Hypofractionation with Tomotherapy: experience at HSR

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Summary

- Classical applied radiobiology
- Hypofractionated RT: pro's and con's
- Hypofractionated protocols at HSR
  - Lung mets (details)
  - Liver mets (details)
  - Pancreatic carcinoma (details)
  - Pleural Mesothelioma (details)
  - ….. further informations in other course lessons (head-neck, prostate, etc)
- Conclusions

Radiobiological basis: from the beginning

The effect of radiation on cells is described by the Linear-Quadratic (LQ) model – extensively verified provided d > 0.5 Gy and dose-rate not too low

$$E = n(\alpha d + \beta d^2) = D(\alpha + \beta d)$$

$$and \quad SF = e^{-E}$$

full recovery in - between

where the α and β are coefficients which describe the radiosensitivity of the cells in the normal tissue /tumour

Classical applied radiobiology: BED

Using different fractionation regimens the model enables one to convert from one regimen to another, by equating *BED*

Biological Effective Dose

$$BED = E/\alpha = D[1 + d/(\alpha/\beta)]$$

Basic assumptions:

- Complete repair of sublethal damage between fractions

- The effects of proliferation are negligible

- Dose distributions are uniform

Classical applied radiobiology: BED

In case of rapid repopulation during treatment:

$$BED = E/\alpha = D[1+d/(\alpha/\beta)] - h(T-T_K)$$

T= Overall treatment time (days)

T_k=Proliferation starts at T_k days (20-30 days)

h=0.4-0.8 Gy/day: Rate of loss after T_k

For tumours with rapid repopulation during treatment the reduction in overall treatment time could increase the local control

Classical applied radiobiology: EQD_2

To convert a total dose D given in fractions of size d into the *isoeffective* total dose EQD_2 given in 2-Gy fractions

assuming $d_{ref} = 2$

$$EQD_{2Gy} = D \frac{d + \frac{\alpha}{\beta}}{2 + \frac{\alpha}{\beta}}$$

Withers formula

(assuming complete repair, negligible repopulation, etc.)

d and D are the doses prescribed for the tumour (…nothing about dose distribution and OAR behaviour)

Classical applied radiobiology: α and β

α/β (Gy): ratio used in the LQ model to quantify the fractionation sensitivity of tissues

Normal Tissues:

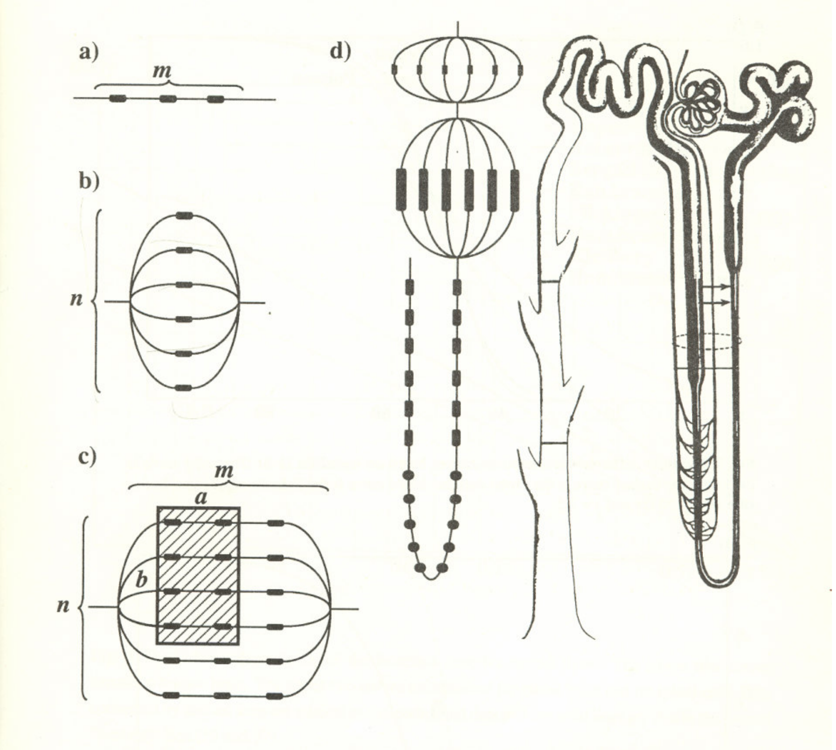
- Low α/β (0.5-6 Gy) late effects, expressed months to years after irradiation
- High α/β (7-20Gy) acute effects, expressed within a period of days to weeks after irradiation

Tumours:

- High α/β (7-20Gy) (few exception in melanomas, sarcomas, prostate (?))

But don't forget the assumptions

• the absorbed dose of the OAR is the same than the absorbed dose of the tumour: while it's quite obvious the fact that if we can half the dose to the OAR we could double the dose/fraction without any incremental risk for the OARs



• No differences have been considered between serial and parallel organs: while the volume effect could have a great influence in the determination of the toxicity of the treatment in all the parallel OARs

Hypofractionation: PRO'S

- Potentially favourable with tumours with high rate of repopulation during treatments
- Favourable for tumour with α/β smaller than α/β for OARs
- Favourable for "small" tumour "within" a "parallel" organ
- Economical advantages and more comfortable for patients (reduction fraction number)

Hypofractionation: CON'S

- Disadvantage for tumours with α/β larger than α/β for OARs
- Potentially detrimental for very radioresistent tumours (hypofractionation may act against the possible effects of redistribution and reoxygenation)

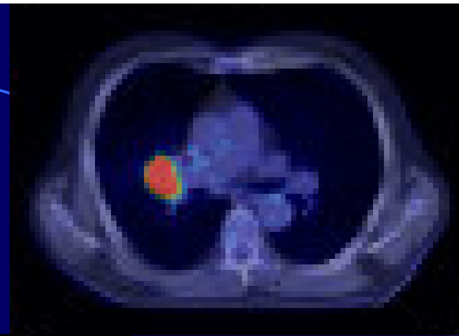
Hypo: open problems

- New complications: using CRT in thorax diseases, the esophagus is the most important serially functioning tissue. Hypofractionated RT may significant increase acute and late effects to other serially functioning tissues (bronchi, vascular pedicles ect).
- Pretreatment healthy tissue function: the use of higher dose/fraction increases complication rate in PTs with a reduced baseline functionality (i.e lung, liver, etc).
- Acute mucosa reaction.
  - Hypo RT (reduced total dose) should lead to a lower acute toxicity (high α/β) BUT:
    - Repopulation is an important mechanism of resistance to radiation!
  - In case of shorter schedule, acute mucosa reaction can become the dose-limiting side effect *[Gortec 1 and Harde1 trials].*
    - its underlying biological process remains unclear.
  - Much more caution is required when combined chemoradiation schedules are used

What is (relatively) new ?

- ❖ Advent of IMRT: Excellent dose painting
  - ❖ More precise coverage of PTVs
  - ❖ High gradient between PTV and OARs
  - ❖ Better sparing of OARs
- ❖ RT unit with Image System. Reduced impact of :
  - ❖ set-up errors
  - ❖ organ motion
- ❖ Clinical evidence that a tumoricidal dose, given in large fractions, is tolerated in certain OARs (body stereotactic RT)

TomoTherapy : work-flow at HSR



CT +

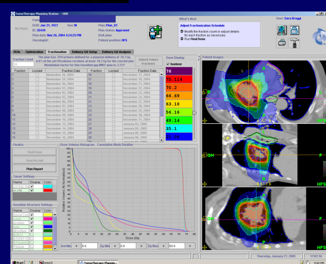
PET → HN, lung, pelvis

NMR → brain, pelvis

4D-PET/CT → lung, pancreas, liver

SPECT → lung

Contouring BTV/GTV and OARs



Planning strategy:

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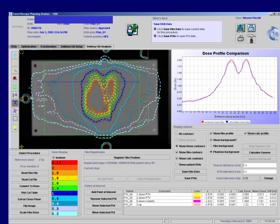
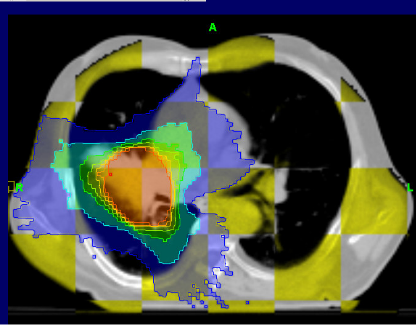
Constraints related to dose/fraction value



Patient dosimetry: Part of QC. Critical cases



Daily MVCT-KVCT match

↓

treatment

TOMOTHERAPY PROTOCOLS AT HSR

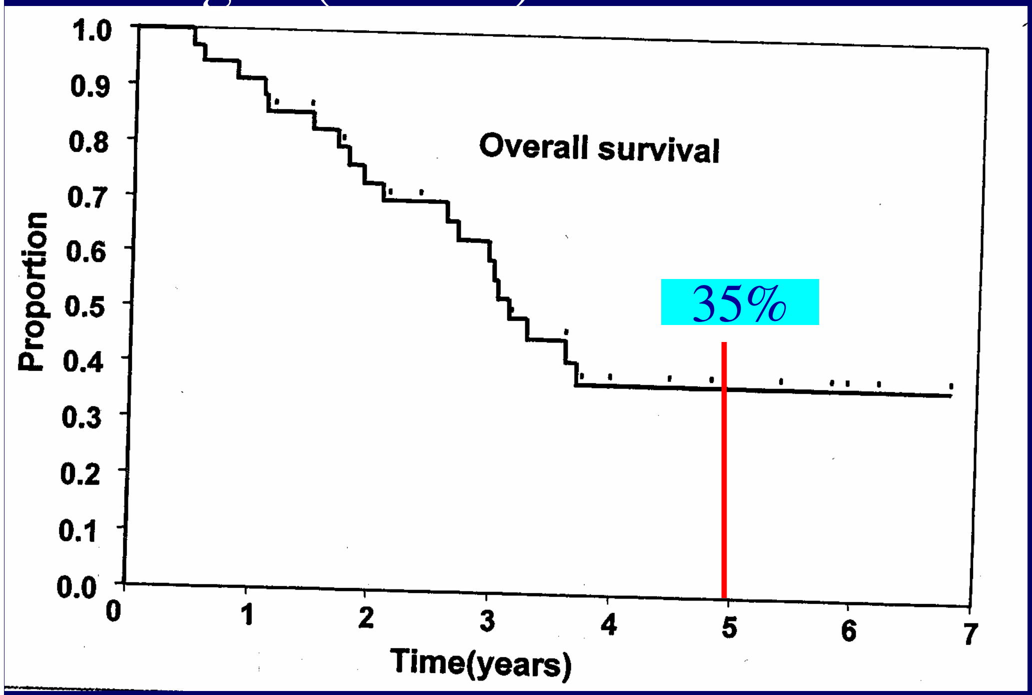
SITE	STAGE	INDICATION	SCHEDULE	
			n fractions	Gy / f
H&N	IVa/b	radical	30	1.8-2.15(2.25)
		adjuvant	30	1.8-2.3
MESOTELIOMA	IIIa/b	radical	25	2.16 SIB: 2.5
PANCREAS	III	Radical	15	2.95 SIB: 3.2—3.9
PROSTATE	pT2-T4pN0	adjuvant	20	2.9
	T1-T3	radical	28	1.85-2.65
LUNG Met	max 3 , < 3cm	radical	6	> 6
LIVER Met	max 4 , < 3cm	radical	5	> 8

Small Lung lesions

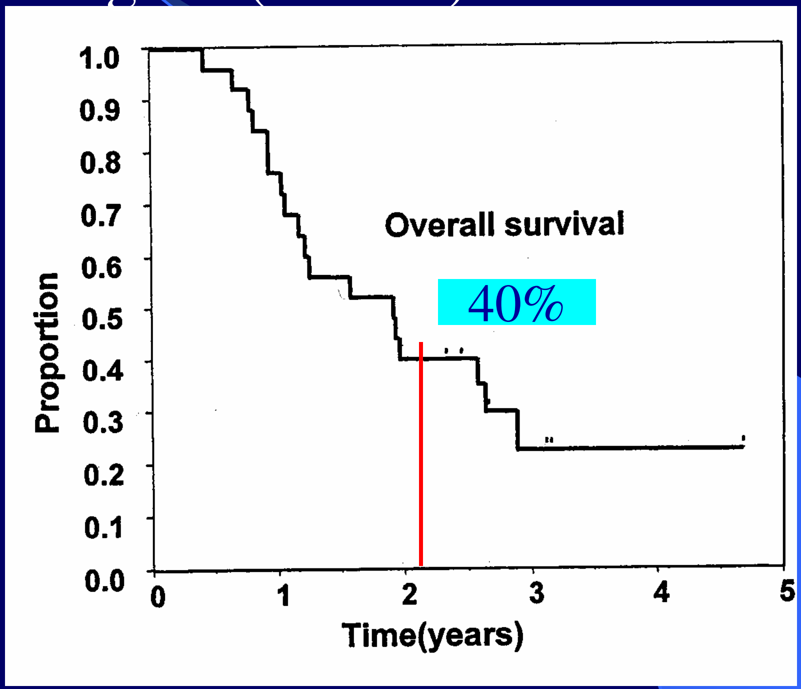
- Relevant articles demonstrate that
  - 3Fx15 Gy in 3 –12 days is a suitable fractionation regimen for lung and liver small lesions
  - lung tumours of size < 3 cm diameter have a TCP of 95% contrasted with 58% for sizes > 3 cm
- The limit of the dose escalation is the maximum acceptable level of toxicity .
  - The limit for the lung is a maximum of 20% of grade II pneumonitis .
- A review of the current regimes reveals a great increase of the dose size and of the BED values, without any clinical evidence of acute and late effects increase

Stereotactic Body Radiation Therapy for NSCLC: clinical outcomes (Karolinska Hospital experience)

Stage I (35 PTs)



Stage III(25 PTs)



8-20 Gy /Fraction (PTV margin)
2-5 fractions
1-2 day intervals

In "Stereotactic Body Radiation Therapy". Kavanagh BD abd Timmerman RD editors

Stereotactic body radiation therapy: clinical outcomes (lung tumours)

TABLE 13-2 Results of Stereotactic Body Radiation Therapy for Early-stage Non–Small Cell Lung Cancer.

Author	No. of Patients	Median Follow-up	Local Control	Survival
Timmerman (57)	37	15 m	83%	54%
Uematsu (47)	43	20 m	100%	3-yr 66%
Nagata[a] (50)	16	16 m	100%	2-yr 79%
Wulf[b] (62)	12	8 m	85%	2-yr 40%
Hara (58)	5	20 m	100%	
Hof (48)	10	15 m	80%	2-yr 64%
Onishi[c] (49)	241	18 m	90%	3-yr 56%
Lee (59)	9	18 m	90%	100%

[a]Only T1 N0 patients shown.
[b]Included some patients with T3 N0 and recurrent disease.
[c]Multiinstitutional study; may contain overlapping patients from other authors.

TABLE 13-3 Results of Stereotactic Body Radiation Therapy for Metastatic Lung Tumors.

Author	No. of Targets	Median Follow-up	Local Control
Blomgren (63)	14	8 m	92%
Uematsu (47)	23	20 m	100%
Nakagawa (61)	21	10 m	95%
Nagata (50)	9	18 m	66%
Wulf (62)	11	8 m	85%
Hara (58)	18	12 m	78%
Lee (59)	19	18 m	88%

TABLE 13-4 Complications of Lung Stereotactic Body Radiation Therapy.

Author	No. of Patients	Dose	Grade 3 Toxicity
Uematsu (47)	66	30–76 Gy, 5–15 fx	0%
Nakagawa (61)	22	15–24 Gy, 1 fx	0%
Nagata (50)	40	40–48 Gy, 4 fx	0%
Wulf (62)	61	26–37.5 Gy, 1–3 fx	3%
Hara (58)	23	20–30 Gy, 1 fx	4%
Hof (48)	10	19–26 Gy, 1 fx	0%
Onishi[a] (49)	241	18–75 Gy, 1–22 fx	2%
Lee (59)	28	30–40 Gy, 3–4 fx	0%
Blomgren (63)	13	15–45 Gy, 1–3 fx	
Timmerman (51)	37	24–60 Gy, 3 fx	5.4%

Fx, fraction.
[a]Multiinstitutional study; may contain overlapping patients from other authors.

In "Stereotactic Body Radiation Therapy". Kavanagh BD abd Timmerman RD editors

Small Lung lesions: hypofractionated stereotactic body radiotherapy

Literature data:

- Medically inoperable stage I NSCLC
  - Local Control: 71-95%
  - Survival (2-3y): 55-71%
  - Toxicity (grade 3-5) significantly associated with:
    - Tumor location: perihilar/central region (11-fold higher risk)
    - Tumor volume: > 10 mL (8-fold higher risk) The limit for the lung is a maximum of 20% of grade II pneumonitis .
- **JAPANESE MULTI INSTITUTIONAL RETROSPECTIVE TRIAL**
  - **CUMULATIVE LOCAL CONTROL RATE ACCORDING TO BED**
    - **BED < 100 Gy : 5 y LC=36.5%**
    - **BED > 100 Gy : 5 y LC=84.2 %**

P<0.001

Lung mets (Phase I) protocol at HSR: Hypofractionated with dose-escalation

- Simulation CT: 4D-CT/PET
- 4D target volume:
  - PTV1: tumor region (4D_GTV+BTV +5/5/7 mm)
- Daily MVCT scan

Dose escalation study:
D=36 – 54 (60) Gy (6 fr; 2 weeks)
BED_{10}= 57.6 – 102.6 (120) Gy

4D-PET/CT : WORKFLOW (1)

- respiratory training (verify/instruct regular breathing)
- ^{18}F-FDG injection (50 kBq/Kg)
- rest for 60 minutes
- vacuum pillow , patient supine , 3 marks on the thorax , free regular breathing
- conventional whole-body PET/CT
- 4D-CT (on the region of interest)
- 4D-PET (on the region of interest)
- image processing and reconstruction (Advantage Win , GE)

4D-PET/CT : WORKFLOW (2)

Standard PET/CT (PET/CT st) : staging

4D CT :

- inspiratory phase (CT insp)
- expiratory phase (CT exp)
- all respiratory phases (CT sum ; MIP method)

4D PET :

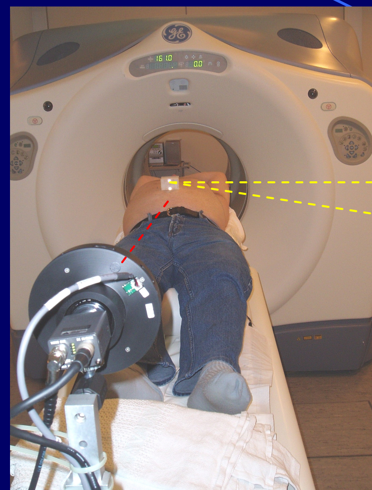
- all respiratory phases (PET sum)

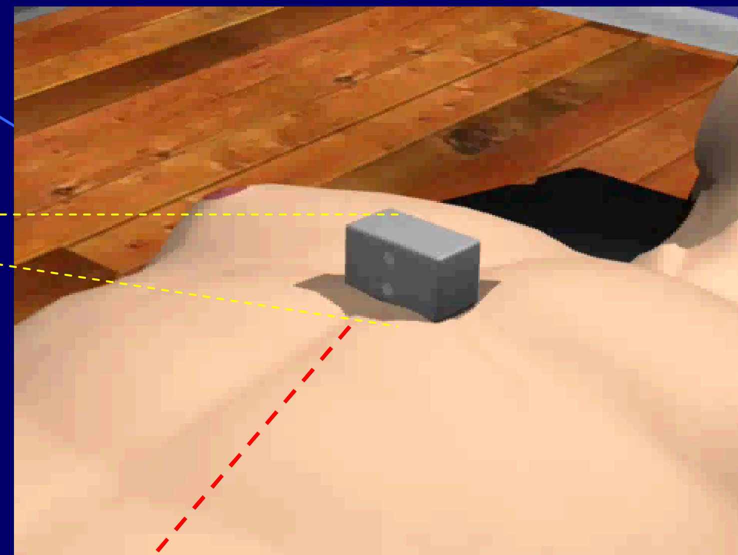
} coregistered

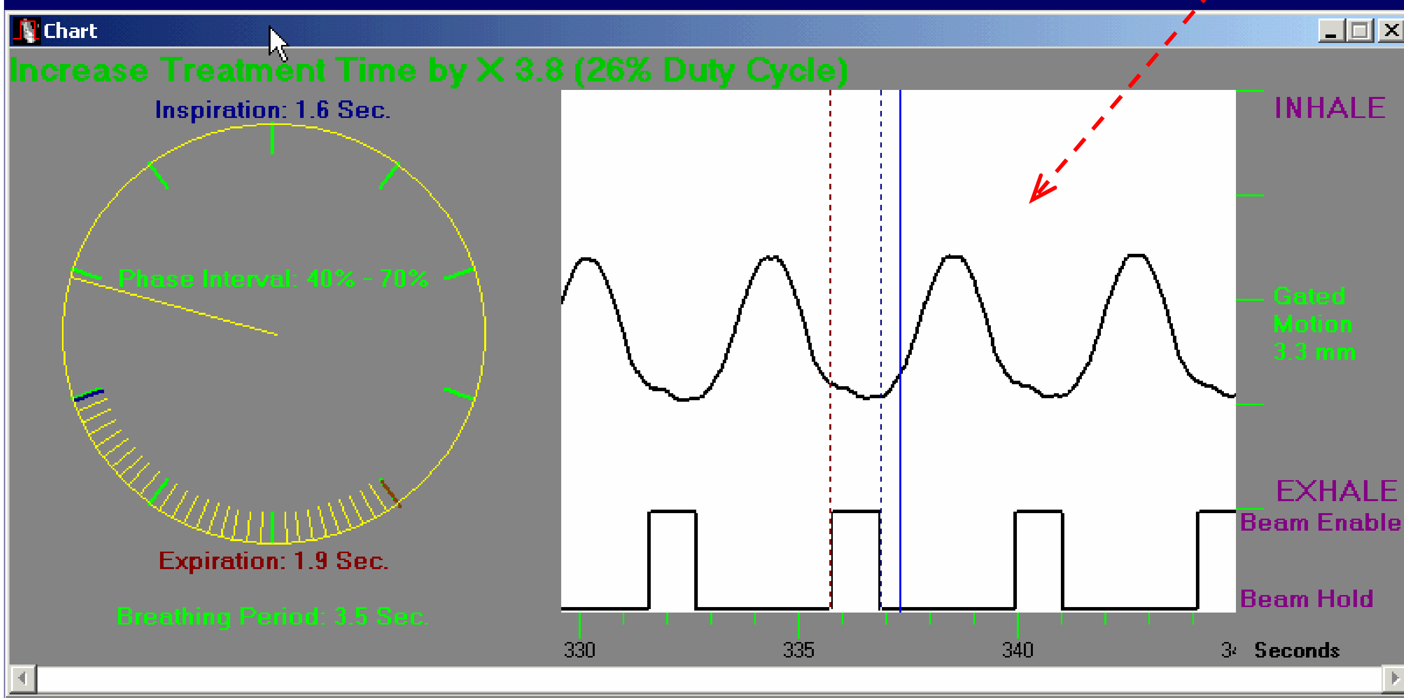
Respiratory Gating Techniques
4D PET/CT

- Integrated PET/CT system with at least 70 cm gantry opening
- Standard RTP pallet (FLAT TABLE)
- High –precision patient positioning / immobilization devices
- 4D PET/CT Hardware for Respiratory Gating
- Respiratory monitoring system

RPM Respiratory Gating™ System

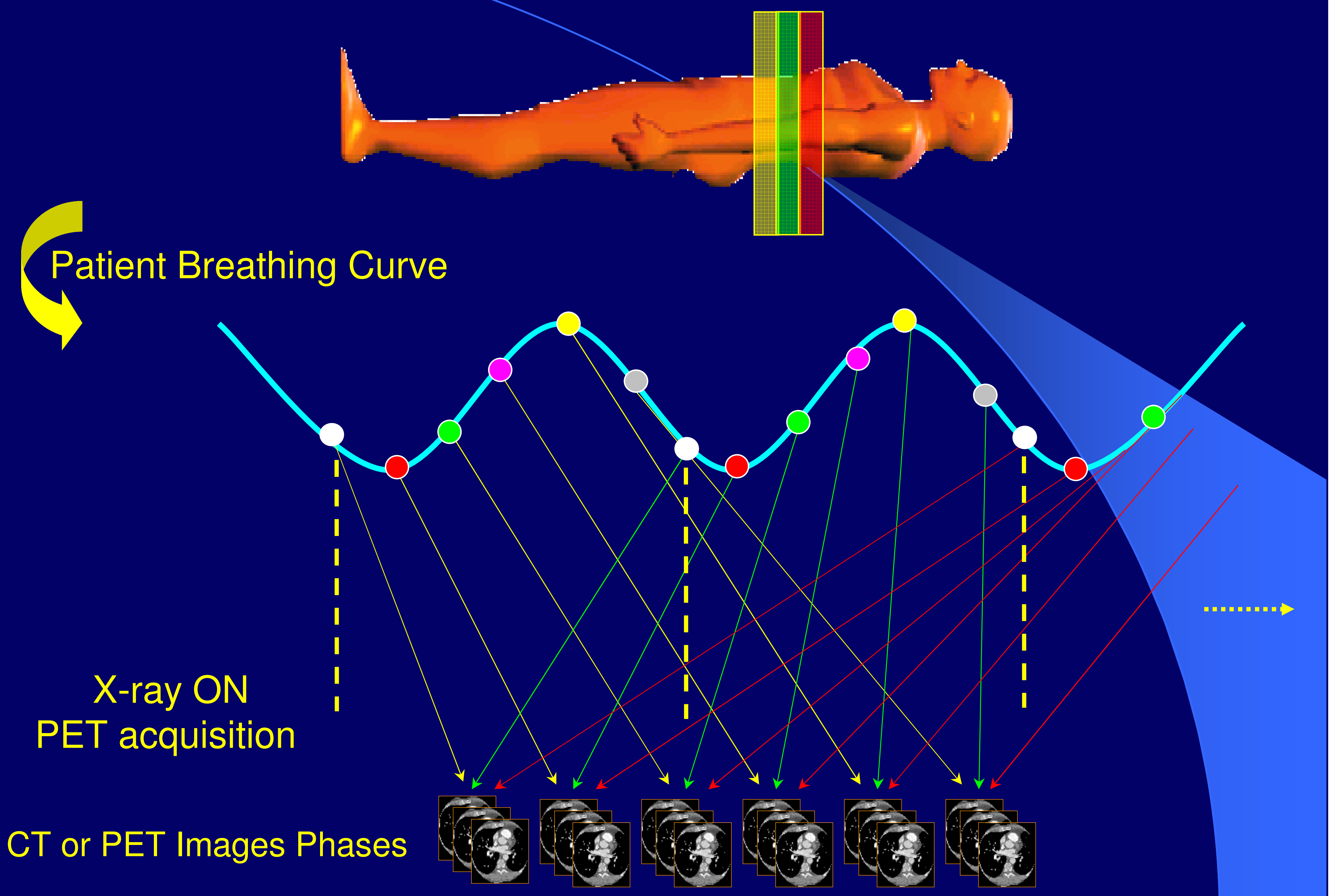






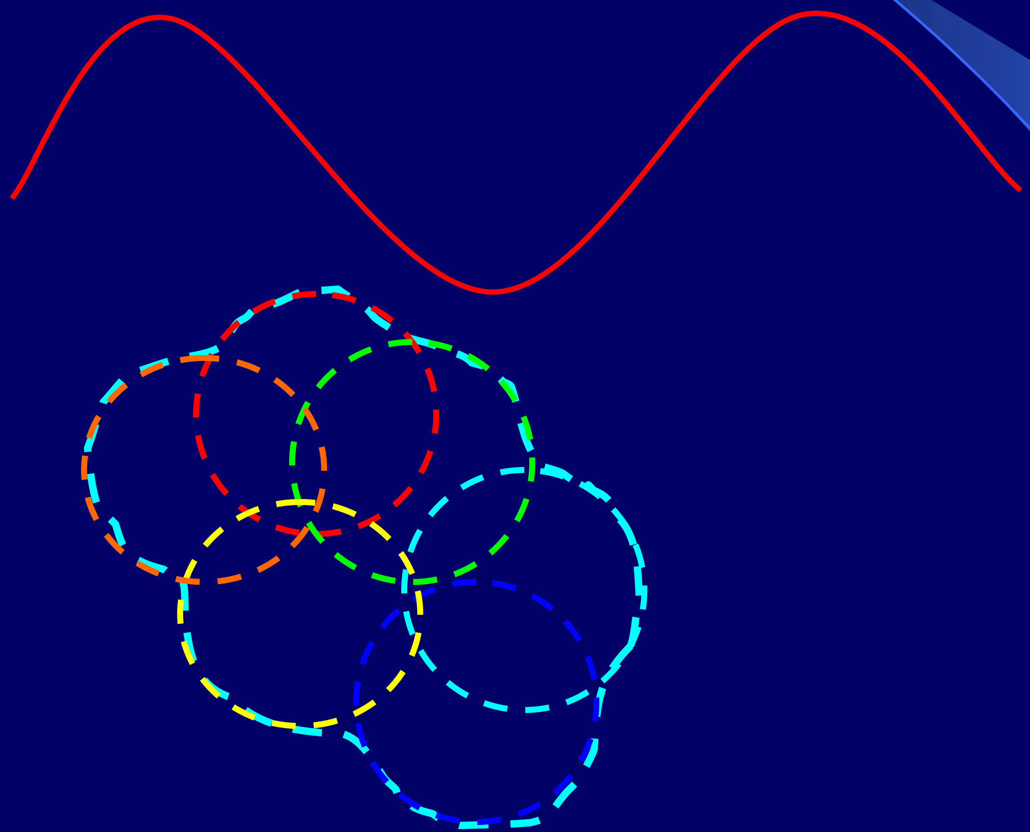
TM : Varian Medical Syster
Gating School Copenhagen

4D Data Sorting



Goal:

Define the target volume and the volume of space that encompasses tumor motion.



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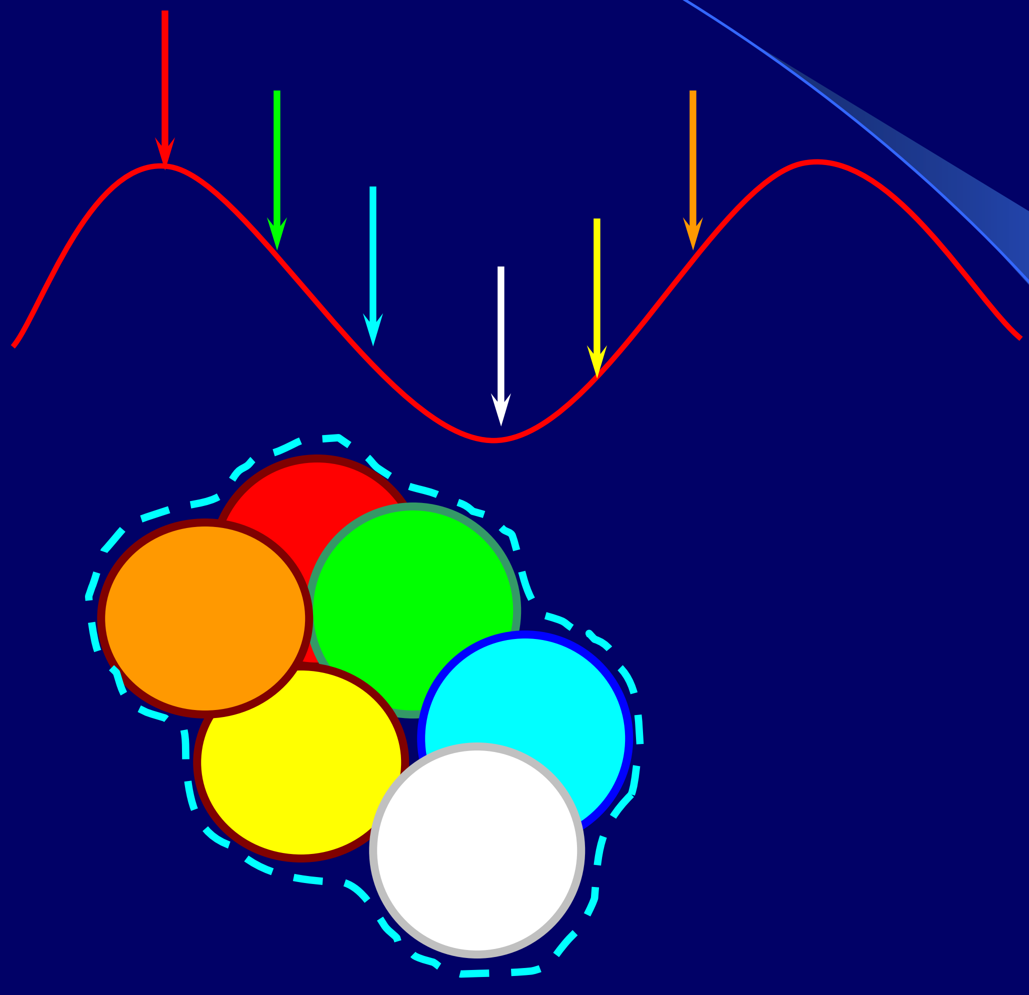
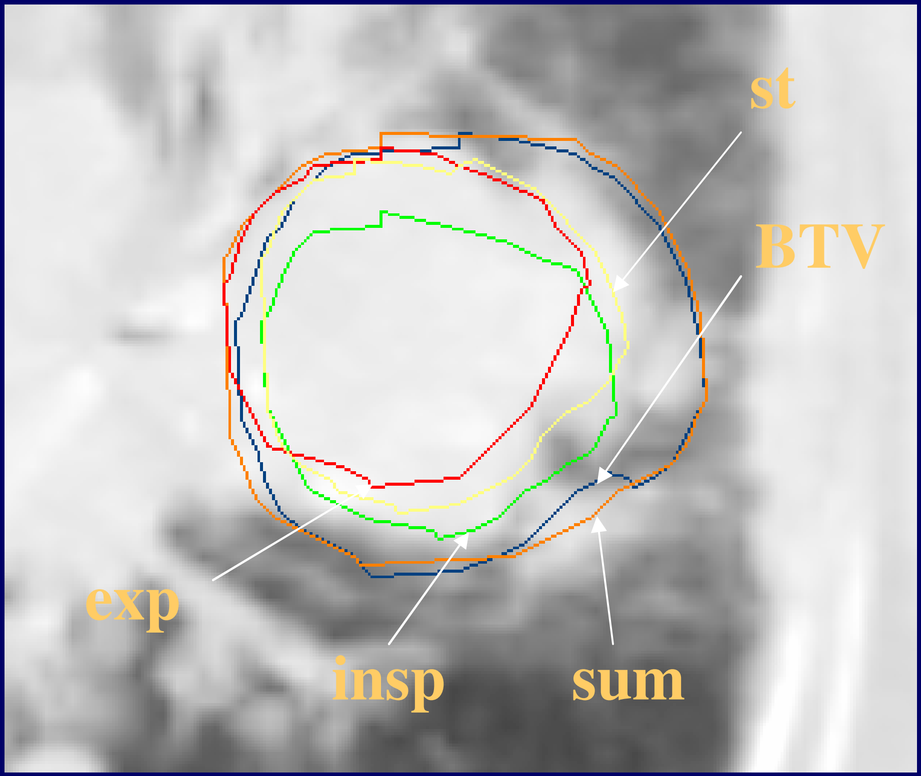
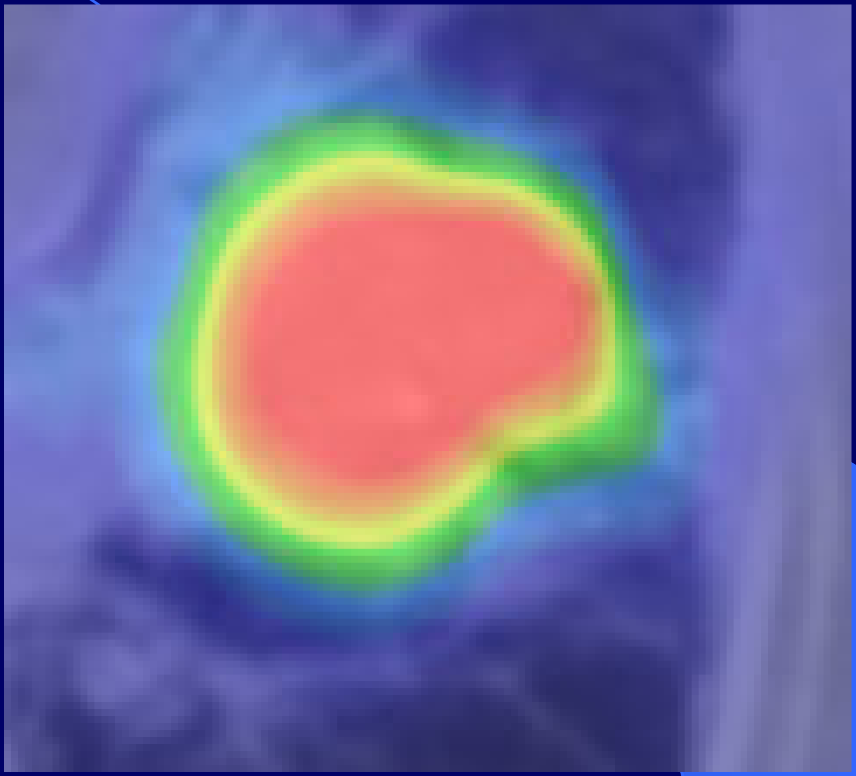


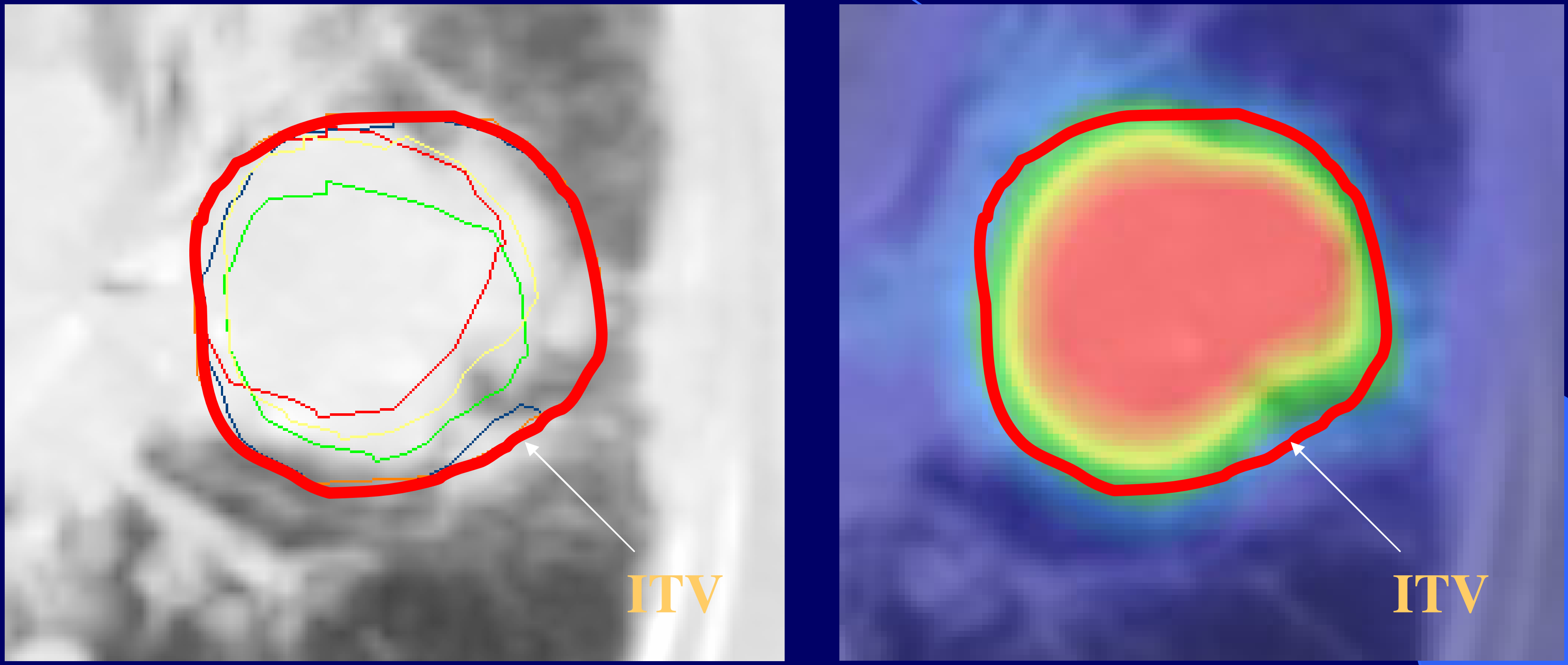
4D-PET/CT CONTOURING





HSR , Milan

4D-PET/CT CONTOURING



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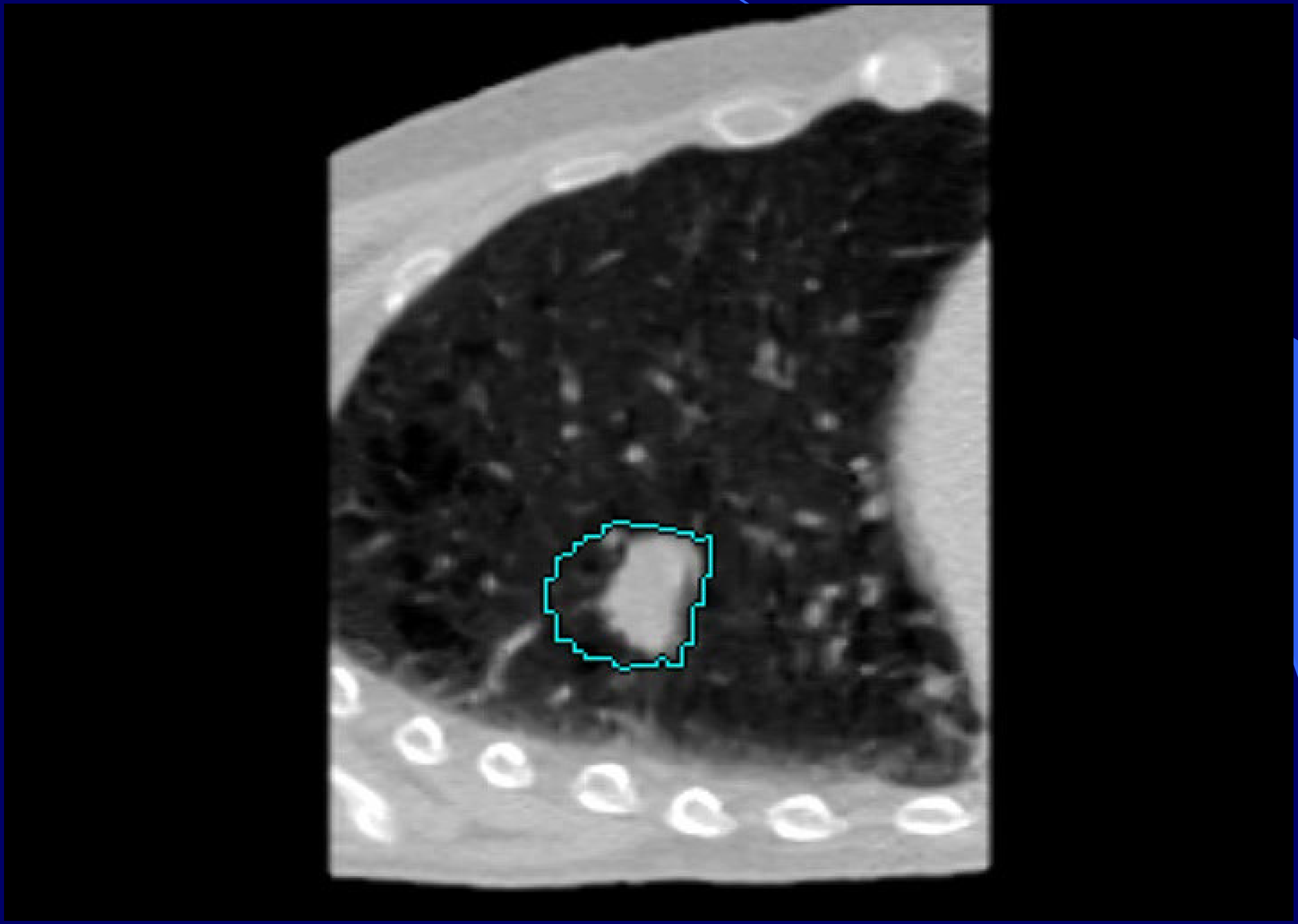
4D CT

Cine Review



ITV

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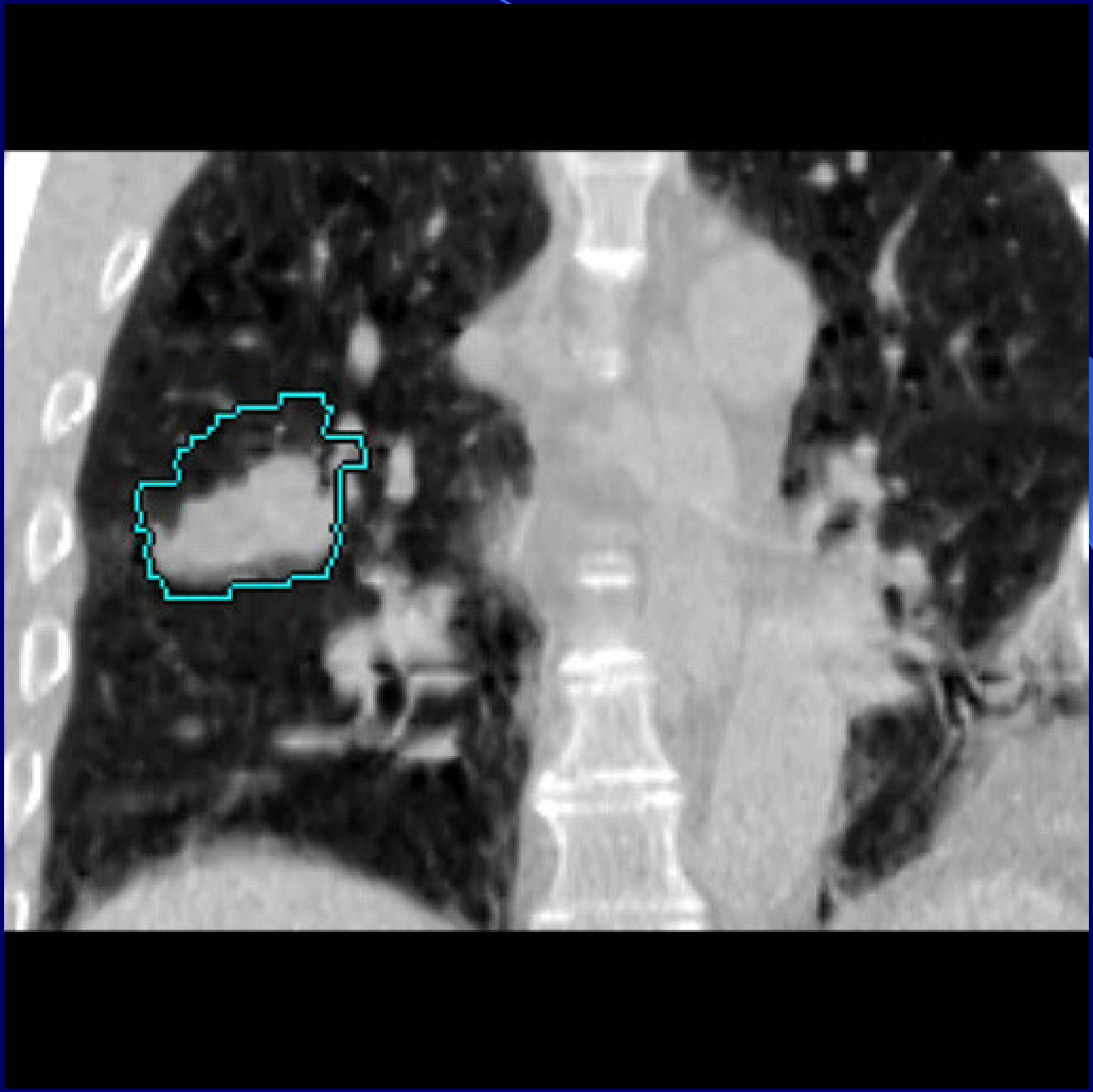
4D CT

Cine Review

ITV



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PATIENTS

Pt	Primary tumor	Lung mts location
1FE	lung	left lower lobe
2PV	uretra	right middle lobe
3FF	lung	right upper lobe
4RF	hepatocarcinoma	right middle lobe
5LD	kidney	right upper lobe

PET/CT VOLUMES

"standard"	"4D"
GTVst	**GTVsum (= ITV)**
CTVst = GTVst + 2mm	CTVsum = GTVsum + 2mm
ITVst = CTVst + 5-15 mm*	
PTVst = ITVst + 3,3,5 mm	**PTVsum** = CTVsum + 3,3,5 mm

* according to location

RESULTS

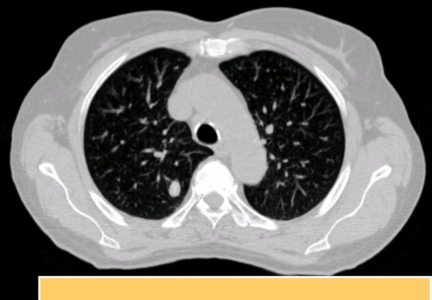
	GTVst (cc)	GTVsum (cc)
Mean ± SD	17.51±30.83	19.64 ±31.86

	PTVst (cc)	4DPTVsum (cc)
Mean ± SD	135.96±121.61	42.44±55.69

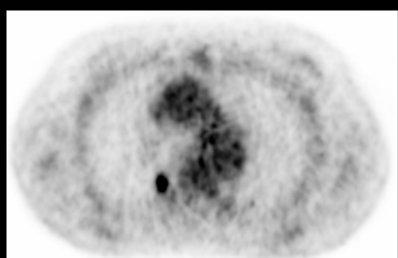
	R (spatial reproducibility index)	
	GTVst vs GTVsum	PTVst vs PTVsum
Mean±SD	0.45±0.32	0.23±0.12

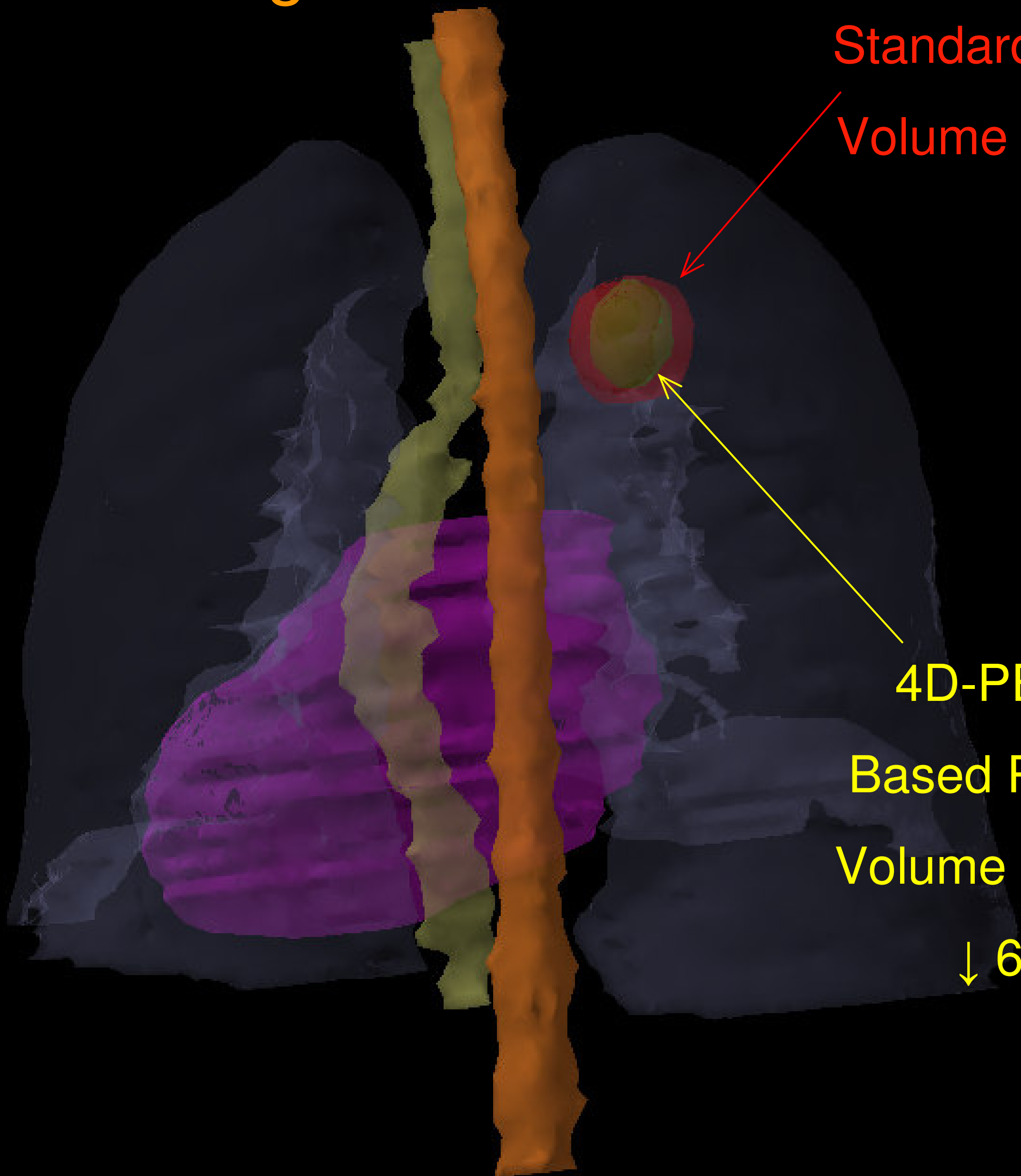
Lung tumour

CT



PET





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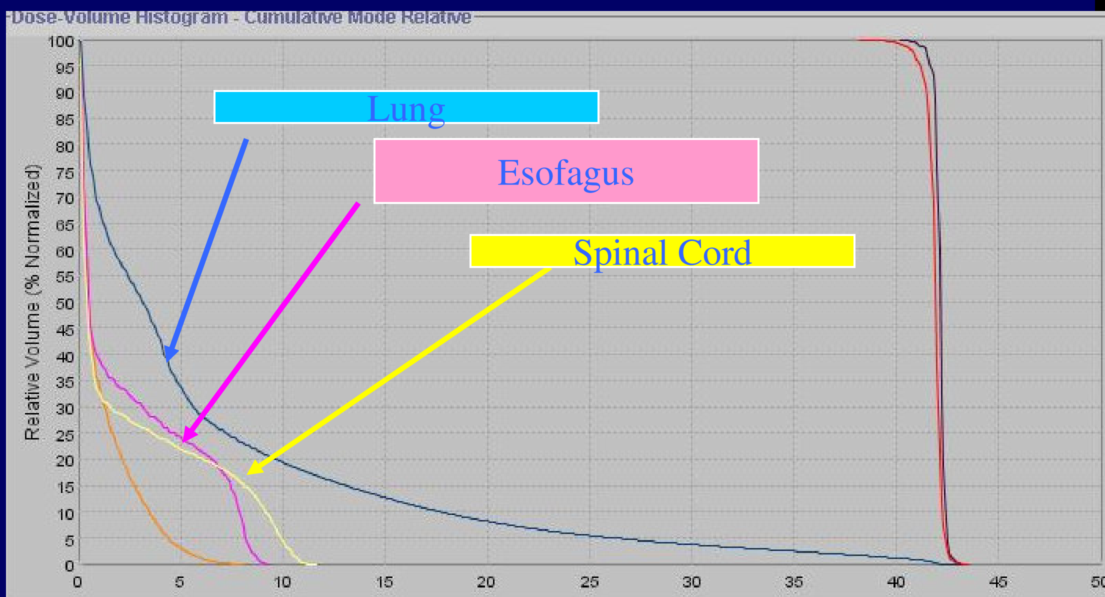
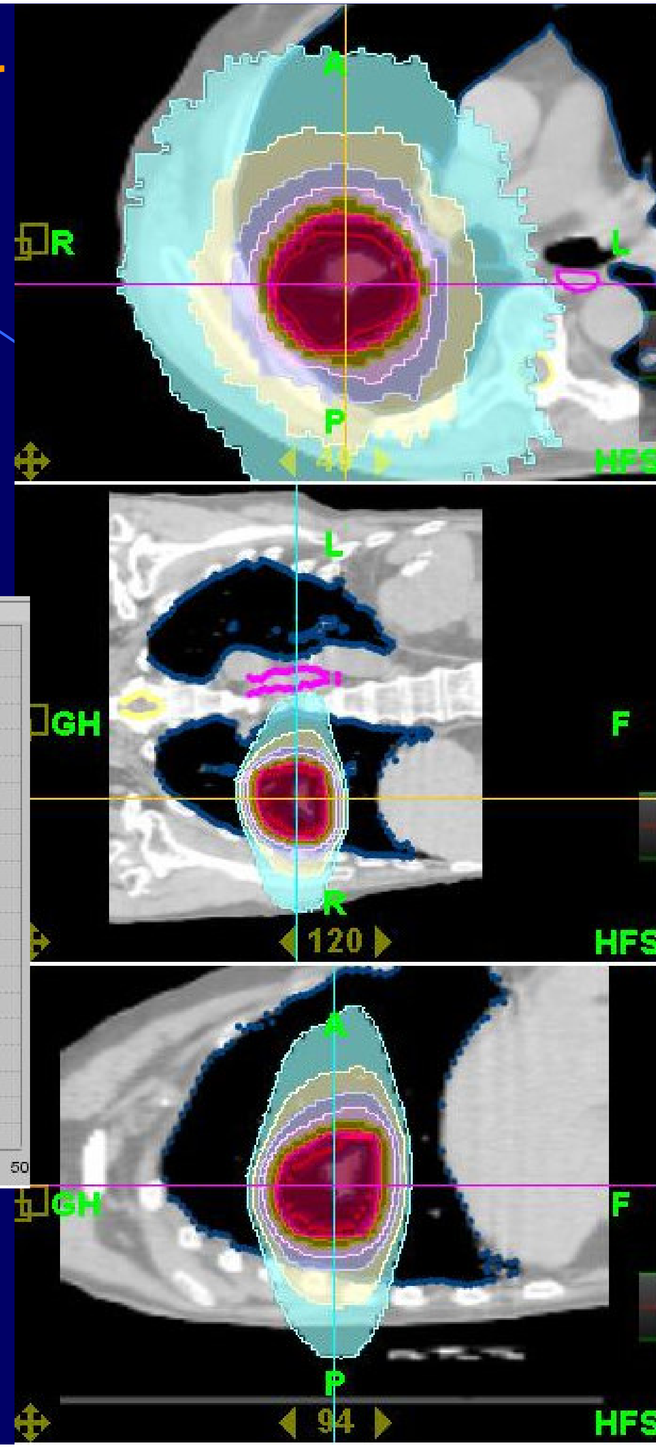
Lung tumour

IMRT allows a "good dose painting" of PTVs while sparing the adjacent normal tissue structures

⇒This allows the development of Hypo-fractionated protocols.





Dose 54Gy= 9 Gy x 6 fractions

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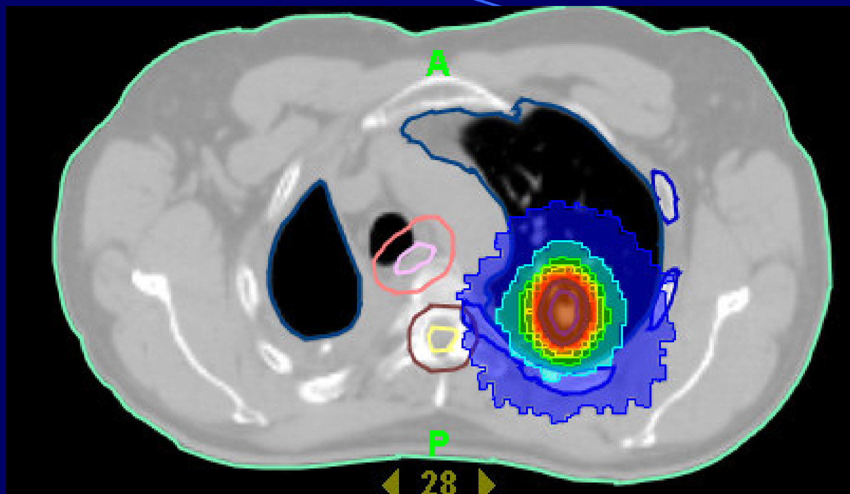
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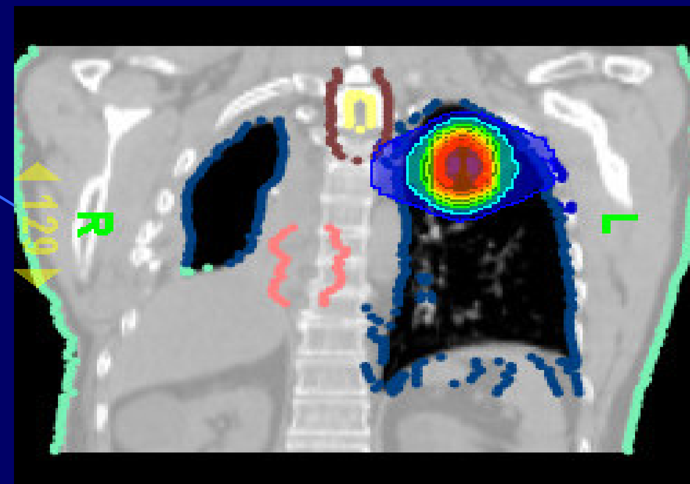
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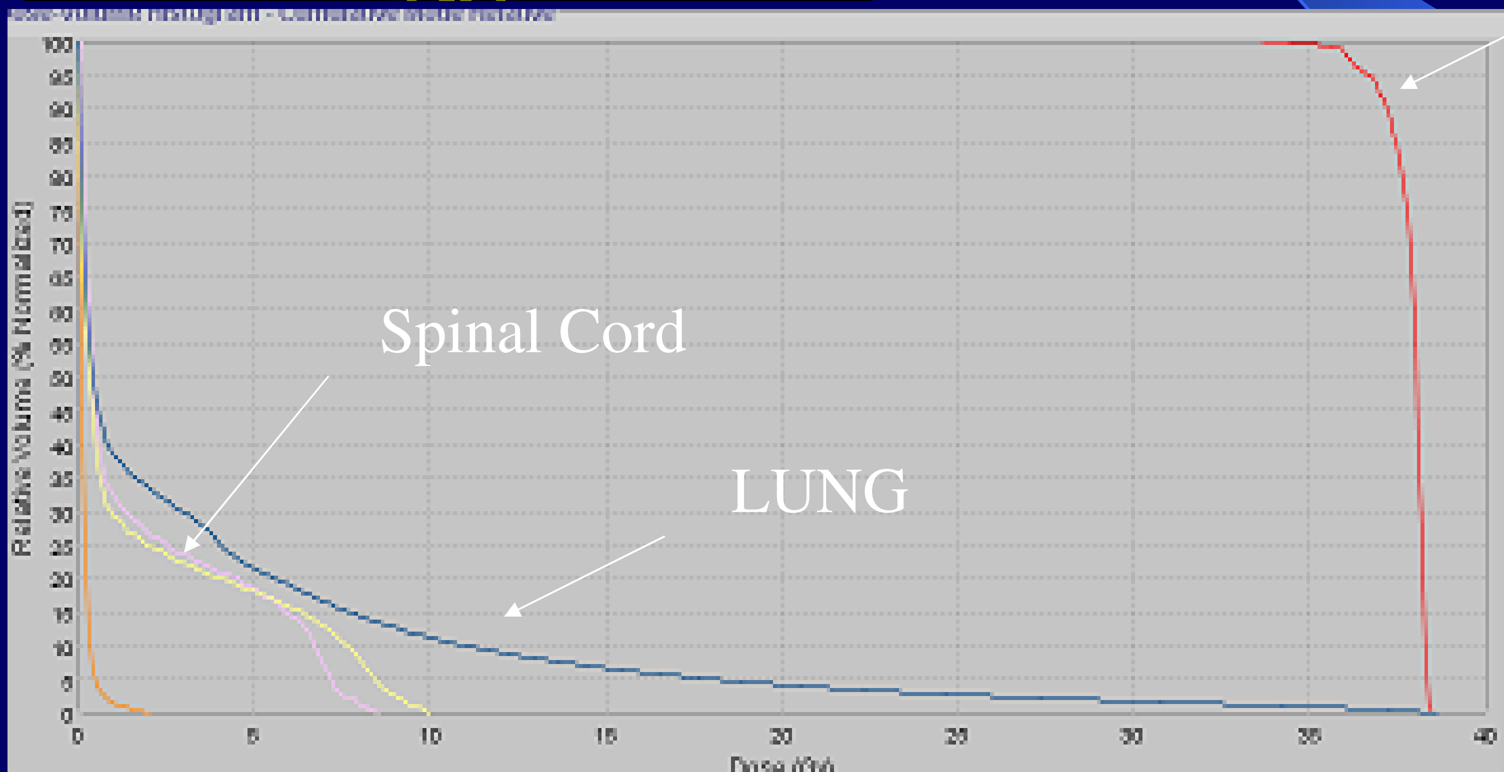
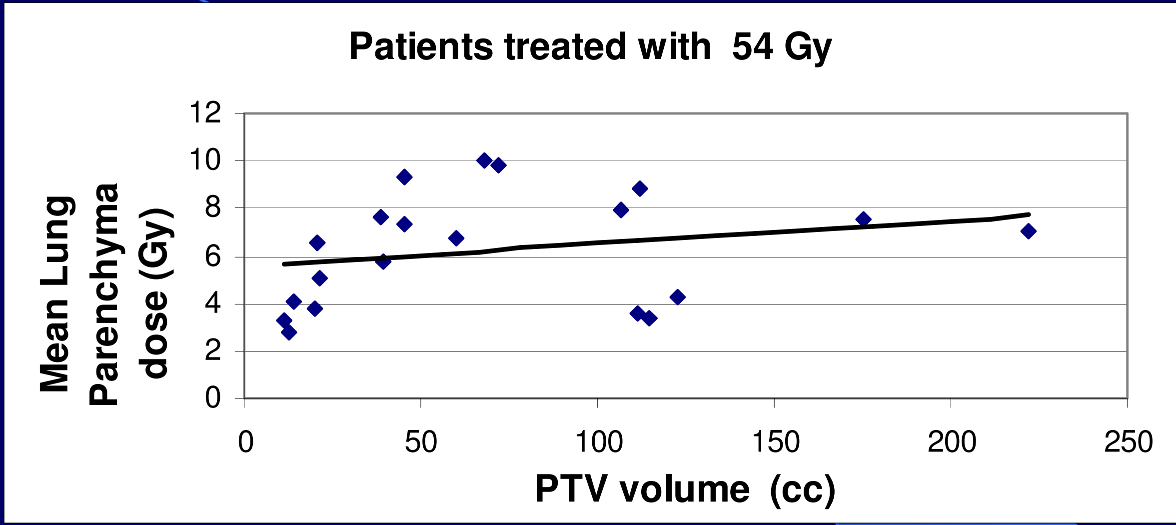

PTV
Spinal Cord
LUNG
Relative Volume (% Normalized)
Dose (Gy)

Lung Met (single lesion): HT plan data

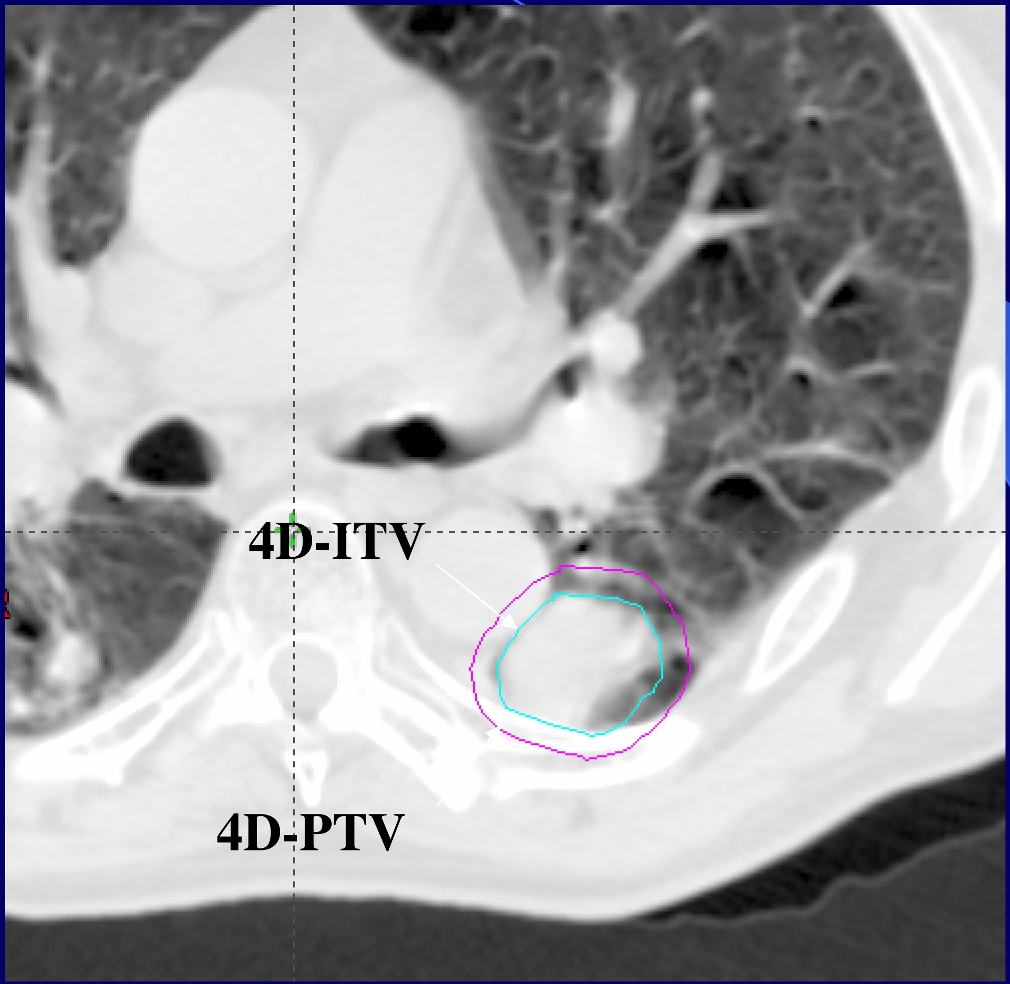
- **20 Patients**
- **54 Gy, 6 fractions**
- **PTV vol: 71.6±58.1 cc**
- **Delivery time:19.8±6.0 min**

(block on contralateral Lung)



	D95	D_mean	D_max	V10
PTV	51.8±0.8			
Heart		3.4	22.7	8.4%
Esoph		4.1	18.2	16.0%
Sp cord			11.5	
Lung Par		6.5		18.5%

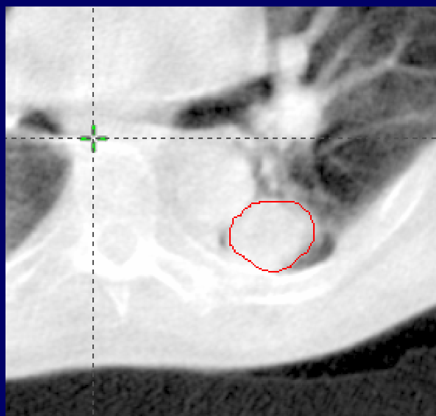
MV-CT AND 4D-PTV REPRODUCIBILITY : METHODS



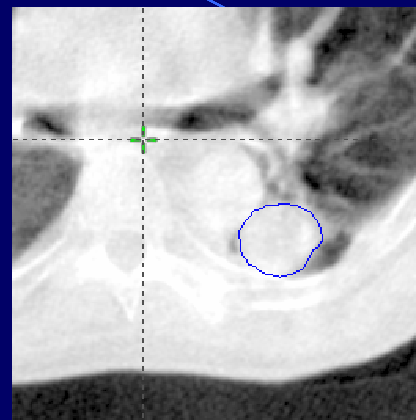
Male , lung mts

48 Gy/6 fs

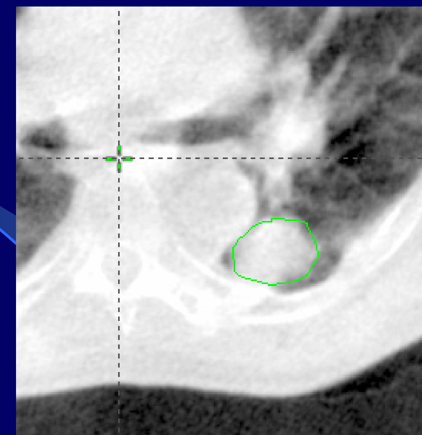
MV-CT



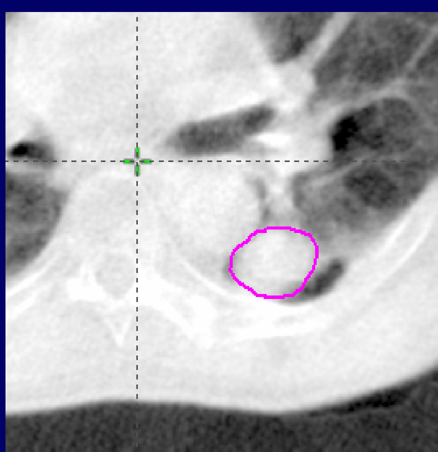
MV-CT 1



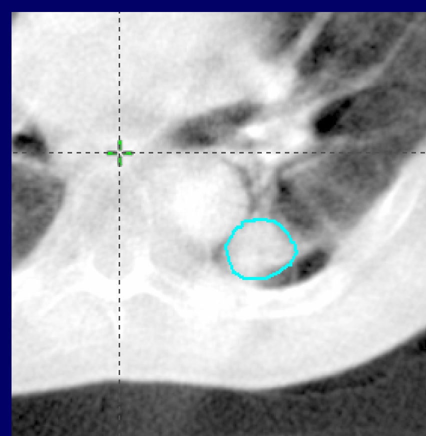
MV-CT 2



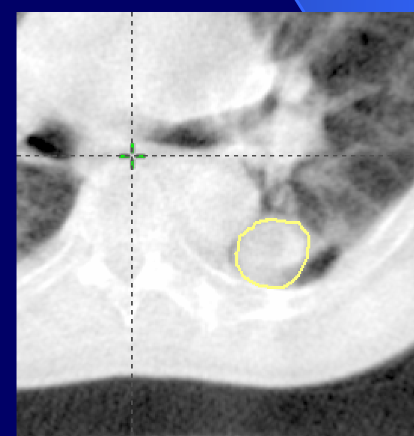
MV-CT 3



MV-CT 4

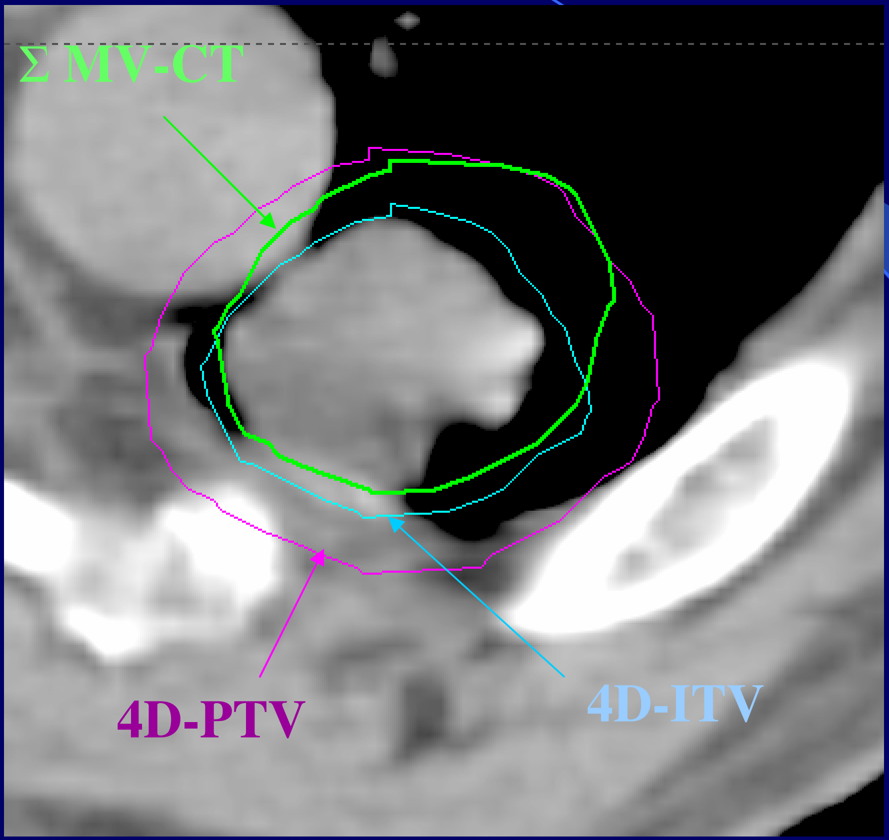


MV-CT 5

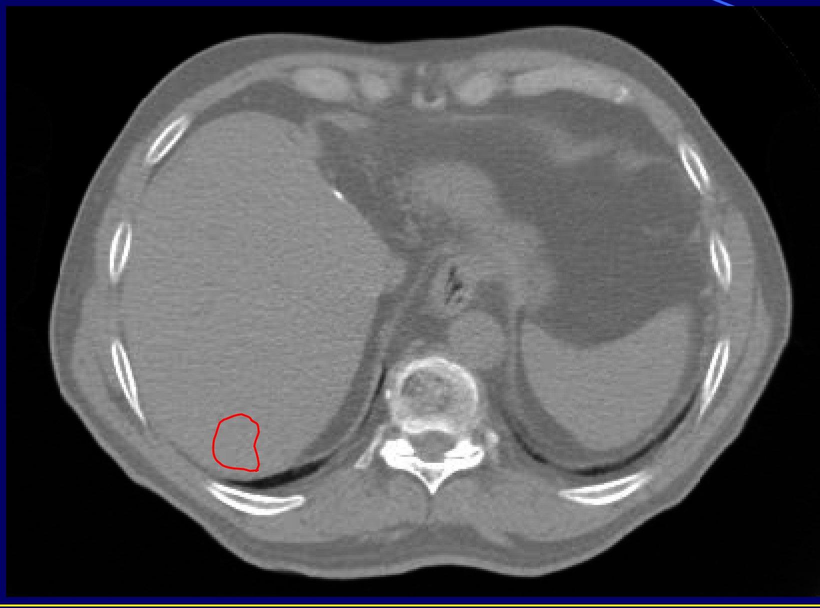


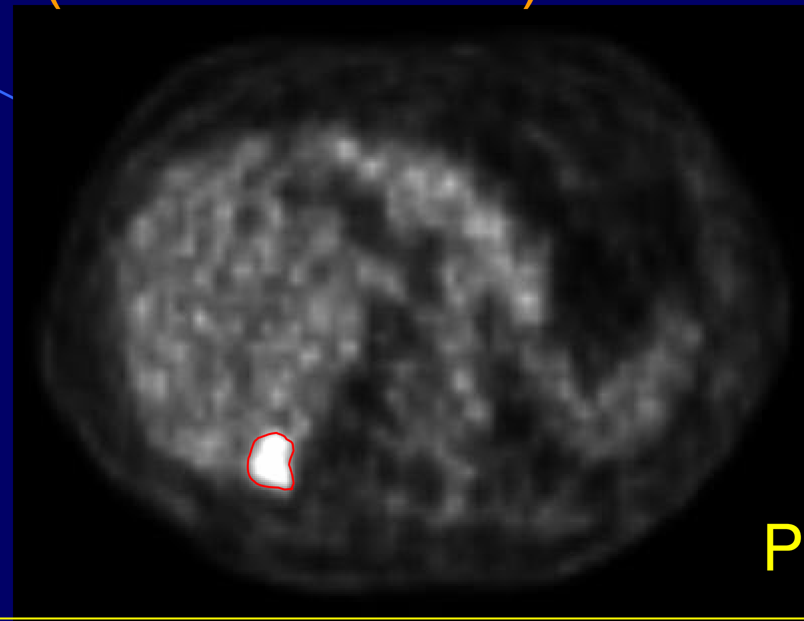
MV-CT 6

VOLUME COMPARING

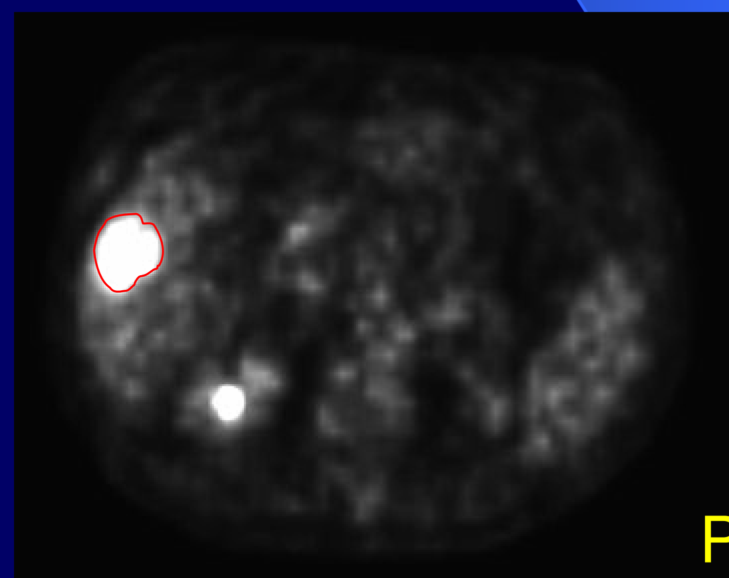


Target definition (difficult on CT)





Pat.1



Pat.2

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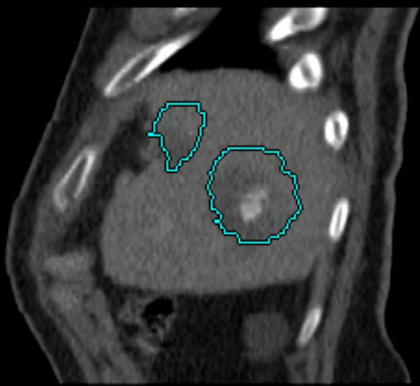
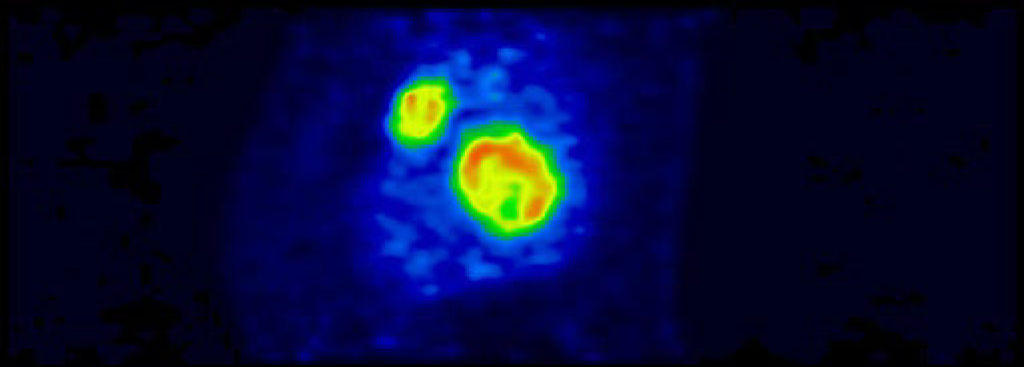
4D CT & 4D PET



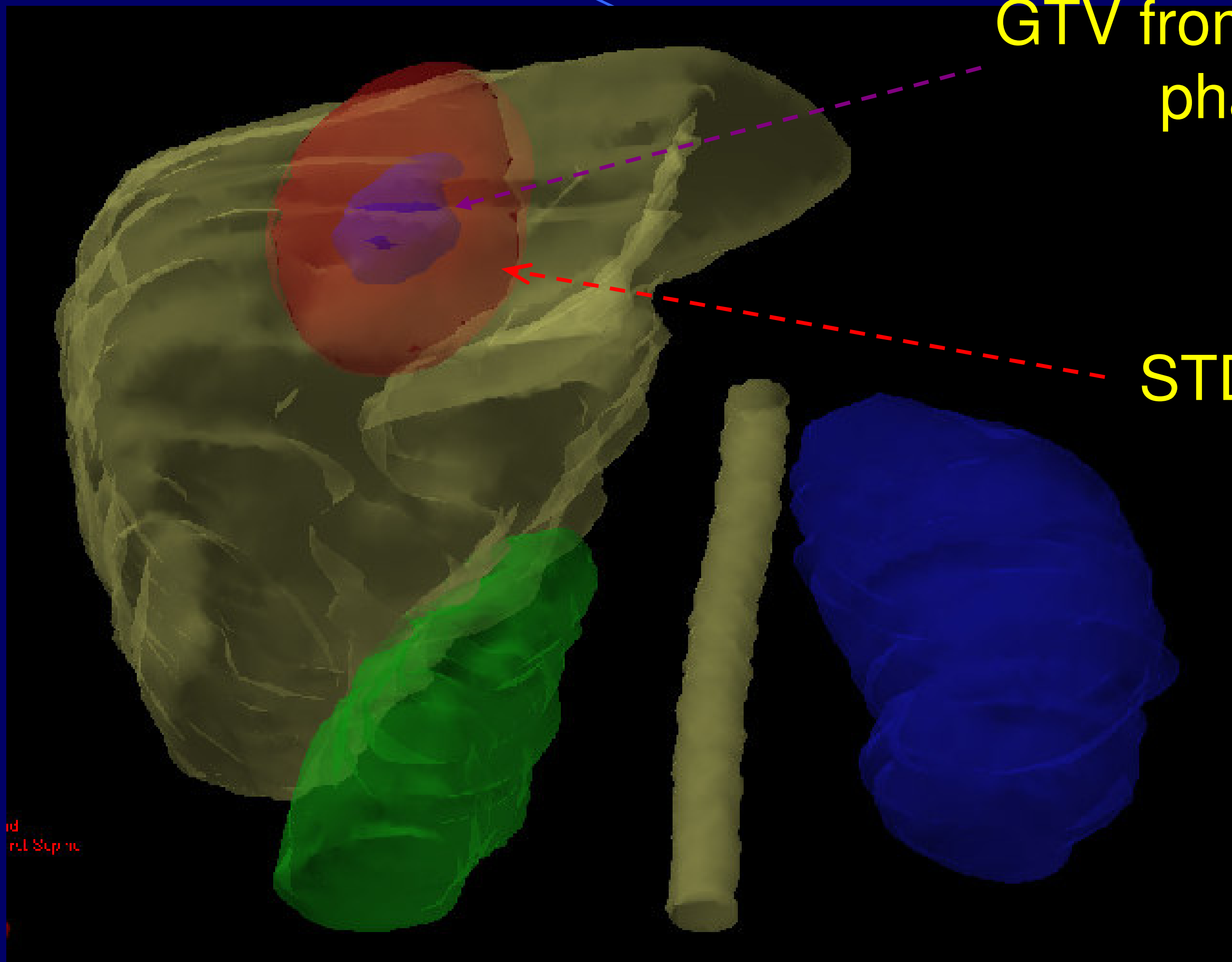
4D-CT
with c.m.



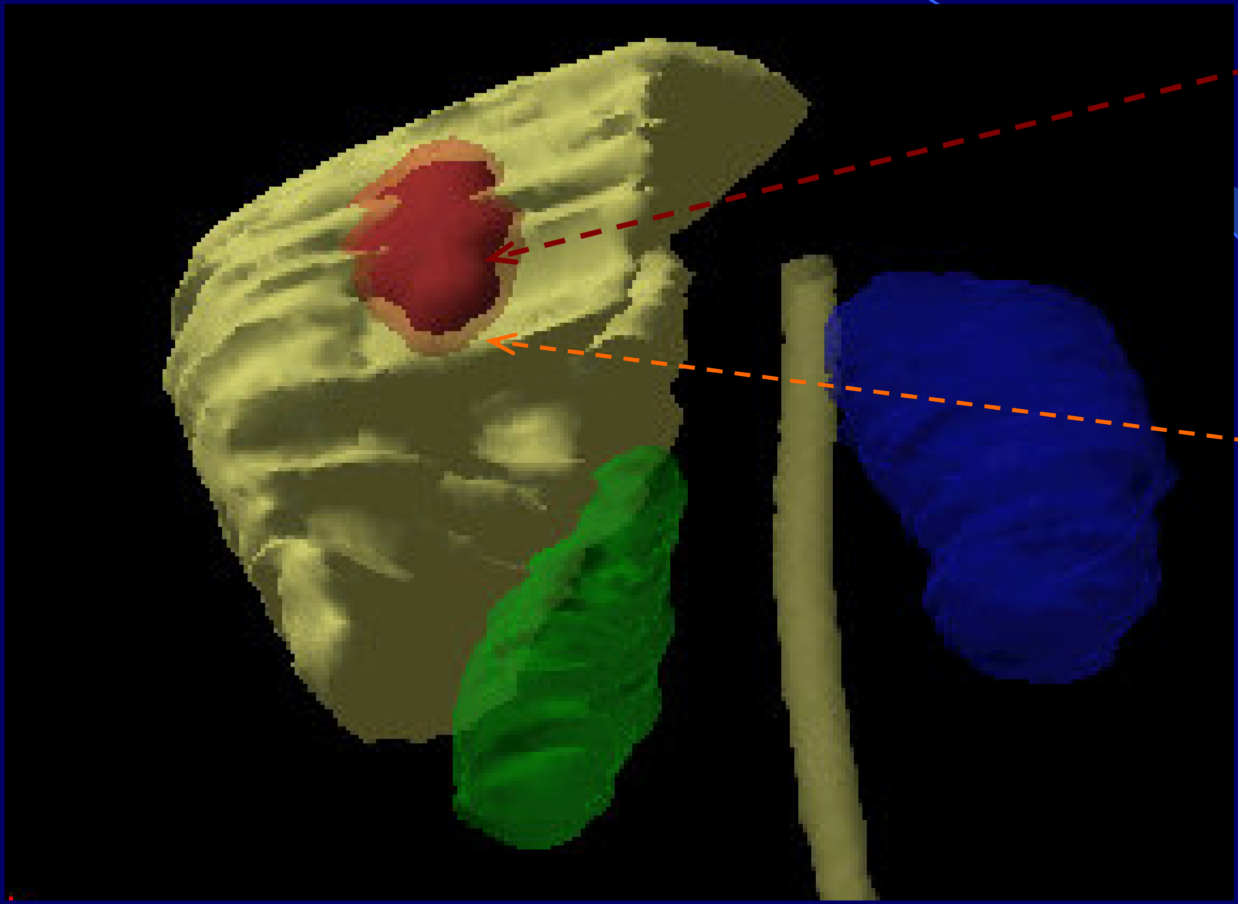
4D-PET

HSR-Milano

Liver tumour



Liver tumour

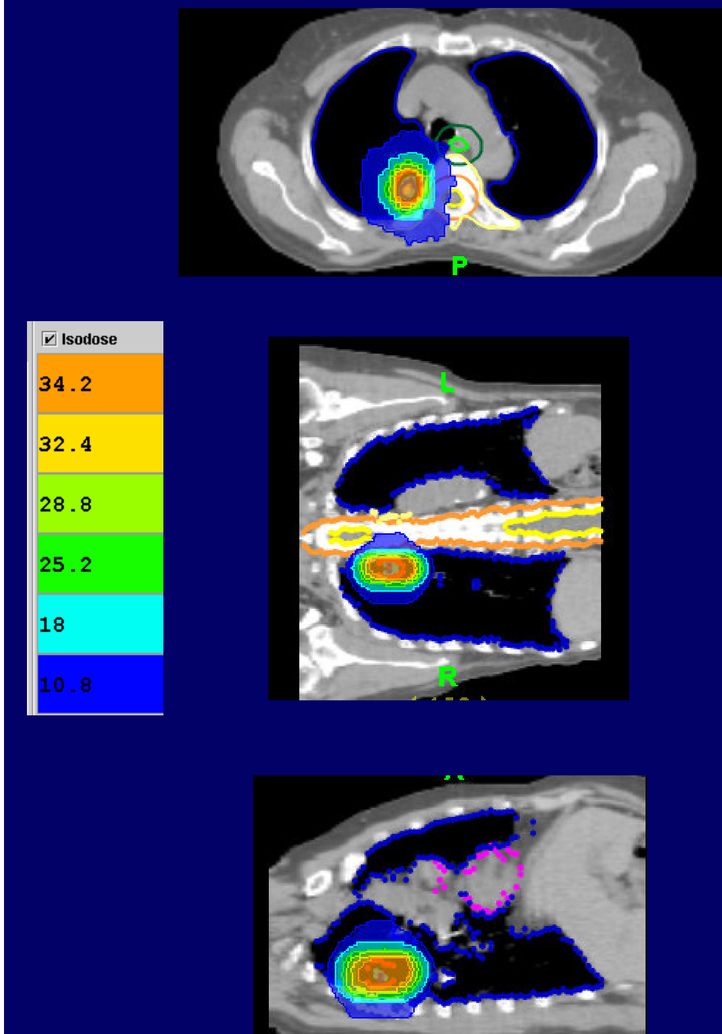


40Gy : 8Gy /fr

HSR-Milano

LUNG mts :

TOXICITY

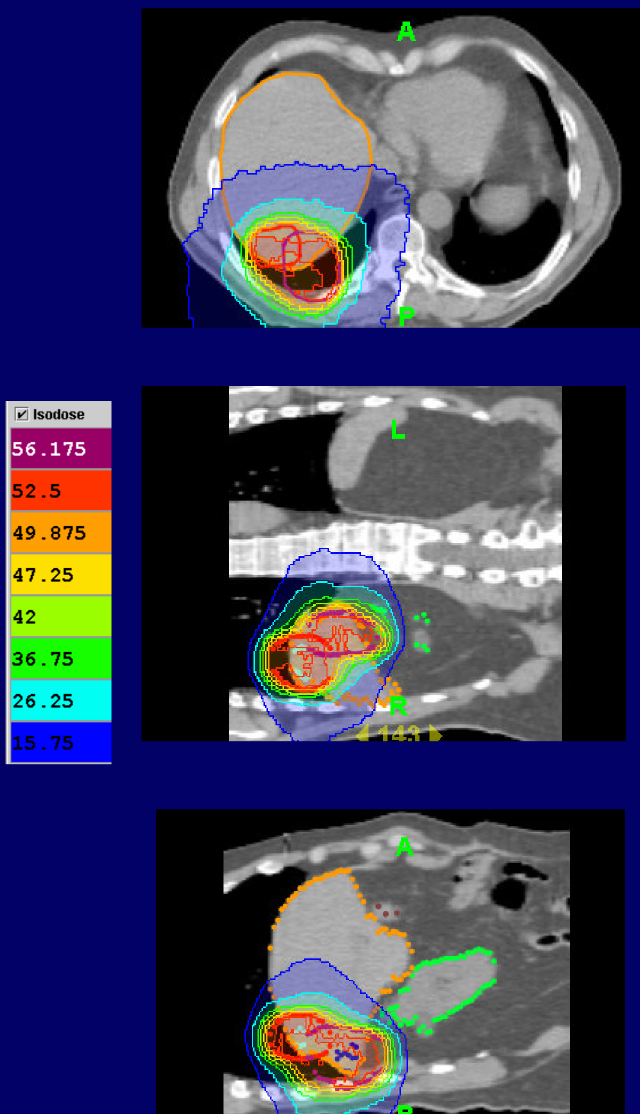


Treatment	Dose (Gy)	Late Tox
Radical , Mts (30 pts)	36-54 (6 fs)	• Pulm : G1 (2/30)

RC 80%
FU 24 ms

LIVER mts :

TOXICITY



Treatment	Pts	Dose (Gy)	Late Tox
11 pts	11	40 (5 fs)	• Nausea : G1 (2/11)

RC 75%
FU 26 ms

Pancreatic Tumor protocol (Phase I): Hypofractionated with dose-esacalated SIB on infiltrated vessels

- Simulation CT: 4D-CT synchronized to concomitant infusion of non-iodinate contrast medium.
- Two 4D target volumes:
  - PTV1: tumor region (4D-GTV1 +5/5/7 mm) (NOT CTV, similar approach: Murphy IJROBP 2007]
  - PTV2 infiltrated vessels + 10 mm (4D-GTV2 +5/5/7 mm).
- Definition of overlap (stomach+duodenum) with PTV1 if > 5 cc
- SIB on PTV2 WITH concurrent to 5-FU continuous infusion (c.i.) or capecitabine

hSR

Pancreatic Tumor : protocol (II)

- Doses:
  - PTV1 (and overlap if defined) : 44.25 Gy in 15 fractions
    - $EQD_2(\alpha/\beta=10\ Gy) = 47.75\ Gy$
  - PTV2: 48-55(58) Gy in 15 fractions
    - $EQD_2(\alpha/\beta=10\ Gy) = 52.8—67.0\ Gy$

… ??? correction for overall treatment time ???

$$BED= E/\alpha= D[1+d/(\alpha/\beta)]-h(T-T_K)$$

Tk=25 d

h=0.5 Gy

Pancreatic Tumor : protocol (III)

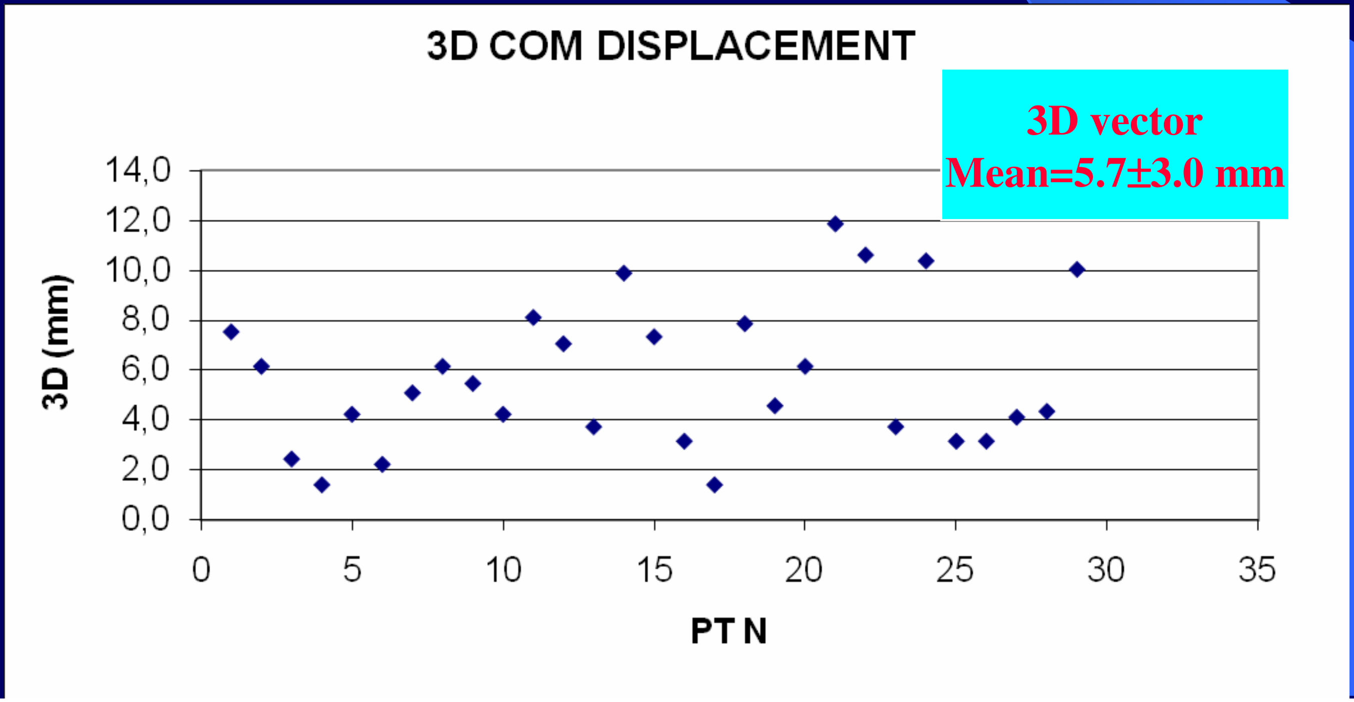
correction for overall treatment time: just an extimation !

D (Gy)	fr	OTT (d)	BED (Gy)	BED* (Gy)	ΔBED
50 (std)	25	33	60	56	
44.25 (PTV1)	15	19	57.3	57.3	+2.3%
55 (PTV2)	15	19	75.2	75.2	+34%

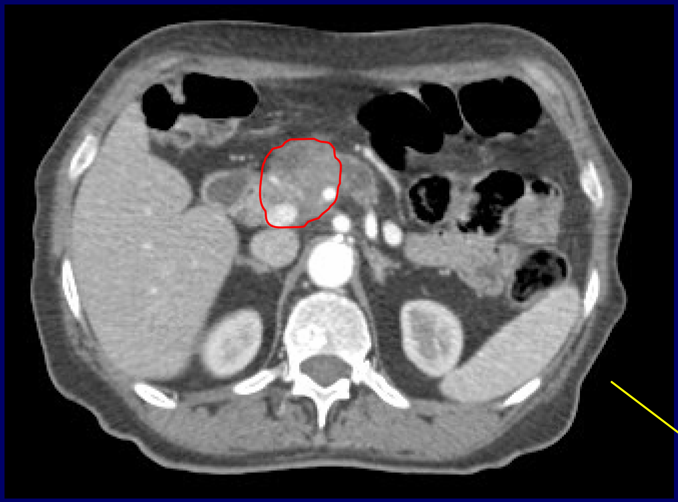
Pancreatic tumor respiratory related motion

- 29 Patients with (contrast enhanced) 4D-CT, quite breathing
- 3D distance between center-of-mass (COM) of the GTV drawn on the end-inhalation and end-exhalation phases

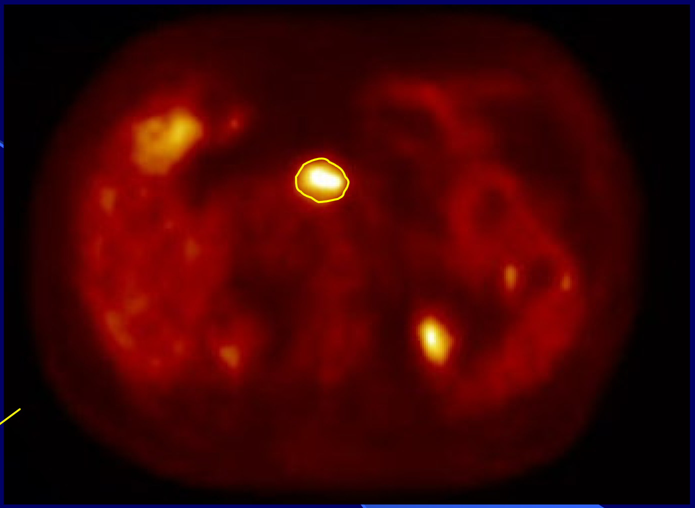
3D vector:
45% ≤ 5 mm
8% > 10 mm
Max = 12 mm



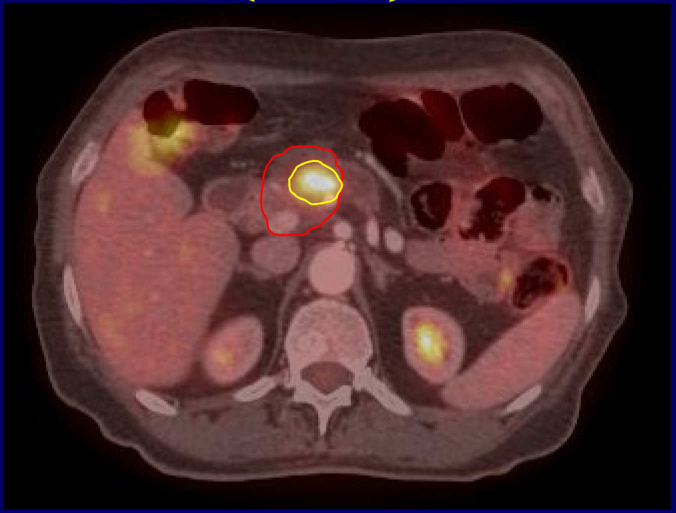
Pancreatic Tumour: imaging for volume definition



4D-CT
with c.m.

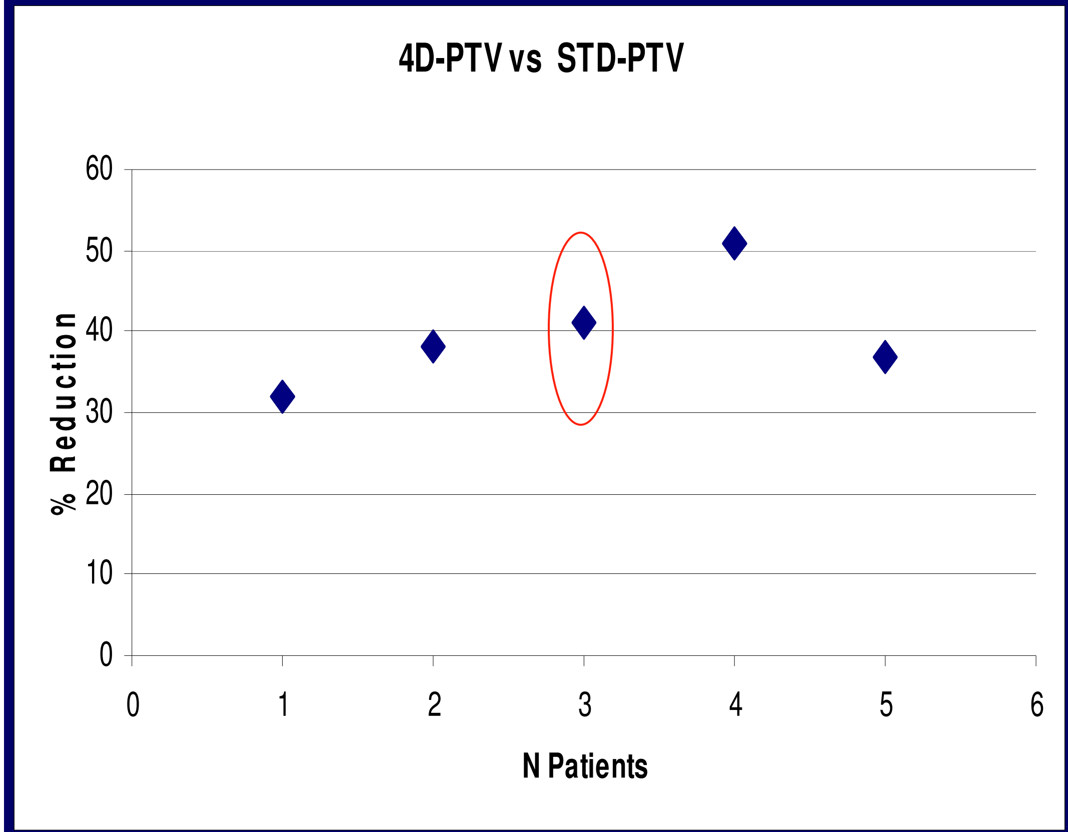


4D-PET

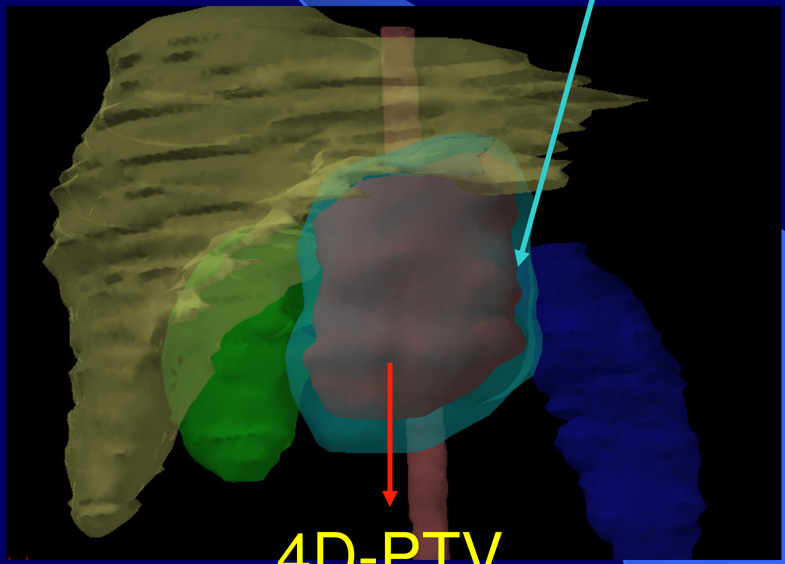


Fused
PET /CT

Pancreatic Tumour



Patient N 3



↓ 40%

HSR-Milano

ST-PTVs 3DCRT vs 4D-PTVs 3DCRT

		3DCRT Targets			
Organ	DVH Parameters	ST-PTV (Mean Values)	4D-PTV (Mean Values)	Organ Spared (%)	P
Stomach	D_mean	22.6	17.6	22%	0.007
	V20	48.5	39.7	18%	0.01
	V50	13,9	8.3	40%	0.004
Duode-num	D_mean	35.0	30.1	24%	0.01
	V20	69.9	63.4	9%	0.01
	V50	36.1	25.3	29%	0.01
Kidney	D_mean	9.0	6.9	23%	0.03
	V20	18.5	13.2	28%	0.05
	V30	11.2	7.7	31%	0.06

ST-PTVs 3DCRT vs 4D-PTVs 3DCRT

ST-PTV vs 4D-PTC: GEOMETRIC RESULTS

4D-PTVs resulted smaller than ST-PTVs in all pts

4D-PTVs were 36% smaller than ST-PTV (mean value 187 cm3 vs 295 cm3, p=0.0006)

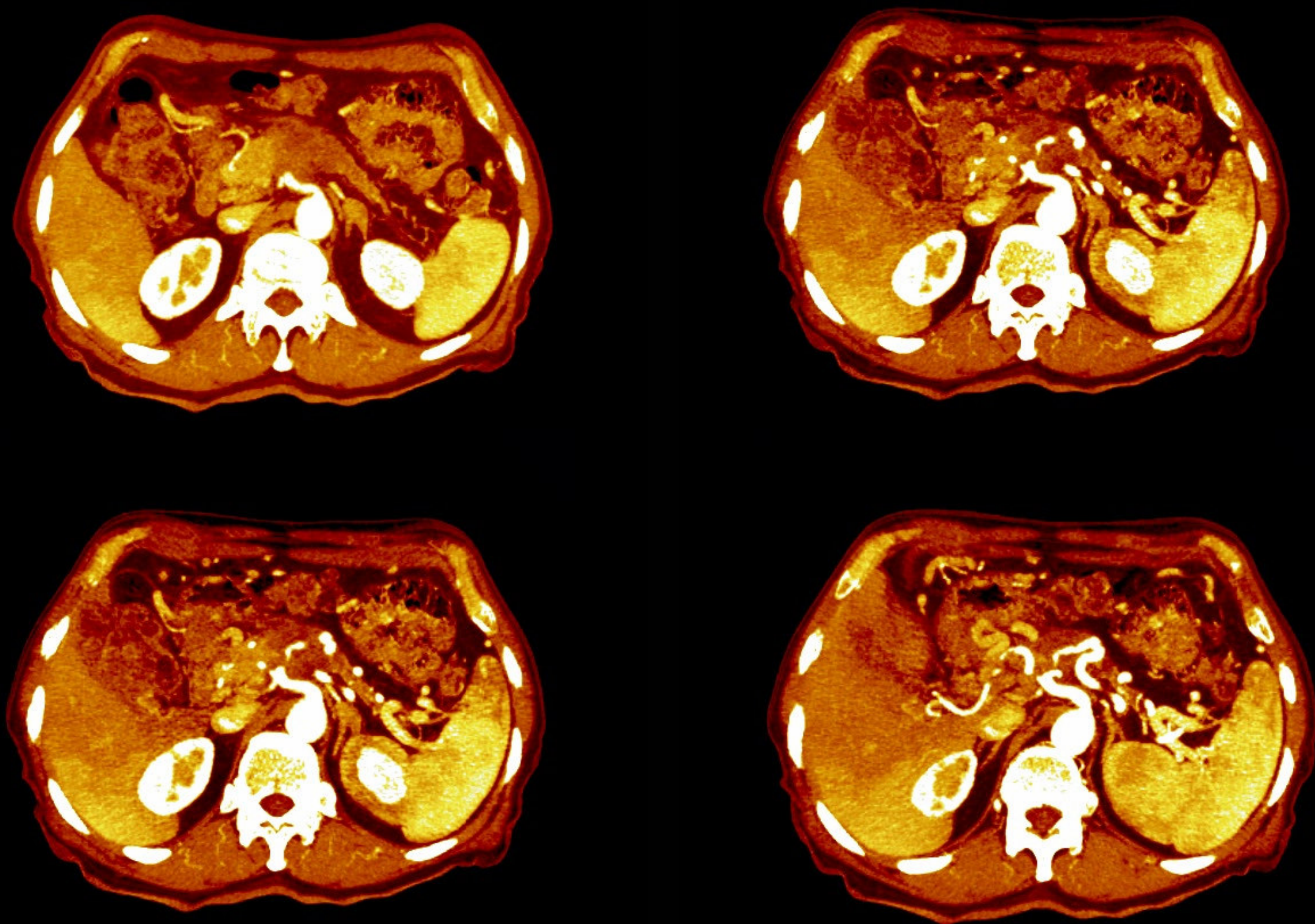
Overlapping volumes between 4D-PTVs and stomach resulted 59% smaller than overlapping volumes between ST-PTVs and stomach (mean value 7 vs 18 cm3, P=0.0014)

Overlapping volumes between 4D-PTVs and duodenum resulted 43% smaller than overlapping volumes between ST-PTVs and duodenum (mean value 9 vs 16 cm3, P=0.006)

3DCRT vs TOMOTHERAPY

		Target = 4DPTVs			
Organ	DVH Parameters	3DCRT (Mean values)	TOMO (Mean values)	Organ Spared (%)	P
Stomach	D_mean	17.6	16.5	8%	0.36
	V20	39.7	29.2	29%	0.004
	V50	8.3	4.3	48%	0.001
Duode-num	D_mean	30.1	24.6	17%	0.003
	V20	63.4	50.5	20%	0.001
	V50	25.3	12.7	49%	0.001
KIdney	D_mean	6.9	13.3	-48%	0.0006
	V20	13.2	18.0	-26%	0.16
	V30	7.7	1.2	84%	0.01

Pancreatic Tumour



HSR-Milano

Pancreatic Tumour: two 4D-PTV

4D-PTV1

“Vascular region ”

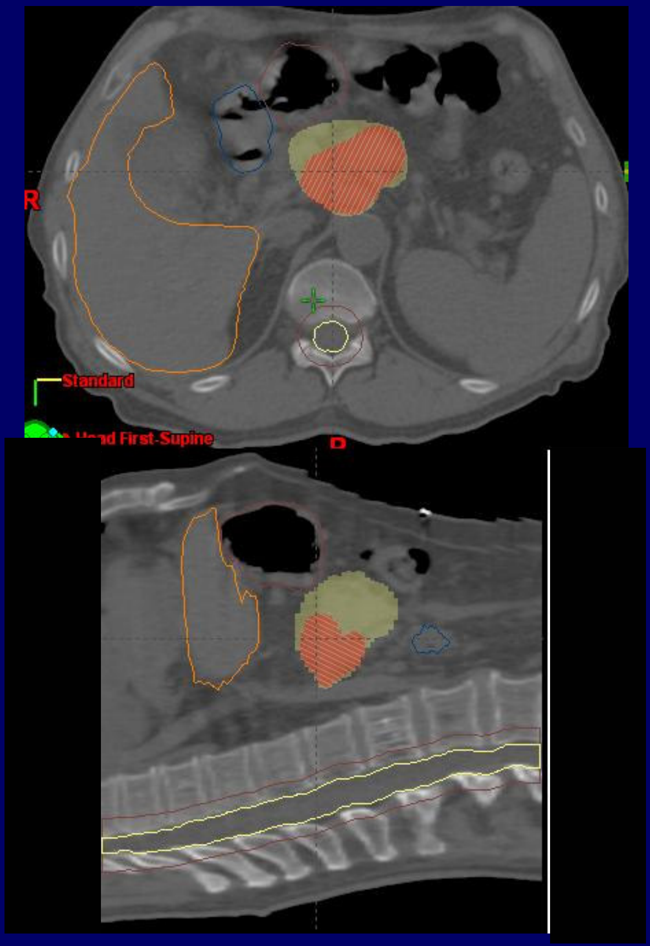
(48-55 Gy, 15 fr)

4D-PTV2

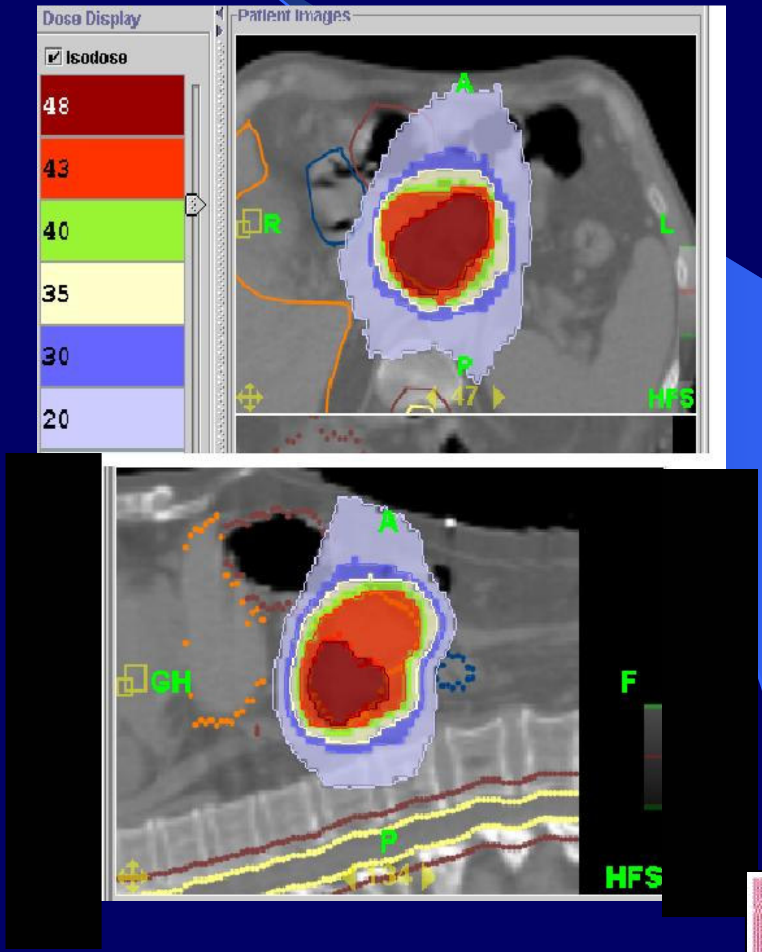
(44.25 Gy, 15 fr)

Pancreatic Tumour: HT plan

two 4D-PTV



Dose distribution

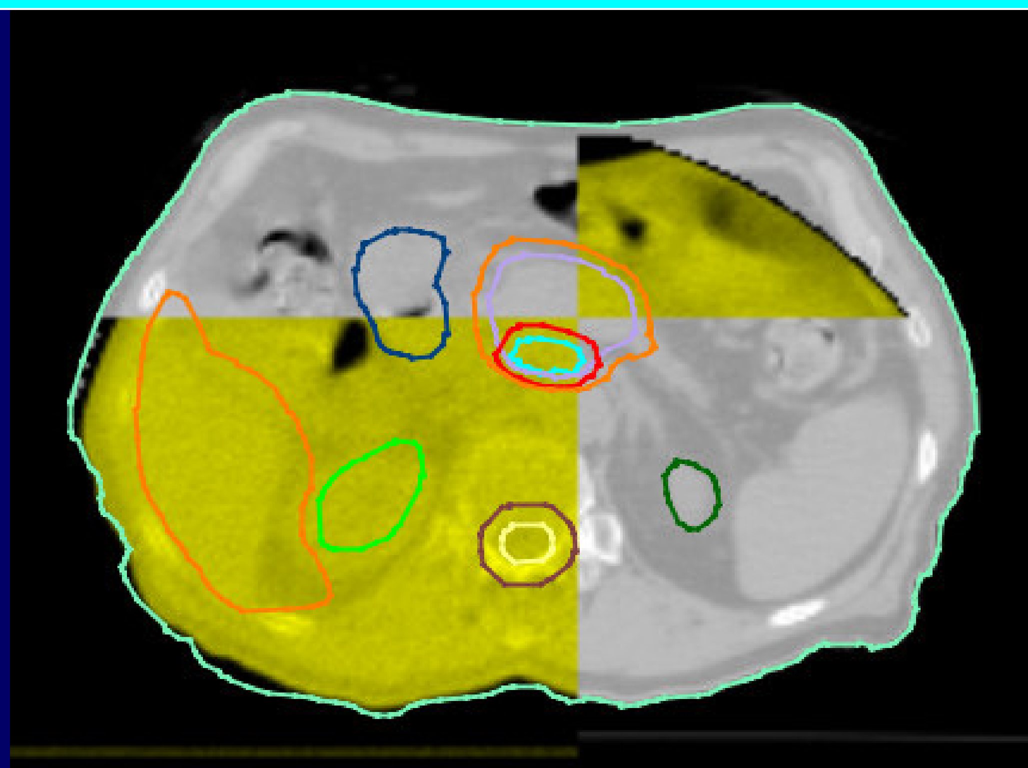


Daily MVCT-KVCT match

A two step procedure:

- a fully automatic registration based on bony anatomy

- matching adjusted through direct visualization **(overlapping of the 12th costo-vertebral joints and of inter vertebral spaces; aorta, vena cava, and the origins of their main vessels, etc)**



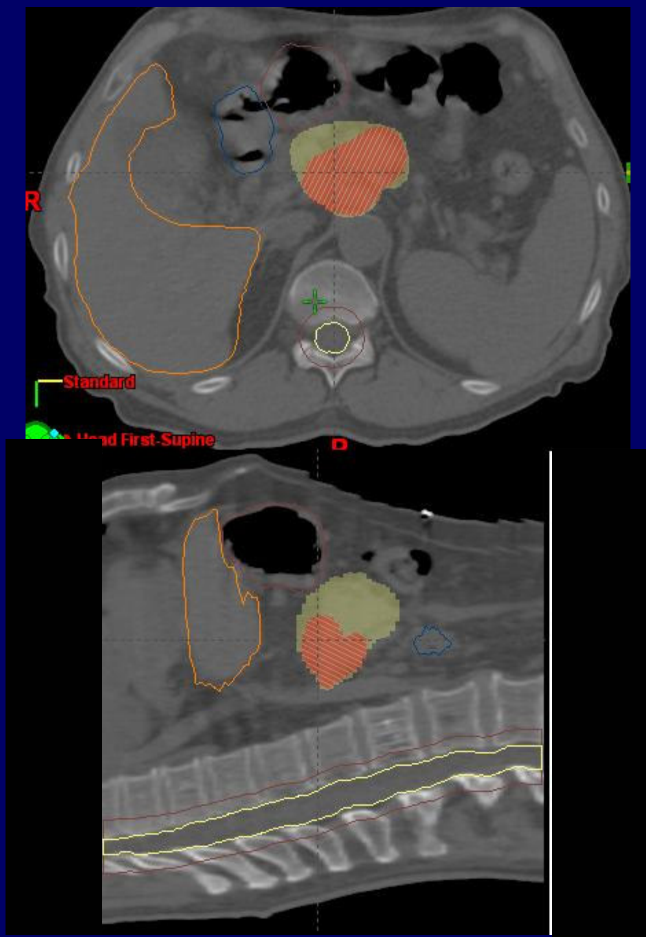
Difference between "bone" and "operator" matching

- **12Pts, 180 daily MVCT**
- **For the three main axes, the deviation between bone matching and the final direct visualization**

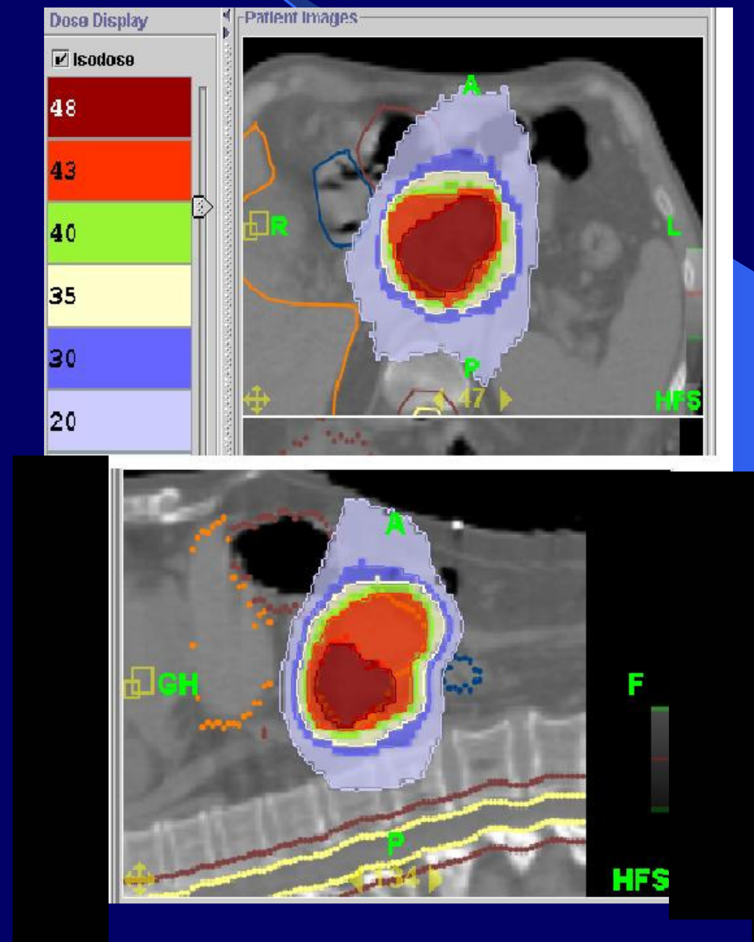
	LR	**CC**	**AP**	**3D**
≥ 3 mm	6.8%	9.6%	3.4%	19.2%
≥ 5 mm	3.4%	4.5%	2.3%	9.0%
≥ 7 mm	2.3%	4.0%	1.1%	4.5%
Max shift	10mm	7mm	5mm	13mm

Pancreatic Tumour: HT plan

two 4D-PTV



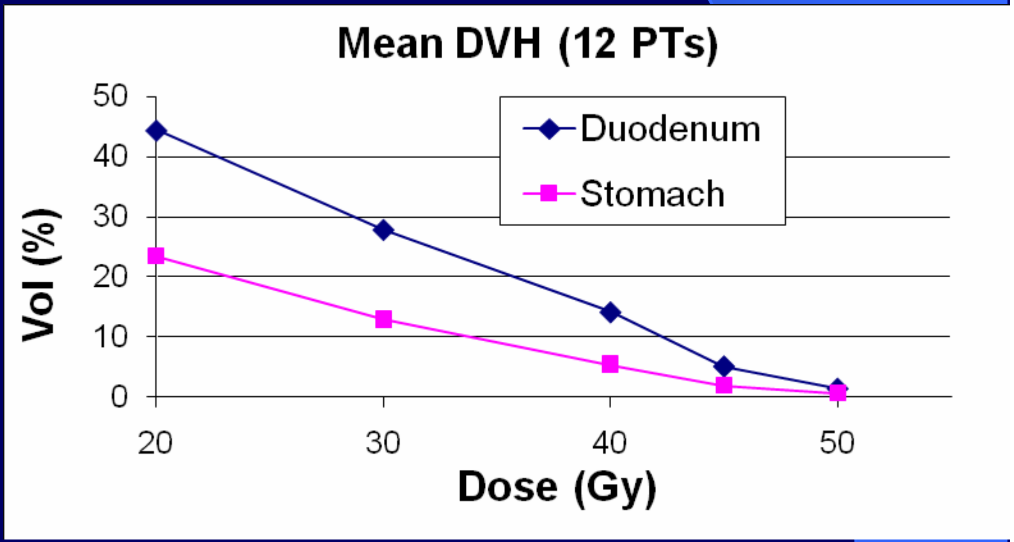
Dose distribution



HT plan strategy

OAR	2.95Gy	3.67Gy
Spinal cord $\alpha/\beta = 2$	D_{max} = 36.3 Gy	D_{max} = 31.7Gy
PR-Spinal cord $\alpha/\beta = 2$	D_{max} = 40.4 Gy	D_{max} = 35.3 Gy
Liver (RILD) $\alpha/\beta = 3$ NTCP: 4%	D_{med} =22.1Gy	D_{med} =19.7 Gy
DUODENUM $\alpha/\beta = 3$	V36 < 33%	V32 < 33%
STOMACH $\alpha/\beta = 3$	V36 < 25%	V32 < 25%

- Constraints modified according to the dose/fraction on PTV1 (… to stress the optimization with higher dose/fraction values)
- For more critical structure (stomach, duodenum): as low dose level (on overall DVH) as reasonable achievable without compromising PTV coverage



PANCREATIC CANCER

RESULTS

DOSE LEVELS:

I level, 48 Gy: 4 pts
II level, 50 Gy: 6 pts
III level, 52Gy: 3 pts
IV level, 55 Gy: 3 pts

SD	**53%**
PR	**27%**
PD	**20%**
Median FU	**18 m**

G3 TOXICITY:

Gastric ulcer: 1 pt at the II level

Gastro-duodenitis: 1 at the IV level

COMMENTS:

Three more pts will be enrolled at the IV level
The planned final dose to PTV2 is 58 Gy

Malignant Pleural Mesothelioma: dose escalation protocol with SIB on BTV

- **Simulation CT + PET**
- **Two target volumes:**
  - **PTV1: tumor region (CTV + 10 mm)**
  - **BTV: FDG_PET avid region**
- **DOSES:**
  - **PTV: 54 Gy 25 fr (12 PTs)**
  - **BTV: 62.5 Gy 25 fr (11 PTs)**

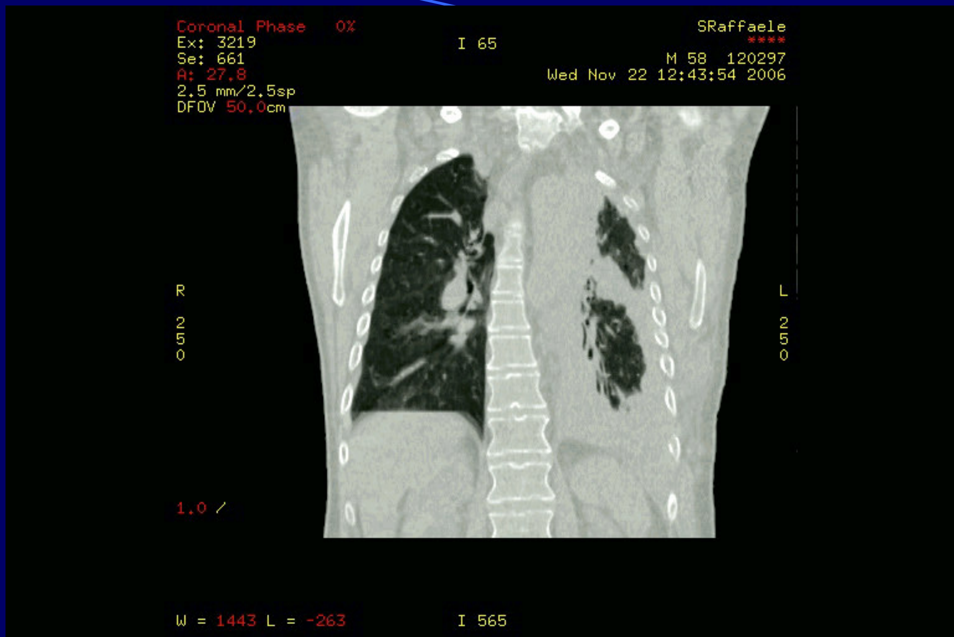
Malignant Pleural Mesothelioma

DOSE-DEPENDENT PULMONARY TOXICITY AFTER POSTOPERATIVE INTENSITY-MODULATED RADIOTHERAPY FOR MALIGNANT PLEURAL MESOTHELIOMA

Rice et al. IJROBP 2007
63 Pts, 21% non-cancer-related deaths
10% pulmonary related deaths

and may further improve local tumor control. With strict attention to limiting the MLD and V_{20} as much as possible, it is usually feasible to safely administer therapeutic doses to the entire planned target volume. Currently, we aim to keep the MLD at <8.5 Gy and the mean V_{20} at <7%; ideally, both should be even lower if possible. In centers

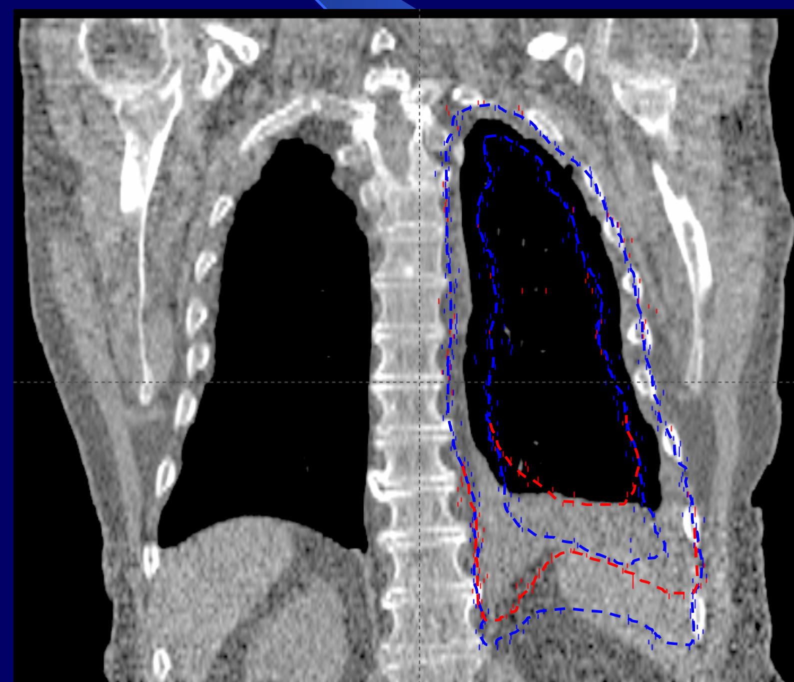
Conclusion: The results of our study have shown that fatal pulmonary toxicities were associated with radiation to the contralateral lung. V_{20} was the only independent determinant for risk of PRD or non–cancer-related death. The mean V_{20} of the non-PRD patients was considerably lower than that accepted during standard thoracic radiotherapy, implying that the V_{20} should be kept as low as possible after extrapleural pneumonectomy.



Involved lung respiratory pattern:

Usually reduced motion !

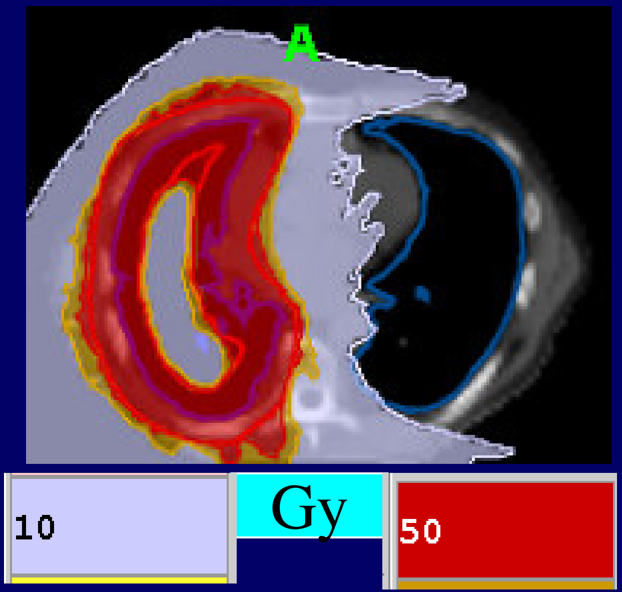
Rare exceptions ⇒ 4D imaging

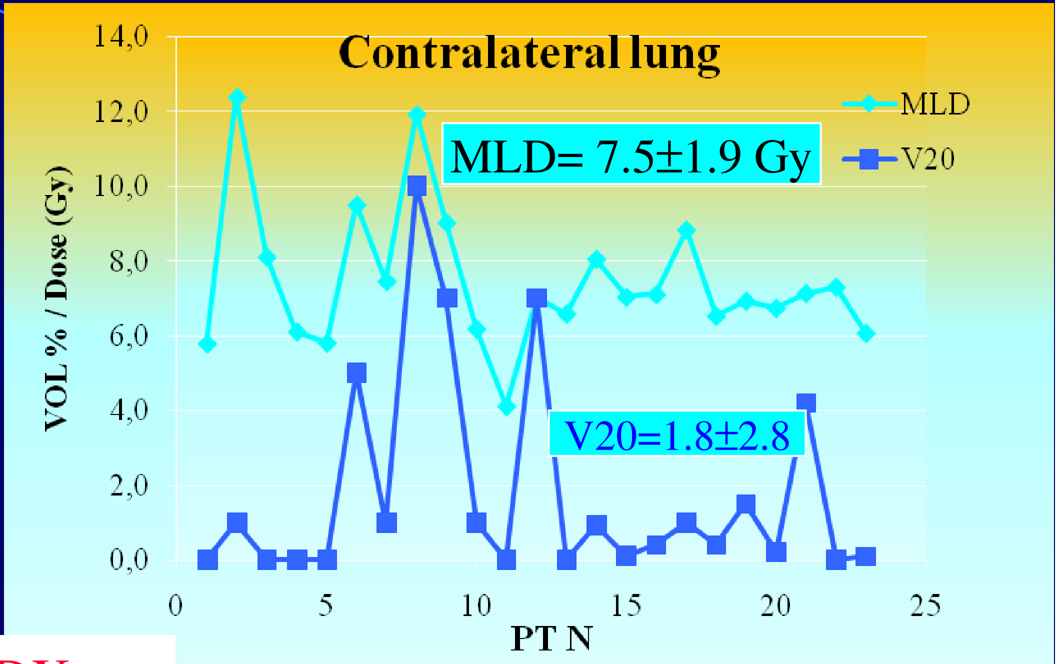


--- End Inspiration

--- End Expiration

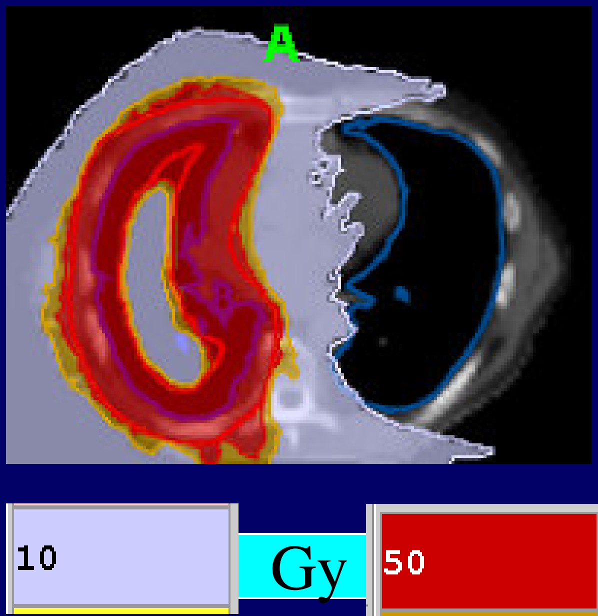
Pleural mesothelioma : HT plan data

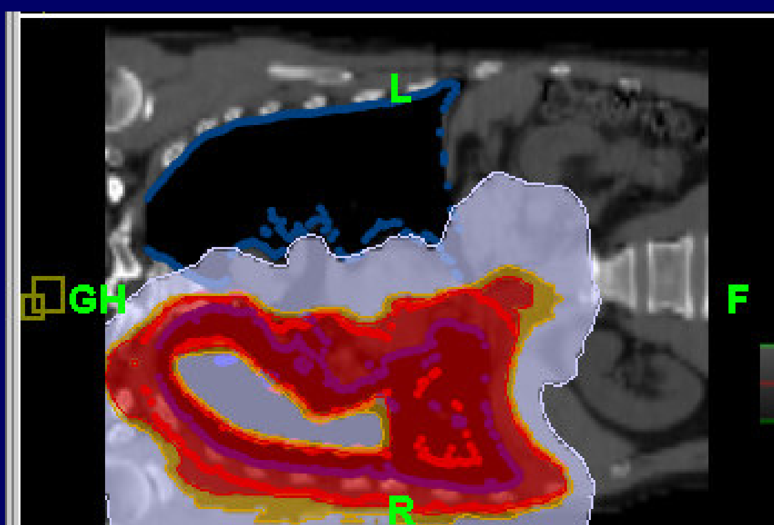




	Meso SX	Meso DX
Heart		
D_mean	28.5±5.0	23.2±2.9
Liver		
D_mean	7.7±2.3	23.0±4.0
Sp Cord		
D_max	40.3±5.0	

Pleural mesothelioma : TOXICITY AND RESPONSES





TWO GROUPS

*** Group 1 (56 Gy, 12 Pts)**

Median Survival= 5 months (0-32 m)

No early-late tox > G1 RTOG

1 CR, 4 PR, 7 PD

*** Group 2 (+ SIB on BTV 62.5 Gy, 11 PTs**

3 G3 RTOG Lung Tox

4 PR, 3 SD

Median survival: 7 (1-12) months

Conclusions

- **Modern IMRT-technology** guarantees a dose delivery which conforms more closely to the shape of the PTV and improves OAR DVHs

- Both lung a liver tumours have been treated using hypofractionated RT with limited acute or long term normal tissues reactions

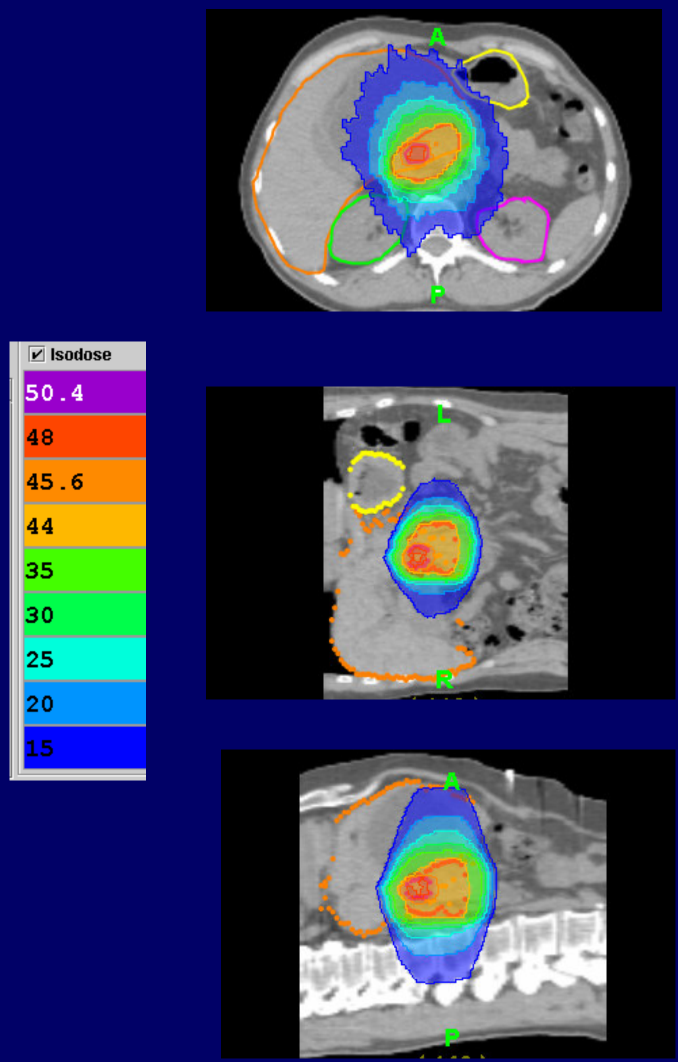
- Certain dose and volume limitations are necessary BUT their limits are still under evaluation

- Daily MVCT scan for (hard) hypofractionated protocol

Acknowledgements

- **Medical Physics DPT**
- **Radiotherapy DPT**
- **Nuclear medicine DPT**

PANCREAS : TOXICITY AND RESPONSES



SIB DOSES

- 48 Gy (4 PTs)
- 50 Gy (6 PTs)
- 52 Gy (3 PTs)
- 55 Gy (3 PTs)

Early G3 toxicity: 7%

SD	53%
PR	27%
PD	20%
Median FU	18 m