Heavy Ion Therapy Research Integration

ORGAN MOTION - ABDOMEN

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This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101008548

RESPIRATORY MOTION

HITRI plus
Heavy Ion Therapy Research Integration

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RESPIRATORY MOTION

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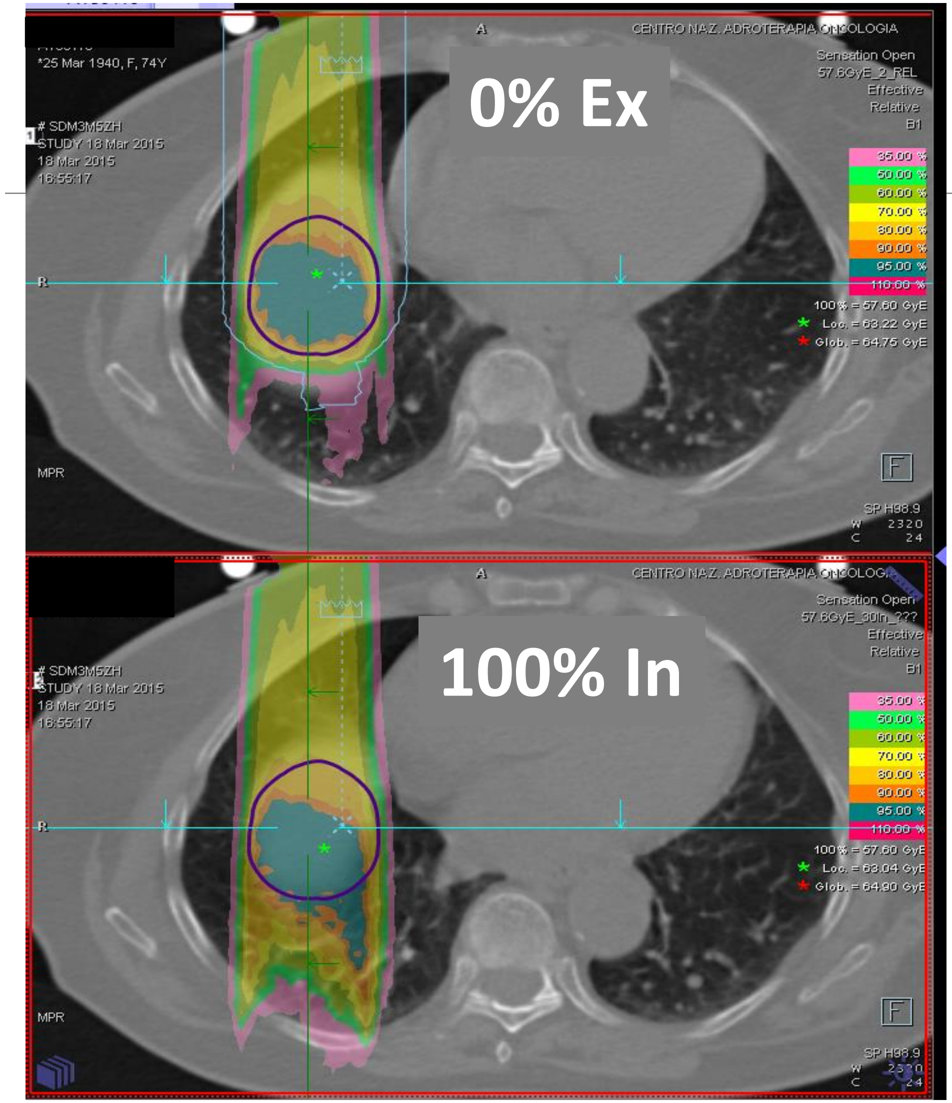
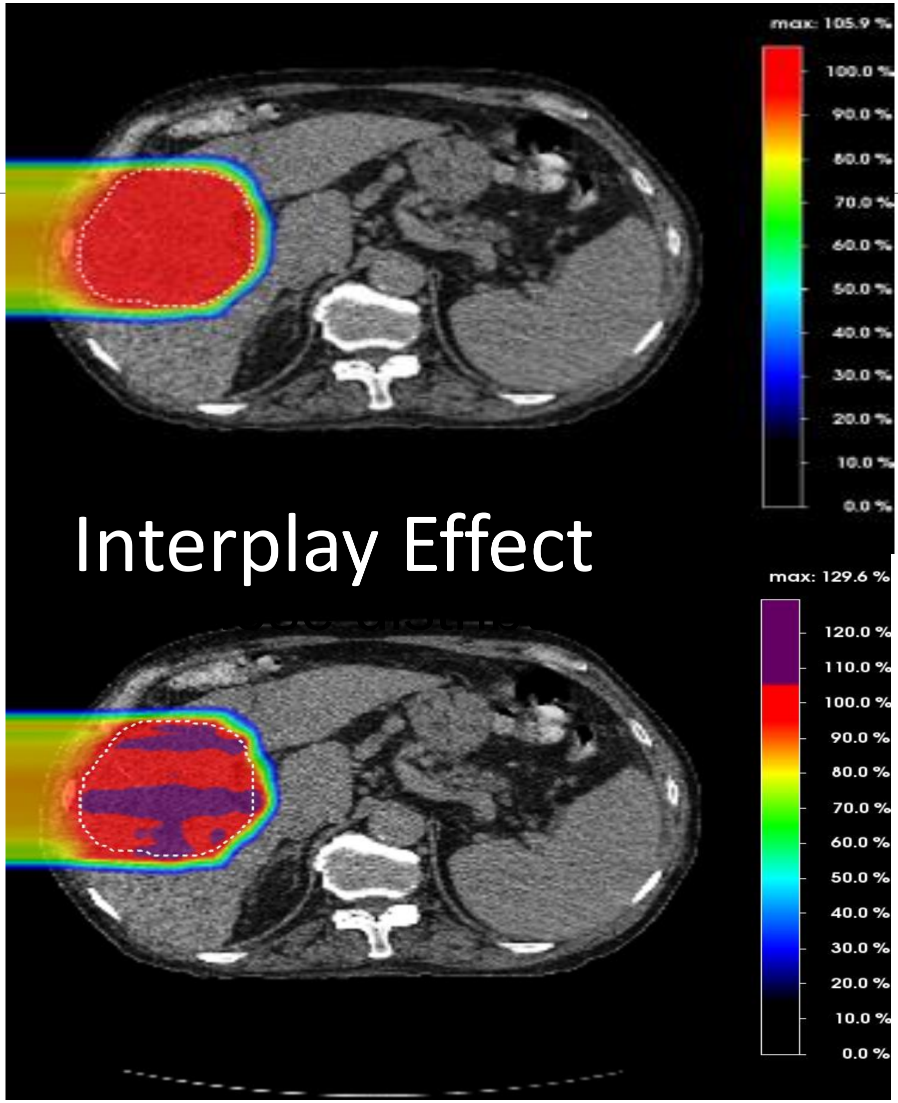
Breathing phase





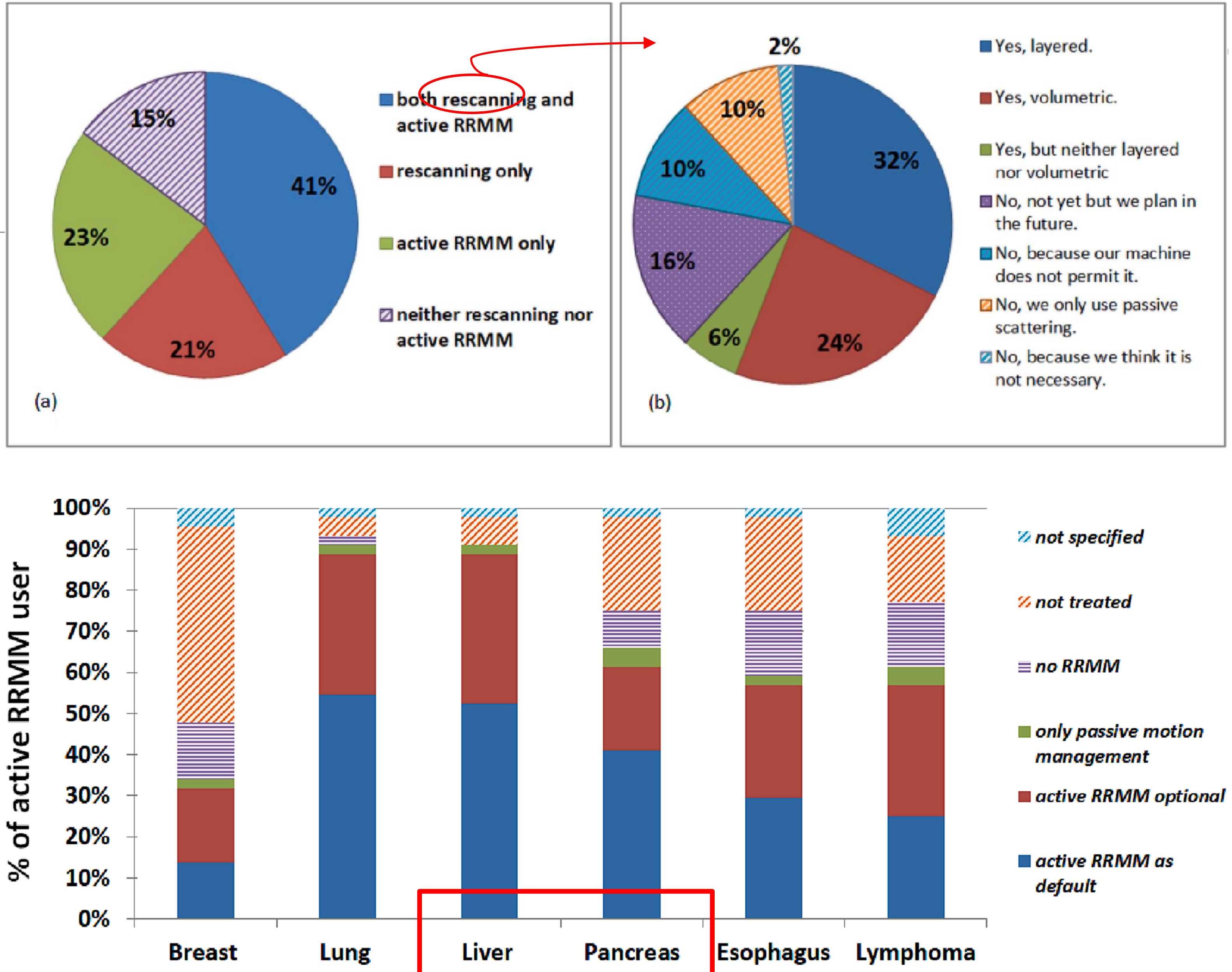
Static case

~6mm S-I motion

Boye et al, Med. Phys. 40 (2013)

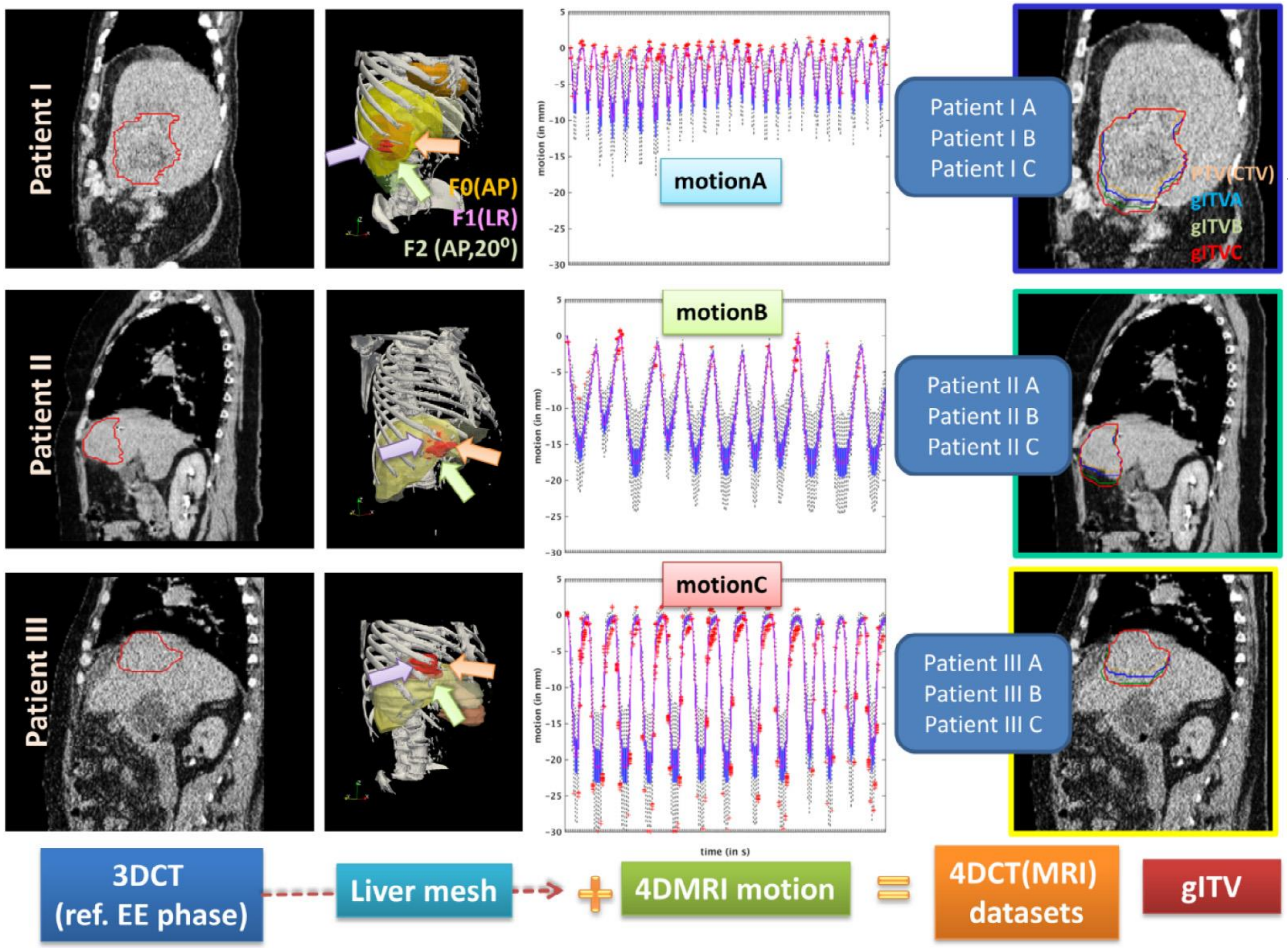
MOTION MANAGEMENT

- Which type(s) of RRMM methods are used, for which sites?
- 70 responses - 17 countries [Europe (23/23), Japan (22/23), USA (20/38)]
- 85% of the 68 clinically operational used RRMM (41% rescanning & active methods)
- 64% used active-RRMM for at least one site, mostly with gating guided by an external marker



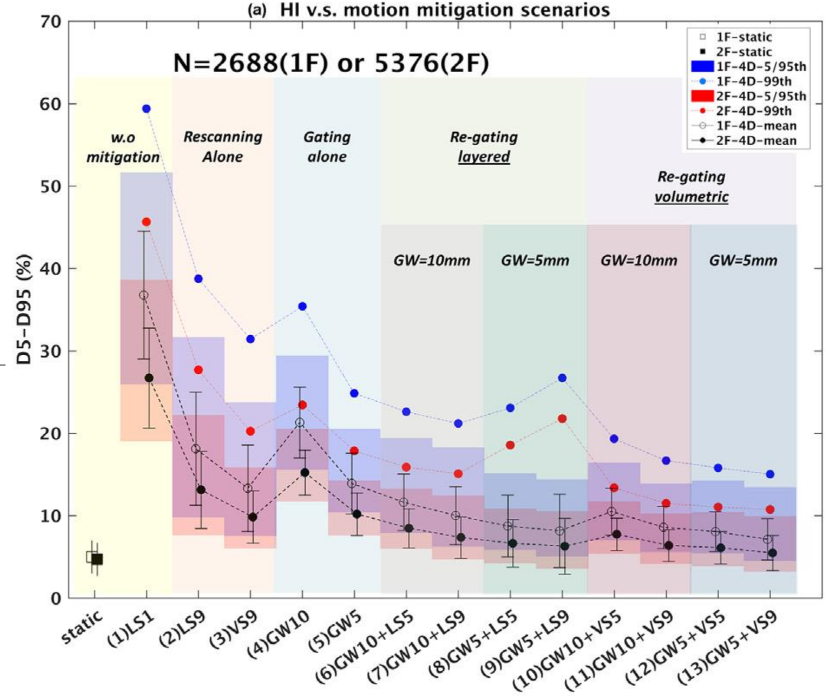
Y. Zhang et al. PHYRO 2023 (26)

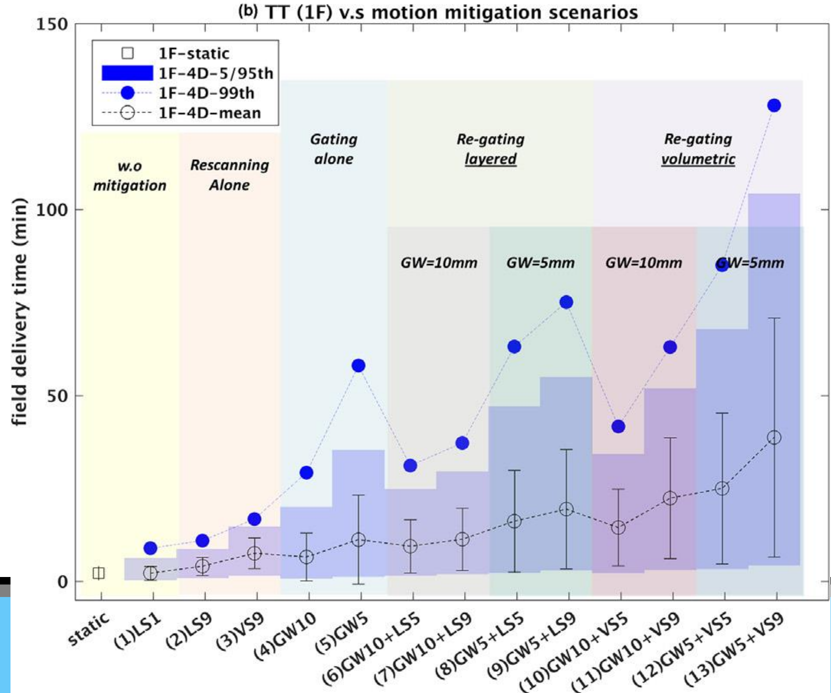
LIVER



< 10 mm

> 10 mm
→ 20 mm





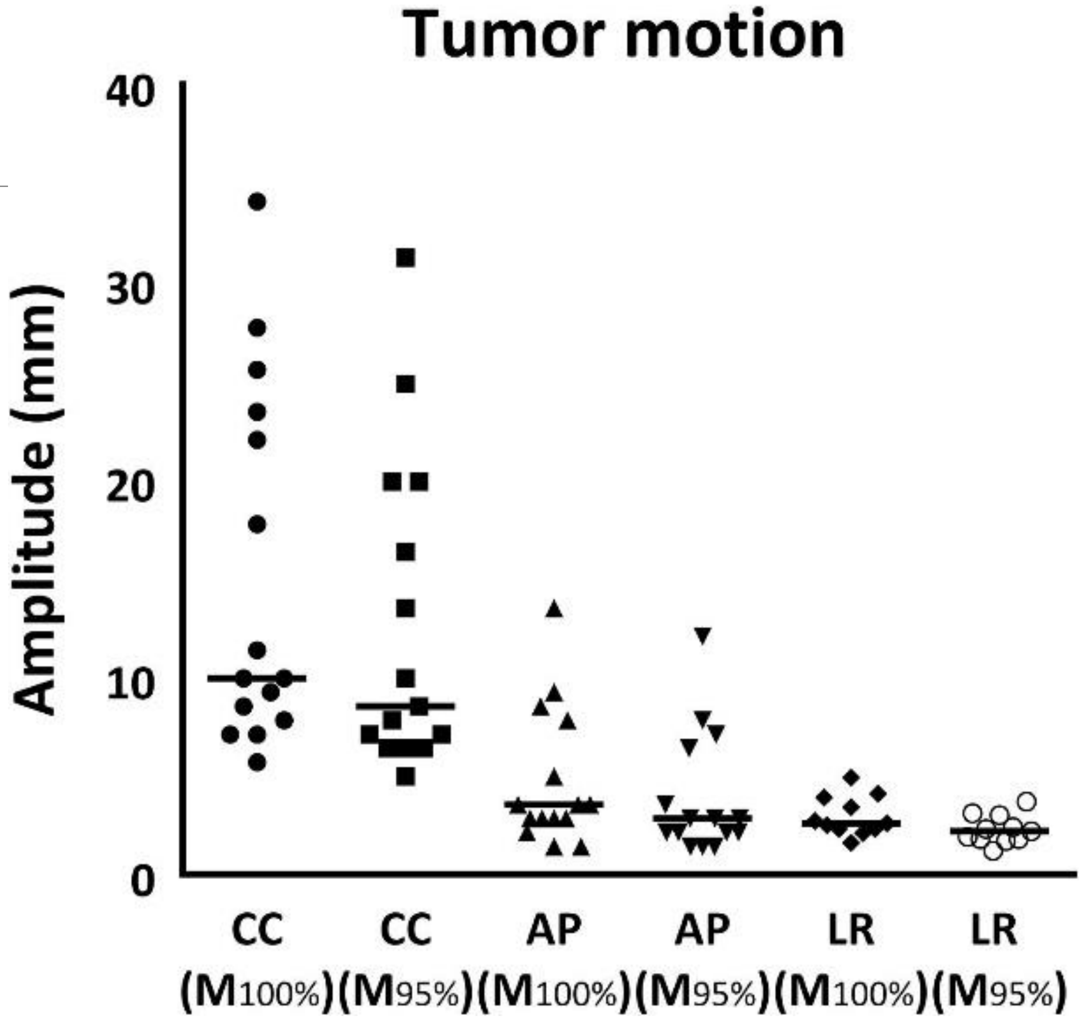
Y. Zhang et al. Radiotherapy and Oncology (2016; 2018)

PANCREAS

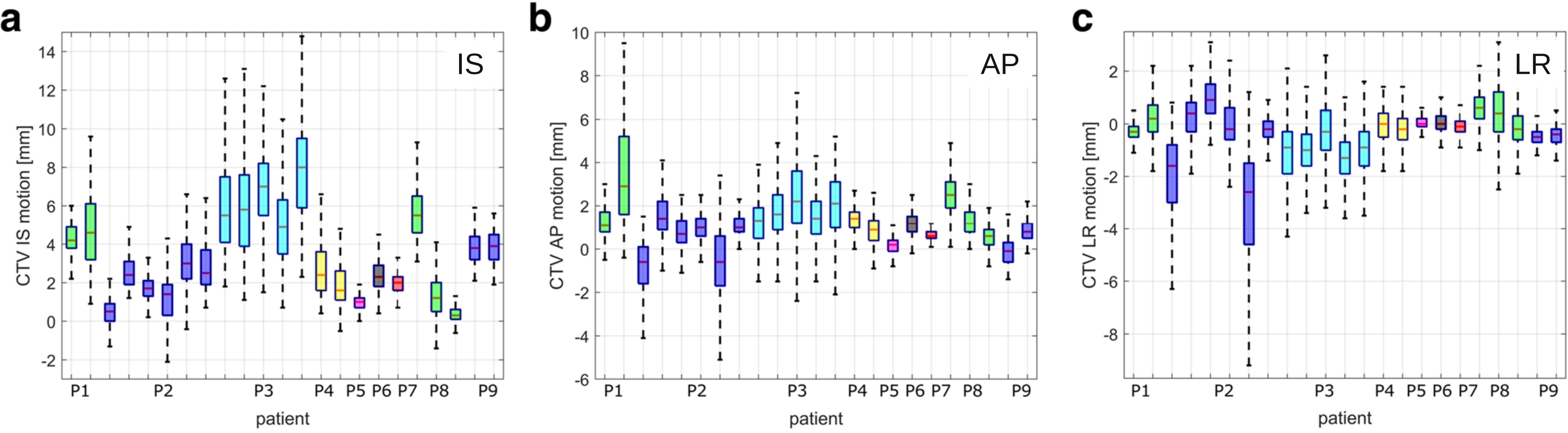
- Two cine MRIs of 60s, 15 pancreatic patients, to quantify tumor motion in CC, LR, AP.

→ The largest tumor motion was CC: average peak-to-peak amplitude of 15 mm (range 6–34 mm); AP: 5 mm (range 1–13 mm); LR: 3 mm (range 2–5 mm).

→ The end exhale position was the most stable position in the breathing cycle and tumors spent more time closer to end exhale than end inhale.



PANCREAS

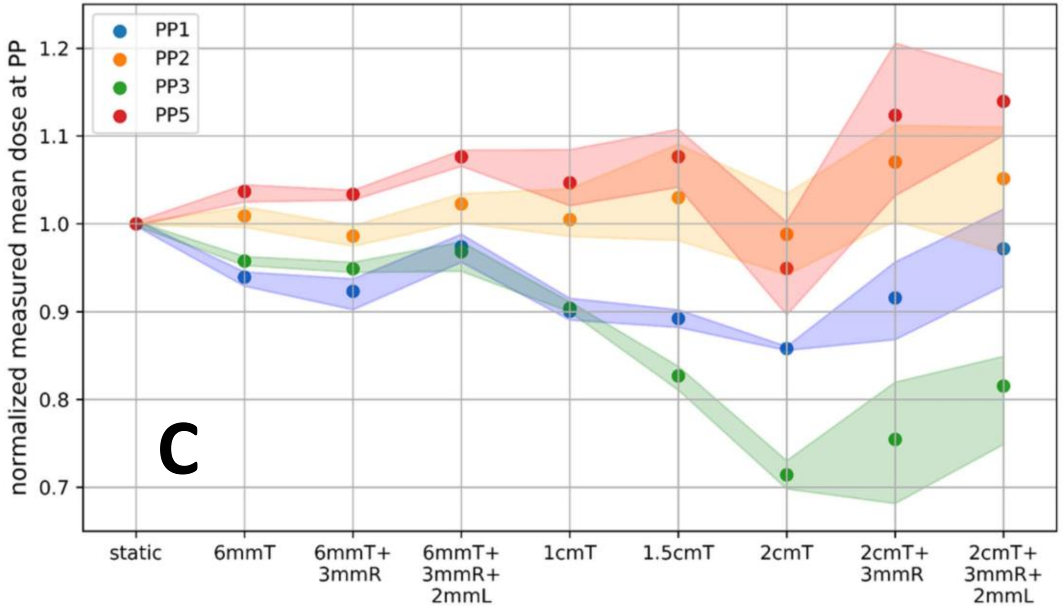


Repeated 4DMRI – 9 pts → Motion distributions of all voxels inside the CTV between end-inhale and end-exhale breathing phases for the respective numbers of available 4DMRI data sets → Max motion up to 15 mm

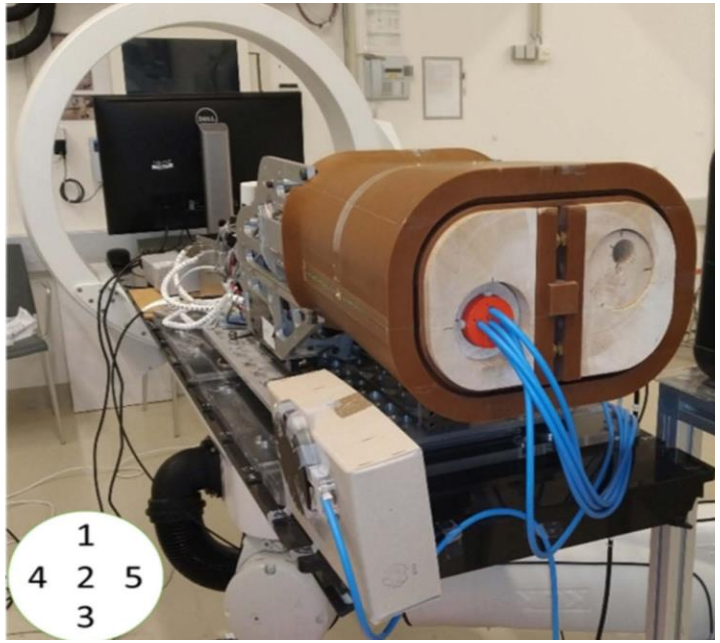
(Batista et al 2018 – up to 12.7 mm based on 4DCT)

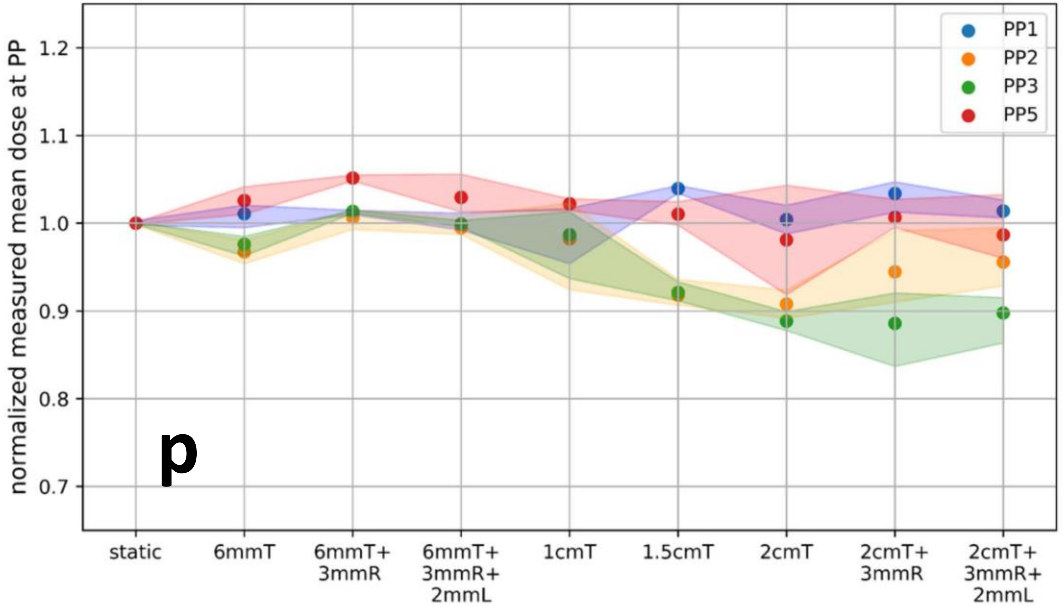
CARBON vs PROTON

- The dose in the tumour centre was deteriorated up to 10% for carbon ions - up to 5% for protons.
- Dose deviations in the penumbra increased by a factor of two for carbon ions vs protons, ranging from 2 to 30% for an increasing motion amplitude depending on the beam intensity.



ARDOS
Advanced Radiation DOSimetry phantom



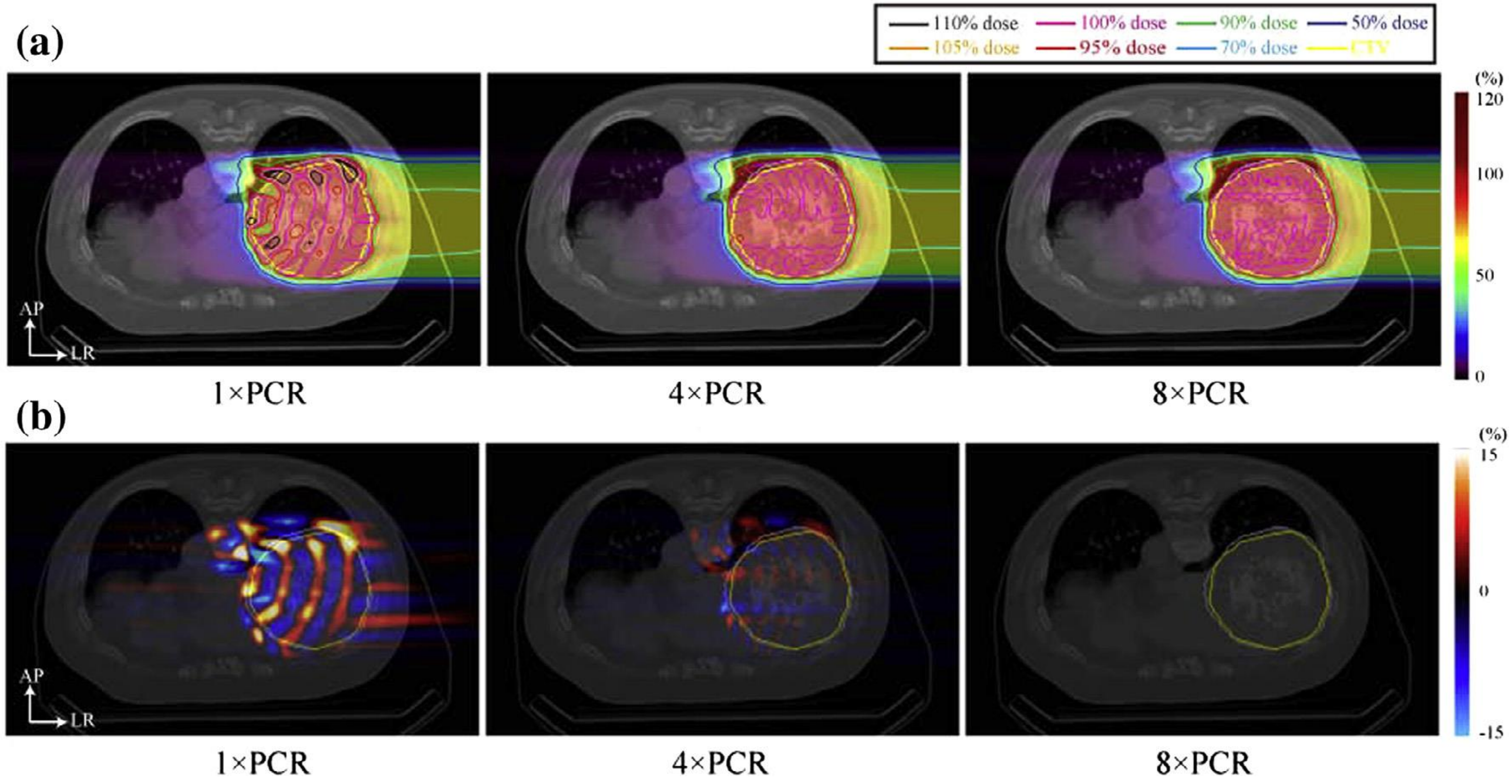


HITRI plus
Heavy Ion Therapy Research Integration

Lebbink F et al. Cancers 14 (2022)

LIVER - Layered PCR & Field-specific FTV

- Free-breathing 4DCT in 30 hepatocellular carcinoma
- 2 ⊥ field with layered PCR (1-10)
- 45 Gy(RBE) to FTVs in 2 fx
- Good dose conformity > 4 PCR
- ≈ D_{95}, $D_{max/min}$ and HI with or without gating
- Liver V_{10}, esophagus and cord D_{max} < 40% with gating
- Total time increased by about 50% with gating



LIVER

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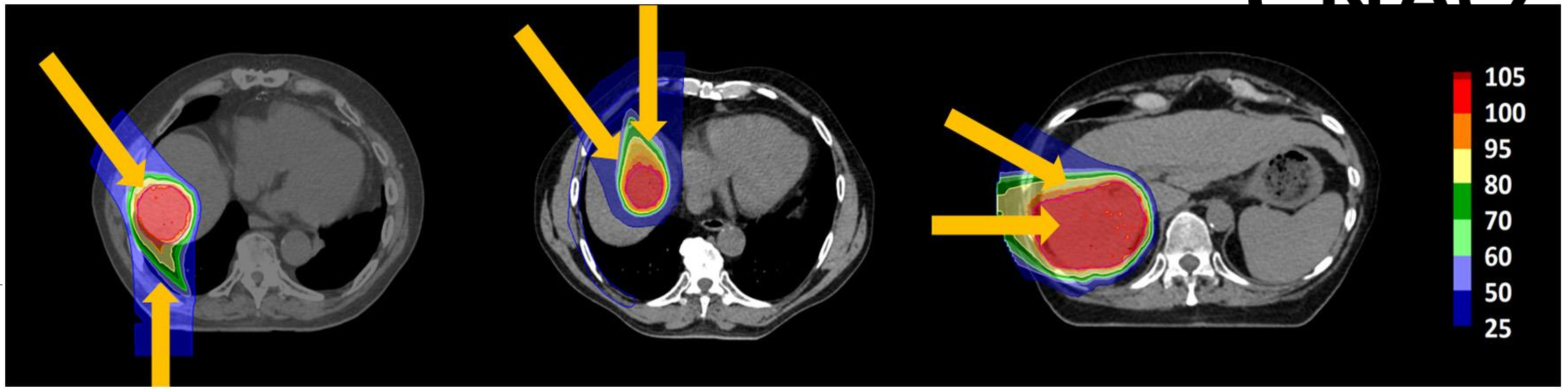
1. Breath hold: Active breath coordinator (ABC) was the first choice if the patient could cooperate with ABC and hold their breath for 20–30 sec at the end of inspiration (BH patients);
2. Gating: Anzai respiratory gating system was the second choice when the patient breathed smoothly and regularly (gating patients)
3. Abdominal compression: It was used for patients who failed with both ABC and the Anzai respiratory gating system. After abdominal compression, the tumor moving should be ≤5 mm (AC patients).

Carbon ion radiotherapy with pencil beam scanning for hepatocellular carcinoma: Long-term outcomes from a phase I trial

Zhengshan Hong et al. Cancer science 2022

LIVER



- Forced breath-hold (ACB) and monitored with an optical tracking system.
- 3 simulation CTs to estimate the anatomical variability intra-fraction and generate an ITV (5^{th} – 10^{th} inter-fraction).
- The interplay effect (between breath-hold) had a limited impact
- Positioning images confirmed that breath-hold & PTV margin were adequate to compensate for inter- and intra-breath-hold variations
- The mean number of breath-holds per fraction and per field was 9.9 (range 5.8–15.9) and 2.5 (range 1.4–3.9)
- The median breath-hold duration per patient was 12.5 s (9.7–14.5) and the rest time between breath-holds was 99 s (57.2–217.2)

Clinical implementation of pencil beam scanning proton therapy for liver cancer with forced deep expiration breath hold

ABDOMINAL TUMORS

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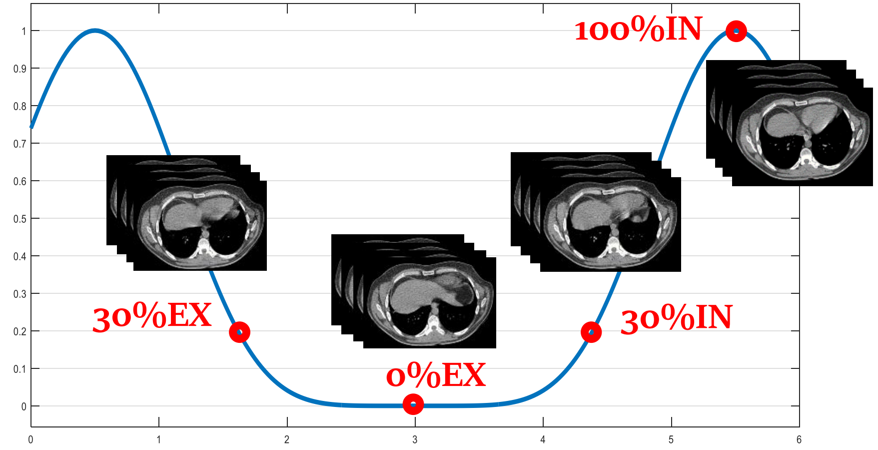
→ Thermoplastic mask → thoraco-abdominal compression
- Diaphragm displacement in 27 pts (5 ± 4) mm range (1 ÷ 14) mm
- tumor displacement in 10 pts* (6 ± 3) mm range (1 ÷ 12) mm

→ **4DCT:** External pressure sensor (Anzai Medical, Japan) after > 24 hrs (8 phases)

→ 4D robust plan opt on **0% Ex** (5% - 5 mm + 30% IN + RE1 0% EX)
→ Robust evaluation and recalculation on extreme phases
→ Weekly RE-4DCT
→ Gated (**30% DC**) free-breathing & 5 times Layered rescanning

Planning 4DCT



GATING & RESCANNING

Table 1
Flatness and field size values measured on the EBT3 films exposed using the experimental set-up shown in Fig. 1.

Test	Ion type	Flatness (%)	Field size (mm)
(a) Static (reference)	Carbon ions	4.3	60
(b) Moving phantom, no motion mitigation strategy applied, horizontal beam scan	Carbon ions	[a]	[a]
(c) Moving phantom, no motion mitigation strategy applied, vertical beam scan	Carbon ions	[a]	[a]
(d) Moving phantom, repainting alone (N = 7), horizontal beam scan	Carbon ions	[a]	[a]
(e) Moving phantom, gating alone, horizontal beam scan	Carbon ions	9	60
(f) Moving phantom, gating and repainting (N = 5), horizontal beam scan	Carbon ions	6.1	60
(g) Static (reference)	Protons	3.1	60
(h) Moving phantom, no motion mitigation strategy applied, vertical beam scan	Protons	[a]	[a]
(i) Moving phantom, gating alone, vertical beam scan	Protons	4.8	60
(j) Moving phantom, gating and repainting (N = 5), vertical beam scan	Protons	4.6	60

[a] Dose distribution so strongly distorted to make flatness and field size determination meaningless.

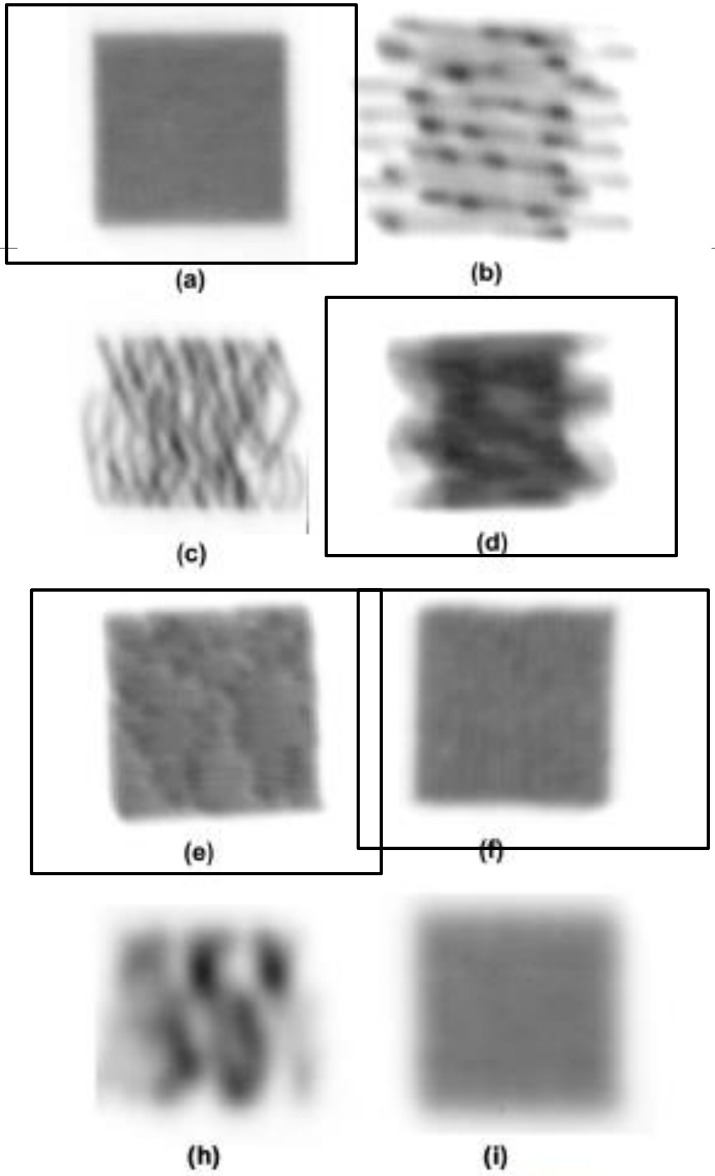


Fig. 3. Examples of EBT3 films exposed using the set up shown in Fig. 1 and under the most significant conditions reported in Table 1, for carbon ions (a–f) and protons (h, i).

STATIC

RESCANNING (7)

GATING & RESCANNING

M. Ciocca Physica Medica 2016

END -TO-END TESTING

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4D strategies for lung tumors treated with hypofractionated scanning proton beam therapy: Dosimetric impact and robustness to interplay effects

Edoardo Mastella [a,*], Silvia Molinelli [a], Andrea Pella [a], Alessandro Vai [a], Davide Maestri [a], Viviana Vitolo [a], Guido Baroni [a,b], Francesca Valvo [a], Mario Ciocca [a]

- → 4D robust optimization
- → 4D dose delivery
- → Interfraction variation
- → Varaible breathing pattern

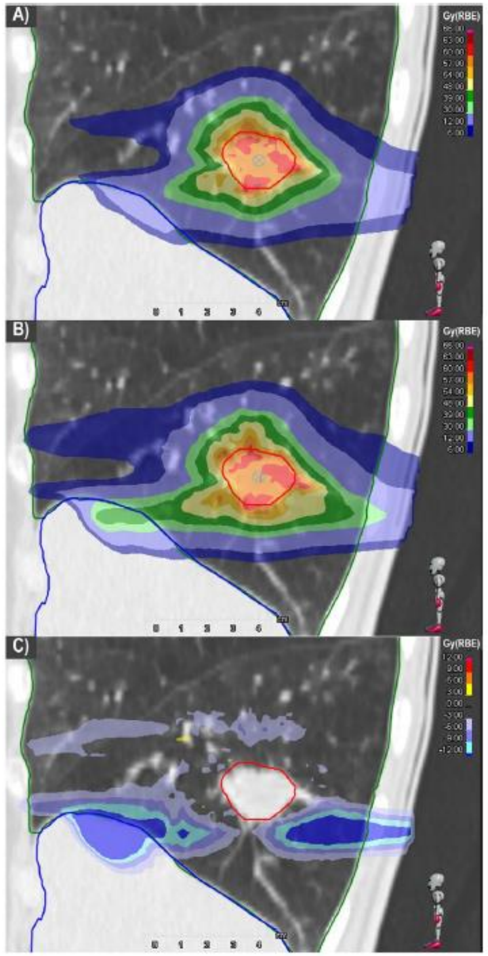


Fig. 2. Dose distributions for patient P20: (A) 4D robustly optimized plan including three breathing phases; (B) 4D plan using the whole breathing cycle; (C) dose differences between (A) and (B). The GTV is delineated in red, the lung in green and the liver in blue.

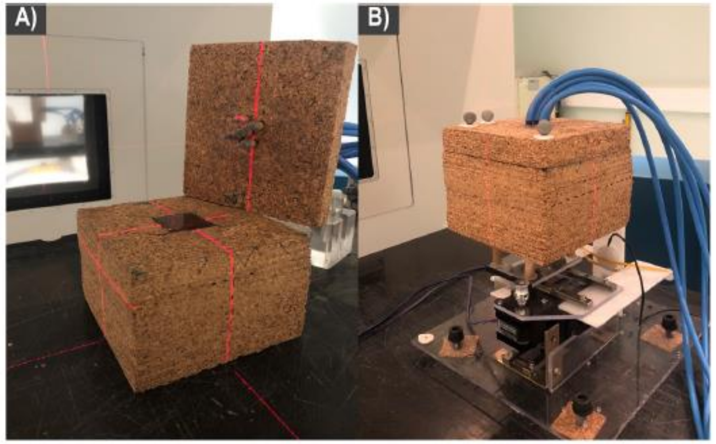


Fig. 1. (A) The lung phantom used for dynamic quality assurance measurements (B) mounted on three moving platforms.

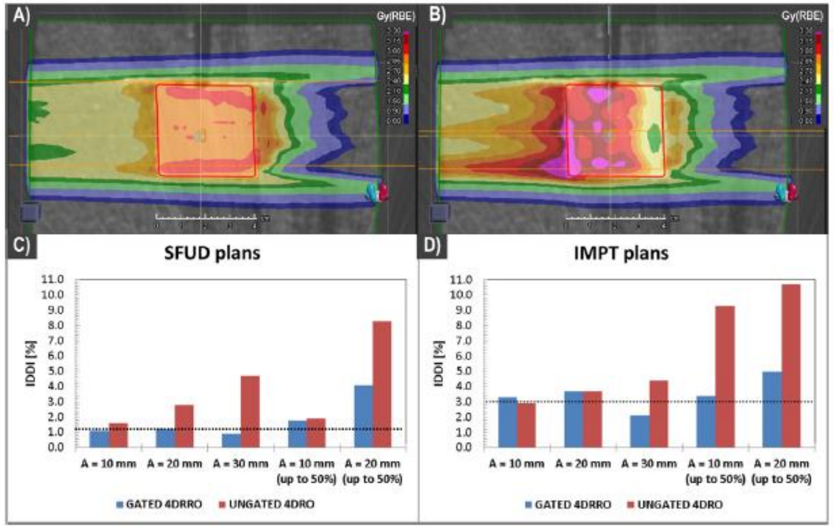
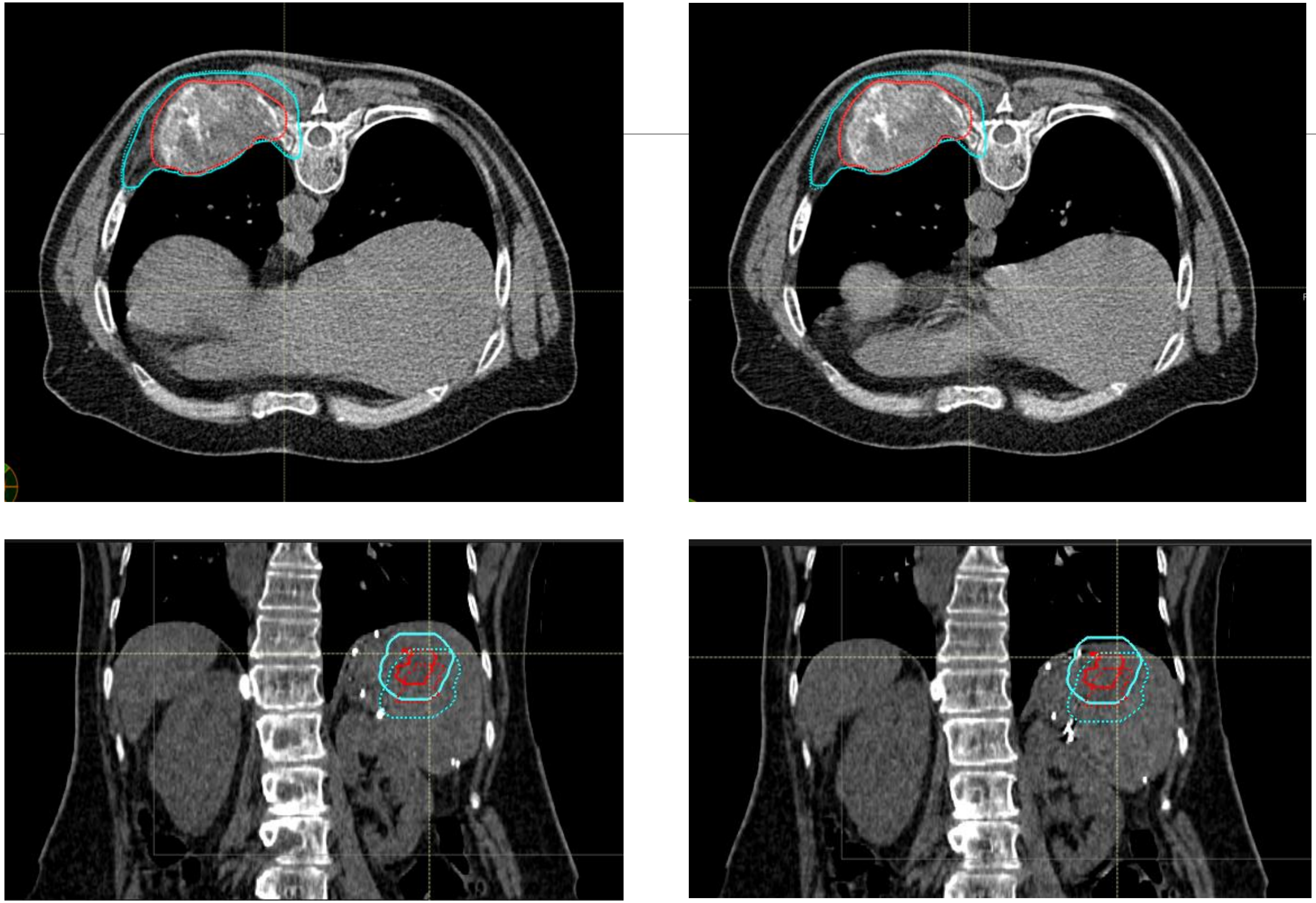


Fig. 3. Horizontal beam dose distributions planned using 4D restricted robust optimization (4DRRO) and an amplitude (A) – 10 mm: (A) SFUD and (B) IMPT plans. Calculated absolute dose deviation (|DD|) for the (C) SFUD and (D) IMPT plans as a function of motion amplitude; the dotted lines refer to the static cases. Target motion irregularities were simulated for amplitudes of 10 and 20 mm, as percentage deviation of nominal value up to 50%. 4DRRO plans were delivered in combination with gating and 5 rescans, full 4DRO plans were delivered only with rescanning.

Mastella E *et al*. Radiother Oncol 2020

4DCT - INTRA-FRACTION

Max Exhale



Max Inhale

INTRA-FRACTION

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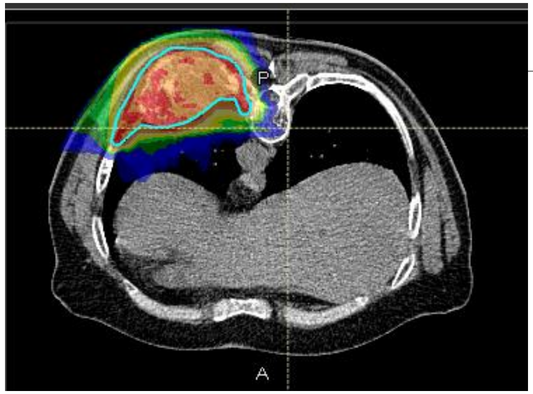
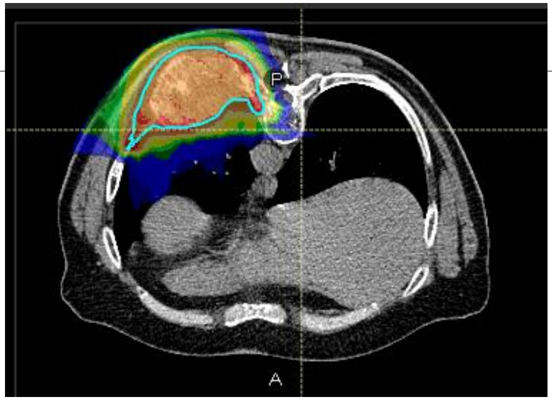
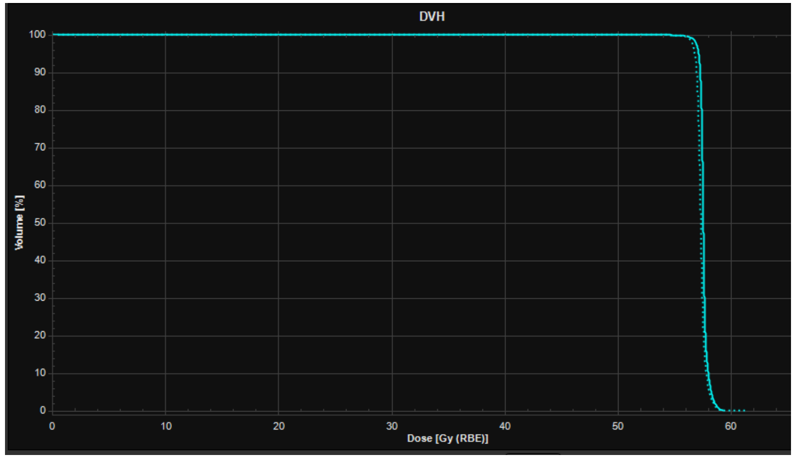
Max Exhale



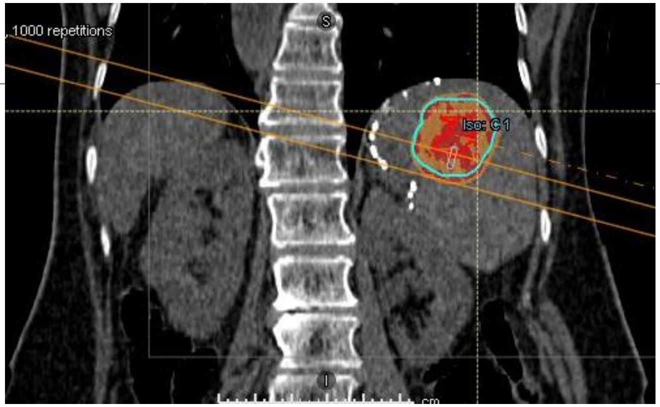
Max Inhale



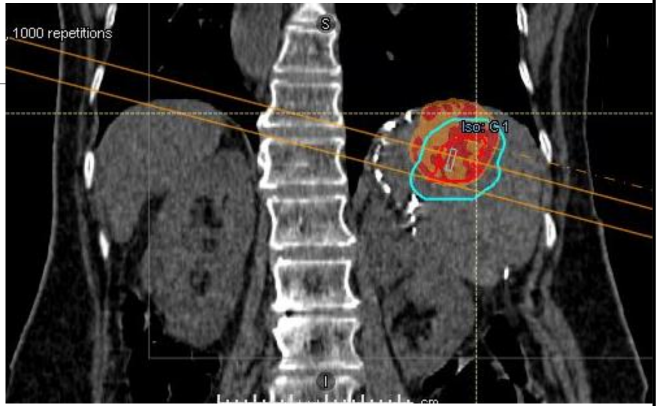


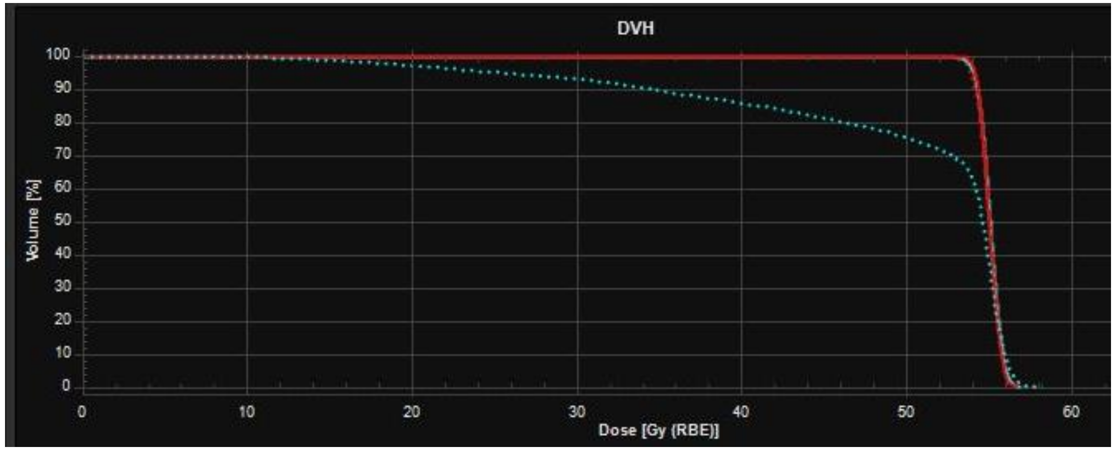
NO GATING

Max Exhale



Max Inhale





GATING

4DCT - INTER-FRACTION

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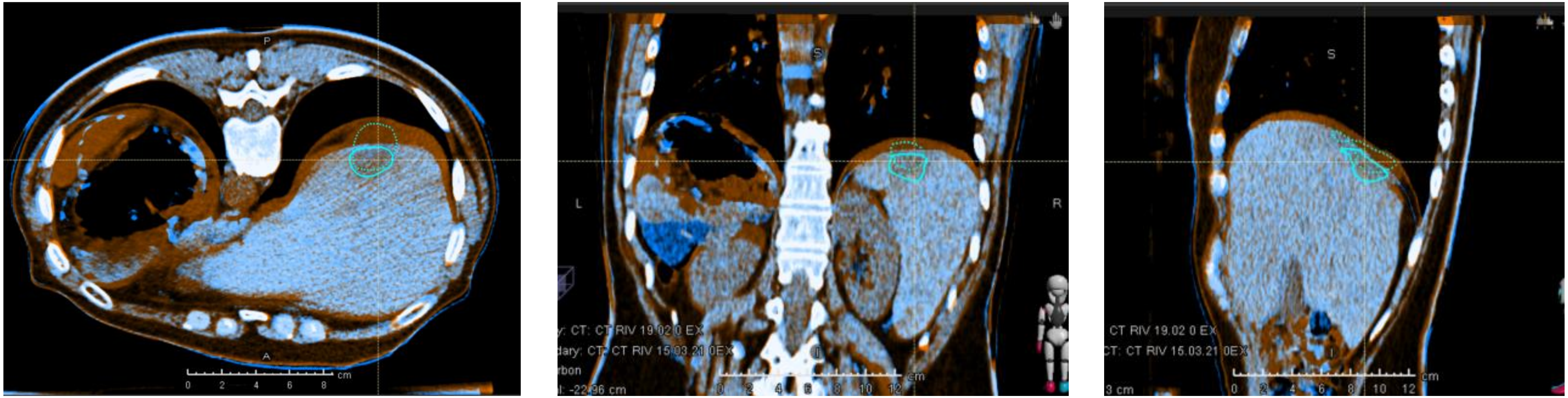
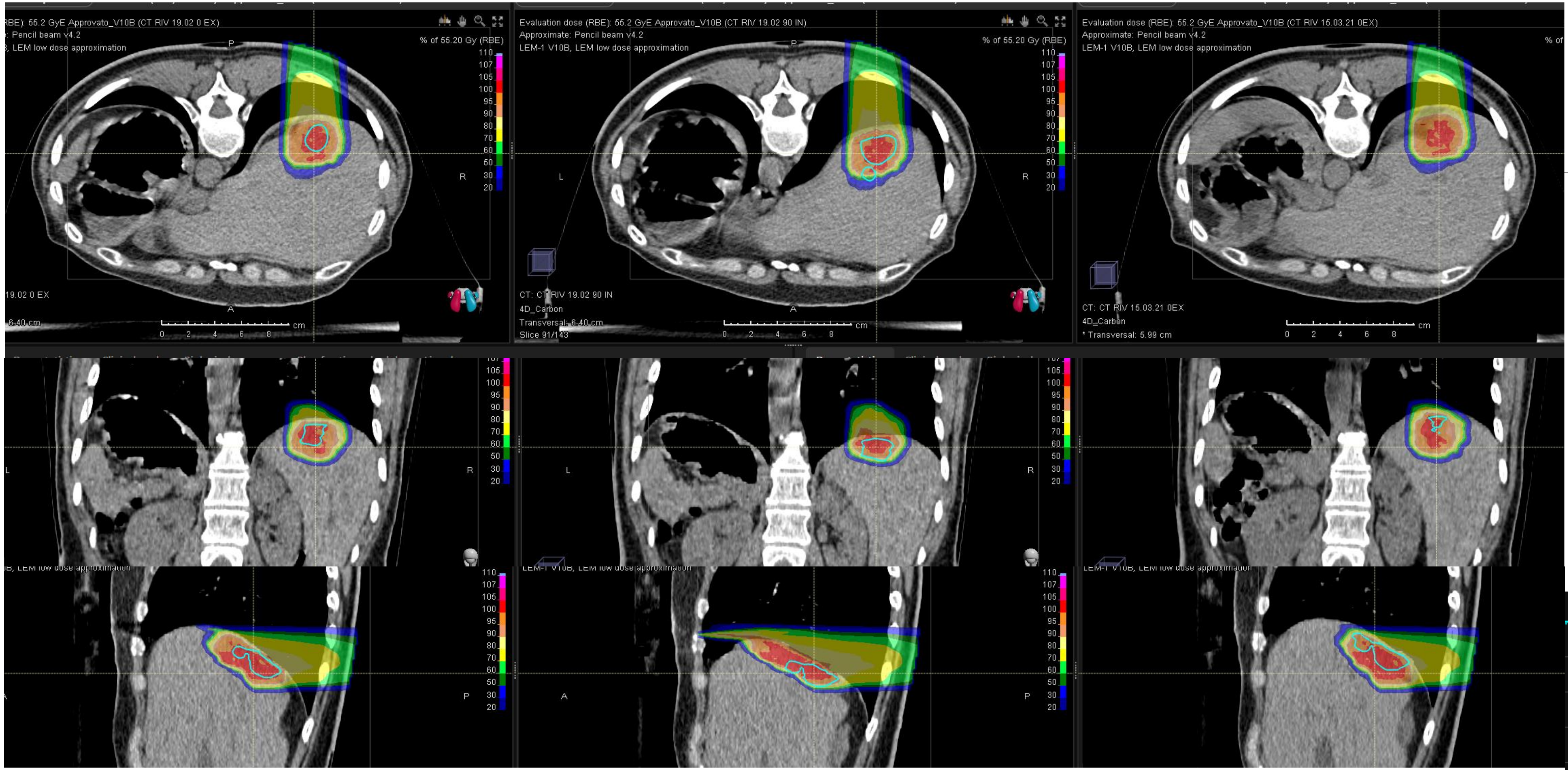
… And then we check it again (ideally on-line… at least every week)



15 March → 19 March

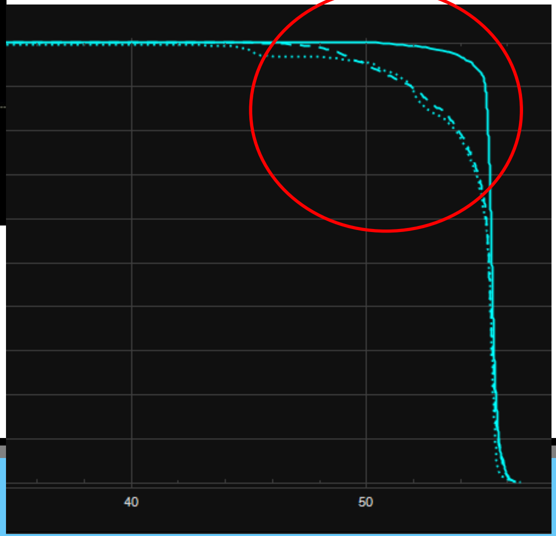
4DCT INTRA AND INTER-FRACTION



Max Exhale Plan

Max Inhale Plan
INTRA-FRACTION

Max Exhale RE1
INTER-FRACTION



4DCT INTER-FRACTION

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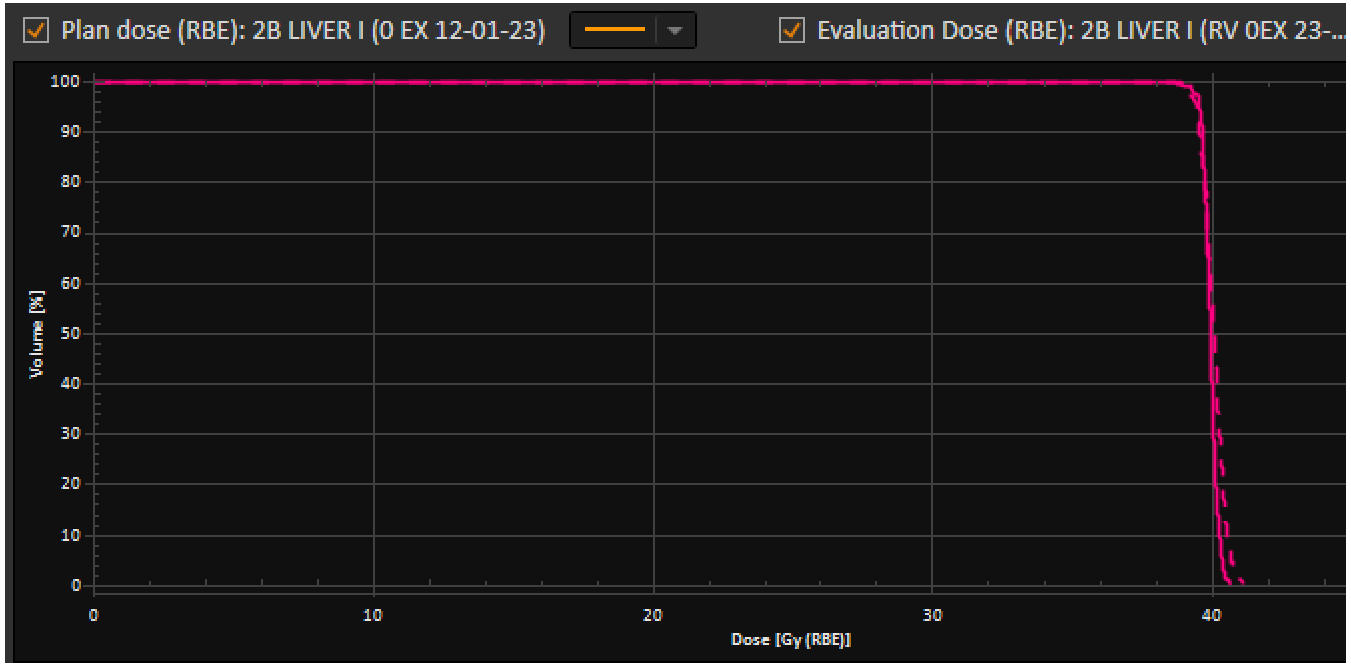
Same patient – two years after
Oligo-recurrent high grade serous cell ovarian cancer



ORGAN MOTION (INTRA-FRACTION VARIABILITY)

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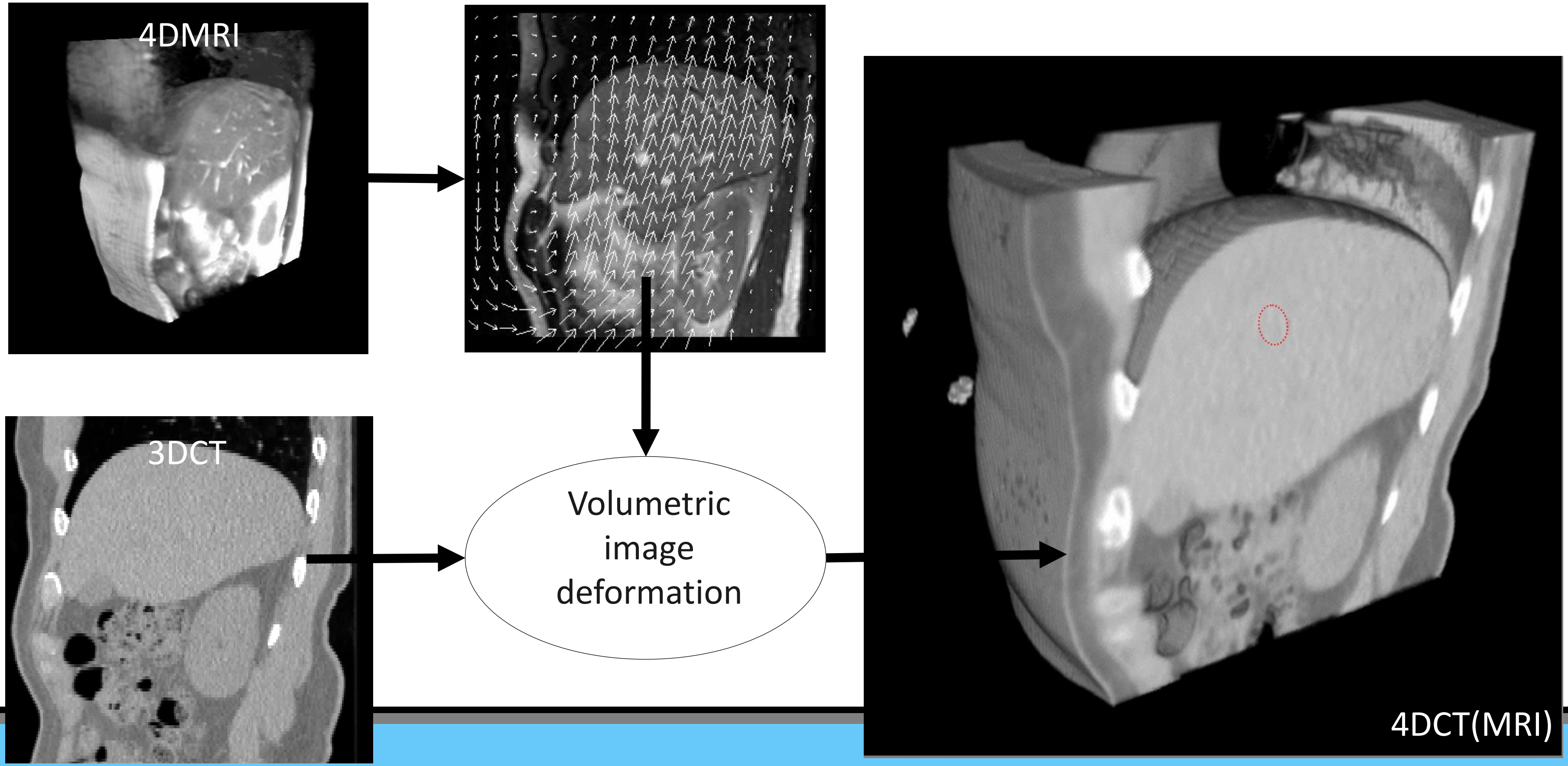
→ 4DCT is a snap-shot of the patient breathing pattern (adding dose to the patient)

→ MRI allows radiation-free repeated scans and fast dynamic sequences for time-resolved imaging providing information on <u>inter-</u> and <u>intra-</u>fraction variations of respiratory motion (tens of minutes)

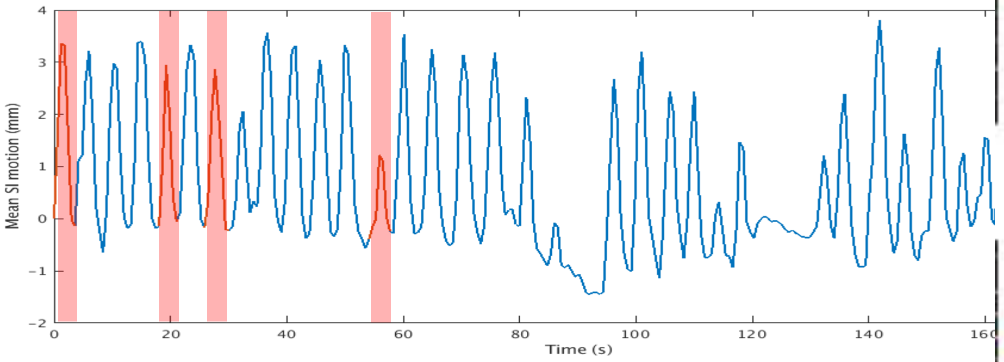
→ Generation of virtual 4DCT from 4DMRI?

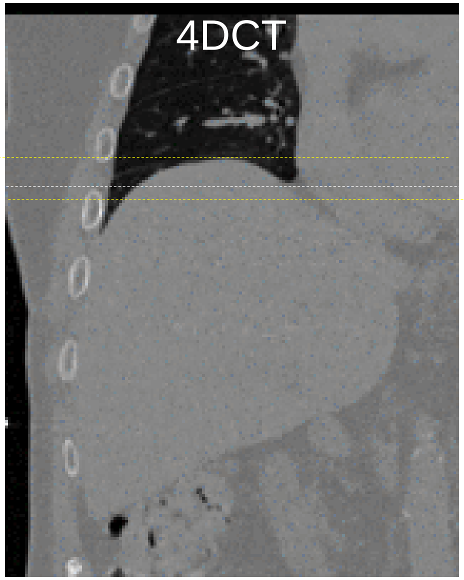


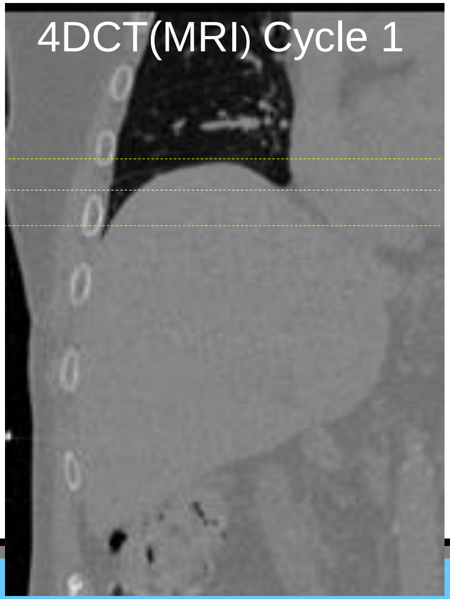
BREATHING VARIABILITY - 5D

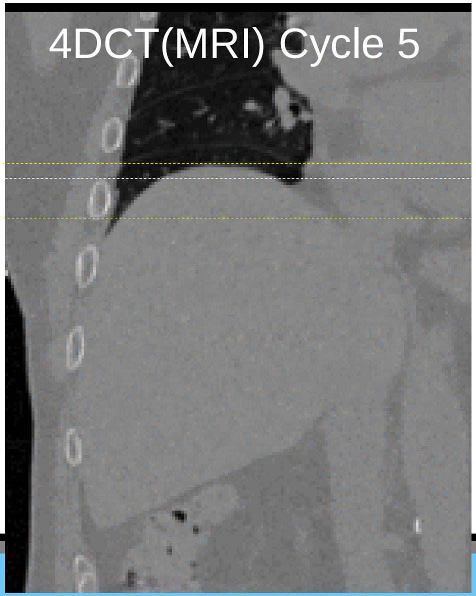
→ Evaluate intra-faction cycle-to-cycle variability

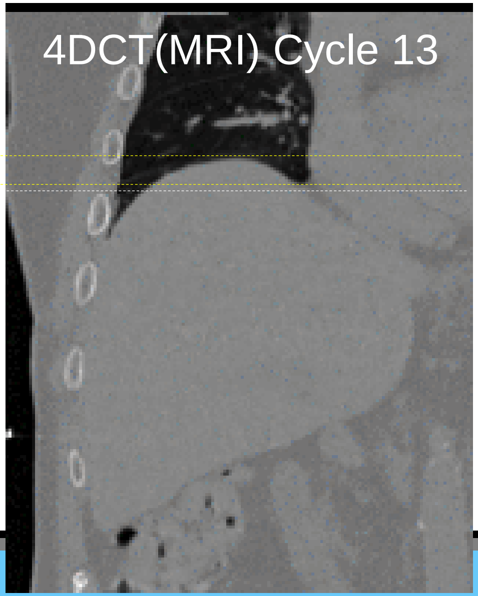
g cycles for
n partner hospital
om 4DMRI
PSI

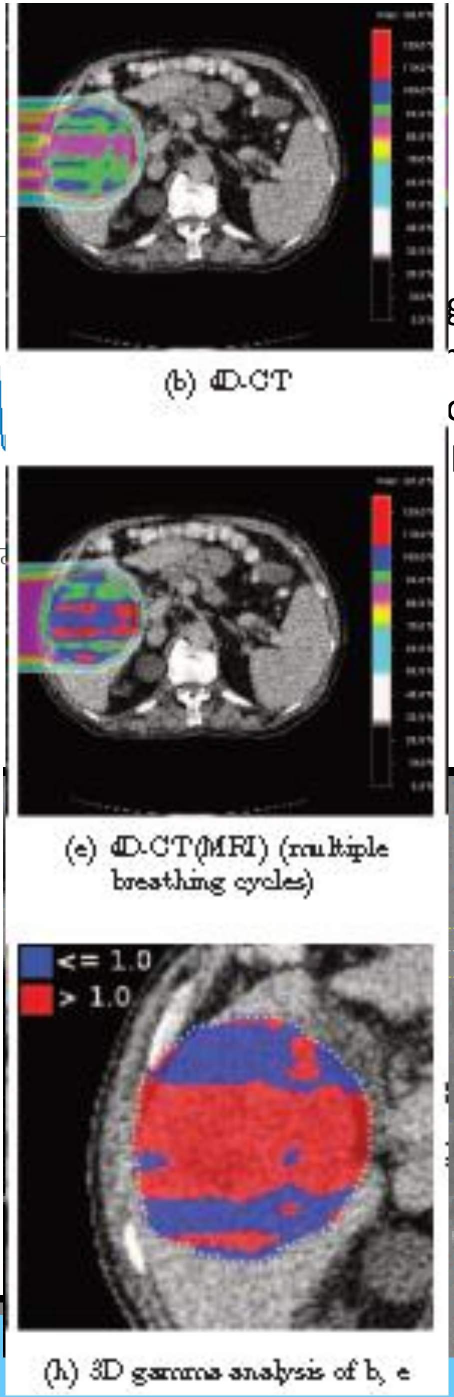












(b) 4DCT

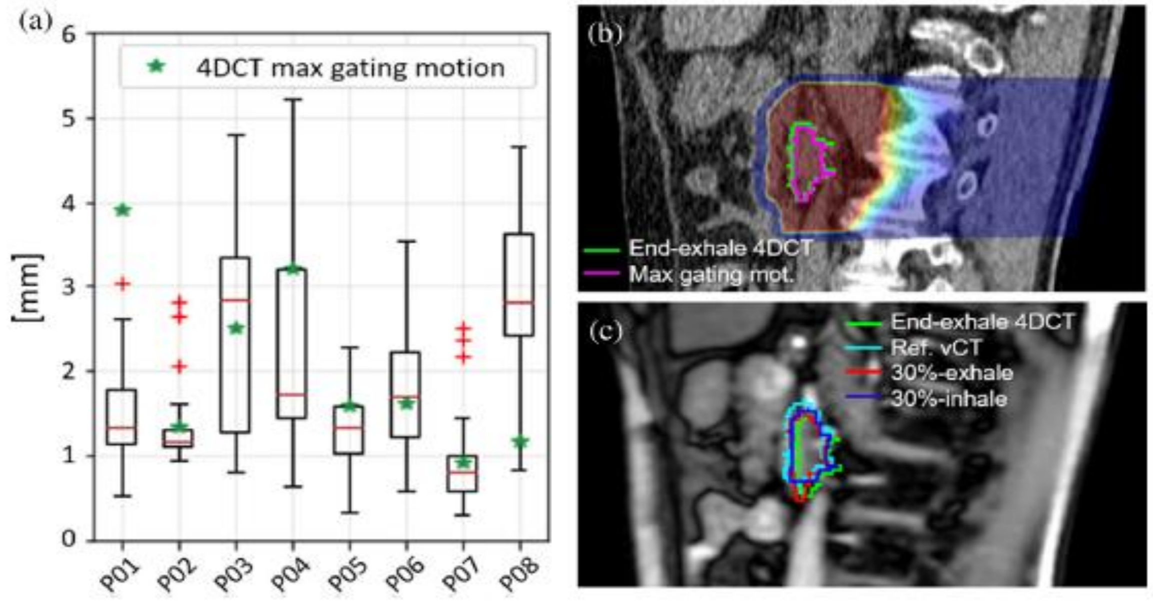
(e) 4DCT(MRI) (multiple breathing cycles)

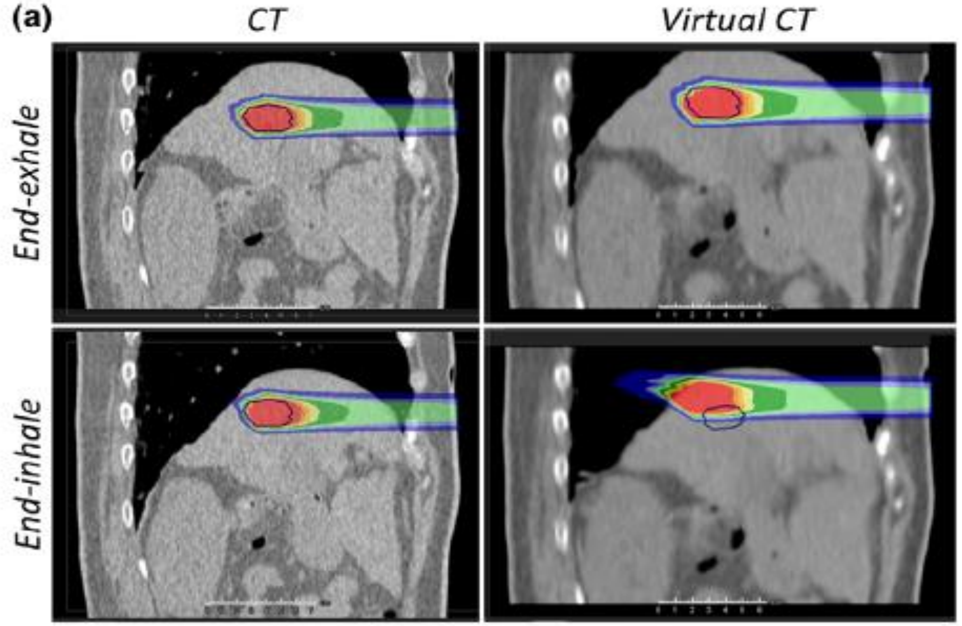
(h) 3D gamma analysis of b, e

Boye et al Med Phys 2013

BREATHING MOTION AMPLITUDE

→ Synthetic 4DCT from 4DMRI acquired at patient simulation for 9 abdominal pts treated at CNAO to evaluate the breathing variability on a cycle-to-cycle base (vs planning 4DCT) and estimate dosimetric related uncertainties





BREATHING VARIABILITY - 5D

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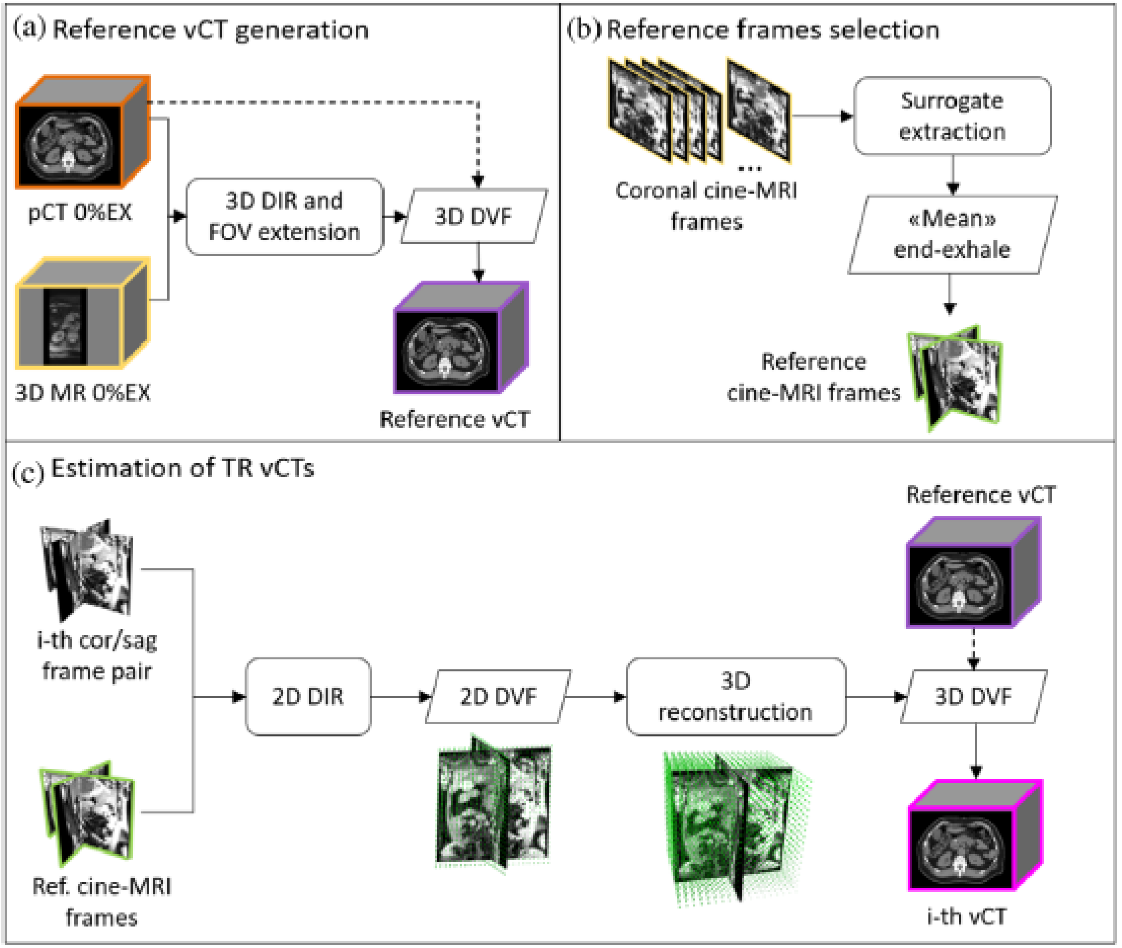
→ Off-line evaluation of intra-faction **cycle-to-cycle** variability in the gating window



- → Median inter-fraction motion 3.3– 12.1 mm
- → Median CTV *D*95% variation -0.4%
- → Cycle-to-cycle tumor displacement 1.35 mm
- → Cycle-to-cycle *D*95% variation -3.9%
- → intra-fraction cycle-to-cycle OARs dose variations were limited

4D DOSE TRACKING

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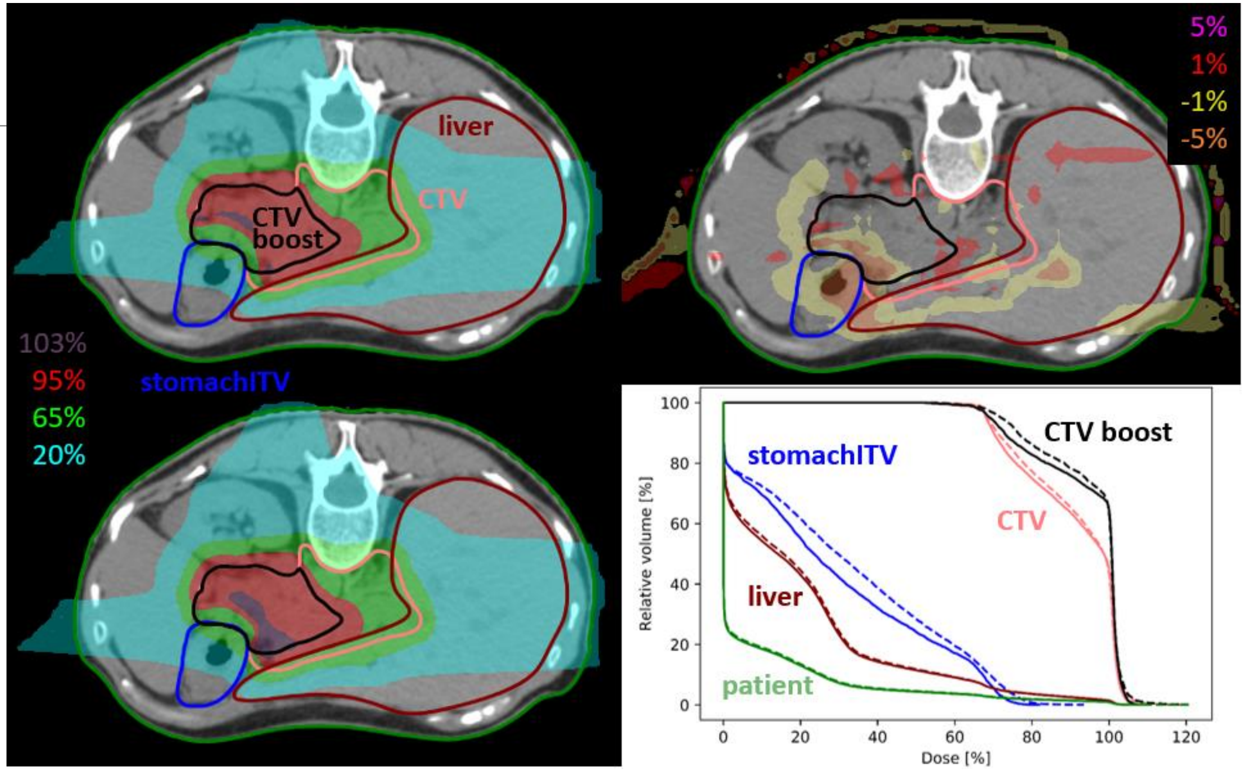
Distribute spots over 4DCT phases /fraction based on delivery log files, breathing signal, DIR between different phases and planning CT.

→ Compute dose on the different phases based on the determined spot distribution

→ Map doses to the reference phase through DIR and accumulate the mapped doses

→ Accumulate the 4DDT dose of each fraction to get the full treatment course dose

→ The hypofractionated proton robust plan optimization (2 to 4 beams) showed to be robust against intra-fractional movements up to 3.7 mm.



Patient Breathing Motion and Delivery Specifics Influencing the Robustness of a Proton Pancreas Irradiation

GI ORGAN VARIATION (FILLING, SHAPE AND POSITION)

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101008548

INTER-FRACTION – ORGAN FILLING

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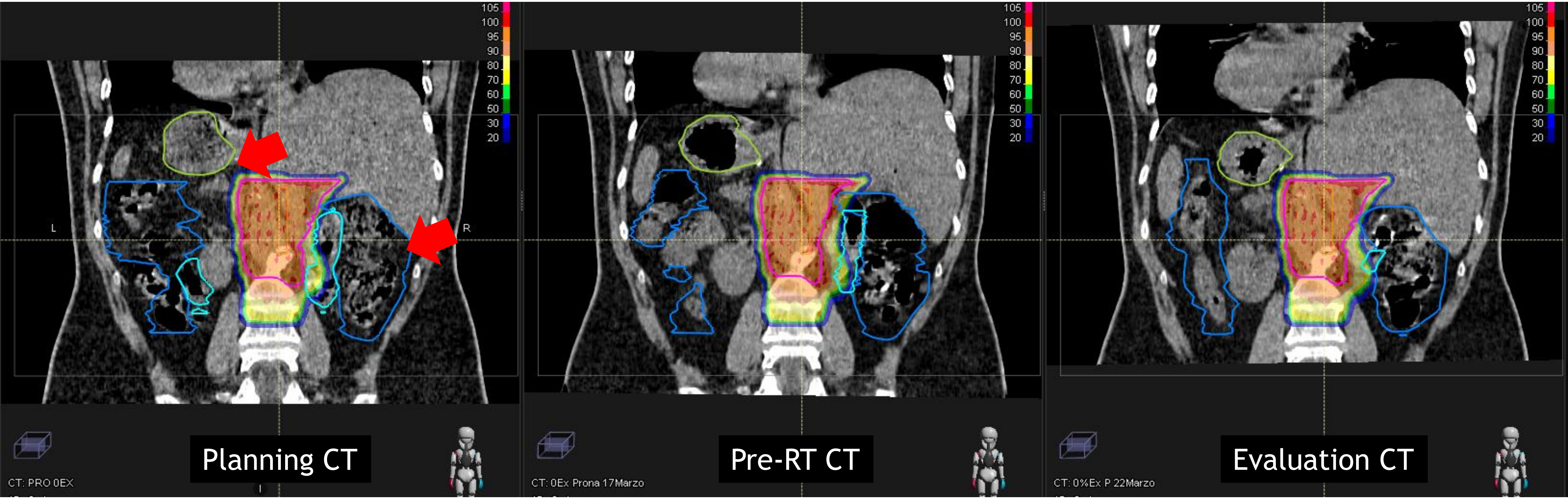
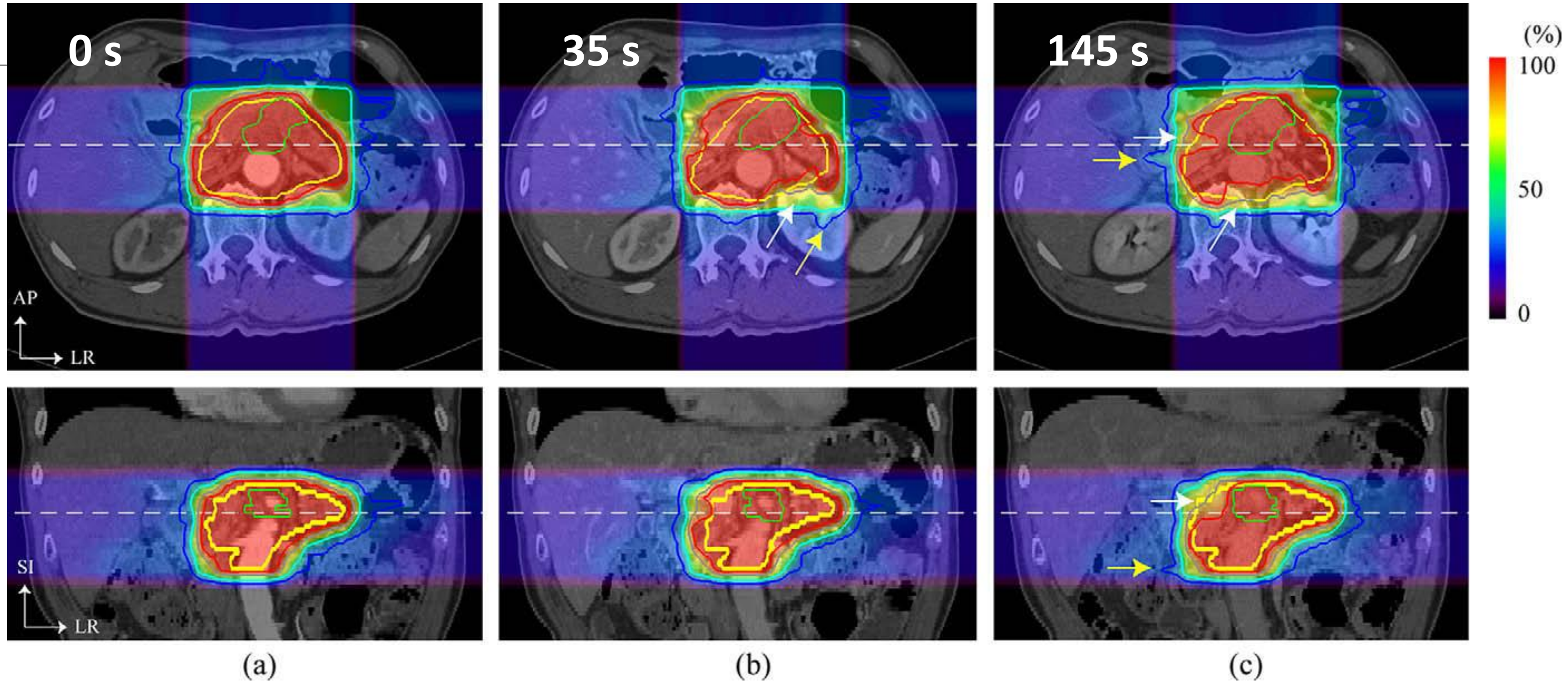
Pancreatic treatment



≈ weekly re-evaluation 4DCT

INTRA-FRACTION - ORGAN FILLING

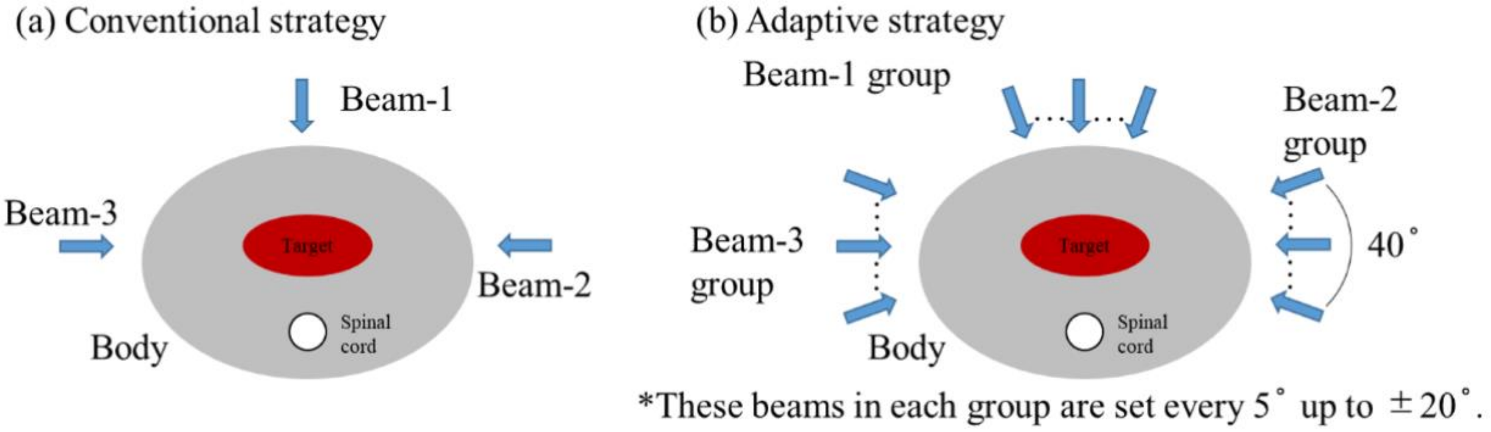
- 10 patients subject to multiple-phase dynamic CT under breath-holding. The arterial–venous phase and arterial–delayed phase intervals were 35 and 145 s
- Beam overshoot (yellow arrows) and undershoot (white arrows) were observed at the scan interval of 35 and 145 s
- CTV dose conformation and OARs sparing were degraded due to bowel gas movement, particularly from the anterior and left directions

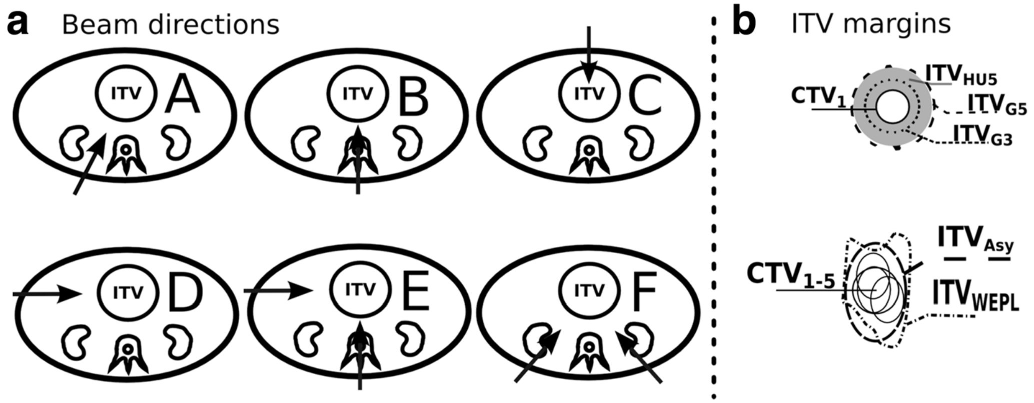


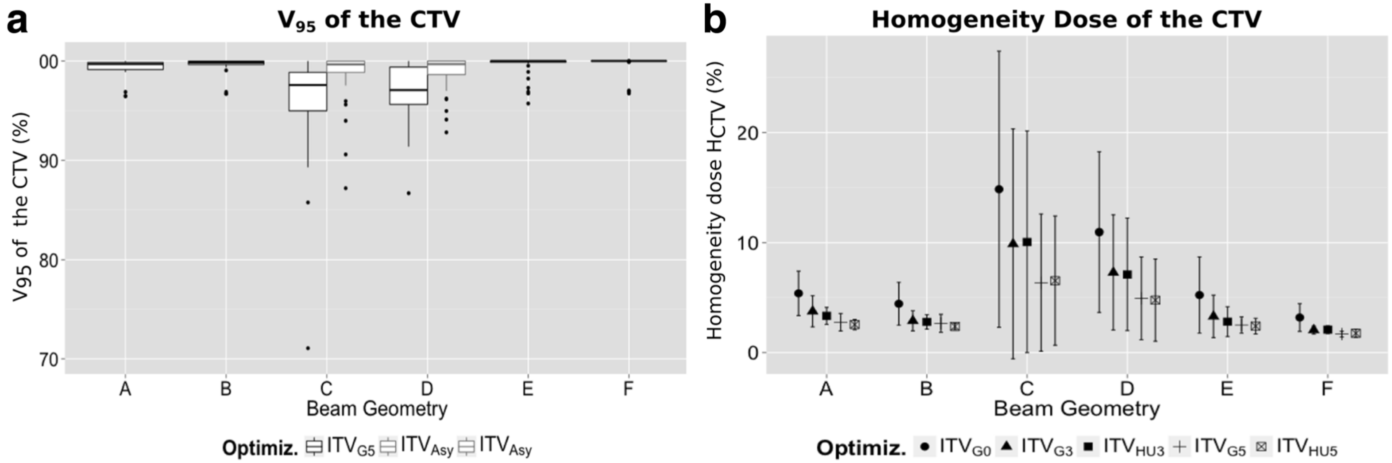
Kumagai M et al IJROBP 73, 2009

BEAM SELECTION

- Multiple beams prepared with a 5° step over ± 20° around the clinical
- Best beam selected based on > CTV V95% on daily CT

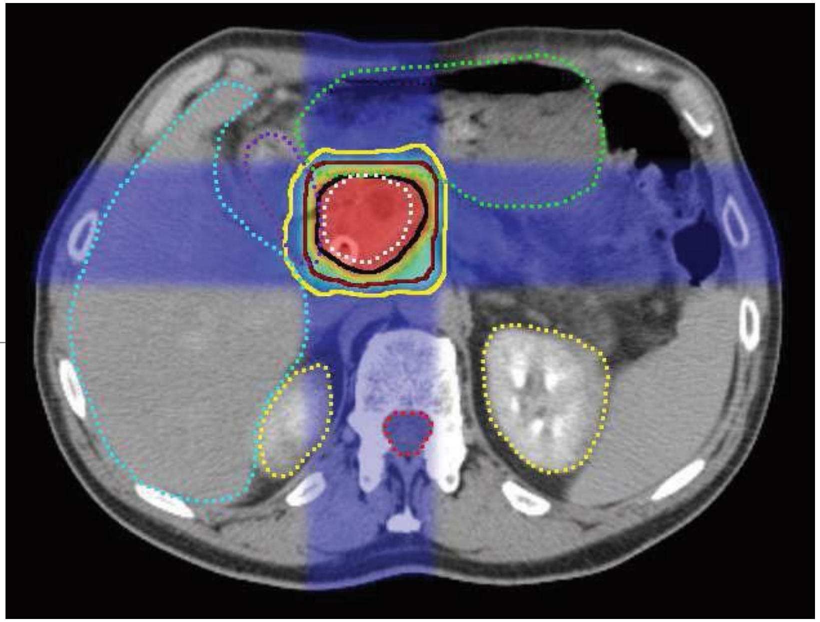


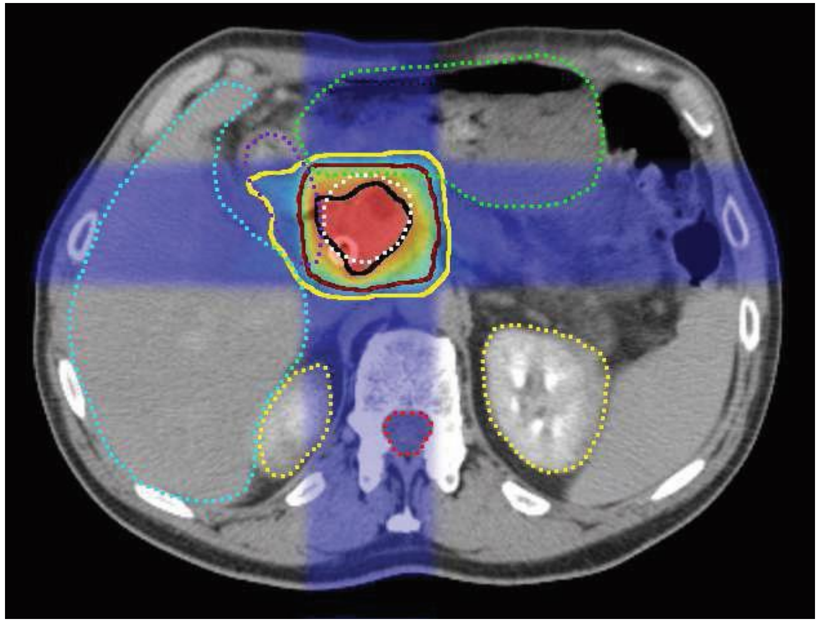




INTER-FRACTION - ORGAN FILLING

- CBCT for online adaptive planning → reduced image quality due to restricted field of view, lower soft-tissue contrast, and inequivalent relation between CBCT voxel values and HU.
- Fraction dose calculations using daily CBCT. The planning CT was deformably registered to each CBCT; gastrointestinal gas volumes were delineated on the CBCTs and copied to the deformed CT.
- Fractionated radiotherapy using photons is highly robust against interfractional anatomical changes. In proton and carbon ion therapy, such changes can severely reduce the dose coverage of the target (ΔD98% >10%).

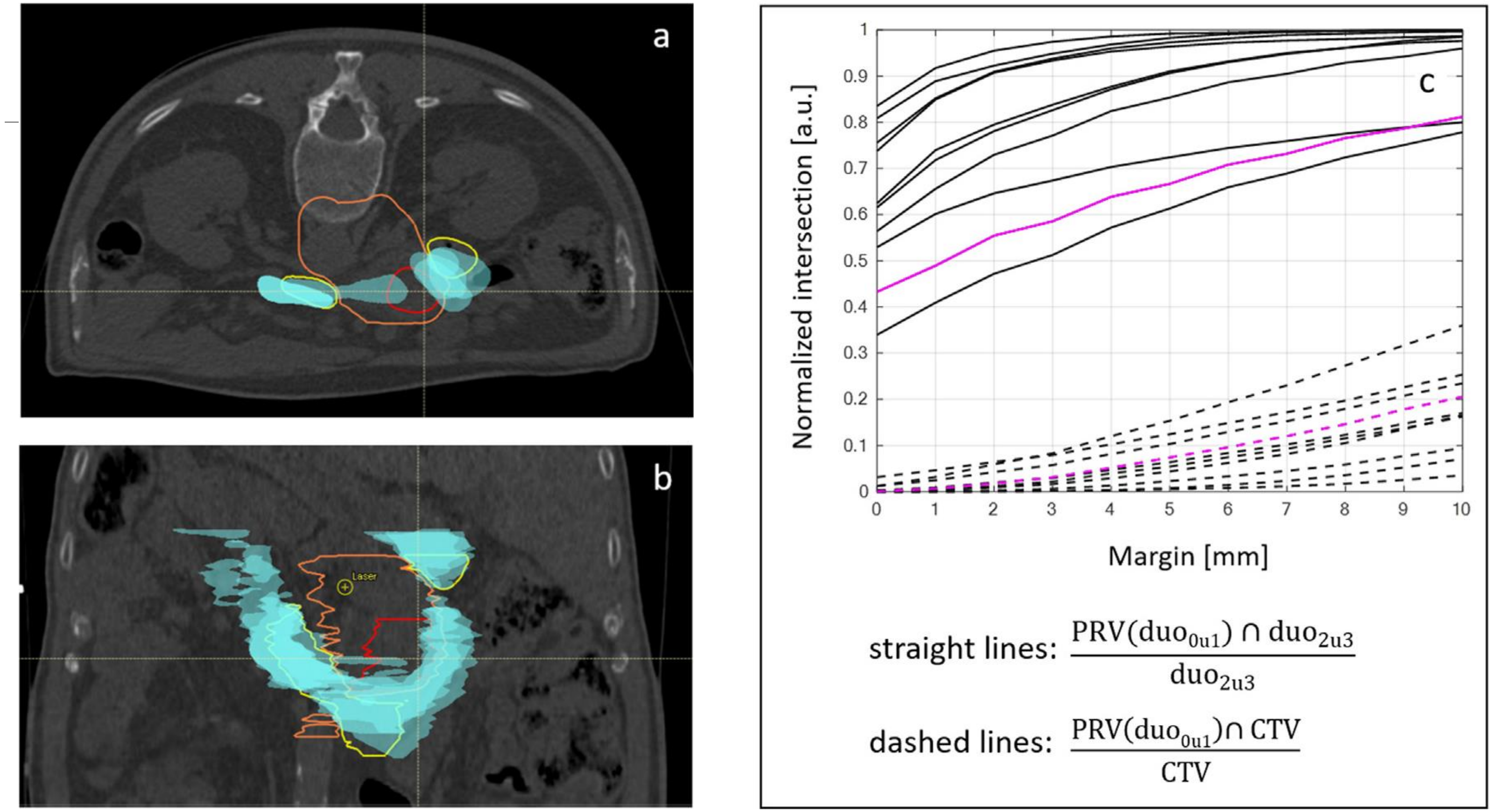




A C Houweling *et al* Phys. Med. Biol. **62** (2017)

IS CBCT ENOUGH? Pancreatic treatment

CNAO
Centro Nazionale di Adroterapia Oncologica



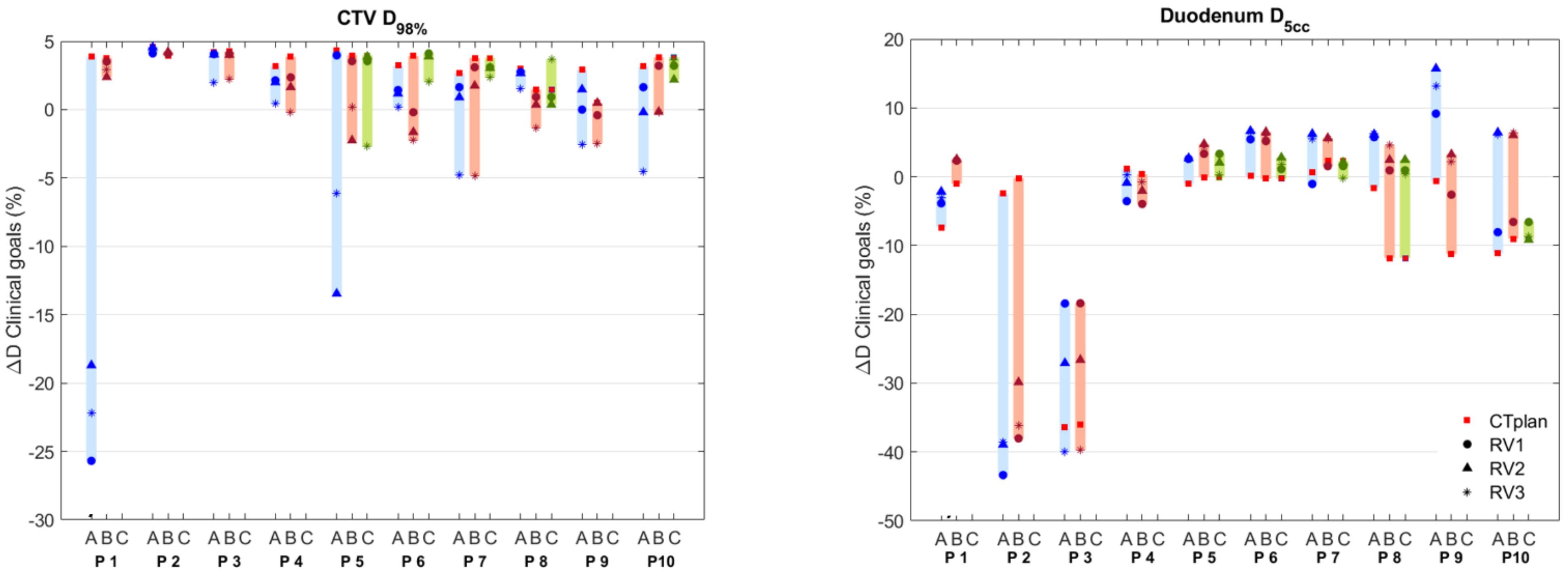
Daily IGRT
In-room CT
(Possibly MR)

OFF-LINE PLAN ADAPTATION

CNAO
Centro Nazionale di Adroterapia Oncologica

→ Thoraco-abdominal (4D) – (CT Planning + 1st RE) + weekly RE

→ Robust optimization on multiple anatomical scenarios



Molinelli S et al. Radiother Oncol 176, 2022

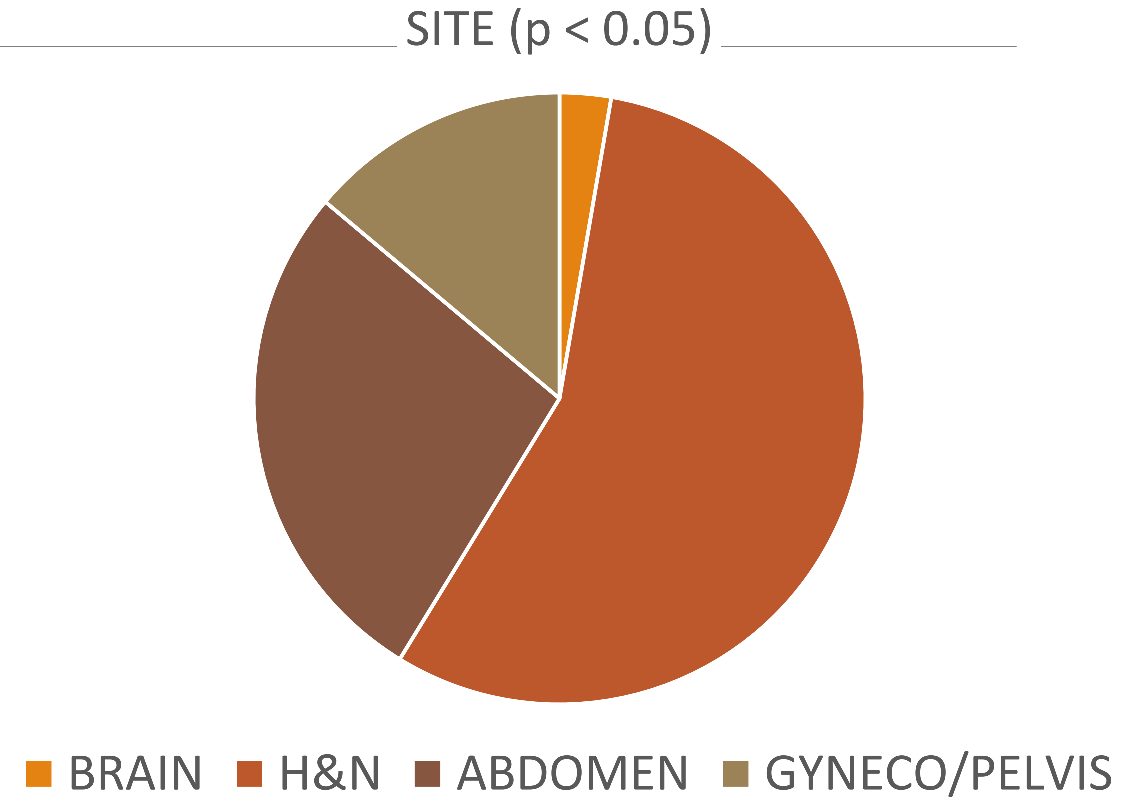
OFF-LINE PLAN ADAPTATION

CNAO - 485 patients (1 yr – no eye)

→ 340 (70%) RE-CT (at 22 days on average)

→ 87 1 RP
→ 20 >1 RP
} 31%

→ 78% Target coverage



Courtesy of A. Vai

THANK YOU

Heavy Ion Therapy Research Integration

Centro Nazionale di Adroterapia Oncologica

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