ORGAN MOTION MANAGEMENT

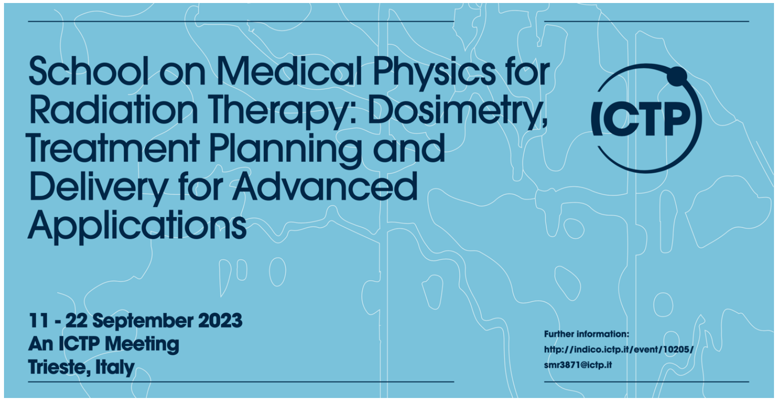
CARLO CAVEDON
MEDICAL PHYSICS UNIT
UNIVERSITY HOSPITAL OF VERONA - ITALY

ICTP School of Medical Physics for Radiation Therapy
TRIESTE – ITALY – 11-22 SEPTEMBER 2023

The Abdus Salam
International Centre
for Theoretical Physics

United Nations
Educational, Scientific and
Cultural Organization

IAEA
International Atomic Energy Agency



ORGAN MOTION IN RADIATION ONCOLOGY

- **respiratory motion**
  - *pseudo-regular motion – predictable in a short interval (50-500 ms)*
- **skeletal-muscular motion**
  - *irregular motion – can be controlled*
- **cardiac motion**
  - *(pseudo-)regular motion – generally not explicitly accounted for in RT*
- **gastrointestinal motion**
  - *unpredictable – can be partly limited*
- **genitourinary system – e.g. bladder filling**
  - *large displacements - can be partly limited*

RESPIRATORY MOTION IN RADIATION ONCOLOGY

AAPM REPORT NO. 91

The Management of Respiratory Motion in Radiation Oncology

Report of AAPM Task Group 76

July 2006

RESPIRATORY MOTION – organs that move with respiration

SHALLOW BREATHING RANGE OF MOTION

- **lung**	up to 50 mm
- **esophagus**	
- **liver**	up to 40 mm
- **pancreas**	up to 35 mm
- **breast**	
- **prostate (!)**	
- **kidneys**	up to 40 mm
- **…**	

RESPIRATORY MOTION IN RADIATION ONCOLOGY

Table 2. Lung tumor–motion data. The mean range of motion and the (minimum–maximum) ranges in millimeters for each cohort of subjects. The motion is in three dimensions (SI, AP, LR).

Observer	Direction		
	SI	AP	LR
Barnes[85]: Lower lobe	18.5 (9–32)	--	--
Middle, upper lobe	7.5 (2–11)	--	--
Chen et al.[84]	(0–50)	--	--
Ekberg et al.[26]	3.9 (0–12)	2.4 (0–5)	2.4 (0–5)
Engelsman et al.[28]:			
Middle/upper lobe	(2–6)	--	--
Lower lobe	(2–9)	--	--
Erridge et al.[101]	12.5 (6–34)	9.4 (5–22)	7.3 (3–12)
Ross[76]: Upper lobe	--	1 (0–5)	1 (0–3)
Middle lobe	--	0	9 (0–16)
Lower lobe	--	1 (0–4)	10.5 (0–13)
Grills et al.[91]	(2–30)	(0–10)	(0–6)
Hanley et al.[77]	12 (1–20)	5 (0–13)	1 (0–1)
Murphy et al.[87]	7 (2–15)	--	--
Plathow[220]: Lower lobe	9.5 (4.5–16.4)	6.1 (2.5–9.8)	6.0 (2.9–9.8)
Middle lobe	7.2 (4.3–10.2)	4.3 (1.9–7.5)	4.3 (1.5–7.1)
Upper lobe	4.3 (2.6–7.1)	2.8 (1.2–5.1)	3.4 (1.3–5.3)
Seppenwoolde et al.[67]	5.8 (0–25)	2.5 (0–8)	1.5 (0–3)
Shimizu et al.[52]	--	6.4 (2–24)	--
Sixel et al.[92]	(0–13)	(0–5)	(0–4)
Stevens et al.[66]	4.5 (0–22)	--	--

AP: anterior–posterior; LR: left–right; SI: superior–inferior.

RESPIRATORY MOTION IN RADIATION ONCOLOGY

Table 3. Abdominal motion data. The mean range of motion and the (minimum–maximum) ranges in millimeters for each site and each cohort of subjects. The motion is in the superior–inferior (SI) direction.

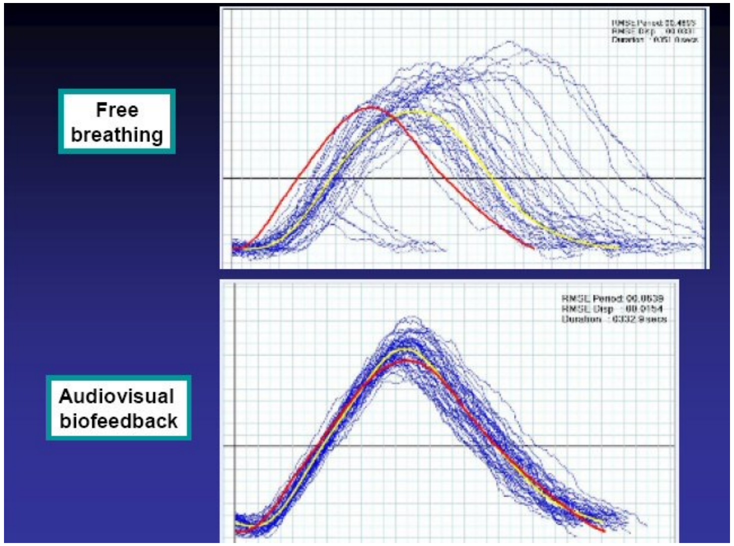
Site	Observer	Breathing mode	
		Shallow	Deep
Pancreas	Suramo et al.[74]	20 (10–30)	43 (20–80)
	Bryan et al.[75]	20 (0–35)	--
Liver	Weiss et al.[89]	13 +/– 5	--
	Harauz et al.[90]	14	--
	Suramo et al.[74]	25 (10–40)	55 (30–80)
	Davies et al.[68]	10 (5–17)	37 (21–57)
Kidney	Suramo et al.[74]	19 (10–40)	40 (20–70)
	Davies et al.[68]	11 (5–16)	--
Diaphragm	Wade[80]	17	101
	Korin et al.[79]	13	39
	Davies et al.[68]	12 (7–28)	43 (25–57)
	Weiss et al.[89]	13 +/– 5	--
	Giraud et al.[78]	--	35 (3–95)
	Ford et al.[86]	20 (13–31)	--

SOURCES OF INFORMATION – RESPIRATORY MOTION

- **radiography** (e.g. double exposure or cine)
- **fluroscopy** (with or without fiducial markers)
- **ultrasound**
- **CT** and **4D-CT** (amplitude- or phase-based / prospective or retrospective / …)
- **MR** and **4D-MR**
- **PET** and **4D-PET**

MITIGATION OF MOTION AND MOTION IRREGULARITY

- patient **training**
- audiovisual **feedback**
- oxygen administration?



	Air	O_2
Breath Hold time (sec)	20 (11-40)	100 (85-230)
% O_2 Pre BH	95% (90-97)	100%
%O_2 After BH	94%(90-97)	100%

M Romano, C Cavedon, A Porcaro, M Palazzi, M Gabbani, N Marciai, A D'Amico, S Dall'Oglio, F Pioli, MG Giri, A Grandinetti, "Does pre-radiation oxygen breathing prolong deep inspiration breath hold?" ASTRO meeting 2013

R George et al., "Audio-visual biofeedback for respiratory-gated radiotherapy: Impact of audio instruction and audio-visual biofeedback on respiratory-gated radiotherapy", Int J Rad Onc Biol Phys 65, 924-933 (2006)

RESPIRATORY MOTION – 5 MAJOR STRATEGIES FOR MANAGEMENT

- **motion encompassing** techniques

- **breath-hold** techniques

- **forced shallow-breathing** techniques

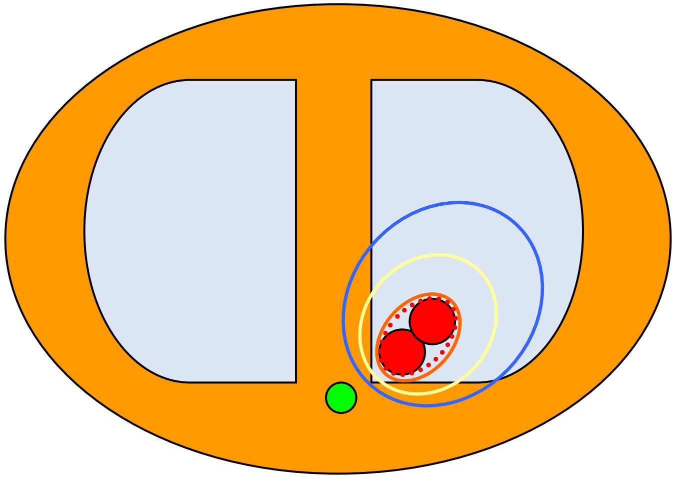
- **respiratory-gating** techniques

- **respiration-synchronized** techniques (**tracking**)

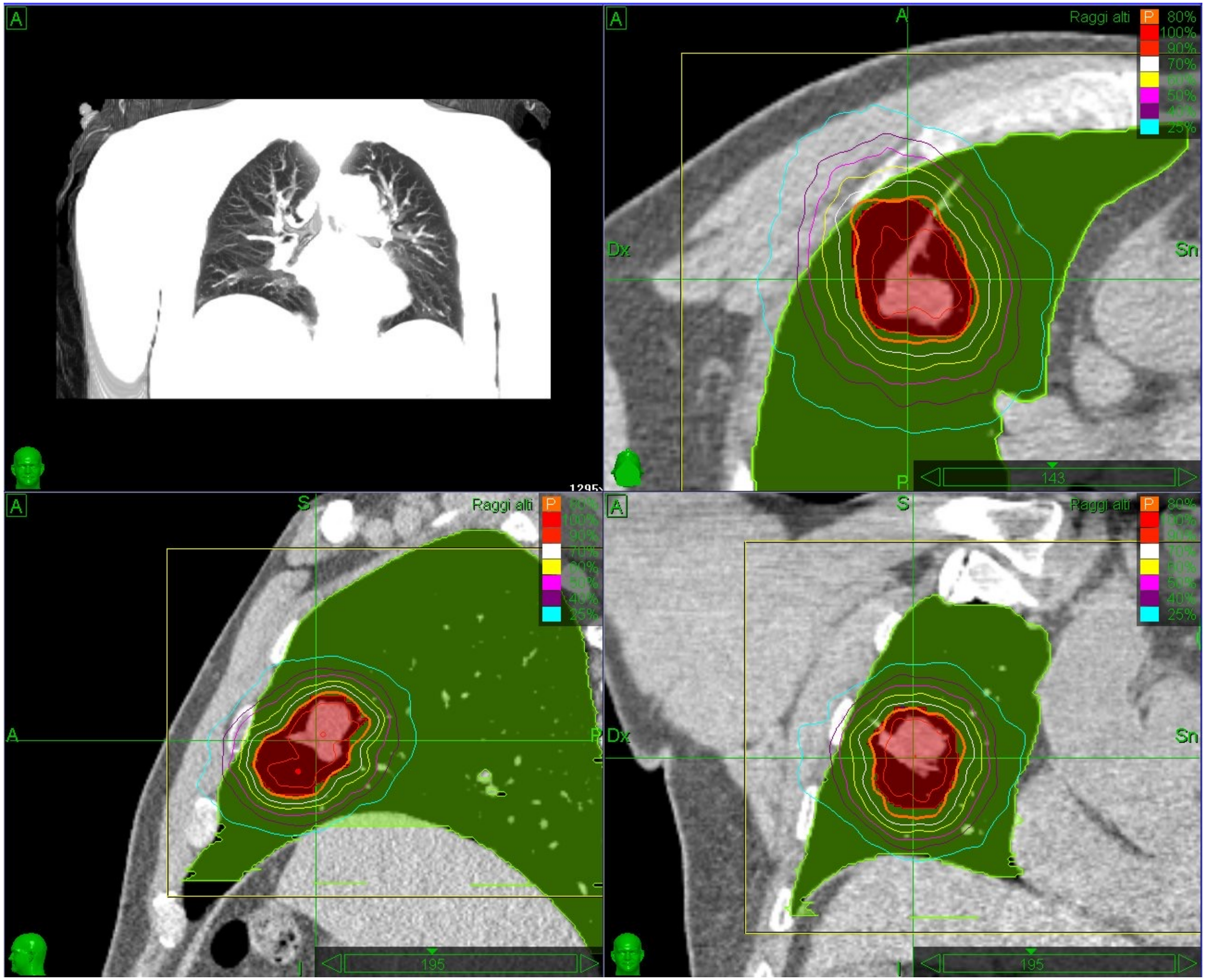
RESPIRATORY MOTION - IMPLICIT MANAGEMENT

- **motion encompassing** techniques
  - *concept: treat the whole volume defined by the envelope of positions during respiration*

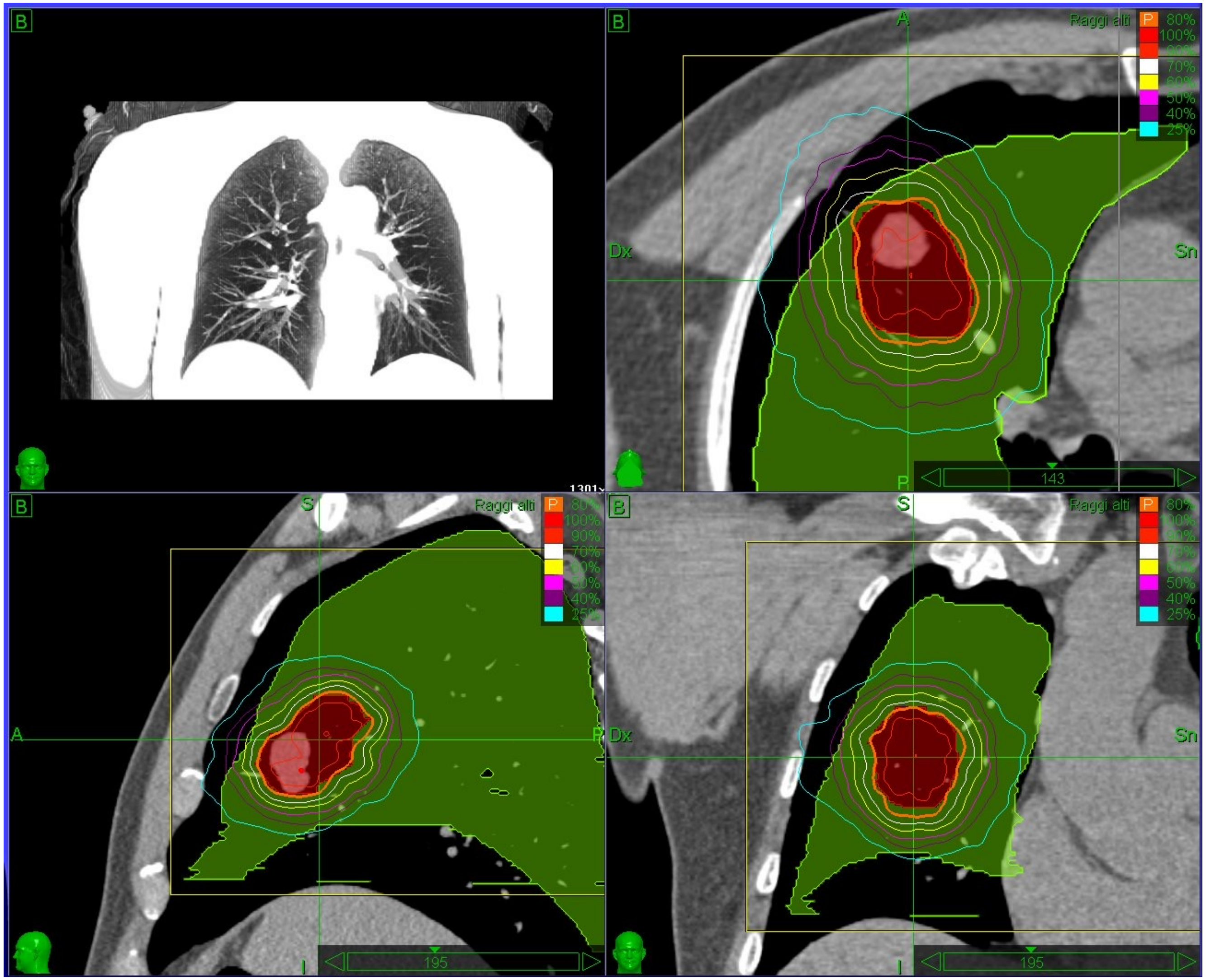
- **ITV = internal target volume** (ICRU 62) = CTV+IM



MOTION ENCOMPASSING – EXAMPLE - expiration

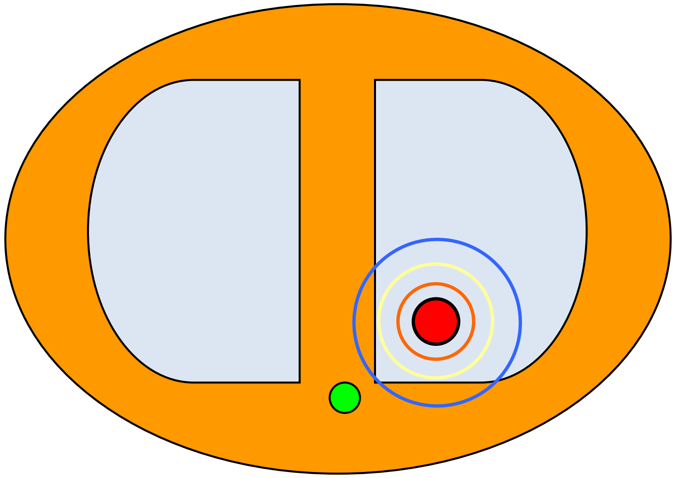


MOTION ENCOMPASSING – EXAMPLE - inspiration

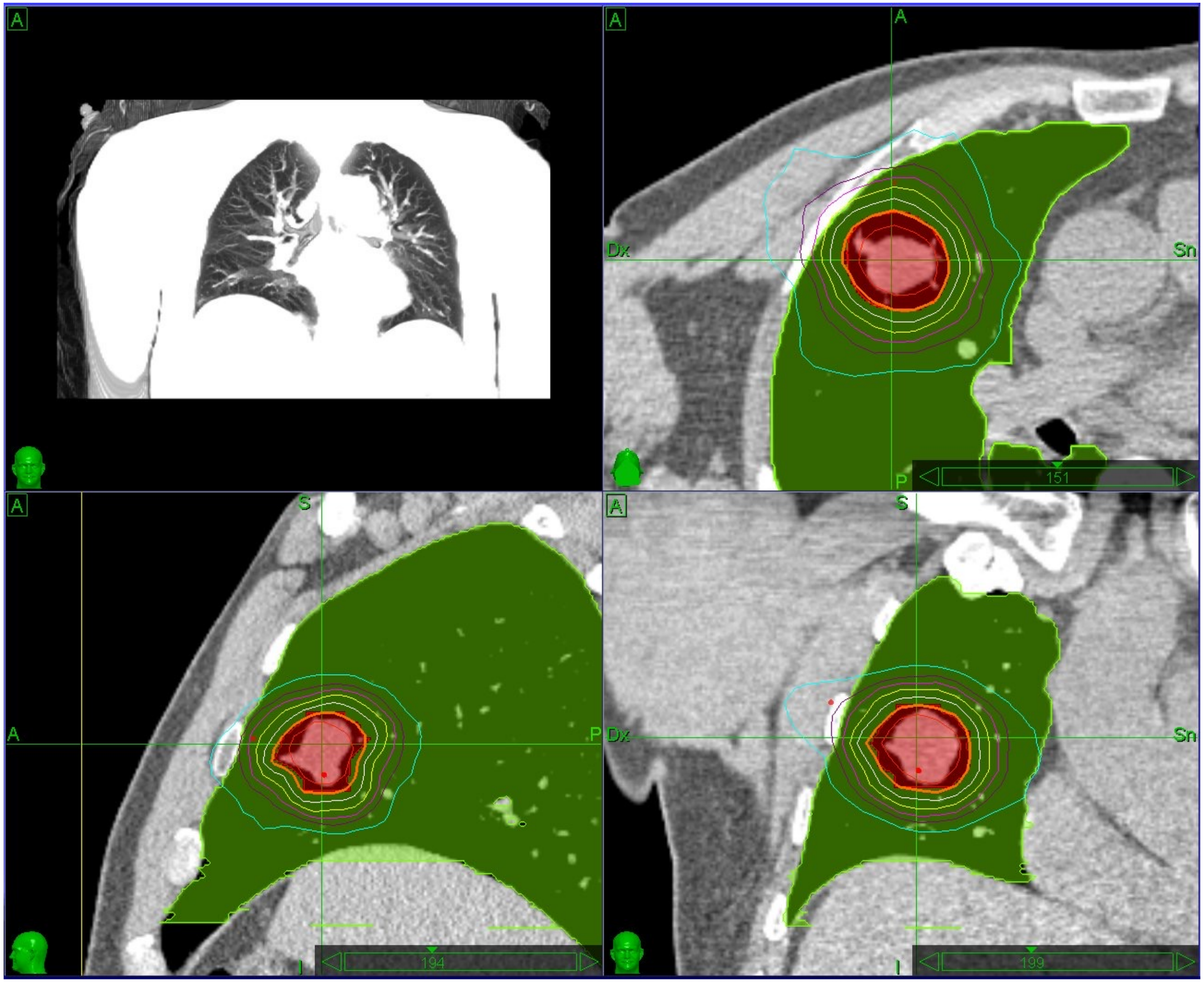


RESPIRATORY MOTION – EXPLICIT MANAGEMENT

- **respiratory gating** techniques
  - *concept: treat only when the target is within the "gating window"*
  - *volume / normal tissue preservation*
  - *long treatment times*



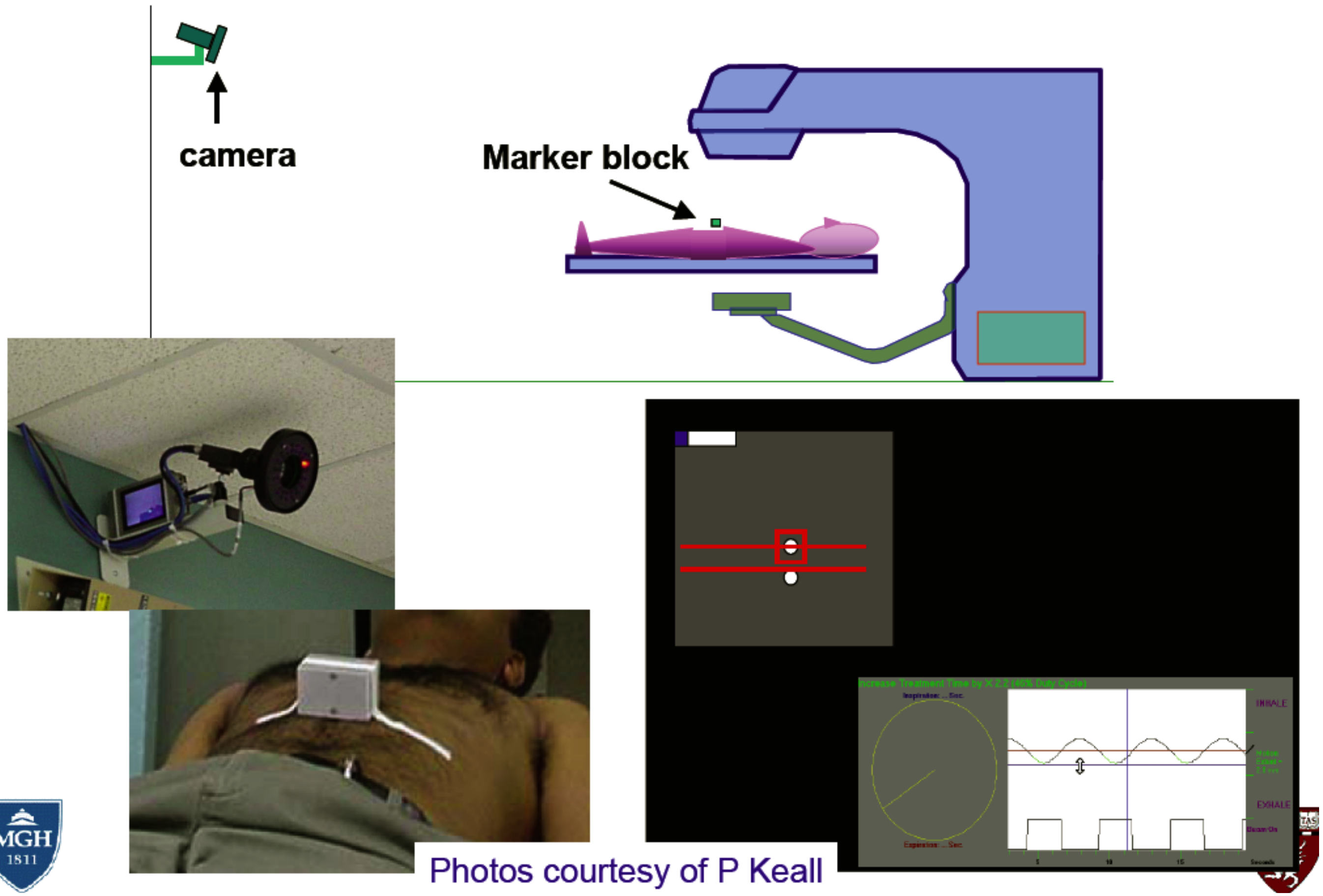
RESPIRATORY GATING – EXAMPLE



RESPIRATORY GATING

- surrogate signal needed to describe motion in real time

[13/48]



Photos courtesy of P Keall

RESPIRATORY GATING – need for surrogate signal

- possible inaccuracy from the relation between tumor motion and surrogate signal

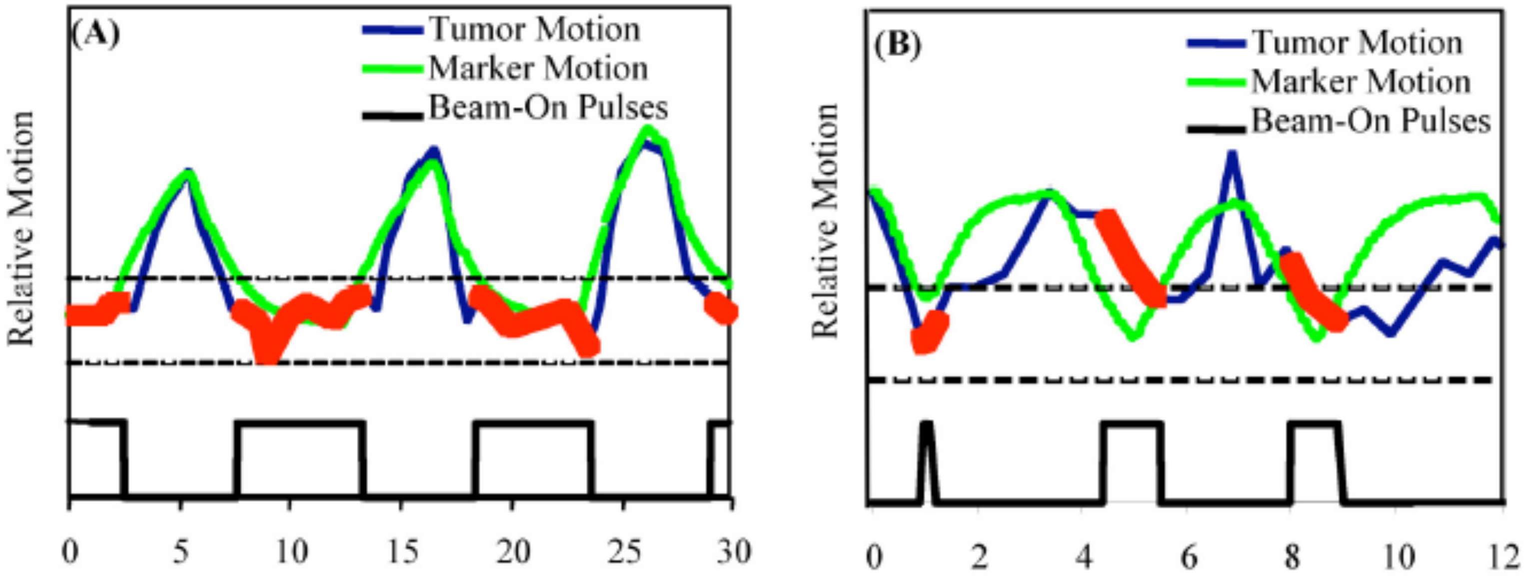
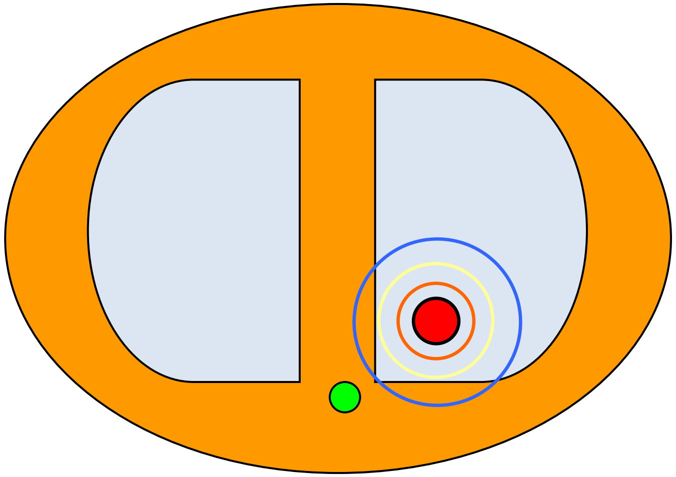


Figure 7. Comparison of external marker block motion with internal motion of the clinical target volume (CTV) for a patient with (a) no phase shift and (b) a patient with significant phase shift. The respiratory gating thresholds are set using the external marker block motion. The beam-on pulses are highlighted in red over the internal CTV position. [Reproduced from reference 227: *Int J Radiat Oncol Biol Phys*, vol 48, "Clinical experience with a commercial respiratory gating system." C. R. Ramsey, D. D. Scaperoth, and D. C. Arwood, pp. P164-165. © 2000, with permission from Elsevier.]

RESPIRATORY MOTION – EXPLICIT MANAGEMENT

- **respiratory tracking (synchronized)** techniques
  - *concept: redirect beam to the target position in real time*
  - *volume / normal tissue AND treatment time preservation*

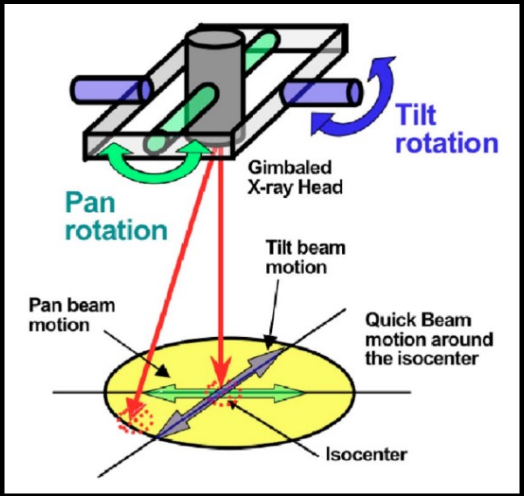


RESPIRATORY MOTION – EXPLICIT MANAGEMENT

- **respiratory tracking (synchronized)** techniques

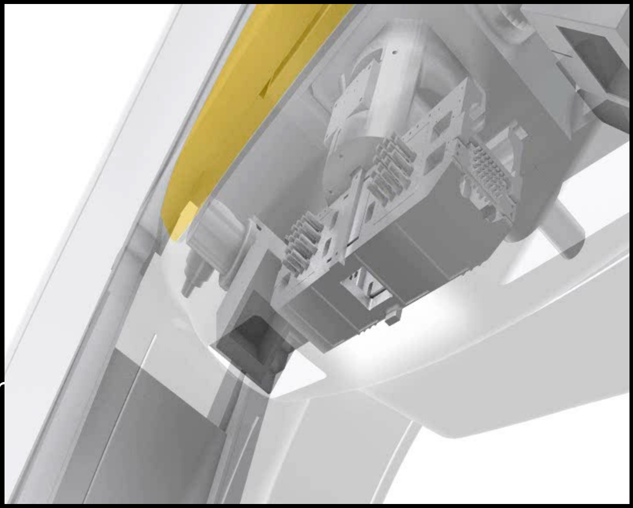
VERO system (BrainLab/MHI)

Gimbaled linac/MLC assembly



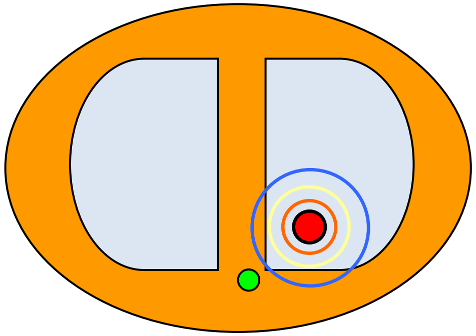
Gimbals tilt/pan : ± 4.4 cm (at iso)
Gimbals oscillation speed : 0.5 Hz
Gimbals position accuracy : 0.1 mm

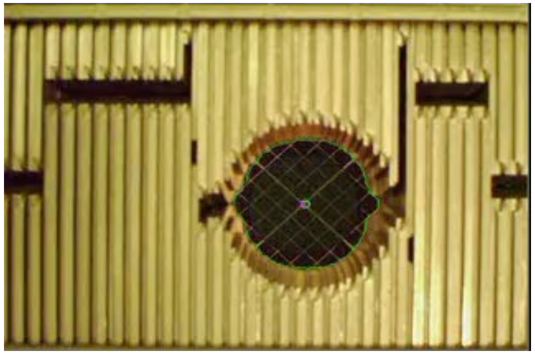
C-band linac: 6 MV beam
Gantry rotation : [-185° ,185°] ± 1°
O-arm rotation : [-60° ,60°] ± 1°
No collimator/MLC rotation
MLC leaves : 60 x 5 mm single focus
Max. field size : 15 x 15 cm
Couch : 5D (lat, long, vert, roll, pitch) ± 6th degree by O-arm



RESPIRATORY MOTION – EXPLICIT MANAGEMENT

- **respiratory tracking**
  - MLC tracking (and couch) tracking (limited availability)
  - clinical trials ongoing (lung, prostate)
  - new systems recently available – possibly increased use

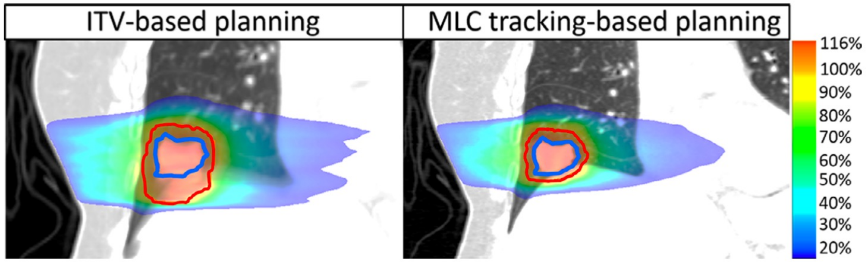


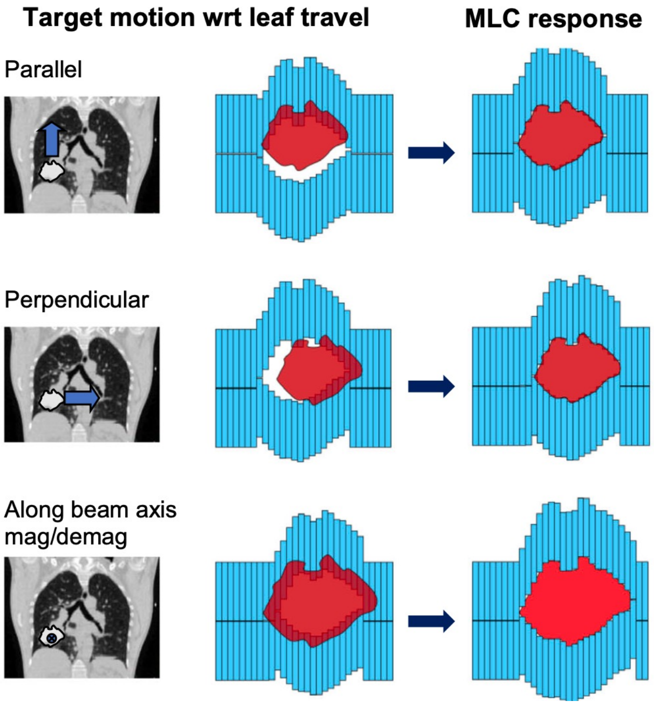


VIDEO Supplementary Material from: Keall PJ et al., AAPM Task Group 264: The safe clinical implementation of MLC tracking in radiotherapy. Med Phys. 2021 May; 48(5):e44-e64

MOTION MANAGEMENT IN USE

- **MLC tracking: dosimetric benefit**
  - sparing of irradiated volume
  - reduced dosimetric uncertainties
  - MLC can compensate motion in 3D (limitations posed by max leaf speed)



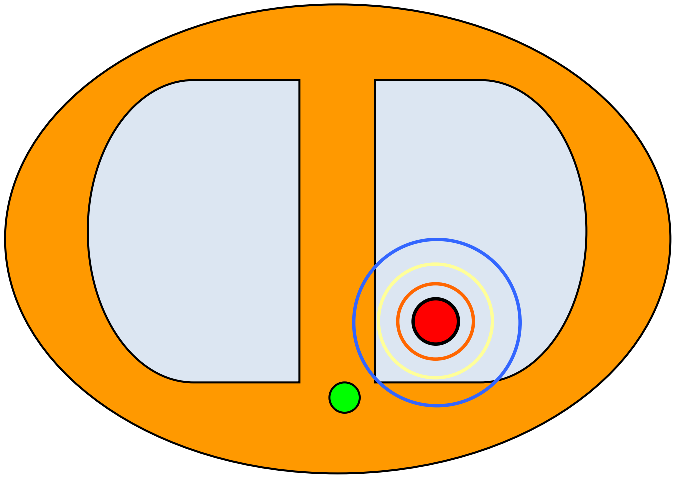


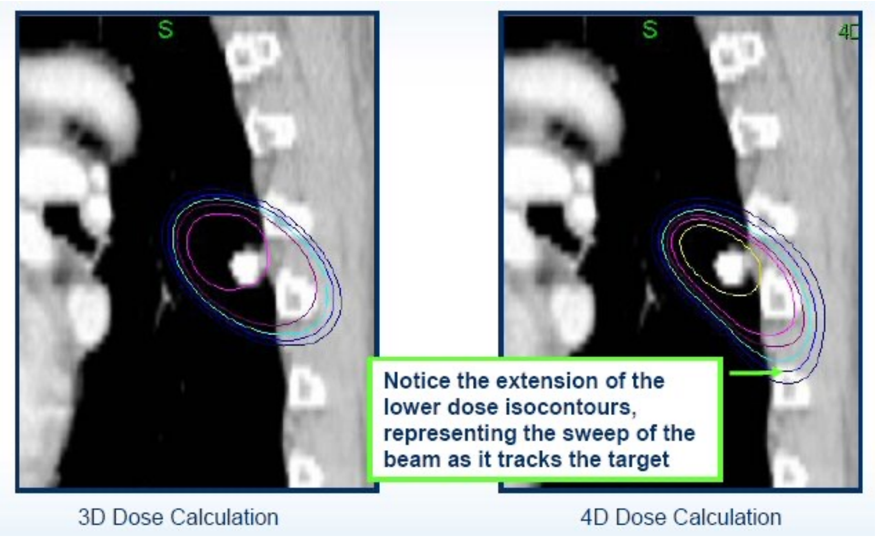
Keall PJ, Sawant A, Berbeco RI, Booth JT, Cho B, Cerviño LI, Cirino E, Dieterich S, Fast MF, Greer PB, Munck Af Rosenschöld P, Parikh PJ, Poulsen PR, Santanam L, Sherouse GW, Shi J, Stathakis S. AAPM Task Group 264: The safe clinical implementation of MLC tracking in radiotherapy. Med Phys. 2021 May;48(5):e44-e64. doi: 10.1002/mp.14625. Epub 2021 Mar 23. PMID: 33260251.

RESPIRATORY TRACKING

- **need for 4D PLANNING**

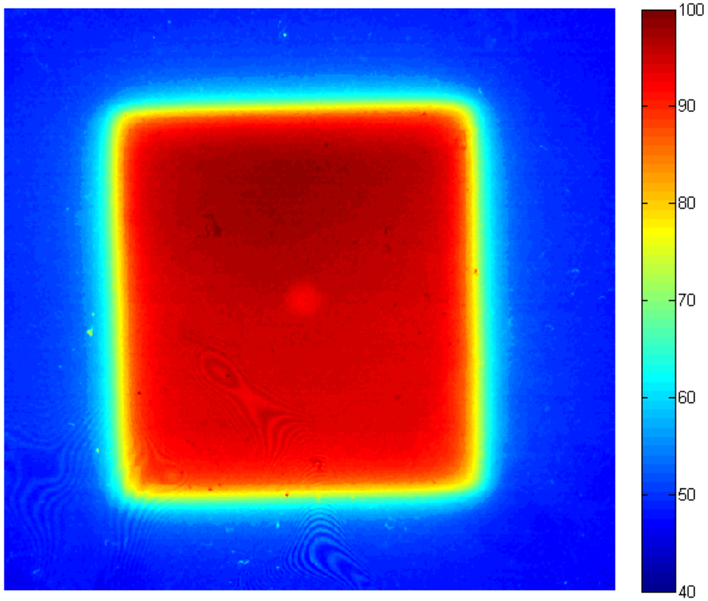
- planning on one phase does not guarantee dosimetric accuracy on nearby tissues

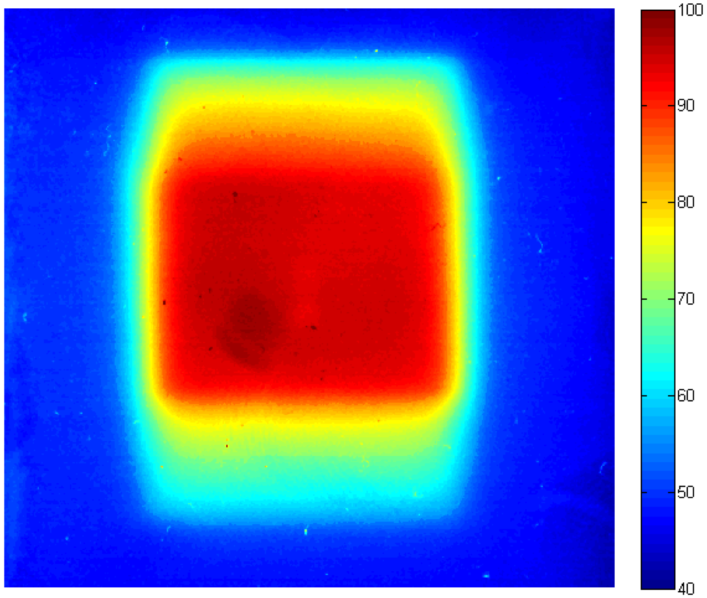




- 4D planning requires a complete description of the respiratory phase (e.g. 4DCT – see below)

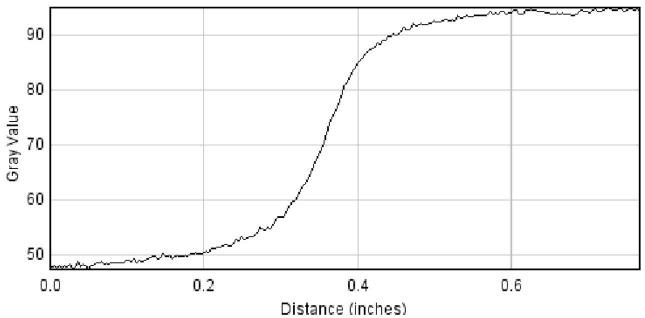
ACCURACY OF DOSE DISTRIBUTION – GATING

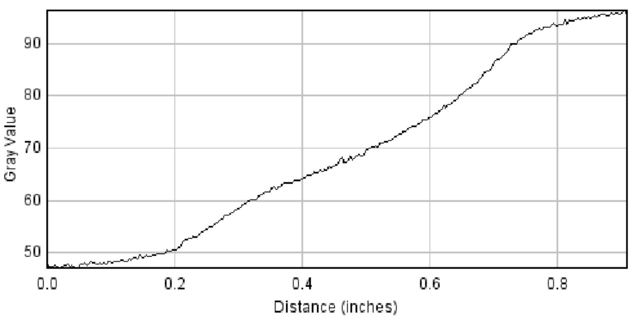




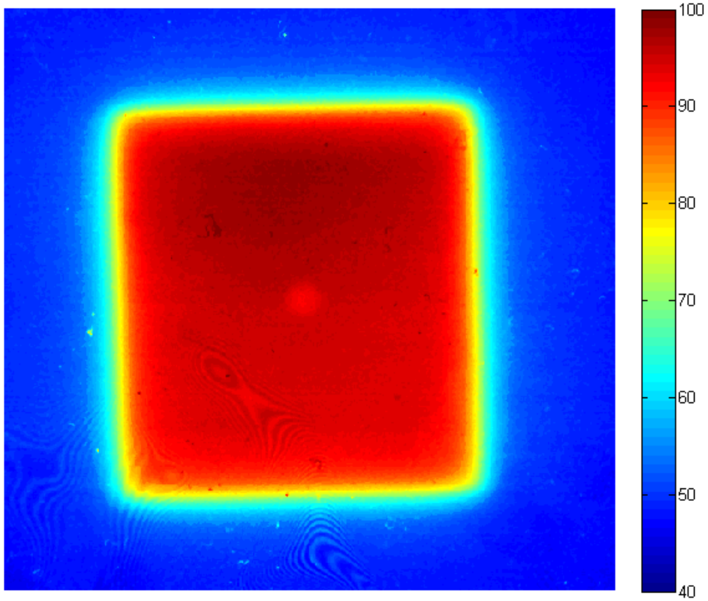
RPM system – static target

RPM system – moving target
no motion control

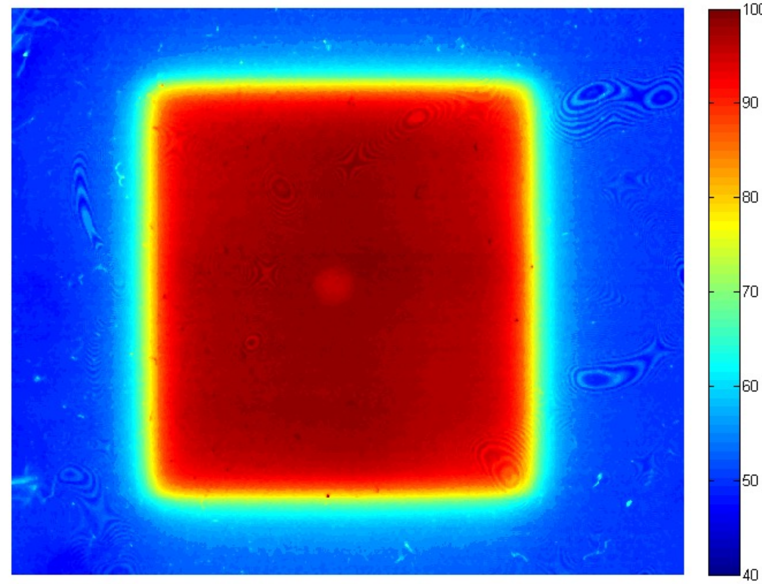




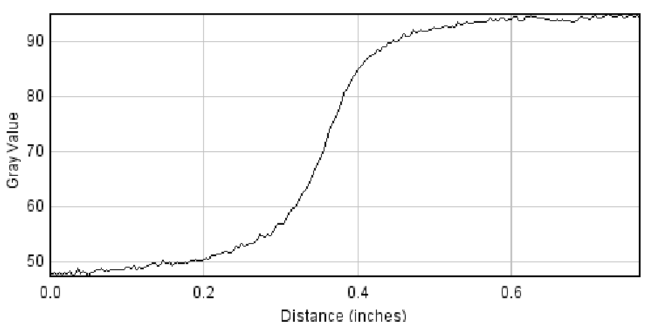
ACCURACY OF DOSE DISTRIBUTION – GATING

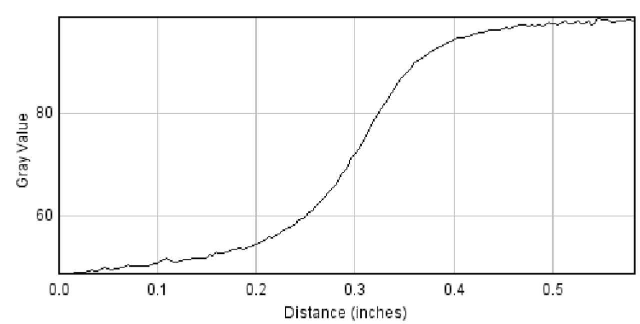


RPM system – static target



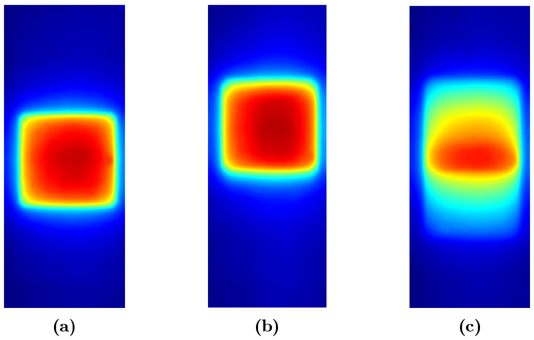
RPM system – moving target
gating system activated

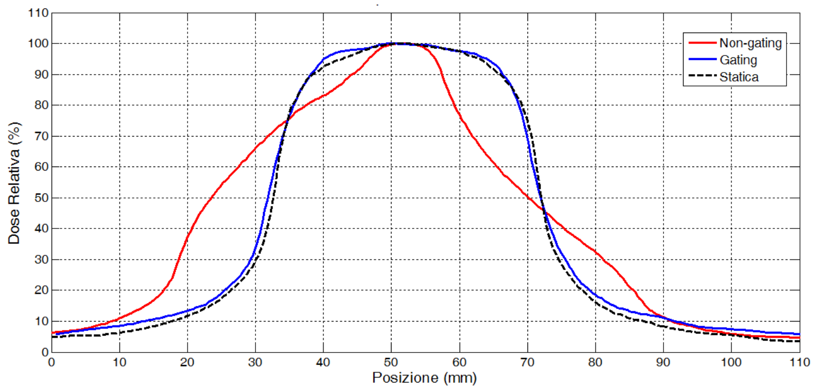




ACCURACY OF DOSE DISTRIBUTION – GATING

- **respiratory gating and tracking**
  - need for dedicated QA





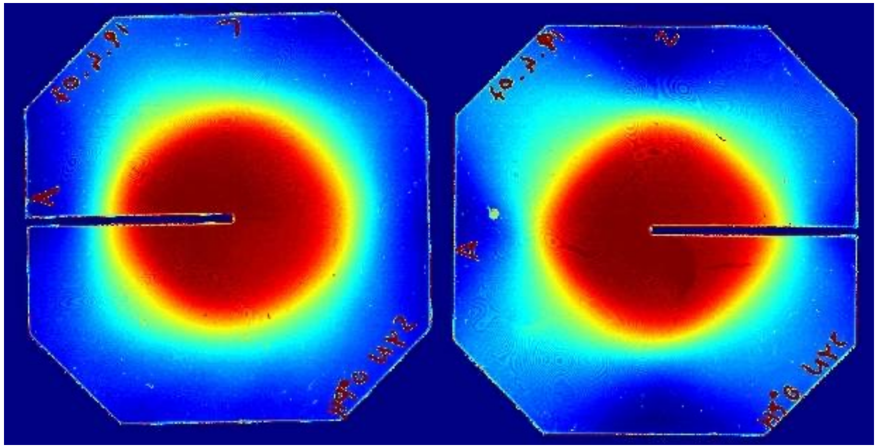
Comparison of dose distributions

- *left: static irradiation*
- *center: mobile target, gating activated*
- *right: mobile target, no gating*

Dose profiles

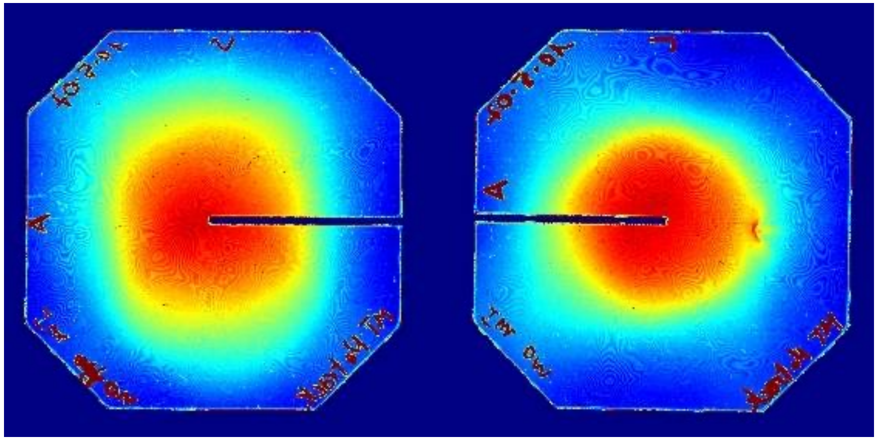
- *dotted black: static irradiation*
- *blue: mobile target, gating activated*
- *red: mobile target, no gating*

ACCURACY OF DOSE DISTRIBUTION – TRACKING


Cyberknife: static target

dose gradient

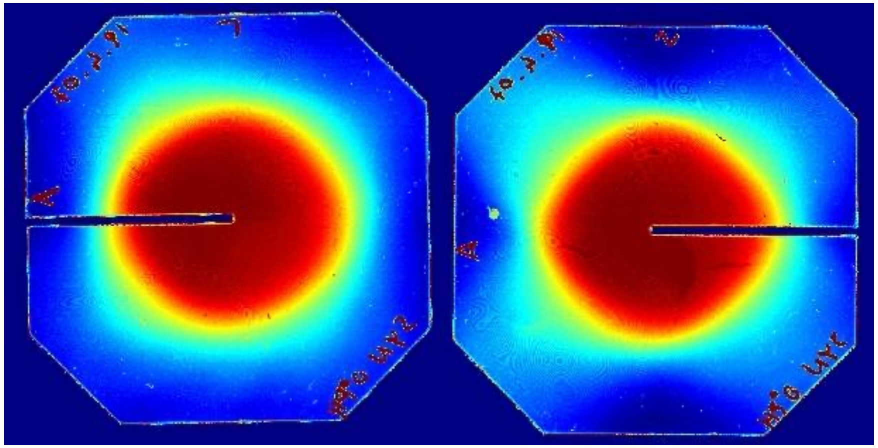
277 cGy/mm


Cyberknife: moving target without motion control

dose gradient

88 cGy/mm

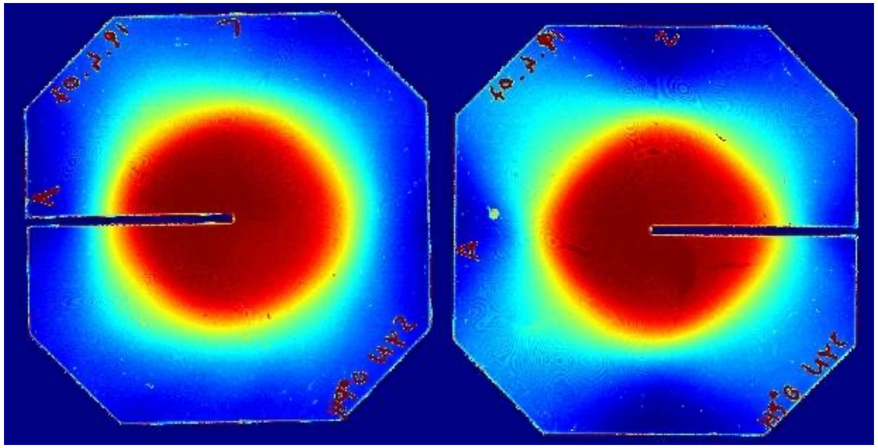
ACCURACY OF DOSE DISTRIBUTION – TRACKING



Cyberknife: static target

dose gradient

277 cGy/mm

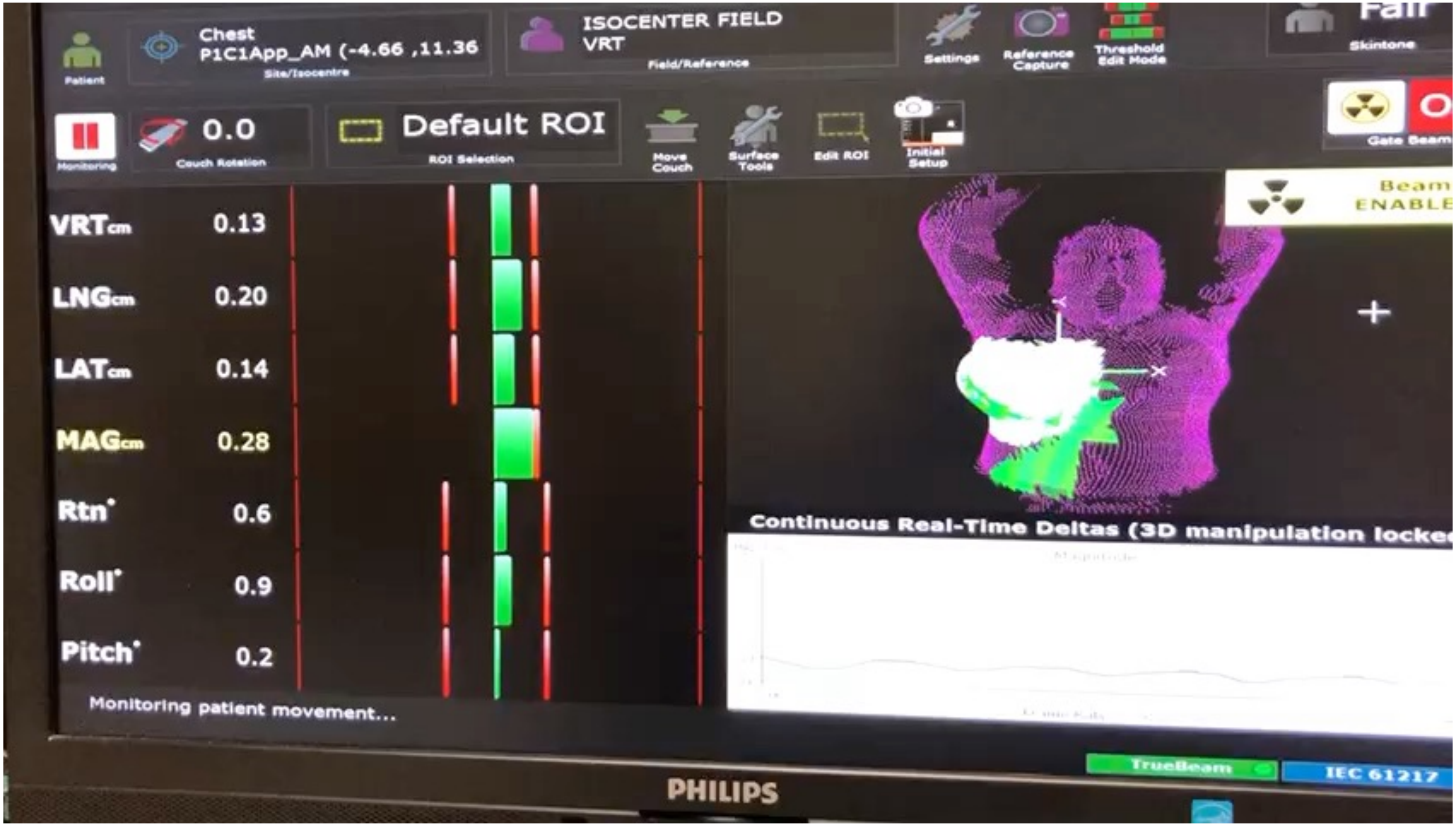


Cyberknife: tracking

dose gradient

273 cGy/mm

Example of gating in the clinical practice: real-time optical monitoring



MOTION MANAGEMENT IN USE

- **Survey** on practice and technology use in SRT and SBRT Delivery (2020)
  - results for lung SBRT – motion managenent system

Motion Management System	
Motion encompassing (ITV)	36.4%
Gating	11.3%
Breath-Hold	6.9%
Tracking (x-rays)	6.5%
Motion restriction (abdominal compression)	14.0%
Other, or multiple systems	24.9%

Chetvertkov M, Monroe JI, Boparai J, Solberg TD, Pafundi DH, Ruo RL, Gladstone DJ, Yin FF, Chetty IJ, Benedict S, Followill DS, Xiao Y, Sohn JW. NRG Oncology Survey on Practice and Technology Use in SRT and SBRT Delivery. Front Oncol. 2020 Nov 27;10:602607. doi: 10.3389/fonc.2020.602607. PMID: 33330102; PMCID: PMC7729187.

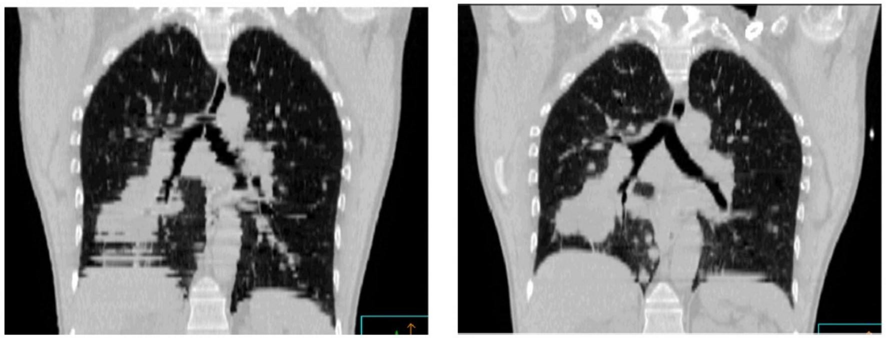
MOTION CONTROL IN IMAGING FOR TREATMENT PLANNING AND TREATMENT VERIFICATION

- need for **temporal coherence** between **imaging** for treatment planning and **treatment** administration

- imaging shall **describe the treatment condition**

- **quantitative imaging** (e.g. BTV based on SUV map) shall account for motion in order to avoid **quantification errors**

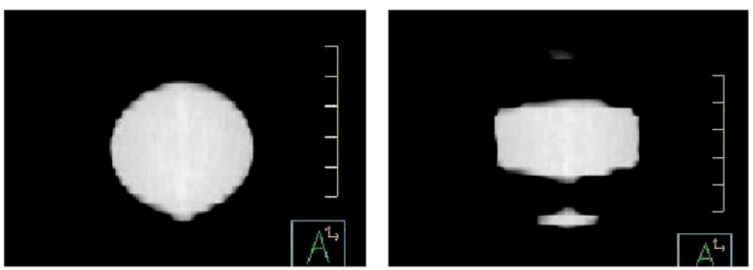
MOTION CONTROL IN IMAGING FOR TREATMENT PLANNING AND TREATMENT VERIFICATION



(a) (b)

Figure 1. Coronal views of CT scans of the same patient taken during free breathing (FB) (a) and with respiratory-gated scanning at exhale (b). [Reproduced from reference 53: P. J. Keall, V. R. Kini, S. S. Vedam, and R. Mohan, "Potential radiotherapy improvements with respiratory gating," *Australas Phys Eng Sci Med* 25(1):1–6, Figure 1. © 2002, with permission from APESM.]

- effect of motion on a free-breathing patient (CT left) and at exhale (right)



(a) (b)

Figure 2. Coronal views of CT scans of a static sphere (a) and a sinusoidally moving sphere (b) (2-cm range of motion and a 4-second period). [Reproduced from reference 56: S. S. Vedam, P. J. Keall, V. R. Kini, H. Mostafavi, H. P. Shukla, and R. Mohan, "Acquiring a four-dimensional computed tomography dataset using an external respiratory signal," *Phys Med Biol* 48(1):45–62, Figure 1. © 2003, with permission from IOP Publishing Limited.]

- static sphere seen at CT (left) and effect of sinusoidal motion (right)

4D-CT: principle

4DCT – how to use the information

- **Consistency** between imaging – planning - delivery

4D-CT volume

free-breathing delivery
motion encompassing
(estimation of target range)

breath-hold

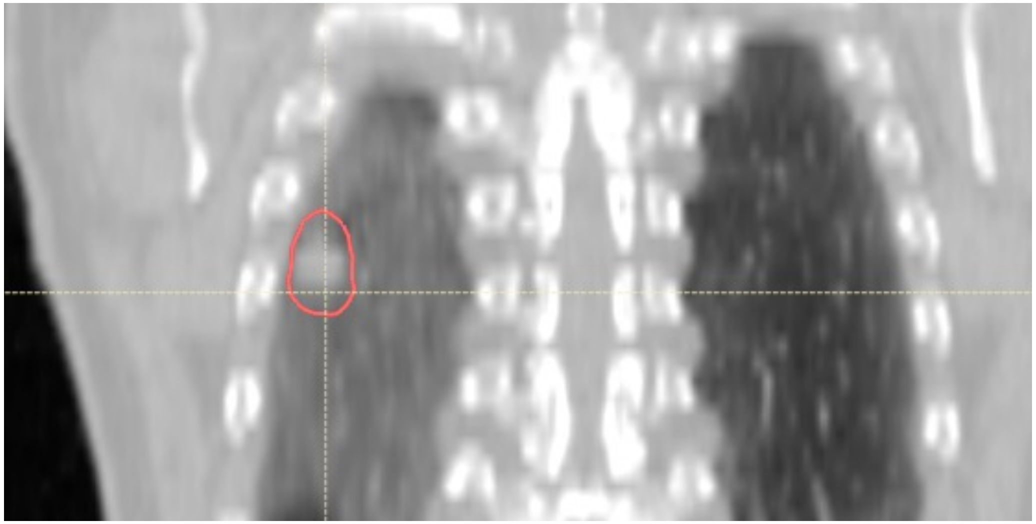
forced shallow-breathing

respiratory gating

respiratory tracking

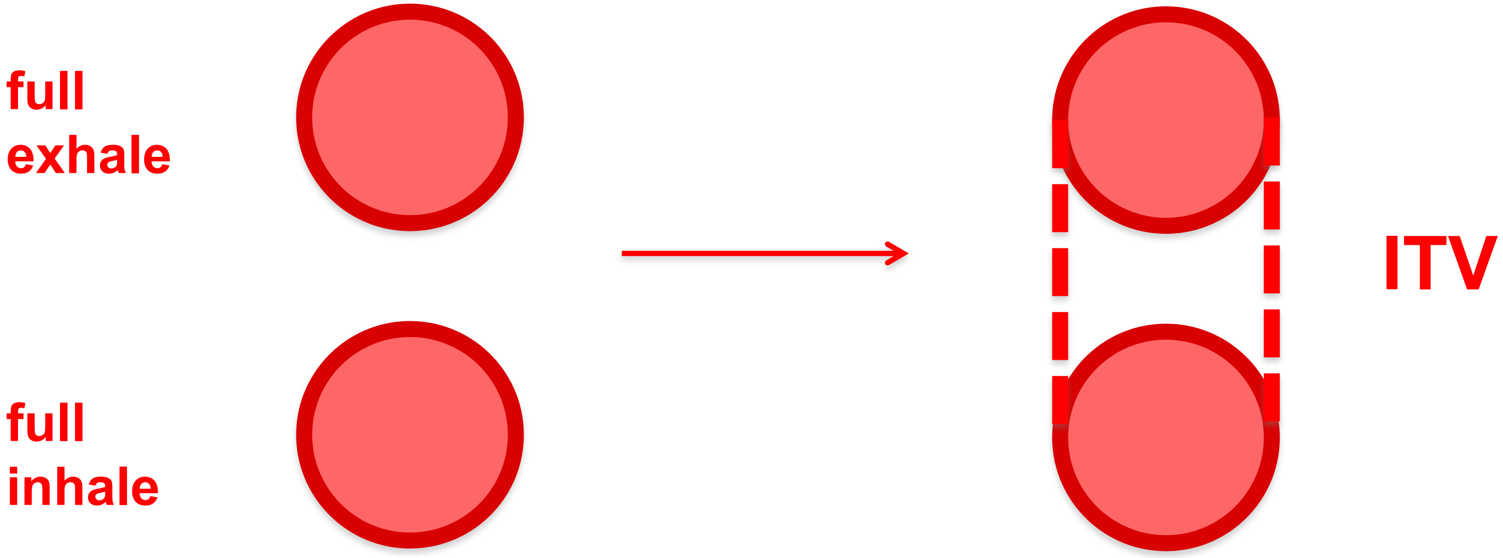
4DCT – derived volumes

- **ITV** from 4DCT phases
- **manual or auto-propagated** contours on all phases



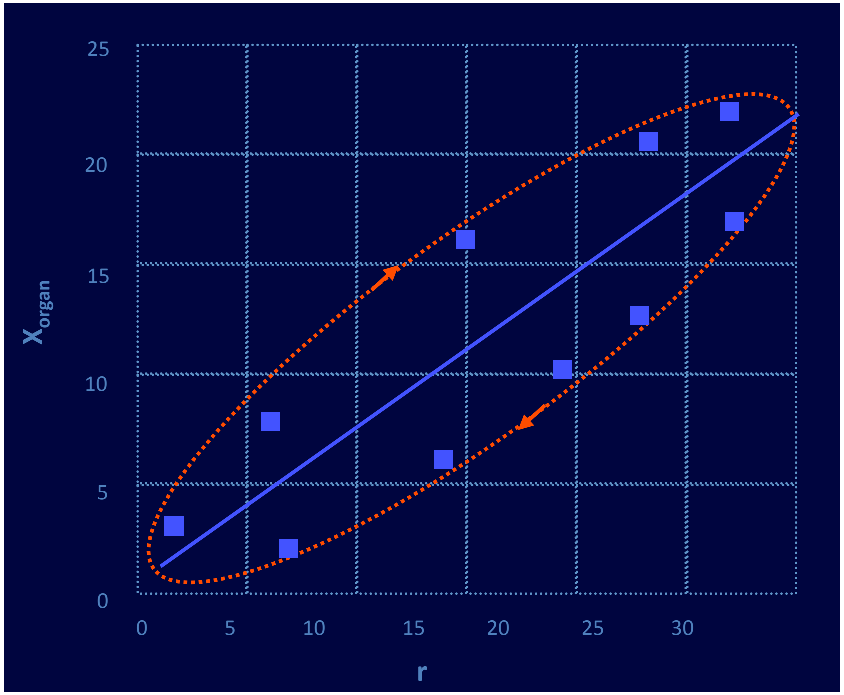
4DCT – derived volumes

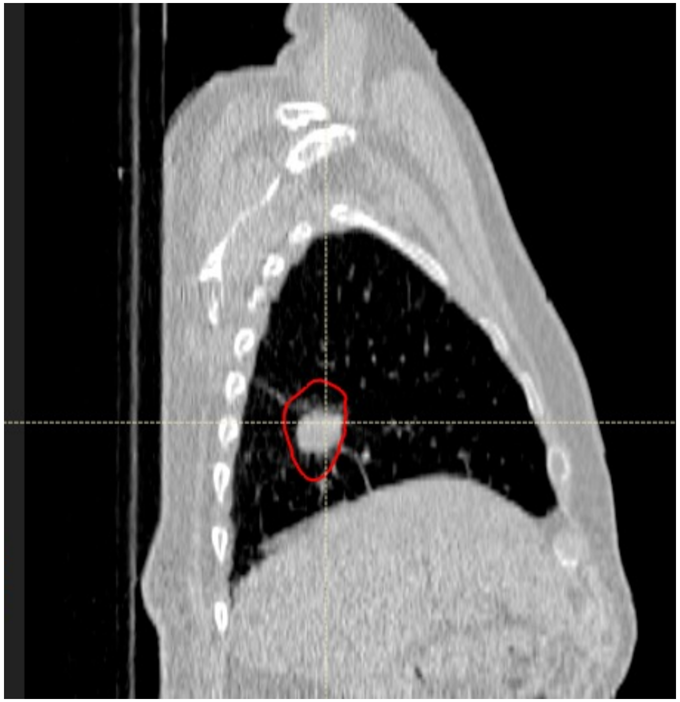
- **ITV** from 4DCT phases
- **full inhale** and **full exhale** sufficient?



4DCT – derived volumes

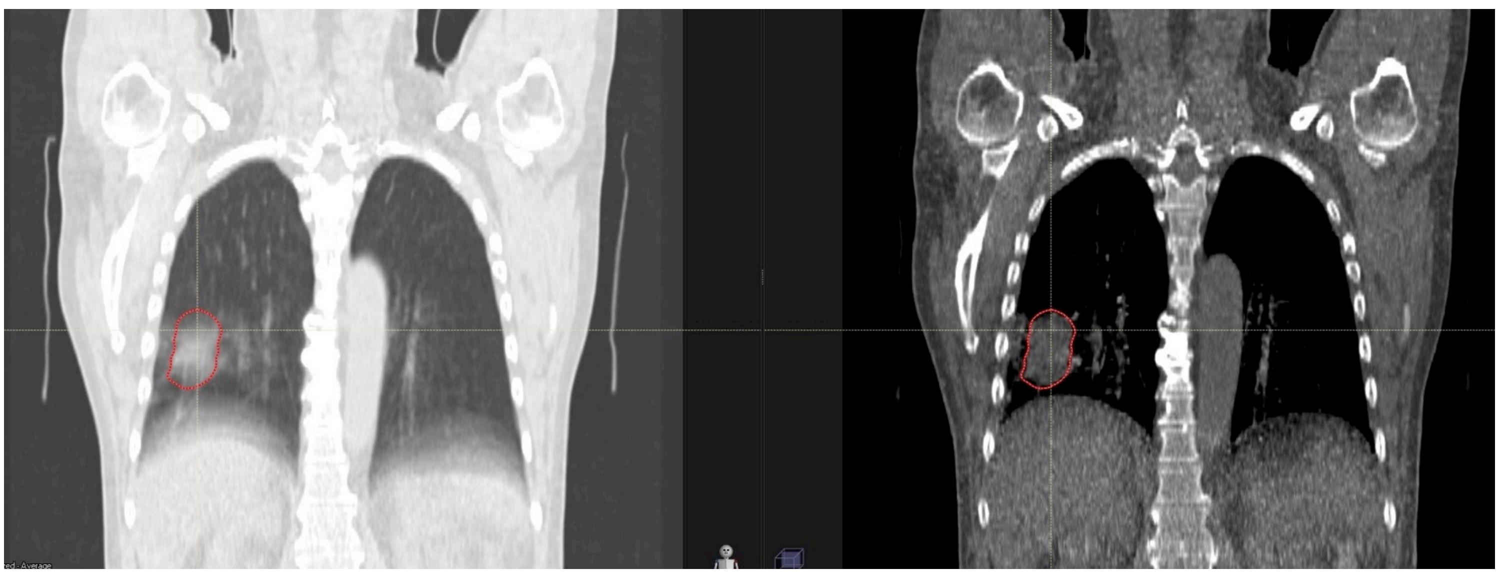
- **hysteresis** in the respiratory cycle (A→B ≠ B→A)
- static anatomy ≠dynamic evolution





4DCT – derived volumes

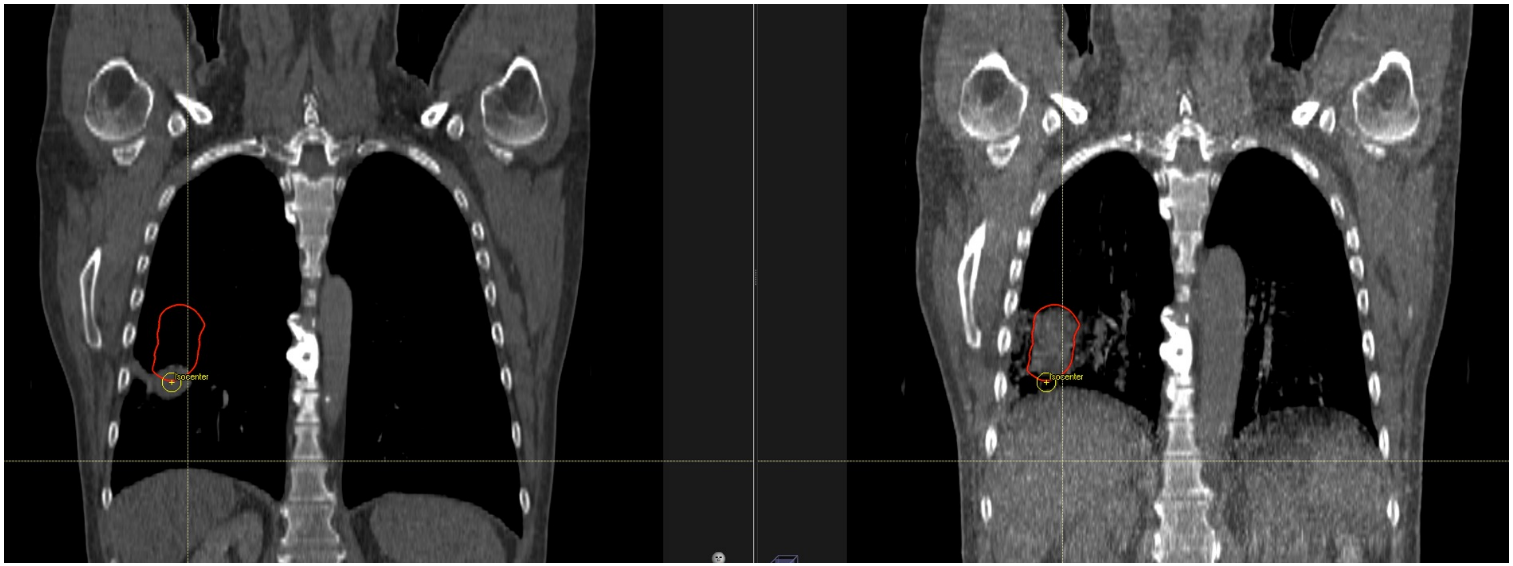
-**maximum** (or minimum*) **CT** **=> ITV**
-**average CT** **=> dose calc**
** pay attention to HU values of target vs. surrounding tissue!*



average CT **maximum CT**

4DCT – derived volumes

-**maximum** (or minimum*) **CT** **=> ITV**
-pay attention to normal vs. deep inhale/exhale!



planning CT (inhale)

maximum CT

4D-CT: modes of operation

- **prospective** acquisition
  - *x-ray on* only in the phase chosen for acquisition (e.g. full exhale)
  - dose sparing – limited information
  - useful e.g. in breath-hold treatment

- **retrospective** sorting
  - *redundant acquisition – "a posteriori" sorting*
  - higher dose –full information
  - necessary e.g. for 4D planning and to estimate the full envelope of positions – tumor trajectory

4D-CT: how to use the information

- information from 4D-CT used for planning shall be **coherent with the delivery technique**, e.g.:

  - *free-breathing treatment => MIP or other method to estimate envelope of positions*

  - *gating and breath-hold: use the phase(s) that will be used to treat*

  - *tracking: use all information for 4D planning*

4D-MR: methods

- **4D-MR** is less frequently used for RT treatment planning than 4D-CT
- **Breath-hold**
  - long acquisition times
  - poor reproducibility
  - dynamic behaviour might be poorly described in breath-hold
- **Cine-MR / Echo Planar Imaging (SSh, EPI, …)**
  - poor spatial resolution
  - artifacts at tissue interfaces
- **4D-MR - sorting**
  - external surrogate: volume, strain-gauge, IR markers …
  - internal surrogate: pencil-beam excitation, 2D slice-stacking
  - generally available as phase-based (limited TR => limited T2 weighting)

4D-MR: methods

- “navigator” sagittal slice
- sorting based on diaphragm position and vascular details
- axial slice acquisition at 2.8 Hz
- acquisition time ~ 1h (200 frames/slice)

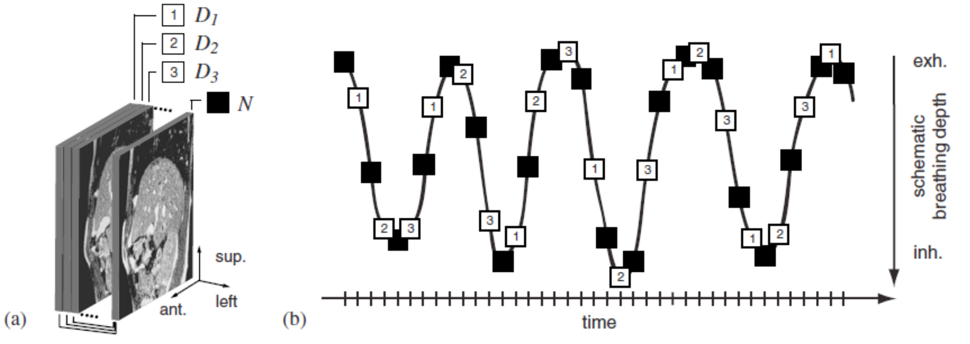


Figure 1. (a) Sagittal slices covering the volume of interest. One dedicated slice *N* is used as navigator slice for image sorting. (b) Interleaved acquisition of data and navigator frames.

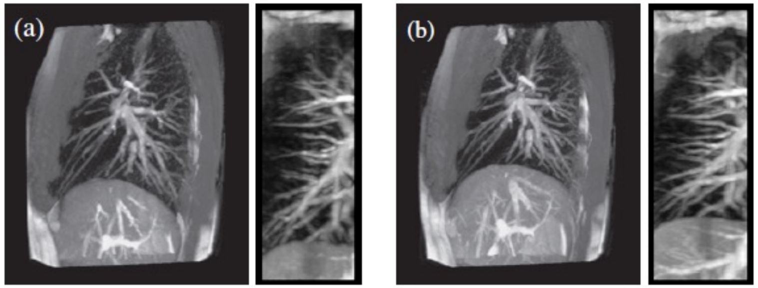


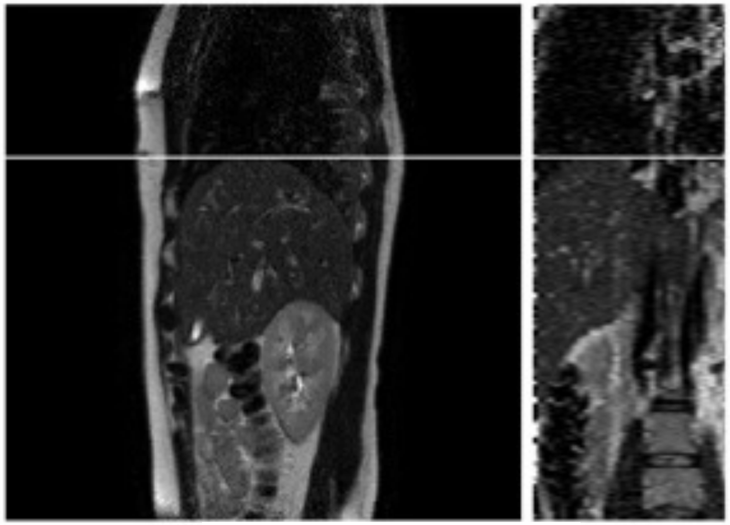
Figure 6. Sagittal and coronal maximum intensity projections after 3D interpolation showing the right part of the lung at (a) inhalation and (b) exhalation.

- very good temporal resolution
- generates deformation maps that can be used in CT etc.
- potentially useful for *dose tracking* in treatment adaptation
- sensitive to breathing irregularities
- not clinically available yet with full functionality

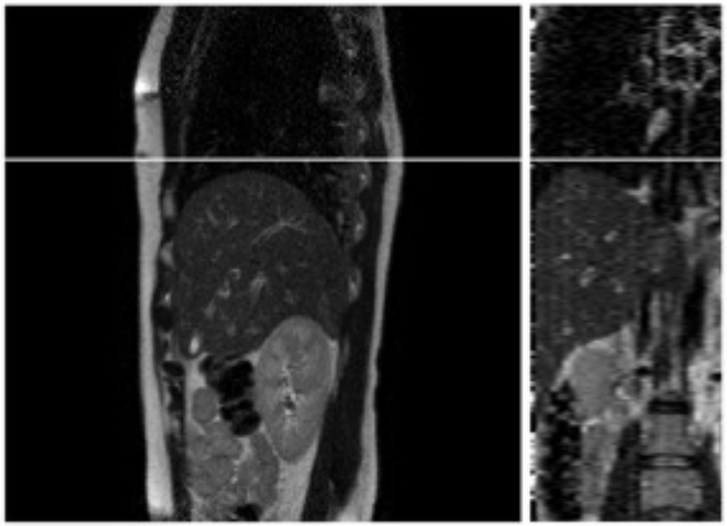
M von Siebenthal et al., “”4D MR imaging of respiratory organ motion and its variability”, Phys. Med. Biol. 52, 1547-1564 (2007)

4D-MR: methods

- 4D-MRI in RT is constantly growing
- generally phase-based triggering => T1-weighting only (limited TR – comparable to breathing cycle => non applicable to new quantitative techniques)
- recent studies on amplitude-based triggering (strain gauge) => T2 weighting



max expiration



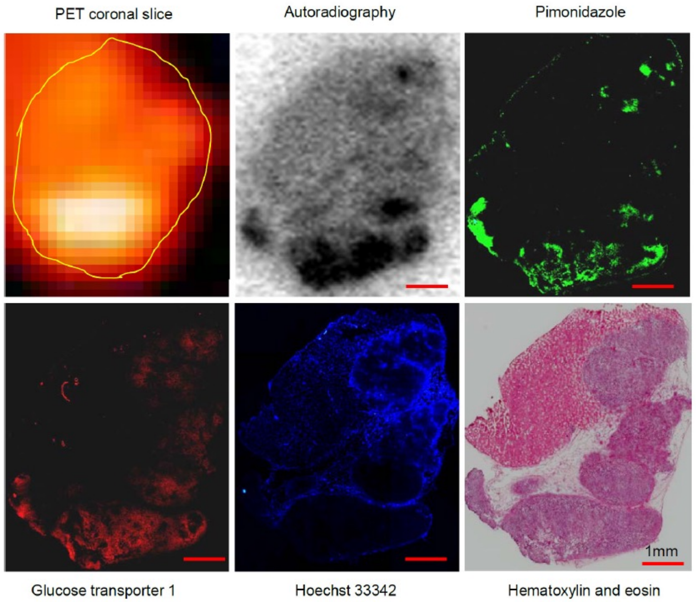
max inspiration

Y Hu, SD Caruthers, DA Low, PJ Parikh, S Mutic, "Respiratory Amplitude Guided 4-Dimensional Magnetic Resonance Imaging", Int J Radiation Oncol Biol Phys, Vol. 86, No. 1, pp. 198e204 (2013)

PET-CT: quantitative imaging

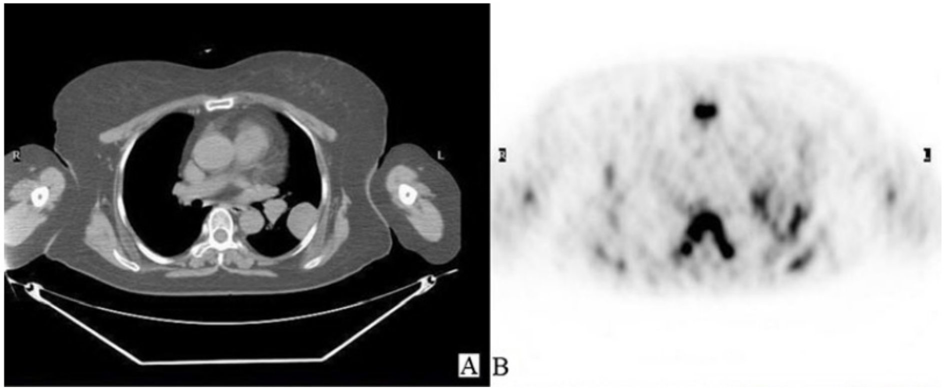
- reference volumes based on SUV (^{18}F-FDG)
- imaging of hypoxia (^{18}F-MISO, ^{64}Cu-ATSM, …)
- cell proliferation (^{18}F-FLT)
- transport of amino acids – synthesis of proteins (^{18}F-FET)
- neo-angiogenesis
- …

=> *dose-painting by numbers*?



example of ^{18}F-MISO PET-CT – accumulation in hypoxic areas (NSCLC – animal model)

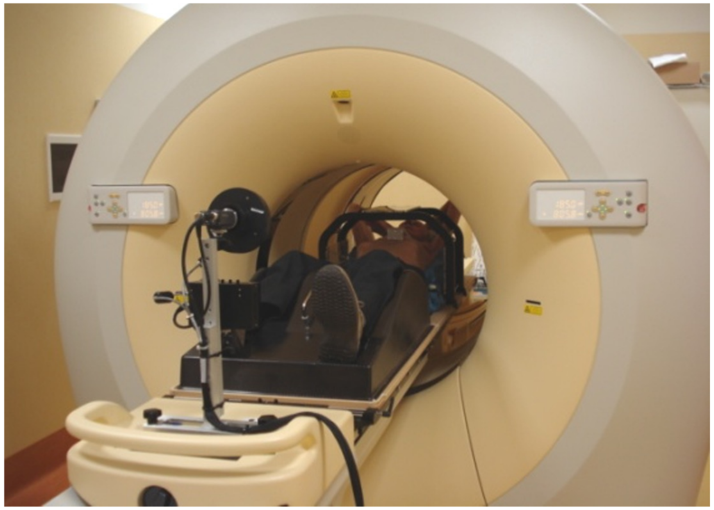
T Huang et al., “^{18}F-misonidazole PET imaging of hypoxia in micrometastases and macroscopic xenografts of human non-small cell lung cancer: a correlation with autoradiography and histological findings”, Am J Nucl Med Mol Imaging 2013;3(2):142-153



example of ^{18}F-FLT PET-CT – evidence of cell proliferation areas

W Yang et al., “Imaging proliferation of ^{18}F-FLT PET/CT correlated with the expression of microvessel density of tumour tissue in non-small-cell lung cancer”, Am J Nucl Med Mol Imaging 2013;3(2):142-153

4D-PET-CT – INSTRUMENTS *(gating)*



-**gating** – 4D PET-CT

-surrogate signal:

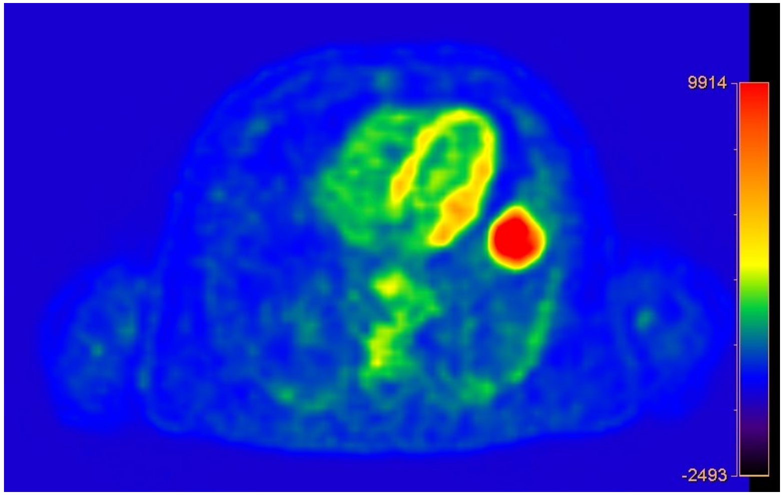
- *optical*
- *“strain-gauge” belt*
- *“tidal volume” measurement*
- *thermometry*
- *…*

-phase-based gating

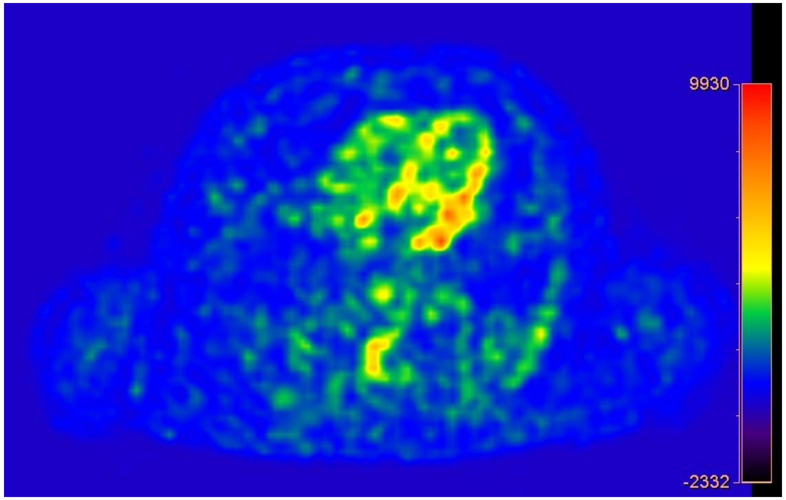
-prospective or retrospective CT

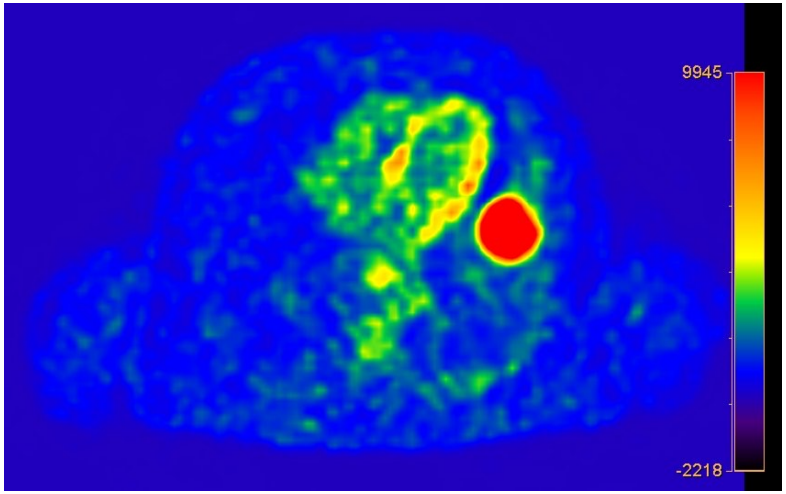
-**loss of SNR** compared to uncontrolled acquisition

4D-PET-CT – INSTRUMENTS *(gating)*

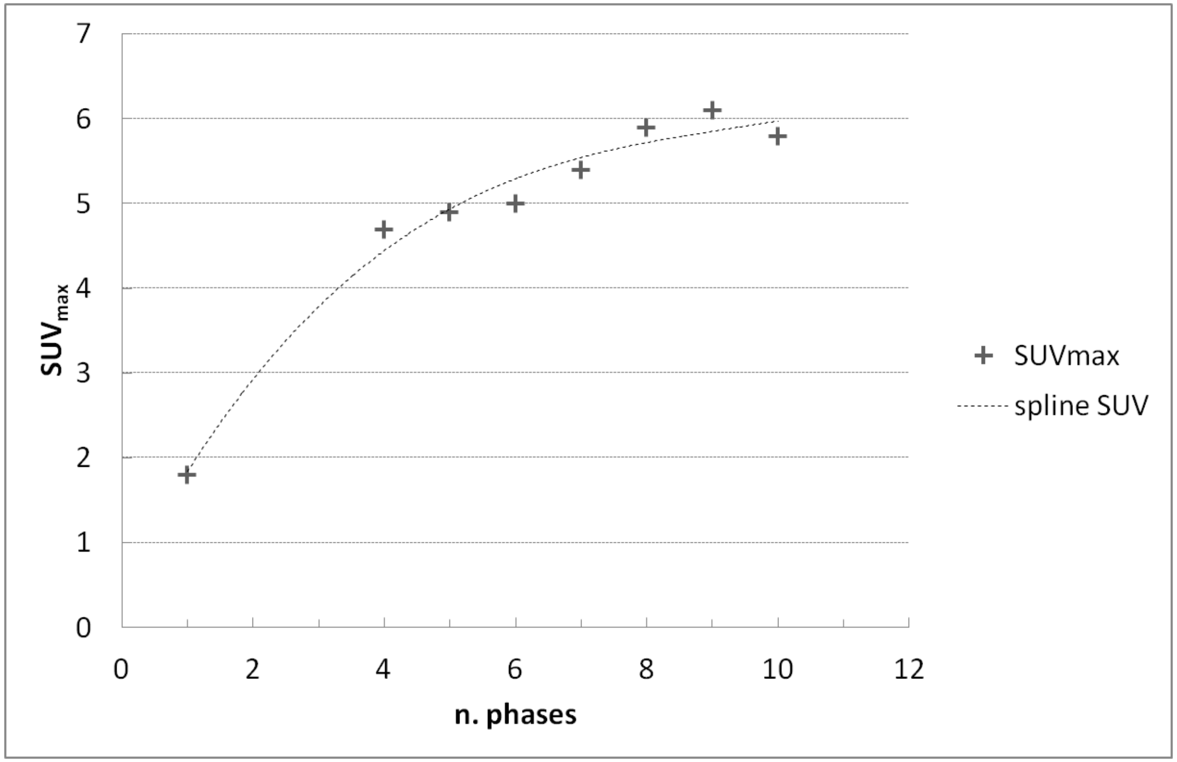


- above: free-breathing uncontrolled acquisition
- lower left: “gated” acquisition - **max inspiration**
- lower right: “gated” acquisition **max expiration**





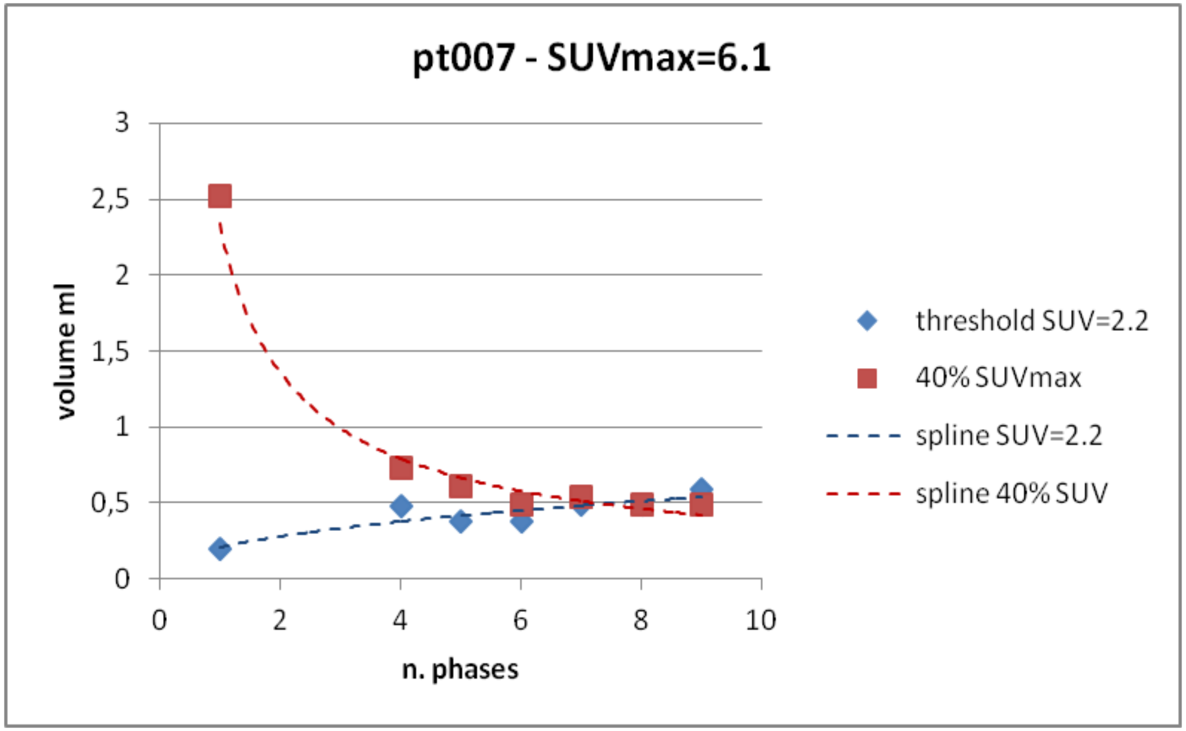
THE EFFECT OF MOTION ON SUV VALUES



- excursion 19 mm
- SUV_{max}=1.8 non-gated
- SUV_{max} =6.1 @9ph

- SUV_{max} in expiration as a function of the number of phase-bins

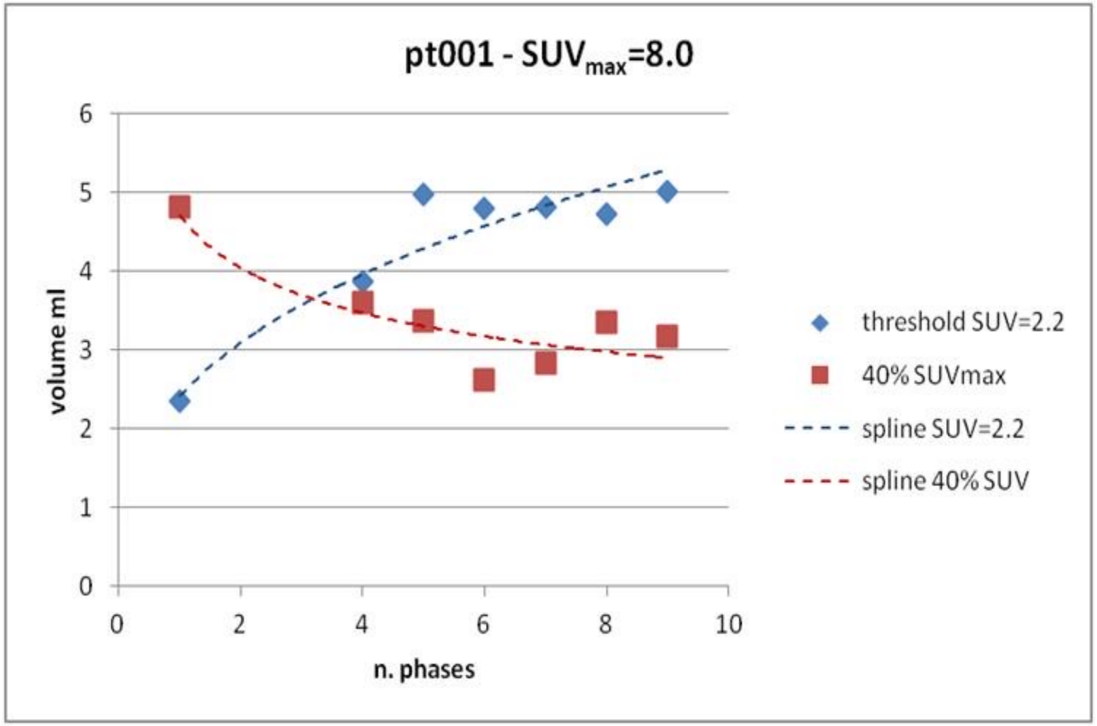
THE EFFECT OF MOTION ON SUV-BASED VOLUMES



CASE 1

- threshold-based algorithms => underestimation of volume
- %SUVmax algorithms => overestimation of volume

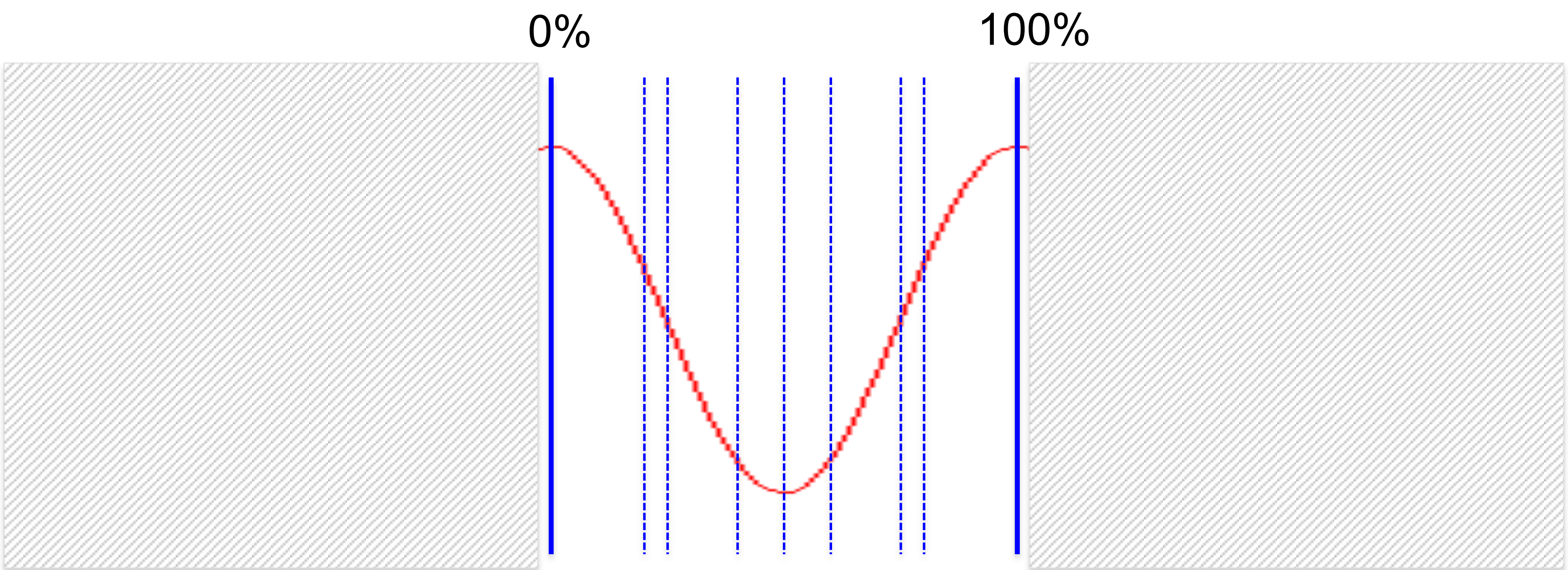
THE EFFECT OF MOTION ON SUV-BASED VOLUMES



CASE 2

- threshold-based algorithms => ?
- %SUVmax algorithms => ?
- more complex algorithms needed for accuracy

GATING in PET-CT – how many phases?



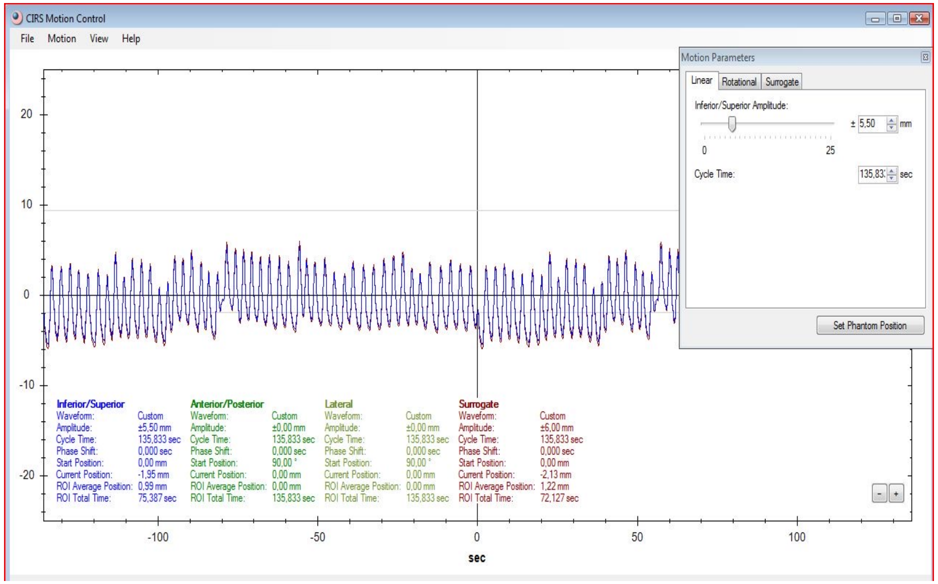
If 0% and 100% correspond to max inhale **and** the breathing pattern is symmetrical, than it is convenient to use an **odd number of phases (5-7)**

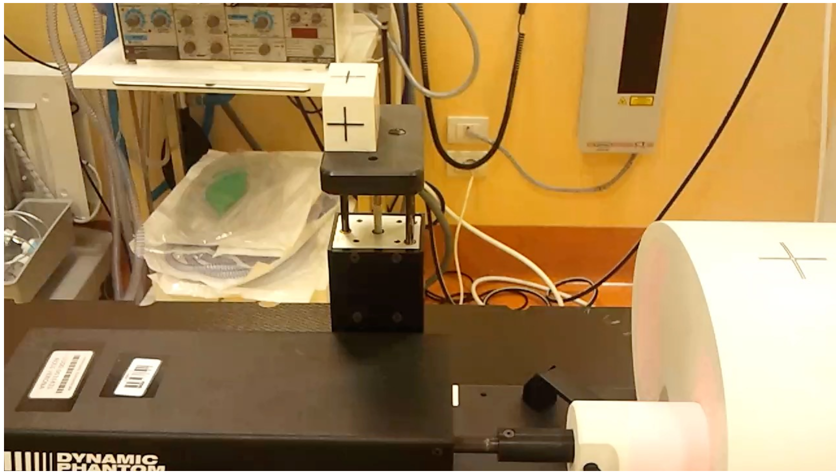
EXPERIMENTAL VALIDATION – VERIFICATION

- use of programmable **motion phantoms** (recommended - AAPM TG76)

- capable of simulating **realistic motion patterns** (ideally, real-patient motion)

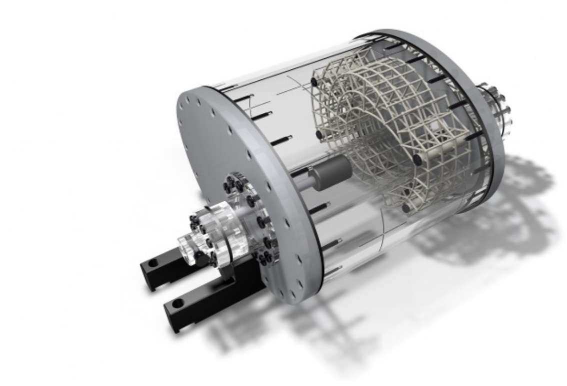
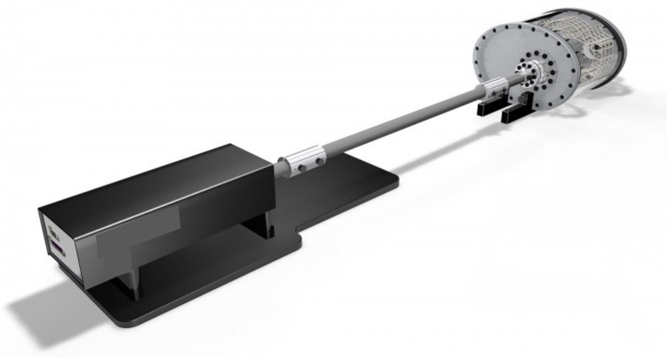
- capable of reproducing both **tumor motion and surrogate motion**

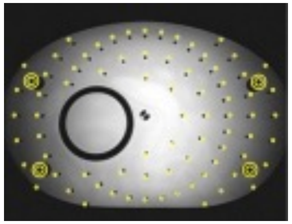




Quality assurance

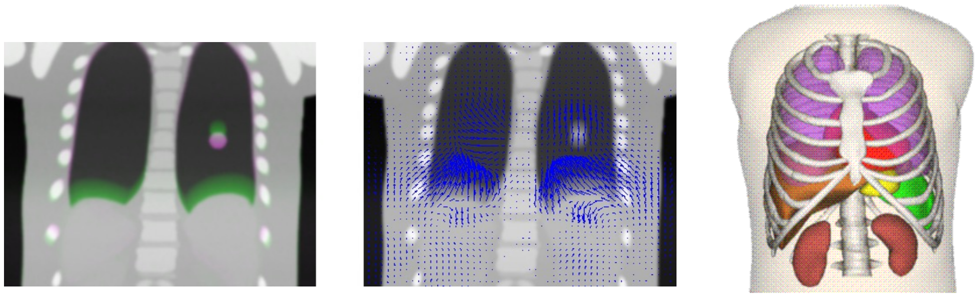
- example of **MR-compatible** motion phantom

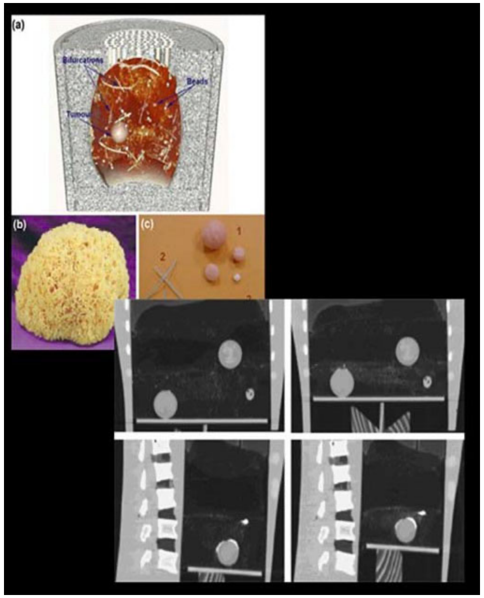


Quality assurance

- virtual phantoms and deformable phantoms
- QA to account for deformations (including accuracy of DIR in dose accumulation)
- virtual phantoms useful but limited in end-to-end tests including treatment delivery

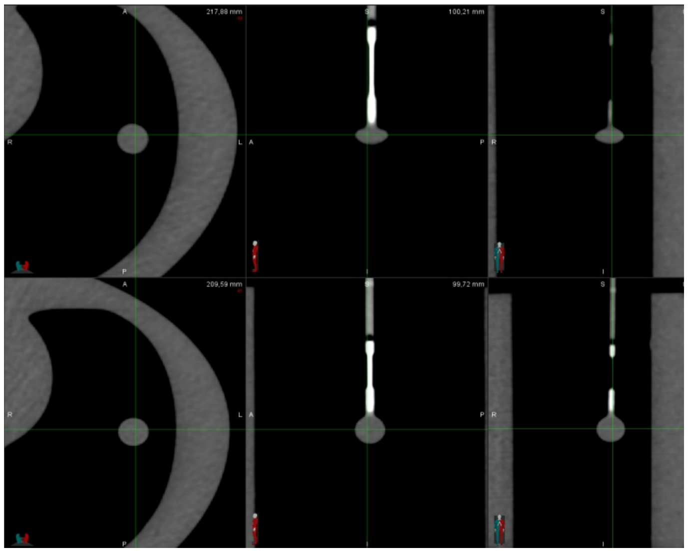


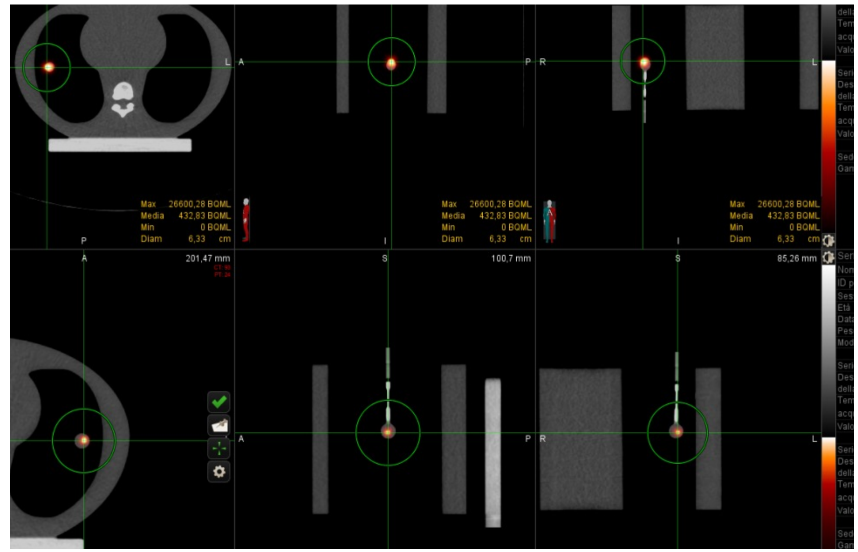
W. Paul Segars and Benjamin M. W. Tsui, “Study of the Efficacy of Respiratory Gating in Myocardial SPECT Using the New 4D NCAT Phantom”, IEEE Trans Nucl Sci, 49(3): 675-679, 2002



M Serban, E Heath, G Stroian, DL Collins, J Seuntjens, “A deformable phantom for 4D radiotherapy verification: Design and image registration evaluation”, Med. Phys. 35, 1094 (2008)

EXPERIMENTAL VALIDATION – VERIFICATION





- available for **4D-CT**
- inserts and accessories for **PET-CT** easily found (or custom-made)
- **3D motion** difficult to reproduce in full detail
- **MR-compatible** instruments not easily found

EXPERIMENTAL VALIDATION – VERIFICATION

- analisys and tests on **system logfiles**
- **consistency checks** (e.g. volume preservation of solid tumors in different respiratory phases)
- **expert judgment** definitely required

TAKE HOME MESSAGES

1. **tumor/organ motion** shall always be considered and accounted for, but an explicit management is not always necessary

2. **explicit methods** of motion management might prolong treatment time and/or introduce significant uncertainties (e.g. of dose to OARs)

3. **temporal coherence** is necessary between imaging used for planning and treatment administration technique

4. **validation – experimental verification** is necessary when implementing a motion-management program (including easily-performed consistency tests)

5. **balance** between accuracy and **clinical applicability** must be considered