MCMA2017

A ROBUST MONTE CARLO TREATMENT PLANNING OPTIMIZATION ALGORITHM FOR DOSE PAINTING CLINICAL IMPLEMENTATION

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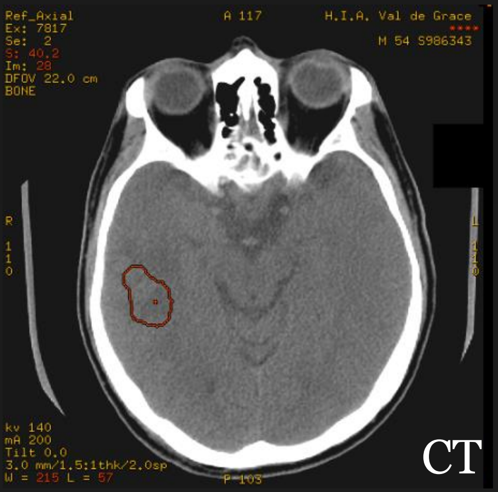
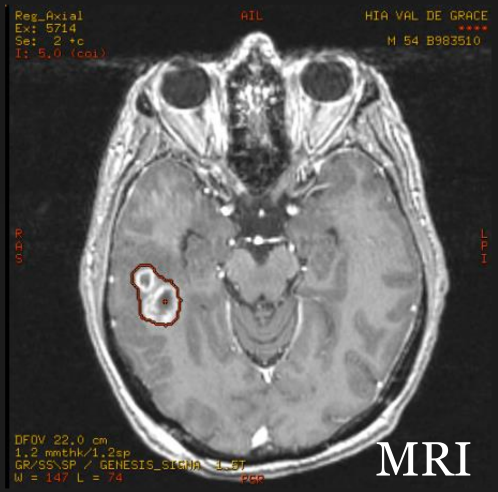
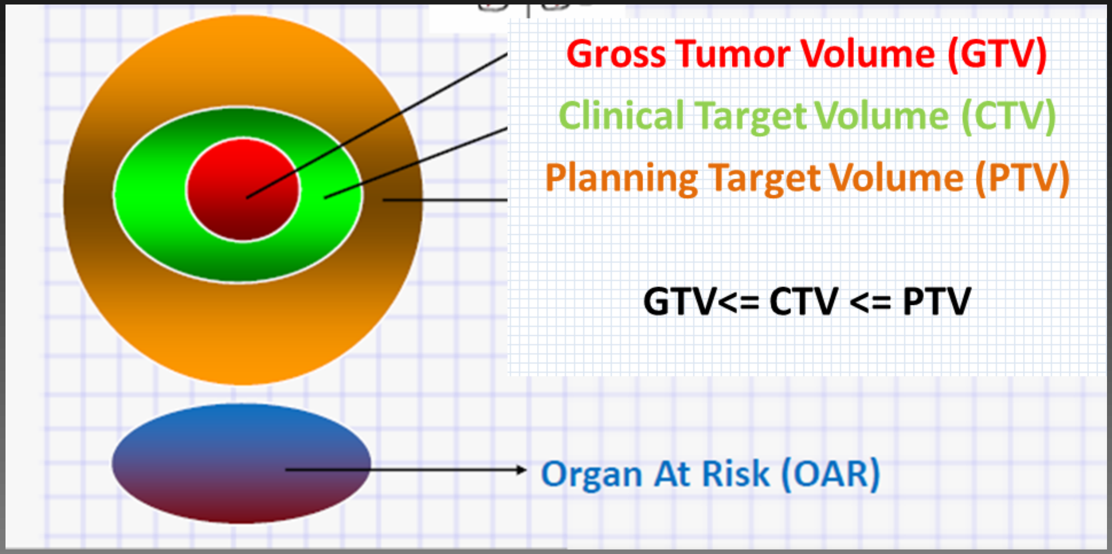
Introduction

Medical imaging in radiotherapy treatment planning.

- Classic role
  - Delimitation based on morphological information
  - Margins for incorporating functional information (movements, extension)





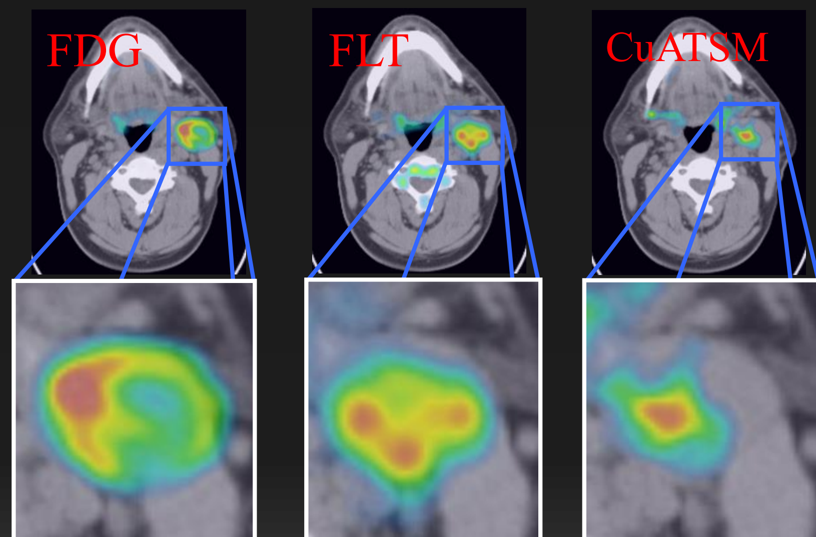


Introduction

- New role → Functional Information

Evolution and characteristics of the lesion

- PET
  - Metabolism
  - Proliferation
  - O_2 concentration
  - Differentiation...
- SPECT
- fMRI



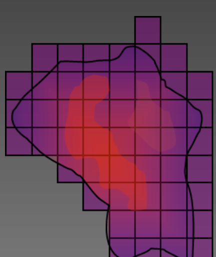
Nyflot et al, Radiother Oncol, 2012

BTV

(Biological Target Volume)

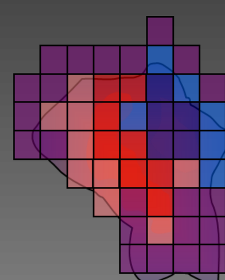
New concepts and protocols

Conventional



- Homogeneous dose to volumes
- Few targets
- Conventional prescription

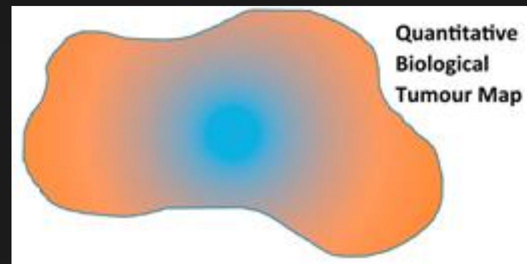
Dose Painting



- Heterogeneous doses
- Multiple targets
- Dose escalation according to functional information

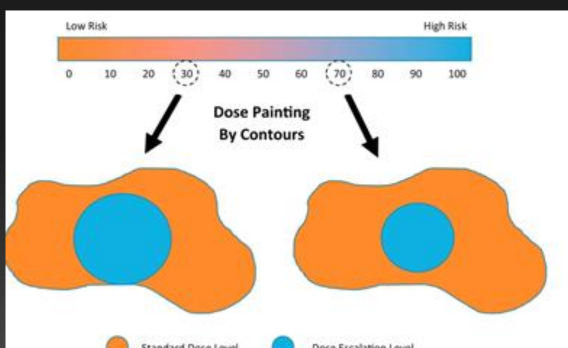
Introduction

Heterogeneous distributions



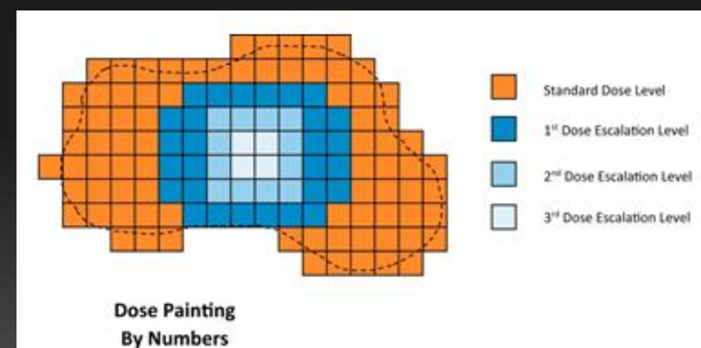
Alonzi et al., Clin Oncol, 2015

Dose Painting by Contour (DPBC)



- Dose escalation based on thresholds
- Dose-to-volume restrictions
- Simultaneous boost strategies in TPS

Dose Painting by Numbers (DPBN)



- Dose escalation based on individual values: TRUE DP
- Dose-to-voxel restrictions
- Commercial TPS: approximations based on dose-volume optimization

Introduction

DP means a new scenario for planning RT

New tools should be incorporated to TPS

(Our proposal)

Dose calculation:

Higher dose gradients within the target require the most accurate dose calculation engine:

Monte Carlo Treatment Planning (MCTP)

Optimization procedure:

A more important role for image into the algorithms

BIOMAP

New restrictions and robustness at the voxel level

Linear Programming (LP)

Material and Methods

http://grupos.us.es/medicalphysics/

Full Monte Carlo Treatment Planning System

- MATLAB platform
- Image processing
- fMC planning
- Optimization
- Evaluation

Material and Methods

PLANNING PROCESS

Functional image processing

Reconstruction protocols and uncertainty assessment

Optimization

Segmentation and Sequencing (DPBC / DPBN)

- Inverse planning
- Generation of apertures based on the image: **BIOMAP**

MU weighting (Voxel level constraints)

Robust optimization based on Linear Programming (**LP**)

Dose Calculation

As accurate as possible → **Full Monte Carlo planning**

Material and Methods

- Functional imaging processing

PET/CT Images (Siemens Biograph mCT 64 scanner of CNA):

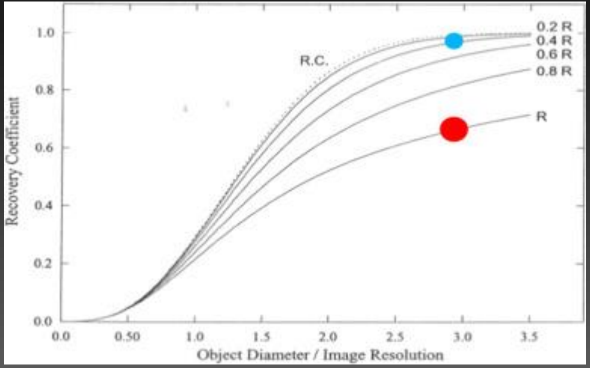
- Location and size of the disease
- Prescription of the dose

Need for **standardized accreditation**

PET reconstruction protocols: EARL / "Radiotherapy"

- Patient protocol simulation
- RT table fitting
- Study of different reconstructions
- Assessment of uncertainties

Recovery coefficients (partial volume effects)

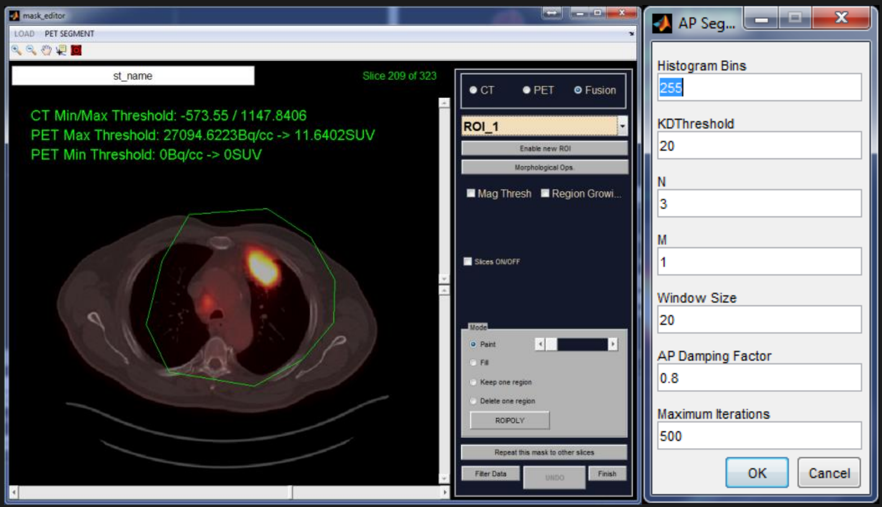


Adapted from: *M.E. Phelps. PET: Molecular Imaging and Its Biological Applications (2004)*

$$RC = \frac{Activity\ concentration\ (measure)}{Real\ activity\ concentration}$$

Material and Methods

- Functional imaging processing

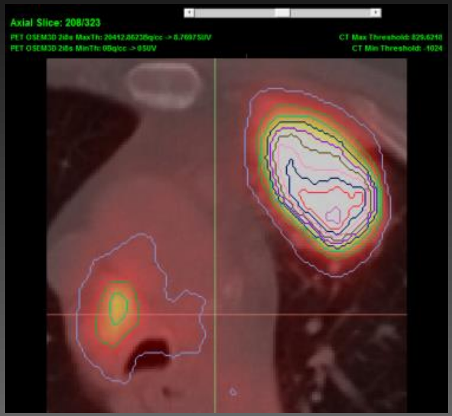


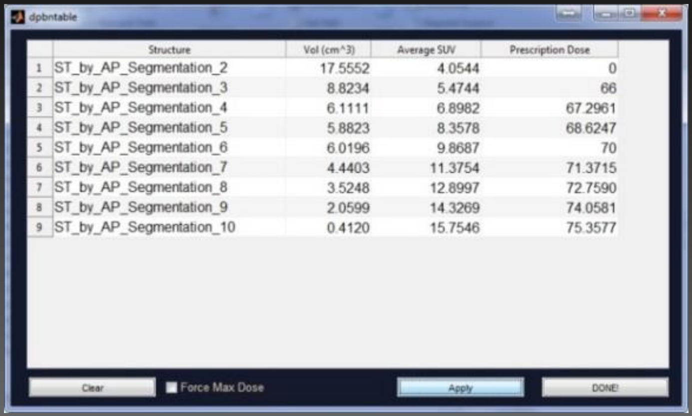
SEGMENTATION ALGORITHM

(*Foster et al., IEEE Trans Biomed Eng, 2014*):

- Clustering according to SUV
- Based on affinity propagation
- Taking into account diffusion PET
- Reduction of uncertainties

Dose prescription map generation





	Structure	Vol (cm^3)	Average SUV	Prescription Dose
1	ST_by_AP_Segmentation_2	17.5552	4.0544	0
2	ST_by_AP_Segmentation_3	8.8234	5.4744	66
3	ST_by_AP_Segmentation_4	6.1111	6.8982	67.2961
4	ST_by_AP_Segmentation_5	5.8823	8.3578	68.6247
5	ST_by_AP_Segmentation_6	6.0196	9.8687	70
6	ST_by_AP_Segmentation_7	4.4403	11.3754	71.3715
7	ST_by_AP_Segmentation_8	3.5248	12.8997	72.7590
8	ST_by_AP_Segmentation_9	2.0599	14.3269	74.0581
9	ST_by_AP_Segmentation_10	0.4120	15.7546	75.3577

$$D_i = D_{low} + \frac{S_i - S_{low}}{S_{high} - S_{low}}(D_{high} - D_{low}), \qquad for\ S_{low} \le S_i \le S_{high}, i = 1, \dots, N$$

Material and Methods

PLANNING PROCESS

Functional image processing

Reconstruction protocols and uncertainty assessment

Optimization

Segmentation and Sequencing (DPBC / DPBN)

- Inverse planning
- Generation of apertures based on the image: **BIOMAP**

MU weighting (Voxel level constraints)

Robust optimization based on Linear Programming (**LP**)

Dose Calculation

As accurate as possible → **Full Monte Carlo planning**

Material and Methods

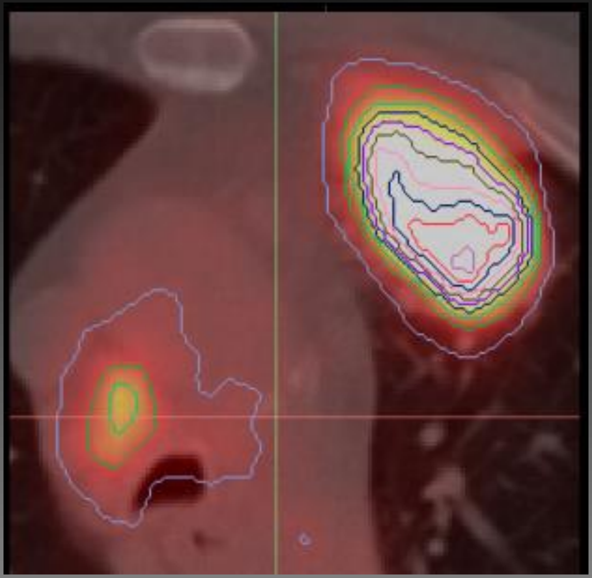
- Optimization: Segmentation and sequencing

Dose Painting By Contours

- Conventional distribution of prescription doses
- Weight optimization: Dose-volume restrictions
- Two planning options:

CONTOURS

INVERSE PLANNING



PLANNING BASED ON DIRECT APERTURES

BIOMAP algorithm
Ureba et al., Med Phys, 2014

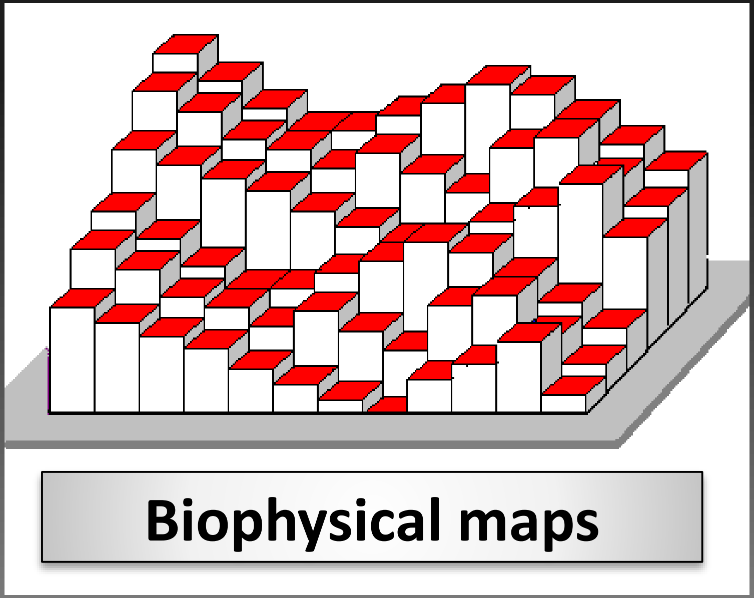
Material and Methods

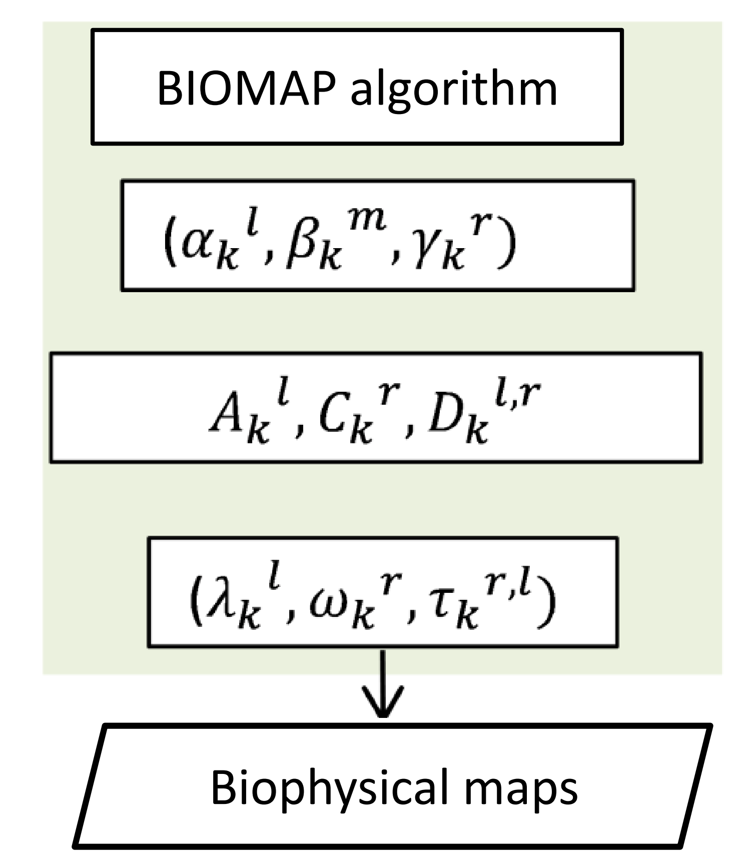
- Optimization: Segmentation and sequencing

BIOMAP algorithm

Ureba et al., Med Phys, 2014

- Based on matrix generation
- Morphological and functional information recruitment



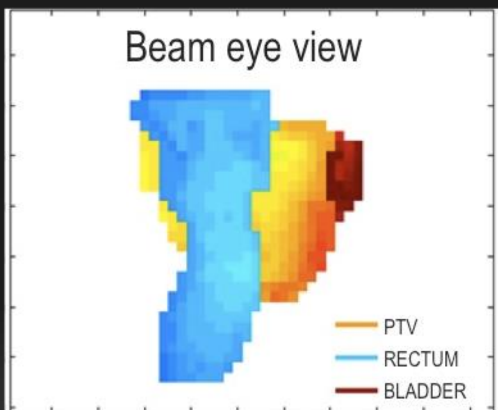


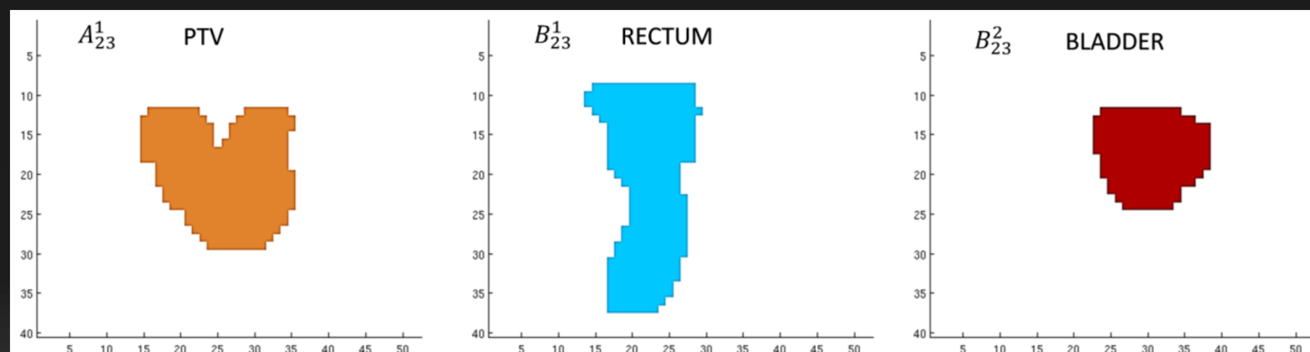
Material and Methods

- Optimization: Segmentation and sequencing

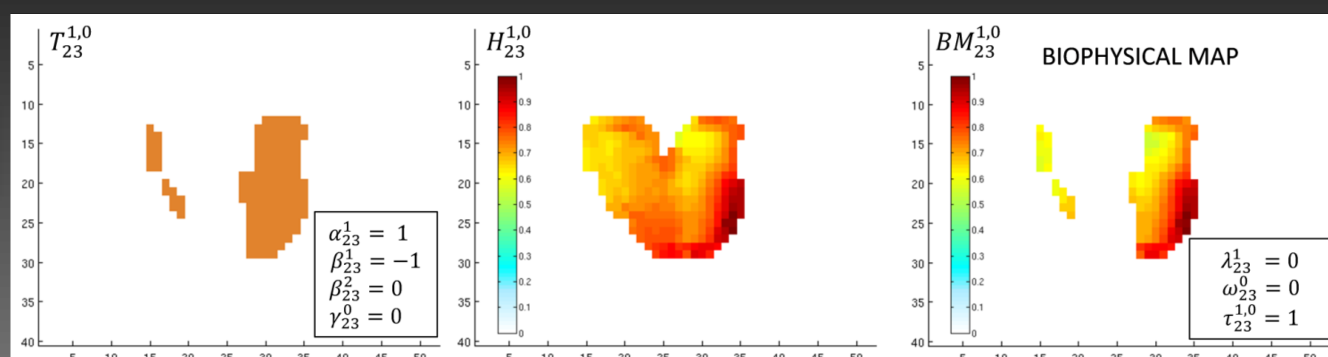
BIOMAP algorithm
Ureba et al., Med Phys, 2014

Based on morphological and functional images:
Adaptive radiation therapy





Biophysical maps



Material and Methods

- Optimization: Segmentation and sequencing

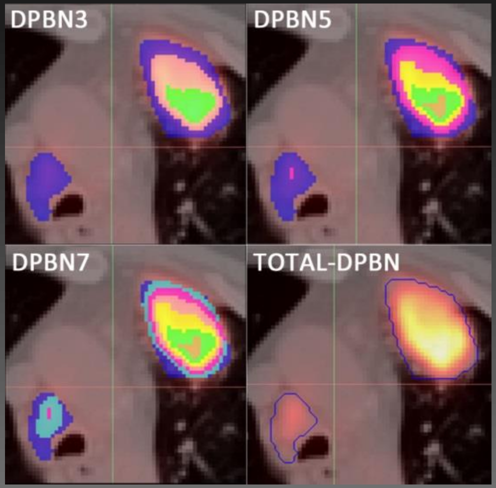
Dose Painting By Numbers

- Heterogeneous distribution of prescription doses
- Weights optimization: dose-voxel restrictions
- Two planning options

INVERSE PLANNING

- LP optimization of beamlets fluence
- Segmentation and sequencing
- 2nd LP optimization of apertures

CLUSTERING



Jiménez-Ortega et al., Phys Med, 2017

PLANNING BASED ON DIRECT APERTURES

BIOMAP algorithm
Ureba et al., Med Phys, 2014

Clusters for apertures generation

Material and Methods

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Dose Calculation

As accurate as possible → **Full Monte Carlo planning**

Material and Methods

- Optimization: Monitor Units Weighting

$$o.f.\quad \sum_{i=1}^{N_{org}} P_i \sum_{j=1}^{N^i_{vox}} x^i_j + \sum_{i=1}^{N_{org}} Q_i \sum_{j=1}^{N^i_{vox}} y^i_j$$

$$\text{subject to}\quad \sum_{j=1}^{N_{total\ beamlets}} \omega_j B_{kj} - x^i_k \le D^i_k \qquad k = 1,\ldots,N_{vox}$$

$$\sum_{j=1}^{N_{total\ beamlets}} \omega_j B_{kj} + y^i_k \le d^i_k \qquad i = 1,\ldots,N_{org}$$

Ureba et al., Med Phys, 2014

LINEAR PROGRAMMING (LP) OPTIMIZATION

Simplification of the problem by random selection of voxels

Dose constraints at the voxel level, rather than volumes

TRUE DPBN option

Material and Methods

- Optimization: Monitor Units Weighting

$$\min \; o.f. \equiv P_{target}^{max} \sum_{i=1}^{N_{target}} x_i + P_{target}^{min} \sum_{i=1}^{N_{target}} y_i + P_{OAR}^{max} \sum_{i=N_{target}+1}^{N} x_i$$

sujeto a

$$\sum_{j=1}^{M} \omega_j d_{ij} - x_i \leq D_i^{max} \Delta_i \qquad i = 1, \dots, N_{target}$$

$$\sum_{j=1}^{M} \omega_j d_{ij} + y_i \geq D_i^{min} \Delta_i \qquad i = 1, \dots, N_{target}$$

$$\sum_{j=1}^{M} \omega_j d_{ij} - x_i \leq D_{OAR}^{max} \qquad i = N_{target} + 1, \dots, N$$

$$x_i, y_i, \omega_j \geq 0 \;\; \forall i, j$$

Jiménez-Ortega et al., Phys Med, 2017

LINEAR PROGRAMMING (LP) OPTIMIZATION

Simplification of the problem by random selection of voxels

Dose constraints at the voxel level, rather than volumes

TRUE DPBN option

ROBUST OPTIMIZATION

- Image uncertainties (dose prescription)
- Geometric uncertainties (positioning / movement)

VOXEL LEVEL

Material and Methods

PLANNING PROCESS

Functional image processing

Reconstruction protocols and uncertainty assessment

Optimization

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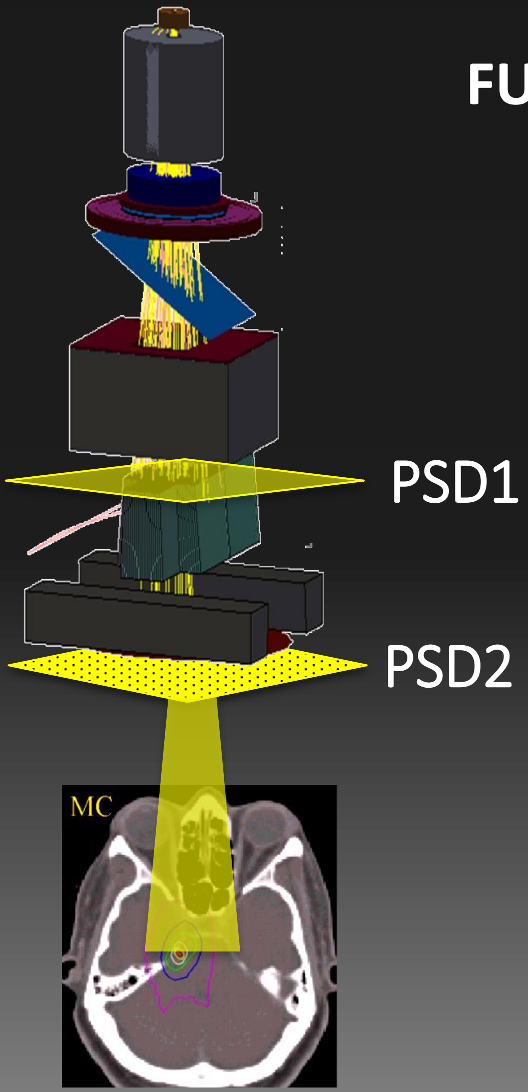
Dose Calculation

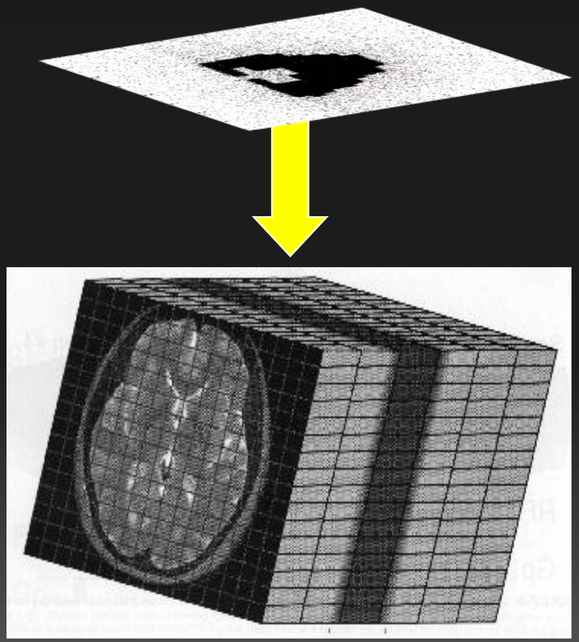
As accurate as possible → **Full Monte Carlo planning**

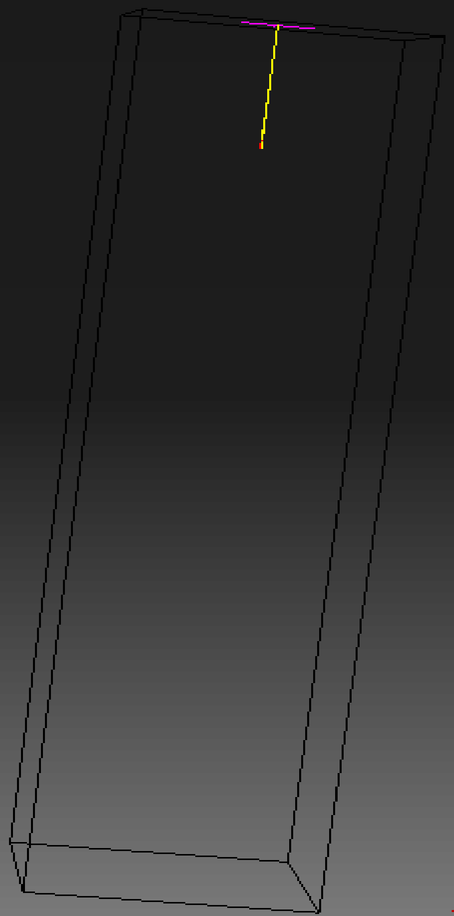
Material and Methods

- Dose Calculation

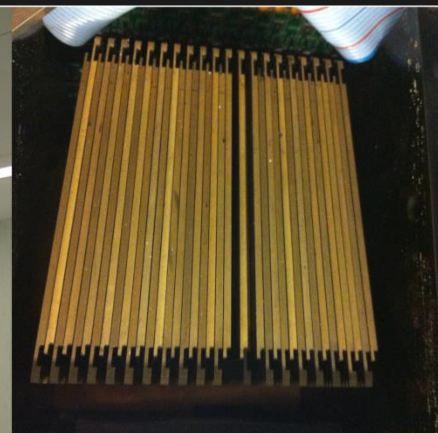


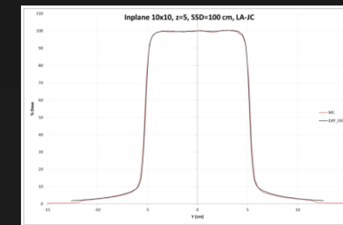
FULL MONTE CARLO PLANNING

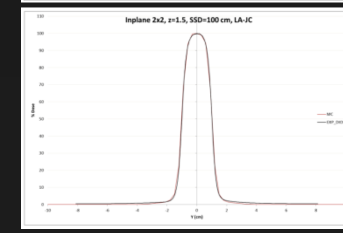


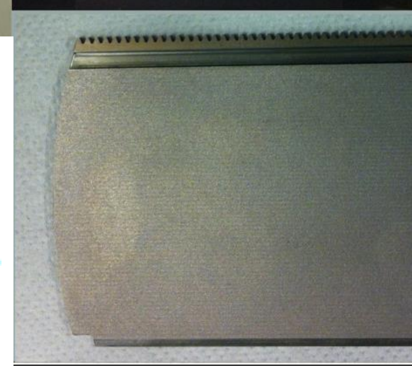


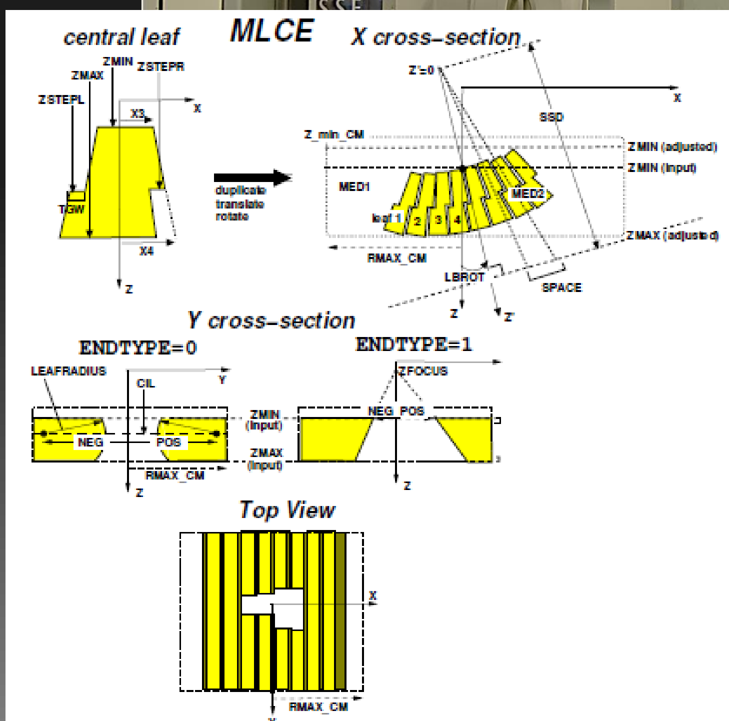
Material and Methods



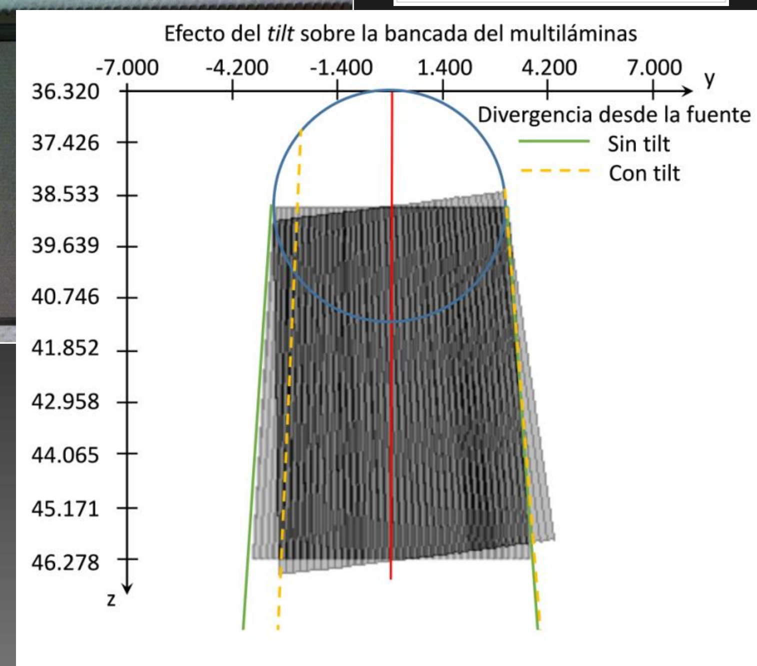








EXPLICIT TRANSPORT OF PARTICLES



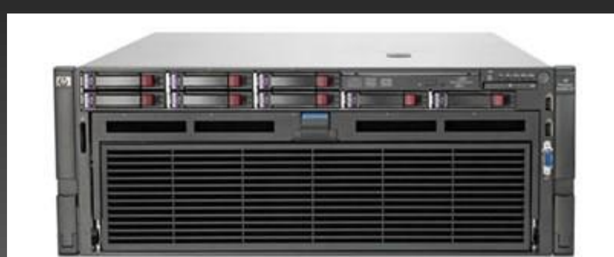
Material and Methods

- Dose Calculation

EGSnrc/DOSXYZnrc/BEAMDOSE

- Linac head: BEAMnrc *(Rogers et al., 2011; Walters et al., 2009)*
- CT patient: BEAMDOSE *(Salguero Castaño, 2008)*

- Parallel Computing *(Leal et al., 2004b; Leal et al., 2001b)*



HP ProLiant DL585 G7
Performance 4 processors
Opteron 2.2 GHz with 12 nodes

Material and Methods

- Dose Calculation: Evaluation

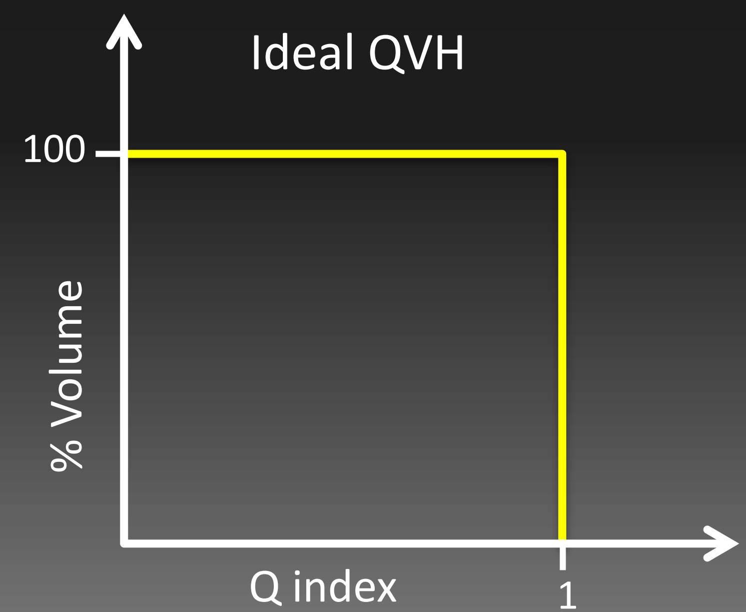
Dose Painting By Numbers

NEW EVALUATION

Quality index per voxel (Q) → QVH

$$Q = \frac{Planned\ dose\ matrix}{Prescribed\ dose\ matrix}$$

$Q_{q_1 - q_2}$ $=$ percentage of Q values between q_1 and q_2



Material and Methods

ROBUSTNESS

CONSIDERATION OF SYSTEMATIC AND RANDOM ERRORS FOR CLINICAL IMPLEMENTATION

Image processing

- Reconstruction protocol: EARL / Radiotherapy
- Segmentation algorithm (Affinity propagation clustering by Foster)

LP Robust Optimisation

$$\min \ o.f. \equiv P_{target}^{max} \sum_{i=1}^{N_{target}} x_i + P_{target}^{min} \sum_{i=1}^{N_{target}} y_i + P_{OAR}^{max} \sum_{i=N_{target}+1}^{N} x_i$$

subject to

$$\sum_{j=1}^{M} \omega_j d_{ij} - x_i \leq D_i^{max} \Delta_i \qquad i = 1, \ldots, N_{target}$$

$$\sum_{j=1}^{M} \omega_j d_{ij} + y_i \geq D_i^{min} \Delta_i \qquad i = 1, \ldots, N_{target}$$

$$\sum_{j=1}^{M} \omega_j d_{ij} - x_i \leq D_{OAR}^{max} \qquad i = N_{target} + 1, \ldots, N$$

$$x_i,\ y_i,\ \omega_j \geq 0 \ \ \forall i, j$$

Voxel uncertainty

- Dose prescription
- Geometric uncertainties

Full Monte Carlo

- Statistical errors in dose calculation (parallelized framework)
- Adaptive anisotropic diffusion filtering (and others)

Evaluation of results

$D =$ MC dose (ΔD *statistical error*)

$D_p =$ Prescribed dose (ΔD_p systematic error)

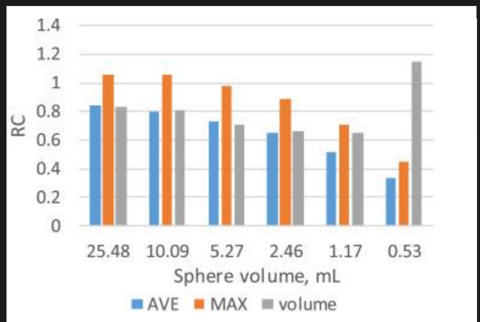
$$Q(D,D_p) = \frac{D}{D_p};$$

$$\Delta Q(D,D_p) = \sqrt{\left(\frac{\partial Q}{\partial D}\right)^2 (\Delta D)^2 + \left(\frac{\partial Q}{\partial D_p}\right)^2 (\Delta D_p)^2}$$

Results

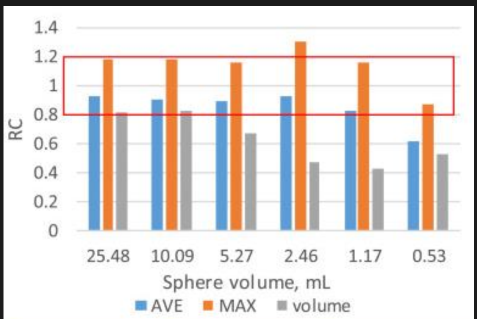
- Functional imaging processing

EARL



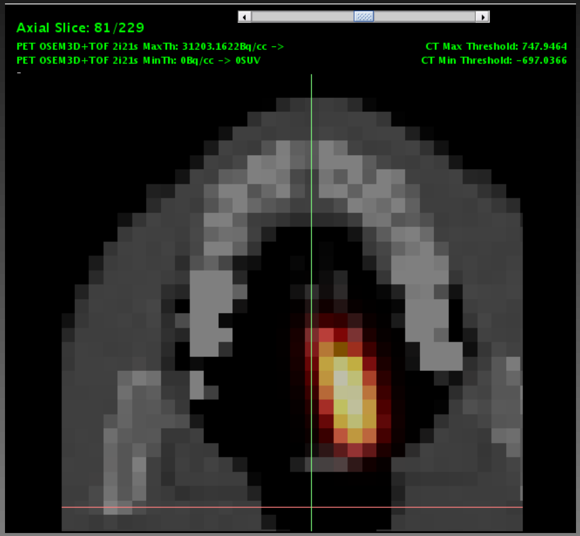
RC AVE	RC MAX	Vol RC
0.71±0.12	0.94±0.13	0.73±0.08

RADIOTHERAPY

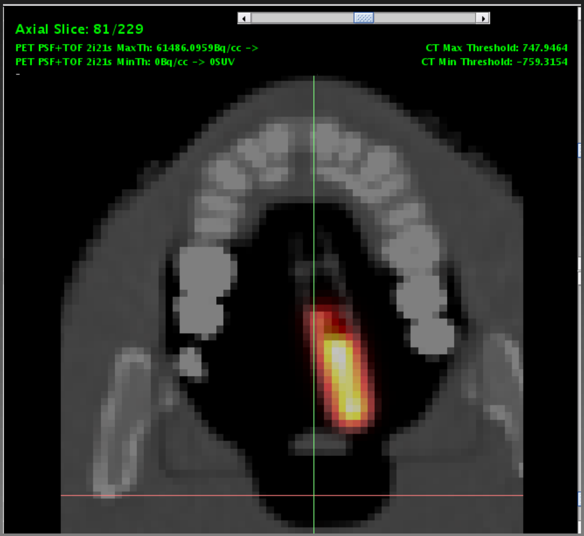


RC AVE	RC MAX	Vol RC
0.89±0.04	1.20±0.05	0.64±0.17

Balcerzyk et al., Nuclear Instruments and Methods A, 2017



Study of uncertainties in SUV values



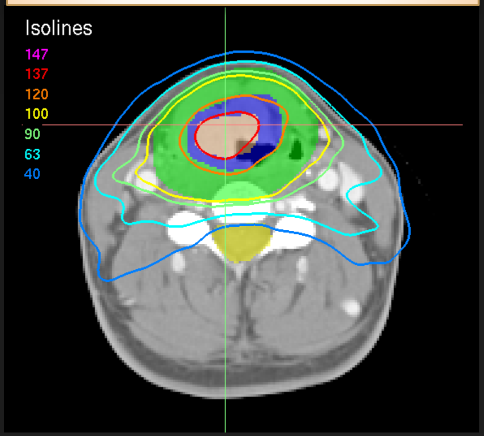
Results

CARMEN: BIOMAP vs Inverse planning

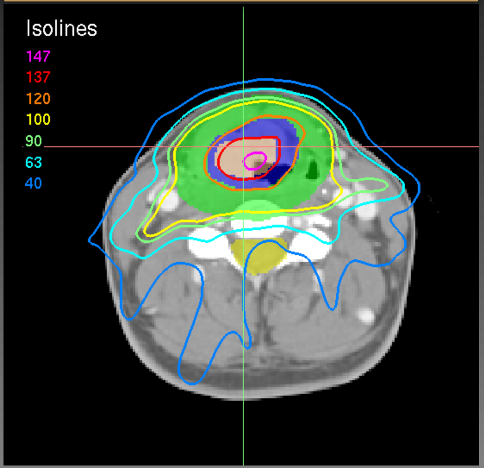
DPBC

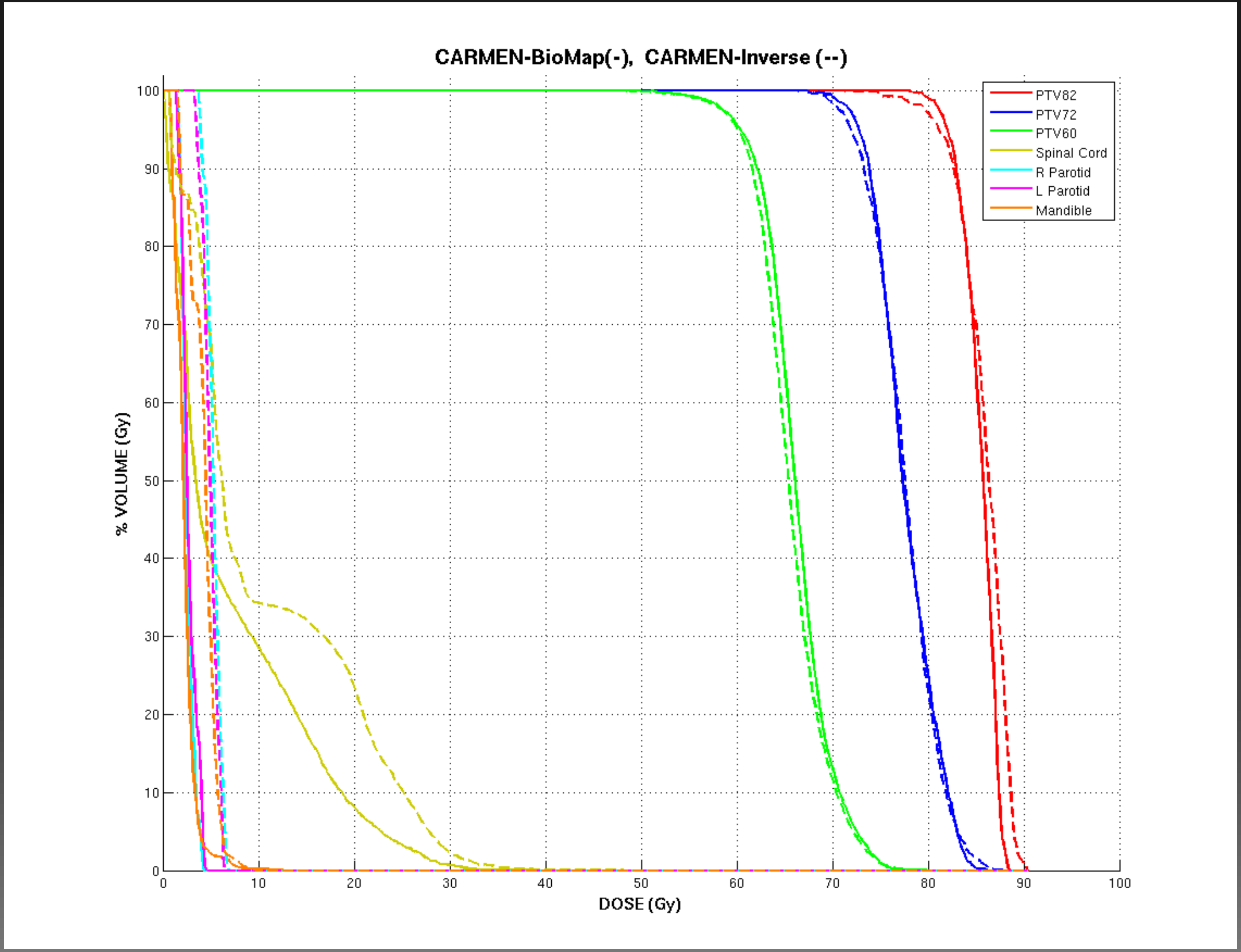
DVH

BIOMAP



INVERSE





Results

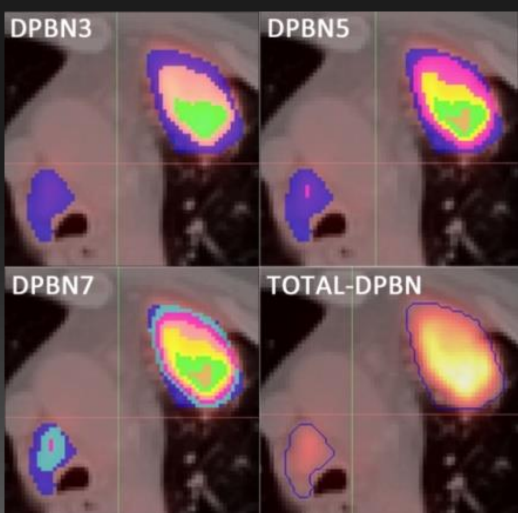
DPBN

CARMEN: Inverse planning (IMRT)

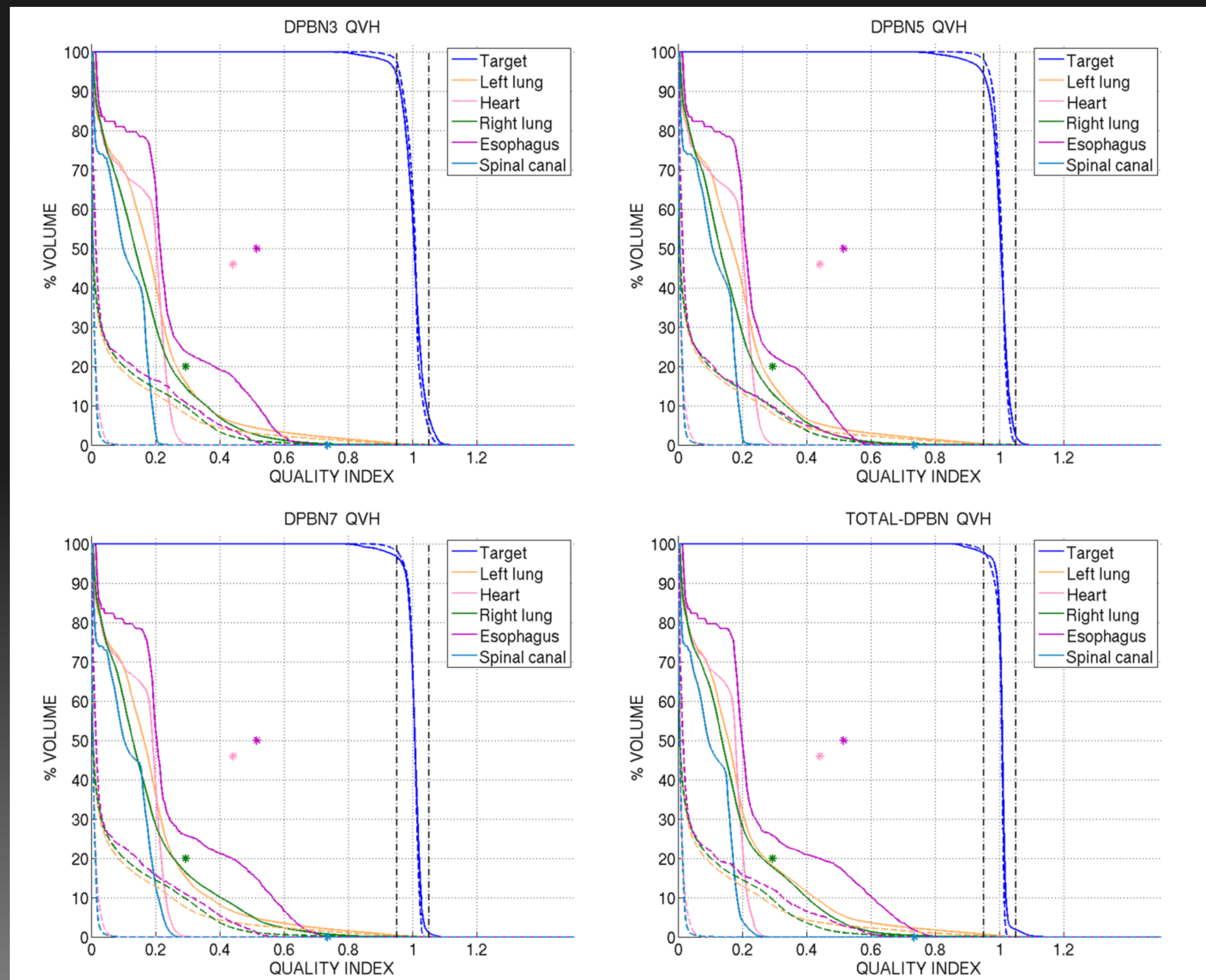
QVH

Apertures ———— *Beamlets* – – – –

Elekta Axesse
(leaves: 4mm)



Jiménez-Ortega et al., Phys Med, 2017

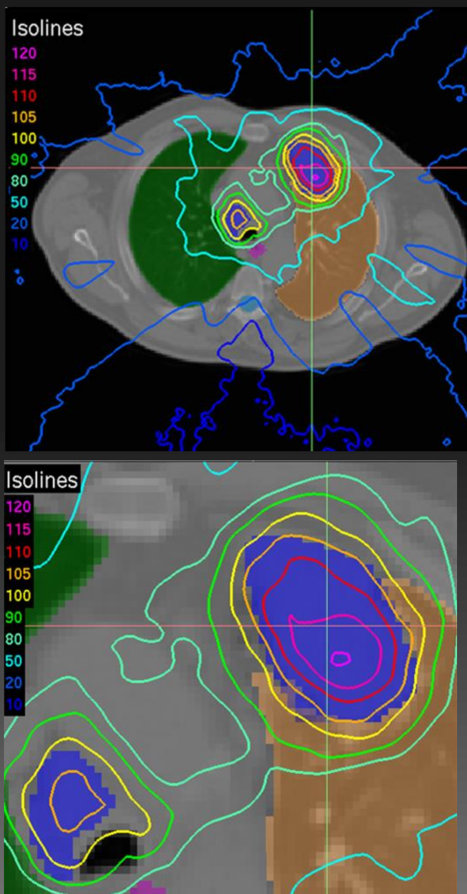


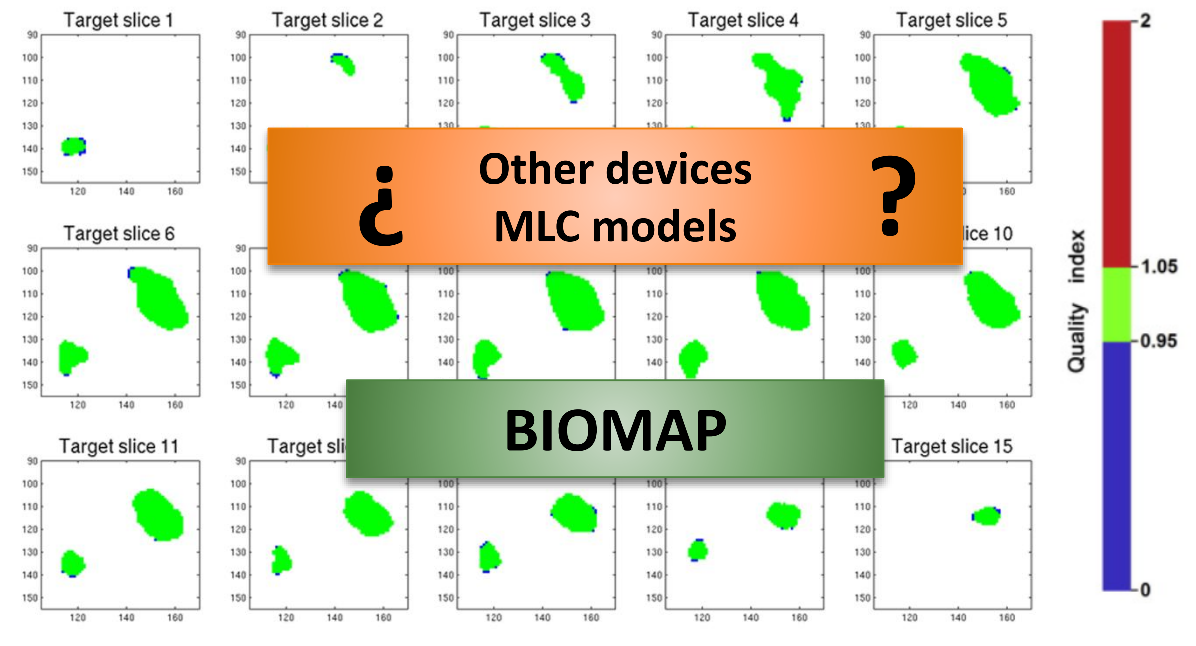
Results

DPBN

CARMEN: Inverse planning (IMRT)

Study	$Q_{0.95-1.05}$ (beamlets)	$Q_{0.95-1.05}$ (segments)	Segments number	MU/fraction
DPBN3	93.3%	86.9%	235	2337
DPBN5	97.7%	91.8%	235	2286
DPBN7	98.1%	95.6%	291	2157
TOTAL-DPBN	**97.8%**	**95.7%**	**351**	**2057** !





¿ Other devices MLC models ?

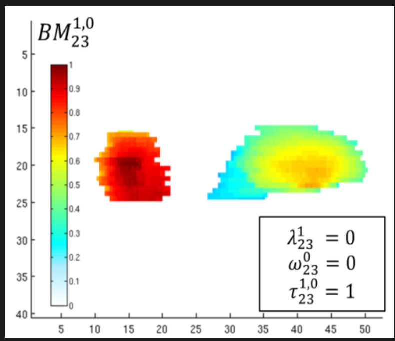
BIOMAP

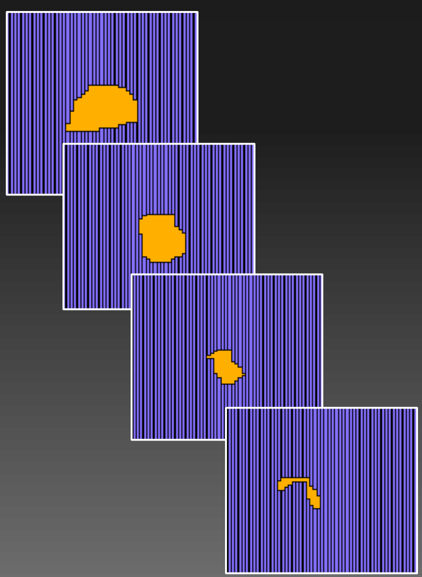
Jiménez-Ortega et al., Phys Med, 2017

Results

BIOMAP Algorithm and Robust LP Optimization

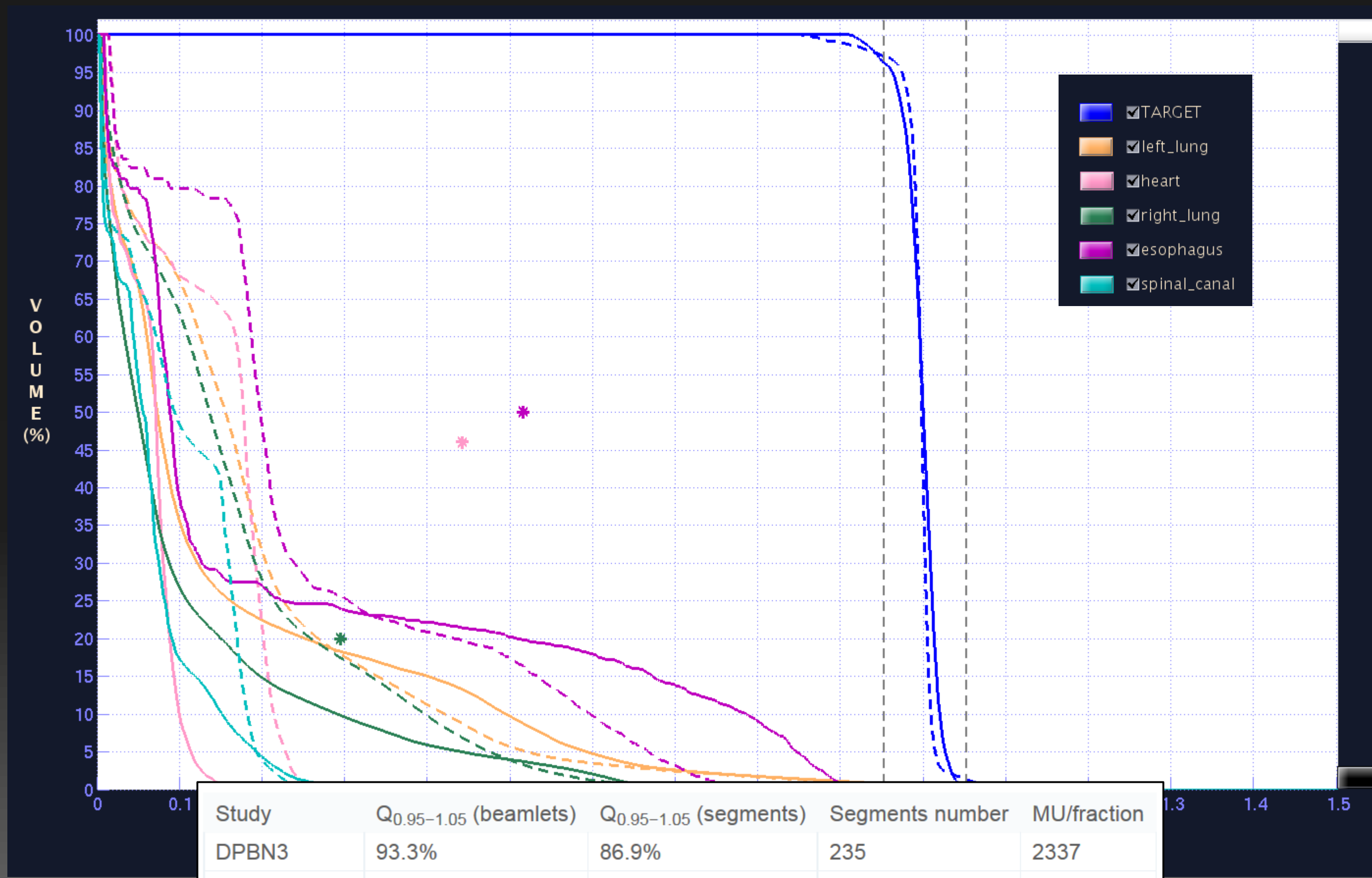
DPBN





QVH

BIOMAP ——— INVERSE - - - -



Study	$Q_{0.95-1.05}$ (beamlets)	$Q_{0.95-1.05}$ (segments)	Segments number	MU/fraction
DPBN3	93.3%	86.9%	235	2337
DPBN5	97.7%	91.8%	235	2286
DPBN7	98.1%	95.6%	291	2157
TOTAL-DPBN	97.8%	95.7%	351	2057
BIOMAP		**98.7%**	**63**	**699**

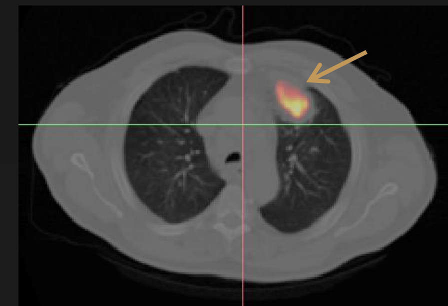
CLINICALLY ACCEPTABLE

Results

DPBN

INITIAL PET

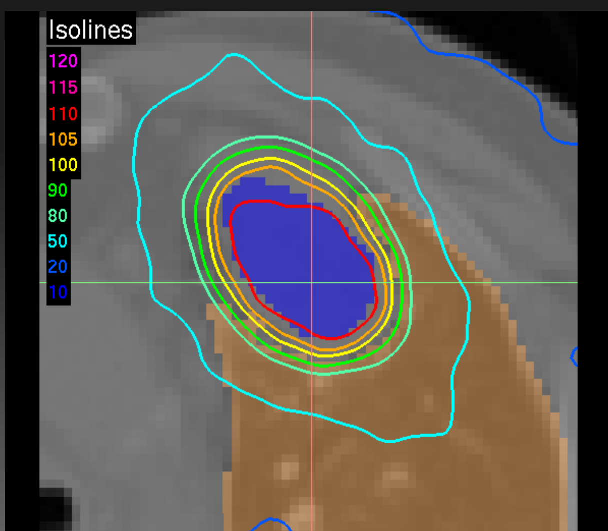
FOLLOW-UP PET



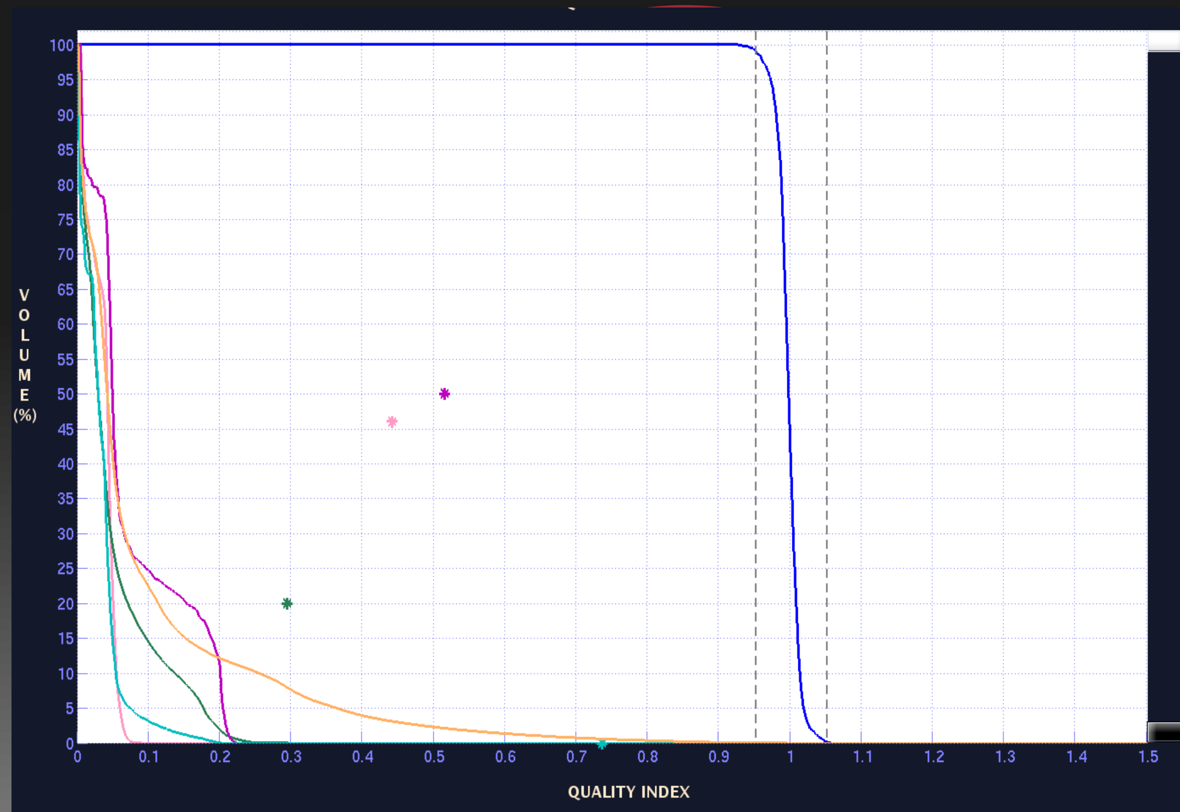
Changes in images:
New biological targets and dose prescription map

CONSEQUENCES OF NO ADAPTATION.

ADAPTIVE RT PLANNING



Normal tissue overdosage



Results

DPBN

Adaptive RT by BIOMAP at the voxel level

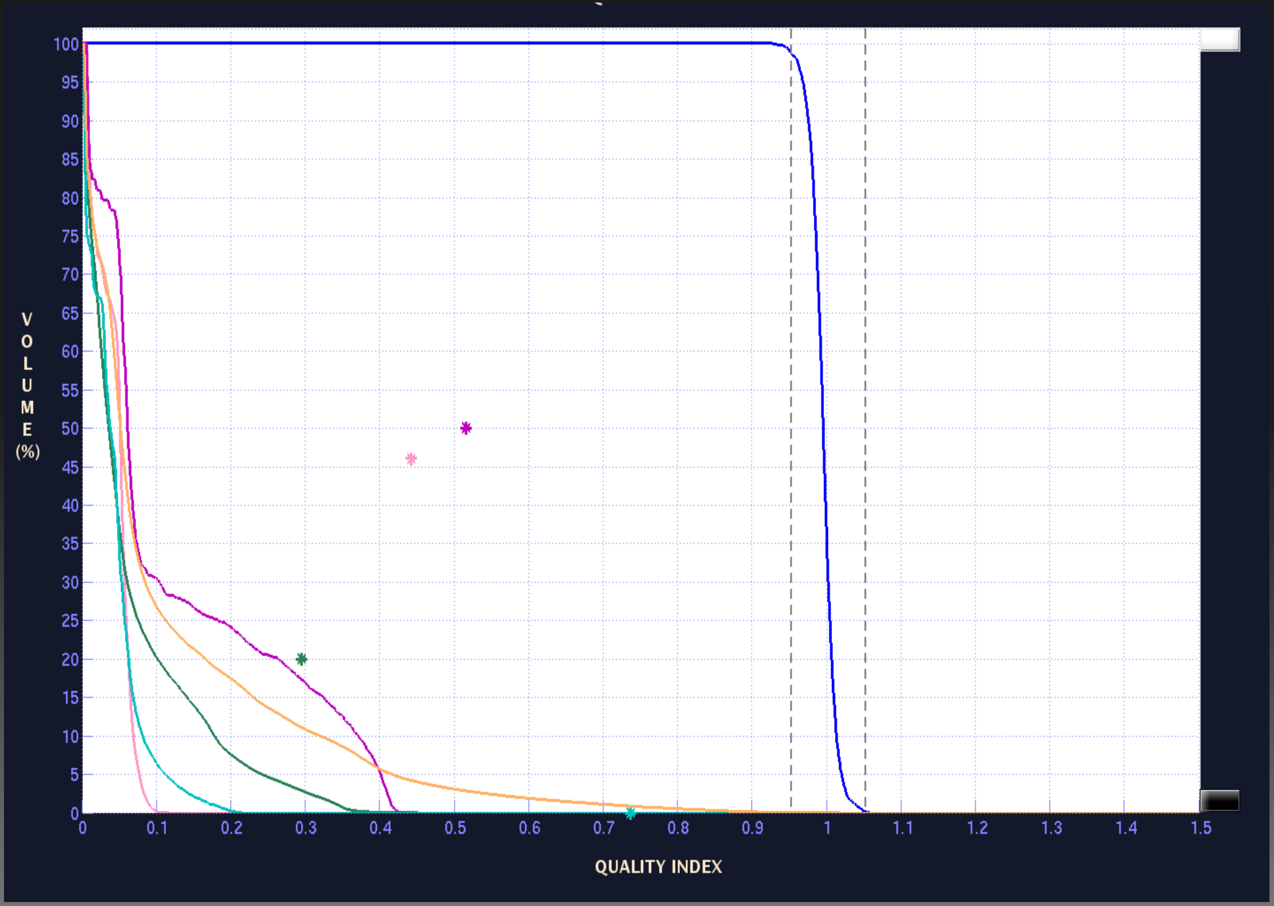
VOXEL LEVEL:
DEFORMABLE REGISTRATION NOT NECESSARY

TOTAL TREATMENT EVALUATION

$$Q_v = \sum_{i=1}^{N} f_i \, Q_v^i$$

Q_v: Q index of voxel v
f_i: fraction weight
N: number of fractions
Q_v^i: Q index of voxel v in fraction i

$Q_{0.95\text{-}1.05}$=98.9%
$Q_{0.97\text{-}1.03}$=96.2%



Conclusions

- In these conditions of **accuracy** and **robustness** (through fMC planning, LP-based optimization and BIOMAP algorithm), we feel confident to move our system for DPBN application into the clinical environment.

- The BIOMAP algorithm, based on the image information, allows the **adaptive** radiation therapy planning at voxel level.

- This solution can be easily extended to other types of functional information such as MRI.

Thanks for your attention

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