SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliero-Universitaria di Modena

Policlinico

Adaptive RT and replanning

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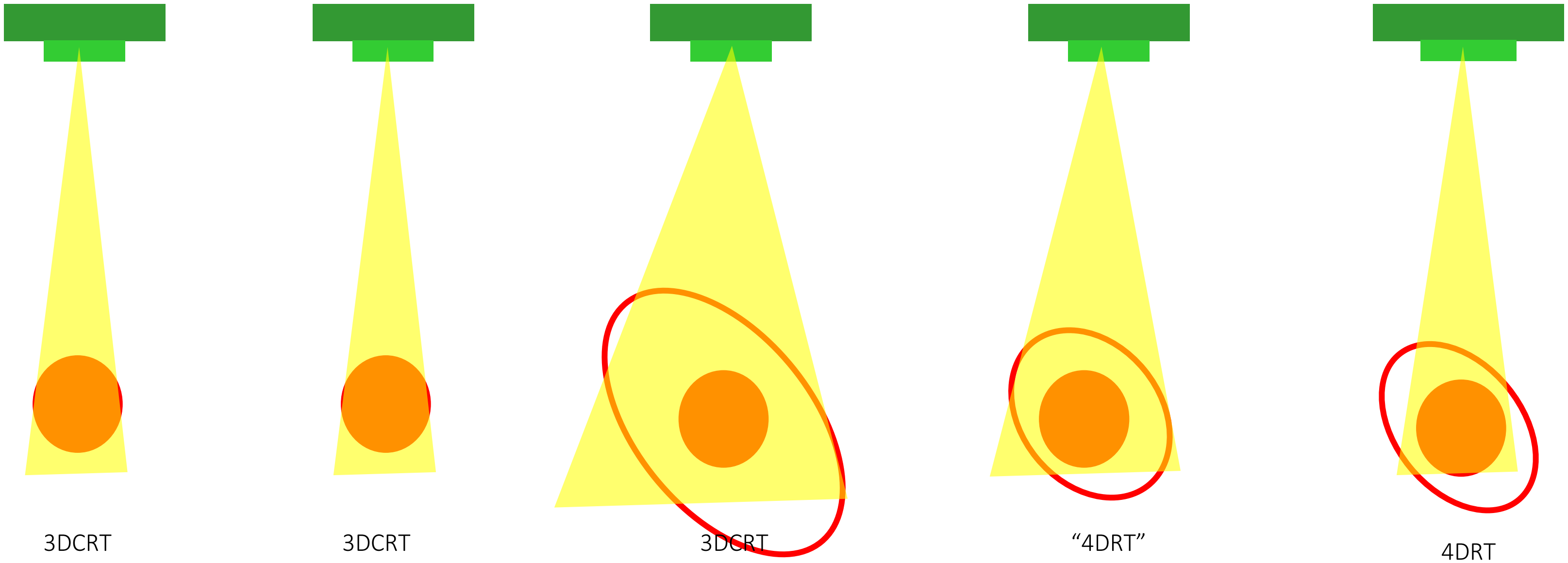
No conflicts of interest to disclose

Define Clinical Objectives and Needs for Future



3DCRT
Static Target

3DCRT
Dynamic Target
NO Motion evaluation

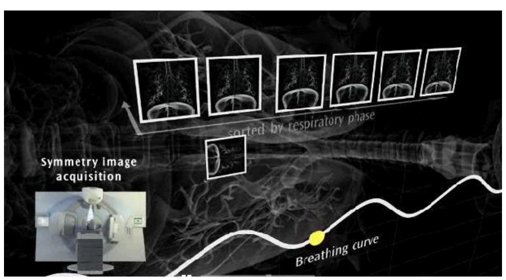
3DCRT
Dynamic Target
4DCT Motion Evaluation (ITV)

"4DRT"
Dynamic Target
4DCT Motion Limitation

Phases beam-on 20-60%
Abdominal Compressor
MIP 4DCT Reconstruction
Deformation analysis
Dose accumulation

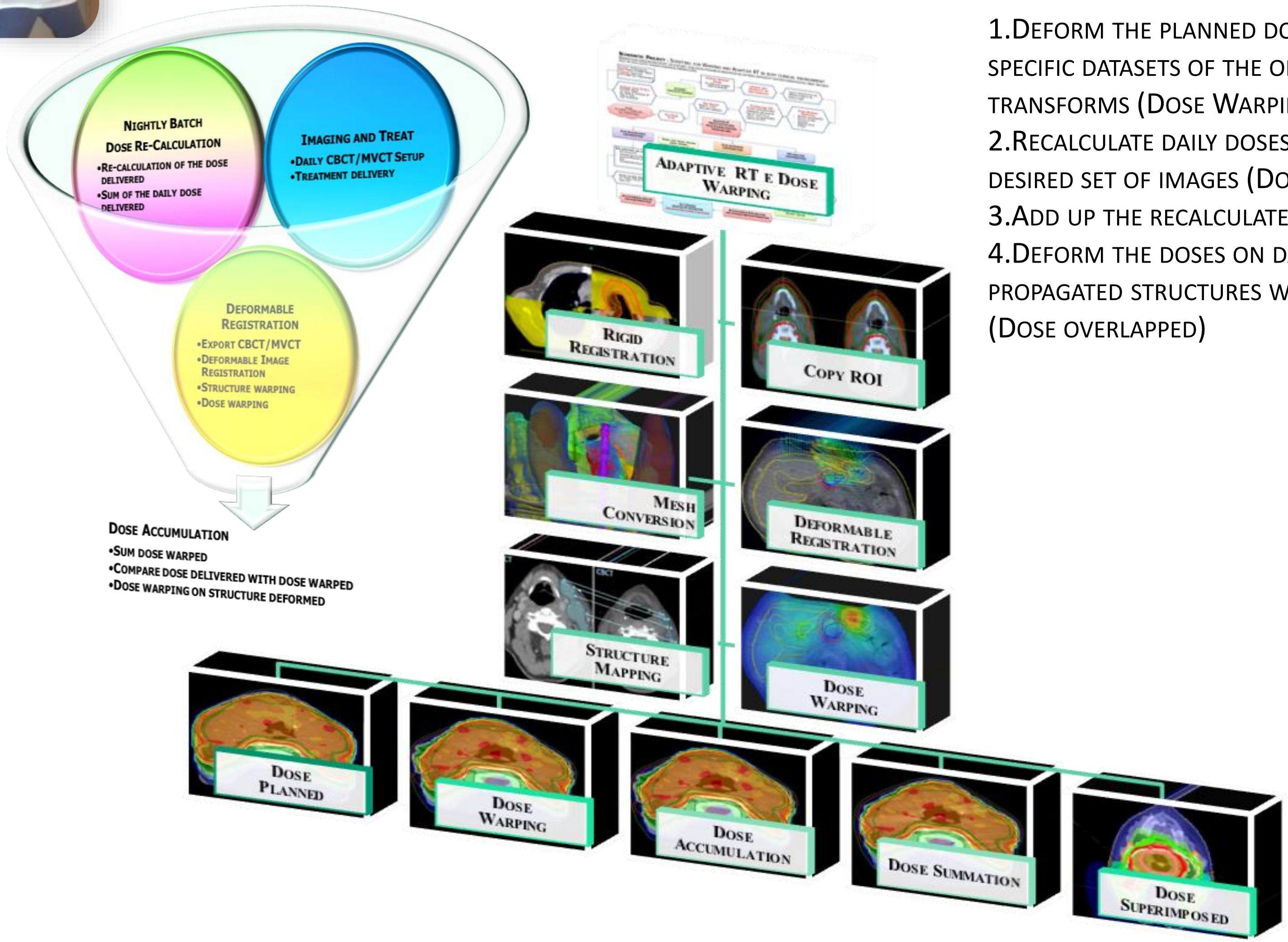
4DRT
Dynamic Target
4DRT Technologies

Internal Marker Tracking
Dynamic MLC
Robotic Couch
Organs Motion Compensation
Daily Adaptive RT
DIBH
Deformable Registration
Dose Accumulation



- Reduce margins?
- Improve delivery efficacy and efficiency?
- Follow time and space evolutions?

Adaptive RT Strategies and deformable registration .. How Many way?



1. Deform the planned doses on images based on specific datasets of the object using elastic transforms (Dose Warping)
2. Recalculate daily doses and deform them on the desired set of images (Dose Accumulation)
3. Add up the recalculated doses (Dose Summation)
4. Deform the doses on dataset of images and propagated structures with elastic algorithms (Dose overlapped)

Guidi G. Metodi predittivi per ART: effetti del movimento d'organo, degli algoritmi di registrazione deformabile e dell'accumulo di dose. PhD Thesis UNIBO-2016.

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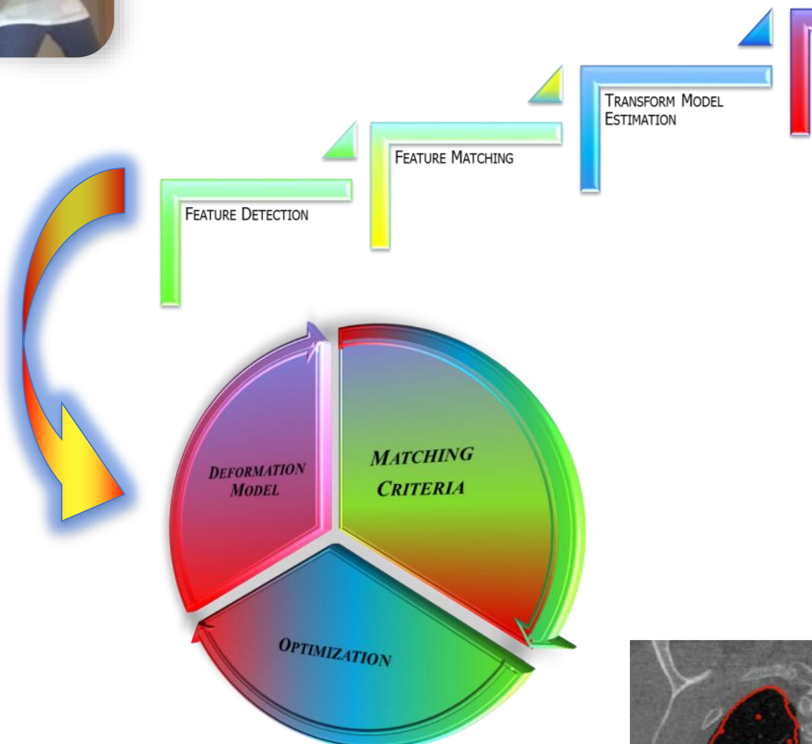
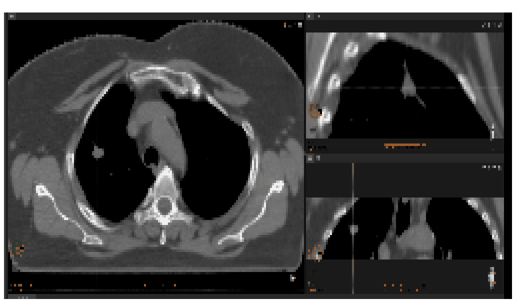
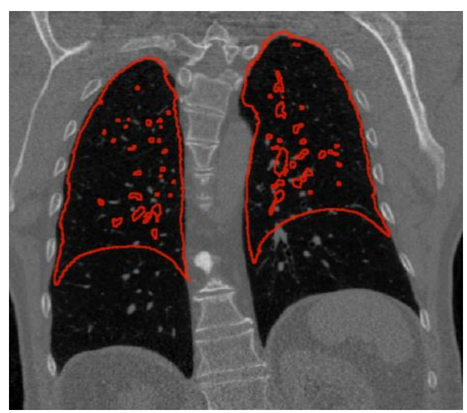
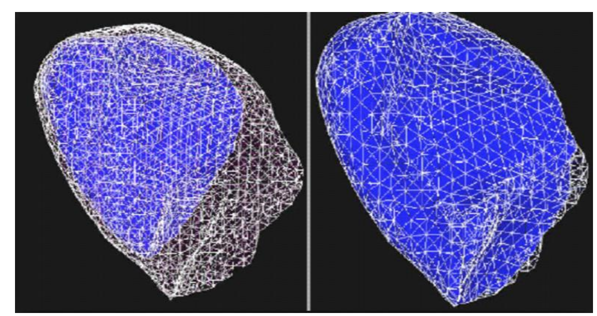
CO-REGISTRATION – ELASTIC TRASFORMATION



- Deformation models
  - Physics-based models
    - Elastic body models
    - Viscous fluid flow models
    - Diffusion models
    - Curvature registration
    - Flows of diffeomorphisms
  - Interpolation-based models
    - Radial basis functions
    - Elastic body splines
    - Free-form deformations
    - Basis functions from signal processing
    - Piecewise affine models
  - Knowledge-based models
    - Statistically-constrained models
    - Biomechanical/biophysical models
  - Task-specific constraints
    - Topology preservation
    - Volume preservation
    - Rigidity constraints

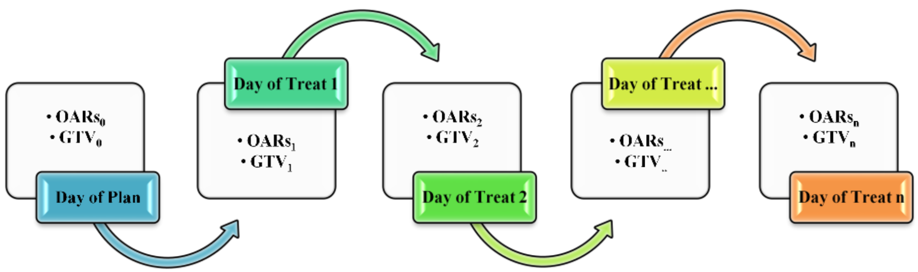


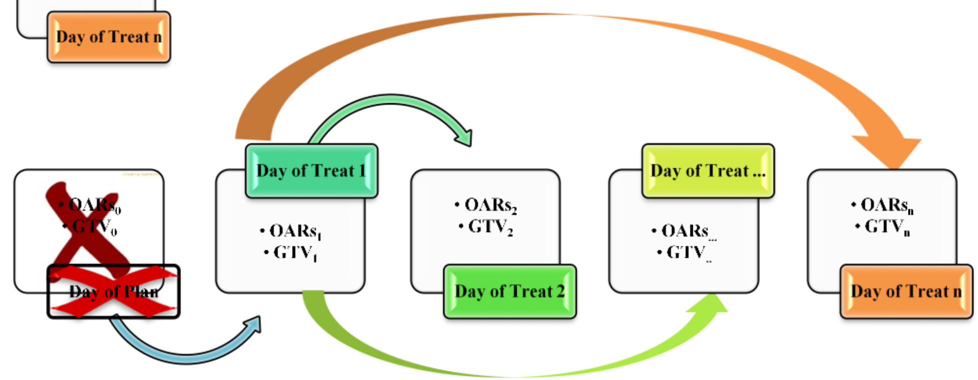


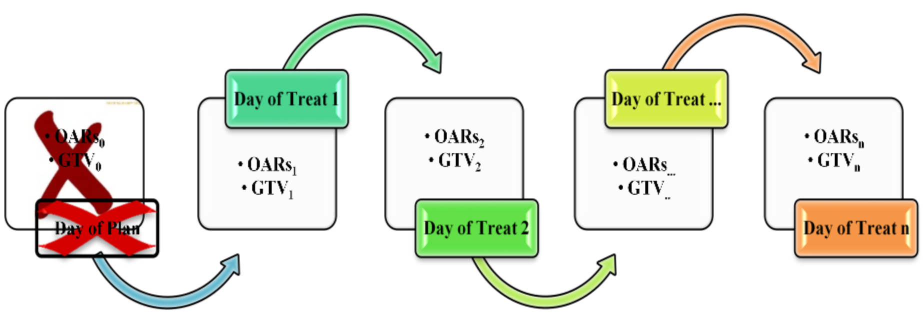


How to study the evolution of volumes and treatment using deformable registration? Types of Models and Possible Analysis

1. Referring to the planning day
2. Referring to the first day of therapy
3. Referring to the previous day







WARPING METHODS PER
DEFORMABLE REGISTRATION, IMAGE-GUIDED RT E ADAPTIVE RT

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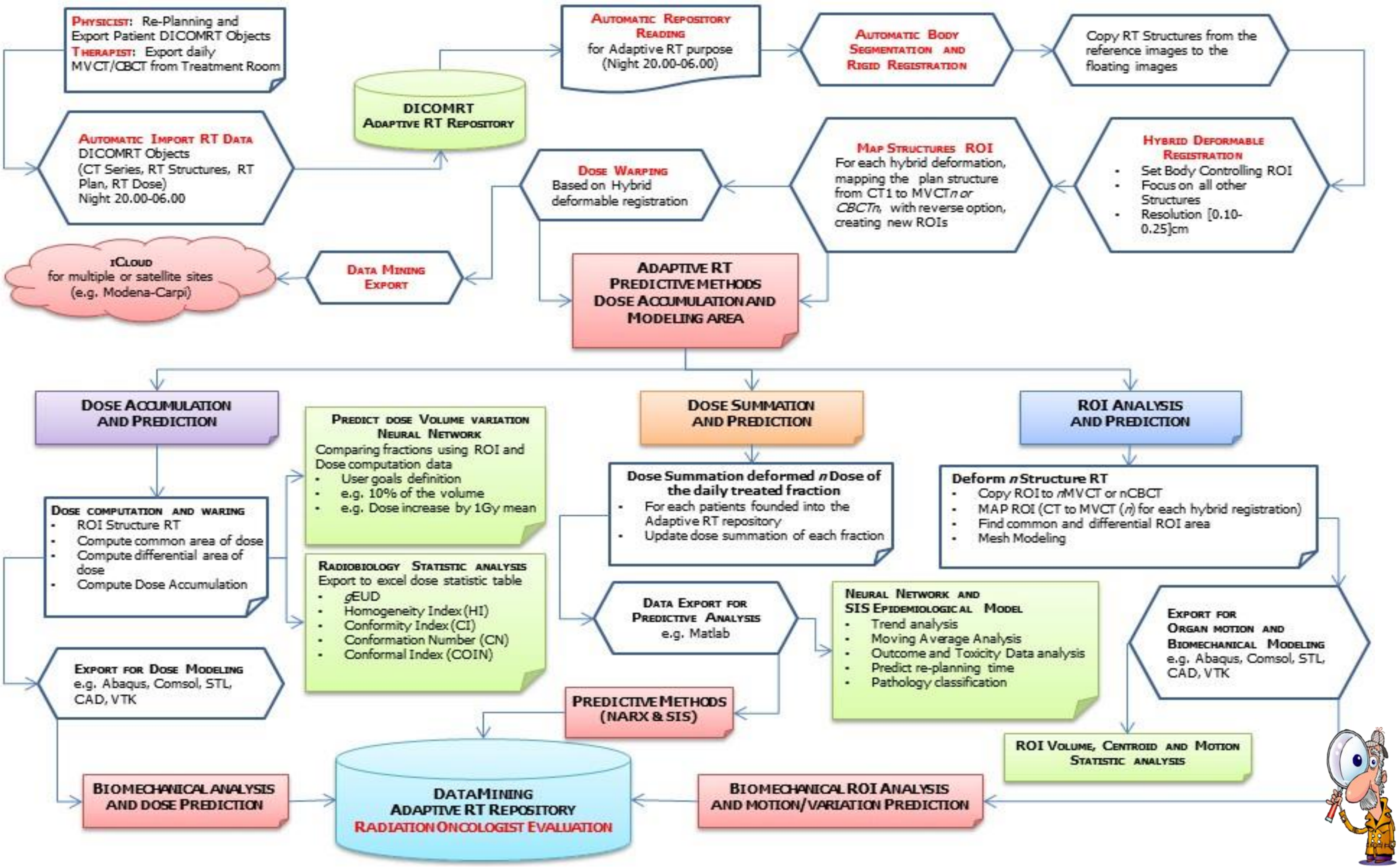
SCHEMATIC PROJECT : SCRIPTING FOR WARPING AND ADAPTIVE RT IN BUSY CLINICAL ENVIRONMENT

PROJECT: DOSE WARPING METHODS FOR IGRT AND ADAPTIVE RT: DOSE ACCUMULATION BASED ON ORGAN MOTION AND ANATOMICAL VARIATIONS OF THE PATIENTS DURING RADIATION THERAPY TREATMENTS (MOH. GR-2010-2318757 PRINCIPAL INVESTIGATOR: GABRIELE GUIDI)



DEFORMABLE IMAGES REGISTRATION IN LITERATURE (TO CLARIFY)

Use of image registration and fusion algorithms and techniques in radiotherapy: Report of the AAPM Radiation Therapy Committee Task Group No. 132

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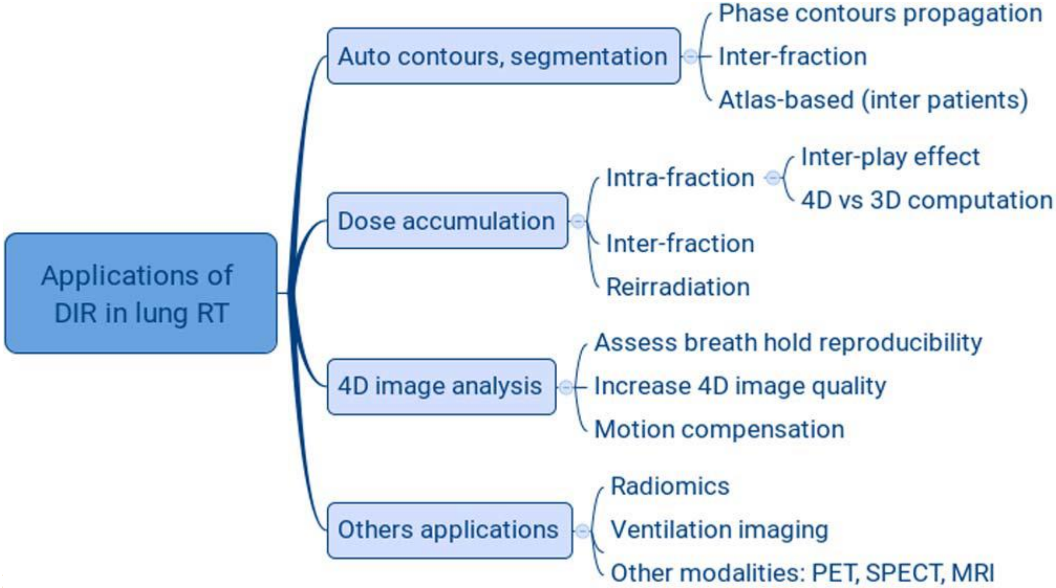

Review Article
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pISSN 2234-1900 · eISSN 2234-3156
ROJ Radiation Oncology Journal

Deformable image registration in radiation therapy

Seungjong Oh, PhD, Siyong Kim, PhD
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Review

Deformable image registration applied to lung SBRT: Usefulness and limitations

David Sarrut[a,b,*], Thomas Baudier[a,b], Myriam Ayadi[b], Ronan Tanguy[b], Simon Rit[a]
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Table 1. Summary of reviewed DIR application

Study	Transformation model	Application	Site
Yan et al. [12]	FEM-based linear elastic	Dose accumulation	Prostate cancer
Christensen et al. [14]	Viscous fluid flow	Dose accumulation	Cervix cancer
Schaly et al. [15]	Thin-plate splines	Dose accumulation	Prostate cancer
Velec et al. [16]	FEM-based linear elastic	Dose accumulation	Lung cancer
Sohn et al. [13]	FEM-based linear elastic	Mathematical modeling	Prostate cancer
Nguyen et al. [17]	FEM-based linear elastic	Mathematical modeling	Liver cancer
Budiarto et al. [18]	Thin-plate splines	Mathematical modeling	Prostate cancer
Oh et al. [19]	Parametric active contour	Mathematical modeling	Cervix cancer
Shekhar et al. [20]	B-splines	Automatic segmentation	Lung cancer and abdomen cancer
Chao et al. [21]	Demons algorithm	Automatic segmentation	Head and neck cancer
Lee et al. [22]	Calculus of variance	Automatic segmentation	Head and neck cancer
Wang et al. [23]	Commercial algorithm (Pinnacle)	Automatic segmentation	Head and neck, prostate, and lung cancer
Reed et al. [24]	Demons algorithm	Automatic segmentation	Breast cancer
Guerrero et al. [25]	Optical flow	Functional imaging	Breath hold CT of lung
Yaremko et al. [26]	Optical flow	Functional imaging	4D CT lung
Yamamoto et al. [27]	Calculus of variance	Functional imaging	4D CT lung

DIR, deformable image registration; FEM, finite element method; CT, computed tomography.

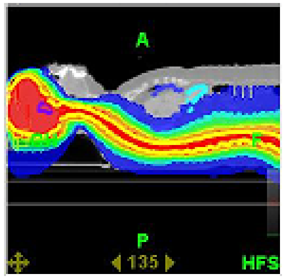
Difference: Different use of the Vector Fields ….

Deformable Image Registration APPLICATIONS

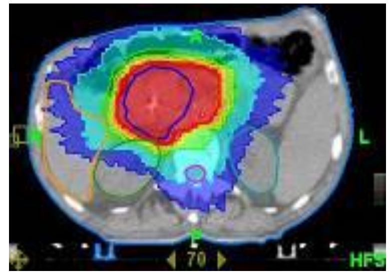
- **Autosegmentation** — Map contours from reference to target image
- **Dose Accumulation** — Estimate the dose delivered from deformable information
- **Mathematical Modeling** — track target / OARs Inter / intra-fx motion
- **Other applications**
  - **Predictive Analysis** — support re-planning by decision making
  - **Functional Imaging** — Evaluate functional data

CLINICAL PRACTICE & RESEARCH AREA

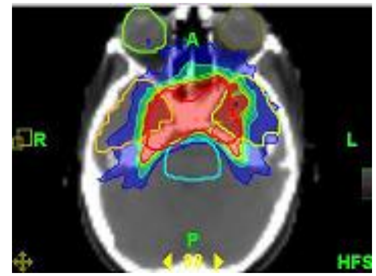
H-N



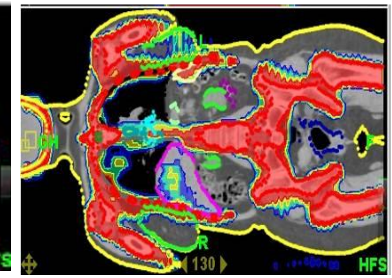
Craniospinal



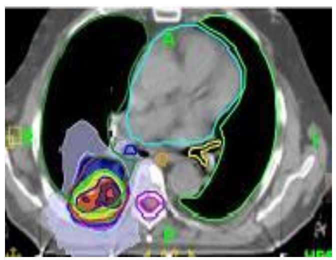
Pancreas



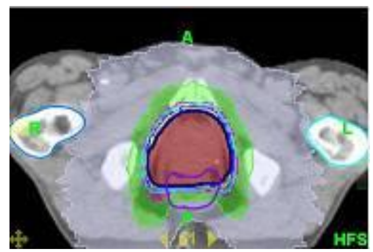
Re-Irradiation



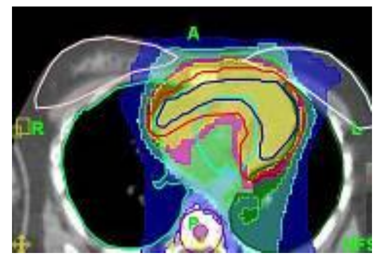
Total Lymphoid Irradiation



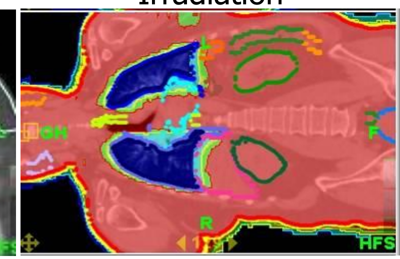
Lung



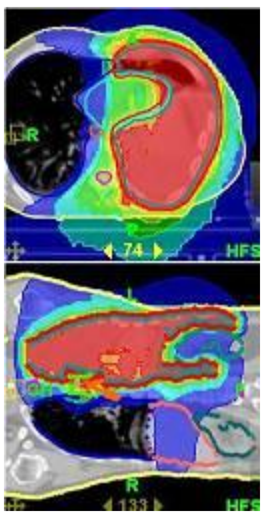
Prostate



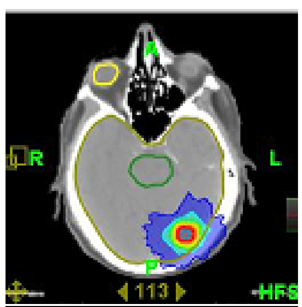
Lymphoma



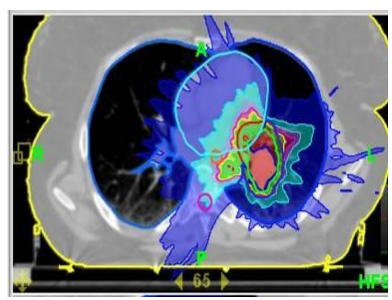
Total Body Irradiation



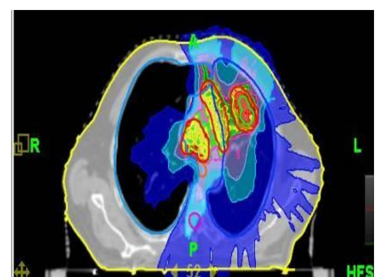
Mesothelioma



Radiosurgery



Lung - SBRT



Multiple Lesions

Bilateral Breast

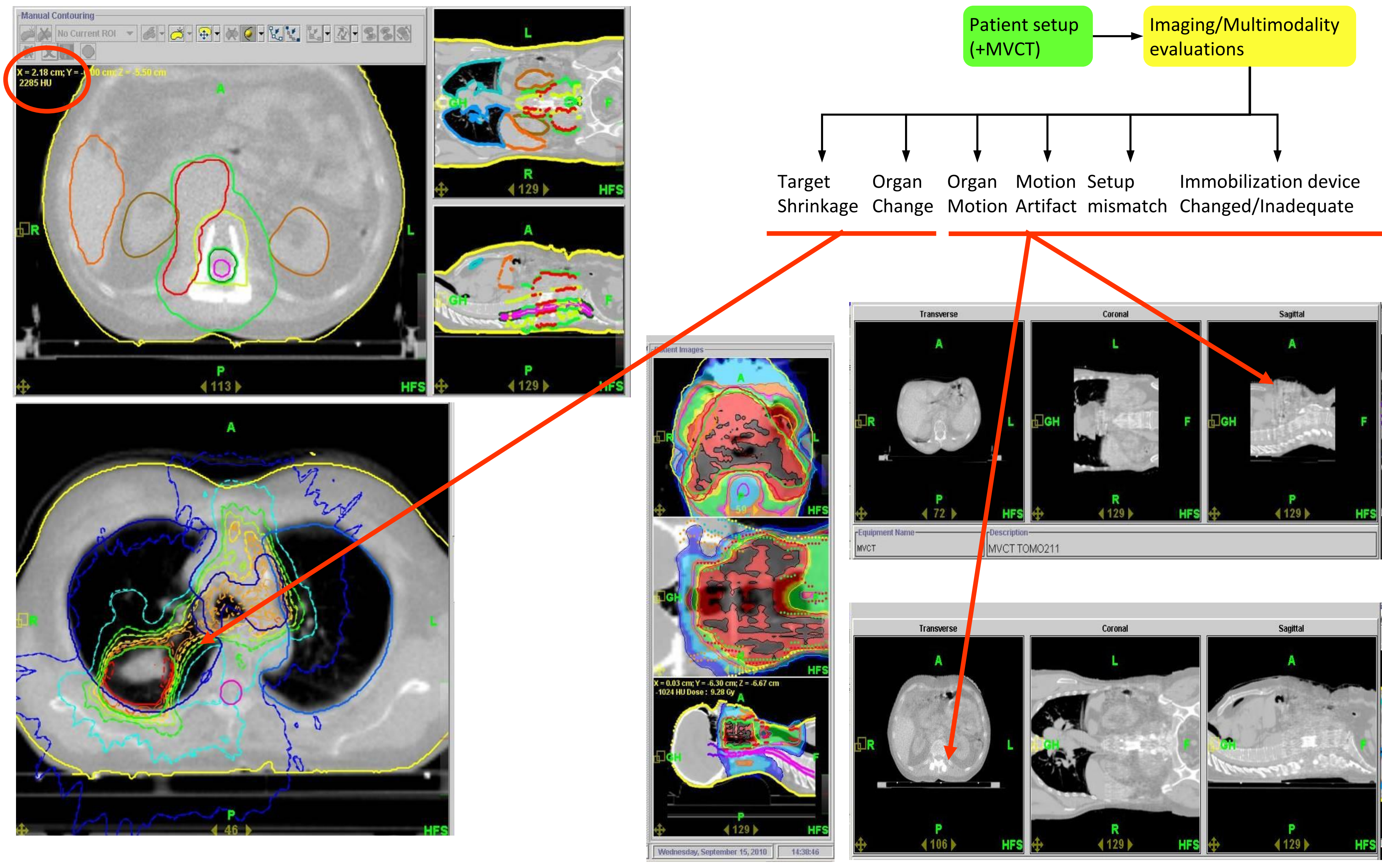
…… preliminary data are consistent with a better tolerance and lower acute toxicity of Tomotherapy treatment compared with other standard treatments using LINAC (3DCRT – IMRT – RCS - SBRT)

ADAPTIVE: HAVING A CAPACITY FOR ADAPTATION

Adaptive Strategies	When	How / What	Time Consuming	Advantages	Disadvantages
External Patient Setup	Daily	•Immobilization Device (i.e. Thermoplastic Mask) •Surface reposition system (i.e. VisionRT)	Fast	•Reproducibility •Re-Adjustment •Monitoring during treatment (i.e. VisionRT)	•External signal surrogate can not detect the real position of the internal organs •Immobilization device could be inadequate after few fractions
Internal Patient Setup	Daily	MVCT	MVCT Resolution (2,4,6mm)	Images can detect the position of the internal organs and the good pre-delivery preparation of the patients	•Extra doses •Low Tissue Contrast •Local or global matching can change the X,Y,Z shift to apply to the patient
Multimodality Imaging (Fusion)	Daily	Not available with Tomotherapy SW, but possible off line with 3th part SW	High	PET, RMI, US, SPECT, Contrast Exams comparison and evaluation Multimodality evaluation	None
MVCT vs. kVCT	•Daily •Weekly	•Dose Re-Calculation on MVCT •Superimpose the dose delivered on new kVCT acquired (3th part SW)	•Long •Only for few patients •Cluster/Console occupancy	•Understand the current delivery of the plan •Evaluate the volume mismatch or over dosage	•Without 4DCT, PET, RMI images integration and/or contrast exams could be done incorrect assumption (i.e. target shrinkage) •Offline images evaluation could be unacceptable with patient delivery performance (e.g. incorrect Tx)
Translation & Rotation	Daily	Mutual information algorithm	Medium (depend on demand and type of Tx)	•Faster if there are no critical structures •Adequate with big volume •Few different algorithm to evaluate soft tissue and bone tissue	•Anatomical global matching can provide abnormal shift of the patients due to the large volume of pixel used by the algorithm (i.e. cord failure position) •Anatomical local matching could lead to unexpected results on the dose distributions (i.e. Lung or liver dose distribution)
Re-Contouring	Daily Weekly	All the structure Only the PTV Only few structures (OARs)	Very high	Adaptive evaluation Evaluate the real volume and condition	•For RS and SBRT misjudgments could do if used without considering some aspects (e.g. Shrinkage of the volume should be done using 4D tools and multimodality images
Re-Planning on MVCT/kVCT	Daily Weekly	•KvCt or MVCT •With/Without Re-Contouring •With/Without Deformations	High	•Evaluation of the daily delivery •Excellent evaluation tools in case of critical cases to monitoring and planning the strategy and follow-up o the Tx	No deformable consideration No automatic tools Dose evaluation on MVCT density Table could create some misjudgments
SW/HW Compensation Dose Accumulation	Daily	•Multimodality images •Deformable registration •Dynamic Jaws/MLC •Robotic Couch	Very High	•Excellent tools for evaluation and adaptive treatment •New era of RT techniques •Evaluation of the motion and shrinkage	At the moment not available, but possible very soon or with 3th part SW

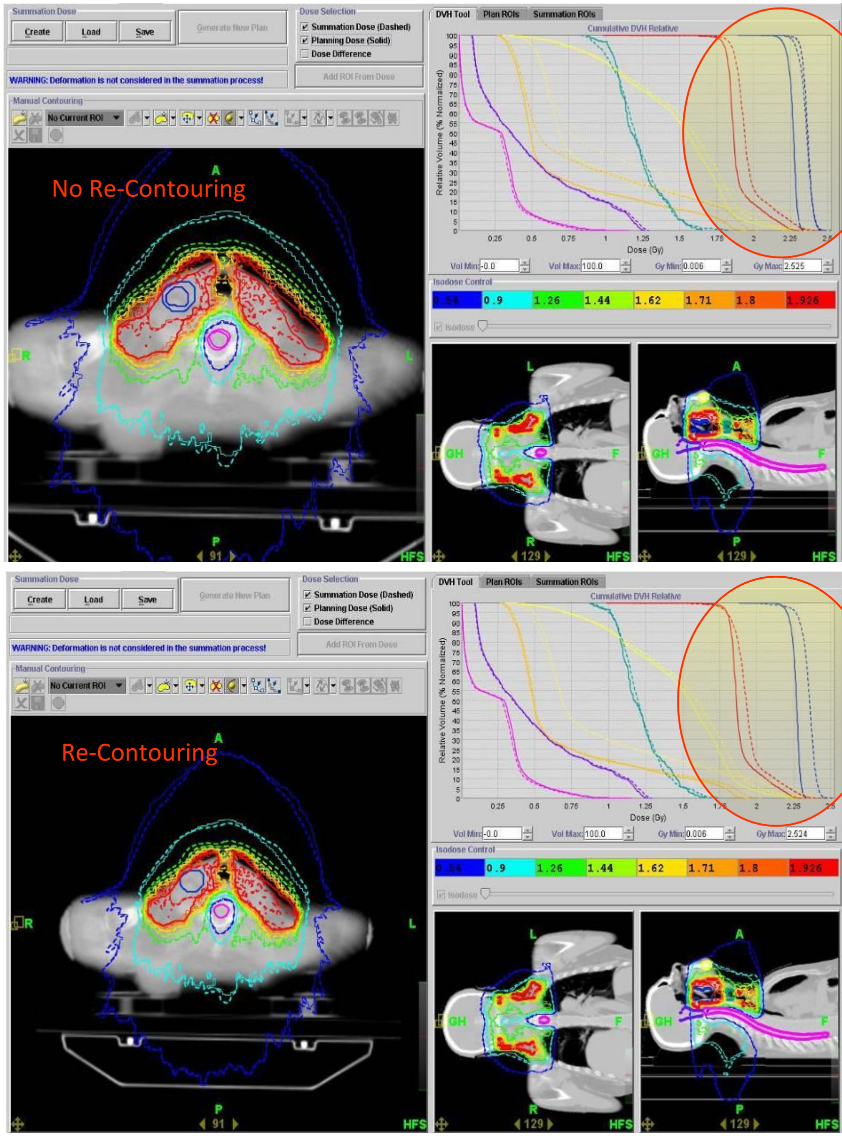
HOW CAN ADAPT? MULTIPLE WORKFLOW AND END-POINTS

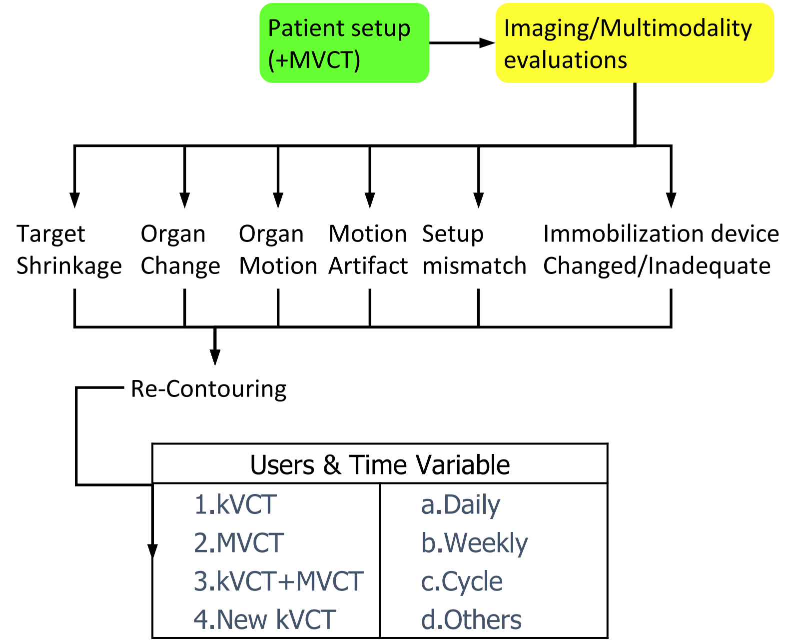
Option 1

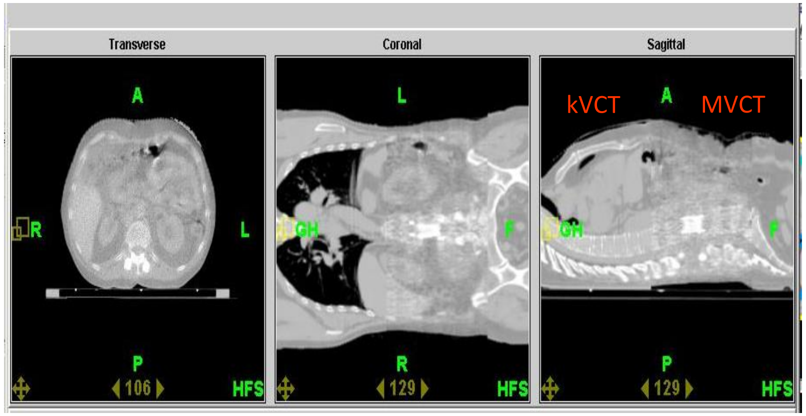


HOW CAN ADAPT? MULTIPLE WORKFLOW AND END-POINTS

Option 2

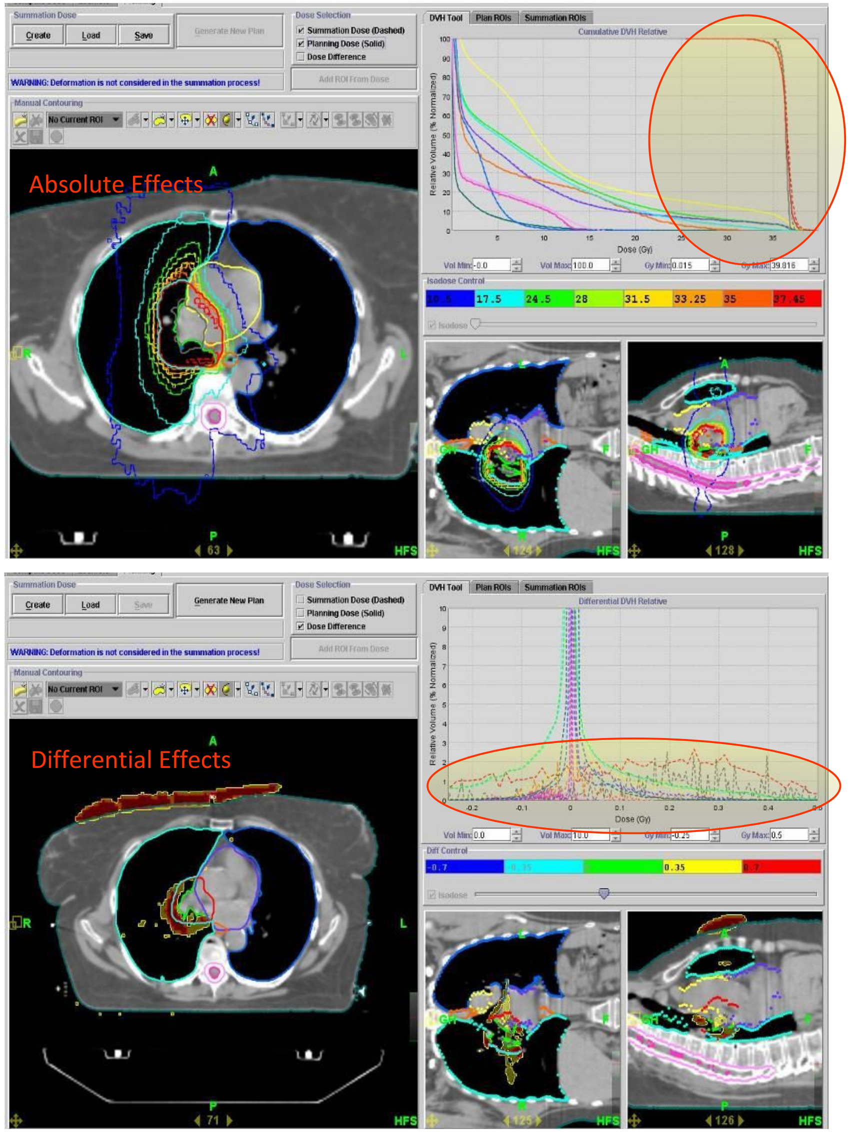






HOW CAN ADAPT? MULTIPLE WORKFLOW AND END-POINTS

Option 3



Patient setup (+MVCT) → Imaging/Multimodality evaluations

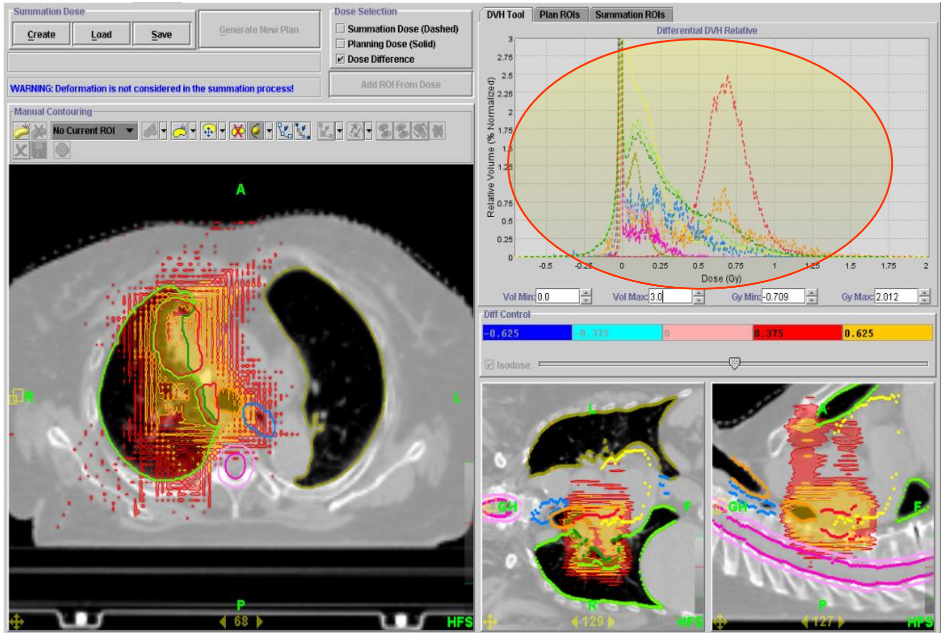
- Target Shrinkage
- Organ Change
- Organ Motion
- Motion Artifact
- Setup mismatch
- Immobilization device Changed/Inadequate

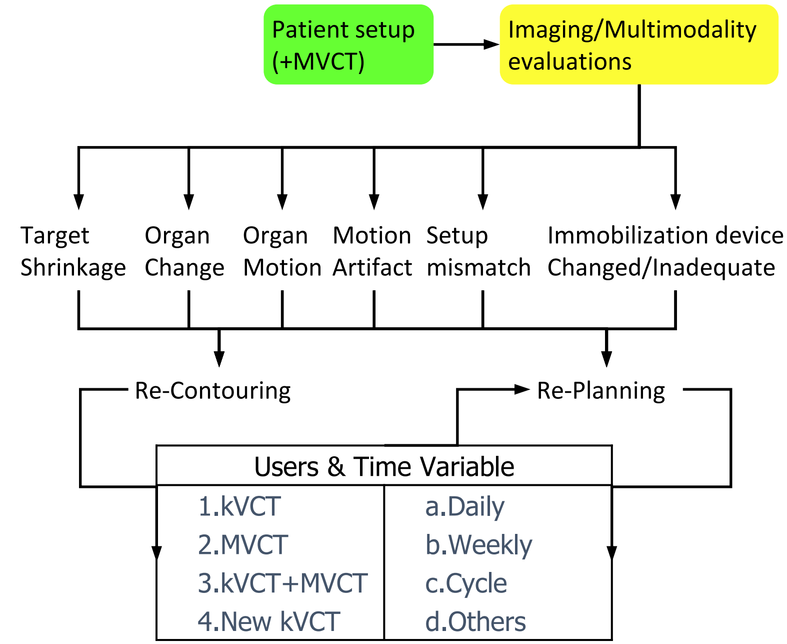
→ Re-Planning

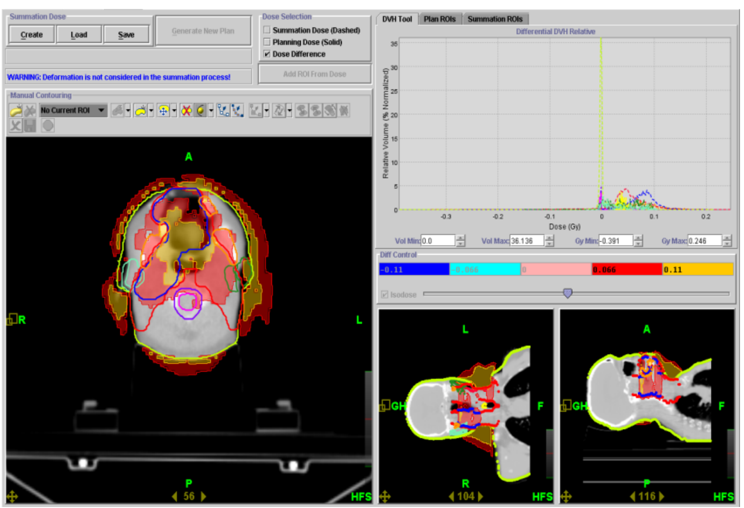
Users & Time Variable	
1.kVCT	a.Daily
2.MVCT	b.Weekly
3.kVCT+MVCT	c.Cycle
4.New kVCT	d.Others

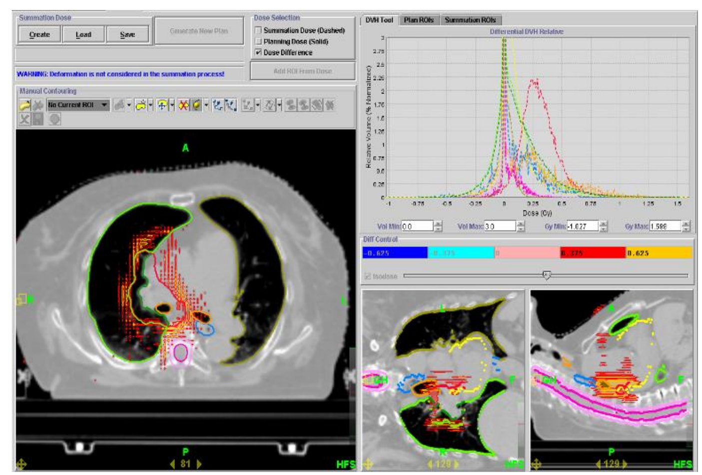
HOW CAN ADAPT? MULTIPLE WORKFLOW AND END-POINTS

Option 4



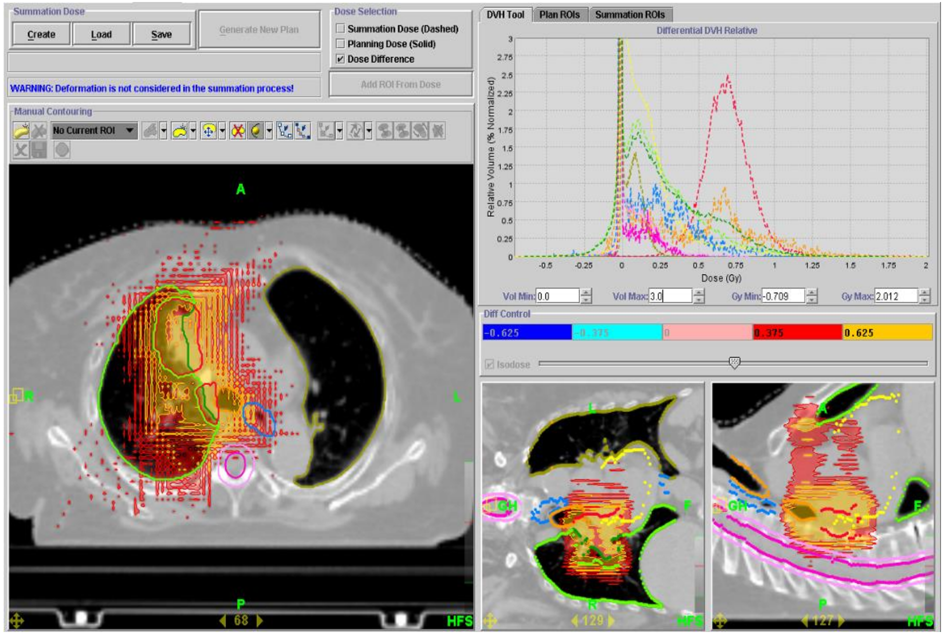


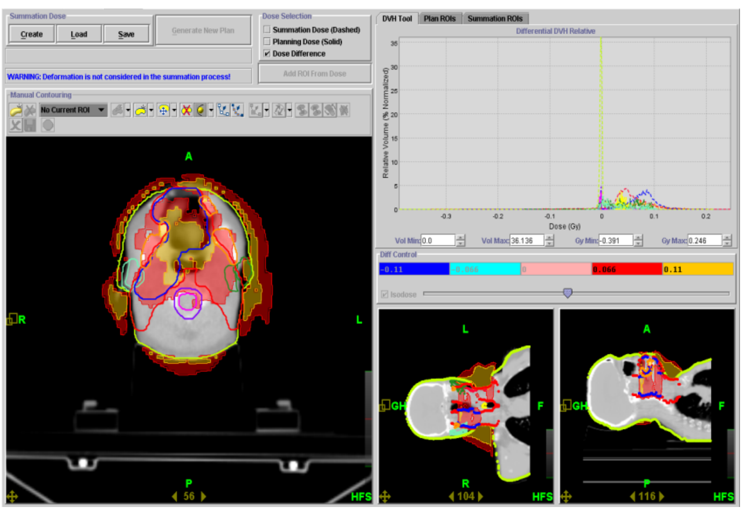


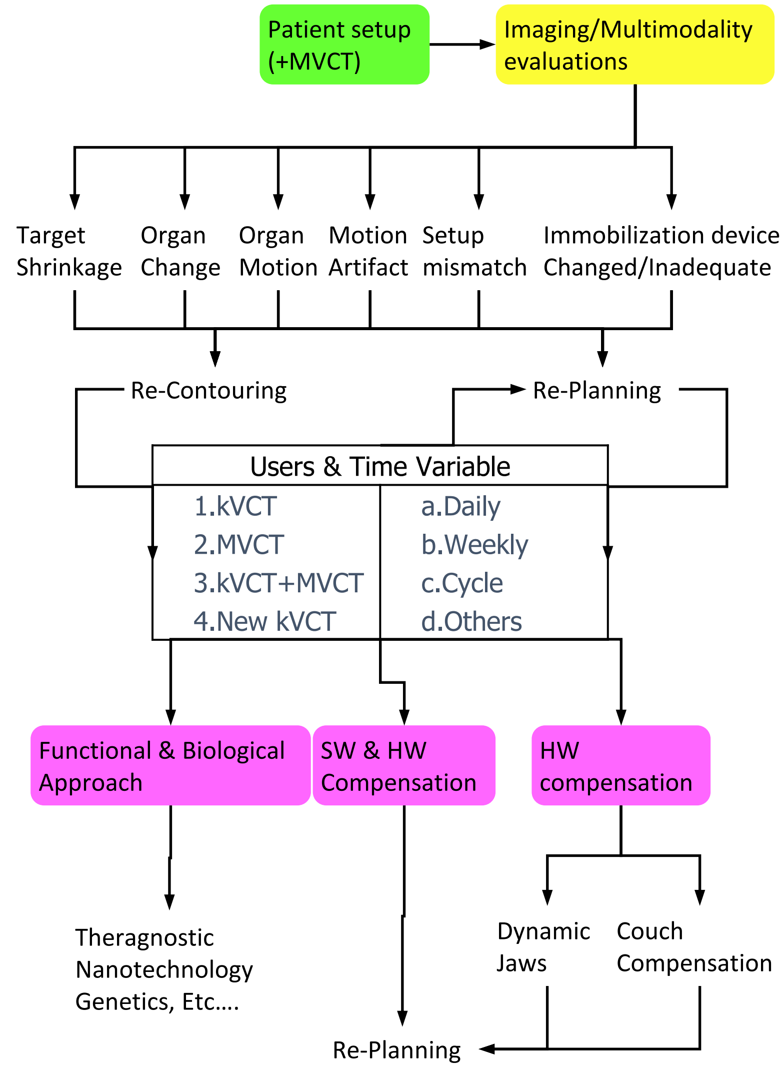


HOW CAN ADAPT? MULTIPLE WORKFLOW AND END-POINTS

Option 5

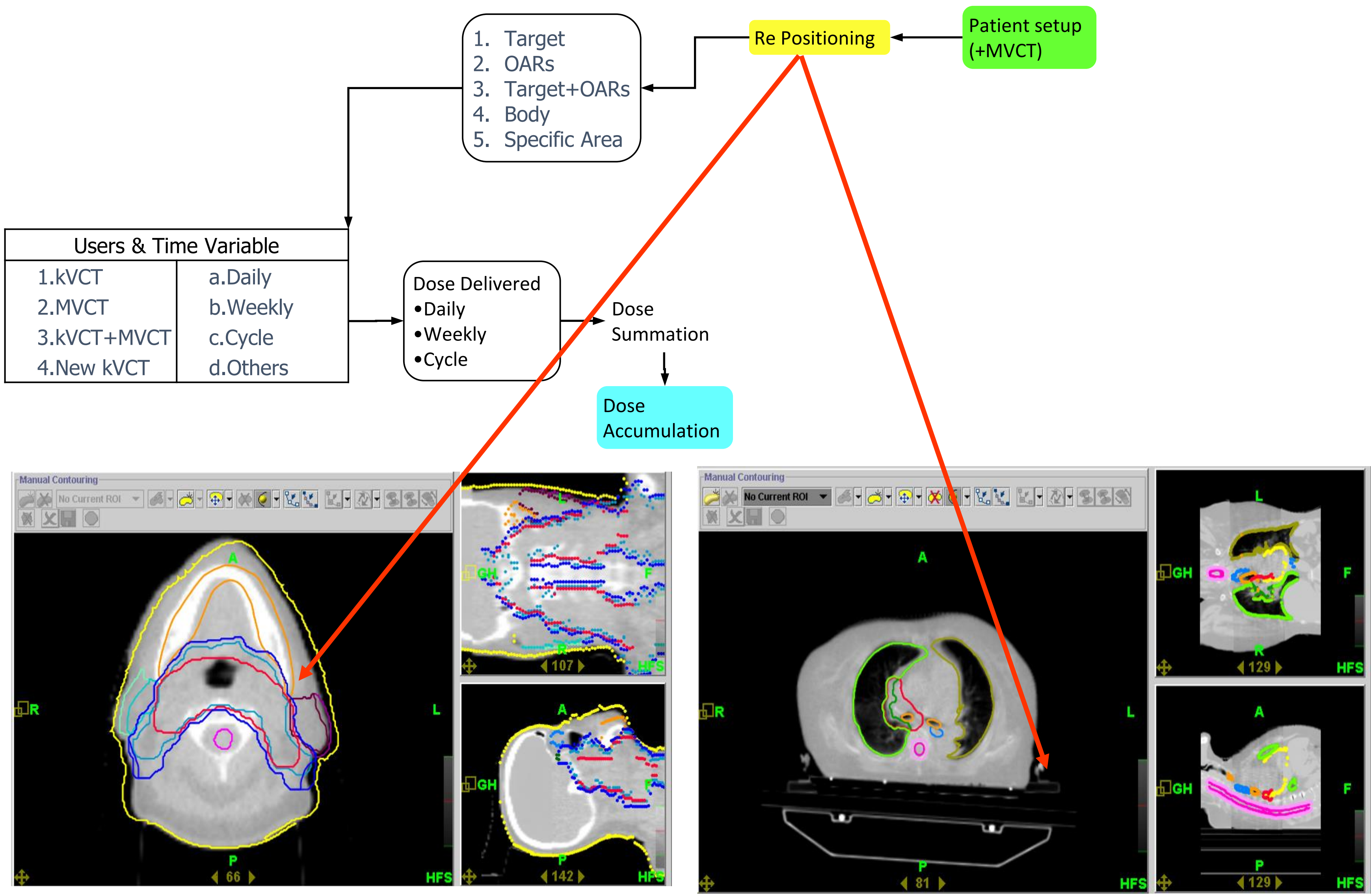






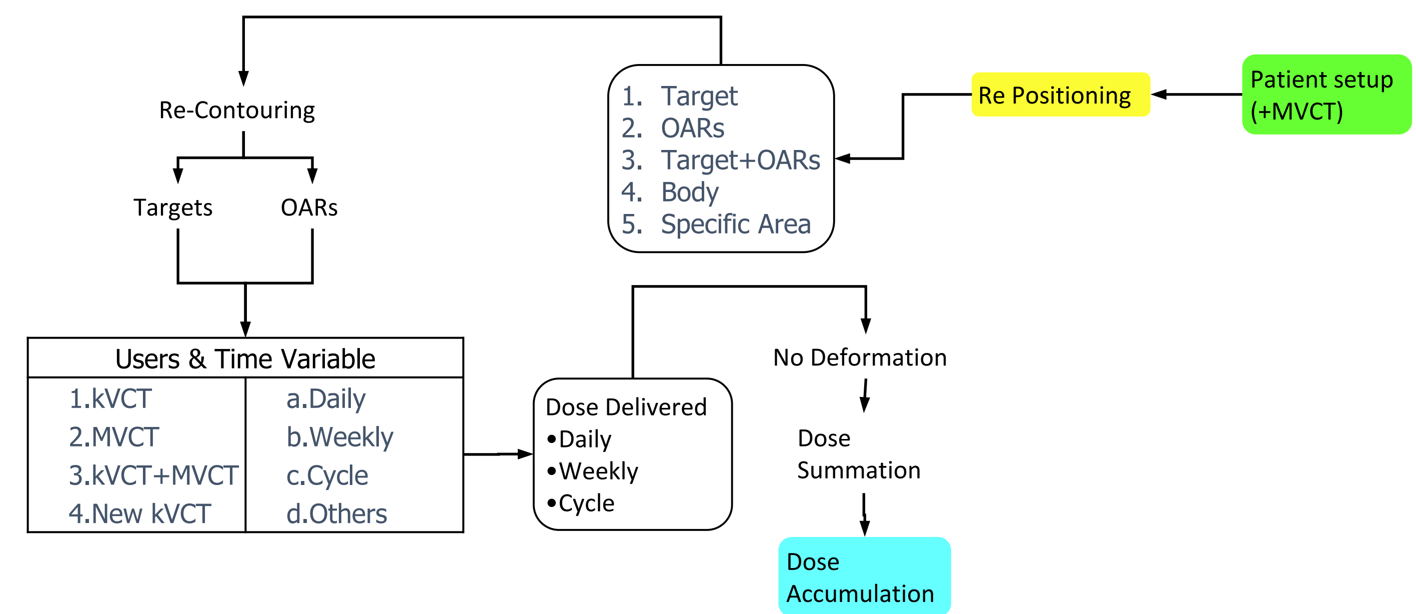
HOW CAN ADAPT? MULTIPLE WORKFLOW AND END-POINTS

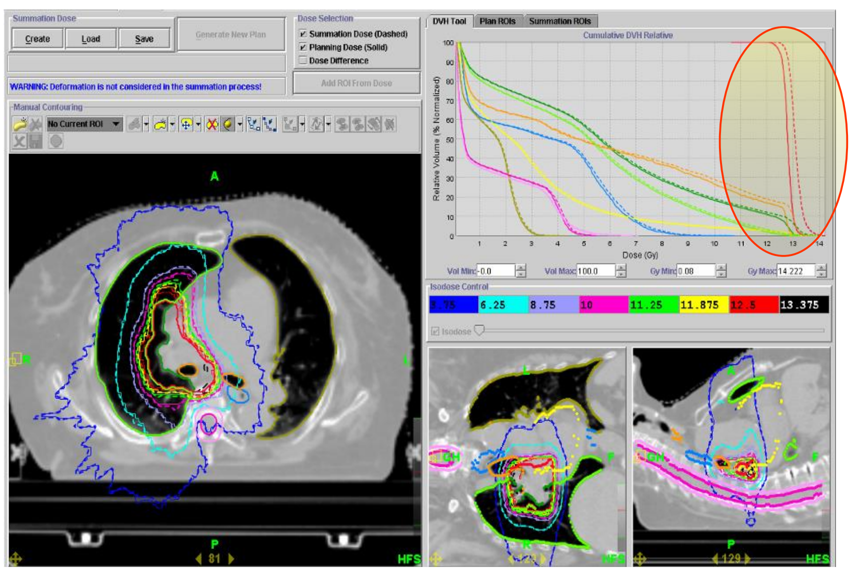
Option 6

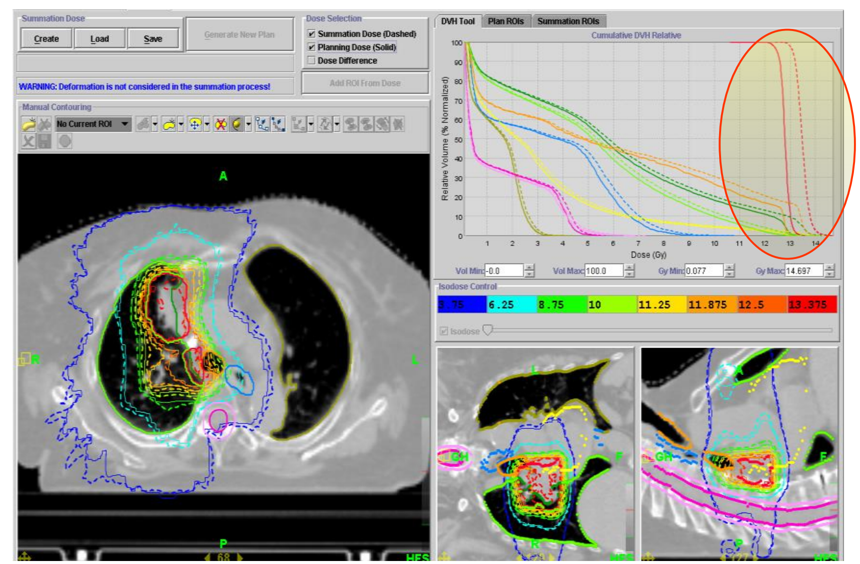


HOW CAN ADAPT? MULTIPLE WORKFLOW AND END-POINTS

Option 7

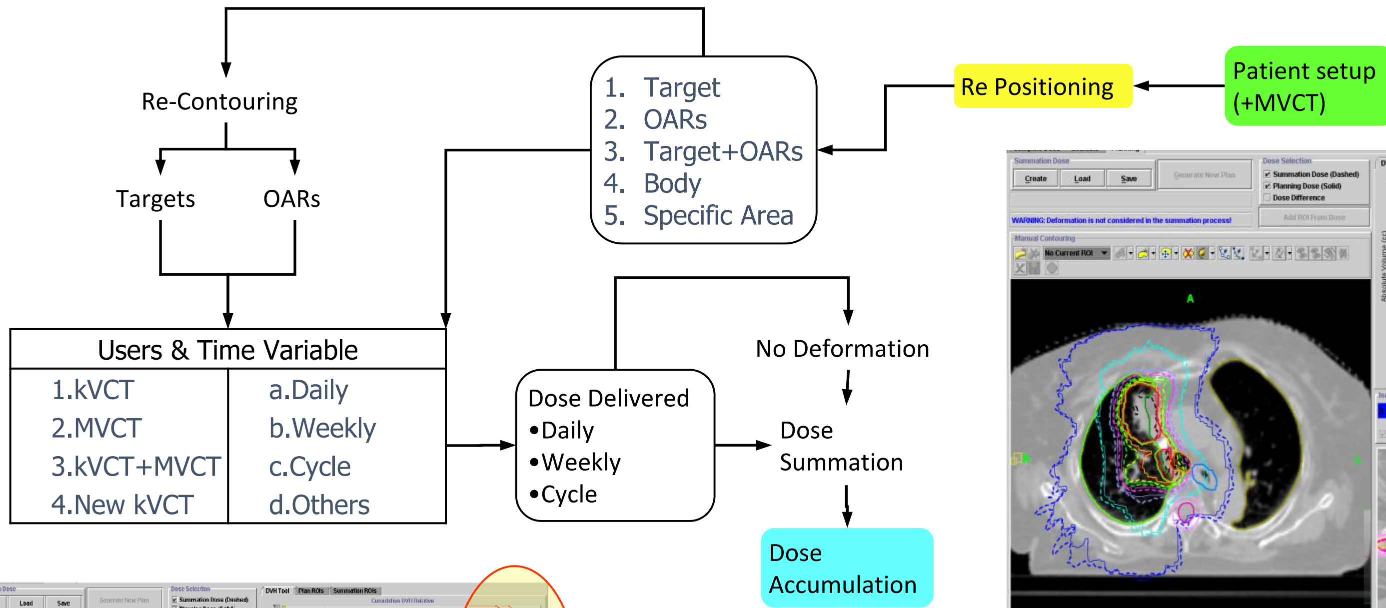


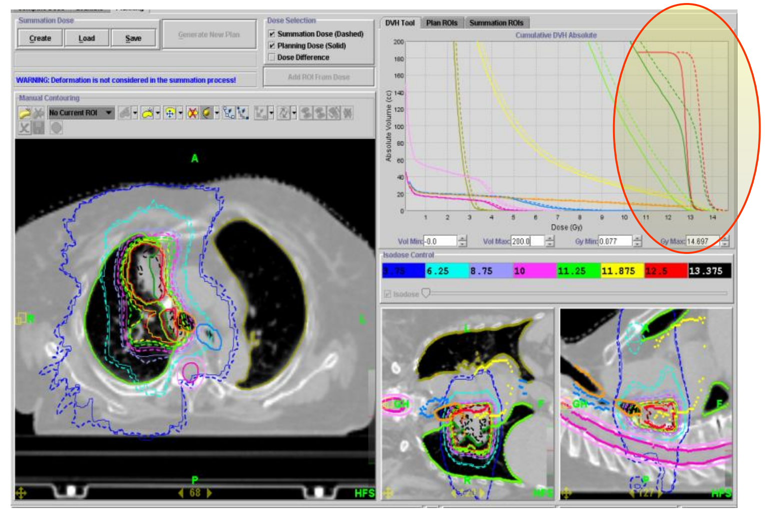


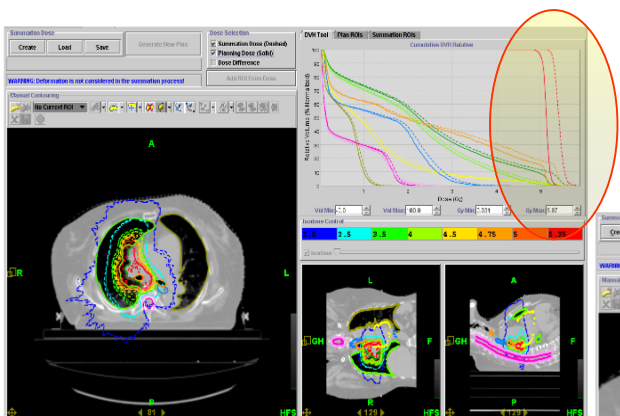


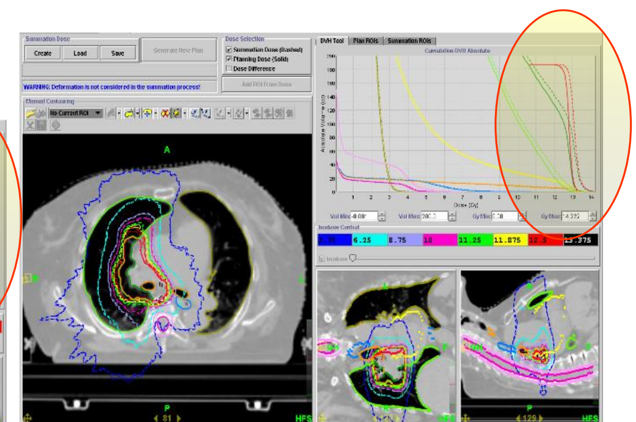
HOW CAN ADAPT? MULTIPLE WORKFLOW AND END-POINTS

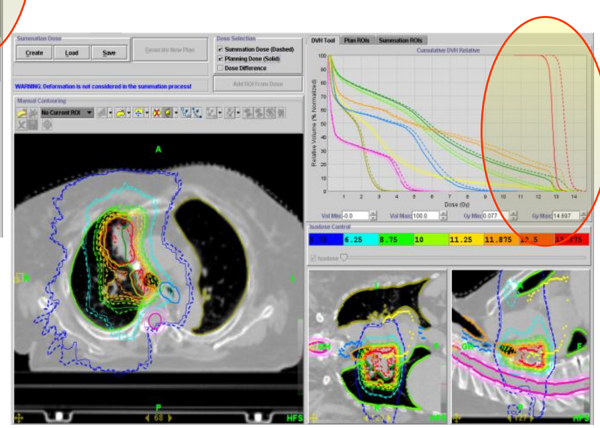
Option 8











HOW CAN ADAPT? MULTIPLE WORKFLOW AND END-POINTS

Option 9

Patient setup (+MVCT) → Re Positioning →

1. Target
2. OARs
3. Target+OARs
4. Body
5. Specific Area

Re-Contouring

Targets | OARs

Users & Time Variable	
1.kVCT	a.Daily
2.MVCT	b.Weekly
3.kVCT+MVCT	c.Cycle
4.New kVCT	d.Others

Dose Delivered
- Daily
- Weekly
- Cycle

No Deformation

Dose Summation

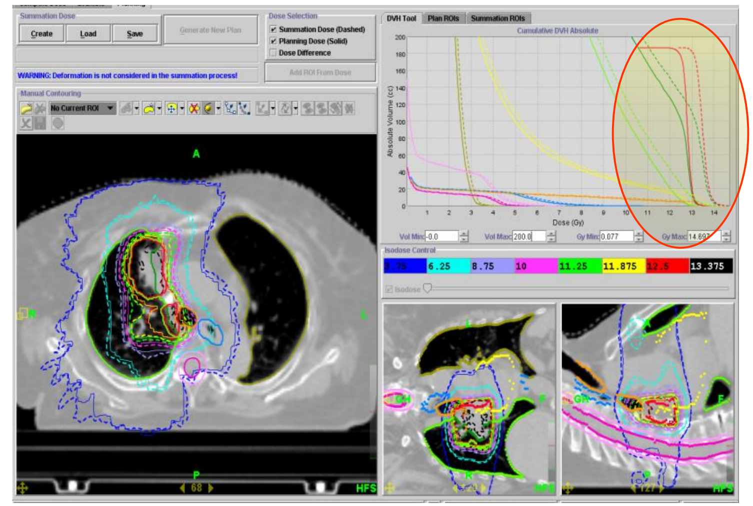
Dose Accumulation

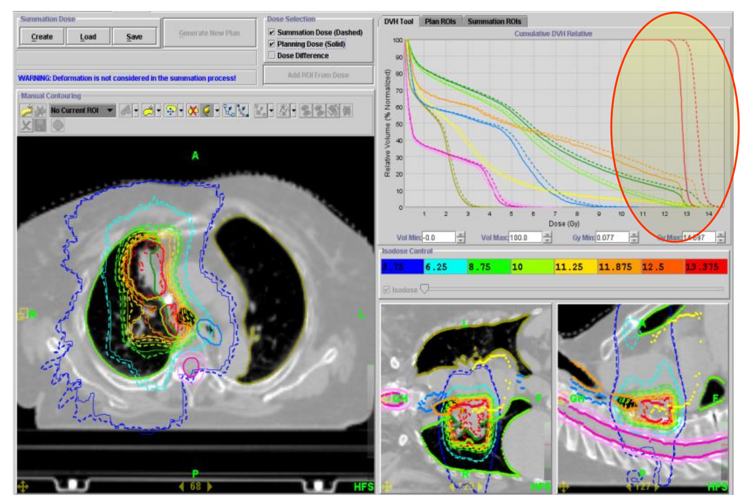
Re-Planning

Users & Time Variable	
1.kVCT	a.Daily
2.MVCT	b.Weekly
3.kVCT+MVCT	c.Cycle
4.New kVCT	d.Others

Adequate Fractionation

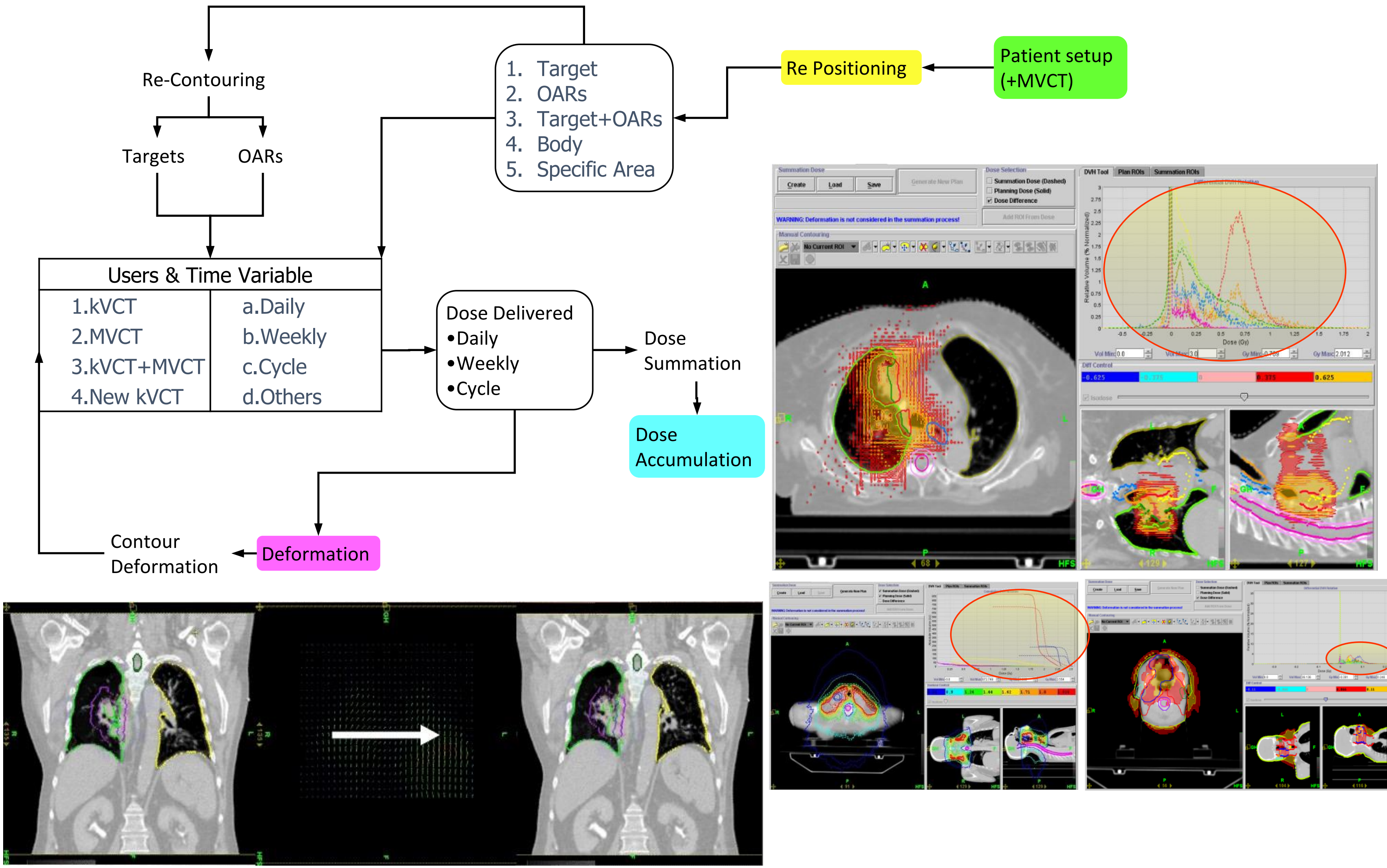
Change with New fractionation





HOW CAN ADAPT? MULTIPLE WORKFLOW AND END-POINTS

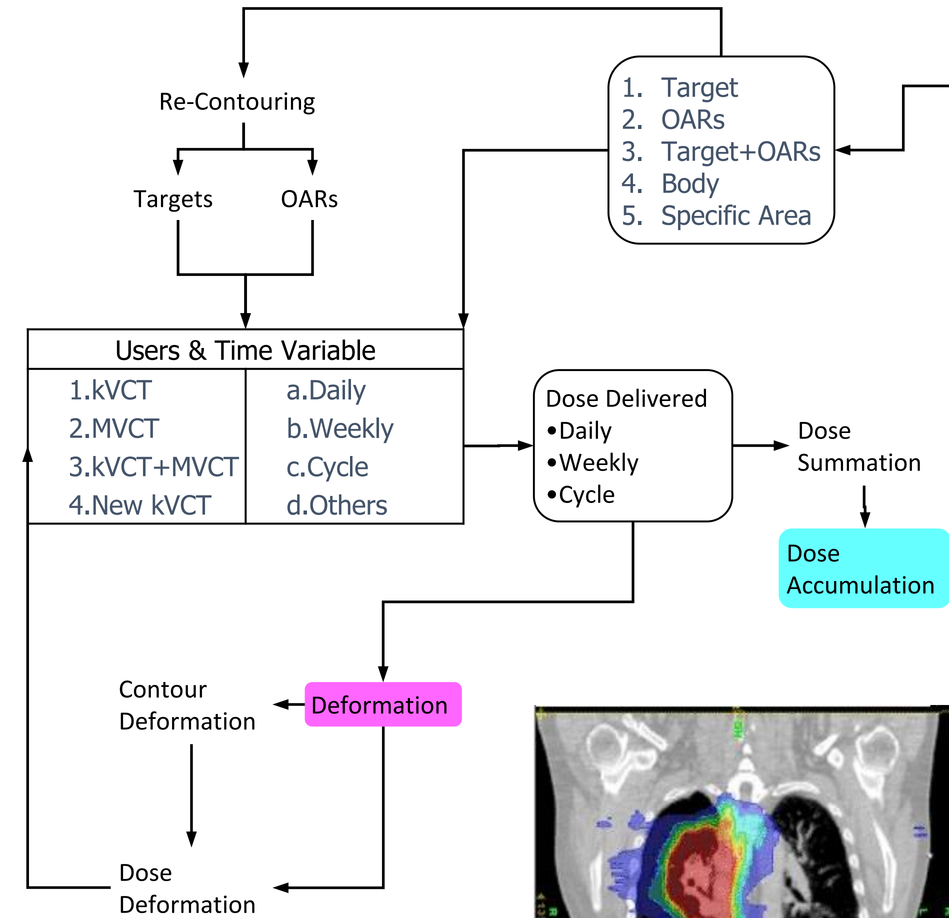
Option 10

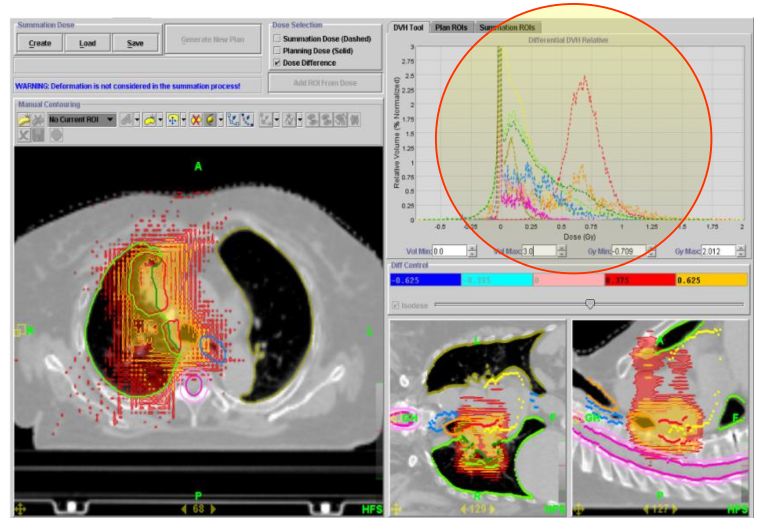


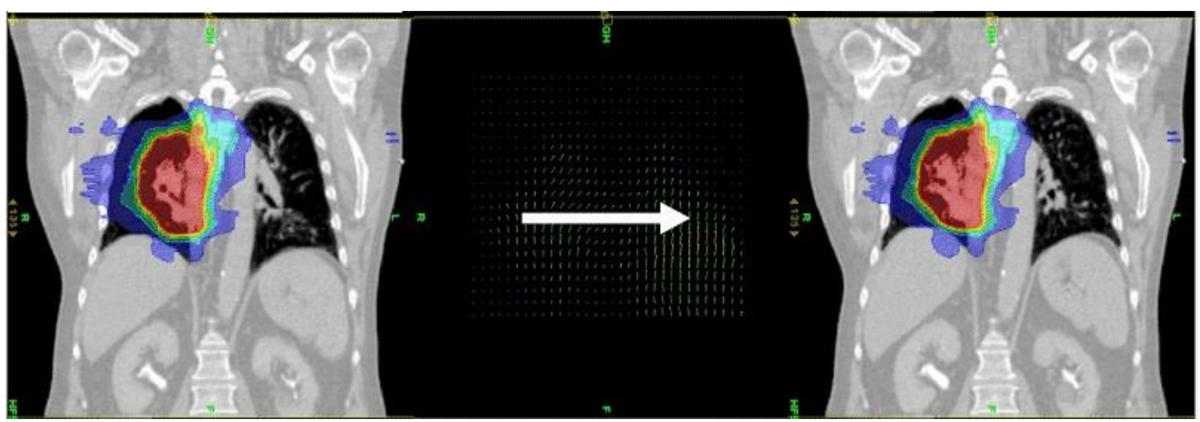
K.Ruchala – Tomotherapy Inc.

HOW CAN ADAPT? MULTIPLE WORKFLOW AND END-POINTS

Option 11



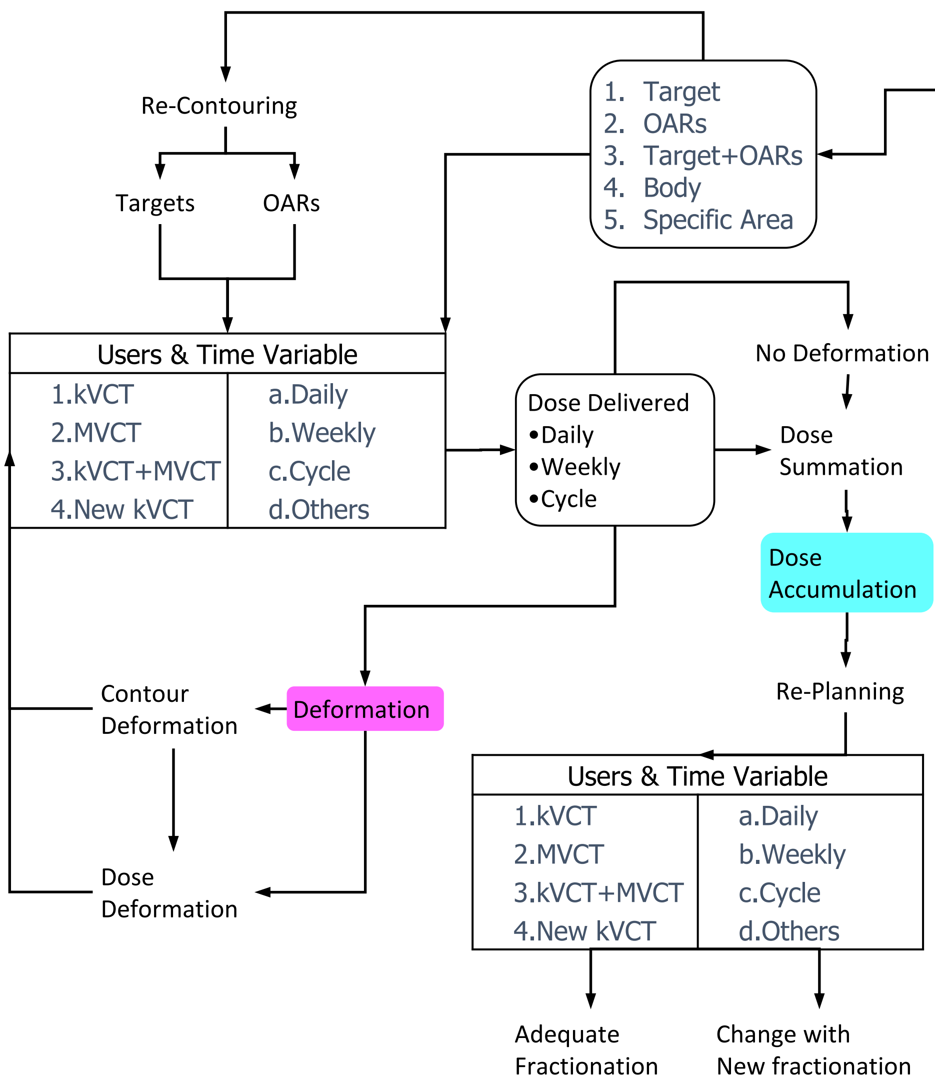


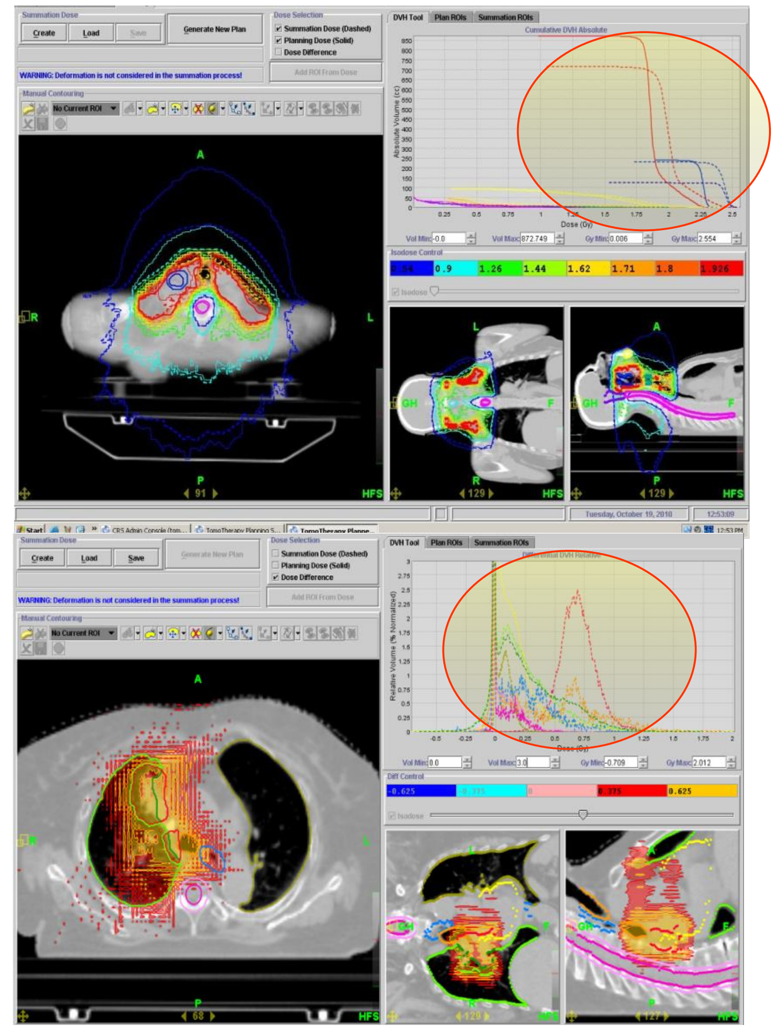


K.Ruchala – Tomotherapy Inc.

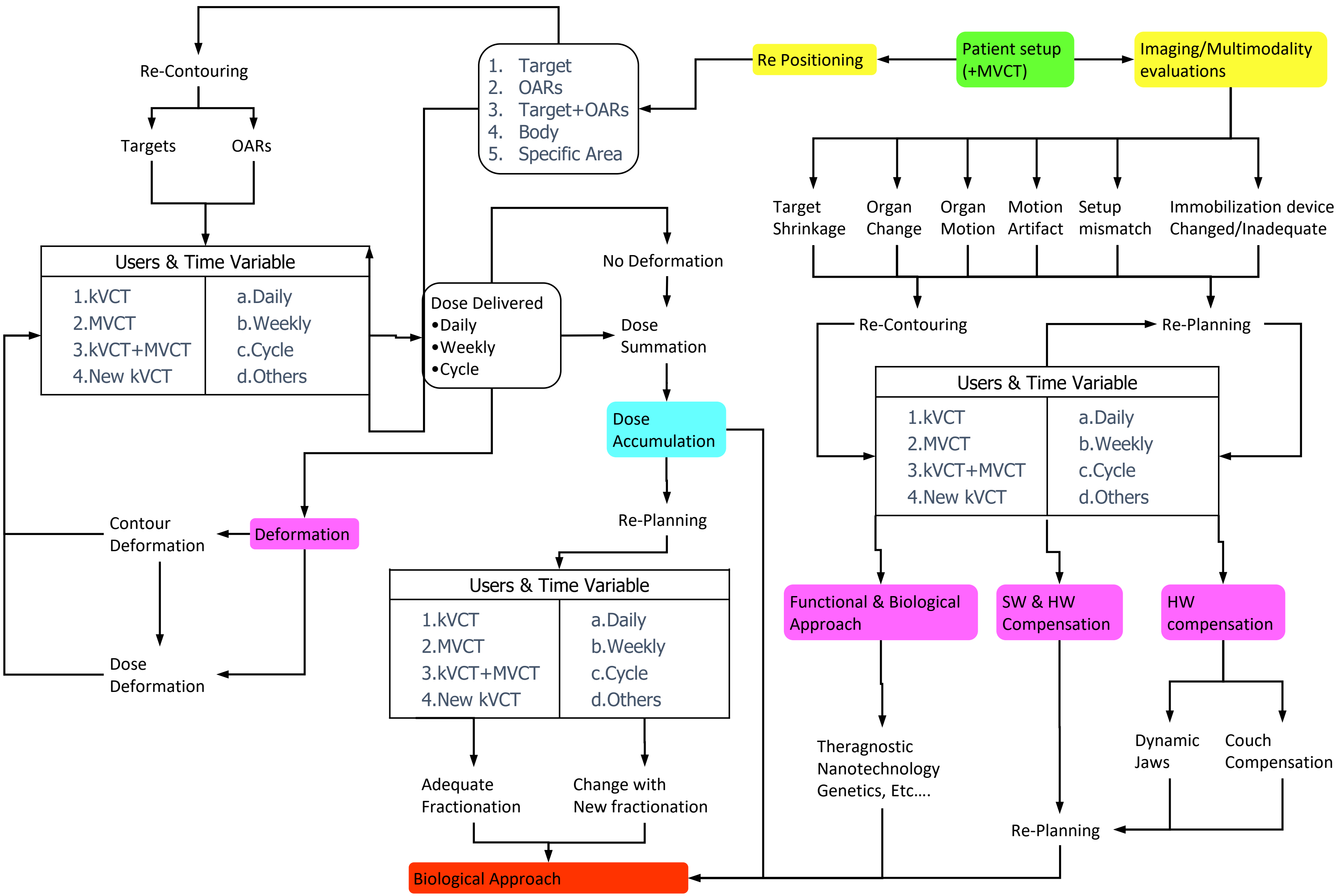
HOW CAN ADAPT? MULTIPLE WORKFLOW AND END-POINTS

Option 12



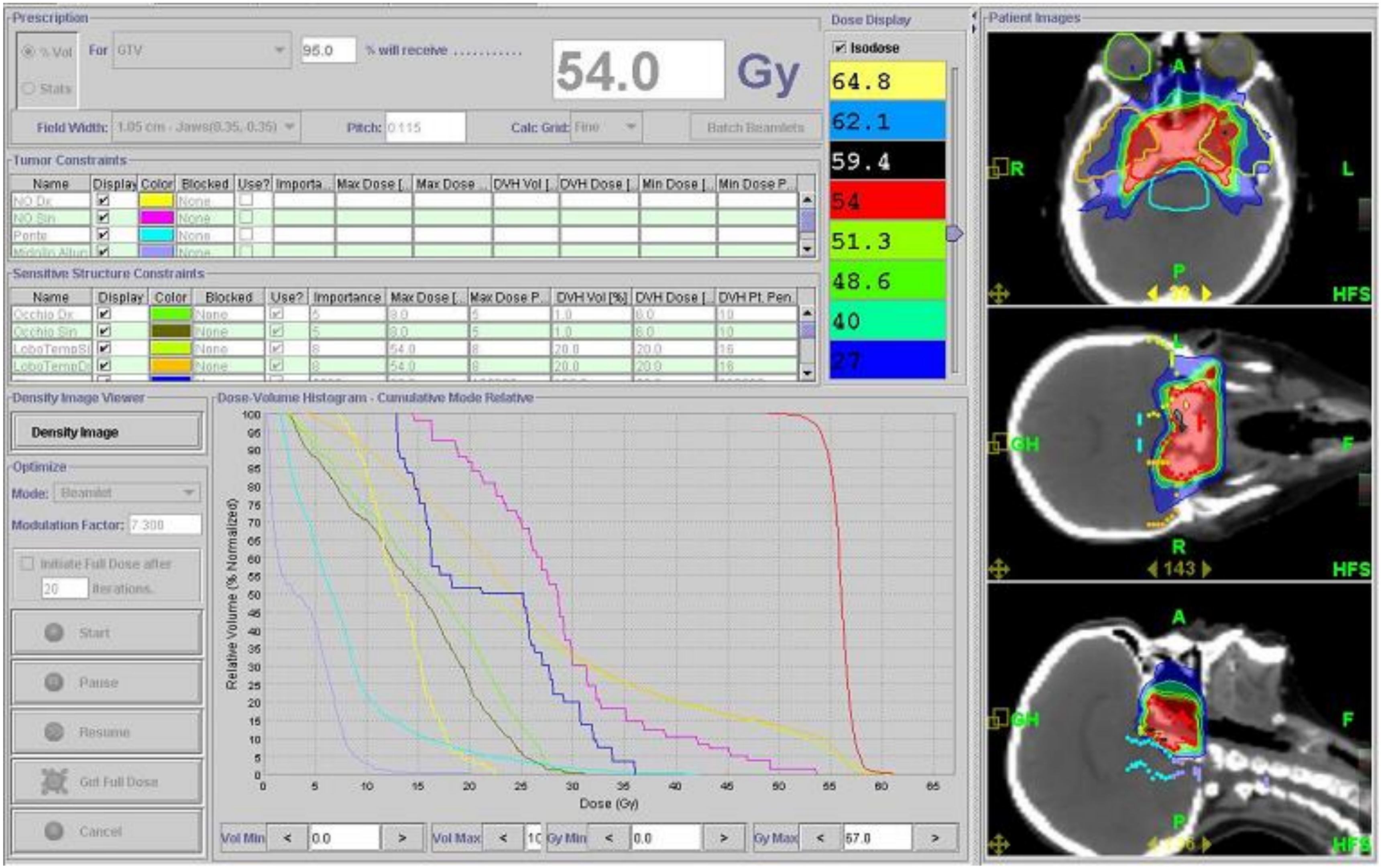


HOW CAN ADAPT? MULTIPLE WORKFLOW AND END-POINTS

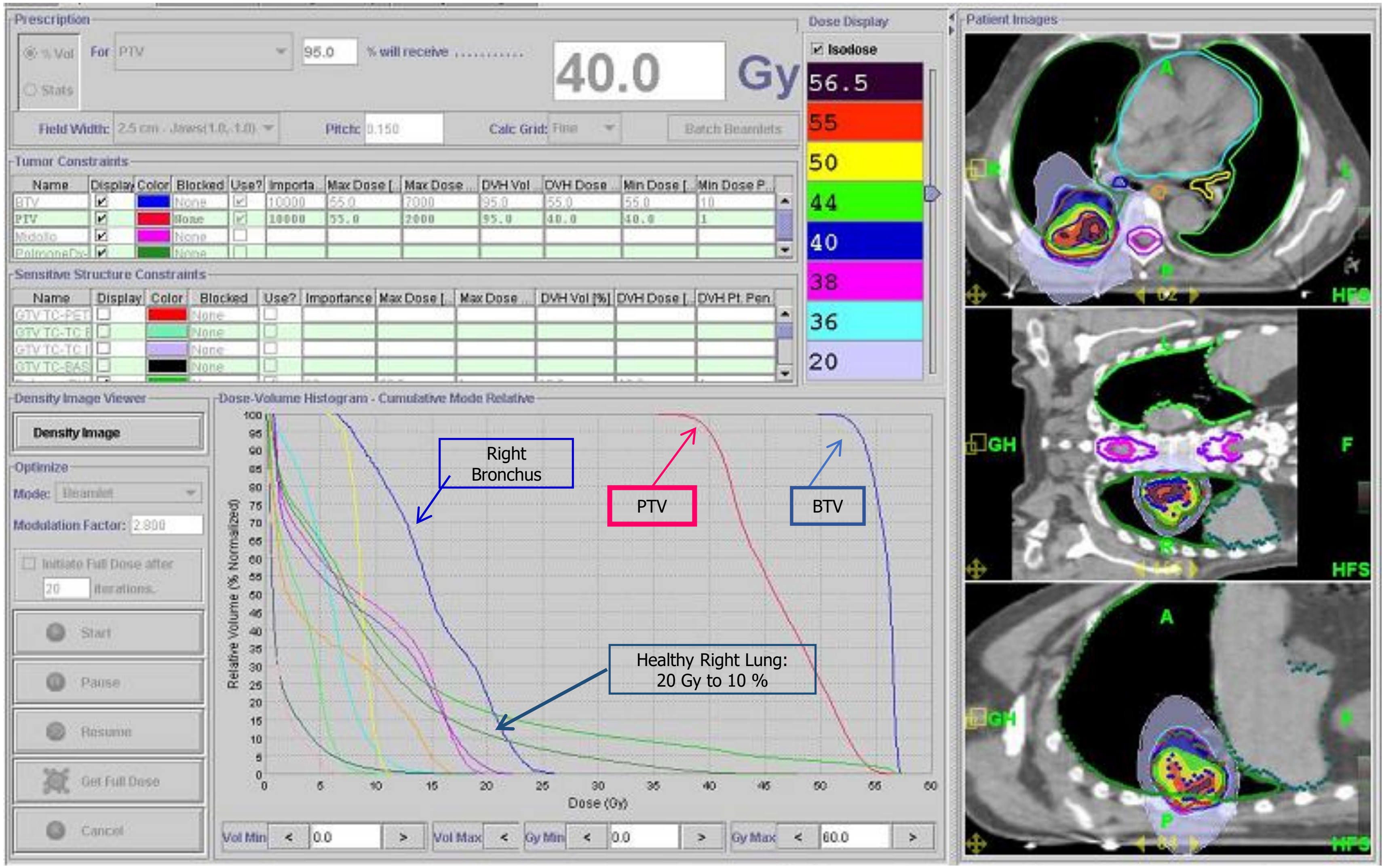


RE-IRRADIATION: HEAD & NECK
(Standard: 54 Gy / 27 Fx - Hyper-fractionation: 54Gy / 36Fx)

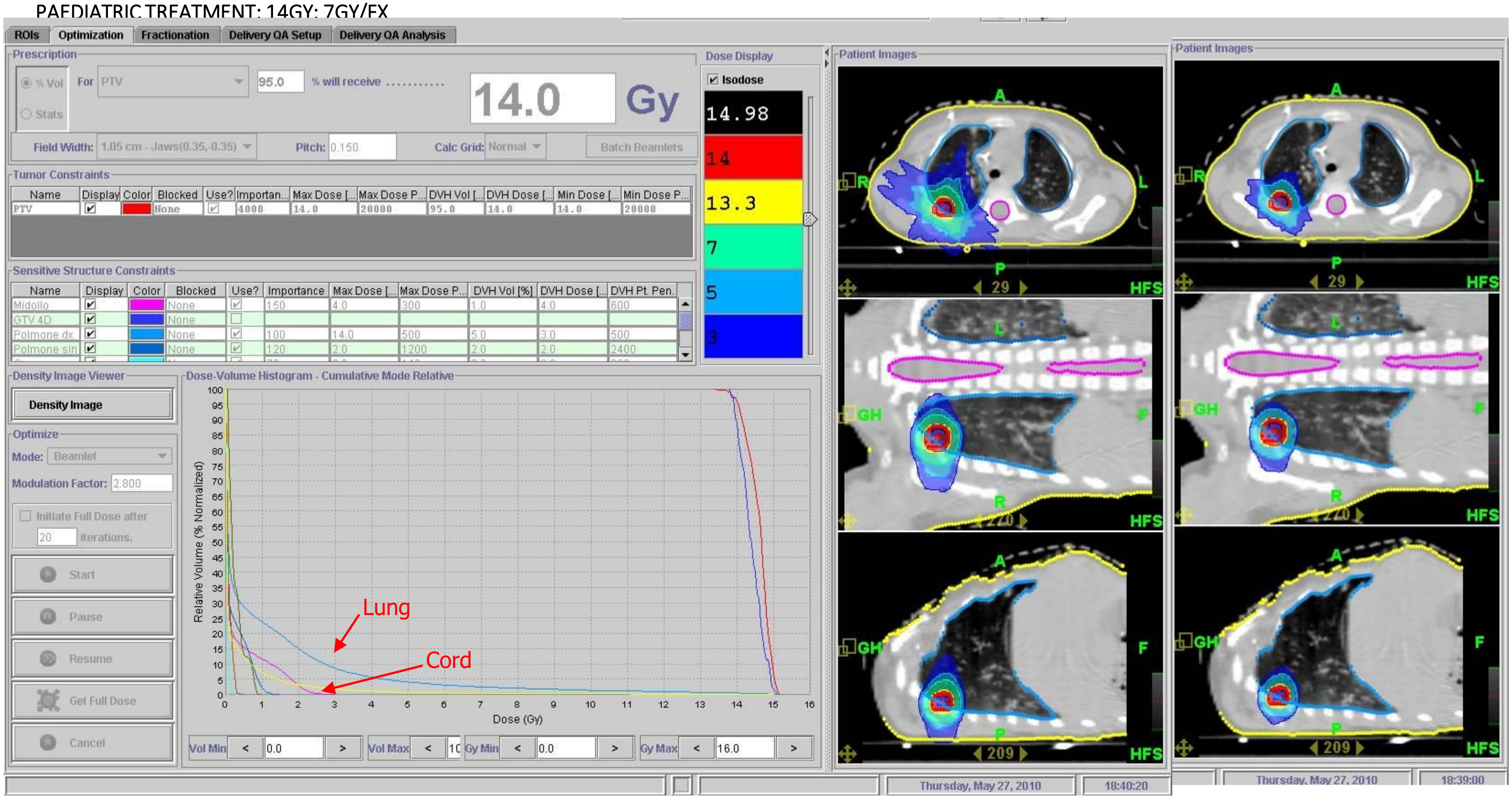
Not RCS but interesting with Tomotherapy



SECONDARY LUNG CANCER RELAPSED AFTER RFA
MULTIMODALITY IMAGE FUSION (SIB: BTV 55 Gy / 5 Fx - PTV 40 Gy / 5 Fx)

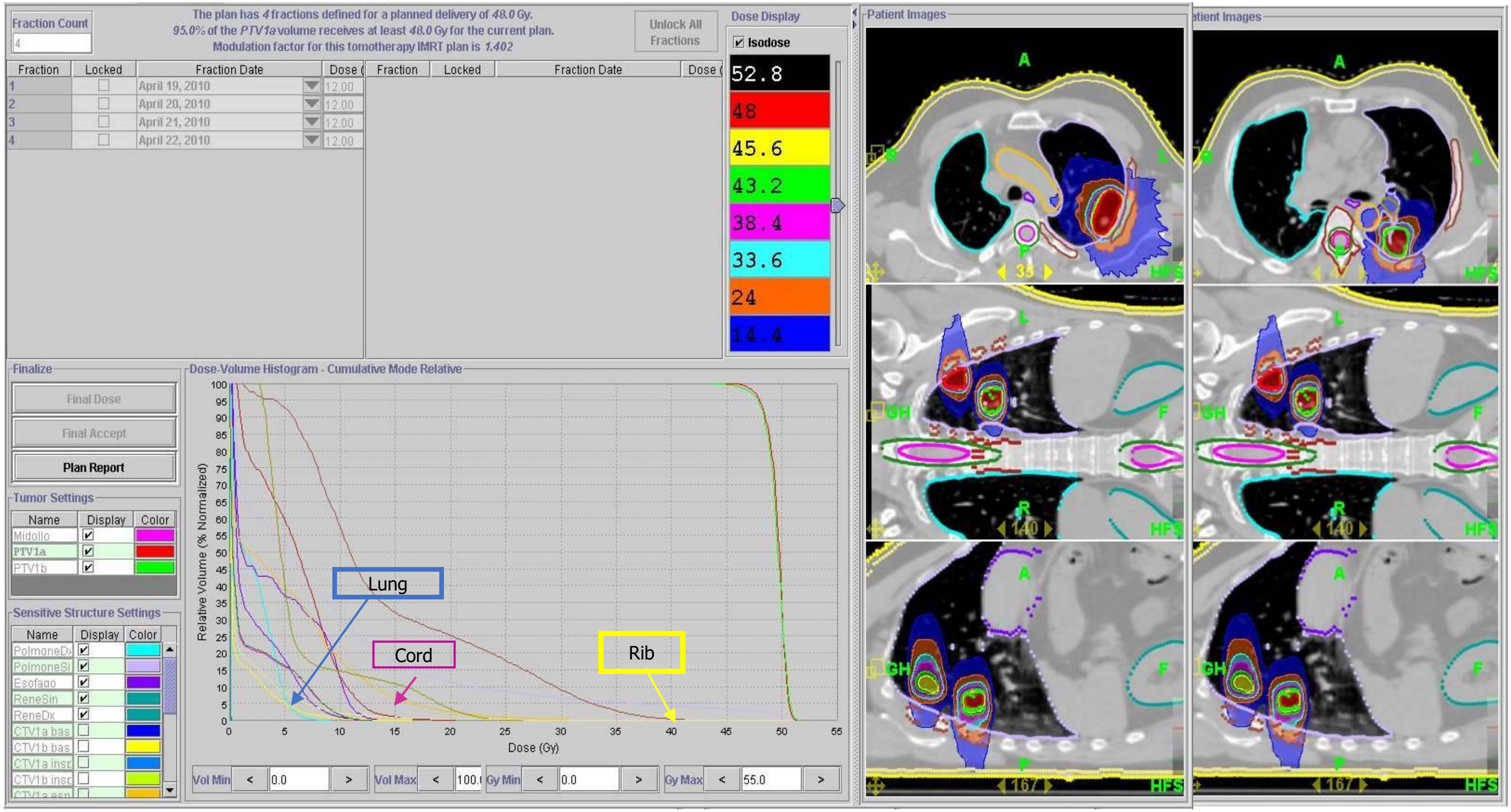


4D CONTOURING FOR SAFETY PLAN….
PAEDIATRIC TREATMENT: 14GY: 7GY/FX



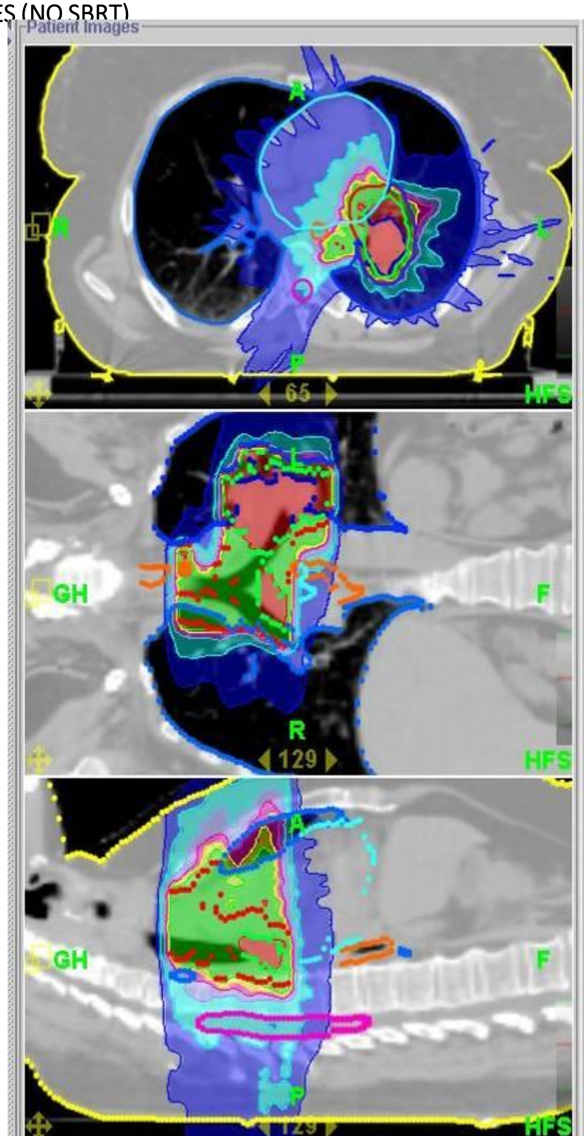
Dosimetric results for paediatric patients using Tomotherapy…
…. with SBRT using LINAC was a problem due the anesthesia and body frame

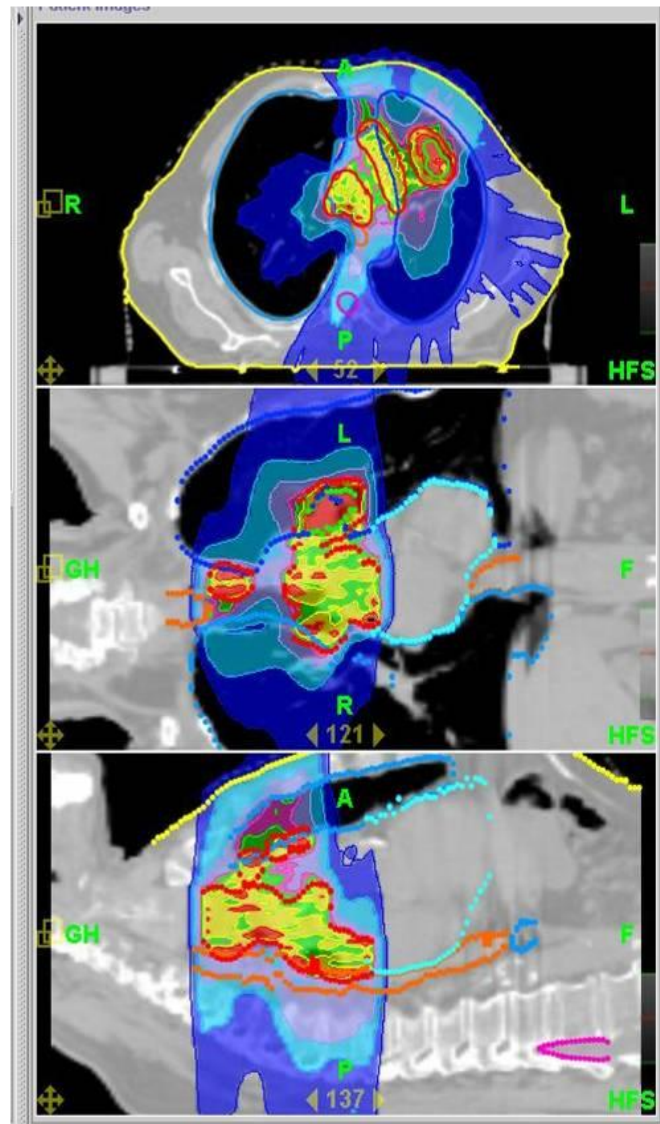
SBRT MULTIPLE LESIONS (48GY / 4 FX)



Not SBRT but interesting with Tomotherapy

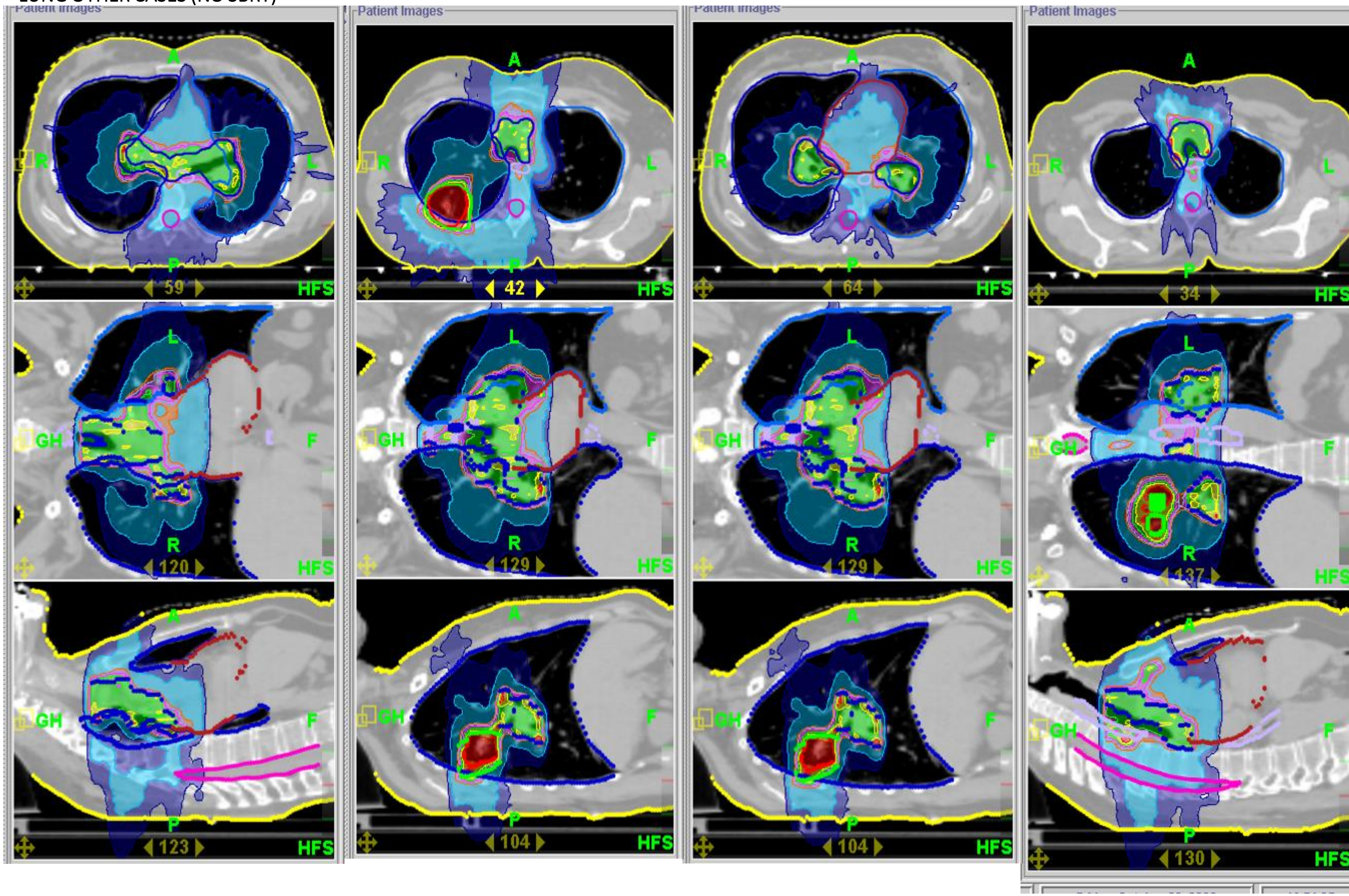
LUNG OTHER CASES (NO SBRT)





Not SBRT but interesting with Tomotherapy

LUNG OTHER CASES (NO SBRT)

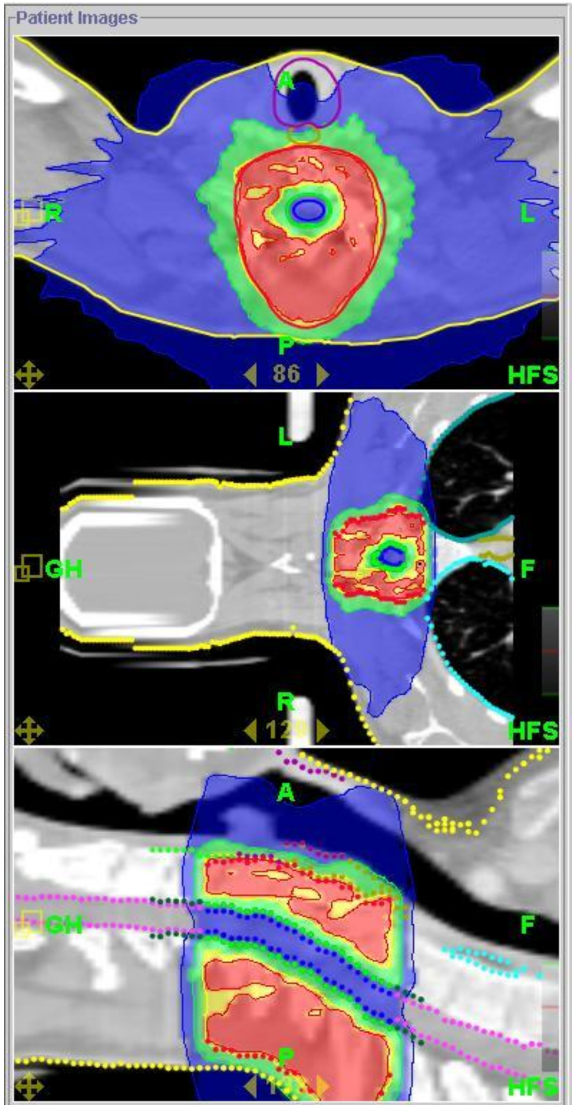


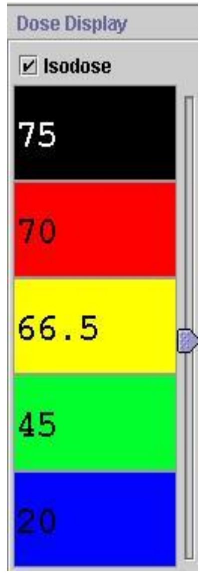
SPINAL SARCOMA
(PTV 70 Gy / 35 FX)

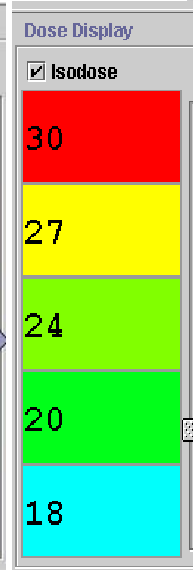
BODY RADIATION THERAPY
PALLIATIVE CASES

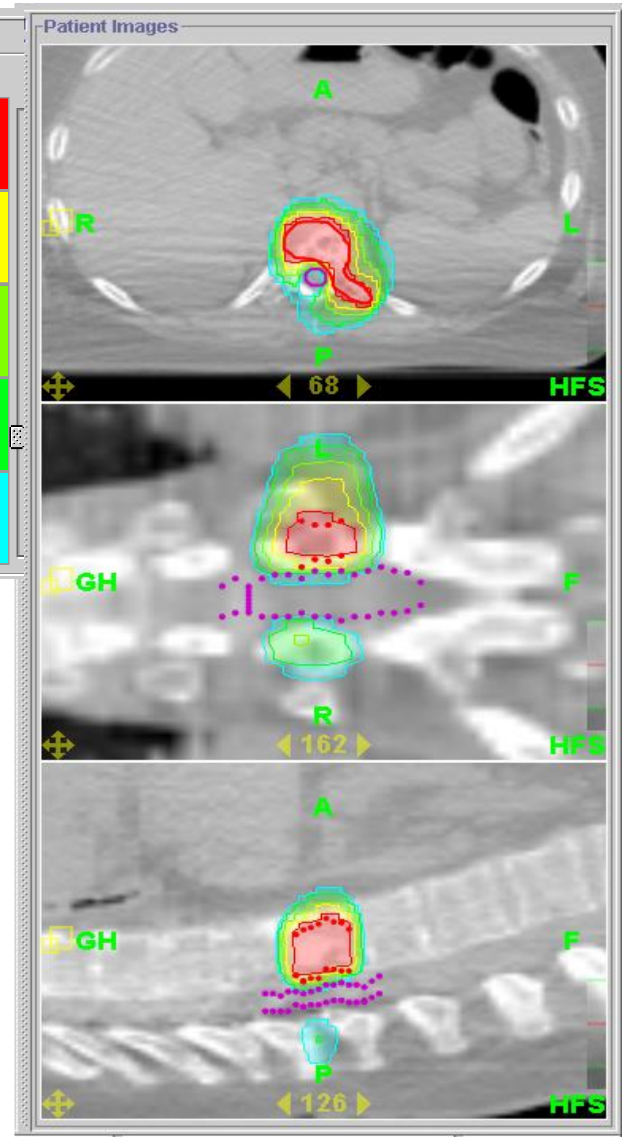
VERTEBRA
(PTV 30Gy)

Not SBRT but interesting with Tomotherapy

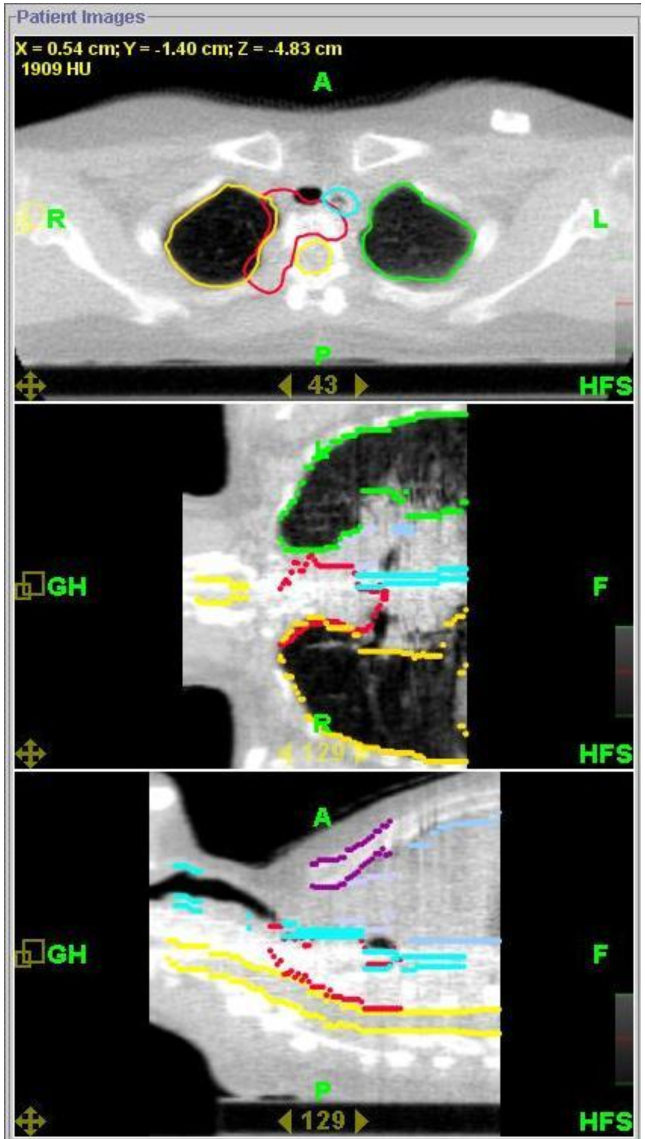




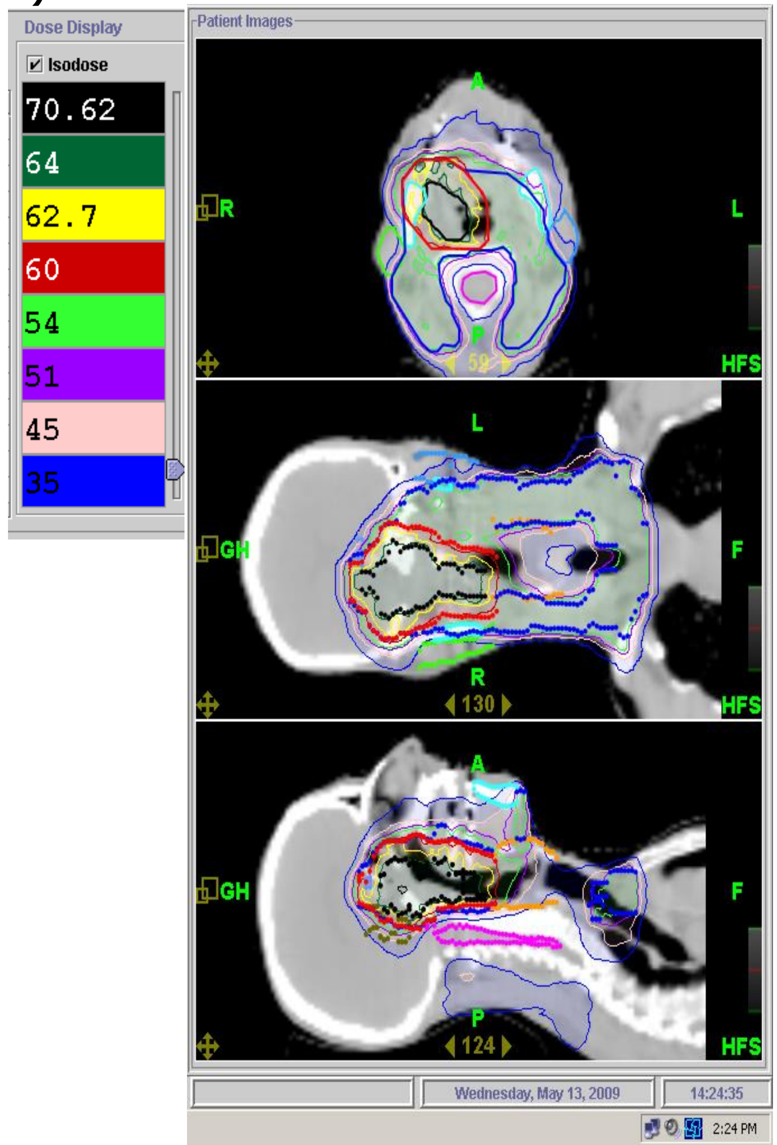




SPINAL METAL PROSTHESIS (Using MVCT)



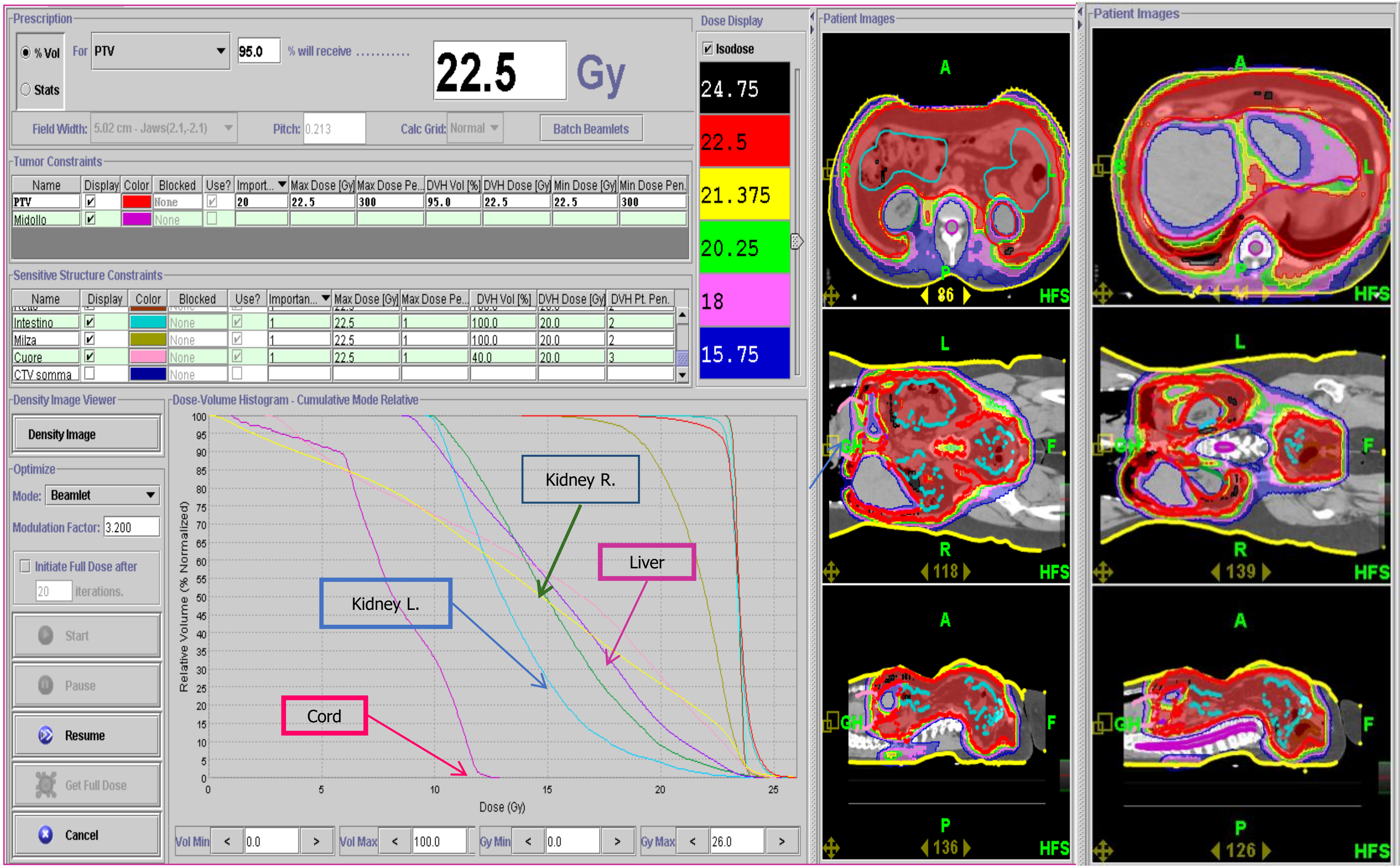
H&N (PTV1:70Gy PTV2:64 Gy PTV3:54 Gy / 33 Fx)



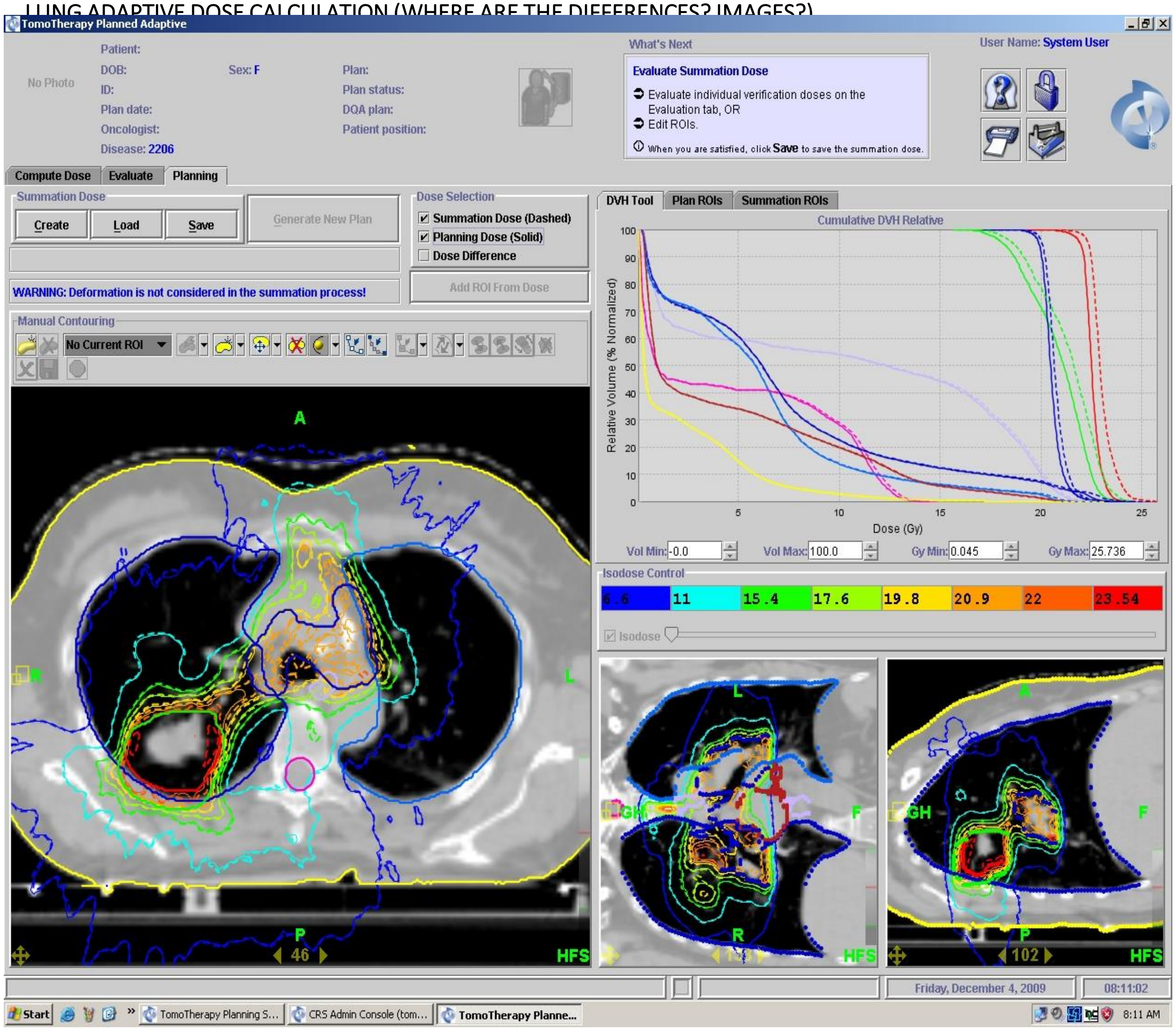
Cases where Adaptive RT could be a need

ABDOMINAL TREATMENT
(PTV 22,5 GY / 15 FX)

Not SBRT but interesting with Tomotherapy



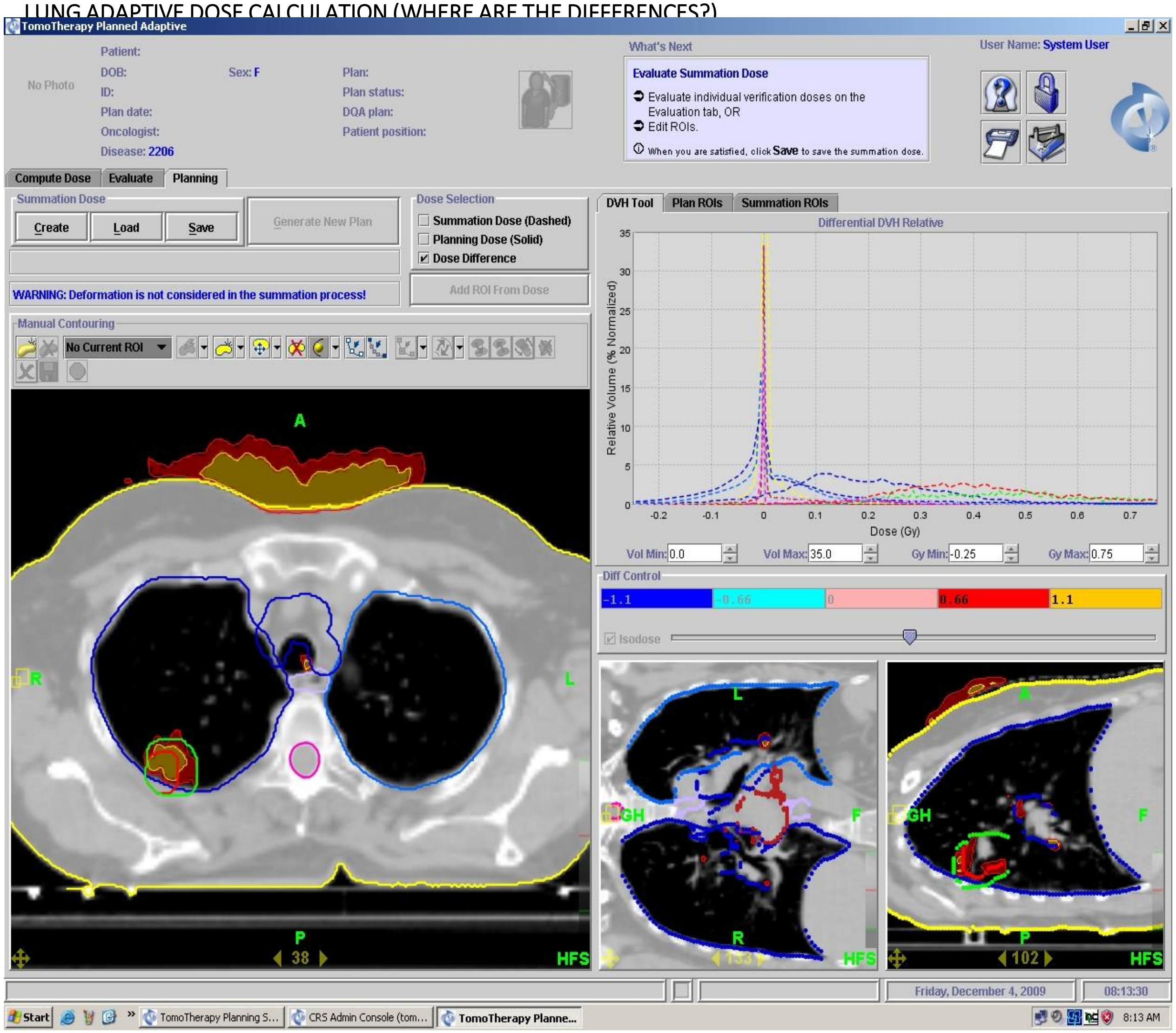
LUNG ADAPTIVE DOSE CALCULATION (WHERE ARE THE DIFFERENCES? IMAGES?)



May be:

1. Dosimetric error due to the algorithm?
2. Target delineation
3. Target Movement (Intra/Inter fraction)
4. Dose Lung Estimation
5. Dose at the interface (Bone/Lung/Fat)
6. Volume effect (image down sampling)
7. MVCT vs. kVCT
8. Morning Dose Output
9. Plan Optimization and Parameters?
10. Operators
    - Doctor
    - Physicist
    - Therapist

LUNG ADAPTIVE DOSE CALCULATION (WHERE ARE THE DIFFERENCES?)



May be:

1. Dosimetric error due to the algorithm?
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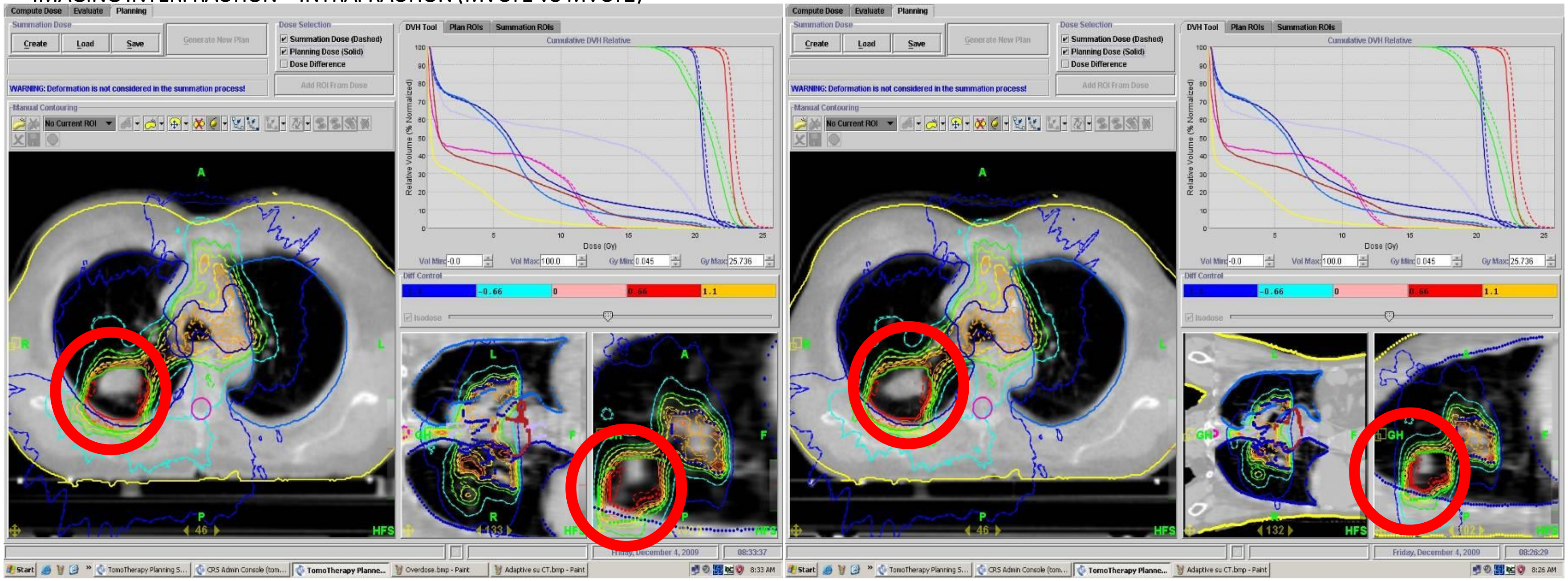
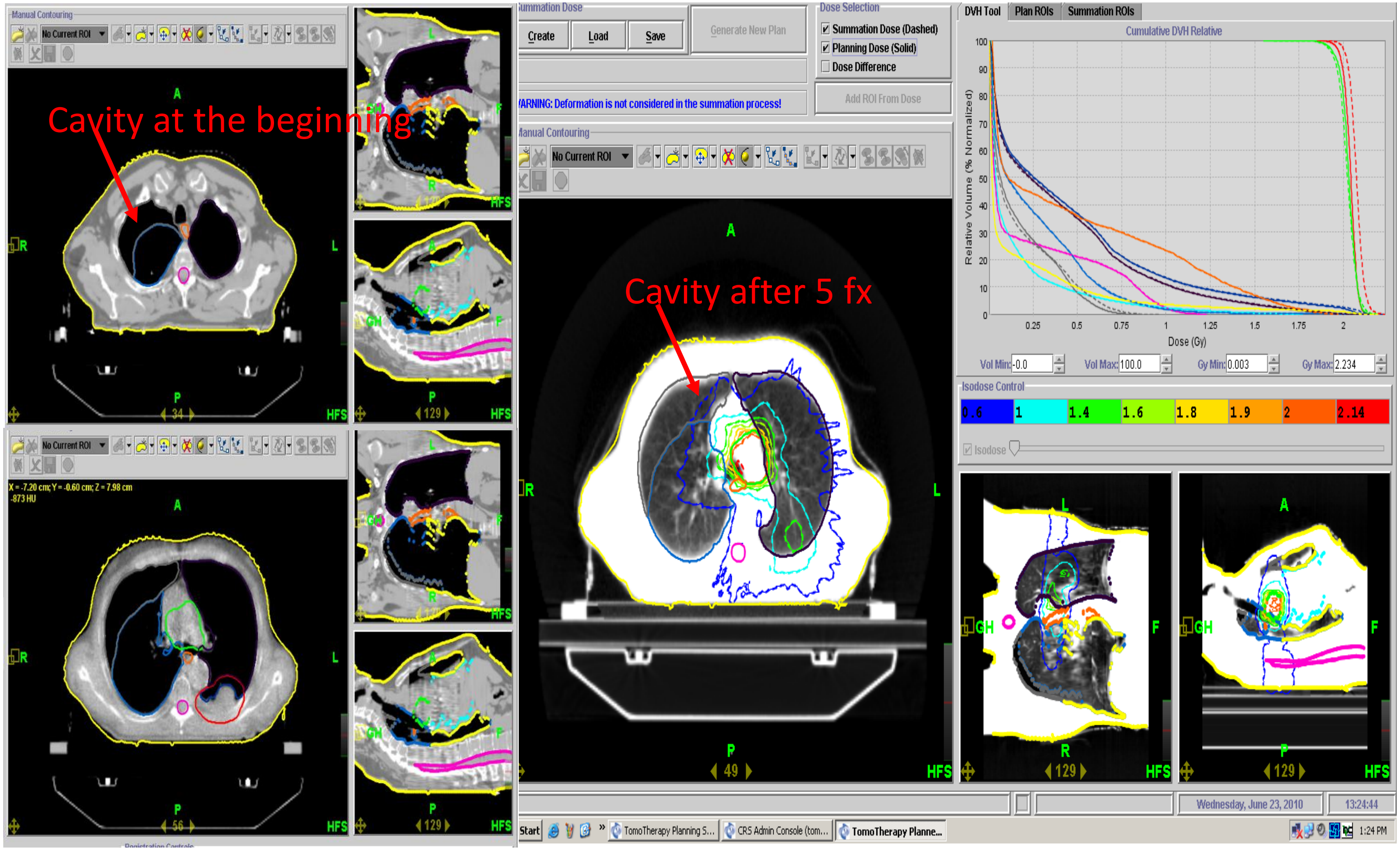
6. Volume effect (image down sampling)
7. MVCT vs. kVCT
8. Morning Dose Output
9. Plan Optimization and Parameters?
10. Operators
    - Doctor
    - Physicist
    - Therapist

IMAGING INTERFRACTION – INTRAFRACTION (MVCT1 VS MVCT2)

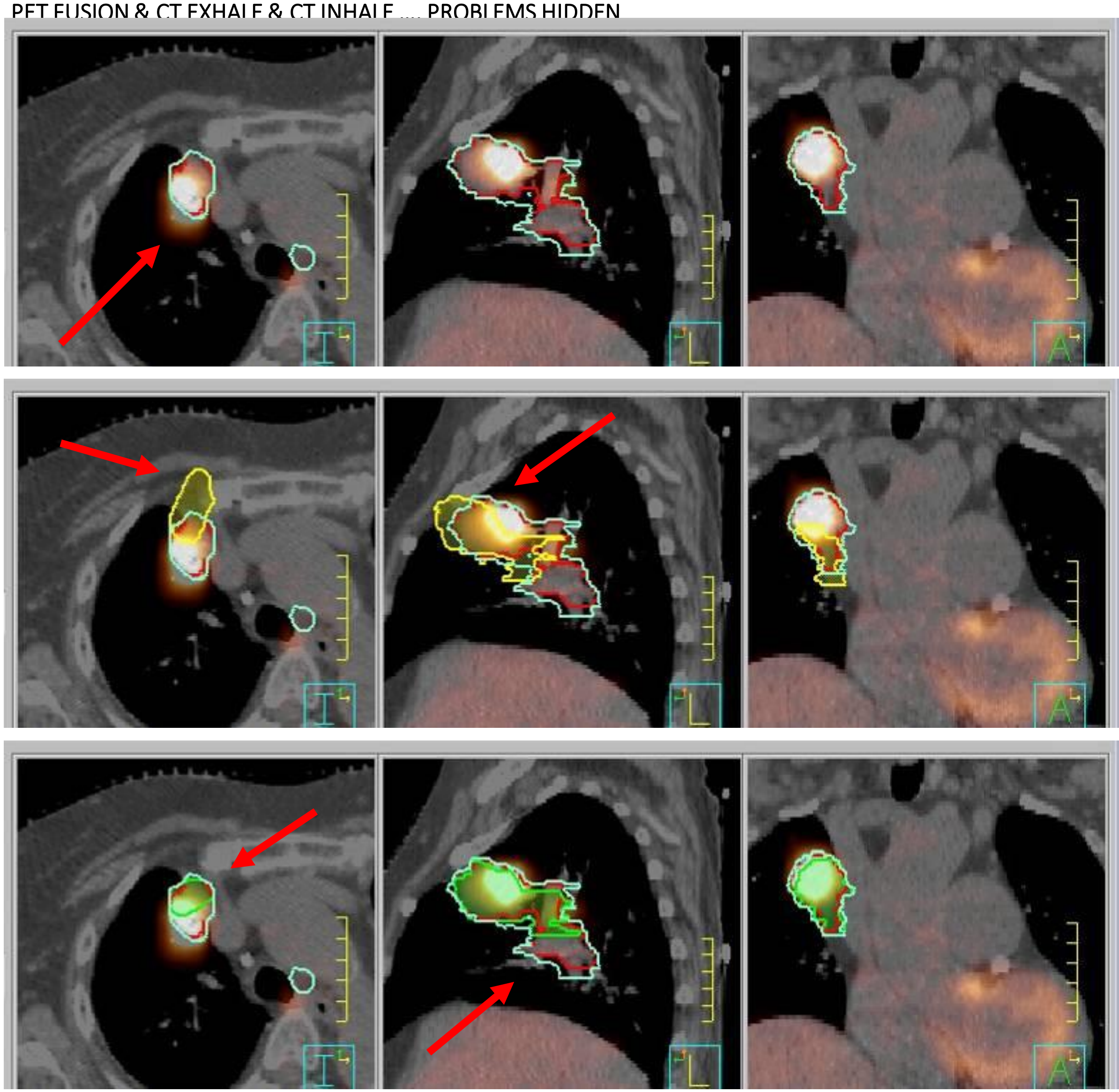


1. Different target dimension?
2. Is Day1 vs. Day2? (Interfraction)
3. Is Time1 vs. Time2 (Intrafraction)
4. Is the tumor shrinkage ?
5. Is the duty cycle? (Breathing)
6. Different dose calculation? (Fine vs. Normal Dose Grid)
   a) Where? In tumour or OAR?
7. Change the dose due to the OARs or Tumour position?
   a. Isn't it during the respiration breathing?
   b. Why should i do a MVCT before and after the treatment?
   c. Why should I believe at the MVCT of multiple days?
8. Is important the Volume effect for goals of the entire treatment?
9. ....

LUNG ADAPTIVE (CAVITY COMPLEXITY)



PET FUSION & CT EXHALE & CT INHALE .... PROBLEMS HIDDEN

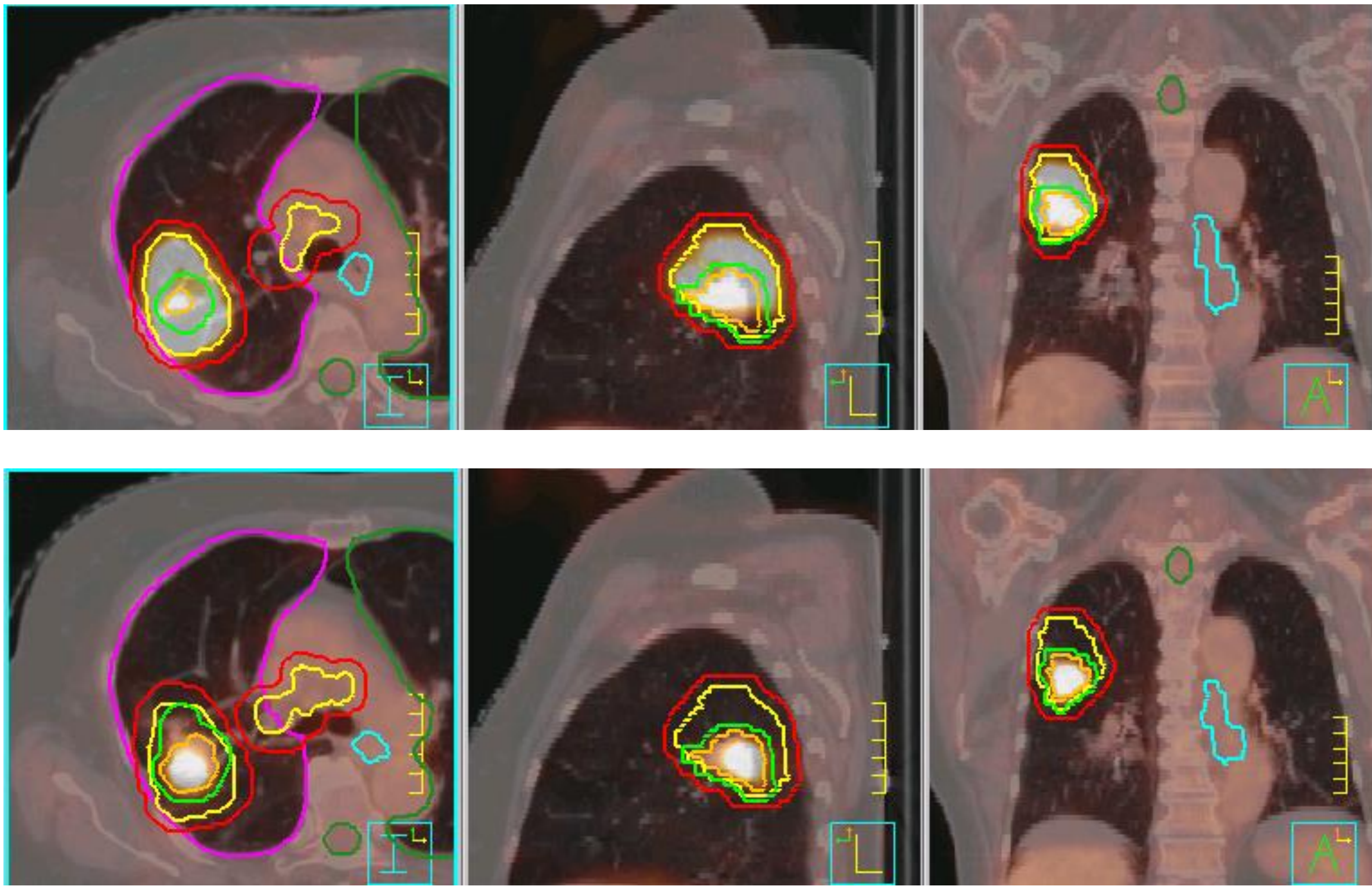


4DCT vs. PET
(GTV4D= Red Contour)

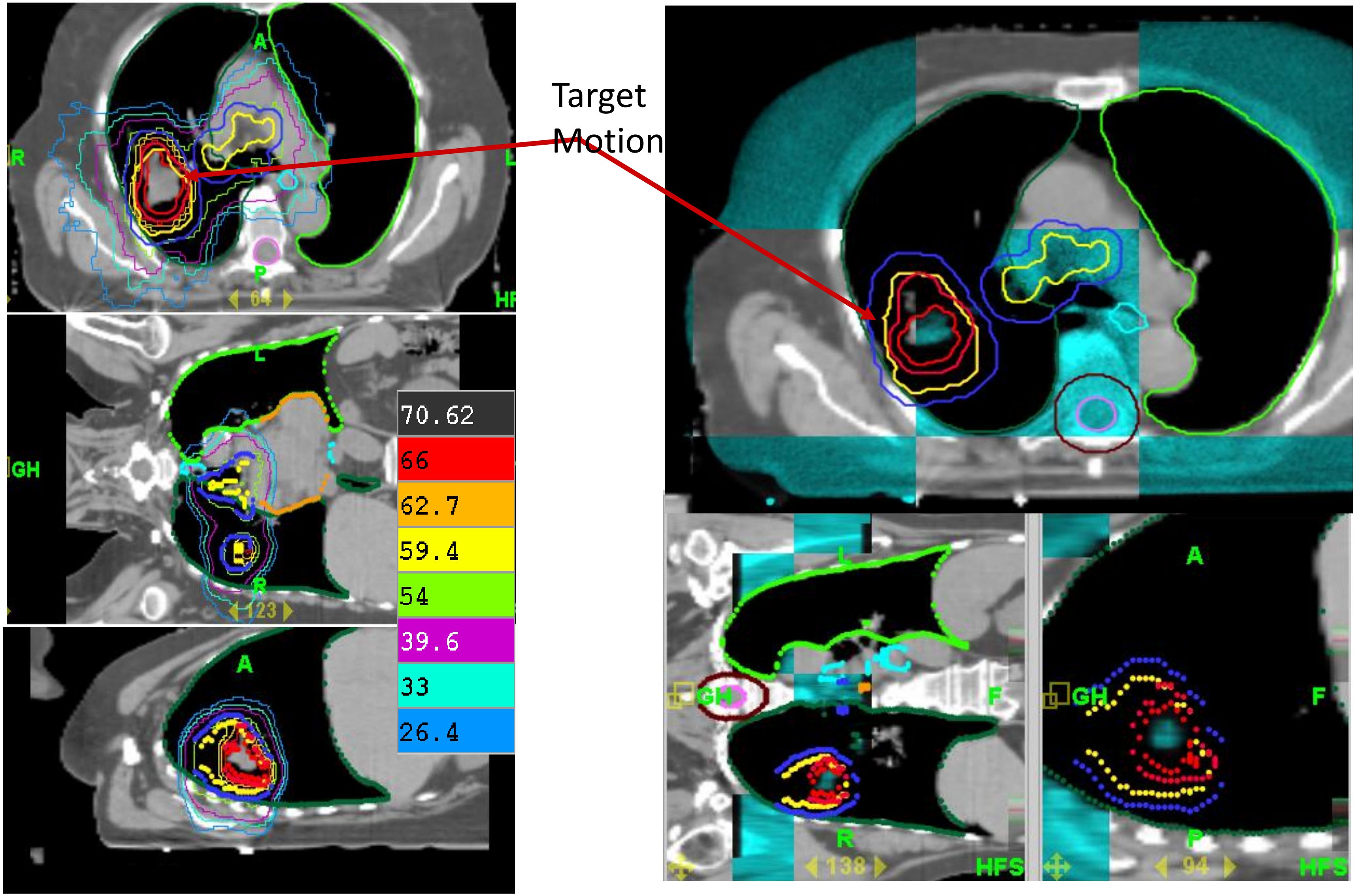
4DCT vs CT with Max Inhale
(GTV Max Inhale=Yellow contour)

4DCT vs CT with Max Exhale
(GTV Max Exhale Green Contour)

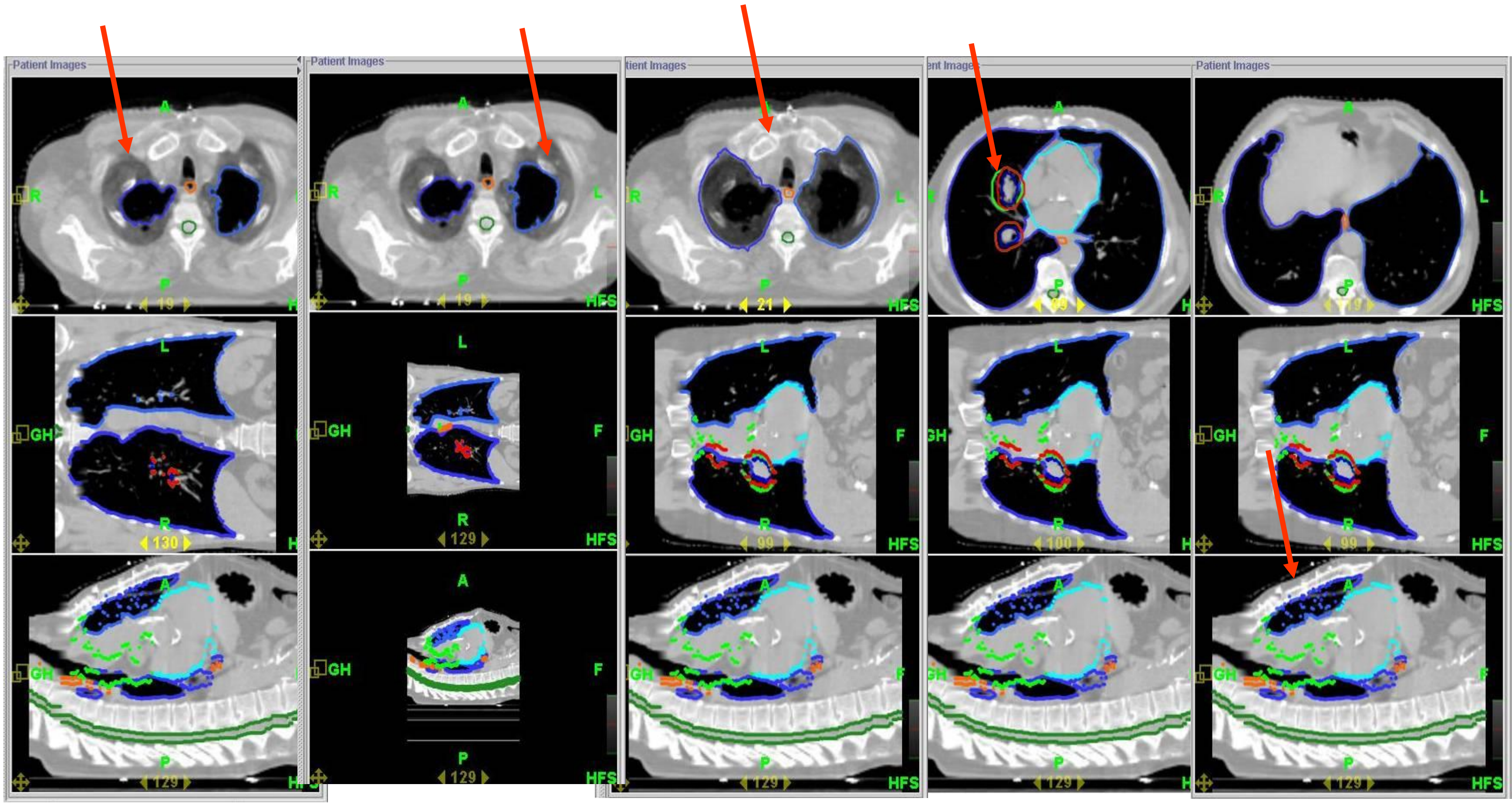
4DCT - MOTION MANAGEMENT
4DPET - MULTI MODALITY IMAGE FUSION



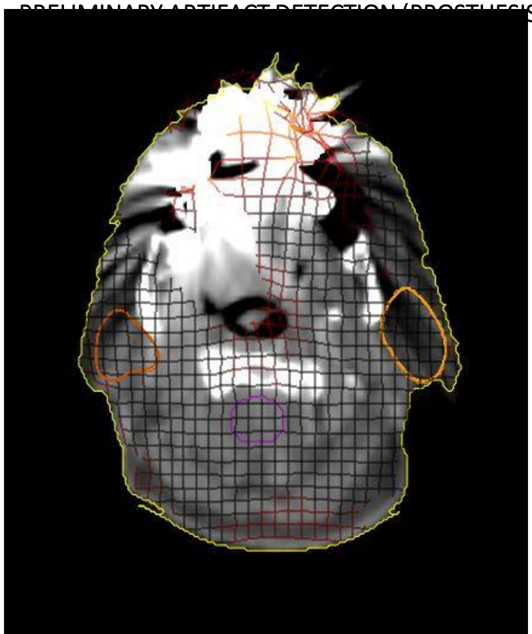
ADAPTIVE RADIATION THERAPY AND MOTION MANAGEMENT (4D-ART: RESEARCH AREA)

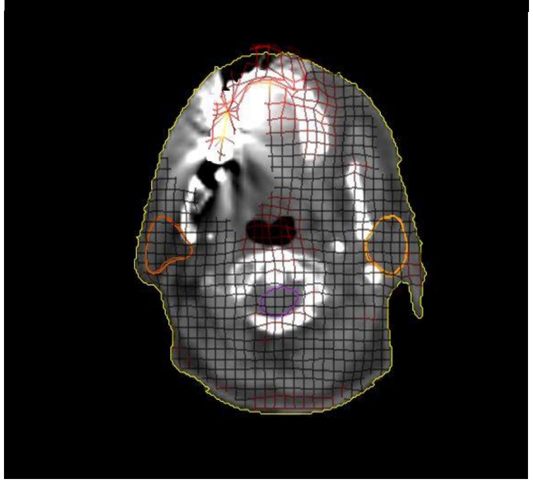


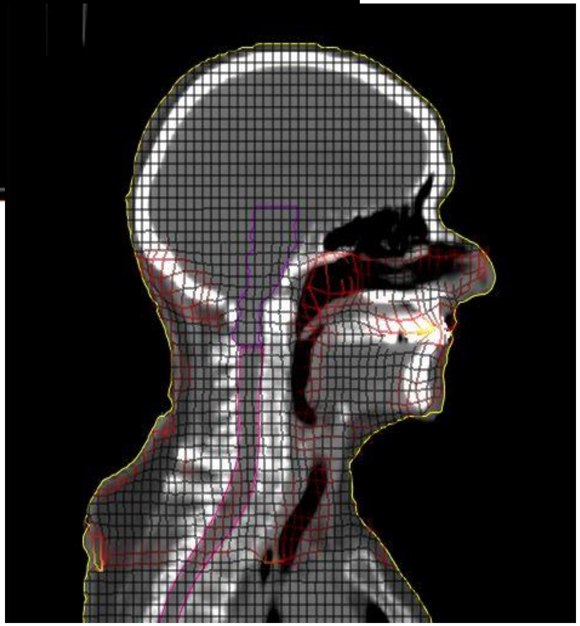
MOTION ARTIFACTS



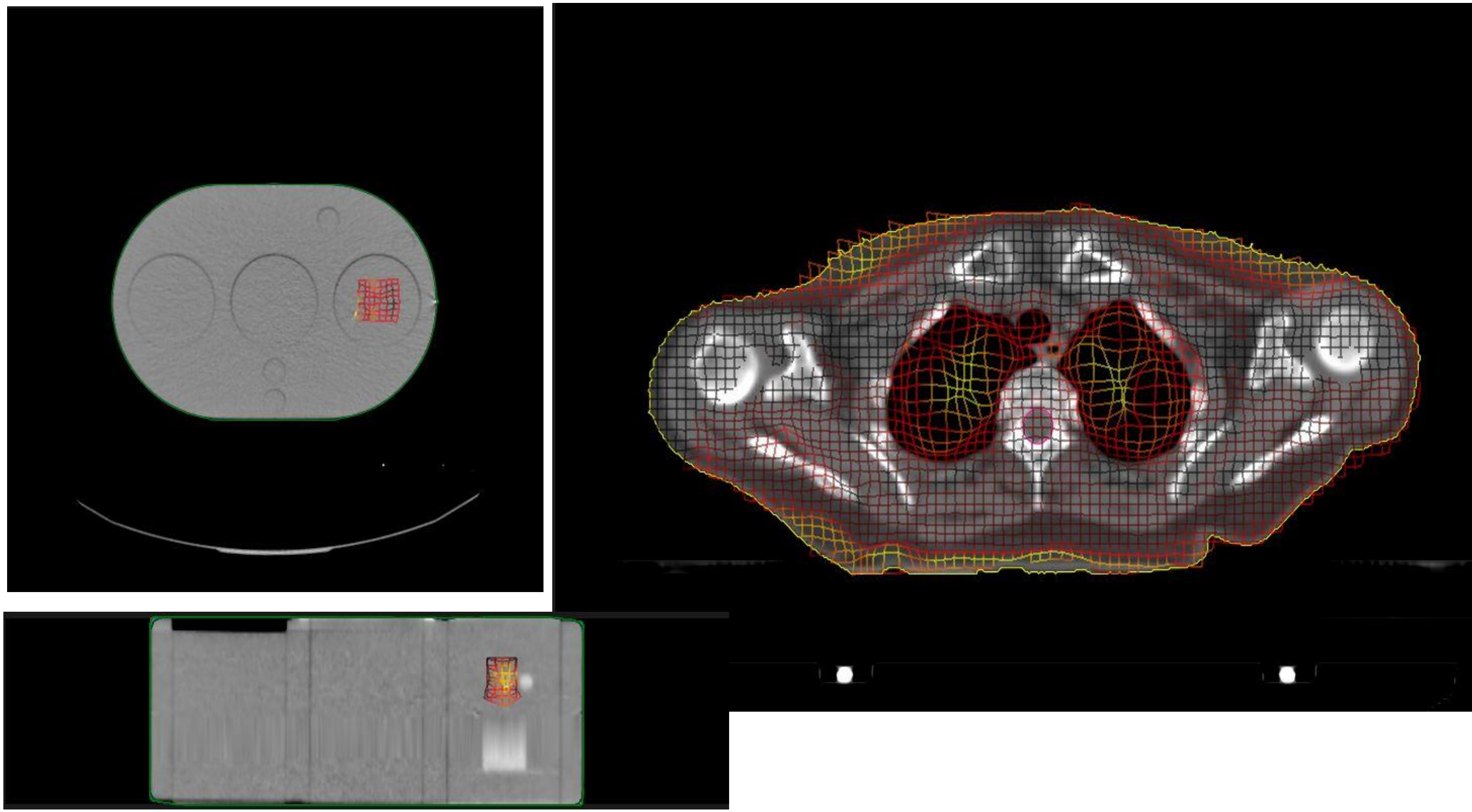
PRELIMINARY ARTIFACT DETECTION (PROSTHESIS)



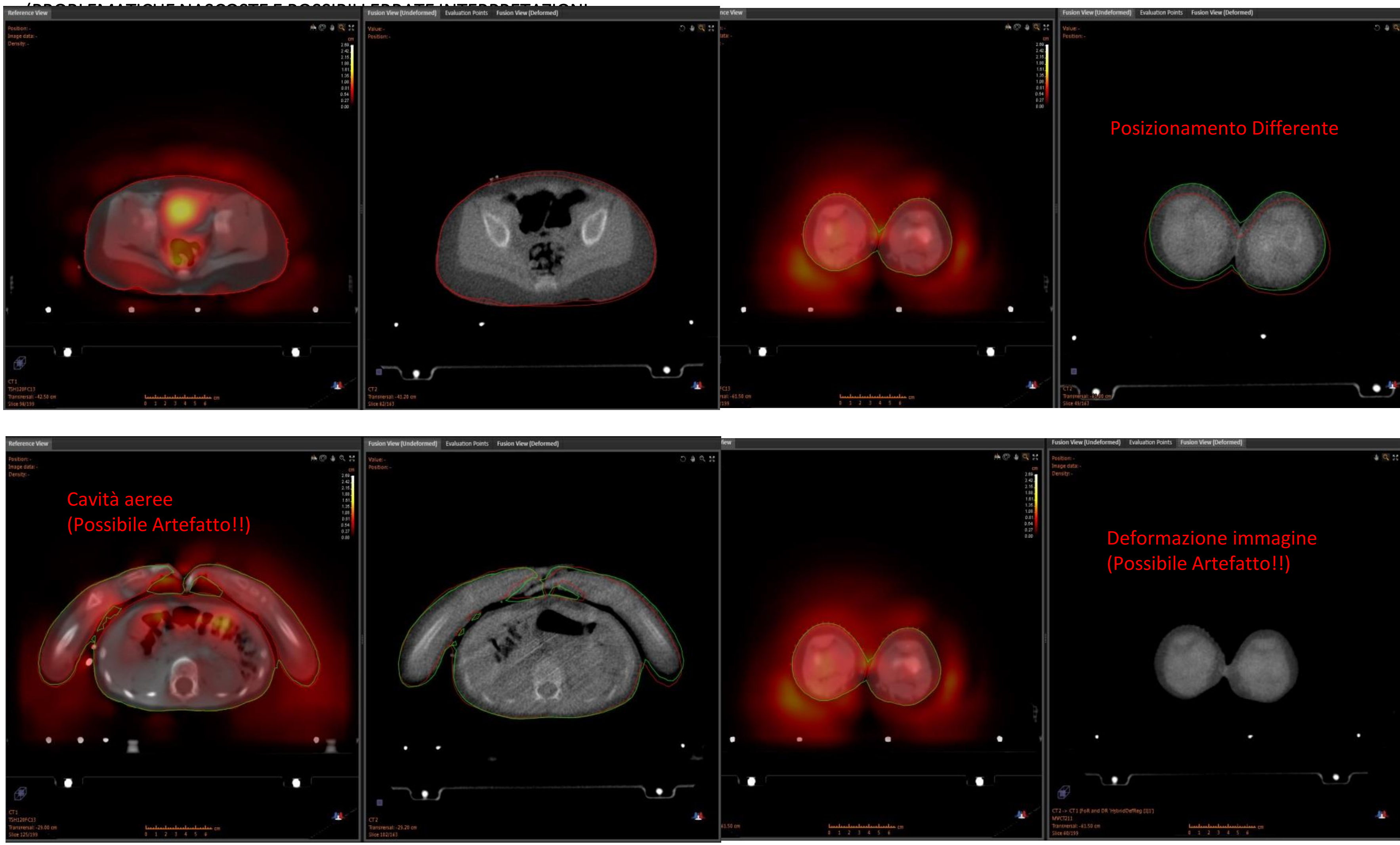




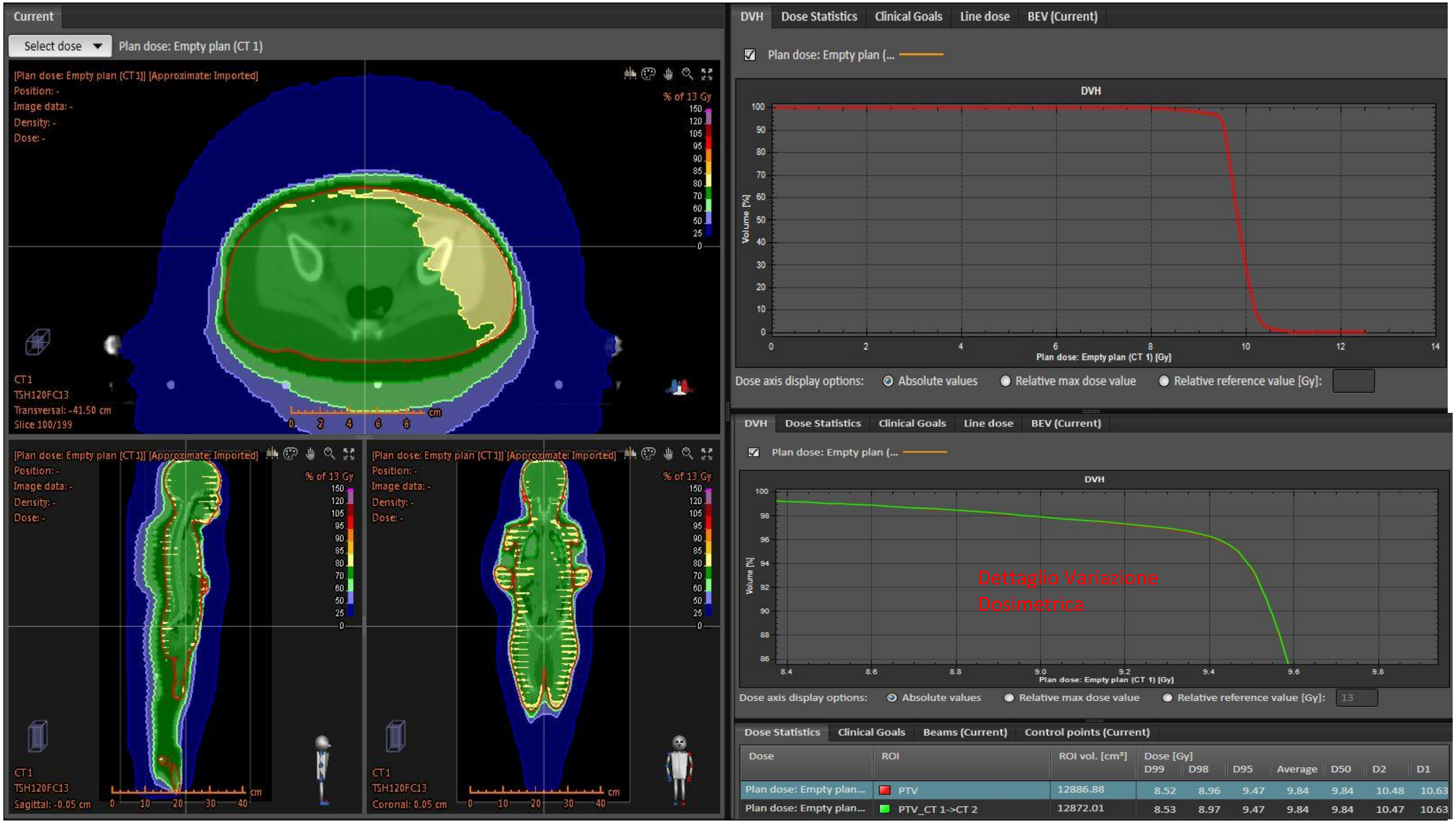
PRELIMINARY 4D DEFORMATION ANALYSIS



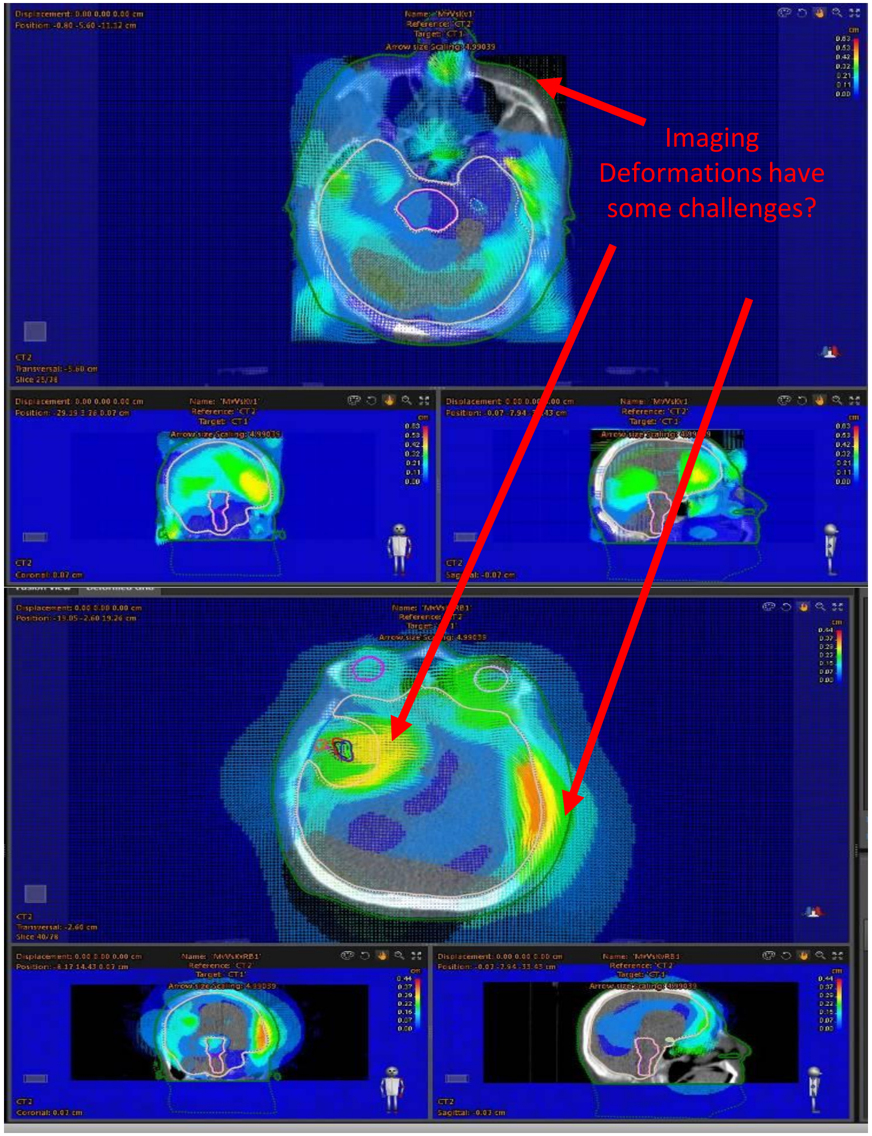
TBI DEFORMAZIONE IMMAGINE E STRUTTURE
(PROBLEMATICHE NASCOSTE E POSSIBILI ERRATE INTERPRETAZIONI



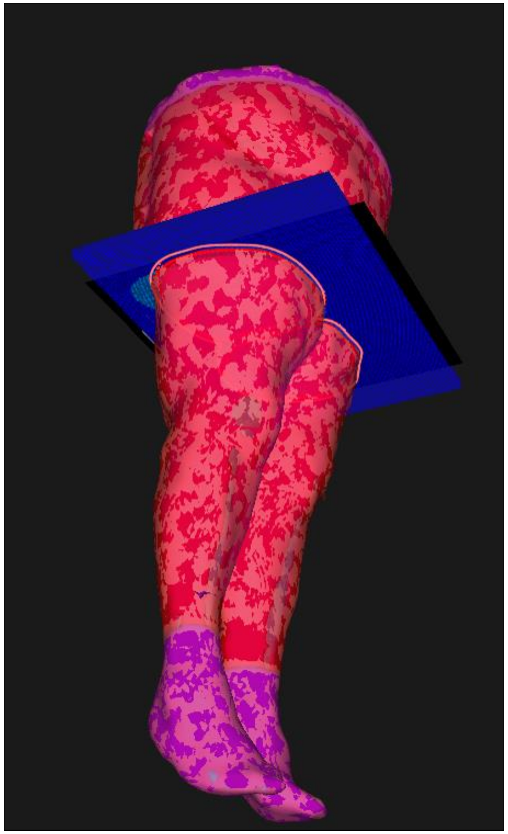
DOSE WARPING – WORK IN PROGRESS

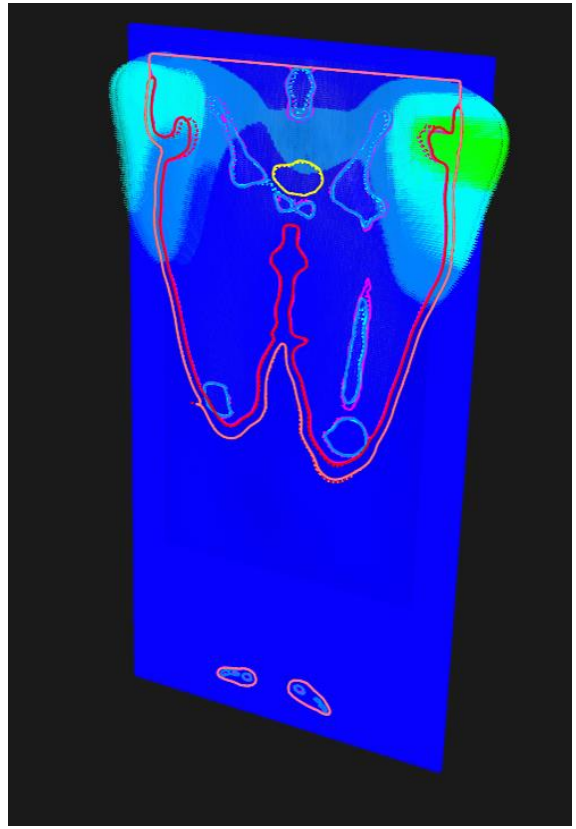


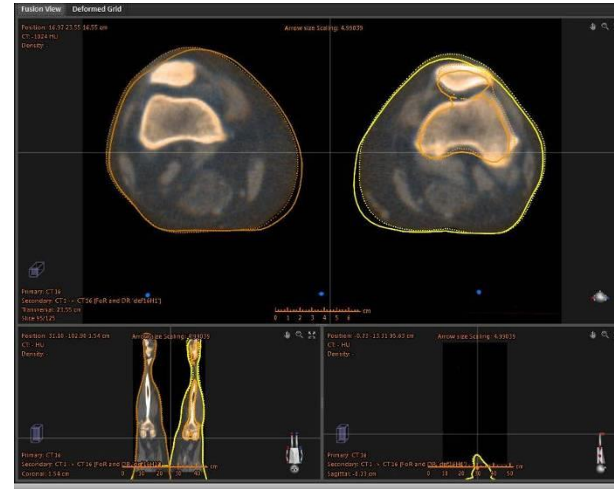
COMPLEX CLINICAL CASES - RADIOSURGERY (AVMS CASES)
CYBERKNIFE IS NOT NECESSARILY A MUST – WE DO IT WITH TOMOTHERAPY IN LESS TIME. NO CLINICAL ISSUES REPORTED AT THE MOMENT

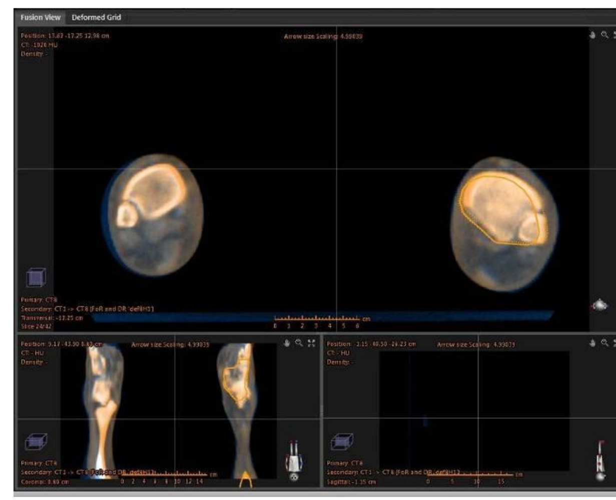


TOMOTHERAPY SKIN IRRADIATION
(E.G. HALF BODY IRRADIATION – TSI (TOTAL SKIN IRRADIATION)





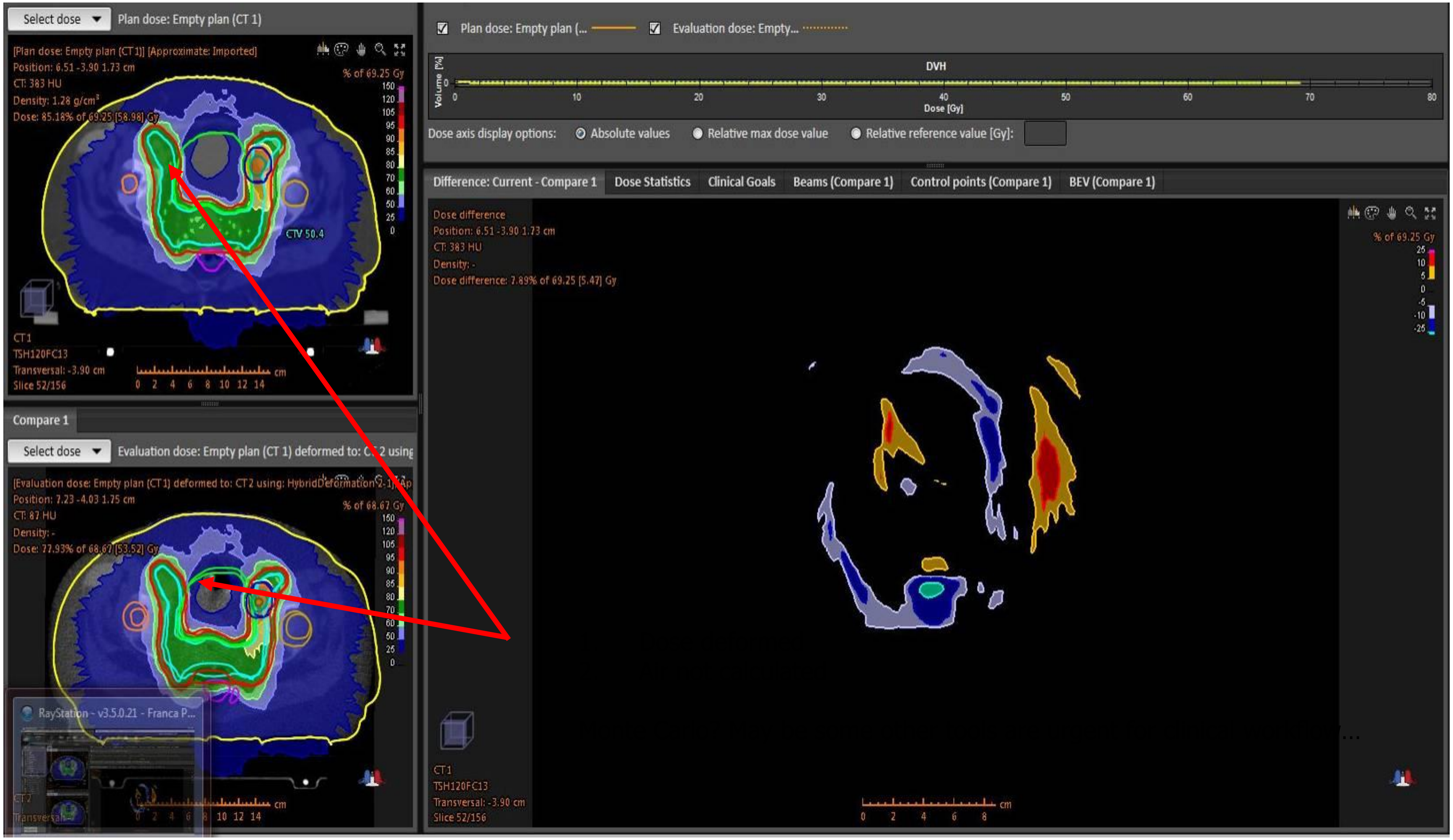




Challenges:
- Due to small PTV Size
- Due to the FOV

Advantages with Tomo +Raystation: deformation could be possible
Some trick in progress

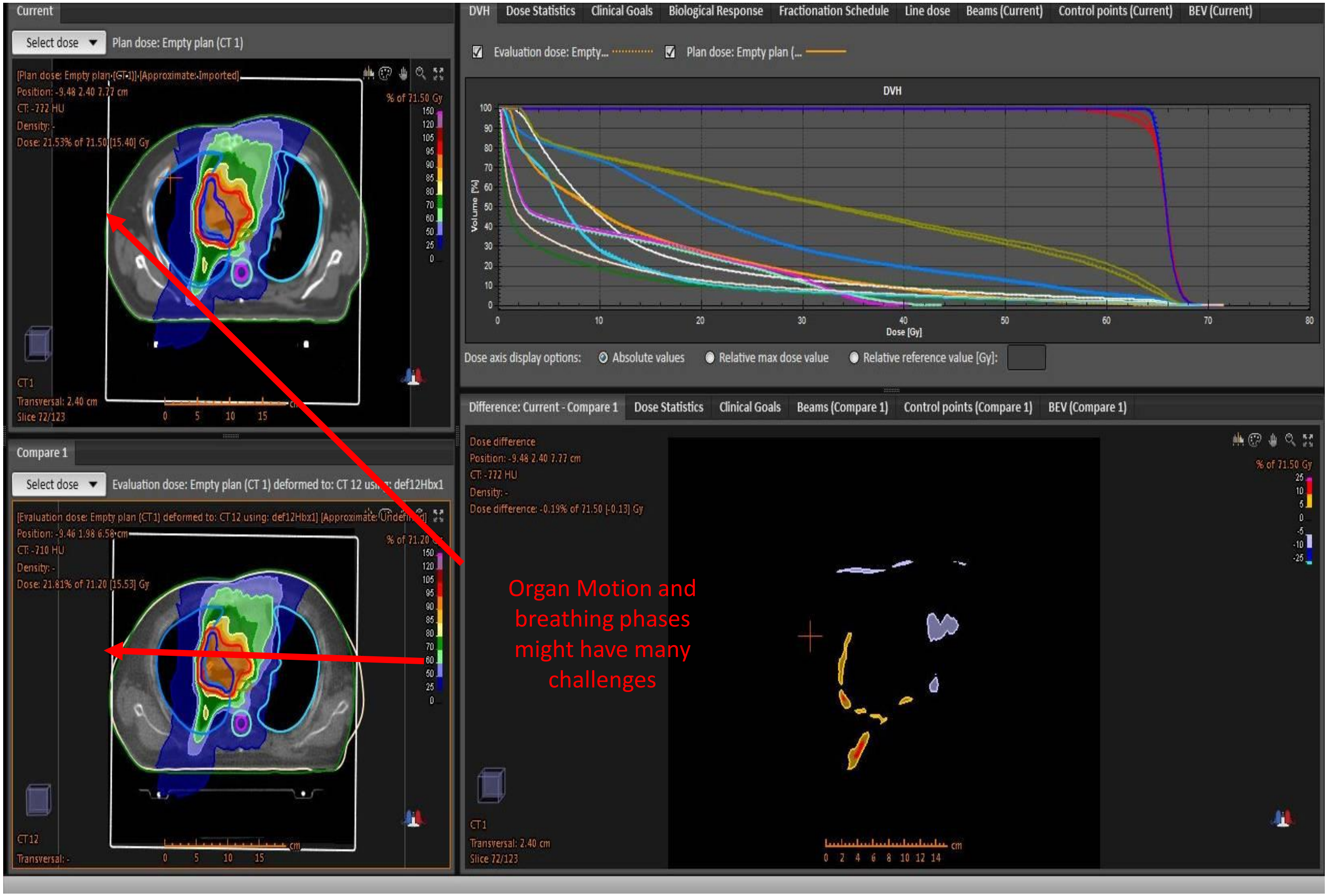
HYPO-FRACTIONATED PELVIS TOMOTHERAPY DOSE DEFORMATION
(DAILY FRACTION EVALUATION - BLADDER AND RECTUM CHALLENGES)



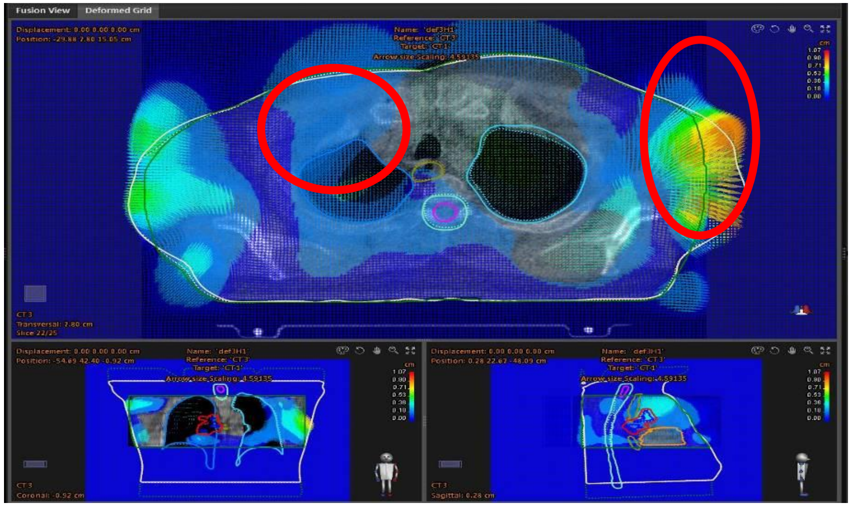
Needs:

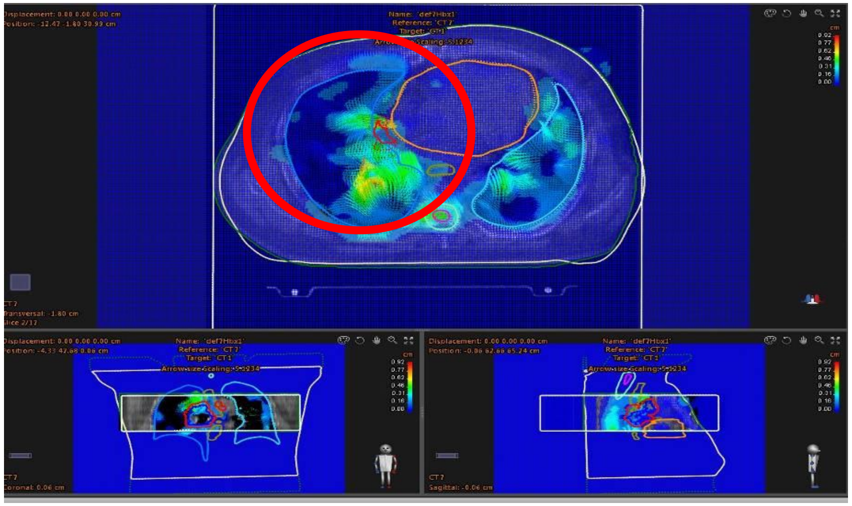
- Not only Raystation is used for calculation
- I should able to use Dicom RT Plan to recalculate dose and perform accumulation

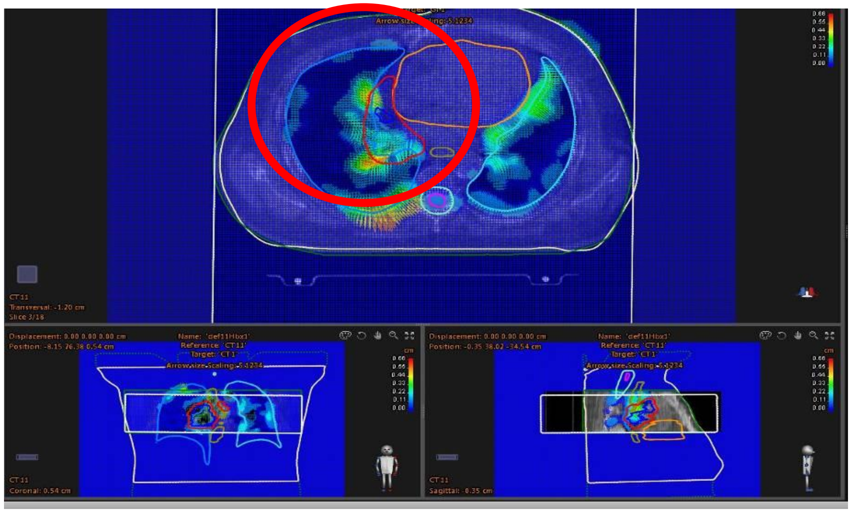
LUNG DOSE DEFORMATION
(....POSSIBLE BUT DVH EVALUATION IS NOT OUR GOALS OR A GOOD CLINICAL PARAMETER).....

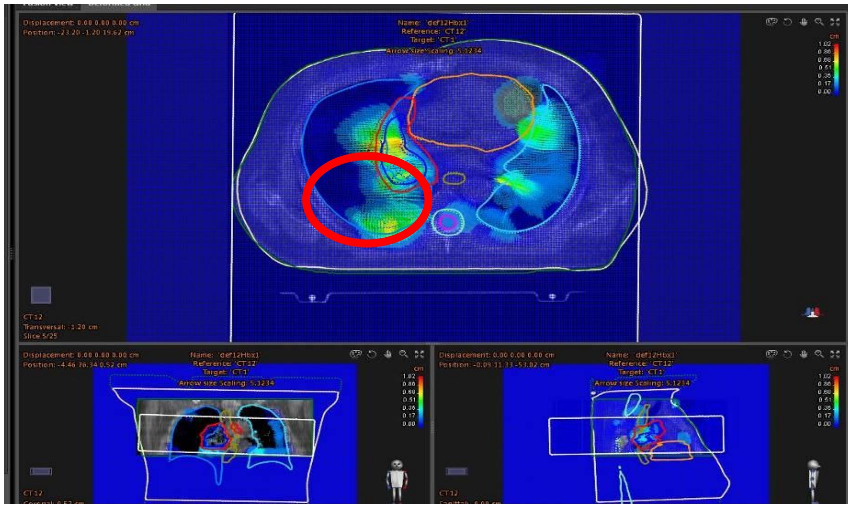


LUNG VECTOR FIELDS (E.G. LUNG)
DIFFERENT DEFORMABLE OPTIONS – DIFFERENT RESULTS ….. BE CAREFUL, WHAT YOU SAY TO THE DOCTORS



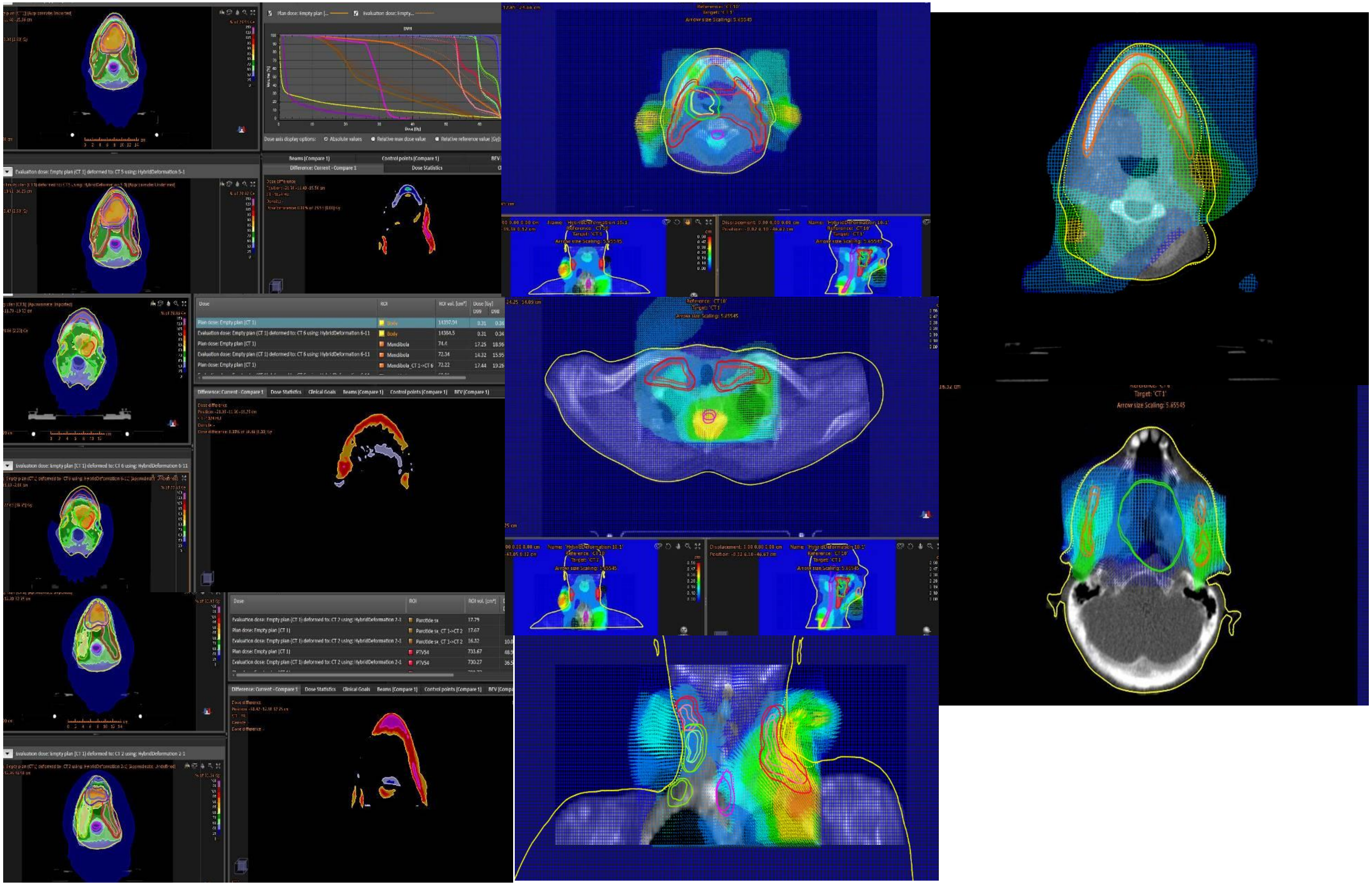




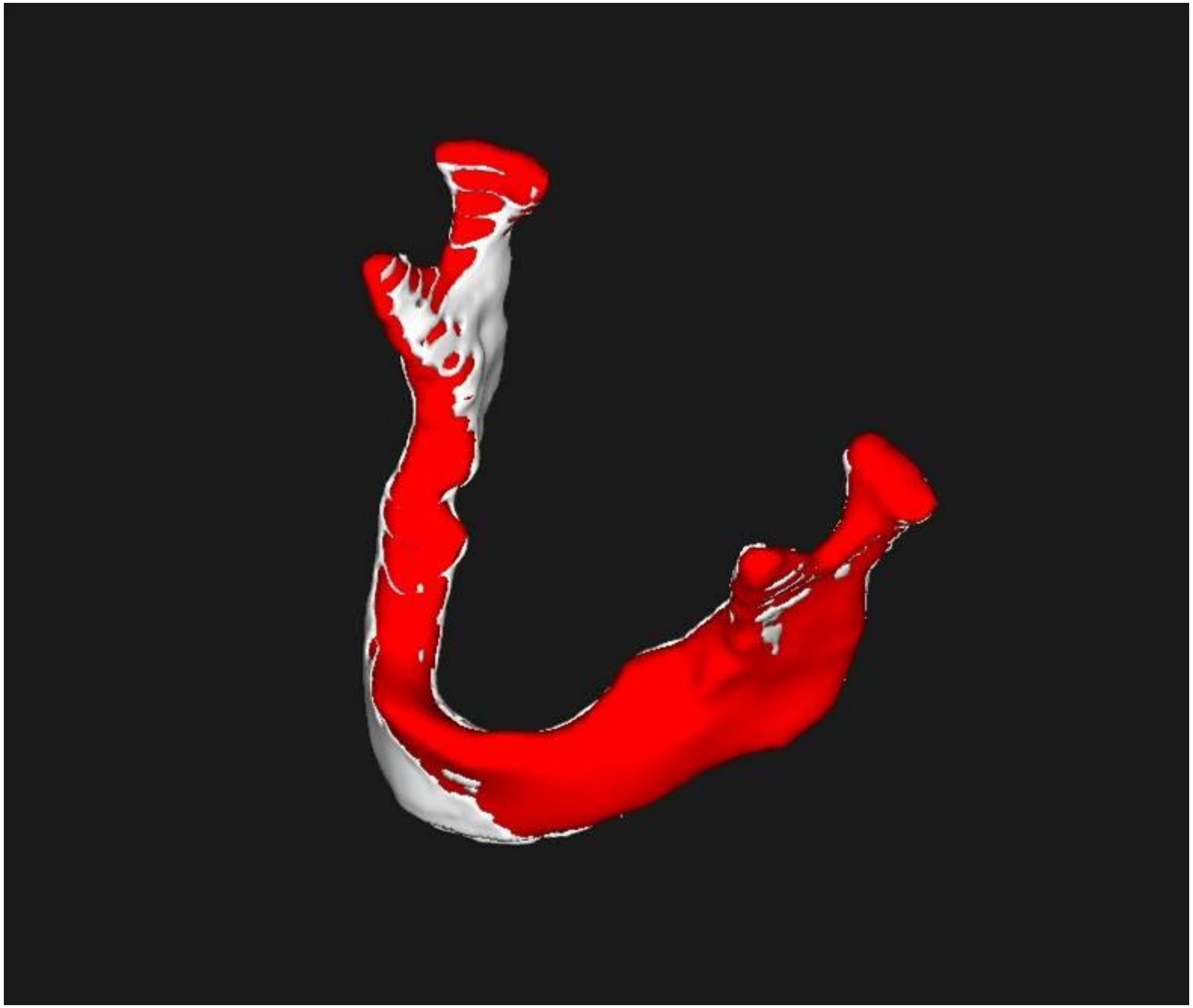


H&N CASES

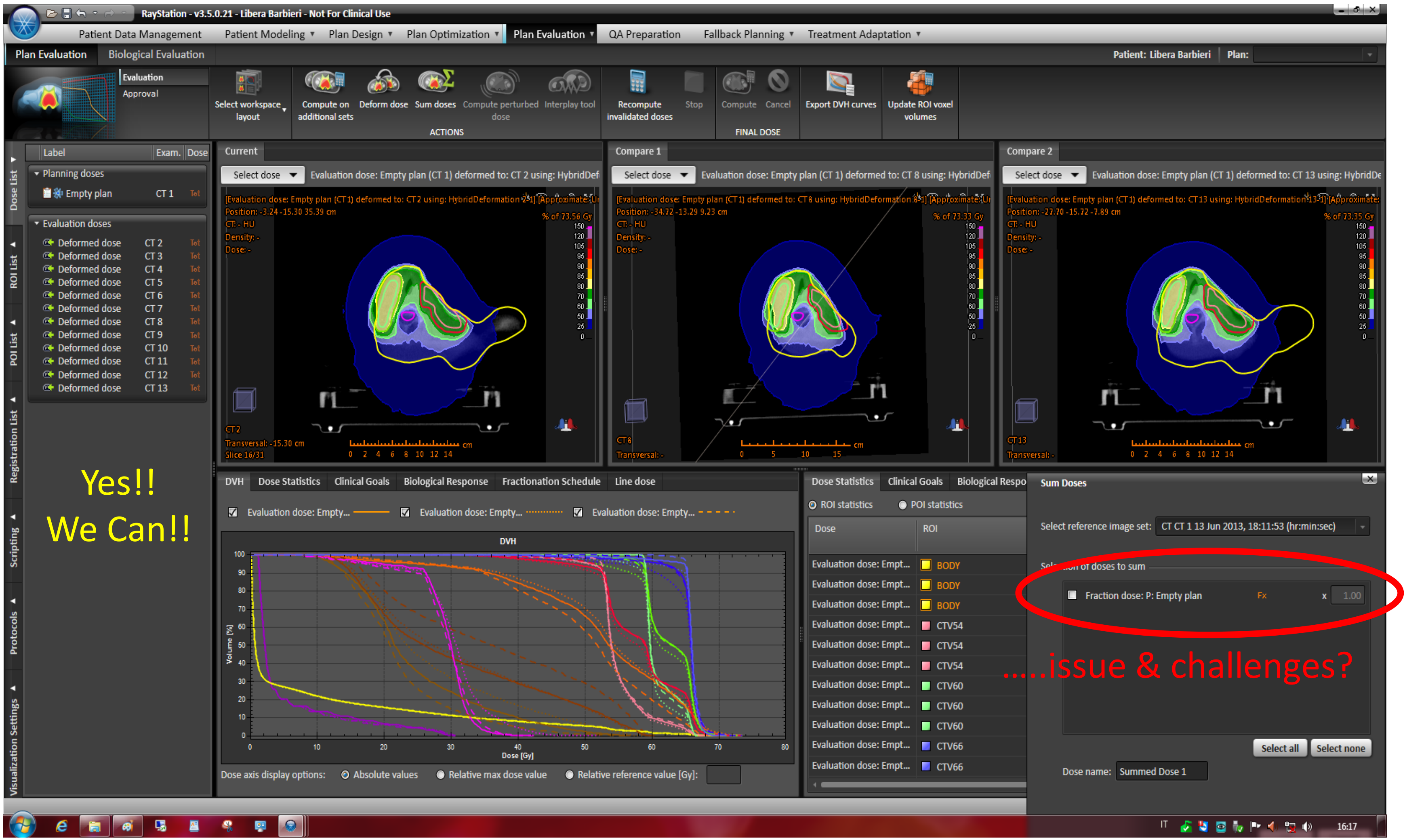
… SOME VARIATION ARE DUE TO IMAGING, ROTATIONS, VOLUME SHRINK OR SOMETHING ELSE? E.G. BIOMECHANICAL ADJUSTMENTS?



BIOMECHANICAL ANALYSIS FROM IMAGING....



DOSE ACCUMUALTION TAKING IN ACCOUNT DAILY IMAGING…
(……IS THIS THE ADAPTIVE RT?)



Challenges, Future Directions and … Open questions

Challenges:

(1) automatic image registration;
(2) more rigorous validation methodology;
(3) robust planning taking DIR uncertainty into account;
(4) ultimate automatization of critical processes in treatment workflow
(5) Mass variation can cause extreme difficulty in mapping voxel-to-voxel radiation doses. The authors believe this is the most challenging obstacle to overcome in DIR application for radiation therapy.

Online ART to become available, the process needs to be automated and **fast**.

With increasingly reliable **DIR** (autocontouring, dose deformation) we can move toward modifying treatment beams online with the aid of an improving suite of daily imaging technologies.

Online art needs to be made **safe**.

There is the open question of whether the potential therapeutic gains from online art are worth the **resources** required…this question cannot be answered fully at this point

Such solutions assume that DIR is a well-solved problem. However, the bladder, rectum, and prostate deform in a nonuniform manner.
This makes the quality assurance of accurately documenting the delivered dose challenging, and novel methods of time Efficient quality assurance are required!

TG-132 (2017)

*This is currently an area of rapid innovation and **caution** should be used when employing these new techniques until they are well understood"*

*«The **use of deformable registration for dose accumulation** and subsequent adaptive re-planning is **outside** of the scope of this task group.*

*It is recommended that these issues be addressed in a **subsequent task group**…»*

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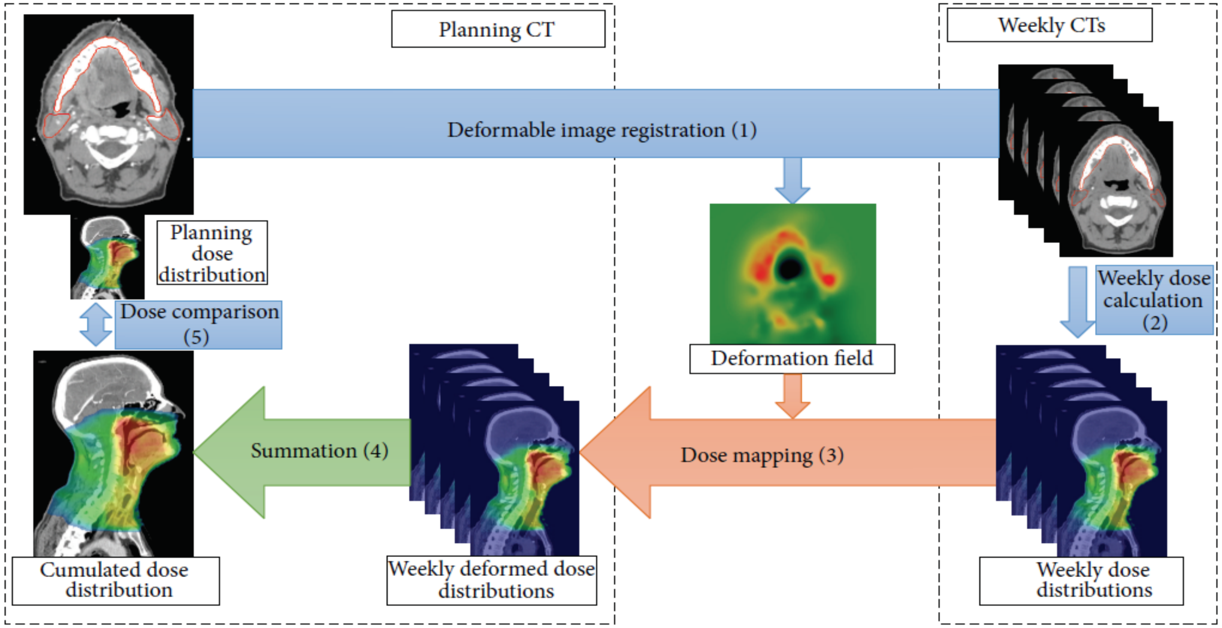
12. Y Vinogradskiy, R Castillo, E Castillo et al. Use of 4-Dimensional Computed Tomography-Based Ventilation Imaging to Correlate Lung Dose and Function With Clinical Outcomes. Int J Radiation Oncol Biol Phys, Vol. 86, No. 2, pp. 366e371, 2013.
13. C Veiga, G Janssens, C-L Teng et al. First Clinical Investigation of Cone Beam Computed Tomography and Deformable Registration for Adaptive Proton Therapy for Lung Cancer. Int J Radiation Oncol Biol Phys, Vol. 95, No. 1, pp. 549e559, 2016.
14. Maffei N, Guidi G, Vecchi C et al. SIS epidemiological model for adaptive RT: Forecasting the parotid glands shrinkage during tomotherapy treatment. Medical Physics 43, 4294 (2016).
15. F. Itta. Biomechanical modeling of parotid glands morphing In head&neck radiation therapy treatments. University of Bologna (2016)
16. S Lim-Reinders, B Keller, S Al-Ward et al. Online Adaptive Radiation Therapy. Int J Radiation Oncol Biol Phys, Vol. 99, No. 4, pp. 994e1003, 2017.

ARTICLES DISCUSSION

DIR for

DOSE ACCUMULATION



Evaluation of Deformable Image Registration Methods for Dose Monitoring in Head and Neck Radiotherapy

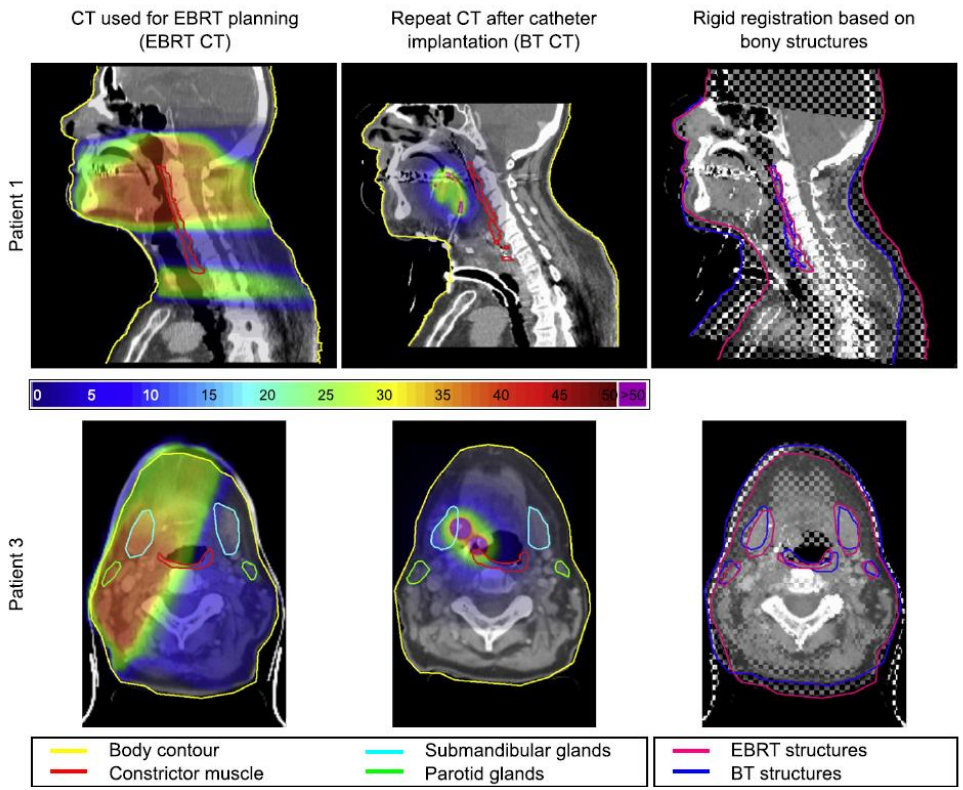
Bastien Rigaud, Antoine Simon, Joël Castelli, Maxime Gobeli,[3] Juan-David Ospina Arango,[1,2] Guillaume Cazoulat,[1,2] Olivier Henry,[3] Pascal Haigron,[1,2] and Renaud De Crevoisier[1,2,3]

N. Maffei

External Beam Radiotherapy (EBRT) + Brachytherapy (BT)

Clinical practice: BT Boosts are optimized independently; dose delivered is **not accounted**

Large anatomic changes:
- Neck dissection
- Catheter insertion
- Patient positioning



Rigid Image Registration
Cannot fully correct
chaneged anatomy

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THREE-DIMENSIONAL DOSE ADDITION OF EXTERNAL BEAM RADIOTHERAPY AND BRACHYTHERAPY FOR OROPHARYNGEAL PATIENTS USING NONRIGID REGISTRATION

Eliana M. Vásquez Osorio, B.Sc., Mischa S. Hoogeman, Ph.D., David N. Teguh, M.D., Abrahim Al-Mamgani, M.D., Inger-Karine K. Kolkman-Deurloo, Ph.D., Luiza Bondar, Ph.D., Peter C. Levendag, M.D., Ph.D., and Ben J. M. Heijmen, Ph.D.

Department of Radiation Oncology, Daniel den Hoed Cancer Center, Erasmus Medical Center, Rotterdam, The Netherlands

Int. J. Radiation Oncology Biol. Phys.
Vol. 80, No. 4, pp. 1268–1277, 2011

AIM: To develop and evaluate a method for adding dose distributions of combined EBRT (46 Gy in 23 fx IMRT) + BT (Pulsed dose-rate: 2Gy+18x1Gy+2Gy) for 5 H&N patients

DOSE ACCUMULATION WORKFLOW

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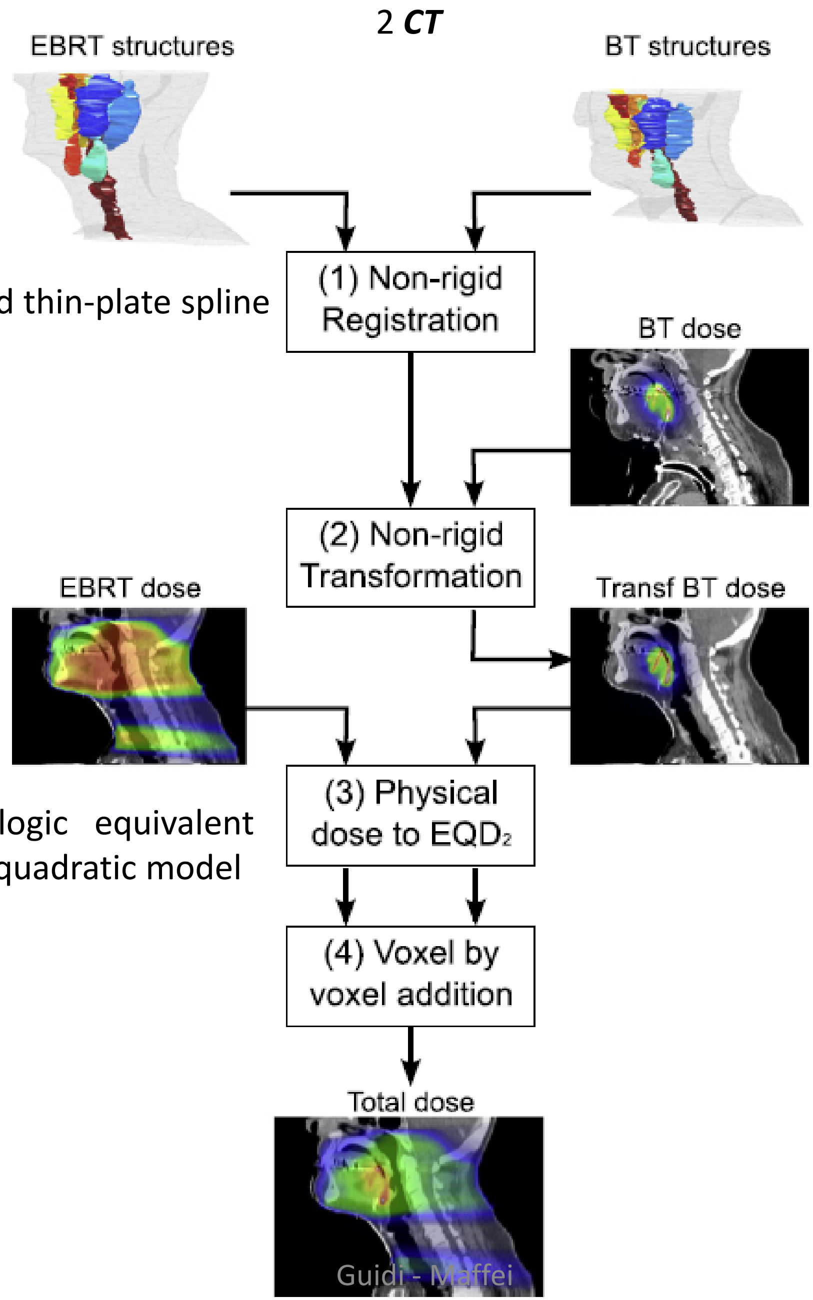


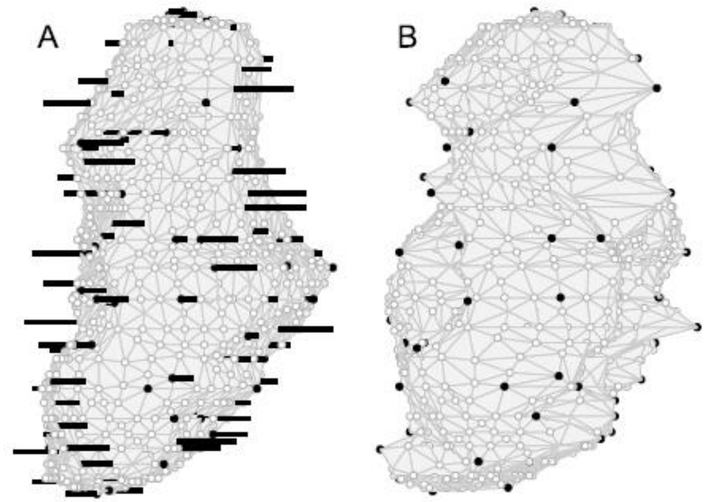
Modeled by regularized thin-plate spline

Conversion to the biologic equivalent dose 2Gy/fx using linear quadratic model

OARs:

- Body
- Chewing muscles
- Swallowing muscles
- Major salivary glands

ROBUSTNESS OF DOSE ACCUMULATION



Perturbations of DIR framework parameters

Points from surfaces by *density radius* (r = 5, 6, 8 mm):

- Small r: more points, > t, more accurate results
- Large r: few points, < t, less accurate results

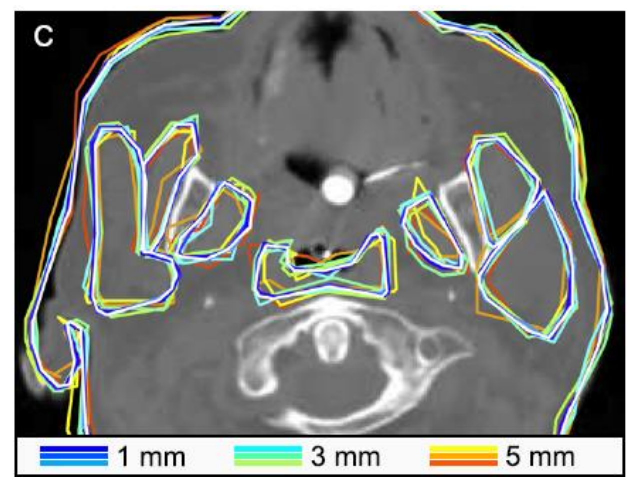
Flexibility by *weight parameter* (λ = 0.5, 5):

- low λ: more flexible transformation
- Large λ: transformation mostly affine

Perturbations in control point distribution

Triangles vertices are grouped in spheres;

Points are randomly replaced by the closest centroid



Perturbations in structures delineations

Random observer variations of 1, 3, 5 mm

Perturbations in α/β values used for EQD2

α/β = 3Gy $\pm$ 10%, 20%

RESULTS

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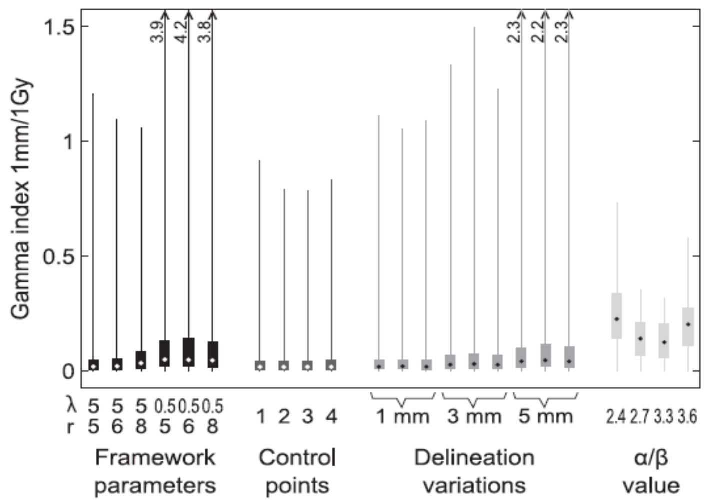
- γ analyses (distance-to-agreement/dose-difference = 1mm/1 Gy)

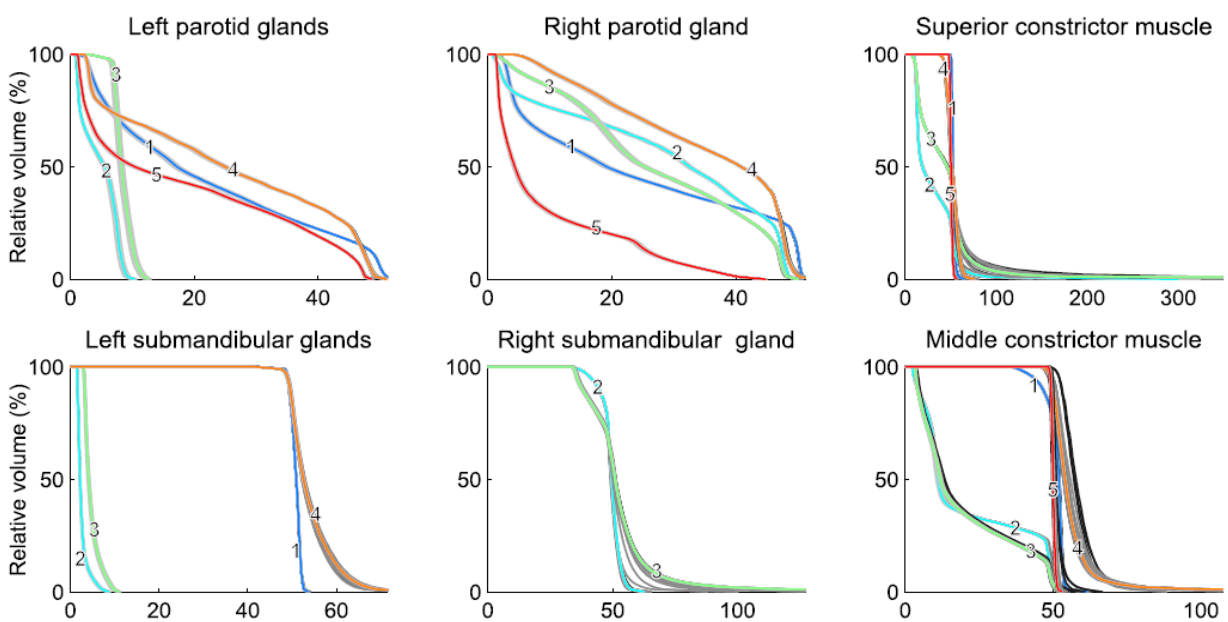


Largest γ Index:

- α/β = 2.4 Gy,
- λ = 0.5
- *r* = 5 mm
- ROIs in high gradient dose

(i.e. constrictor muscles, submandibular gland)

- DVH Analysis



Variations in input parameters

Small perturbations of DVH

ROBUST METHOD

DOSE ACCUMULATION WORKFLOW

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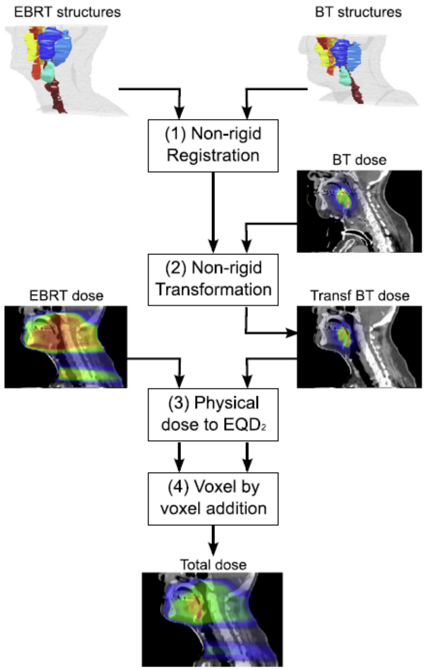
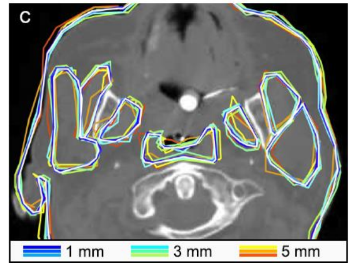
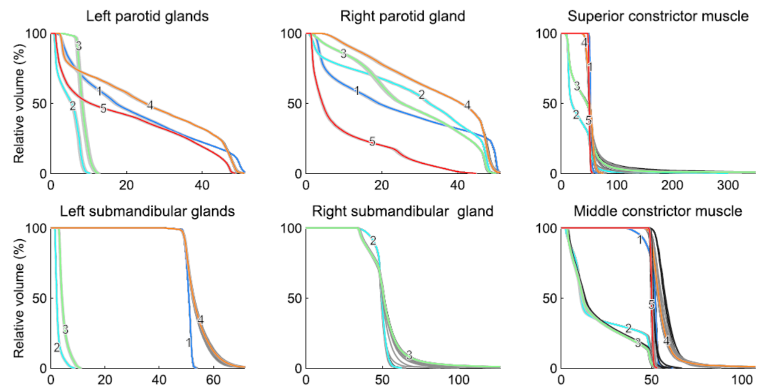




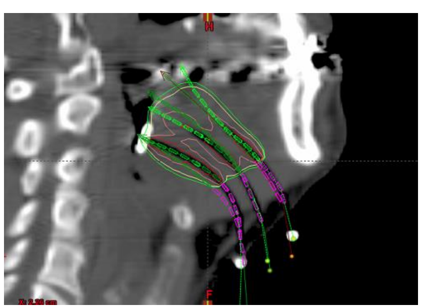


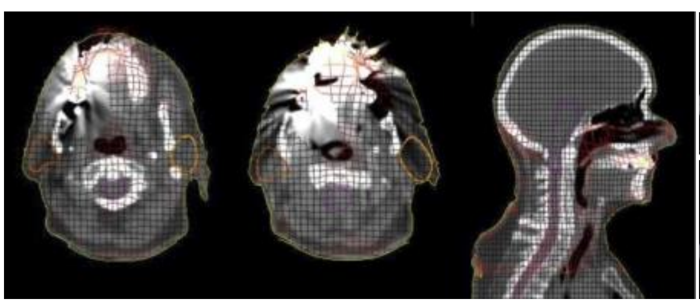
ROIs:

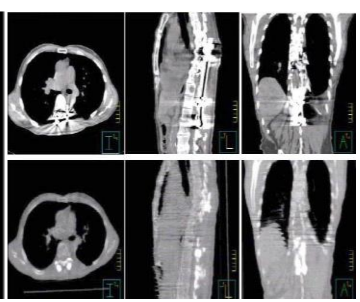
- Body
- Chewing muscles
- Swallowing muscles
- Major salivary glands

REAL «CLINIC WORLD»:

- **Brachy is invasive and not perfectly associate with the images (difference in image acquisition and dose algorithm calculation)**
- **Patients could have prosthesis in tooth. Magically the DIR software could apply deformation to Titenium, and change the DVH**
- **Mucosite or treatment toxicity, can change the dose effect and biological consideration of TCP &NTCP instead the DVH evaluation**







TAKE HOME MESSAGE….. Dose Accumulation algorithm validation

- *Advanced applications are beginning to support daily dose assessment to **propagate contours** and **accumulate dose** over the course of therapy to provide up-to-date **estimates** of anatomical changes and delivered dose* [TG-132]

- **Deformable Image Registration** is a keystone for dose accumulation

- **Dose Recalculation** (rather than the fastest Dose Warping) proves to be more accurate

- **DVHs lack in spatial dose consideration**

- **Pre-processing** and **metric** have a significant impact on the results

- Relationship between **Dose uncertainties** and other factors including the quantitative measurement of **DIR uncertainty** (DSC, surface distance), patient-specific properties (tumor volume, planning heterogeneity) and dose gradient

- Geometrical uncertainties may have different impact on cumulated dose errors depending on dose **gradient**

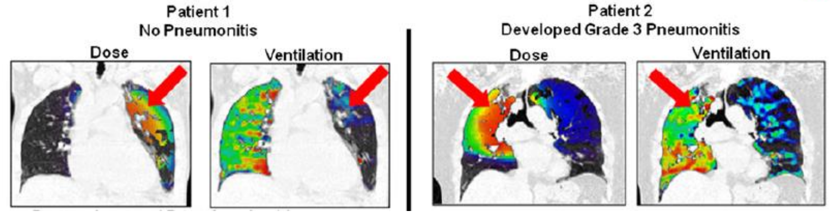
Use of 4-Dimensional Computed Tomography-Based Ventilation Imaging to Correlate Lung Dose and Function With Clinical Outcomes

Yevgeniy Vinogradskiy, PhD,* Richard Castillo, PhD,† Edward Castillo, PhD,‡,§ Susan L. Tucker, PhD,‖ Zhongxing Liao, MD,‡ Thomas Guerrero, MD, PhD,‡,§ and Mary K. Martel, PhD†

*Department of Radiation Oncology, University of Colorado School of Medicine, Aurora, Colorado; †Department of Radiation Physics and ‡Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas; §Department of Computational and Applied Mathematics, Rice University, Houston, Texas; and ‖Departments of Bioinformatics and Computational Biology, The University of Texas MD Anderson Cancer Center, Houston, Texas

Int J Radiation Oncol Biol Phys.

Vol. 86, No. 2, pp. 366–371, 2013



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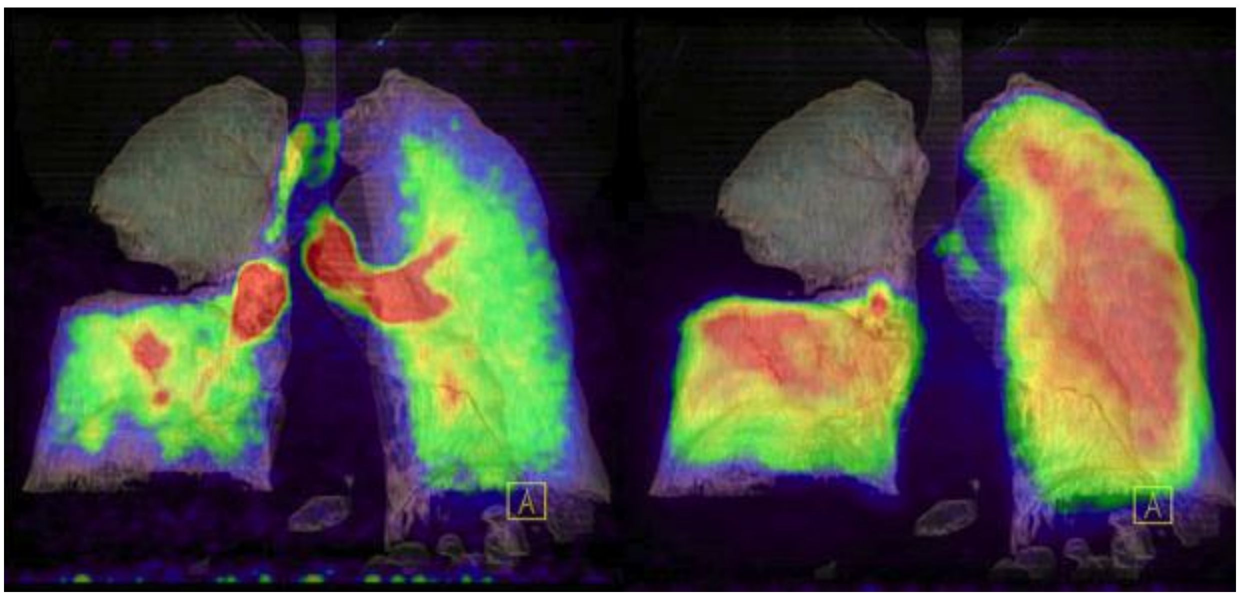
DIR for

FUNCTIONAL IMAGING



High-resolution imaging of pulmonary ventilation and perfusion with Ga-68-VQ respiratory gated (4-D) PET/CT
Article (PDF Available) *in* European Journal of Nuclear Medicine

Ventilation imaging could be important in planning of ablative pulmonary interventions in order to minimize treatment-induced parenchymal injury.

Computed Tomography Ventilation Imaging (**CTVI**) visualize air volume changes during lung motion
IDEA: designing treatment plans that account for lung function

Benefits:

- None preparation of a radio-aerosol or contrast agent,
- No extra dose
- No extra monetary cost
- Use specific multimodality-images

CT ventilation imaging derived from breath hold CT exhibits good regional accuracy with Galligas PET

Enid M. Eslick [a], John Kipritidis [a,b], Denis Gradinscak [c], Mark J. Stevens [b,d], Dale L. Bailey [c,e], Benjamin Harris [d,f], Jeremy T. Booth [b,d], Paul J. Keall [a,*]

[a] *Radiation Physics Laboratory, Sydney Medical School, University of Sydney, Camperdown;* [b] *Northern Sydney Cancer Centre, Royal North Shore Hospital;* [c] *Department of Nuclear Medicine, Royal North Shore Hospital;* [d] *Sydney Medical School – Northern, University of Sydney;* [e] *Faculty of Health Sciences, University of Sydney, Lidcombe; and* [f] *Department of Respiratory Medicine, Royal North Shore Hospital, Australia*

Radiotherapy and Oncology
Volume 127, Issue 2, May 2018, Pages 267-273

AIM: Comparisons of BHCT-based and 4DCT-based CTVIs and PET ventilation for 18 pts

CTVI comparison

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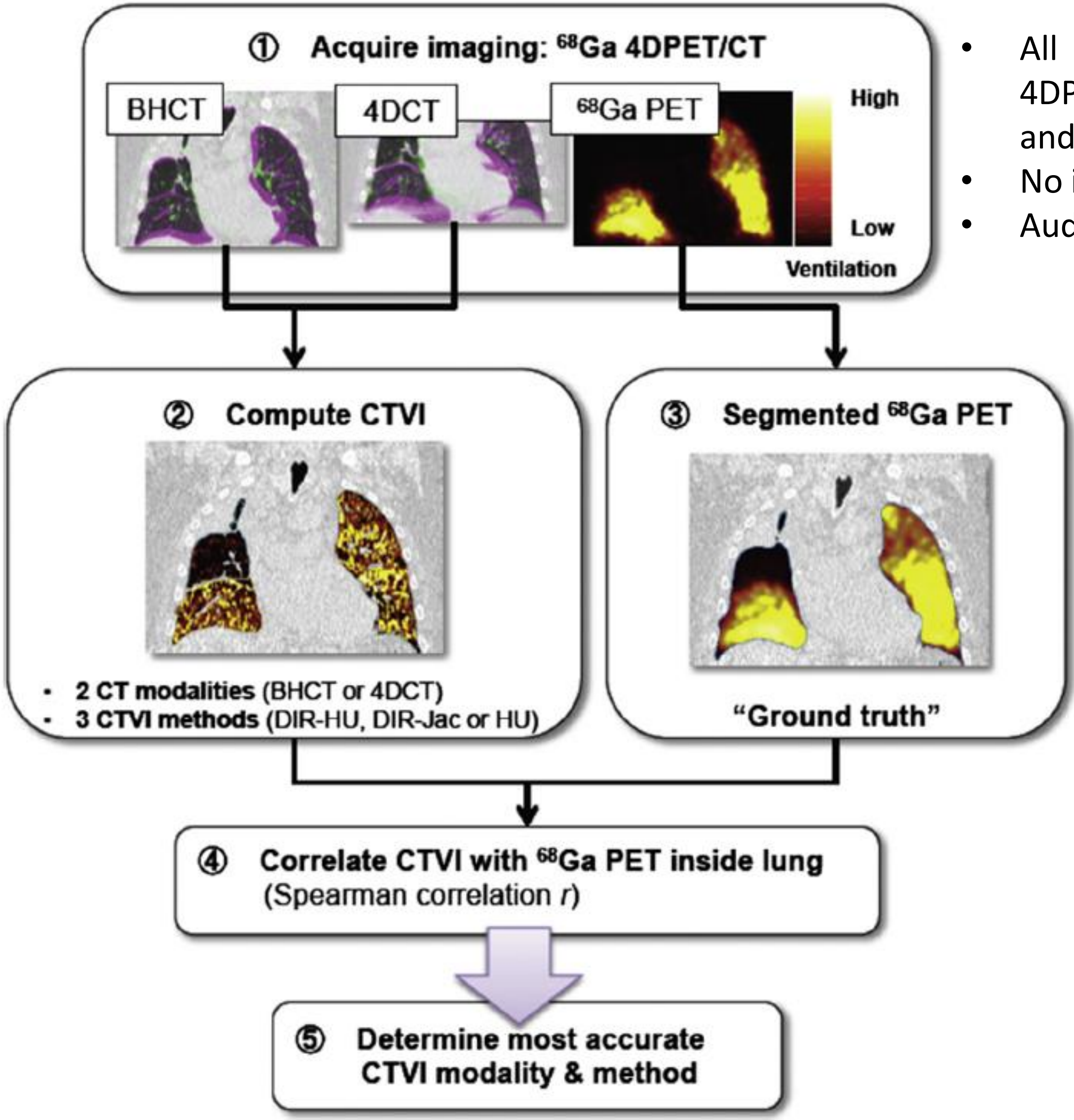

- All acquired in a single session on a 4DPET/CT to minimize time delays and/or patient setup differences
- No immobilization devices
- Audio-visual biofeedback

Results

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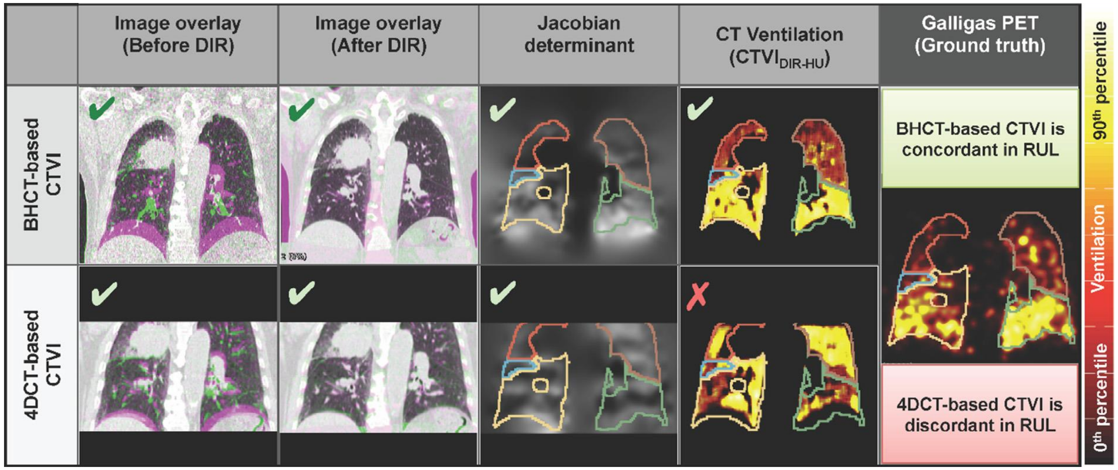
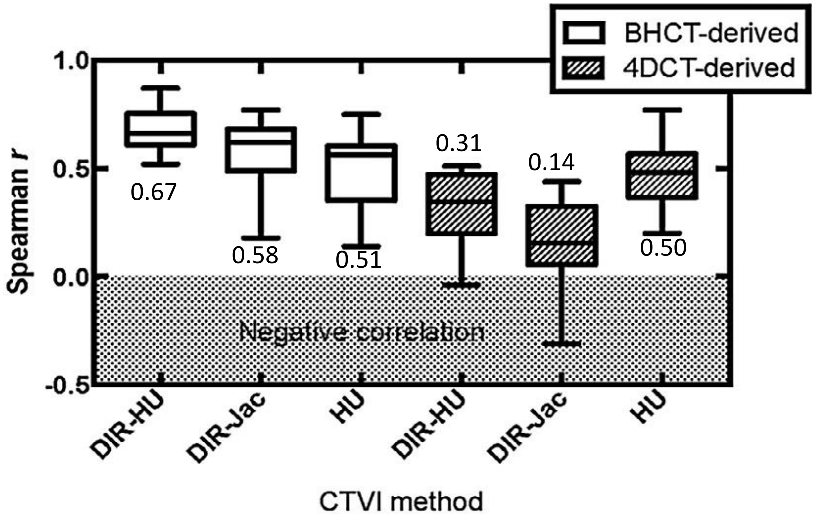


Breth-Hold CT-CTVI has better agreement with Galligas PET



Breath Hold CT-CTVI generated by DIR has higher accuracy than *4DCT-CTVI* (*t-test* $p<0.001$)

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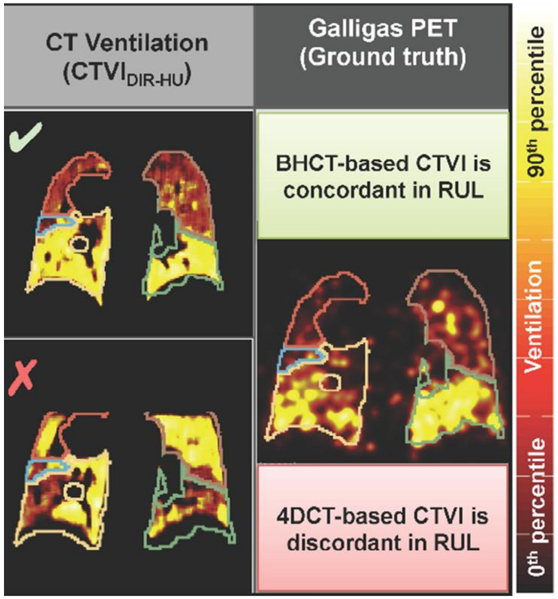
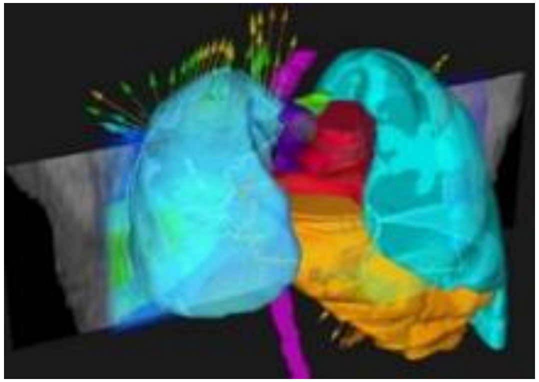
DIR Verified by some *TG-132* metrics:

- Qualitative: *image overlays*
- Quantitative: *Jacobian determinant*
  - BHCT J det > 0
  - 4DCT sometimes J det < 0 (e.g. lung truncated near diaphragm: 12% scans)

onto itself). A Jacobian determinant of less than or equal to zero clearly indicates an erroneous physical modeling of the patient and may indicate an error in the registration or a limitation in the algorithm to handle complex deformation. Any negative values indicate an error in the registration and these areas should be carefully evaluated for their influence on the results and further



Be careful on image truncation due to erroneous DIR usage



Alma Mater Studiorum – Università di Bologna

DOTTORATO DI RICERCA IN

FISICA

Ciclo XXVIII

Settore Concorsuale di afferenza:
02/D1 - FISICA APPLICATA, DIDATTICA E STORIA DELLA FISICA

Settore Scientifico disciplinare:
FIS/07 – FISICA APPLICATA (A BENI CULTURALI, AMBIENTALI, BIOLOGIA E MEDICINA)

METODI PREDITTIVI PER ADAPTIVE RADIATION THERAPY: EFFETTI DEL MOVIMENTO D'ORGANO, DEGLI ALGORITMI DI REGISTRAZIONE DEFORMABILE E DELL'ACCUMULO DI DOSE

Presentata da: Dott. GABRIELE GUIDI

Coordinatore Dottorato	Relatore
Prof. Gastone Castellani	Prof. Giuseppe Baldazzi

Esame finale anno 2016

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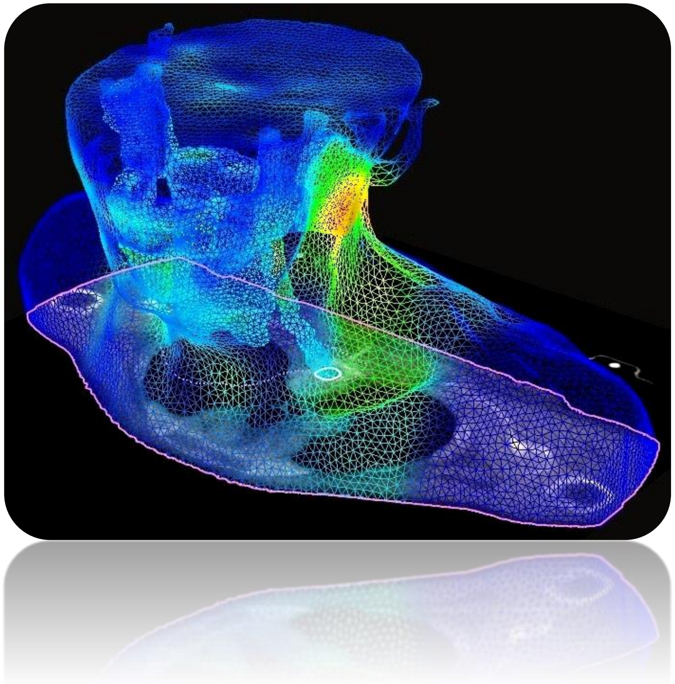
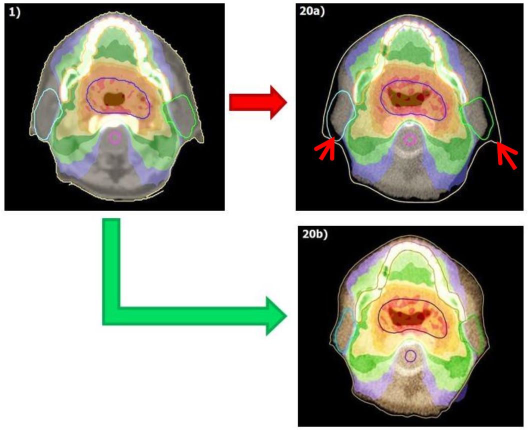
DEFORMABLE IMAGE REGISTRATION

FOR REPLANNING AND PREDICTIVE ANALYSIS





Physica Medica European Journal of Medical Physics

Guidi G et al. *A support vector machine tool for adaptive Tomotherapy treatments: Prediction of Head and Neck patients criticalities.* Physica Medica. 2015; 31: 442-451.

Proton dose distribution is highly sensitive to inter-fraction geometrical changes

Tumor enlargement or atelectasis → increases density / reduces beam penetration → Under-ranging can potentially reduce target coverage!

Tumor regression → reduces density / increases beam penetration → Over-ranging can result in an unplanned dose to OARs!

Re-planning could require

CBCT is an alternative to routine CT imaging.
Advantages:
- Highly accurate positioning in 3 dimensions
- Daily monitoring in treatment position
- Rapid assessment of the “dose of the day”

First Clinical Investigation of Cone Beam Computed Tomography and Deformable Registration for Adaptive Proton Therapy for Lung Cancer

Catarina Veiga, MSc,* Guillaume Janssens, PhD,† Ching-Ling Teng, PhD,‡ Thomas Baudier, BSc,§ Lucian Hotoiu, PhD,§ Jamie R. McClelland, PhD,‖ Gary Royle, PhD,* Liyong Lin, PhD,‡ Lingshu Yin, PhD,‡ James Metz, PhD,‡ Timothy D. Solberg, PhD,‡ Zelig Tochner, MD,‡ Charles B. Simone, II, MD,‡ James McDonough, PhD,‡ and Boon-Keng Kevin Teo, PhD‡

*Proton and Advanced RadioTherapy Group, Department of Medical Physics and Biomedical Engineering, University College London, London, United Kingdom; †Ion Beam Applications SA, Louvain-la-Neuve, Belgium; ‡Department of Radiation Oncology, University of Pennsylvania, Philadelphia, Pennsylvania; §iMagX Project, ICTEAM Institute, Université Catholique de Louvain, Louvain-la-Neuve, Belgium; and ‖Centre for Medical Image Computing, Department of Medical Physics and Biomedical Engineering, University College London, London, United Kingdom

Int J Radiation Oncol Biol Phys, Vol. 95, No. 1, pp. 549–559, 2016

AIM: ART workflow using on-board CBCT in which re-planning of 20 patients treated for lung malignancies is suggested by 3 decision points

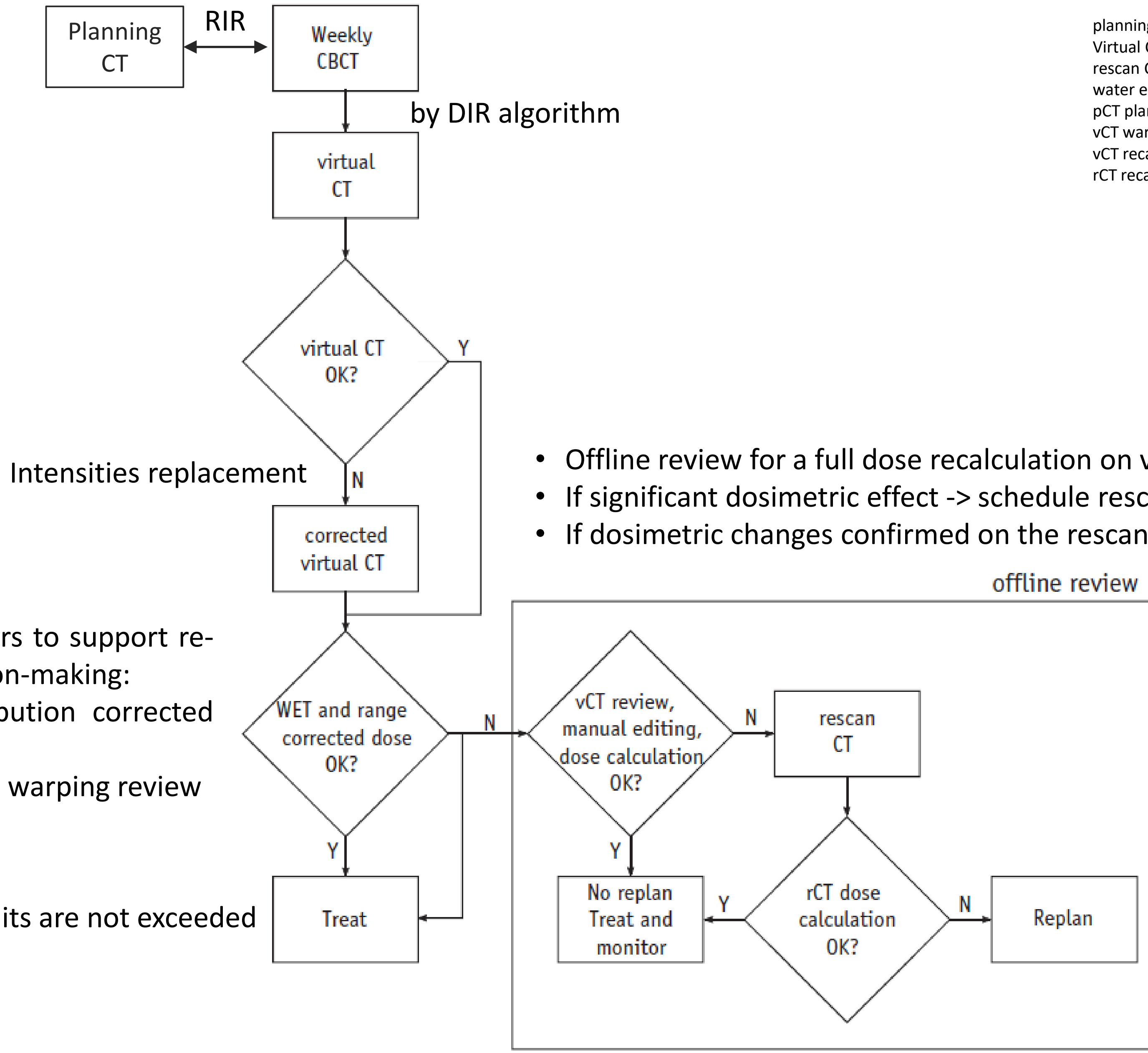
Passive scattering **proton therapy** using 2 treatment fields median dose of 66.3Gy (Co equivalent) in 1.8Gy/fx

Imaging protocol:

- 4D-PET/CT for planning
- weekly CBCT
- rescan 4D CT

Adaptive PT workflow

planning CT (pCT)
Virtual CT vCT
rescan CT (rCT)
water equivalent thickness (WET)
pCT planned dose
vCT warped dose (DvCT-WET)
vCT recalculated dose (DvCT)
rCT recalculated dose (DrCT)

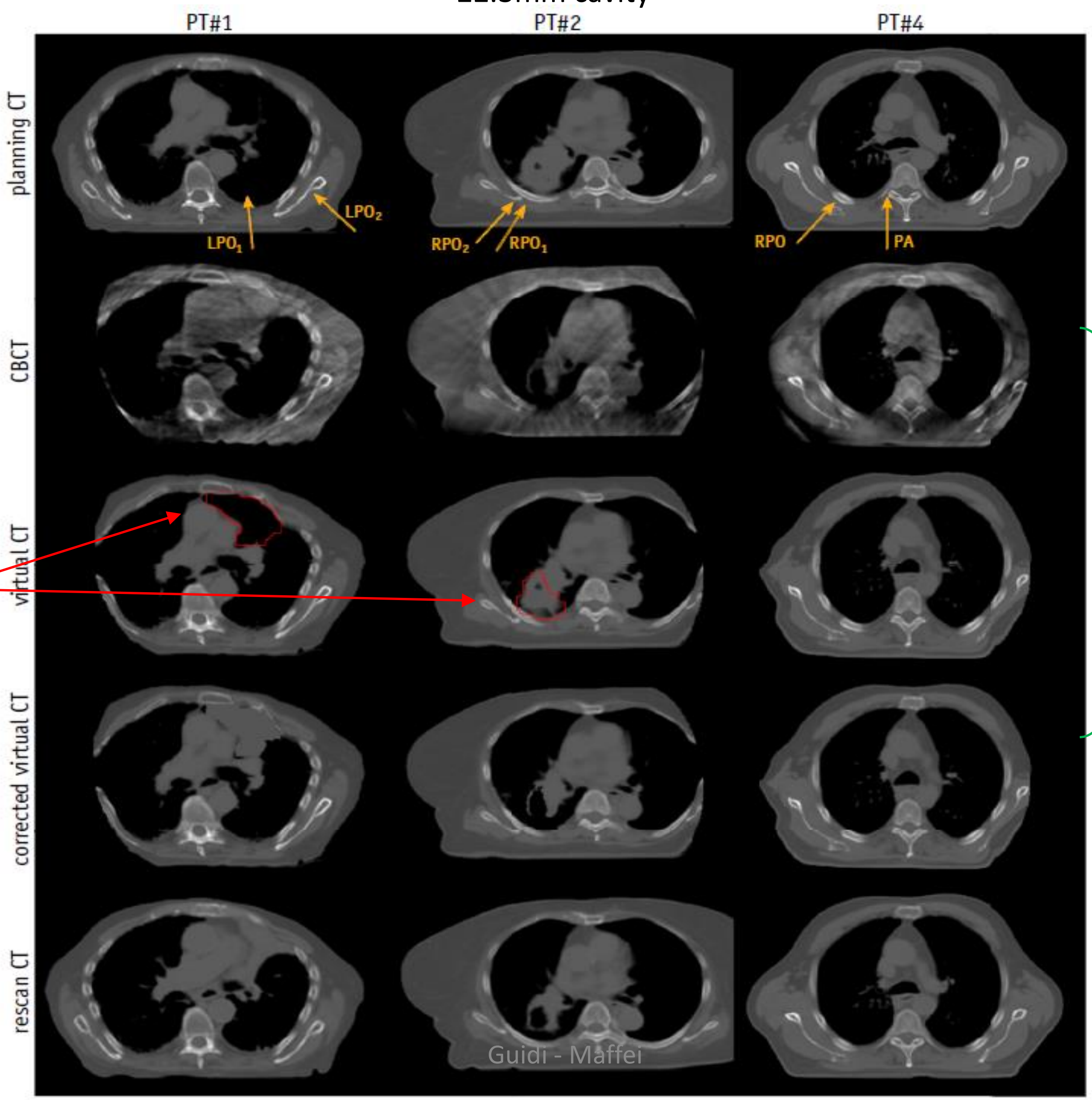


- Offline review for a full dose recalculation on virtualCT
- If significant dosimetric effect -> schedule rescanCT
- If dosimetric changes confirmed on the rescan CT -> **re-plan**

Clinical indicators to support re-planning decision-making:

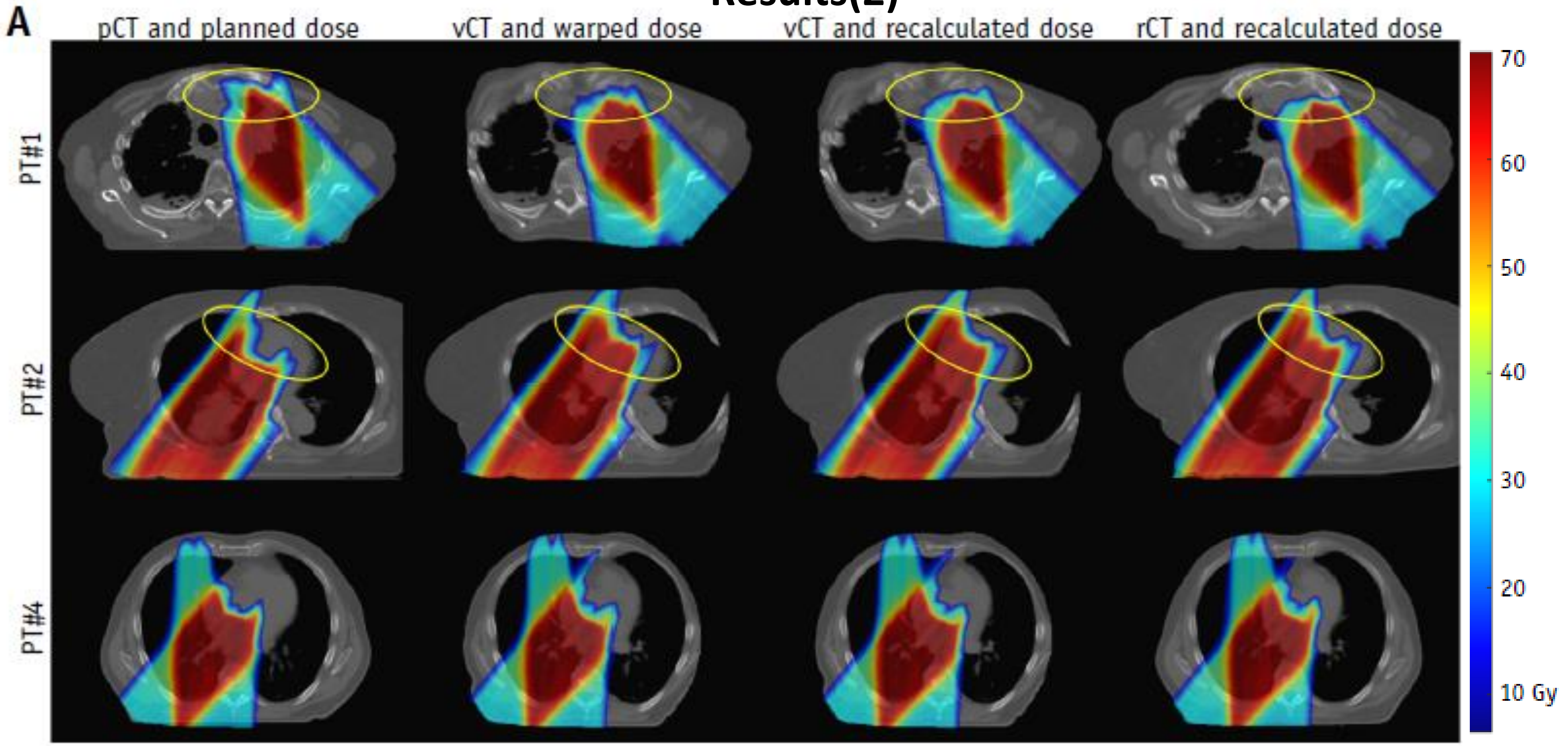
- Dose distribution corrected on WET
- Online dose warping review

Results



Atelectesis
Large tumor shrinkage
22.3mm cavity
Small tumor shrinkage
PT#1
PT#2
PT#4
planning CT
CBCT
virtual CT
corrected virtual CT
rescan CT
LPO$_1$
LPO$_2$
RPO$_2$
RPO$_1$
RPO
PA
Correction
DIR useful to follow changes
Guidi - Maffei

Results(2)



PT#1) Atelectasis increased the WET (>10mm) → under-ranging + loss iCTV coverage

PT#2) GTV shrinkage decreased WET → over-ranging + increased dose to heart, spinal cord

Re-planning predicted on virtualCT

PT#4) small WET changes → Similar dose distributions → Original Plan do not need Re-Planning

Results (3)

- **VirtualCT** scan might play a **complementary** role to RescanCT
- **90% of fields** with WETunder-95%/over-95% > 10mm properly **identified** from VirtualCT
- **2** patients under-ranging; **18** patients over-ranging
- **Dose warping** used as clinical indicator for Re-Planning
- The most issues for **Re-Planning**:
  - Loss of tumor coverage
  - Increase in Dmax to spinal cord
  - Dose over-ranging to heart

Conclusions & Limits

- The workflow is less robust for patients with abnormal internal anatomic changes
- DIR has inherent uncertainties and associated errors, not adequate when tissue appears or disappears (mandatory correction of the virtual CT)
- Loss coverage of the Virtual CT scan due to truncation of the CBCT
- CBCT FOV limitations can result in incomplete information of the external contour.
    - This was problematic for some lateral oblique fields (10% of the field)

From a clinical perspective, 2 scenarios are possible with DIR errors:

1) False-positive : The outcome is an unnecessary CT scan to confirm the replanning. (no dose variation will appears between the CTs)
2) False-negative: DIR errors are larger than real anatomic changes, so unexpected errors will appears in dose delivered

Cit. «All that glitters is not gold”

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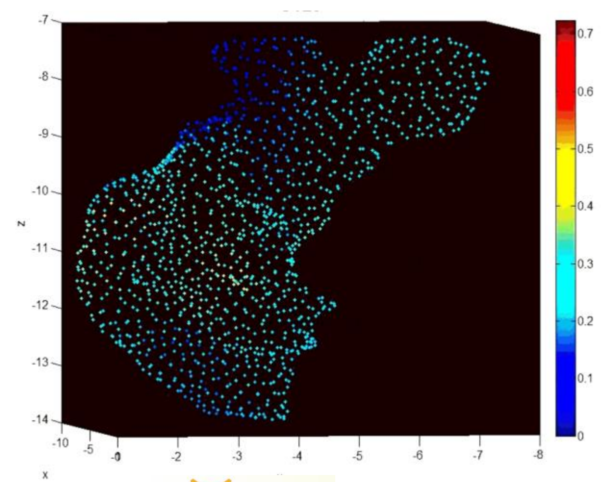
DIR for

MATHEMATICAL MODEL



AAPM2015
REINVIGORATING
SCIENTIFIC EXCELLENCE

Medical Physics
The International Journal of Medical Physics Research and Practice

Guidi - Maffei

Maffei N et al. SIS epidemiological model for adaptive RT: Forecasting the parotid glands shrinkage during Tomotherapy treatment. Medical Physics 43, 4294; 2016

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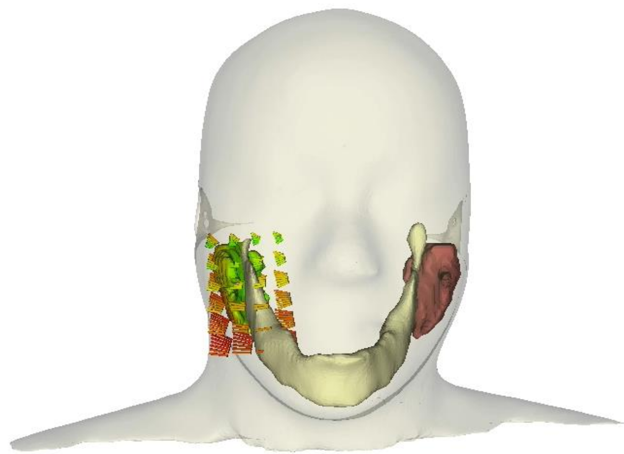

A COMSOL® multyphysics biomechanical model to simulate real parotid glands shrinkage during Radiotherapy Treatments.

G. Guidi (a)*, **N. Maffei** (a,b), **F. Itta** (c), P. Ceroni (a), E. D'Angelo (d), F. Lohr (d), B. Meduri (d)

(a) A.O. U. di Modena, Medical Physics dpt., Modena, Italy
(b) University of Turin, Post Graduate School in Medical Physics, Turin, Italy
(c) University of Bologna, Physics dpt., Bologna, Italy
(d) A.O. U. di Modena, Radiotherapy dpt., Modena, Italy

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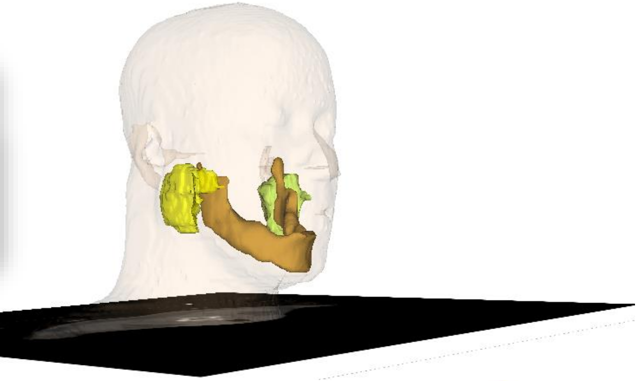
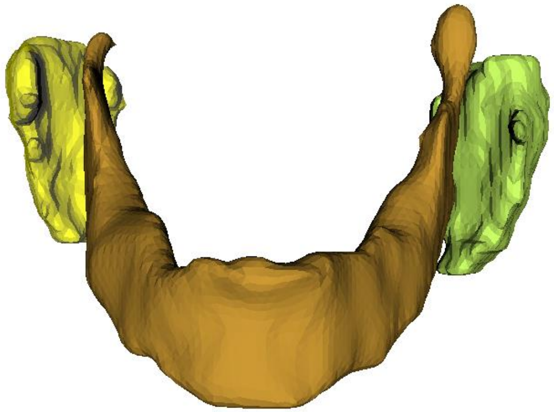
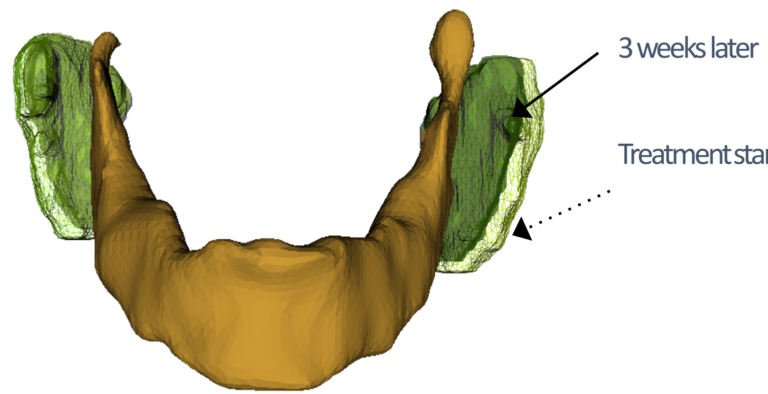
THE HUMAN BODY IS A DINAMIC

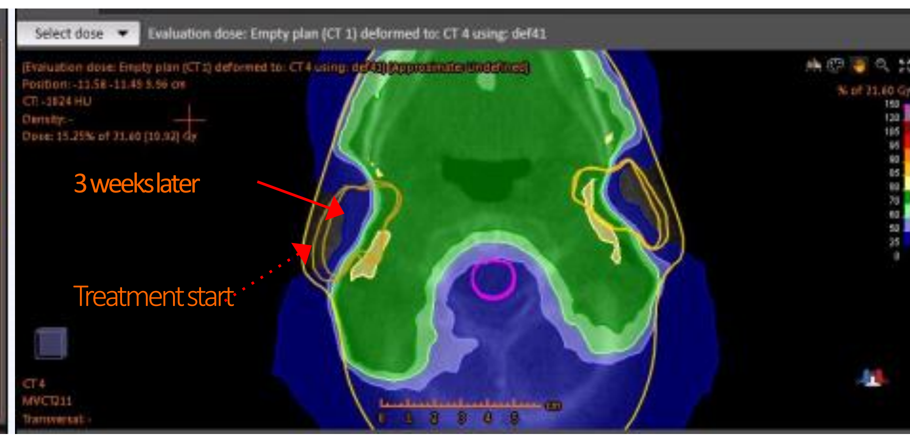


- ❑ Weight loss
- ❑ Tumour shrinkage
- ❑ Alterarion muscle mass

→ PAROTID GLANDS **INTER-FRACTION** DEFORMATION





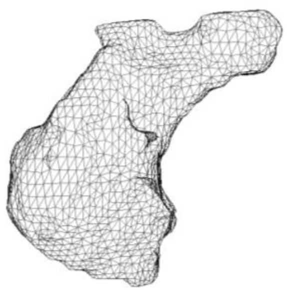


Treatment start
D_{mean}= 25Gy

mid-time course (3 weeks later)
D_{mean}=27Gy

BIOMECHANICAL MODEL IMPLEMENTATIC..

- **PHASE 1** : Image Aquisition of 8 H&N Patients
- **PHASE 2**: 3D Geometrical model creation from segmented structures
- **PHASE 3** : Biomechanical model creation via Finite Element Method (FEM) software



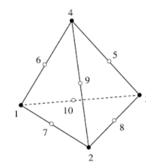
Geometrical model
- Segmentation
- Mesh creation

CT images

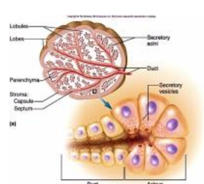
Parotid gland Mechanics

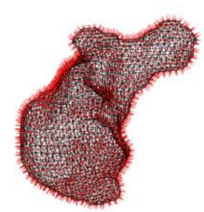
Simulation & Model parameter estimation

- Finite element method



- Linear continuum Mechanics
- Parotid morphing model (acinar cells loss,fixed constrants)

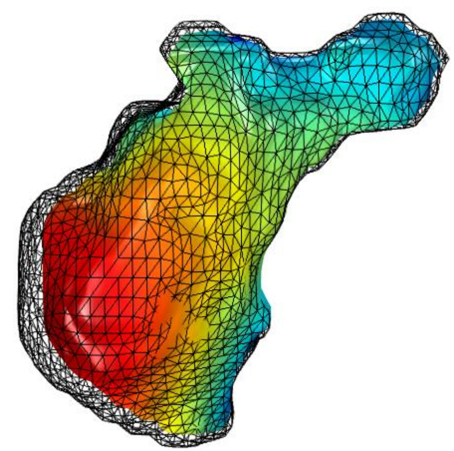




- Parameter Optimization algorithm

Perzonalized Biomechanical simulation

Radiationtherapy plan optimization



PHASE 3 : BIOMECHANICAL MODEL IMPLEMENTATION

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❑ GEOMETRY

❑ MATERIAL

- ❑ Linear elastic
- ❑ Isotropic
- ❑ Homogeneous
- ❑ Navier lamè equation
- ❑ Young's Modulus = ~ 10 kPa
- ❑ Poisson ratio = ~ 0.49
- ❑ Density = 1 (g/cm^3)

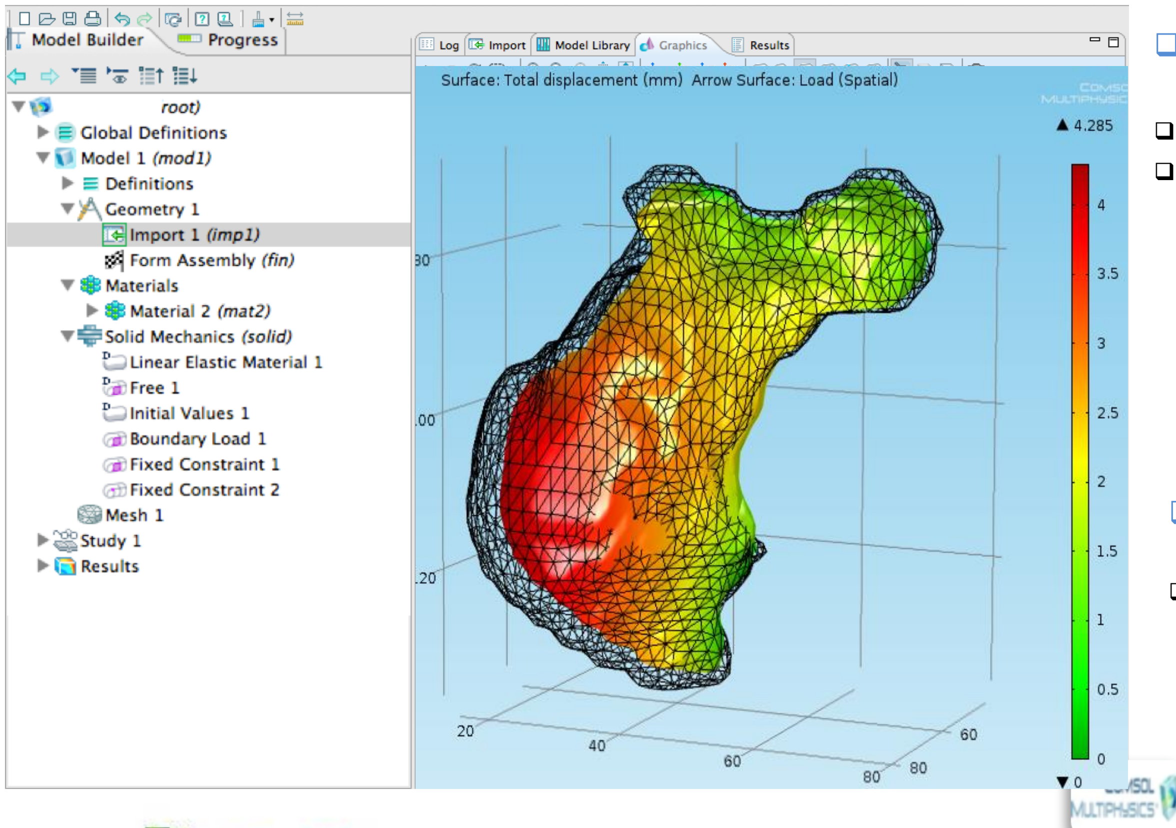
❑ PHYSICS

Load condition based on :

- ❑ Loss of acinar cells
- ❑ Swelling parotid lobuli

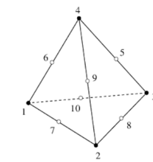
Boundary condition :

- ❑ Motion block carried out by sourranding structures



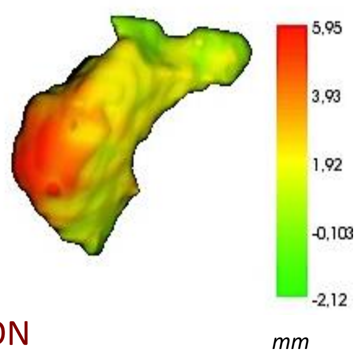
❑ DOMAIN DISCRETIZATION

- ❑ Volumetric mesh creation
- ❑ Domain discretization with 250000 tetrhaedreal elements



❑ RUN STUDY

- ❑ Run simulation for different load condition/Young modulus values to find optimal model parameter



REAL DEFORMATION

$$RMSDE = \sqrt{\frac{1}{n}\sum^{n}(x_{sim} - x_{real})^2 + \frac{1}{n}\sum^{n}(y_{sim} - y_{real})^2 + \frac{1}{n}\sum^{n}(z_{sim} - z_{real})^2} \cdot \sqrt{\frac{1}{3}}$$

OPTIMAL MODEL PARAMETER ESTIMATION COMPARING REAL AND SIMULATED DEFORMATIONS

RESULTS

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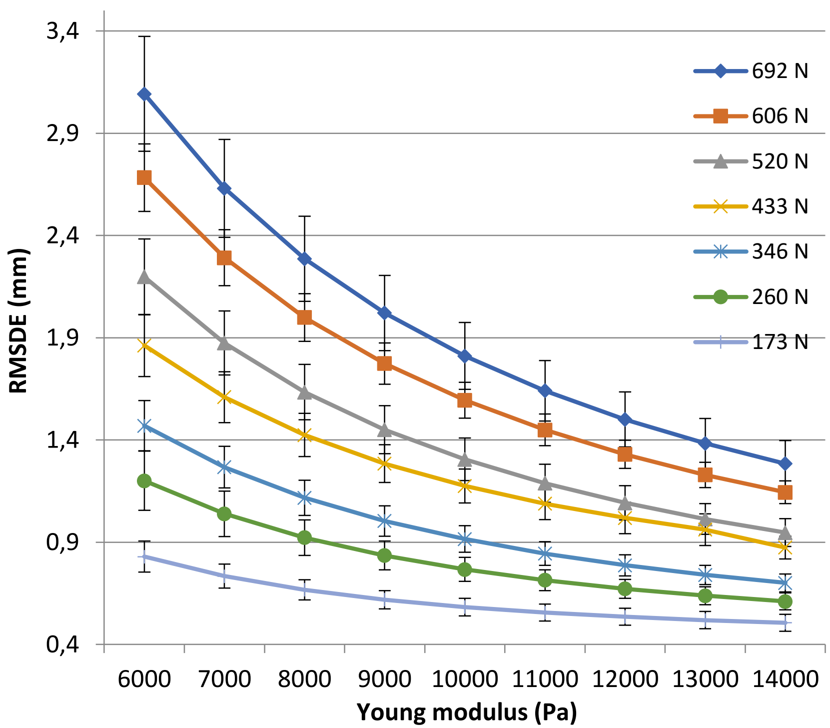
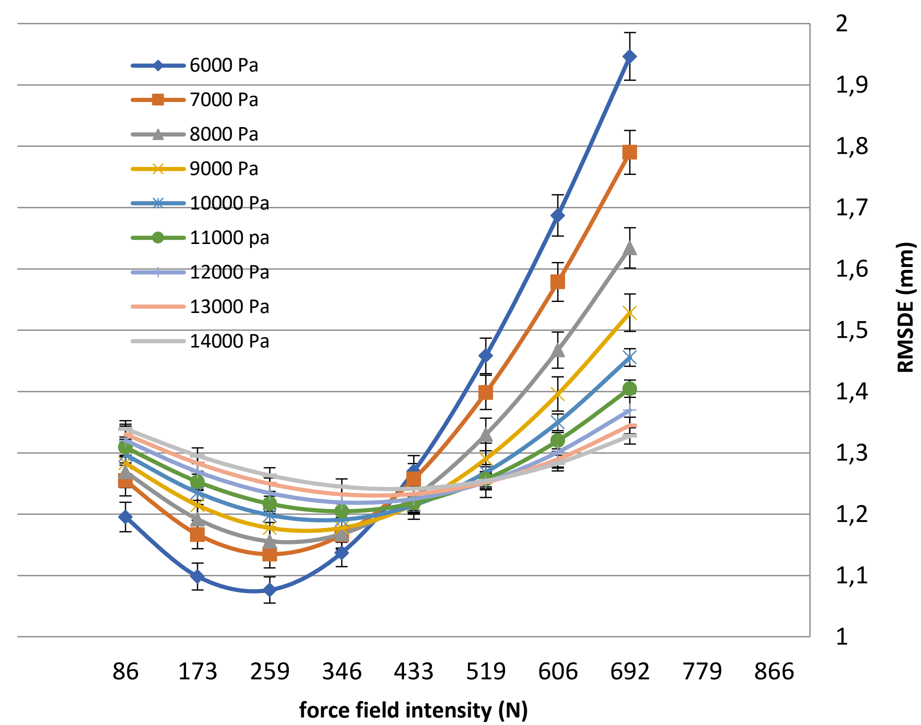
Optimal findings	1 – 15 th day morphing	15– 31 st day morphing
Young's modulus (Pa)	14000	6000
Force field intensity (N)	173	259

- ✓ **NUMBER OF SIMULATIONS PERFORMED : 2016** (16 PGs * 2 periods *9 elastic parameters *7 force intensity)
- ✓ **COMPUTATIONAL TIME PER SIMULATION** (Intel core i7 processor (2.2 Hz) with 4GB RAM) : 7 minutes
- ✓ **MEAN NUMBERS OF FINITE ELEMENTS USED TO SOLVE SINGLE MODEL** : 250000 thetraedral elements

Simulations 1->15th day of morphing :
RMSDE vs Young modulus



Simulations15 th ->31 th day morphing :
RMSDE vs force field



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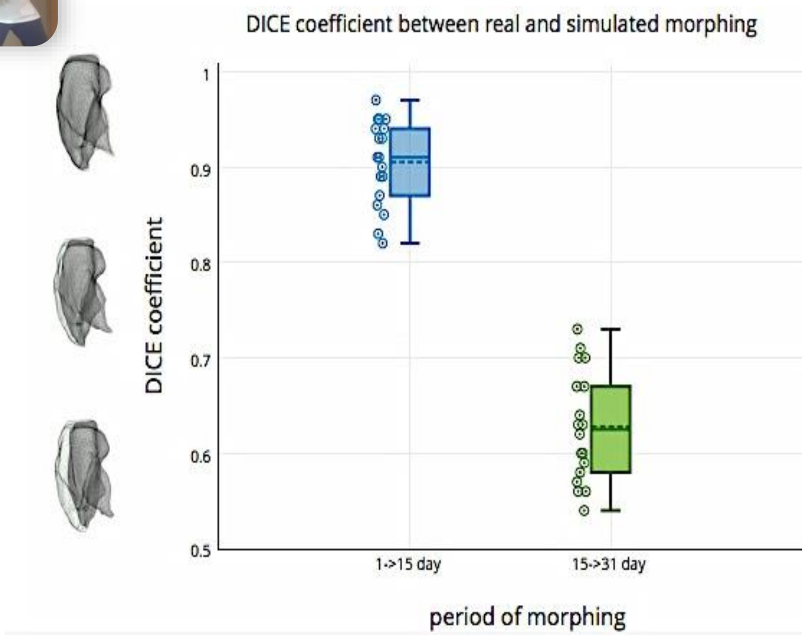
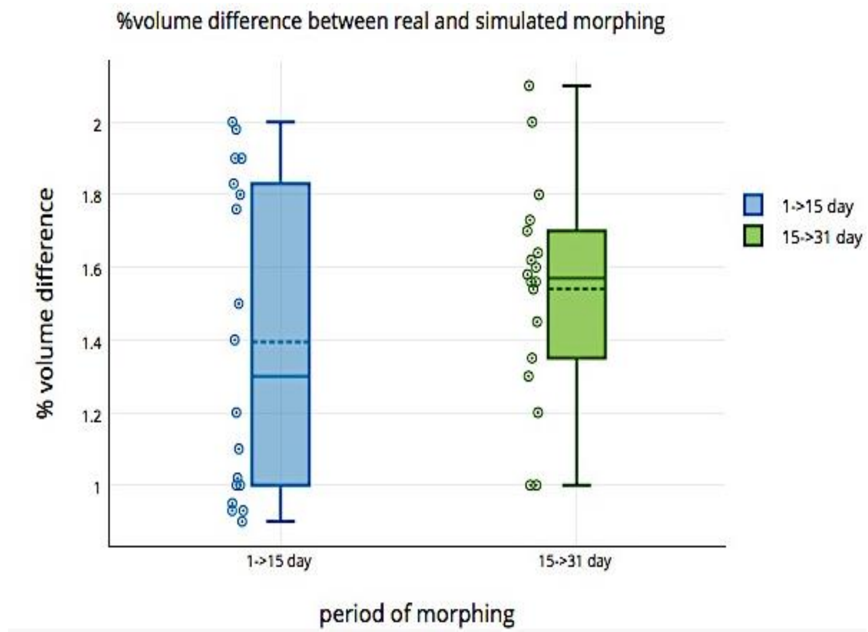
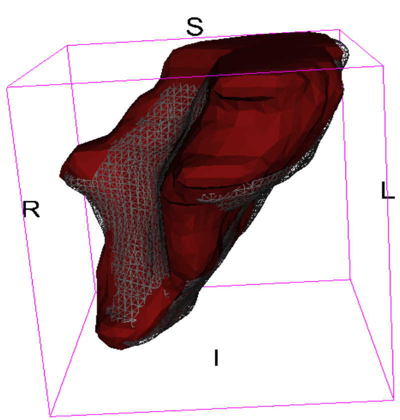
RESULTS

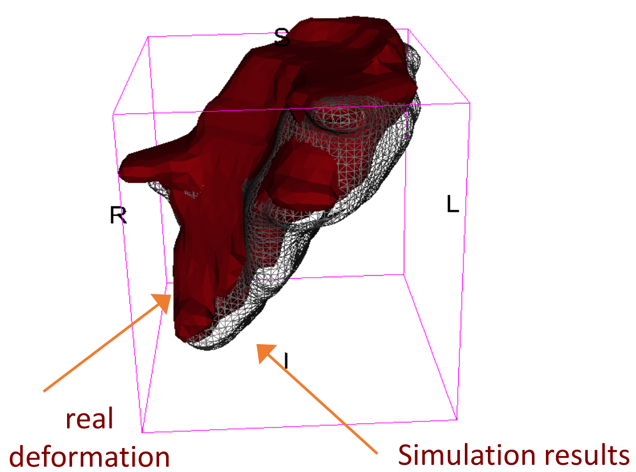




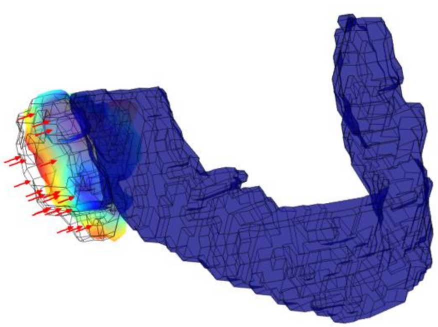
1->15 –th day of morphing



15->31 st day of morphing



- **Patient facial slimming** is the effect we have not considered in our model



CHALLENGES

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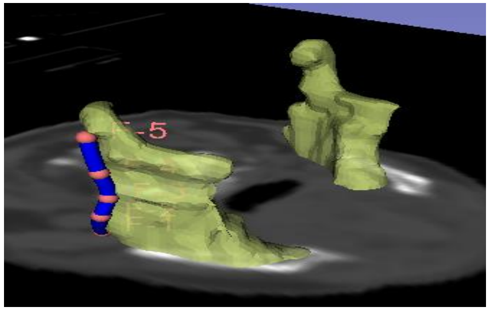
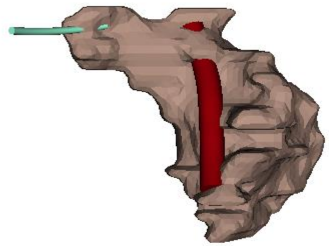
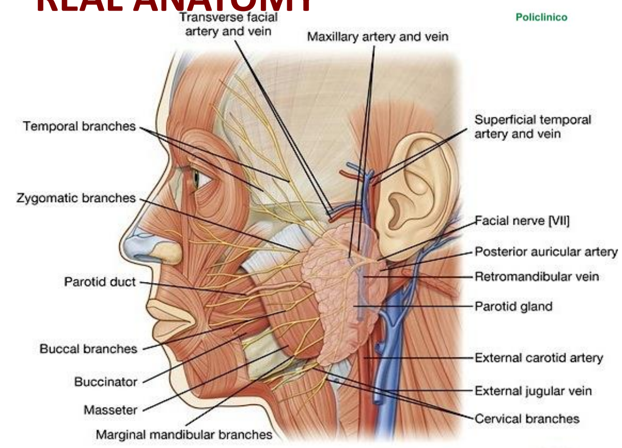
SIMULATED ANATOMY





REAL ANATOMY



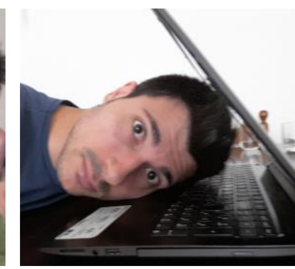
Limited number of anatomical barriers

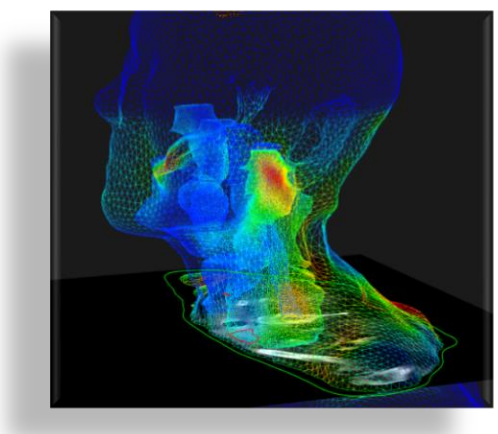
- ✓ **NUMBER OF SIMULATIONS: >2000**

(16 PGs * 2 periods *9 elastic parameters *7 force intensity)

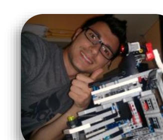
- ✓ **COMPUTATIONAL TIME/SIMULATION** (Intel core i7 with 4GB RAM): **7 min**
- ✓ **MEAN NUMBERS OF FINITE ELEMENTS TO SOLVE SINGLE MODEL** : **250000**

REAL RESULTS



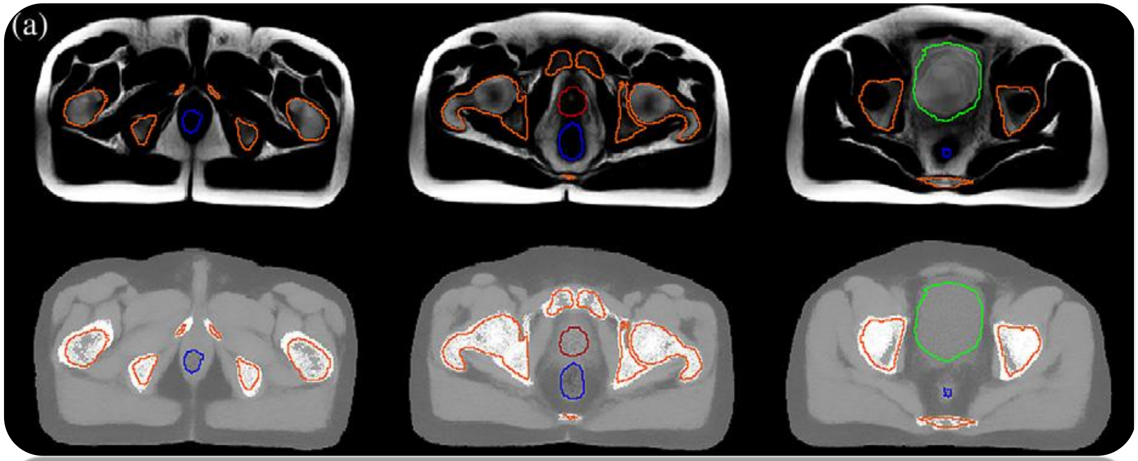


APPLICABLE IN CLINICAL PRATICE FOR ALL OARS?



DIR for

SEGMENTATION



RT dose planning directly on **MRI** scans:

- Reduction of uncertainties due to multimodality image registration
- Superior soft-tissue contrast
- Accurate and robust DIR

- MRI scans could not be calibrated to electron density as standard CT
- RT dose calculations could have challenges on MRI scans

An Atlas-Based Electron Density Mapping Method for Magnetic Resonance Imaging (MRI)-Alone Treatment Planning and Adaptive MRI-Based Prostate Radiation Therapy

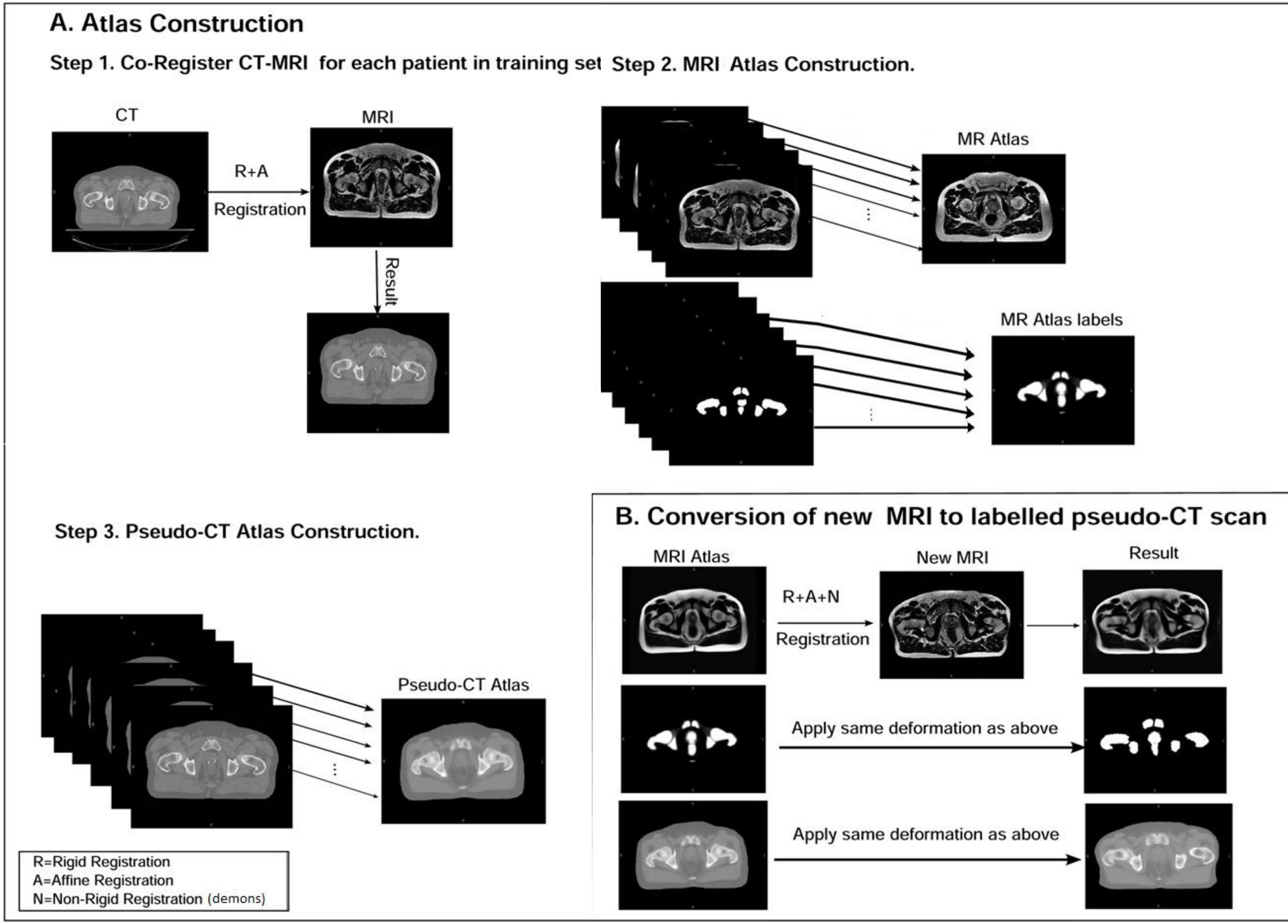
Jason A. Dowling, Ph.D.,* Jonathan Lambert, B.Sc.(Hons),[†,‡] Joel Parker, B.App.Sc.,[†] Olivier Salvado, Ph.D.,* Jurgen Fripp, Ph.D.,* Anne Capp, M.Med.(ClinEpi),[†,‡] Chris Wratten, MB., BS.,[†,‡] James W. Denham, M.D.,[†,‡] and Peter B. Greer, Ph.D.[†,‡]

*Australian e-Health Research Center, CSIRO ICT Commonwealth Scientific and Industrial Research Organisation Information and Communication Technologies Centre, Queensland, Australia; [†]Calvary Mater Newcastle Hospital, New South Wales, Australia; and [‡]University of Newcastle, New South Wales, Australia

Int J Radiation Oncol Biol Phys, Vol. 100, No. 2, pp. 361—373, 2018

AIM: to develop an atlas-based method to map realistic electron densities to MRI scans for dose calculations (39 pts)

Workflow


A. Atlas Construction
Step 1. Co-Register CT-MRI for each patient in training set
CT
MRI
R+A
Registration
Result
Step 2. MRI Atlas Construction.
MR Atlas
MR Atlas labels
Step 3. Pseudo-CT Atlas Construction.
Pseudo-CT Atlas
R=Rigid Registration
A=Affine Registration
N=Non-Rigid Registration (demons)
B. Conversion of new MRI to labelled pseudo-CT scan
MRI Atlas
New MRI
Result
R+A+N
Registration
Apply same deformation as above
Apply same deformation as above

Results

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A **leave-one-out approach** was used for all patients

Site	CT mean HU (±SD)	Pseudo-CT mean HU (±SD)	Two-tailed *t*-test *p* value result
Rectum	−54 (4)	−54 (143)	>0.9
Bladder	9 (0)	9 (6)	>0.9
Bone	339 (10)	340 (85)	>0.9
Prostate	42 (1)	42 (25)	>0.9

Original CT mean HU

Pseudo-CT mean HU

no significant differences (*2-tailed paired t-test*)

Manual Segmentation

Automatic Segmentation

Site	Mean DSC (±SD)
Bone	0.79 (0.12)
Prostate	0.70 (0.14)
Bladder	0.64 (0.16)
Rectum	0.63 (0.16)

pseudo-CT generation

+

automatic segmentation

≈ **3min** (i7 CPU; 8 Gb RAM)
from a whole-pelvis MRI scan

Pseudo-CT used for dose planning

Patients	3D-CRT	Prescription
23	4-field box	70Gy in 35fx
16	5 fields	74Gy in 37fx

Planned Dose on Original-CT

Dose Calculated on Pseudo-CT

Average **Dose difference** @ isocenter = **1.5%** (3cGy)
(Hp0 verified by χ^2 *-test*)

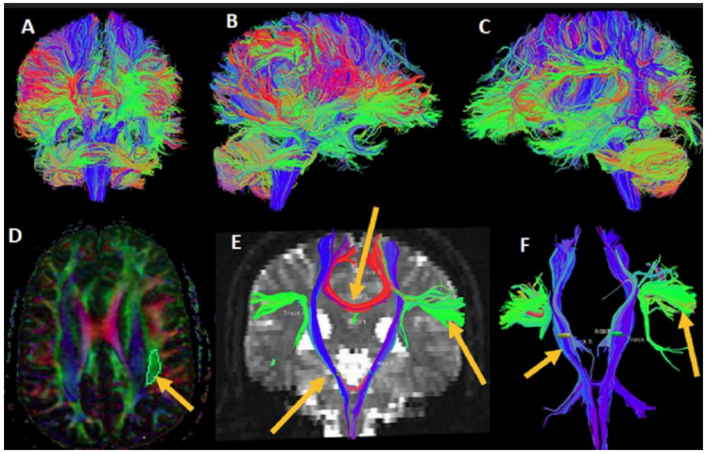
MRI-Only Workflow: Issues and solutions

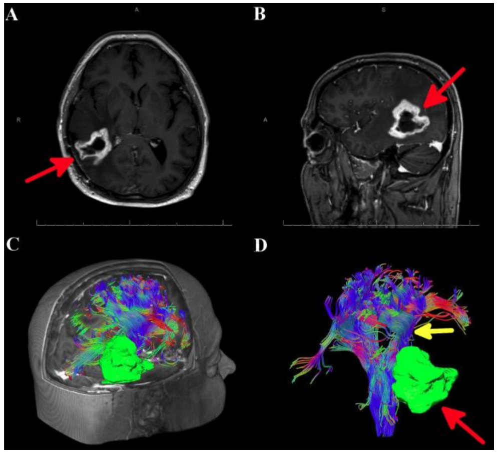
- **CT** provides the electron density required for dose calculations.

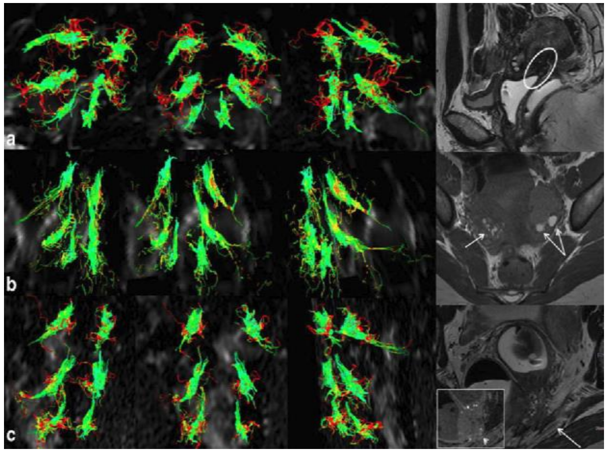
- **CT-MRI** workflow requires image coregistration (registration error approxImately 2 mm)
  - which introducing inaccuracy in anatomic changes between scans (i.e. prostate, bladder, rectal filling).

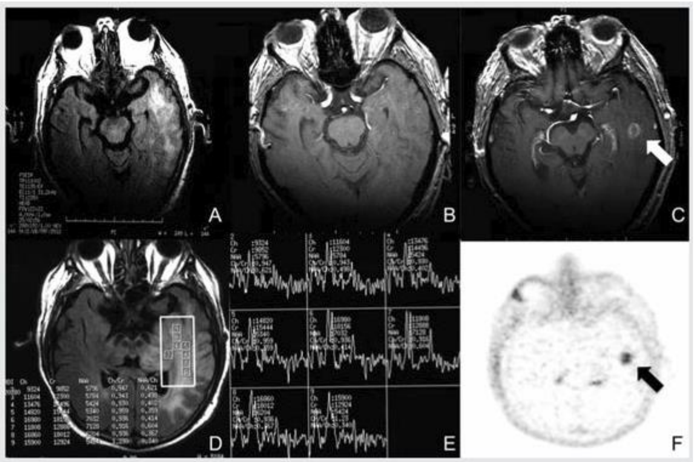
- **MRI-only** workflow requires a synThetic CT or pseudo-CT scan to give the electron density information required for dose calculations
  - A number of methods are available to create a pseudo- or synthetic CT scan, but all the images are not acquired from the patients
  - <u>Tissue segmentation:</u> After manual or automatic segmentation of an MRI data set, assigning separate densities to air, soft tissue, and bone; it gives comparable results to the standard method of a planning CT scan.
    - However, bone segmentation is time consuming using standard MRI sequences, and the value used for the assigned densities must also be relevant
  - <u>Voxel method</u>: Statistical models to differentiate the attenuation of tissue types to allow the automatic conversion of the MRI intensity in each voxel to a HU.
    - Using the information from all voxels, a greater spectrum of attenuation coefficients is obtained for a more accurate dose calculation, rather than the limited number used with tissue segmentation

MANY MANY YEARS A GO…we have USED some OLD software where the ROI where overwritten in Density…Do we have to go back to pencil beam algorithm?









Can you DIR tractography, spectrum and MRI morphing?
Or do we have to loose functional information to use the advanced DIR?

TAKE HOME MESSAGE

- Deformable Image Registration (**DIR**) has the potential to **improve** RT

- **Accumulate dose** over the therapy could **Estimate** anatomical changes and delivered dose

- **BHCT-CTVI** using DIR has better concordance with gold standard **ventilation**; could be used to account lung function during planning

- **VirtualCT** obtained using DIR between OriginalCT - CBCT is **comparable** to a rescanCT.
  It can be used in a fast **online** workflow to support **re-planning** decision making

- Biomechanical **model** based on DIR can **simulate** and **predict** organ warping during treatment

- Atlas method provides the ability to automatically define organs and map electron densities to MRI scans, supporting adaptive MRI-based RT

www.medicalphysicsresearch.weebly.com