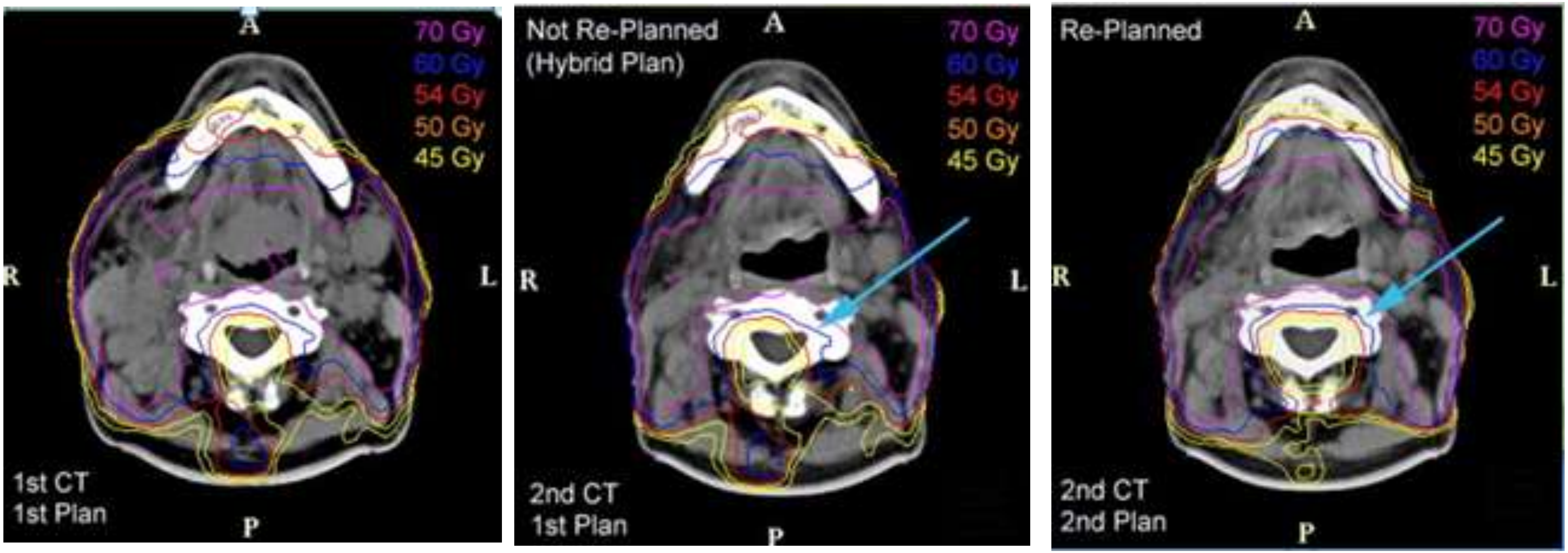
Adaptive Radiotherapy: Personalizing Precision in Radiation Oncology

Dr. Sayan Das, Medica Superspecialty Hospital, Kolkata

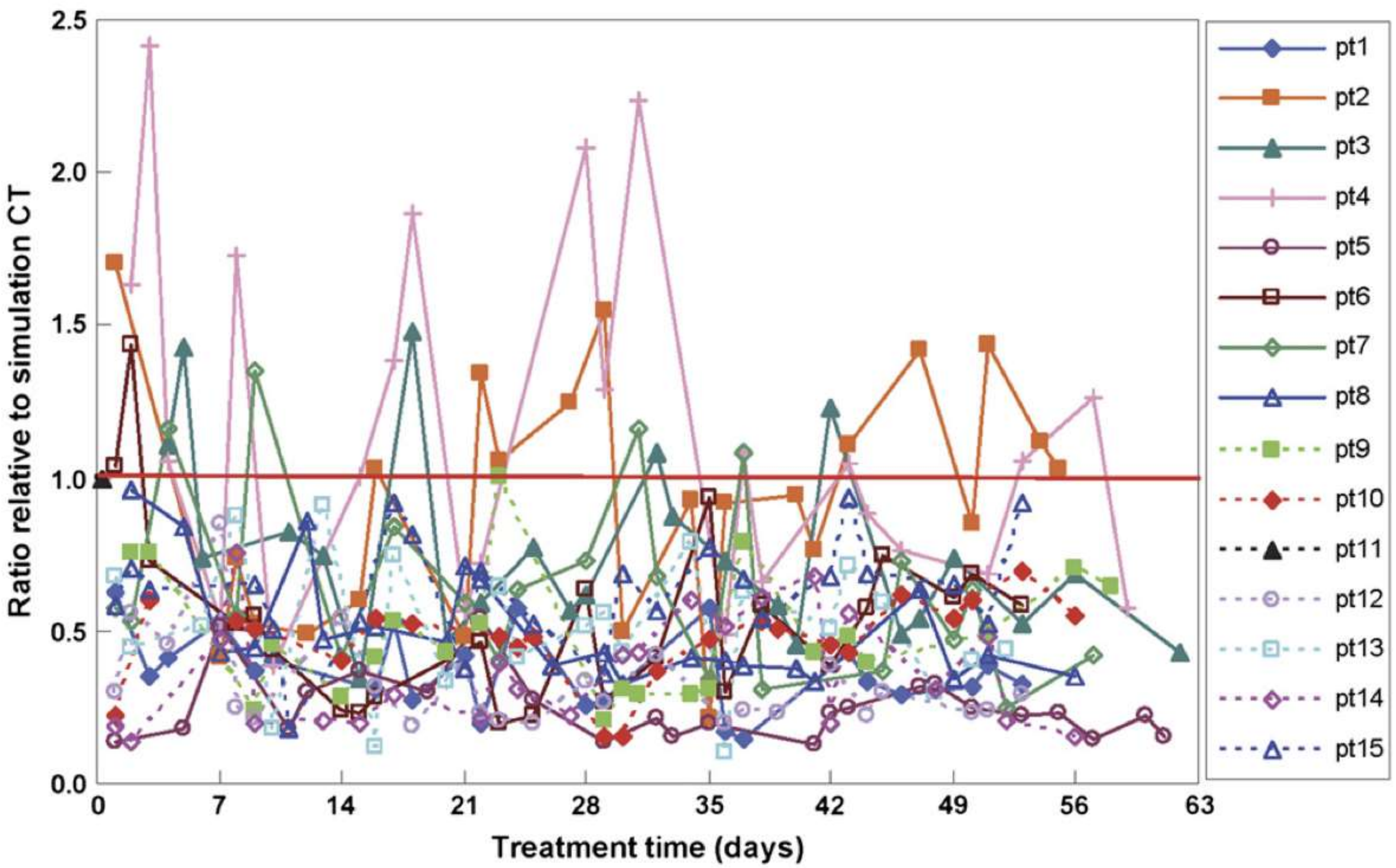
Overview

- What is ART?
- Why do we need it?
- Strategies of ART
- Tools of the Trade
- Online ART/ Real time ART
- Where to use ART? - evidence for ART
- When to Adapt?
- Future of ART



Hansen et al. IJROBP 2007

90% of bladder volumes were smaller than volumes on planning CT



Frank et al. IJROBP 2008

What is Adaptive Radiotherapy (ART)?

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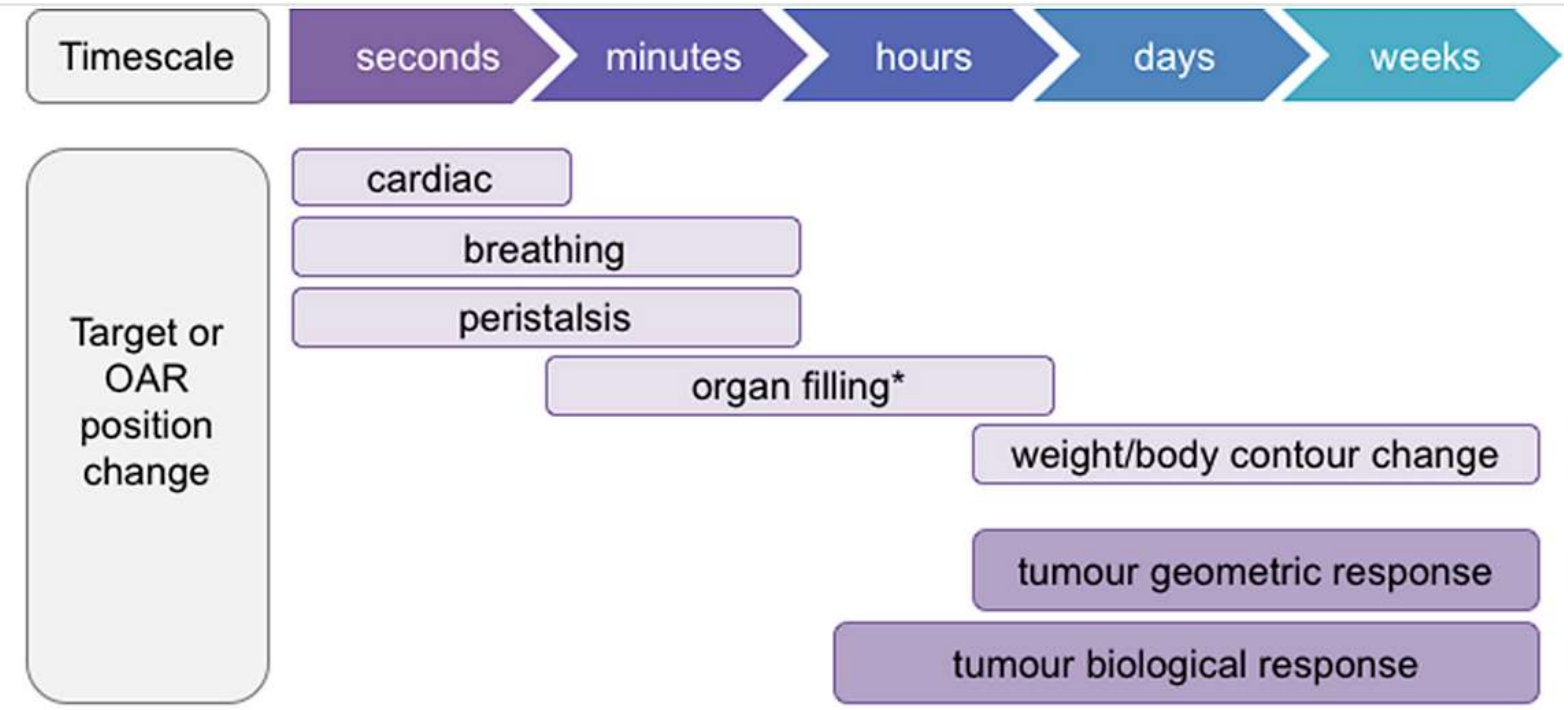
- ART is an advanced approach in radiation oncology that adjusts treatment plans based on anatomical and biological changes during the course of therapy using an imaging feedback loop
- Addresses limitations of static plans in the face of patient-specific variations (e.g. tumor shrinkage, organ motion, weight loss)
- Emerged with advancements in imaging (e.g. IGRT) and planning technology in the early 2000s."

Adaptive radiation therapy

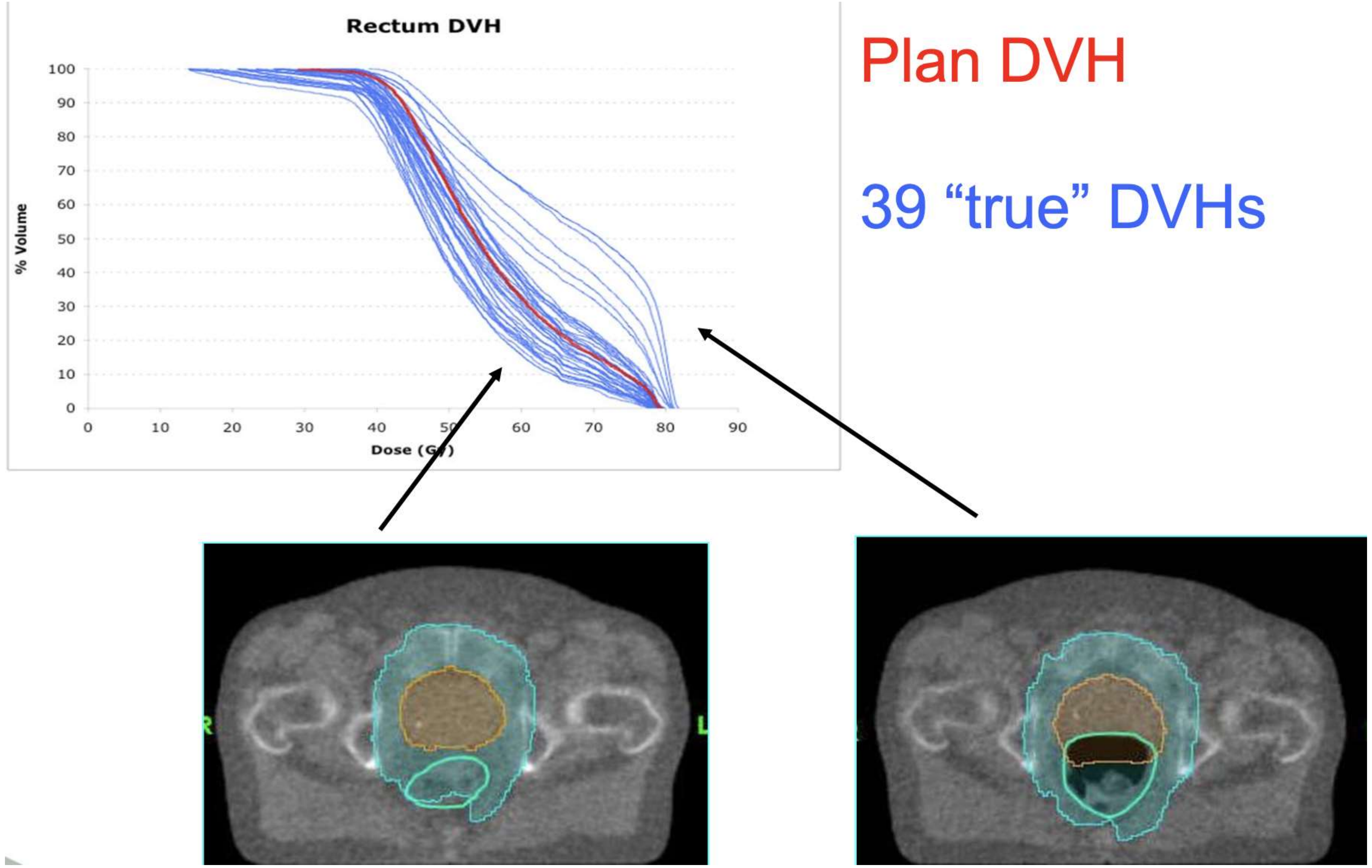
Di Yan†, Frank Vicini, John Wong and Alvaro Martinez
Department of Radiation Oncology, William Beaumont Hospital, Royal Oak, MI 48073, USA

Phys. Med. Biol. 42 (1997) 123–132

Why we need ART? - Anatomical Changes



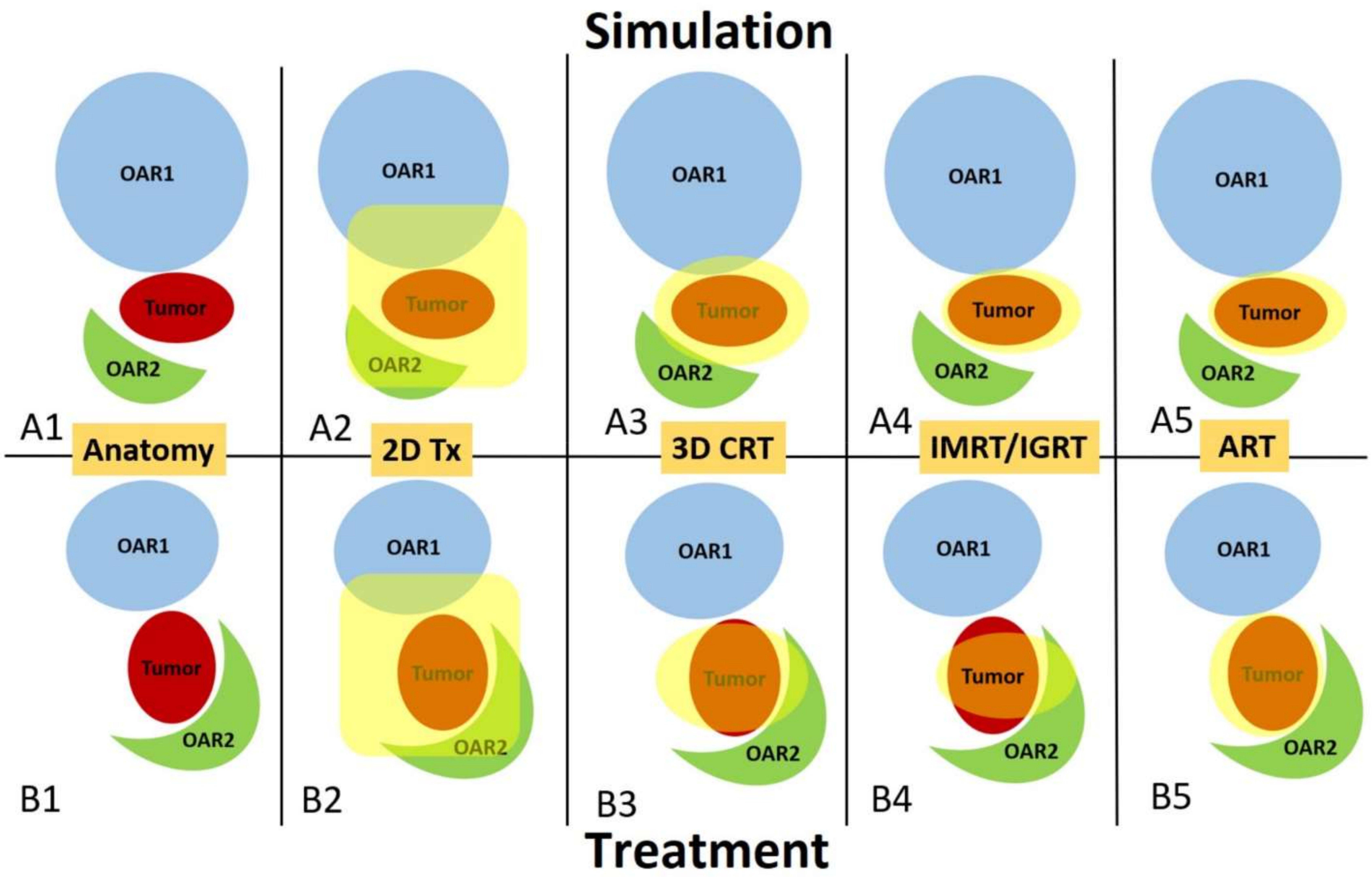
Dosimetric Consequences of Random Changes



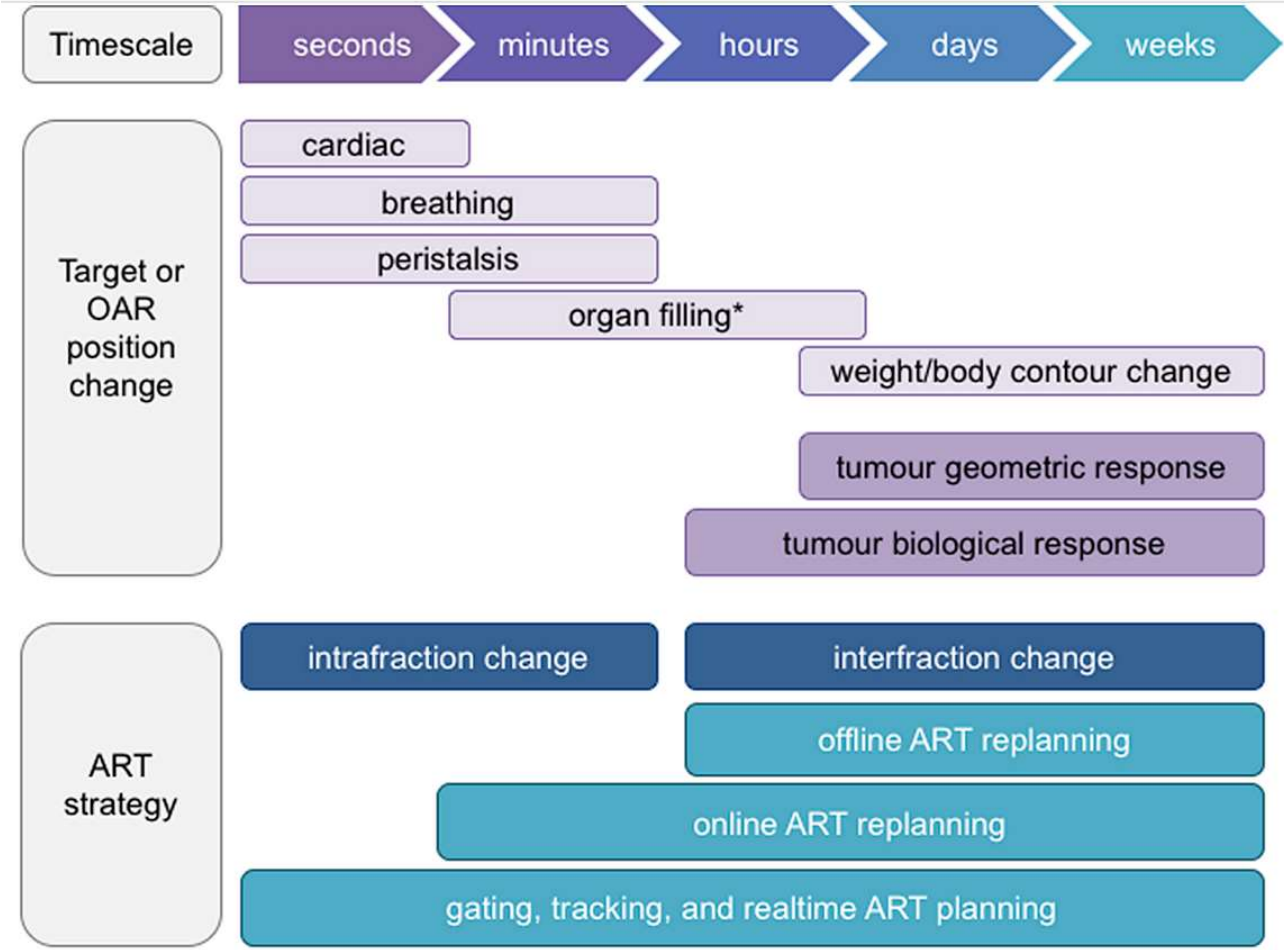
Plan DVH

39 “true” DVHs

Why do we need ART? Impact of Technique



Adaptive Strategies



ART Workflow

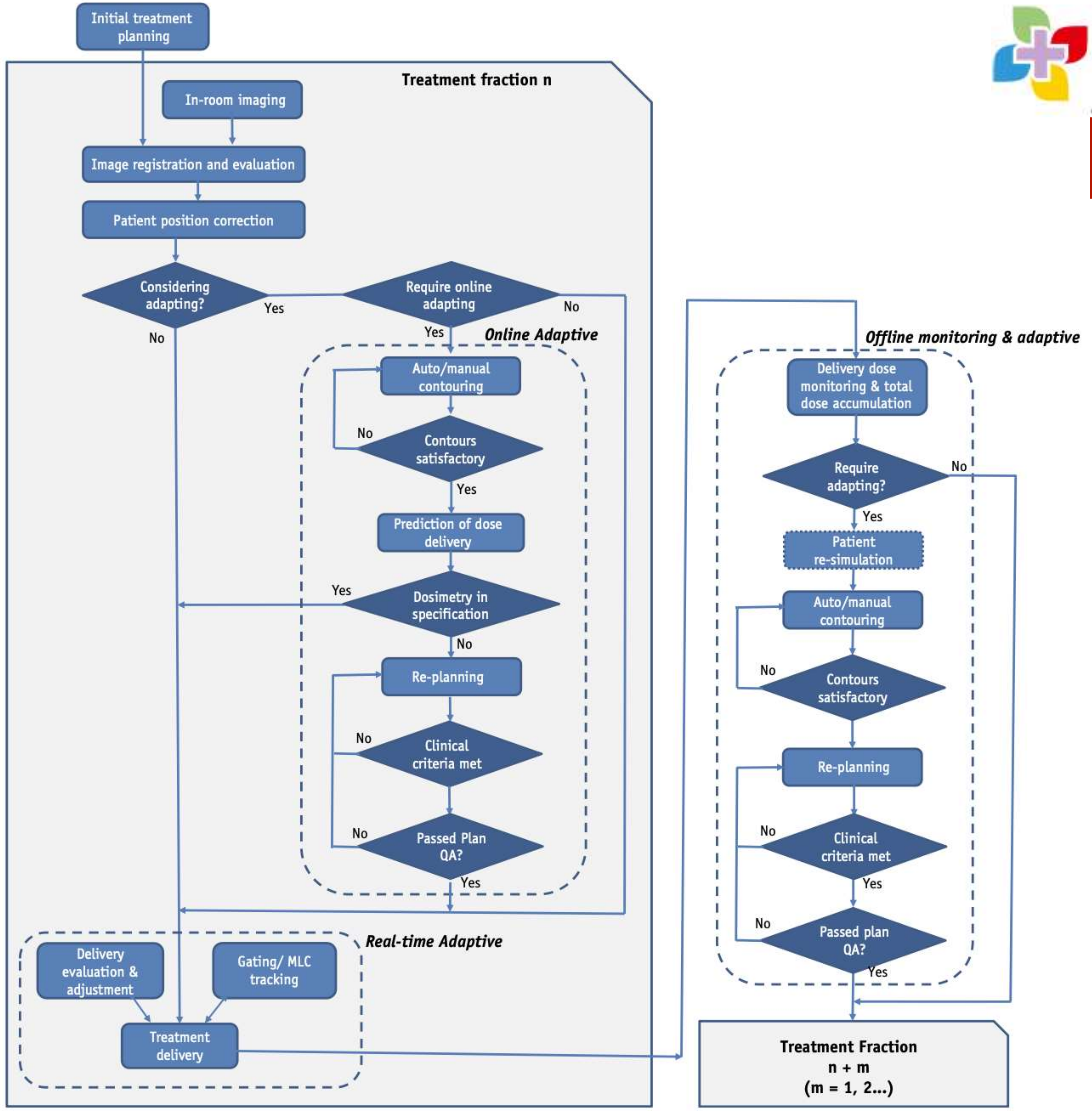
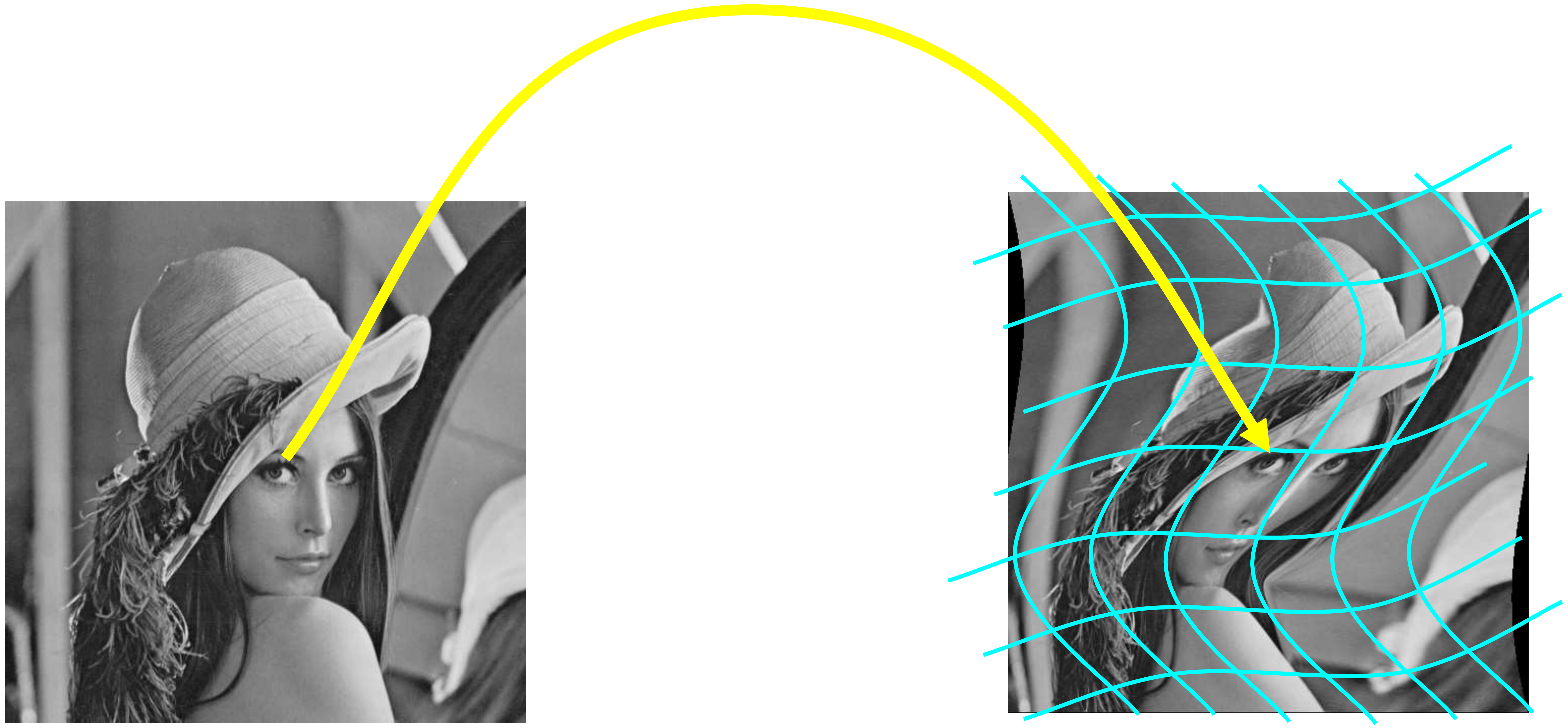


Image Registration

- Rigid
- Deformable (non-rigid)



Fixed Image

Moving Image

Slide Courtesy: Dr Saurabha Kumar

Fixed image

Slide Courtesy: Dr Saurabha Kumar

Moving image

Slide Courtesy: Dr Saurabha Kumar

Registered image

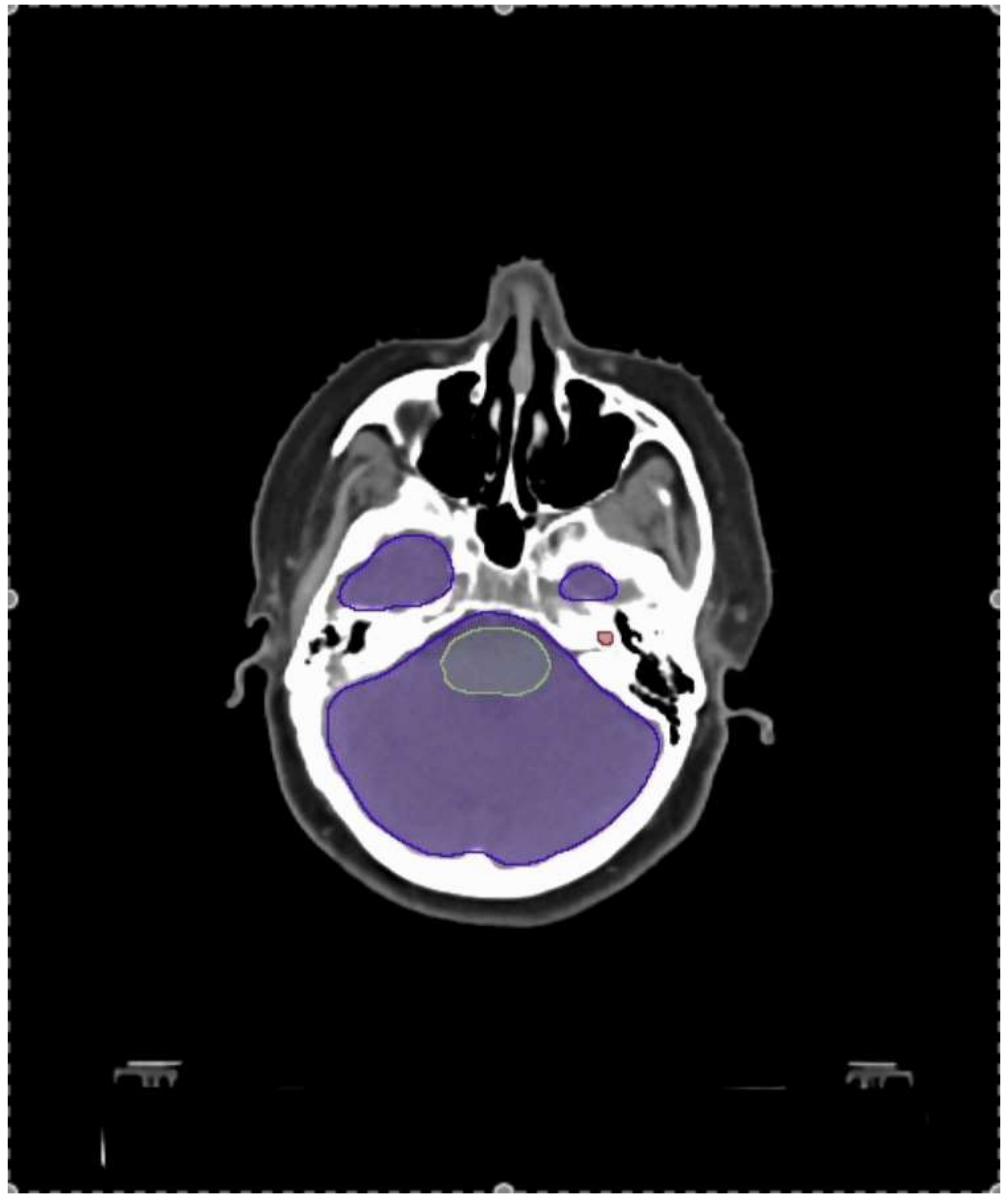
Slide Courtesy: Dr Saurabha Kumar

Registered image

Slide Courtesy: Dr Saurabha Kumar

Auto-Segmentation

- Utility:
  - Efficiency
  - Consistency
  - Workload Reduction
  - ? Accuracy
- Methods:
  - Atlas-Based Methods
  - Deep Learning models, particularly convolutional neural networks
- Examples: Limbus AI/ GE HealthCare Auto Segmentation/ MVision AI



Adaptive Planning: Average Anatomy Model

- Relies on quantification of anatomical changes over the first few of fractions
- An average anatomy model can be estimated by

(1) deformable registration of the planning scan to the scans of the initial fractions,

(2) calculating the average deformation vector field

(3) deforming the planning scan and corresponding structures accordingly to obtain a synthetic scan representing the average anatomical configuration.

- A new treatment plan can subsequently be optimized on the average anatomy model

Adaptive Planning: Library of Plans

- Consists of a library of treatment plans, created “a priori”, to account for expected anatomical changes such as variations in bladder volume
- For each t/t fraction, the best plan from the library is selected, typically using visual comparison
- For practical reasons, only a limited number of plans (2-5) can be generated.
- Application of a LoP strategy is limited to anatomical changes that are dominated by a single variable, such as bladder filling

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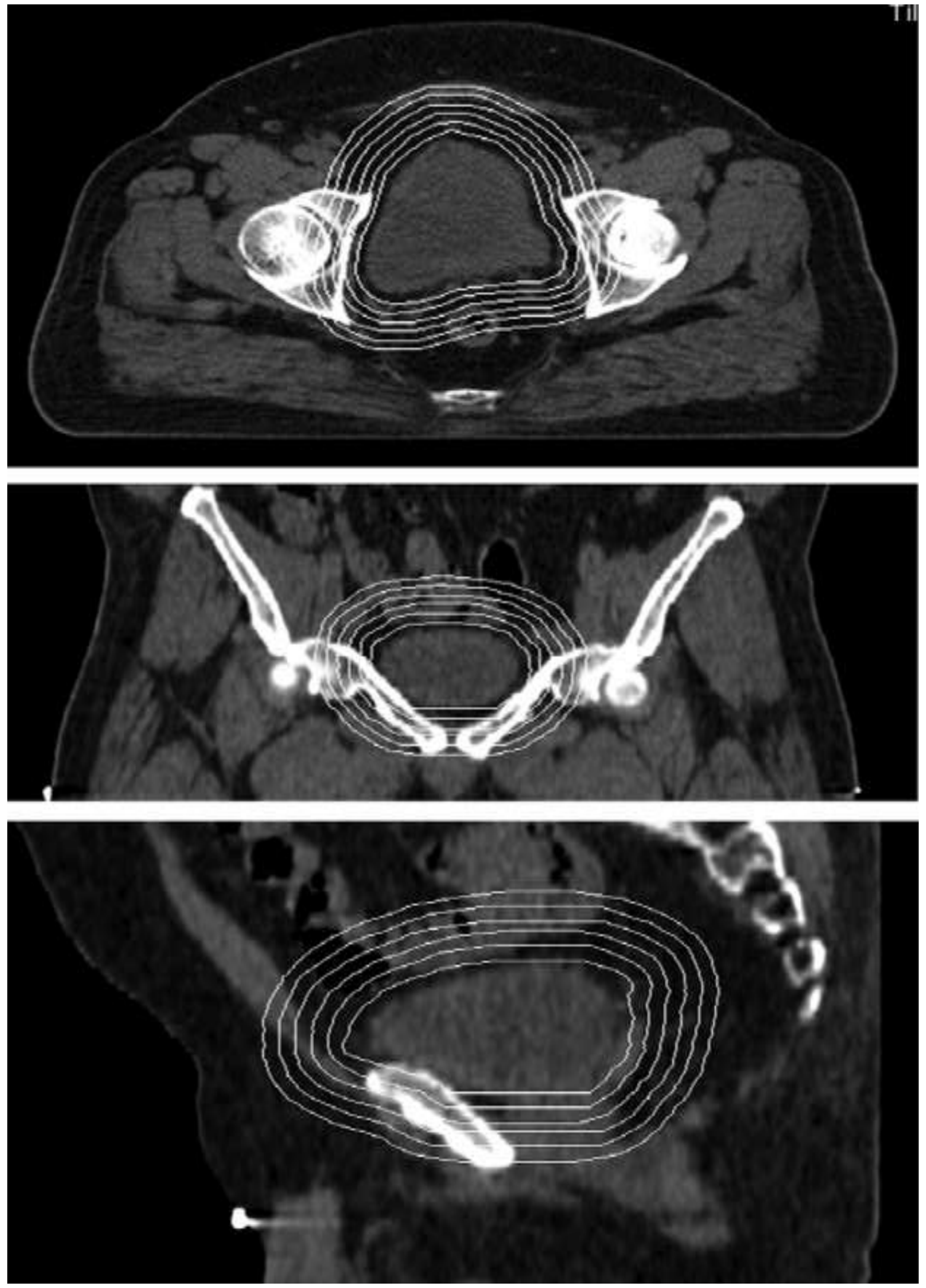
Plan of the Day



Contents lists available at ScienceDirect
Radiotherapy and Oncology
journal homepage: www.thegreenjournal.com
ELSEVIER

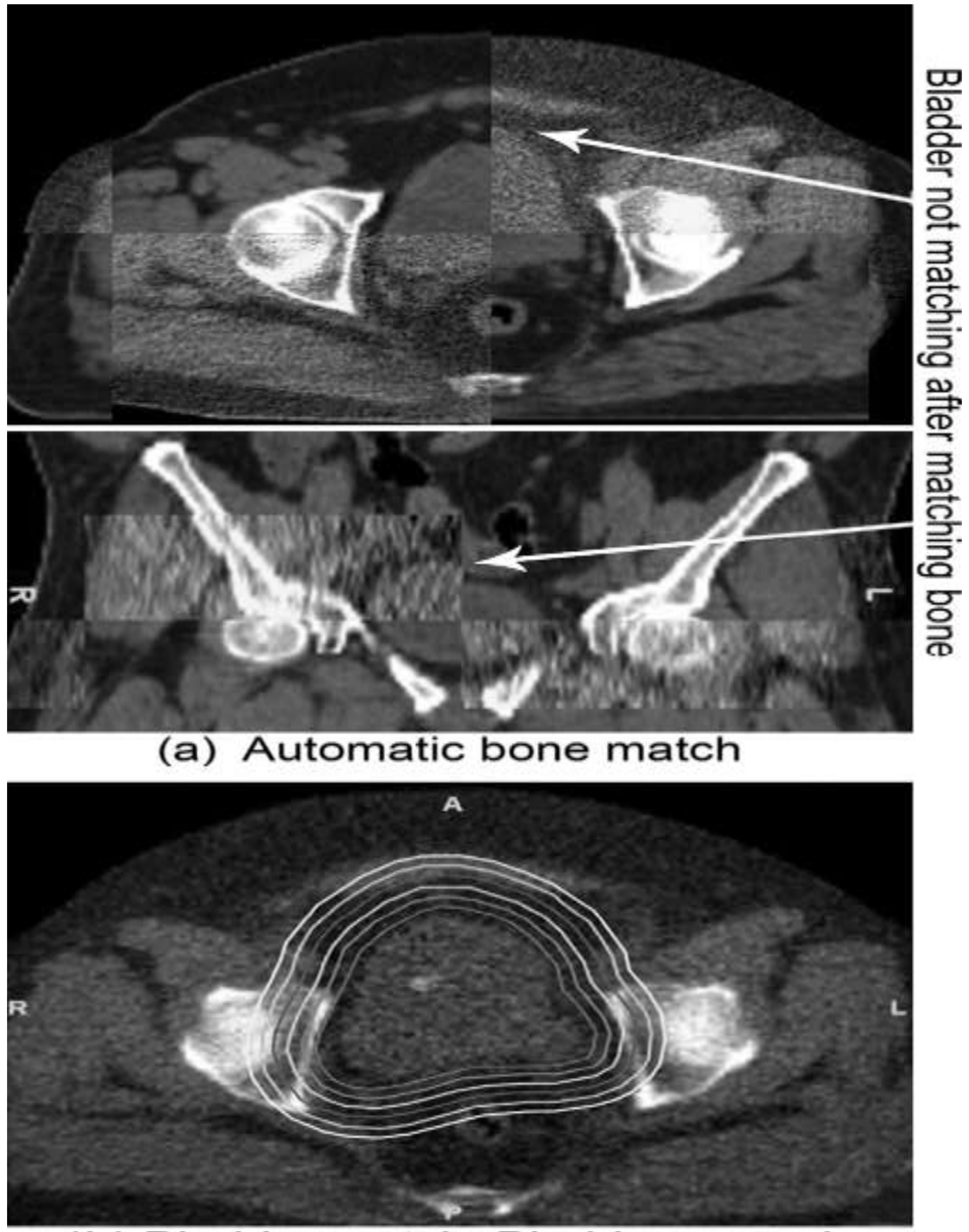
Adaptive radiotherapy

'Plan of the day' adaptive radiotherapy for bladder cancer using helical tomotherapy

Vedang Murthy [a,*], Zubin Master [b], Pranjal Adurkar [b], Indranil Mallick [a], Umesh Mahantshetty [a], Ganesh Bakshi [c], Hemant Tongaonkar [c], Shyamkishore Shrivastava [a]

[a] Department of Radiation Oncology; [b] Department of Medical Physics, Tata Memorial Centre, Mumbai, India; [c] Department of Urology, Tata Memorial Hospital, Mumbai, India

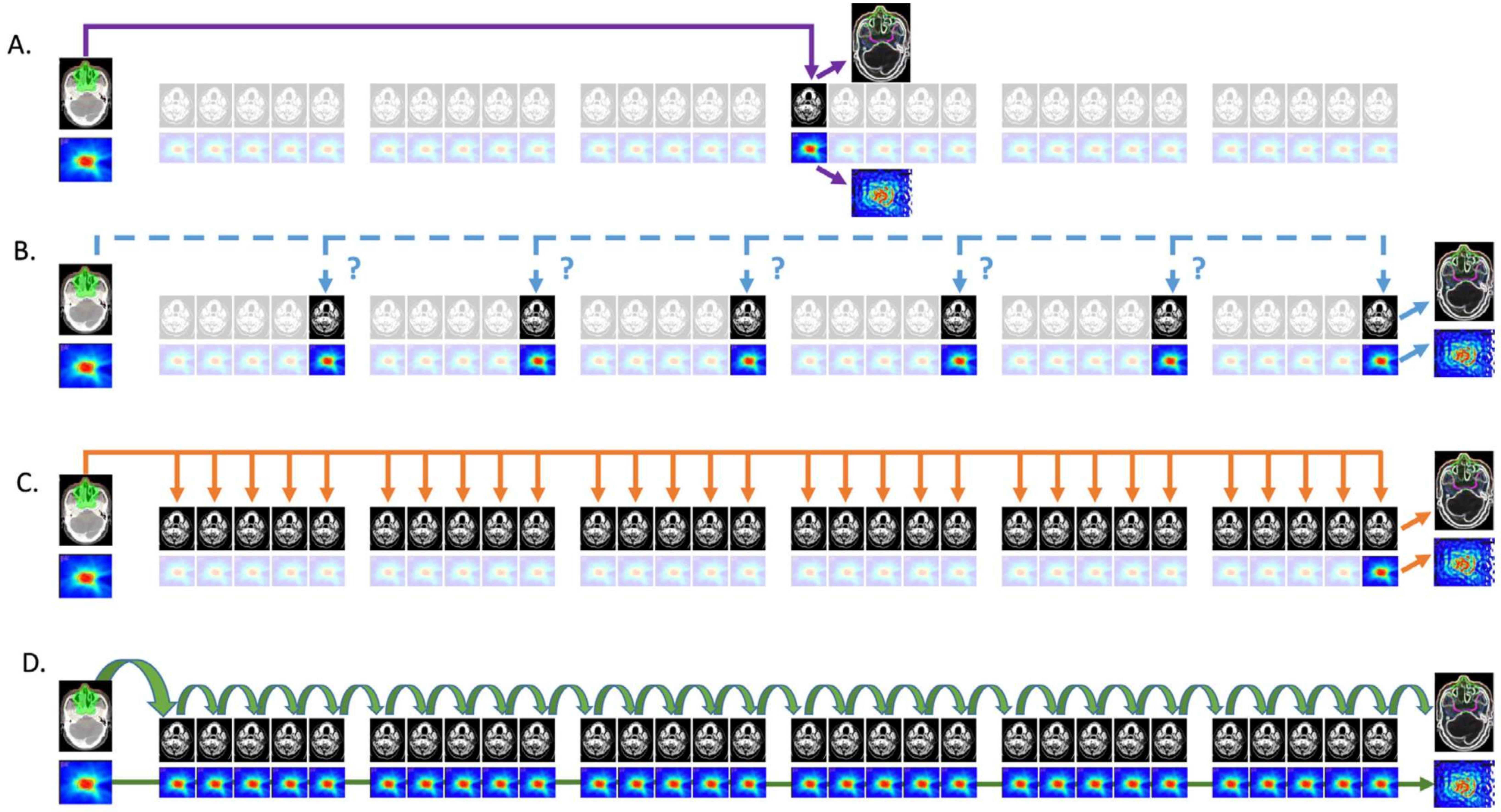
- 6 PTVs for each patient 5 mm to 30 mm isotropically →6 separate IMRT plans
- Treated using Helical tomotherapy with daily MVCT



(a) Automatic bone match

(b) Bladder match: Bladder moved to fit into 5mm PTV

Types of ART Implementation



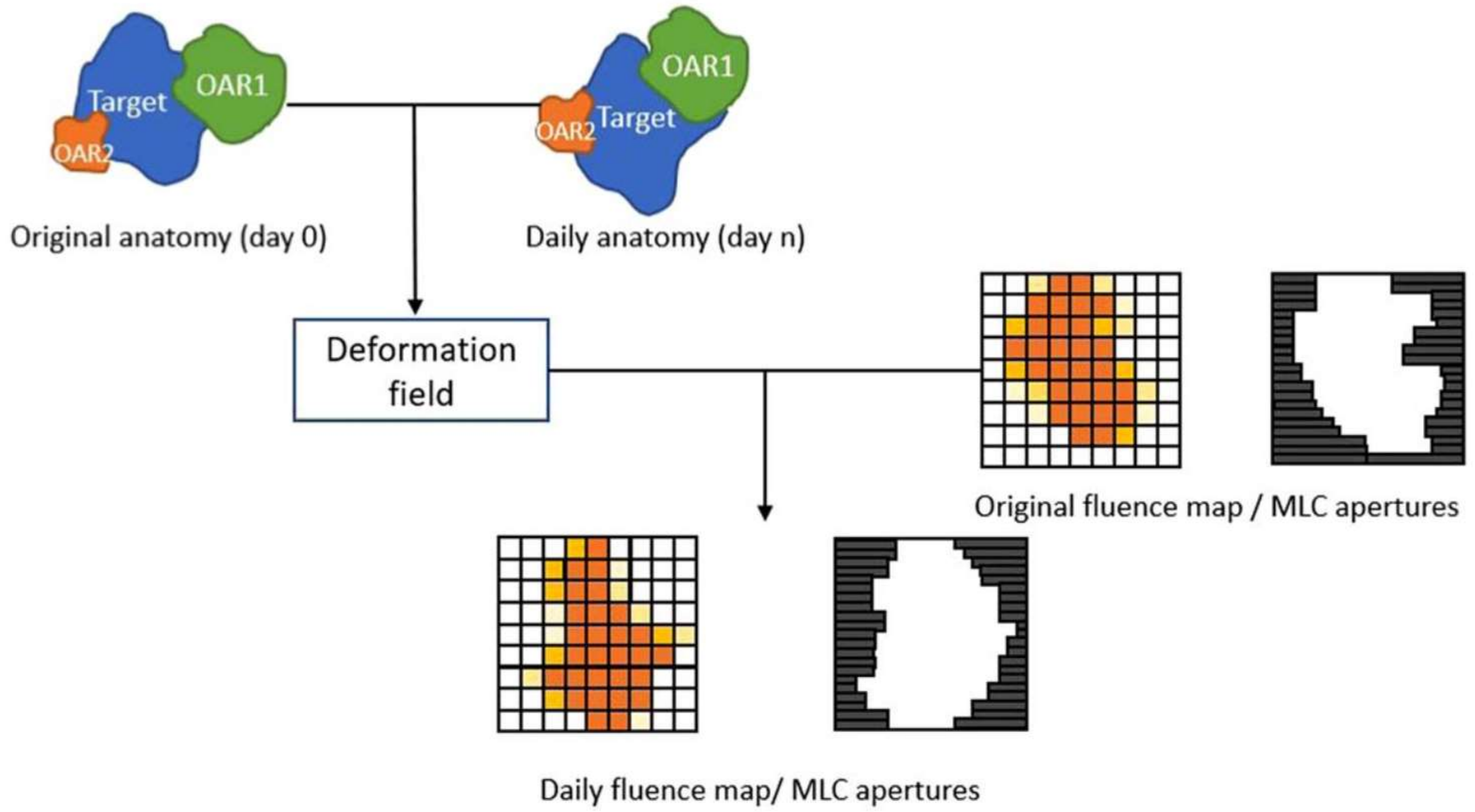
- A. Fixed - interval
- B. Triggered
- C. Serial
- D. Cascade

Online ART

- Useful when tumor or OAR's location and shape may vary on a day-to-day basis, especially in the high dose gradient zone
- Relies on on-couch volumetric imaging techniques for immediate visualization of pt's anatomy and tumor position before each t/t session
- Utilizes advanced TPS that can quickly process imaging data and make in-session adjustments to the t/t plan.
- AI and ML algorithms are increasingly integrated to increase efficiency of in-session adaptations

Rapid Replanning

- In order to minimise replanning times - >
- 1) Plan Deformation method: maintain the initial treatment plan's beam angles and isocenter position; change only the fluence and segment shapes
- 2) Re-optimization method: use the final objective of the initial plan to re-optimize the plan on the new anatomy



QA for Online ART

- Pretreatment, measurement-based patient-specific QA is not practical
- Accuracy of predicted dose delivery is not the most important safety concern
- Fundamentals concerns:

  1) fidelity and reliability of the pretreatment image

  2) re-contouring sufficient to capture the new positions of the OARs and/or target

  3) accurate representation of the relative electron density

- Verify performance of individual machine components by analyzing the machine delivery log files after each t/t
- Portal dosimetry and exit dose analysis

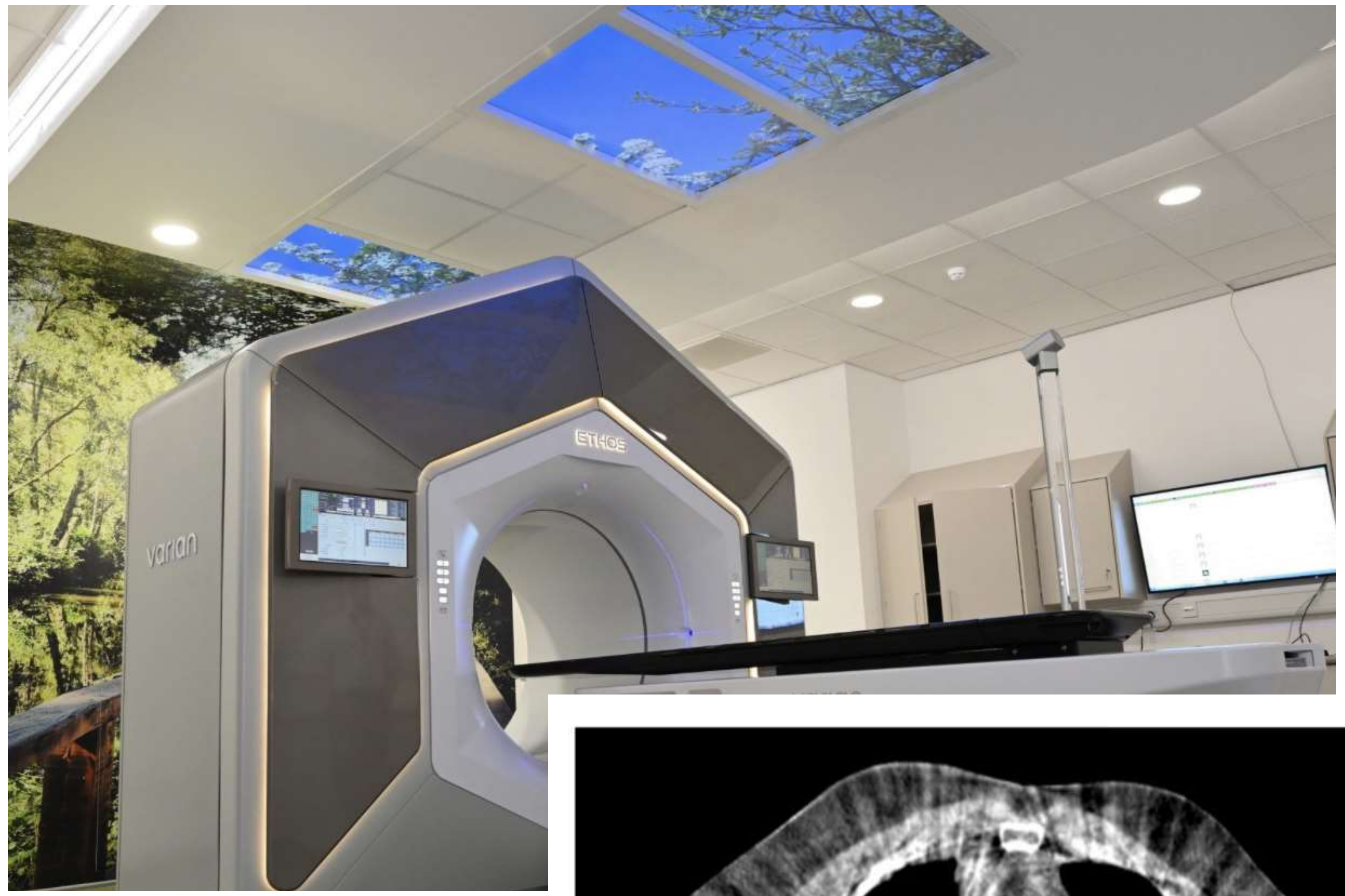
Real-time ART: See - Think - Act

- Respiratory, circulatory, digestive, and muscular systems cause tumor motion on subsecond to minute timescales
- Real-time adaptation of RT t/t delivery increases targeting accuracy of moving lesions fundamentally improving safety and efficacy
- Systems designed for real-time target tracking: CyberKnife (Accuray), Radixact (Accuracy), Vero (Brainlab), Unity (Elekta) or by MLC tracking/ gating
- Calypso 4-D Localization System - using implanted electromagnetic transponders

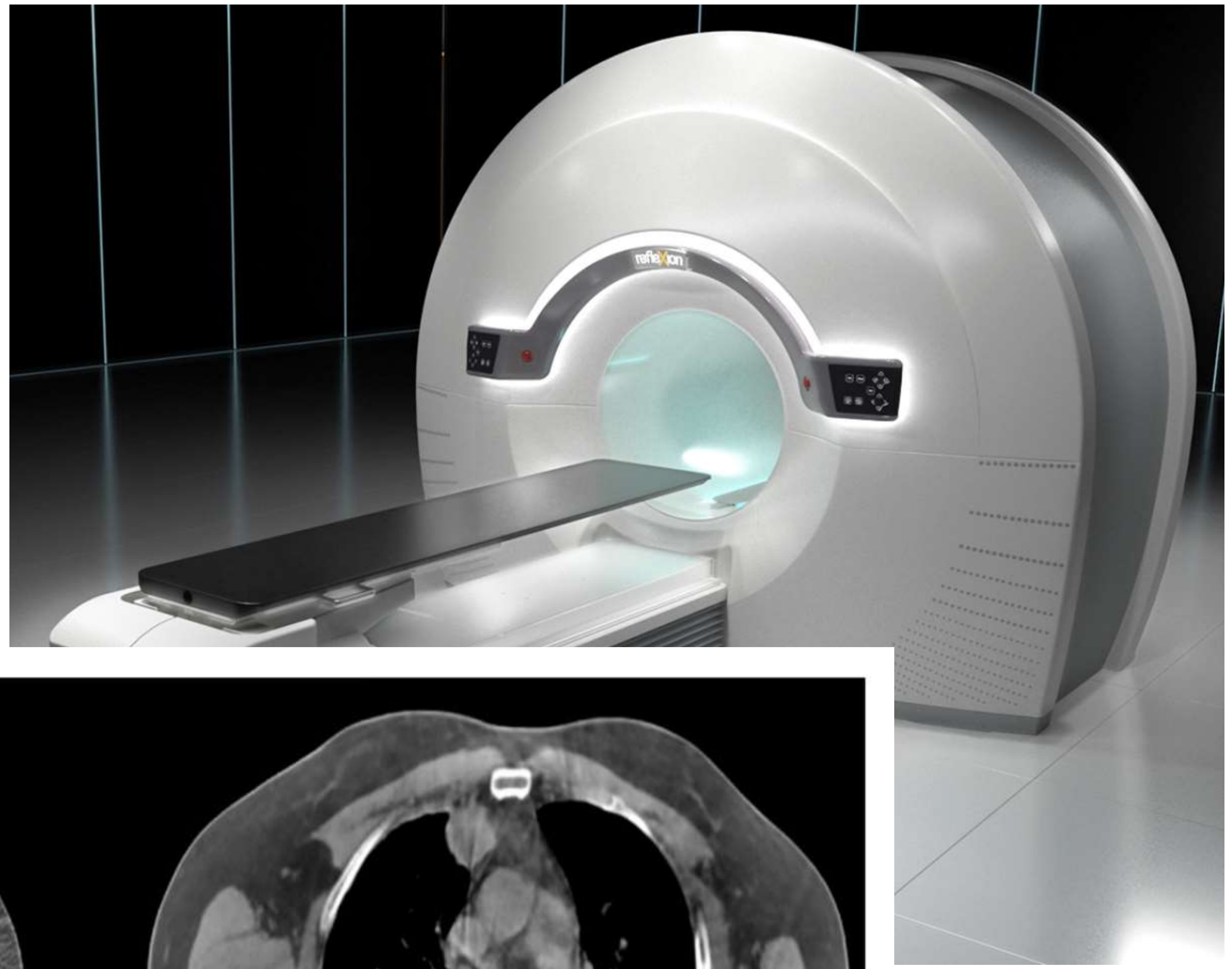
Online ART systems

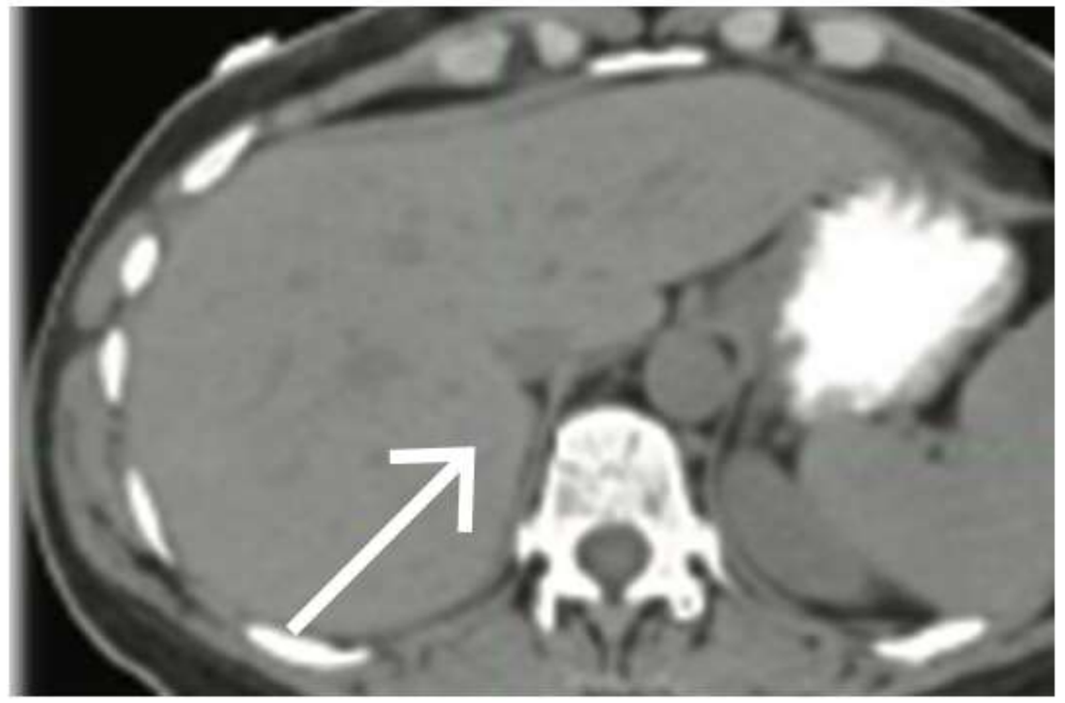
Unity

Ethos

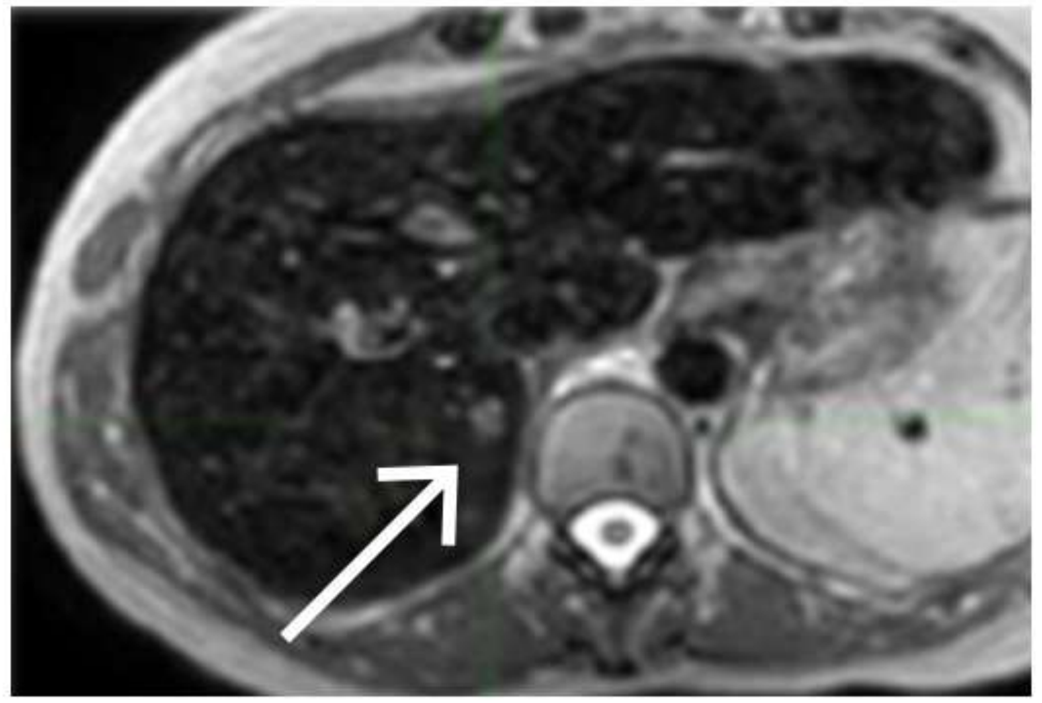


RefleXion

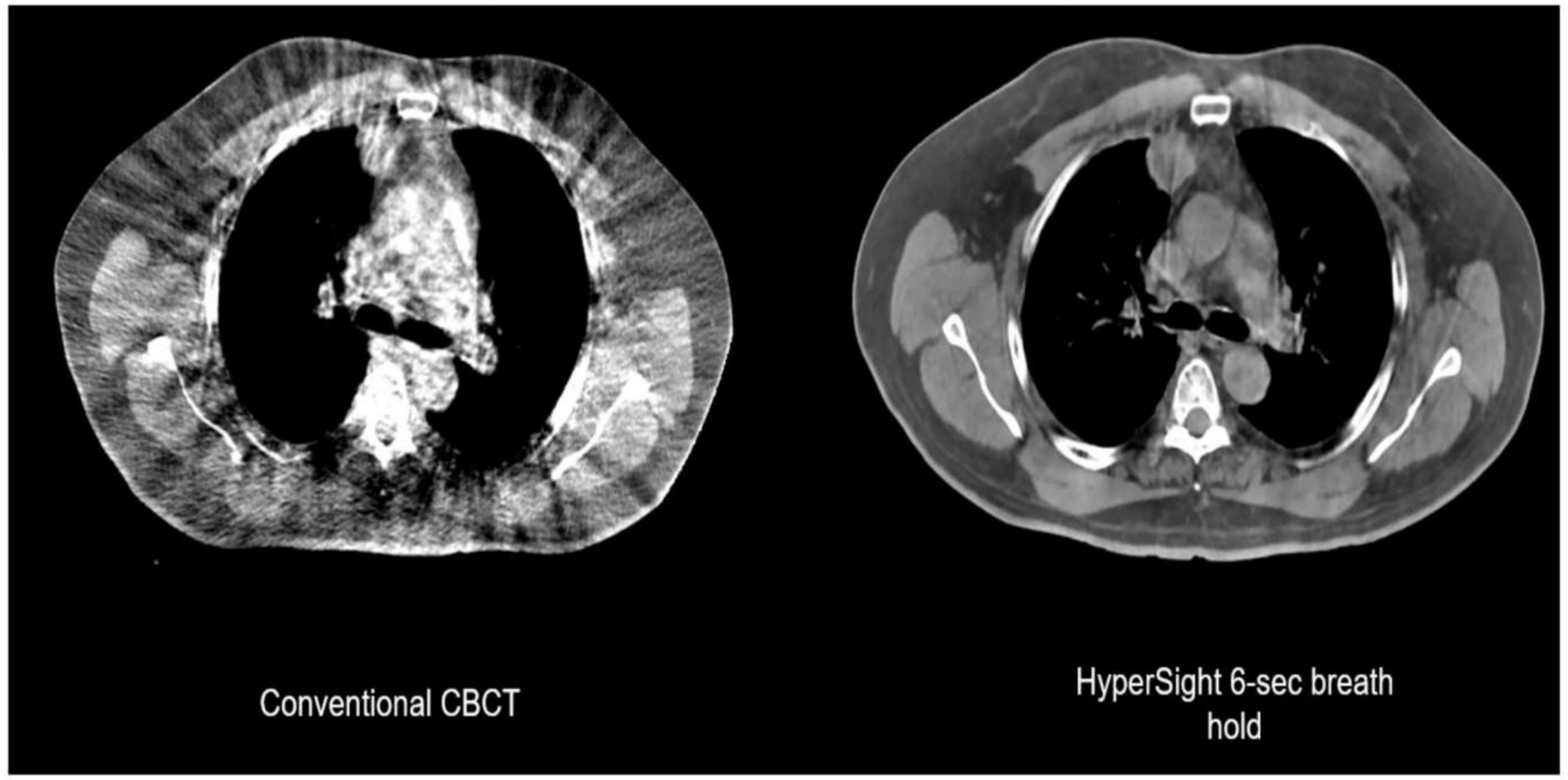




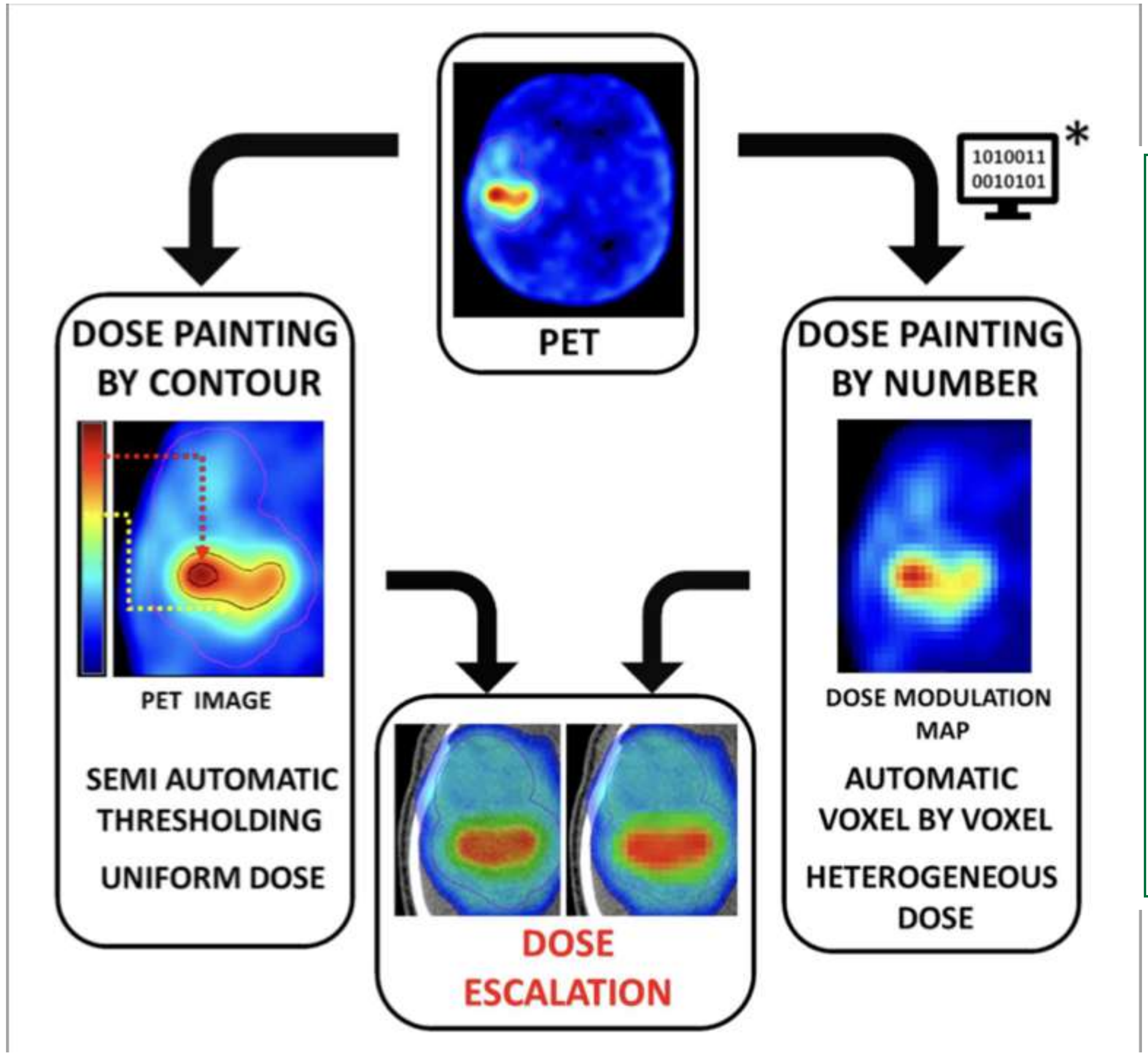
CT

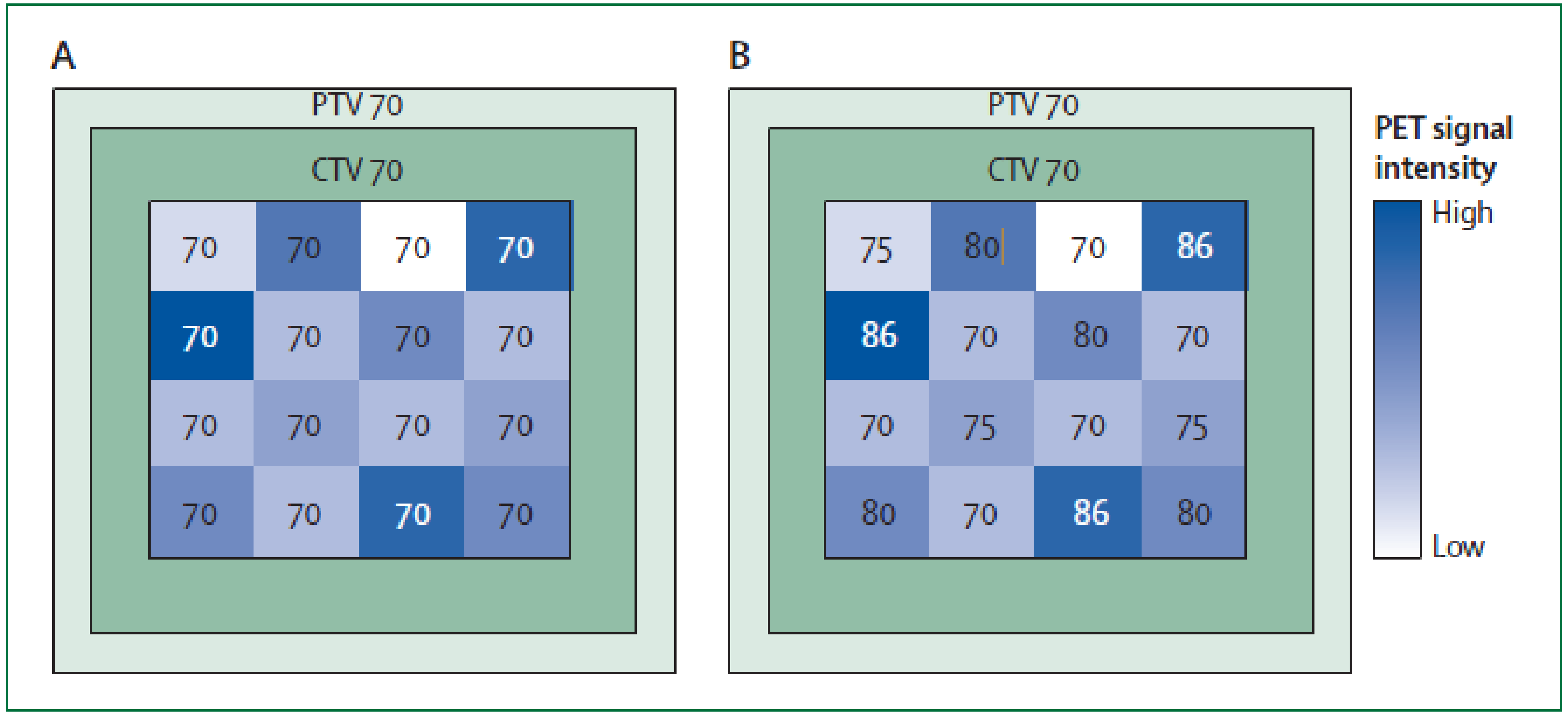


MRI



Biological Adaptive RT





When to Adapt? Frequency of Adaptation

- Optimal timing and frequency of adaptation depends on:

  1) anatomic changes characteristic of the treatment site

  2) time interval of anatomic change

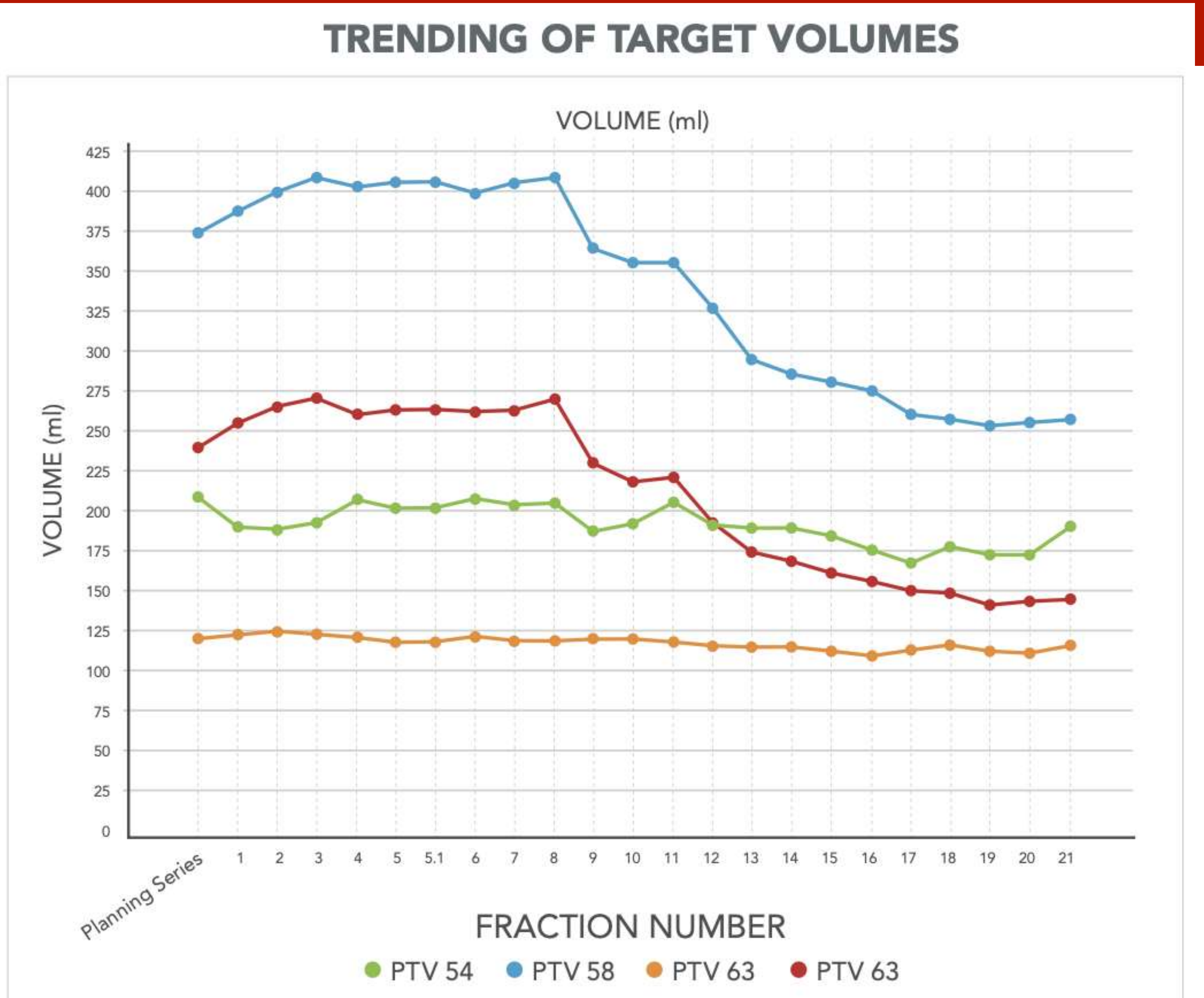
  3) proximity of a given target or an OAR to a steep dose gradient

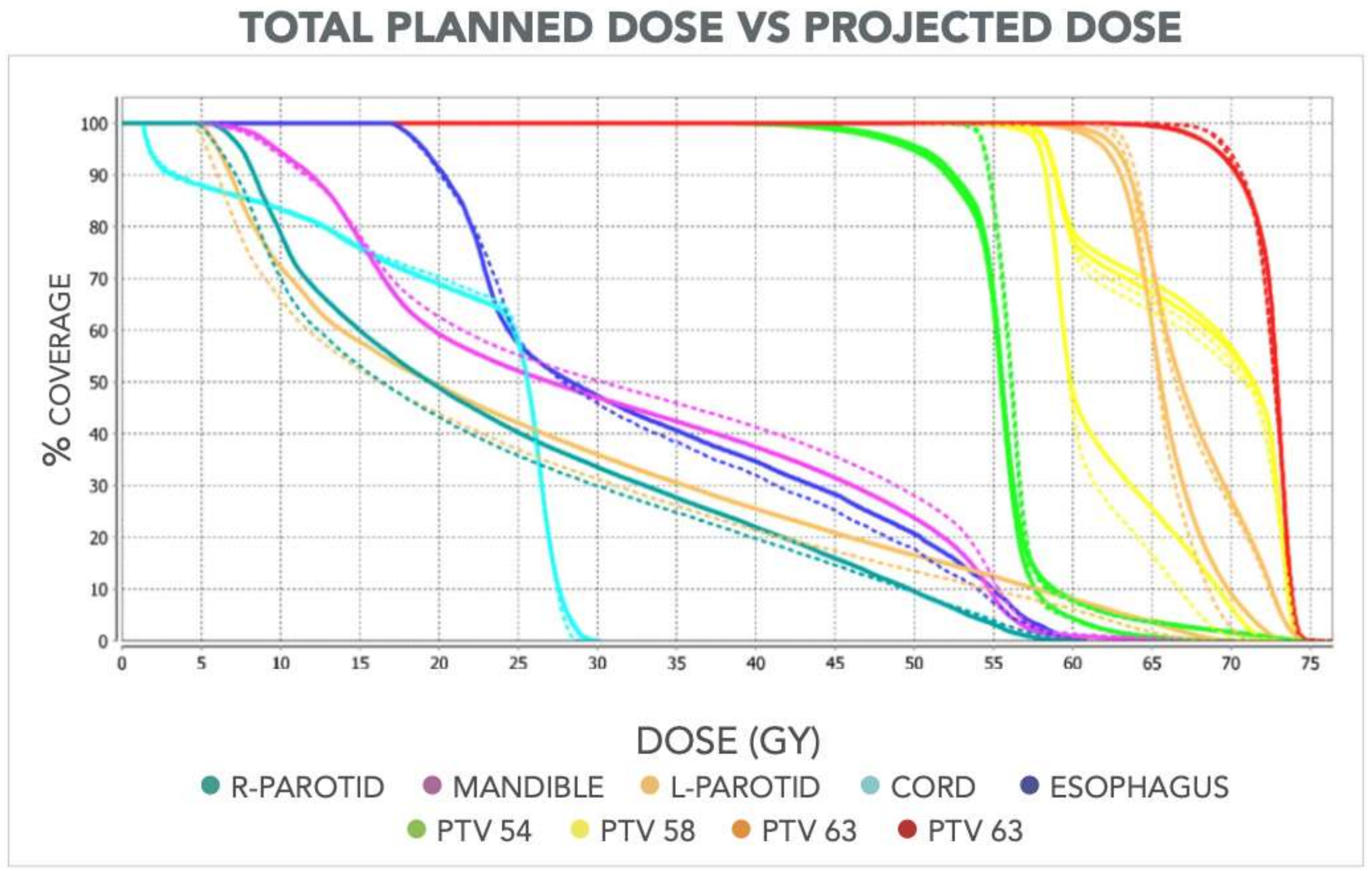
- Timing and frequency of adaptation should balance objectively the clinical value added to pt with considerations of finite resources of the clinic

Precise ART tool

- Allows for automated dose monitoring that may be reviewed offline to assess the need for adaptation

- Automatically creates the merged daily and plan images, deforms the plan contours, calculates dose on the daily image, accumulates the daily dose onto the planning CT, and generates a structured report with dose-volume data





Patterns of Practice

X H&N dominates the adaptive replanning needs

X Offline adaptive is more common
Online protocols (17%) represent the plan library approach and does not include daily replanning.

Table 1
Percentages of respondents (*N* = 177) that apply certain types of ART for specific tumour sites or overall.

Type of adaption	Online plan library	Online daily replanning	Offline protocol	Online or offline protocols	Offline ad-hoc	Any ART
Bladder	15%	0	1%	16%	11%	**27%**
Cervix	6%	2%	5%	13%	19%	**32%**
Rectum	1%	2%	2%	5%	13%	**18%**
Prostate[1]	<1%	3%	6%	10%	18%	**28%**
Head and Neck	0	0	10%	10%	45%	**55%**
Lung	0	0	8%	8%	28%	**36%**
Breast[1]	0	0	<1%	<1%	5%	**6%**
Any site	**17%**	**6%**	**15%**	**31%**	**50%**	**61%**

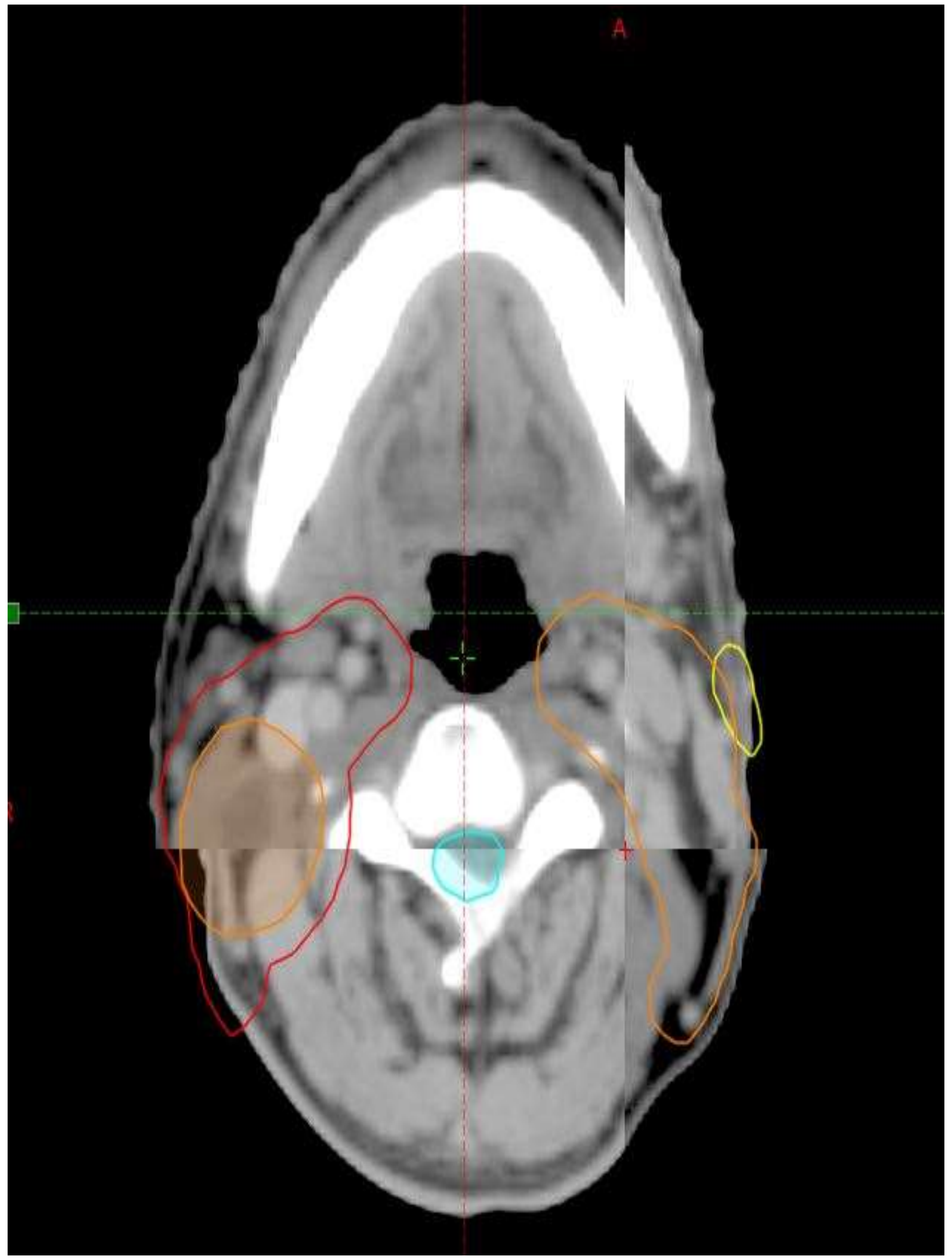
[1] Unspecified type of adaption for one user each.

X Online adaptive replanning is not routine
It was clear that good image quality and high soft-tissue contrast were needed for online daily replanning: 10 users used MR imaging and one used CT.

Radiotherapy and Oncology, Volume 153, December 2020, Pages 88-96

Where ART shines?

- Head & Neck: Tumor shrinkage, salivary gland sparing
- Lung: Atelectasis, tumor motion
- Prostate: Bladder/rectum position variability
- Cervix: brachytherapy boost adaptation
- SBRT of abdominal targets (liver/ pancreas etc)



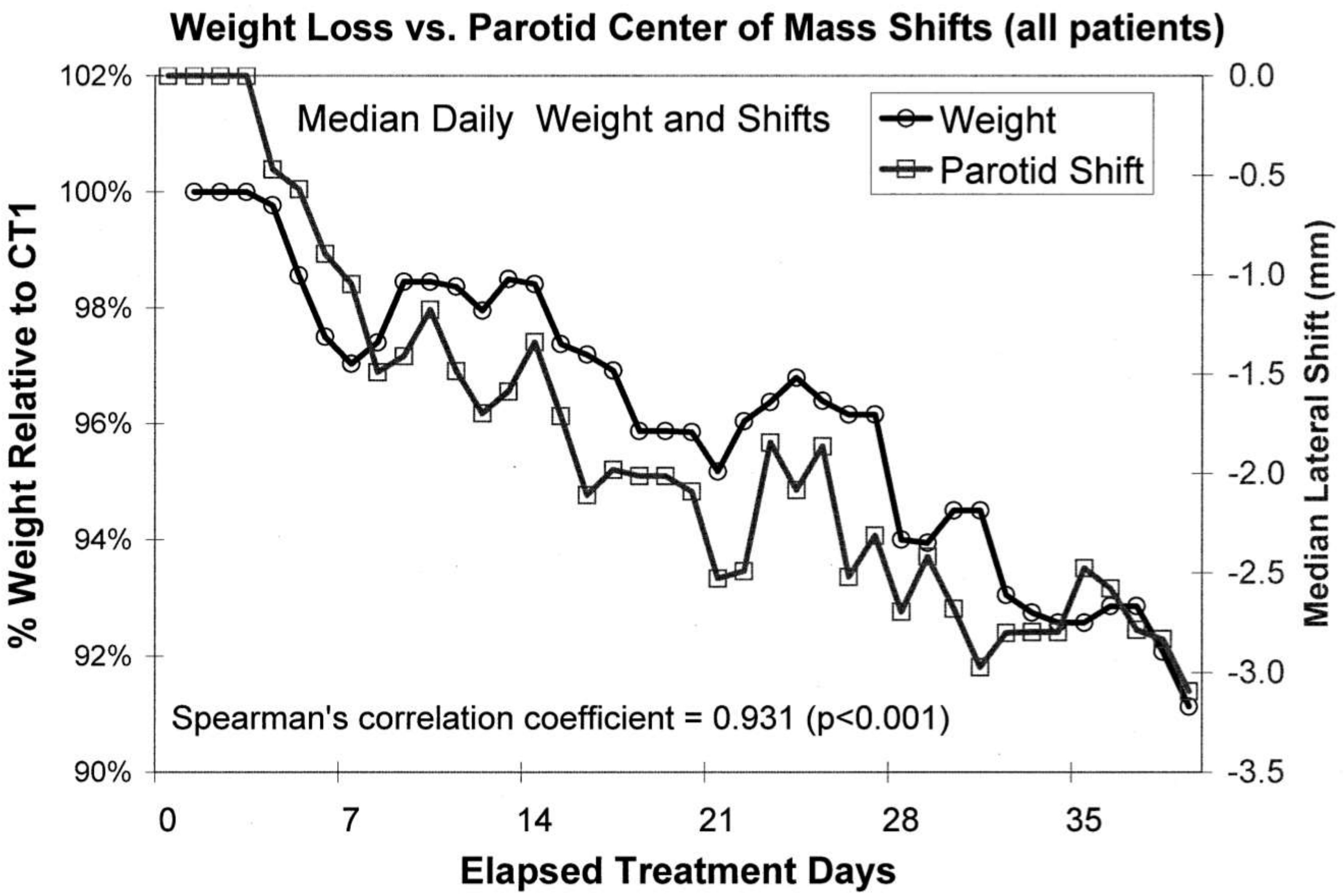
Head and Neck tumors

- Barker et al: quantitative assessment of tumor and parotid alteration via daily imaging in head and neck cancer pts

- Demonstrated a 70% reduction in GTV volume with a median mass displacement of >3 mm at the end of radiation treatment with significant alterations in parotid volumes.

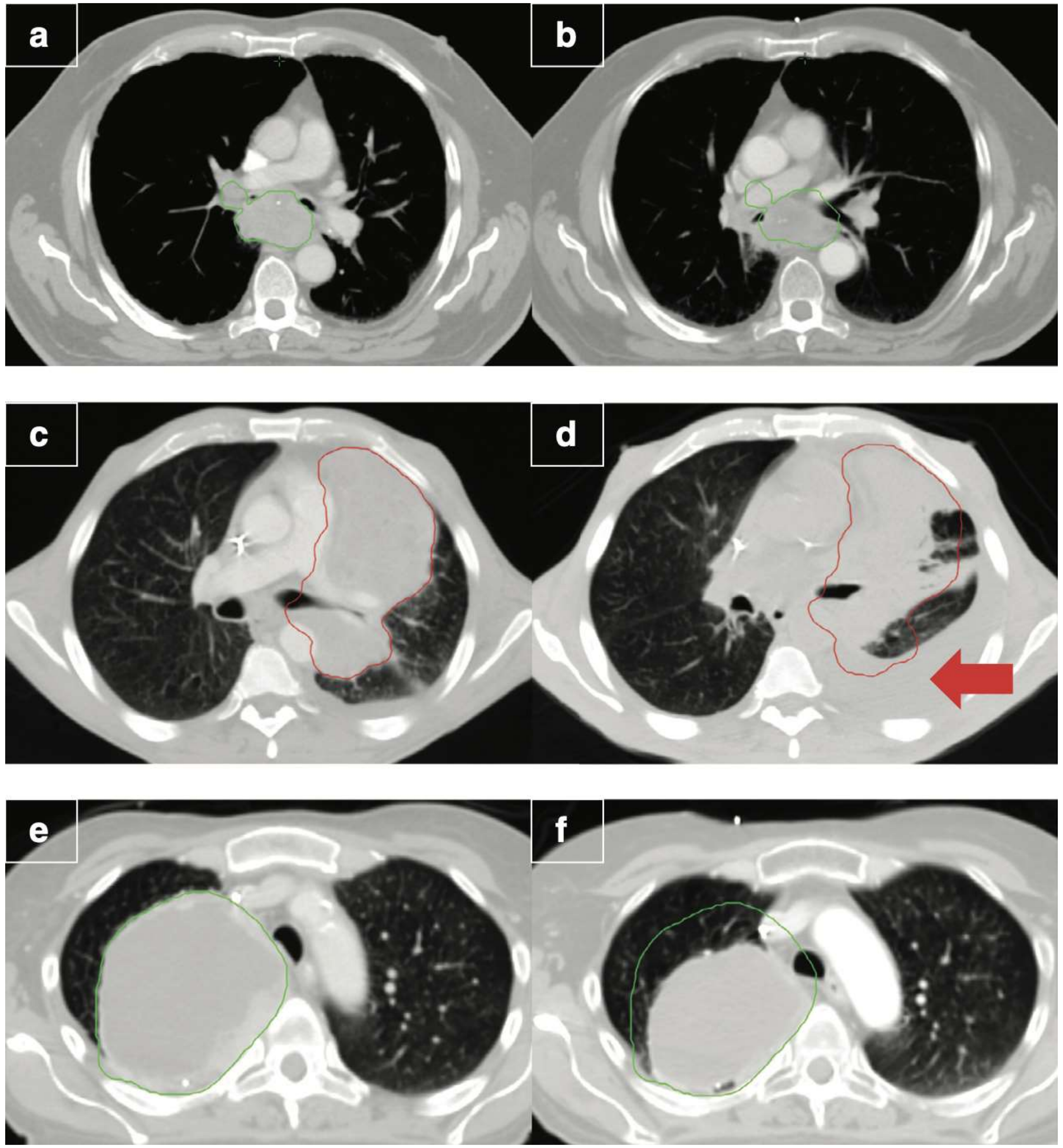
CLINICAL INVESTIGATION **Head and Neck**

QUANTIFICATION OF VOLUMETRIC AND GEOMETRIC CHANGES OCCURRING DURING FRACTIONATED RADIOTHERAPY FOR HEAD-AND-NECK CANCER USING AN INTEGRATED CT/LINEAR ACCELERATOR SYSTEM

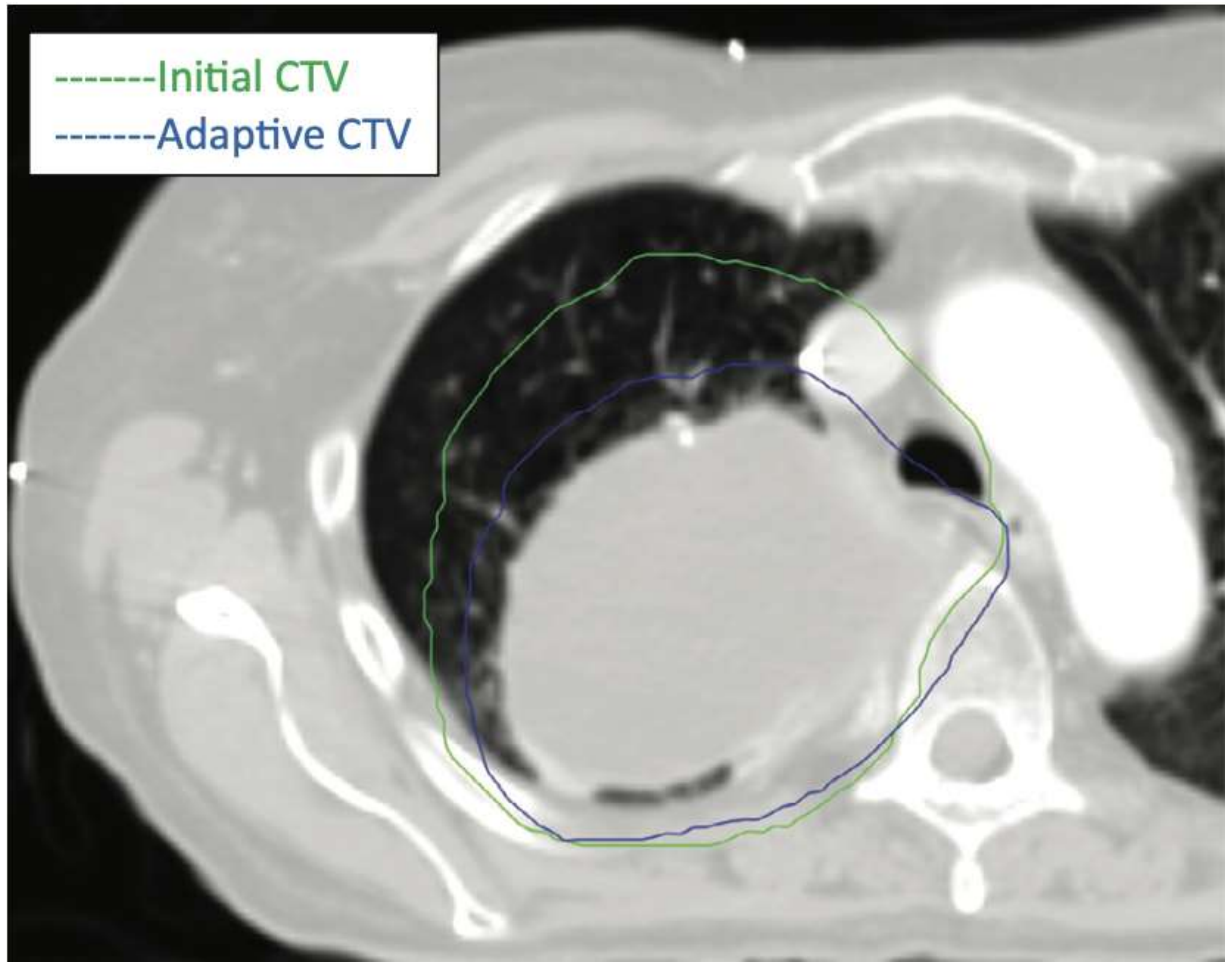


Barker et al. IJROBP 2004

ART in Lung

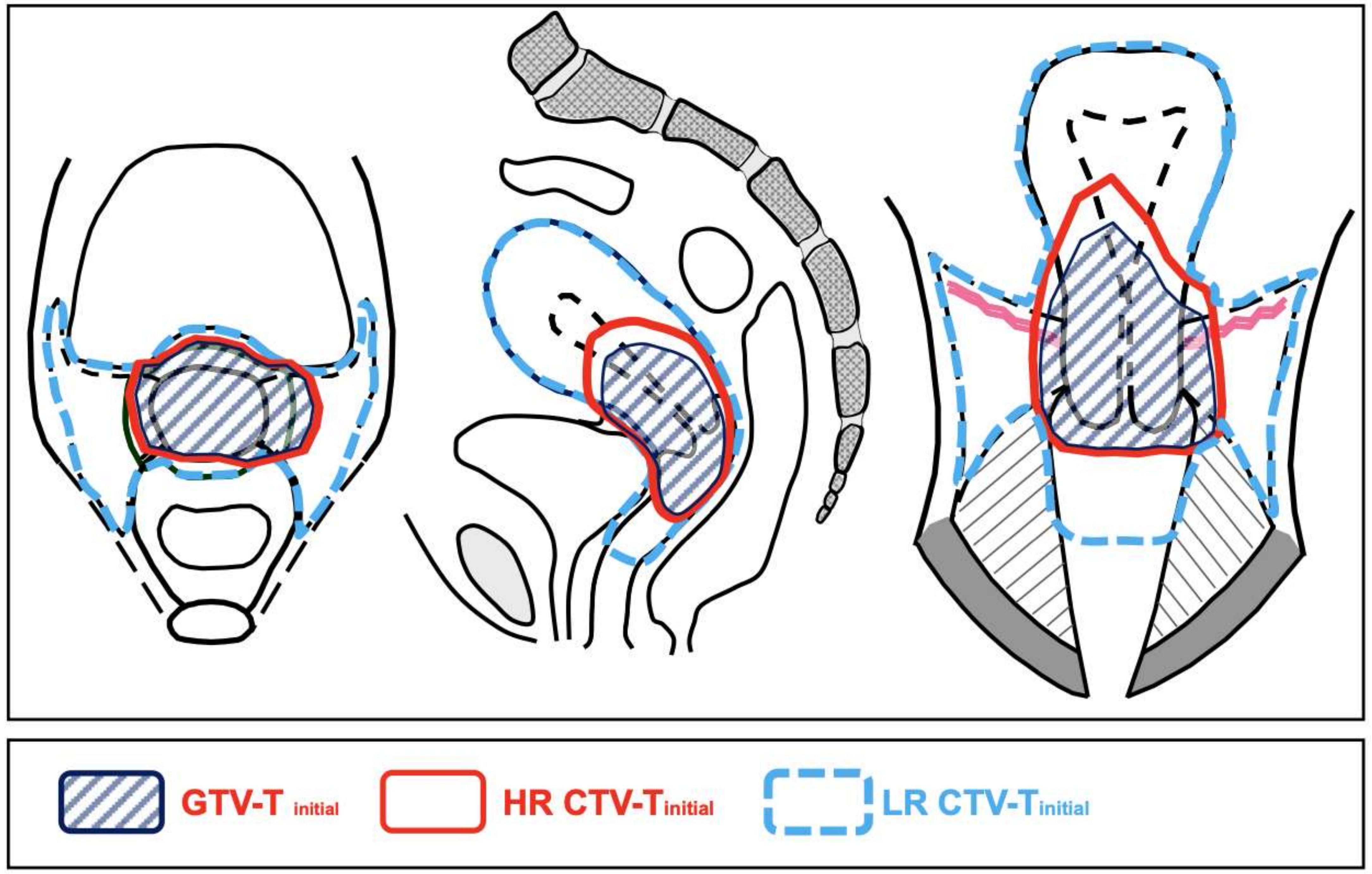


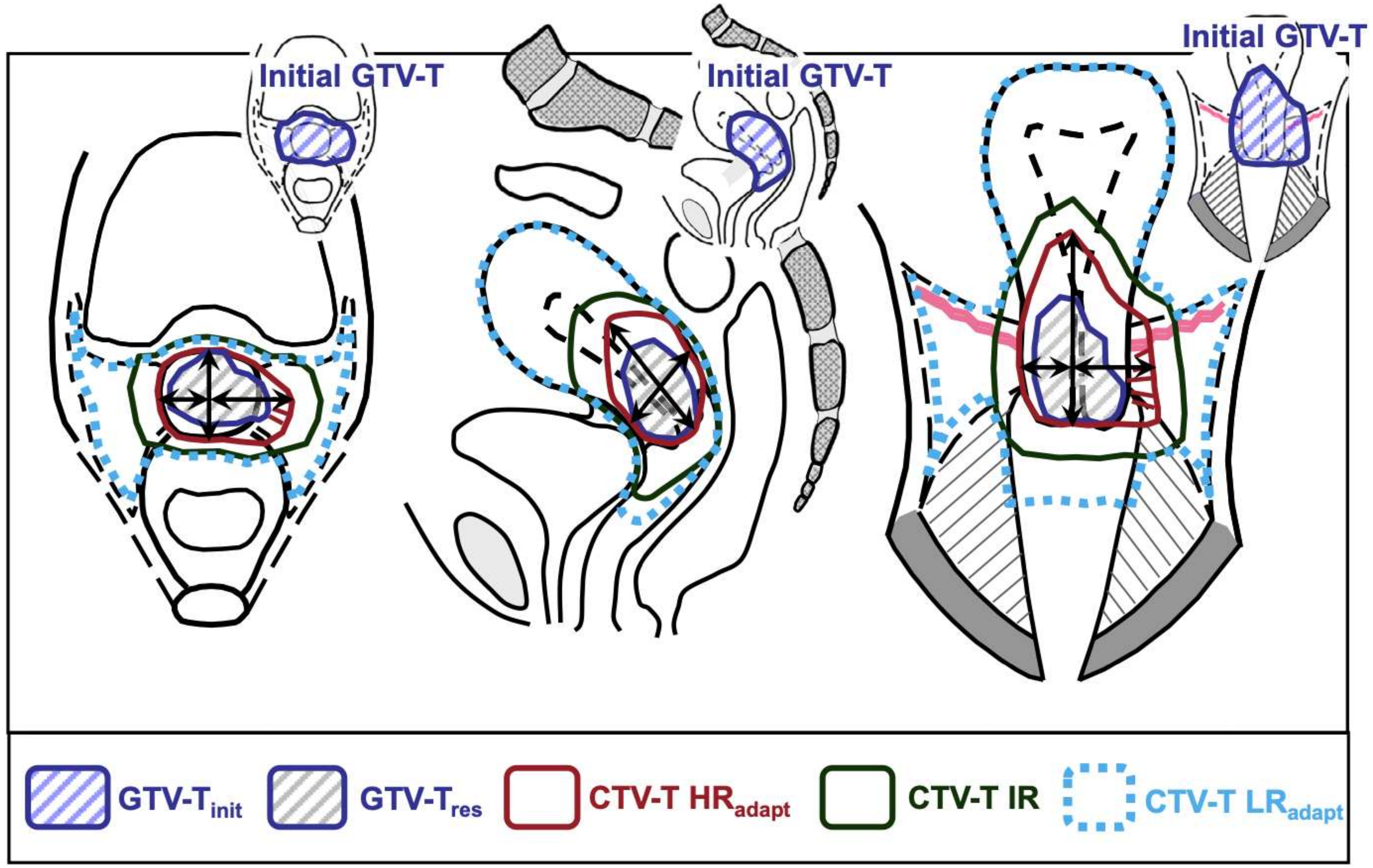
- Tvilum et al: LRC better with ART; no diff in PFS/ toxicity



Tvilum et al. Acta Oncol 54:1430-1437, 2015

Cervical Cancer - Image Guided Brachytherapy





Outcomes with IGBT

Table 1 5-year pelvic failure in Retro-EMBRACE (IGABT) compared with mono- and multicenter historical cohorts[1] and meta-analysis from 2008 on chemoradiation[2] and selected chemoradiation trials[3], all treated with conventional brachytherapy. Crude data are shown for all cohorts (except for Eifel 2004 for IB/IIB and IIIB). For the TATA trials, data are available only for IIIB and IB2/IIB (eligible for surgery), respectively according to the design of these trials. [4]For comparison of the overall pelvic failure rates the different composition of the cohorts in regard to stage has to be taken into account

	n	Stage	IB	IIB	IIIB	Overall[4]	Concomitant Chemotherapy
RetroEMBRACE 2016	731	IB: 17% IIB: 50% IIIB: 20%	4%	11%	25%	13%	77%
Perez 1998[1]	1499	IB: 33% IIB: 29% IIIB: 23%	12%	21%	41%	23%	0%
Barillot 1997[1]	1875	IB: 26% IIB: 29% IIIB: 25%	13%	24%	49%	NA	0%
Vale 2010[1]	471	IB: 11% IIB: 51% IIIB: 23%	NA	NA	NA	22%	100%
Vale 2008[2]	3.128	IB: <24% IIB: 36% IIIB: 38%	NA	NA	NA	23%	50%
Rose 1999[3]	176	IIB: 58% IIIB: 39%	NA	NA	NA	19%	100%
Whitney 1999[3]	169	IIB: 61% IIIB: 34%	NA	NA	NA	>25%	100%
Eifel 2004[3]	195	IB2: 33% IIB: 36% IIIB: 25%	IB2 + IIB: 13%		29%	17%	100%
TATA 2018[3]	317	IB2: 18% IIB: 57%	IB2 + IIB: 14%		-	14%	100%
TATA 2018[3]	424	All IIIB	–	–	29%	29%	100%

Does ART make a difference?

Data Challenging our Optimism

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Primary Results of NRG-RTOG1106/ECOG-ACRIN 6697: A Randomized Phase II Trial of Individualized Adaptive (chemo)Radiotherapy Using Midtreatment ^{18}F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography in Stage III Non–Small Cell Lung Cancer

Authors: Feng-Ming (Spring) Kong, MD, PhD, Chen Hu, PhD, Daniel A. Pryma, MD, Fenghai Duan, PhD, Martha Matuszak, PhD, Ying Xiao, PhD, Randall Ten Haken, PhD, ... SHOW ALL ..., and Mitchell Machtay, MD | AUTHORS INFO & AFFILIATIONS

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Meeting Abstract: 2021 ASCO Annual Meeting I

FREE ACCESS | Symptoms and Survivorship | May 28, 2021

Parotid sparing adaptive radiotherapy in head and neck cancer patients: A study evaluating resource intensiveness and impact on quality of life.

Authors: Shaurav Maulik, Indranil Mallick, Moses Arunsingh, Sriram Prasath, B Arun, and Sanjoy Chatterjee | AUTHORS INFO & AFFILIATIONS

ORIGINAL ARTICLE · Volume 196, 110281, July 2024 Download Full Issue

A multicentric randomized controlled phase III trial of adaptive and 18F-FDG-PET-guided dose-redistribution in locally advanced head and neck squamous cell carcinoma (ARTFORCE)

Anna Liza M.P. de Leeuw [a] · Jordi Giralt [b,c] · Yungan Tao [d] · ... · Coen R.N. Rasch [m] · Jan-Jakob Sonke [a] · Olga Hamming-Vrieze [a] ... Show more

Evidence of ART

Table 3: Clinical Outcomes of Adaptive Radiation Therapy

Clinical Site	ART Type	No. of Patients	Fractionation Scheme	Clinical Outcome: Metric Evaluated	Clinical Outcome: Outcome	Toxicity: Metric Evaluated	Toxicity: Outcome
Oropharyngeal (14)	Offline	22	66–72 Gy, 30–33 fractions	Local control Regional control	100% 95%	Comparison to IMRT	Comparable
NSCLC (30)	Offline	50	45–75 Gy	Local control Median PFS Median OS	70% 8.3 months 30.5 months	Comparison to RTOG 9410 clinical trial	Reduced
Adrenal (36)	Online MRI-guided	52	24–60 Gy, 3–8 fractions			≥ grade 3 toxicity	0%
Prostate (37)	Online MRI-guided	101	36.25 Gy, 5 fractions			≥ grade 2 early GI toxicity ≥ grade 2 early GU toxicity Comparison to HYPRO study	23.8% 5% Reduced
Lung (38)	Online MRI-guided	50		12 months, local control 12 months, OS 12 months, DFS	95.60% 88% 64%	≥ grade 2 toxicity ≥ grade 3 toxicity	30% 8%
Abdomen (22)	Online MRI-guided	20	50 Gy, 5 fractions	6 months, PFS 12 months, OS	89.10% 75%	≥ grade 3 acute toxicity	0%

Impact of AI

- AI-based auto-segmentation algorithms are demonstrating improved accuracy compared to previous model-based and atlas-based algorithms

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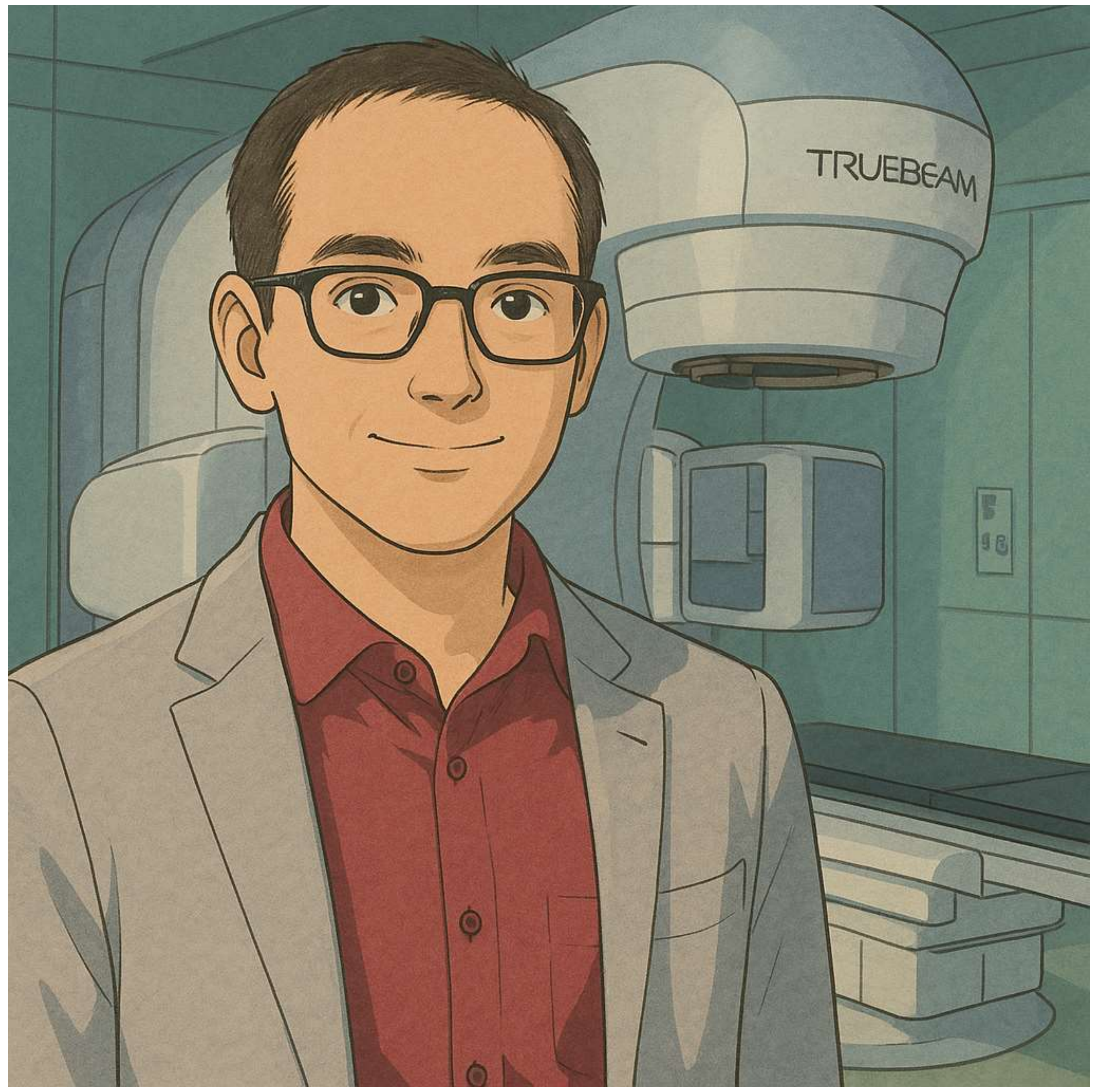


An Artificial Intelligence-Based Full-Process Solution for Radiotherapy: A Proof of Concept Study on Rectal Cancer

Xiang Xia[1,2†], Jiazhou Wang[1,2†], Yujiao Li[1], Jiayuan Peng[1,2], Jiawei Fan[1,2], Jing Zhang[1,2], Juefeng Wan[1,2], Yingtao Fang[1,2], Zhen Zhang[1,2] and Weigang Hu[1,2*]*

- 7 minutes
- 80% cases did not require modifications

Xia et al. Frontiers in Oncology, vol. 10, 2021

Advantage of ART

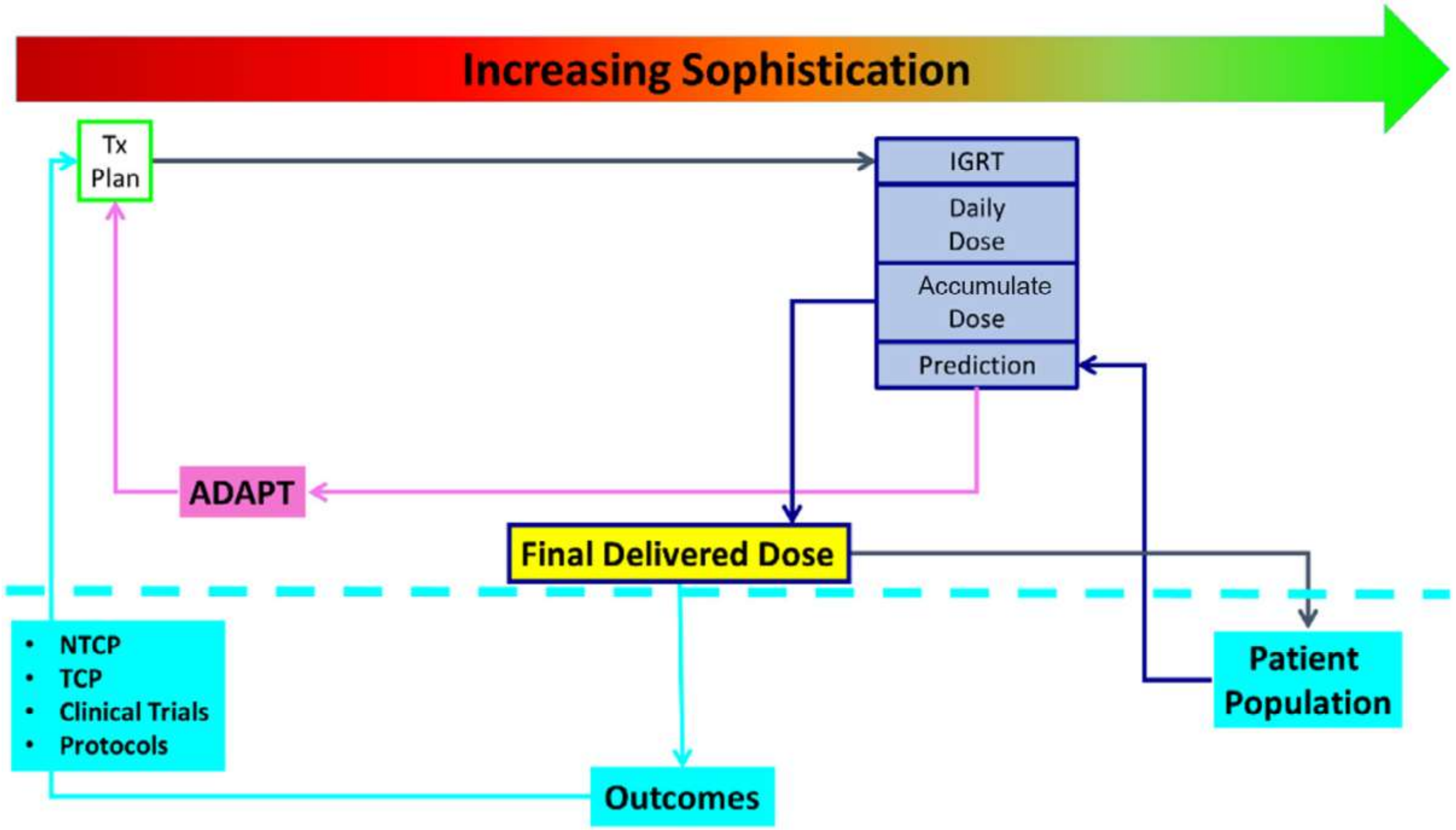
- Improved accuracy
- Reduced margins -> better normal tissue sparing
- Dose escalation

Challenges for ART

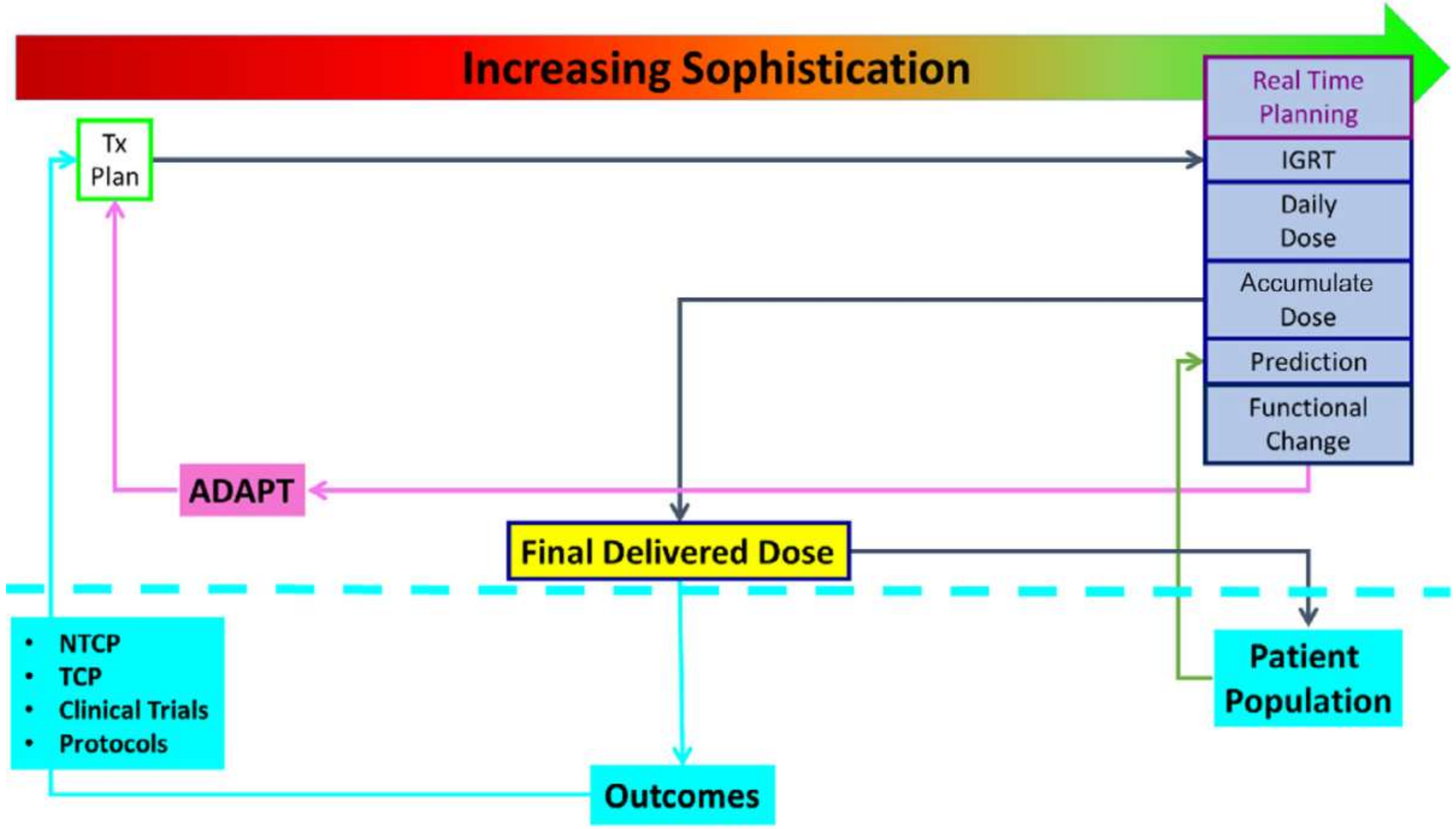
- Added work-load
- Longer daily treatment time
- Limited image quality
- RTT training
- Uncertainty in dose accumulation
- Software or workflow implementation

Future Ahead for ART

Increasing levels of sophistication



Challenge: Cost vs Benefit



Biomarker-driven ART

Key Takeaways

- ART customises radiotherapy by responding to changes
- Enabled by advanced imaging and planning tools
- Enhances precision of radiation delivery, optimizes therapeutic outcomes, and minimizes damage to healthy tissues but requires workflow integration
- AI will further refine efficacy of ART - usher in a new era of personalised radiotherapy

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Adaptive Radiotherapy: where the science of precision meets the **ART** of personalization in the fight against cancer

thank you