University of Otago CPD Workshop, March 2017

Liver Radiation Therapy

(high dose-rate stereotactic ablative radiation therapy to the liver)

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Radiation Therapist, Wellington Blood & Cancer Centre

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Background

Liver malignancies

- Incidence
  - 6th most common cancer diagnosis
  - 5.7% of all diagnoses

  - Primary tumours
    - Hepatocellular carcinoma

  - Liver metastases
    - Colorectal (~10-20% of patients)
    - Breast (~5% of patients)
    - Head & neck, lung, etc

Ananthakrishnan A, Gogineni V, Saeian K. Epidemiology of Primary and Secondary Liver Cancers. *Seminars in Interventional Radiology*. 2006;23(1):47-63. doi:10.1055/s-2006-939841.

Radiation therapy to the liver

- Limitation
  - Toxicity (irradiated volume)
  - Mean dose – 30Gy (TD5/5)
    - Emami et al. (1991)

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- Radiation-induced liver disease (RILD)
  - Fatigue
  - Weight gain
  - Increased abdominal girth
  - Hepatomegaly
  - Anicteric ascites
  - Elevated alkaline phosphatase

Guha, C., & Kavanagh, B. D. (2011). Hepatic Radiation Toxicity: Avoidance and Amelioration. *Seminars in Radiation Oncology*, *21*(4), 256–263. http://doi.org/10.1016/j.semradonc.2011.05.003

Radiation therapy to the liver

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  - Mean dose – 30Gy (TD5/5)
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- Reduce dose to normal liver tissue whilst maintaining therapeutic dose to tumour
  - Increased precision in tumour volume definition (MRI/PET)
  - Increased conformity of dose to the tumour region (treatment planning)
  - Increased accuracy in tracking of tumour on-treatment (treatment delivery)

Stereotactic Body Radiation Therapy (SBRT)

Conventional RT

- 1.8-2Gy per fraction
- 25-30 fractions
- Total dose 45-60Gy

- Maximum dose <107% of prescribed dose
  - Allow function to return to targeted tissue

- ‘Shape’ dose to spare adjacent organs at risk as achievable

SBRT

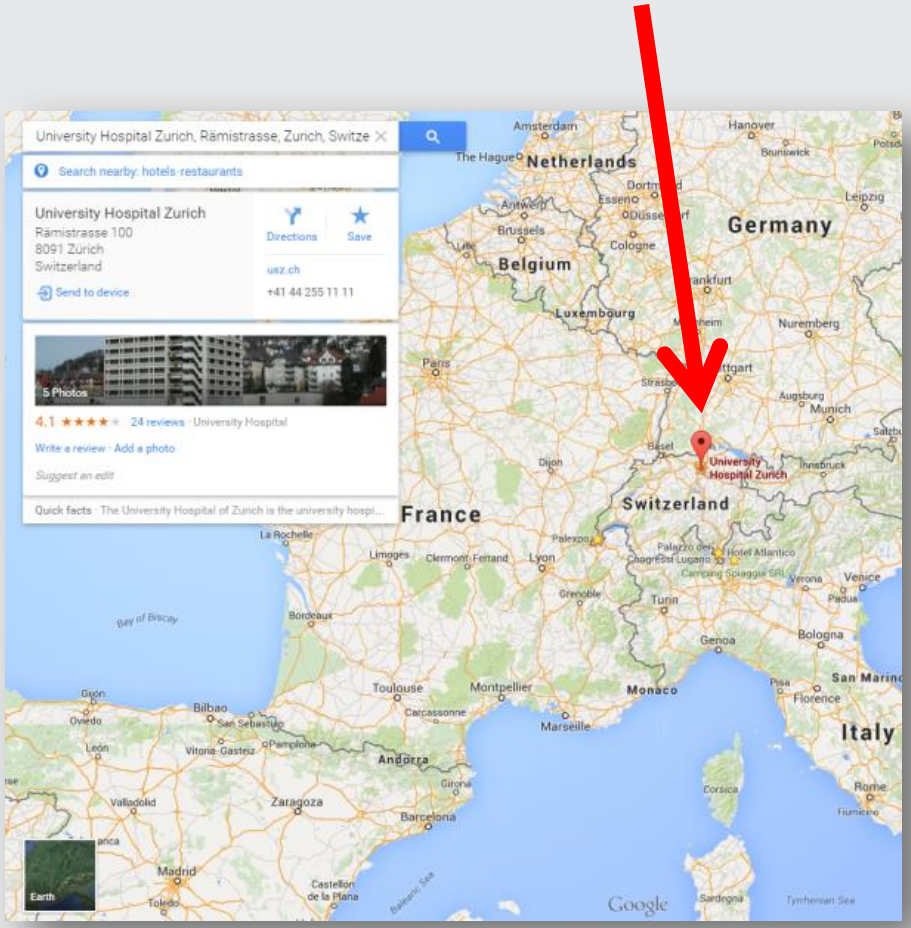
- 6-20Gy per fraction
- 1-8 fractions
- EQD2 80-120Gy

- Maximum dose <140% of prescribed dose
  - Ablative treatment

- High maximum allows steepest possible dose fall-off, sparing adjacent tissue

University Hospital Zurich

- First Varian Truebeam treatment worldwide
  - March 16th, 2010
  - First FFF treatment
- Commence SBRT program
  - Thoracic (lung)
  - Abdominal (liver, renal)



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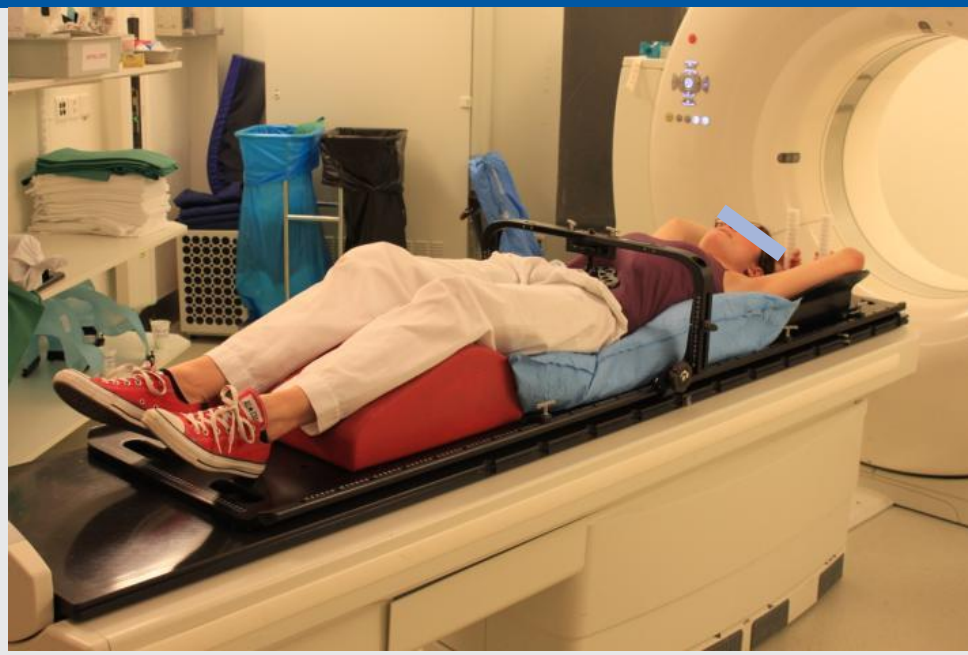
SBRT from the RT's perspective

- **Inter**fractional accuracy
  - Patient position reproducibility
  - Imaging (IGRT)

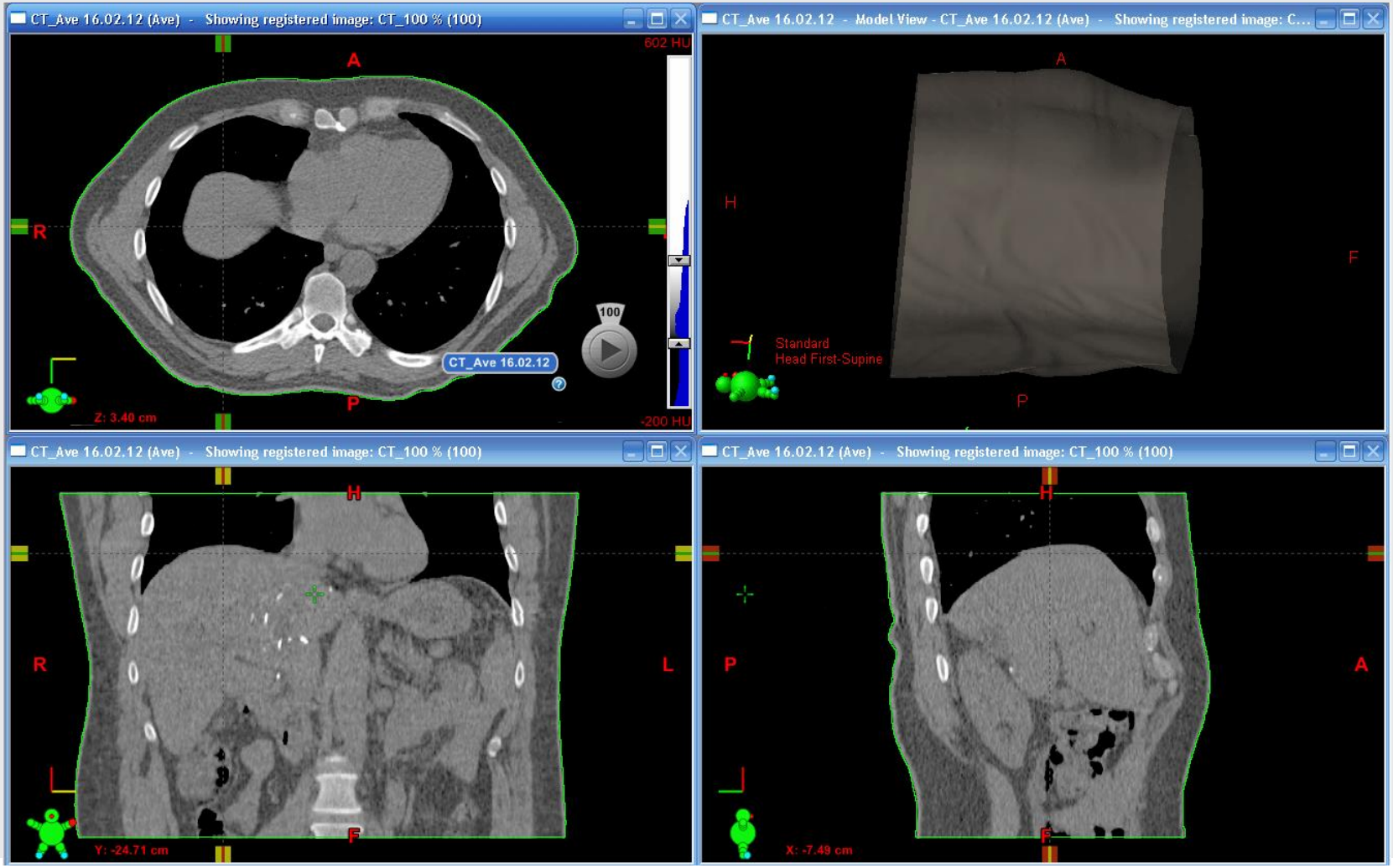
- **Intra**fractional accuracy
  - Patient position stability
  - Imaging (IGRT)
  - Respiratory motion

SBRT: Planning-CT

- CIVCO Body Pro-Lok
  - Wingboard
  - Vacuum Cast
  - Knee fix
- **For lesions near diaphragm:**
  - **With/without abdominal compression**
- **4DCT**
  - Breathing curve amplitude

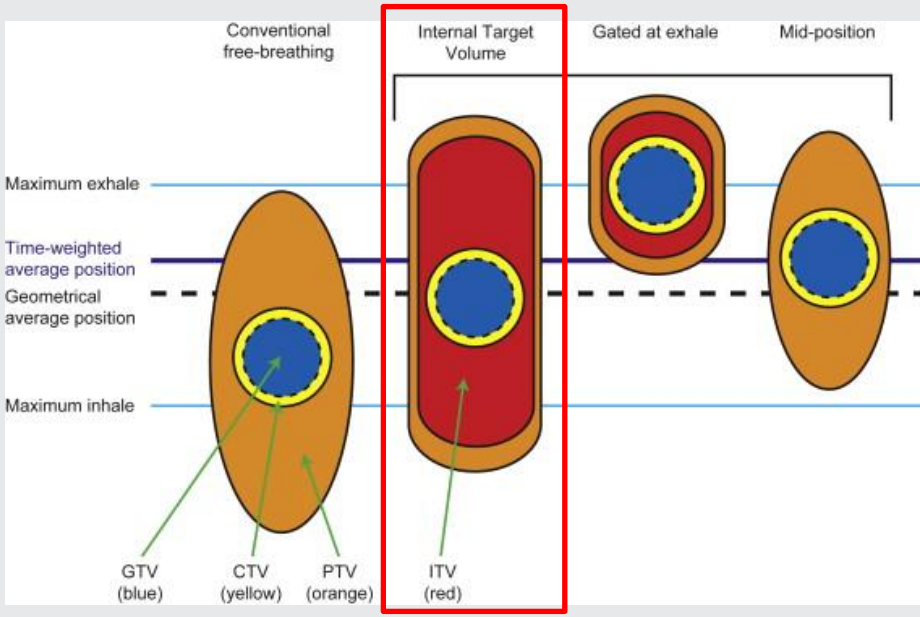


SBRT: Planning-CT (respiratory motion)



SBRT: Planning-CT (respiratory motion)

ITV



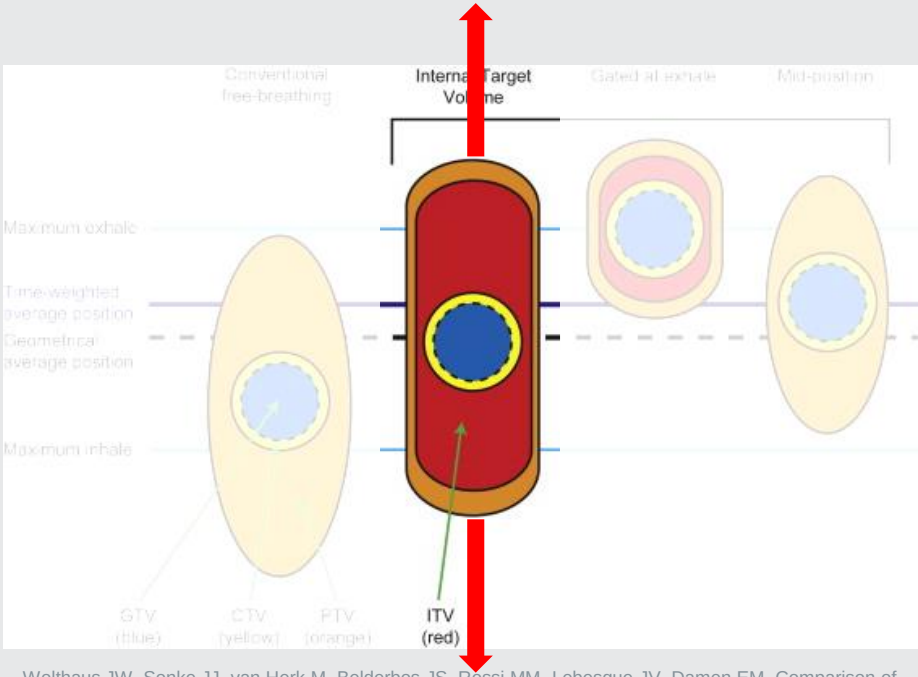
Wolthaus JW, Sonke JJ, van Herk M, Belderbos JS, Rossi MM, Lebesque JV, Damen EM. Comparison of different strategies to use four-dimensional computed tomography in treatment planning for lung cancer patients. Int J Radiat Oncol Biol Phys. 2008 Mar 15;70(4):1229-38.

SBRT: Planning-CT (respiratory motion)

ITV

- ↑Tumor motion = ↑ irradiated volume

- High biological dose of SBRT



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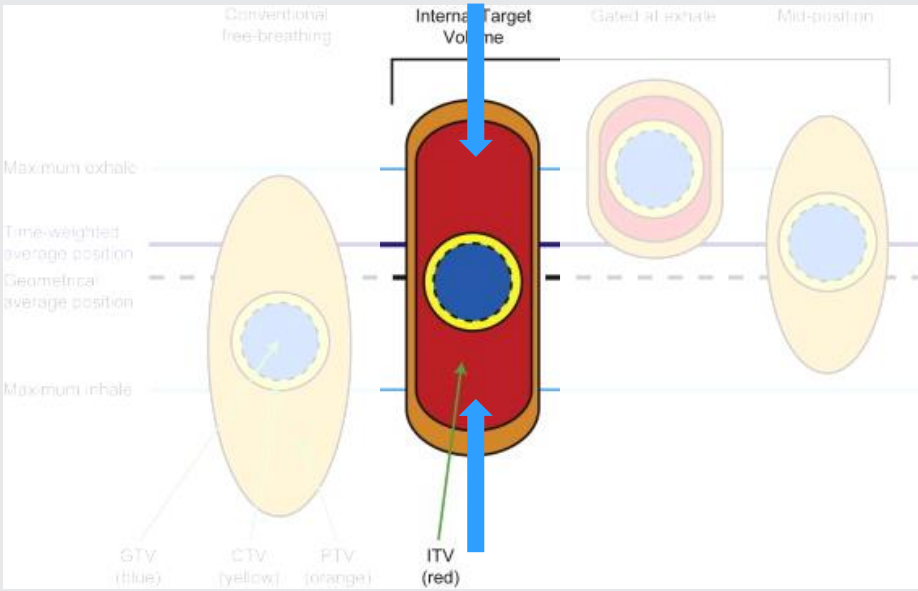
SBRT: Planning-CT (respiratory motion)

ITV

- ↑Tumor motion = ↑ irradiated volume
- High biological dose of SBRT
- **Reduce respiratory motion**
- **Reduce normal tissue component of ITV**
- **Stabilise GTV**



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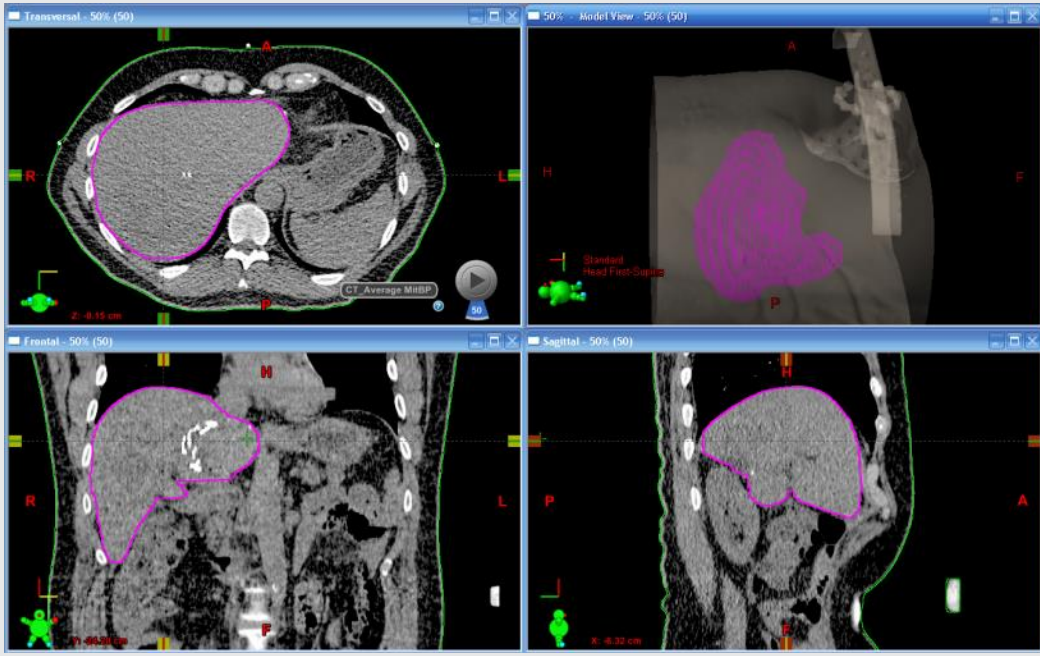
SBRT: Planning-CT (respiratory motion)

Respiratory motion of the liver with/without abdominal compression:

- 10 abdominal SBRT patients
  - 3 excluded (N=7)
- 4DCT scans with/without AC
- Liver contoured at inhale/exhale



SBRT: Planning-CT (respiratory motion)

Respiratory motion of the liver with/without abdominal compression:

- 10 abdominal SBRT patients
  - 3 excluded (N=7)
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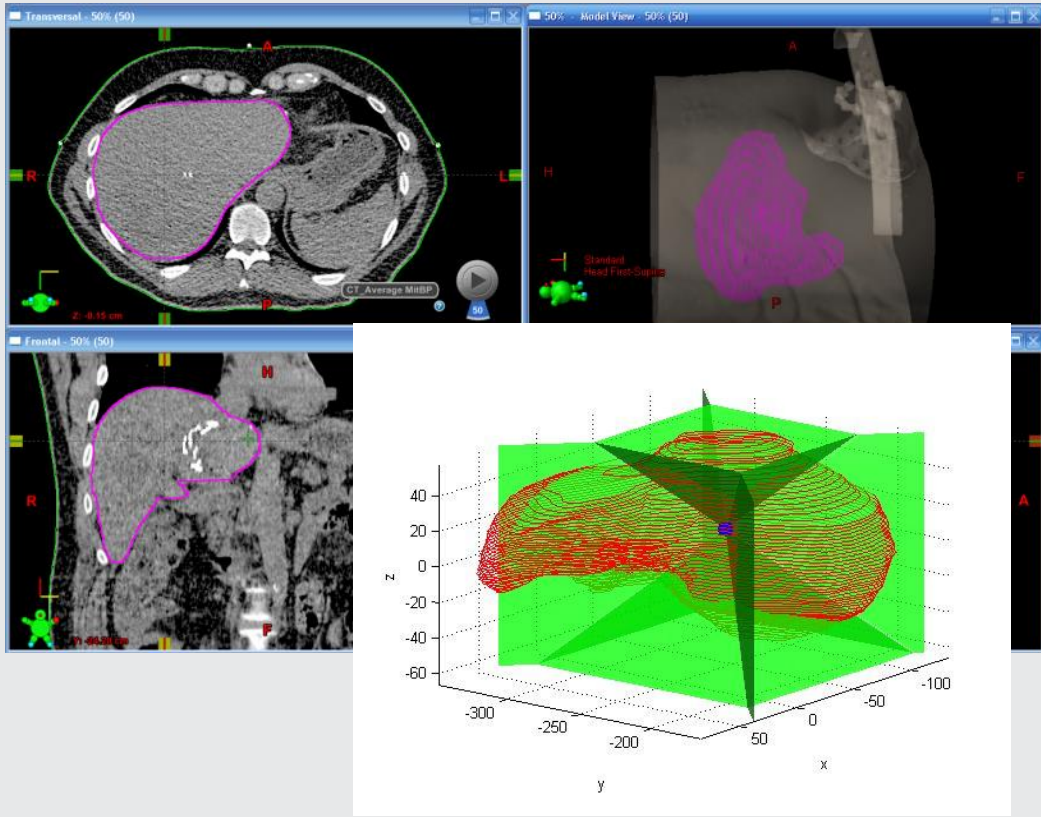
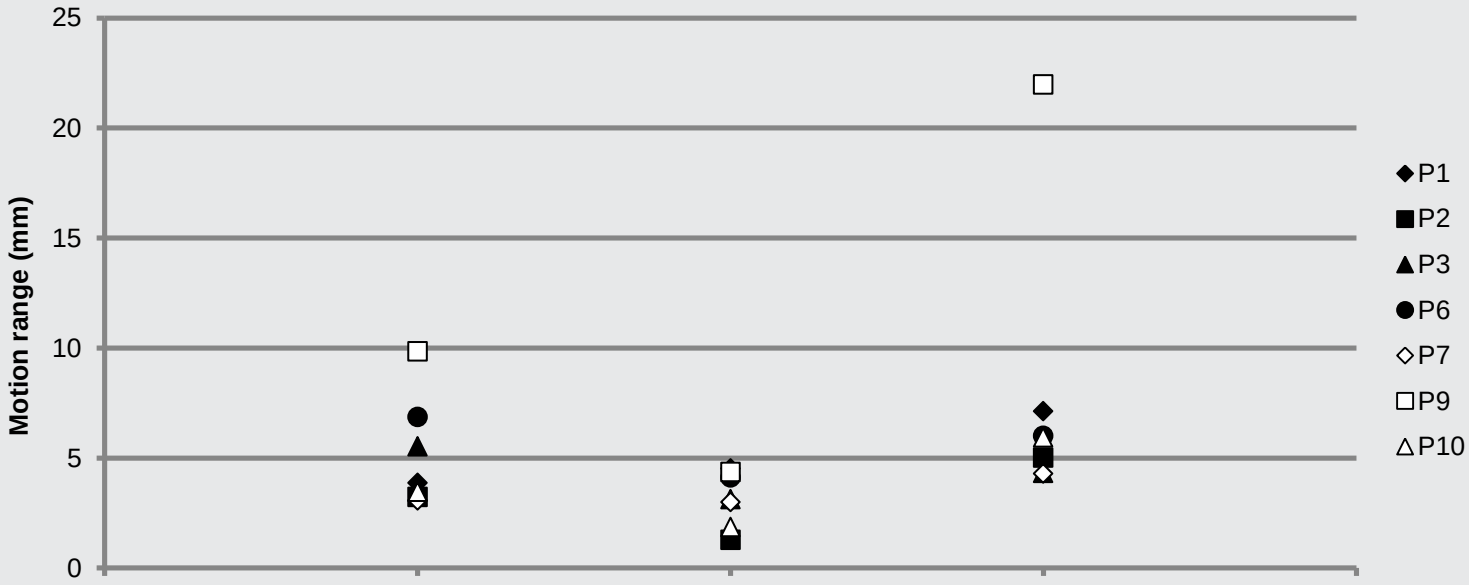
- Liver contoured at inhale/exhale

- MATLAB analysis
  - Comparative motion of whole liver
  - Comparative motion of liver segments



Results: Baseline respiratory motion (without AC)

Whole liver displacement (all patients)

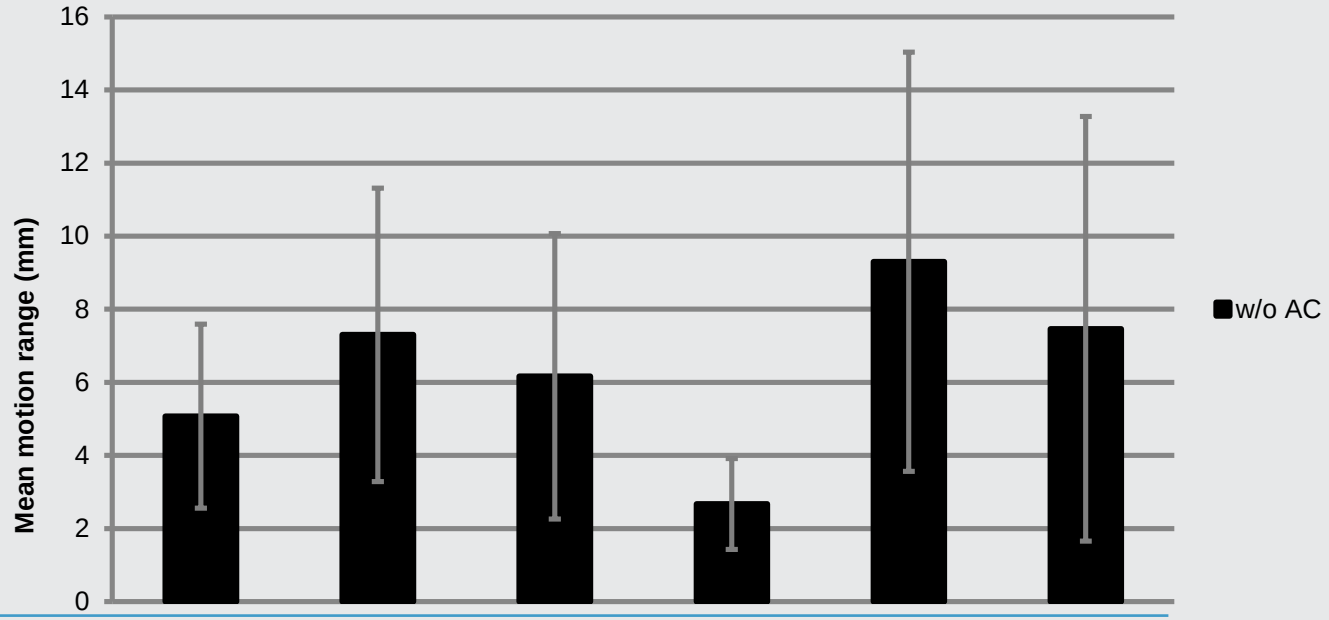


Segment:	Ant/Post	Left/Right	Cran/Caud
Mean	5.12	3.18	7.81
STD	2.51	1.26	6.33

Leong et al. (2013). 4DCT motion analysis of distinct liver regions during respiration with and without abdominal compression. Radiotherapy & Oncology. 106, S63.

Results: Baseline respiratory motion (without AC)

Segmental motion (mean)

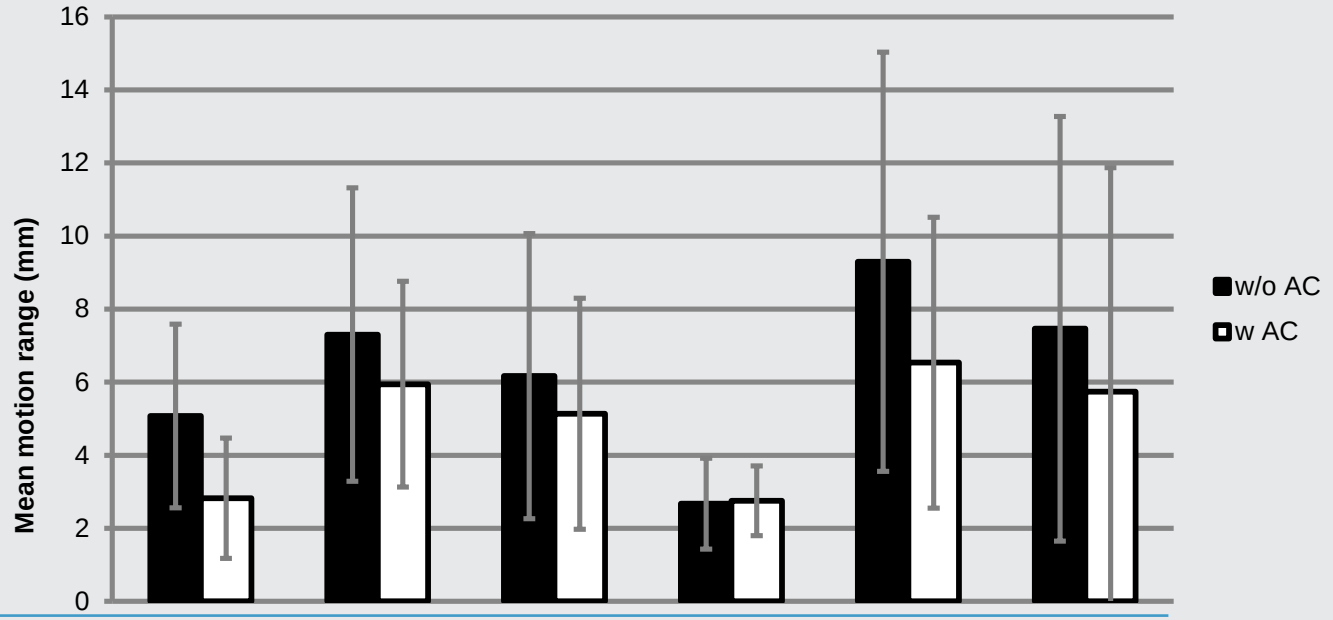


Segment:	Ant	Post	Right	Left	Cran	Caud
Mean	5.07	7.30	6.17	2.67	9.30	7.46
STD	2.52	4.02	3.90	1.24	5.74	5.81

Leong et al. (2013). 4DCT motion analysis of distinct liver regions during respiration with and without abdominal compression. Radiotherapy & Oncology. 106, S63.

Results: Reduction with AC

Segmental motion (mean)



Segment:	Ant	Post	Right	Left	Cran	Caud
Mean reduction	2.25	1.36	1.03	-0.08	2.77	1.72
STD	1.14	2.66	1.68	0.63	2.00	1.21

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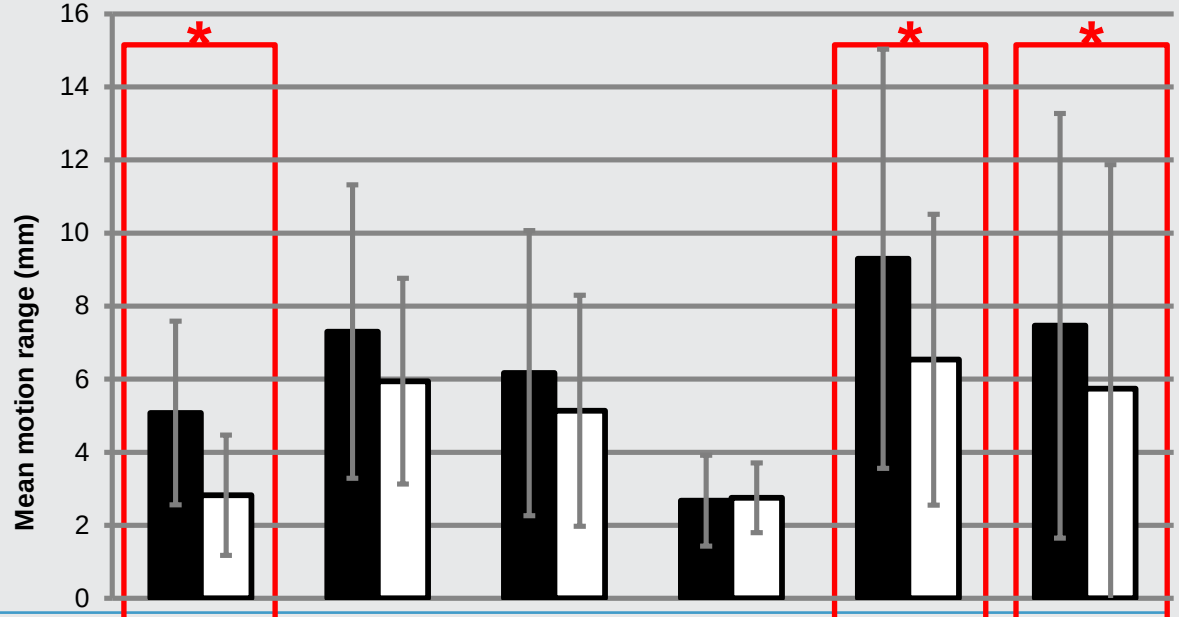

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Mean reduction	2.25	1.36	1.03	-0.08	2.77	1.72
STD	1.14	2.66	1.68	0.63	2.00	1.21

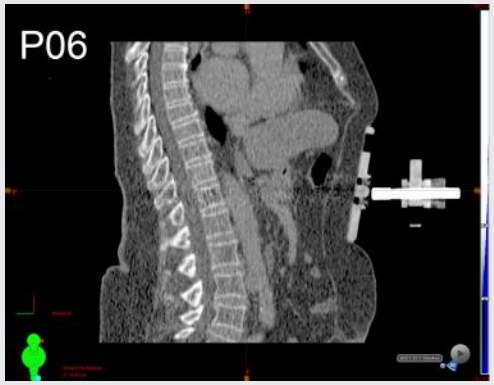
*p<0.05

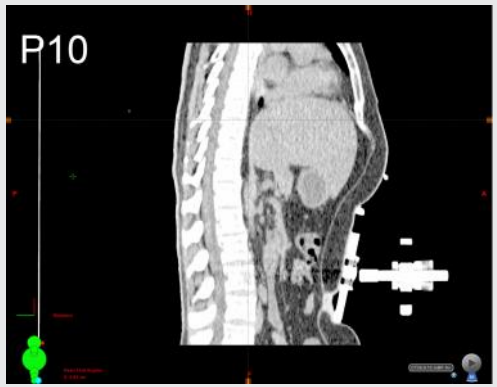
Leong et al. (2013). 4DCT motion analysis of distinct liver regions during respiration with and without abdominal compression. Radiotherapy & Oncology. 106, S63.

Key findings

- Liver segments demonstrate variable respiratory motion (with and without AC)
  - Left segments appear inherently stable
- Cranial, caudal and anterior segments become more stable with AC
- Other segments benefit more variably, or not at all
- Requires validation with treatment data

Inter-patient variation





Alternative immobilisation methods

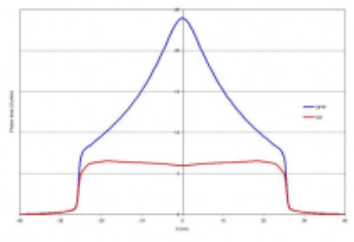
Body fix
www.elekta.com

SBRT: Planning

- Eclipse (v11)
- Standard: 4x12Gy or 3x18Gy (adapted to individual patients)
- VMAT (~2 Arcs)
  - Complete arcs or-
  - Partial arcs (i.e. 30°-180E°) for peripheral lesions
    - Consideration of gantry clearance
- Optimisation/normalisation (adapted from RTOG 0915)
  - 40% inhomogeneity within PTV is allowed (ablative therapy)
    - Dmax ~120-130%
    - Steep dose gradient beyond PTV
  - 95% of PTV receives 100% prescribed dose

SBRT: Planning

- Truebeam STx
- HDMLC (2.5mm)
- Flattening filter free (FFF) mode
  - 10MV FFF: 2400MU/min



- CBCT imaging
- Sub-mm corrections
- Real-time Position Management (RPM)
  - Optical tracking/gating system

SBRT: FFF

Radiotherapy and Oncology 101 (2011) 226–232

Contents lists available at ScienceDirect

Radiotherapy and Oncology

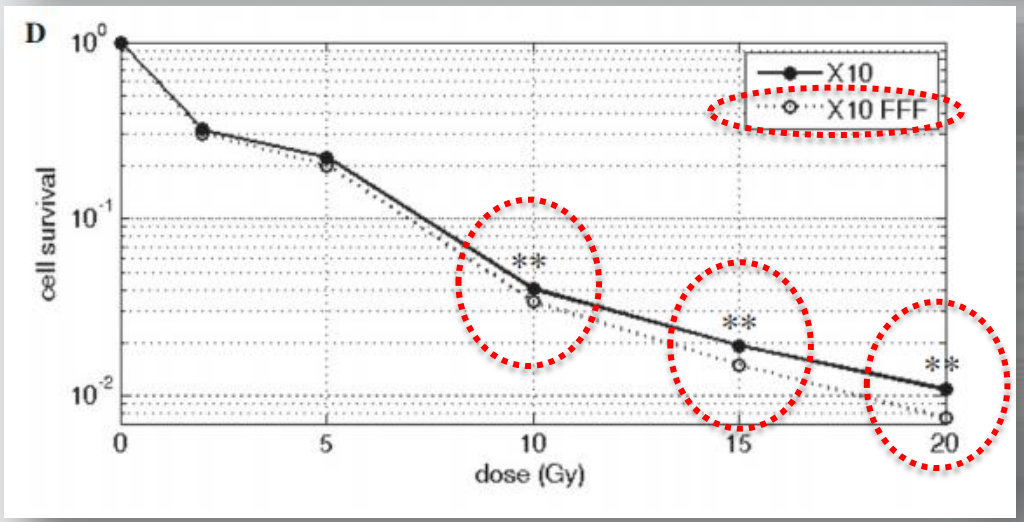
journal homepage: www.thegreenjournal.com

Dose rate

Effect of high dose per pulse flattening filter-free beams on cancer cell survival

Ines Lohse [a], Stephanie Lang [a], Jan Hrbacek [a], Stephan Scheidegger [c], Stephan Bodis [b], Nadia S. Macedo [a], Jianhua Feng [a], Urs M. Lütolf [a], Kathrin Zaugg [a,*]

[a] Department of Radiation Oncology, University Hospital Zürich, Switzerland; [b] Institute of Radiation Oncology, Kantonsspital Aarau, Switzerland; [c] Centre of Applied Mathematics and Physics, Zurich University of Applied Science, Switzerland



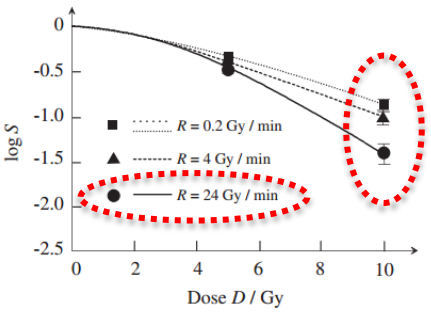


Fig. 4. Surviving fraction of T98G-glioblastoma cells at different dose rates. For 24 Gy/min, the Γ-LQ-model can fit the experimental data with $\alpha = 0.03\ \mathrm{Gy}^{-1}$, $\beta = 0.04\ \mathrm{Gy}^{-2}$ and $\gamma = 0.556\ \mathrm{min}^{-1}$; for 4 Gy/min, γ has to be adapted to $0.361\ \mathrm{min}^{-1}$ and for $R = 0.2$ Gy/min, a good fit can only be achieved by adapting the kinetic constant to $\gamma = 0.0313\ \mathrm{min}^{-1}$.

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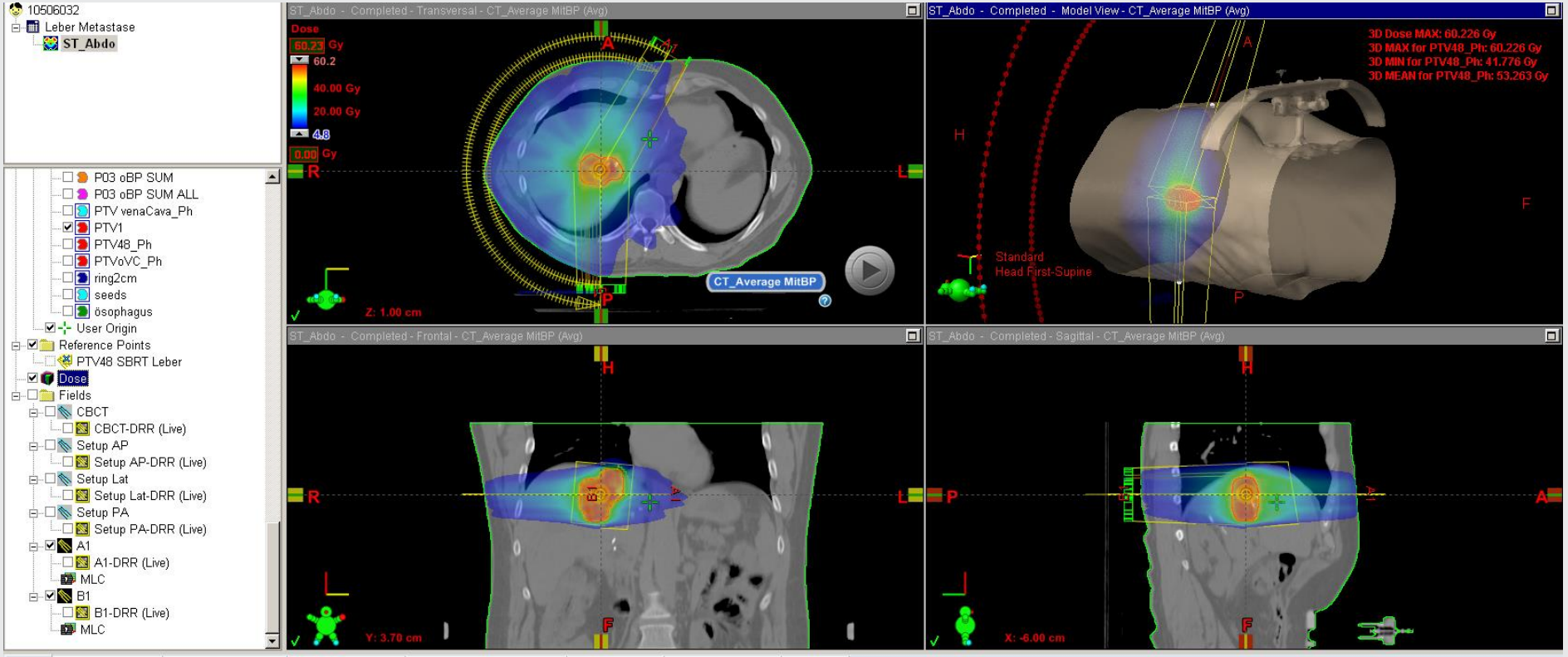
SBRT: Planning

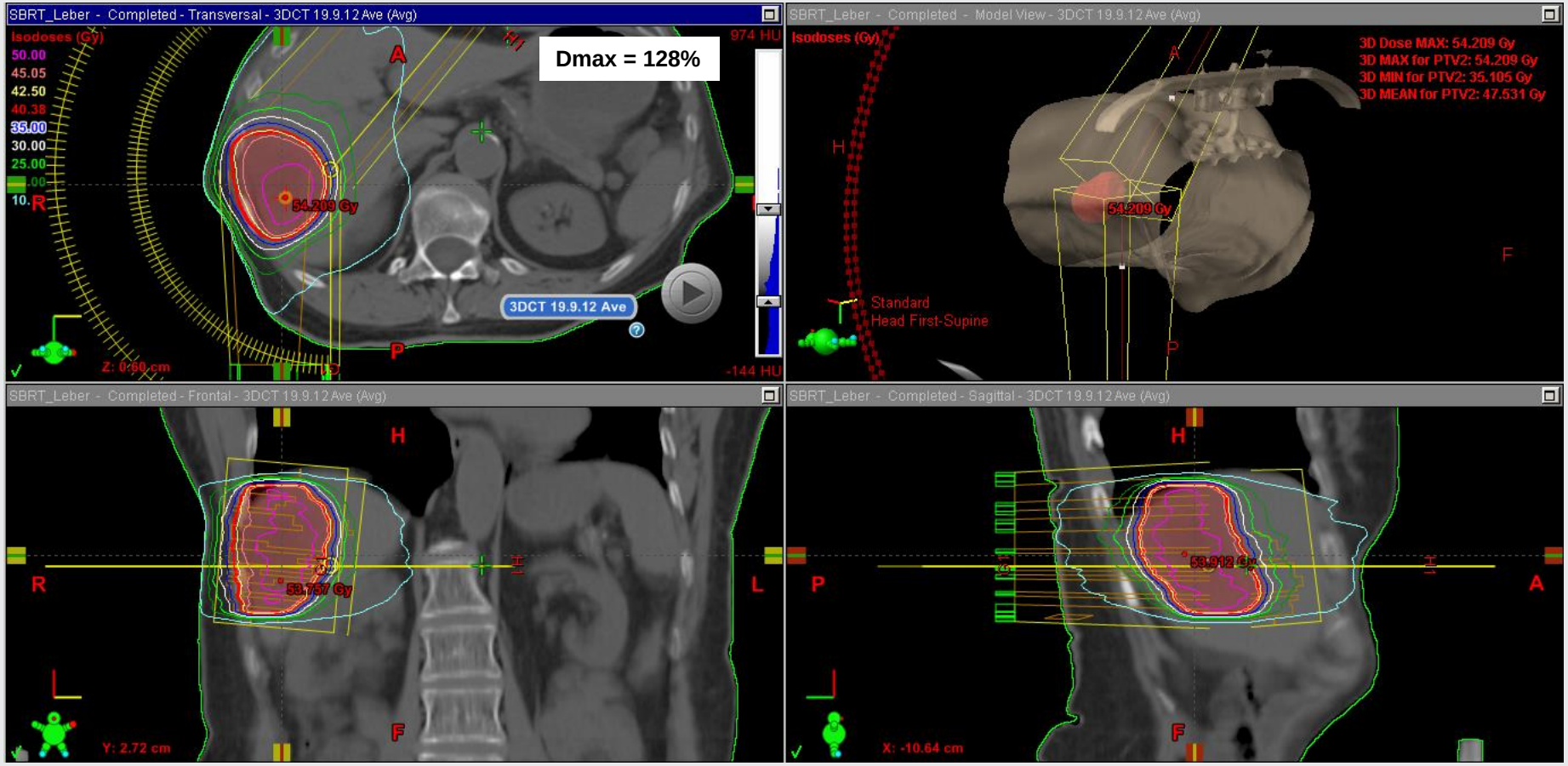


Fields | Dose Prescription | Field Alignments | Plan Objectives | Optimization Objectives | Dose Statistics | Calculation Models | Plan Sum

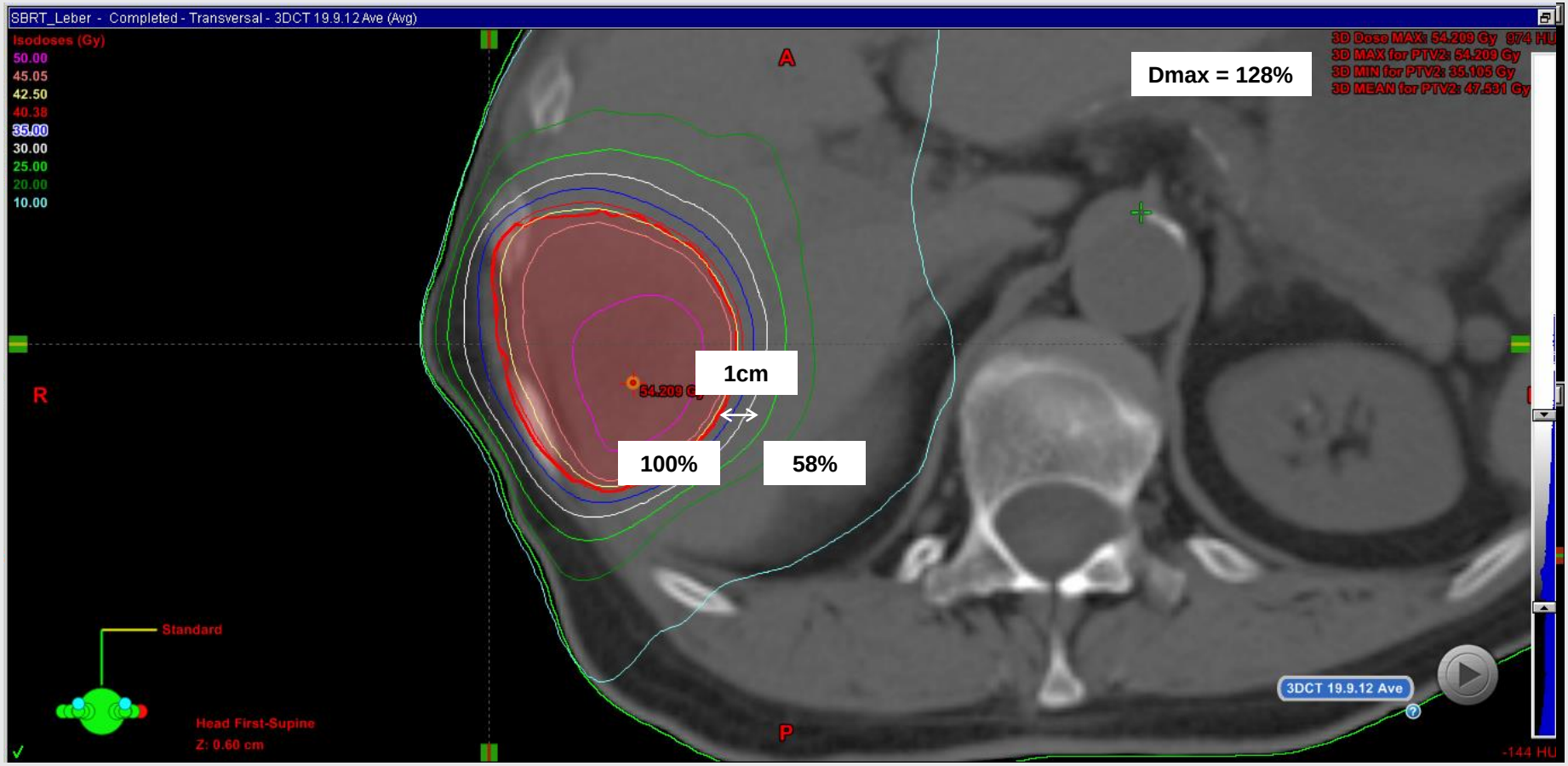
Group	Field ID	Technique	Machine/Energy	MLC	Field Weight	Scale	GantryRtn [deg]	CollRtn [deg]	PatientSupp [deg]	Wedge	CollX [cm]	CollX1 [cm]	CollX2 [cm]	CollY [cm]	CollY1 [cm]	CollY2 [cm]	X [cm]	Y [cm]	Z [cm]	SSD [cm]	MU	Ref. D [Gy]
☑	CBCT	STATIC-I	TrueBeam1001 - 6X		0.000	Varian IEC	0.0	0.0	0.0	None	10.0	+5.0	+5.0	10.0	+5.0	+5.0	-6.00	3.70	1.00	86.8		
☑	Setup AP	STATIC-I	TrueBeam1001 - 6X		0.000	Varian IEC	0.0	0.0	0.0	None	10.4	+2.4	+8.0	7.3	+4.0	+3.3	-6.00	3.70	1.00	86.8		
☑	Setup Lat	STATIC-I	TrueBeam1001 - 6X		0.000	Varian IEC	270.0	0.0	0.0	None	8.1	+5.8	+2.3	8.1	+4.8	+3.3	-6.00	3.70	1.00	86.0		
☑	Setup PA	STATIC-I	TrueBeam1001 - 6X		0.000	Varian IEC	180.0	0.0	0.0	None	11.1	+8.5	+2.6	8.9	+5.4	+3.6	-6.00	3.70	1.00	87.2		
☑	A1	SRS ARC-I	TrueBeam1001 - 10X-FFF	VMAT	1.139	Varian IEC	30.0 CCW 180.1	355.0	0.0	None	6.6	+3.4	+3.2	7.9	+4.0	+3.9	-6.00	3.70	1.00	84.8	1801.8	
☑	B1	SRS ARC-I	TrueBeam1001 - 10X-FFF	VMAT	1.155	Varian IEC	180.1 CW 30.0	95.0	0.0	None	7.4	+3.7	+3.7	7.0	+3.5	+3.5	-6.00	3.70	1.00	87.2	1828.0	

Ready | User: leaid | Group: Erf. MTRA | Site: Main | CAP | NUM | SCRL

SBRT: Planning



SBRT: Planning

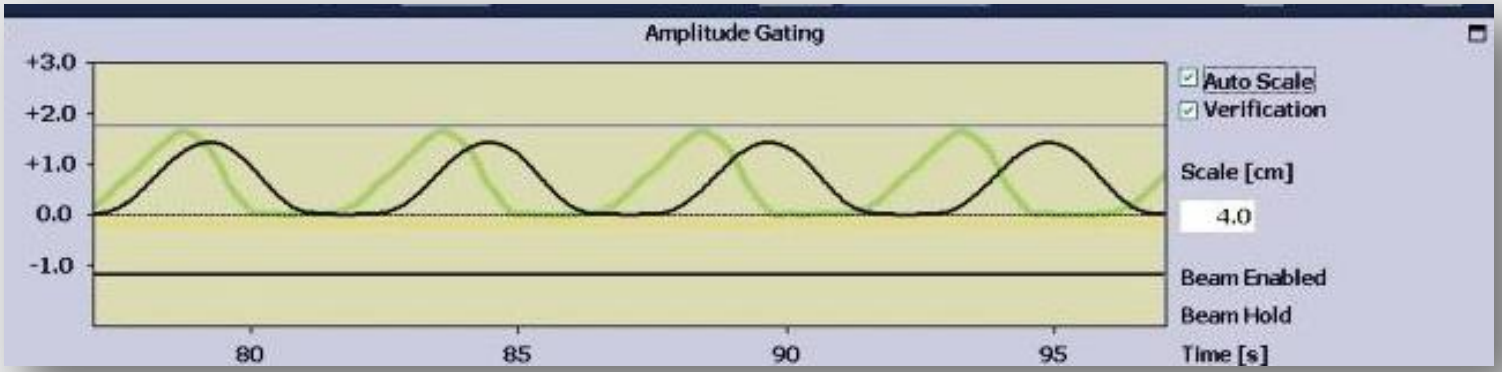


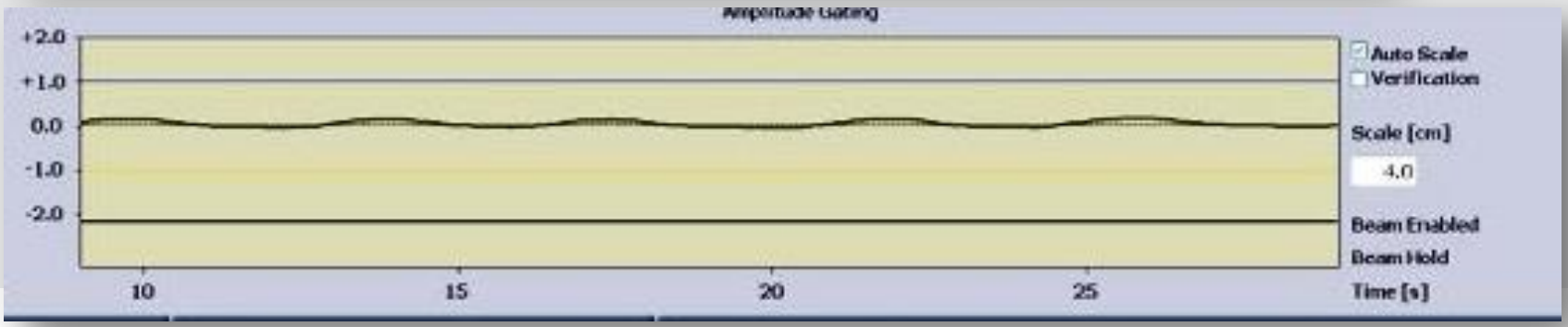
SBRT: Treatment delivery

1. Patient positioning
2. Breathing curve verificiation
3. PreRT-CBCT (consultant present)
   - GTV Match (when visible) + correction
4. Breathing curve verification
5. Treatment delivery + respiratory tracking
6. PostRT-CBCT
   - Repeat match
   - Intrafractional motion assessment

SBRT: Treatment delivery

- Patient set up
  - Check stability/breathing



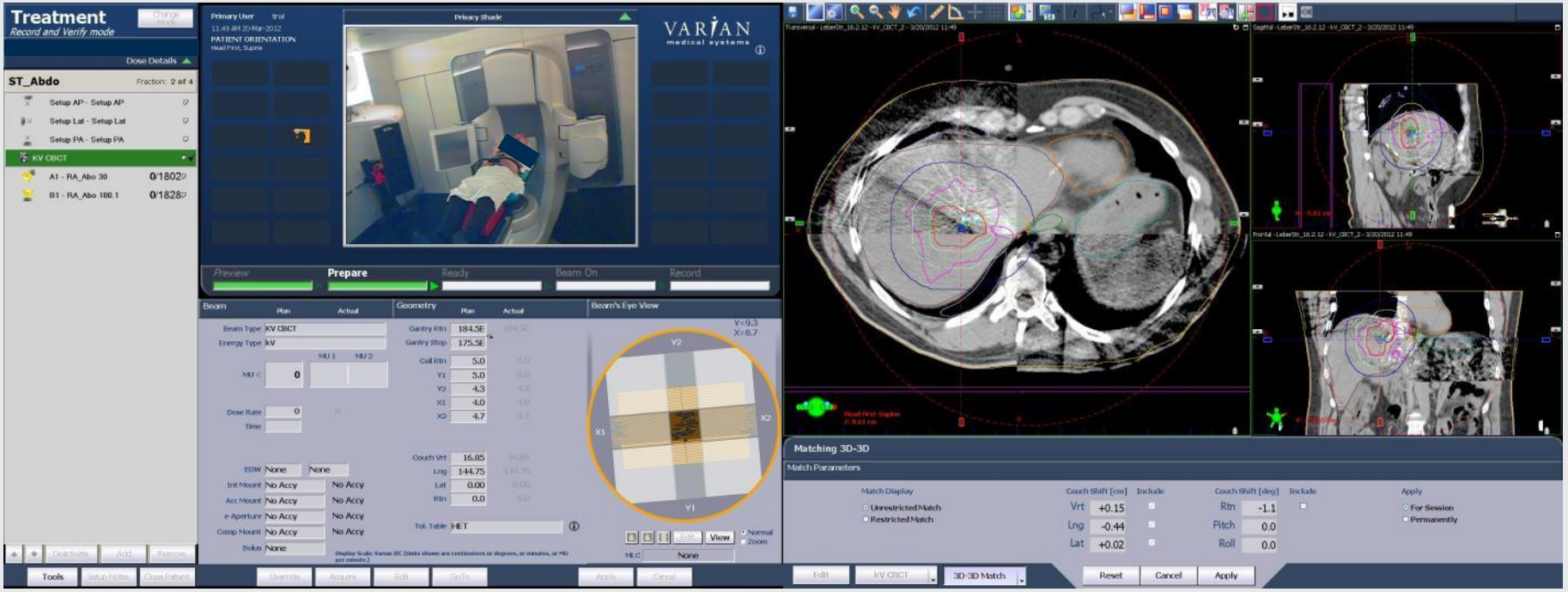


SBRT: Treatment delivery

CBCT

SBRT: Treatment delivery

Matching



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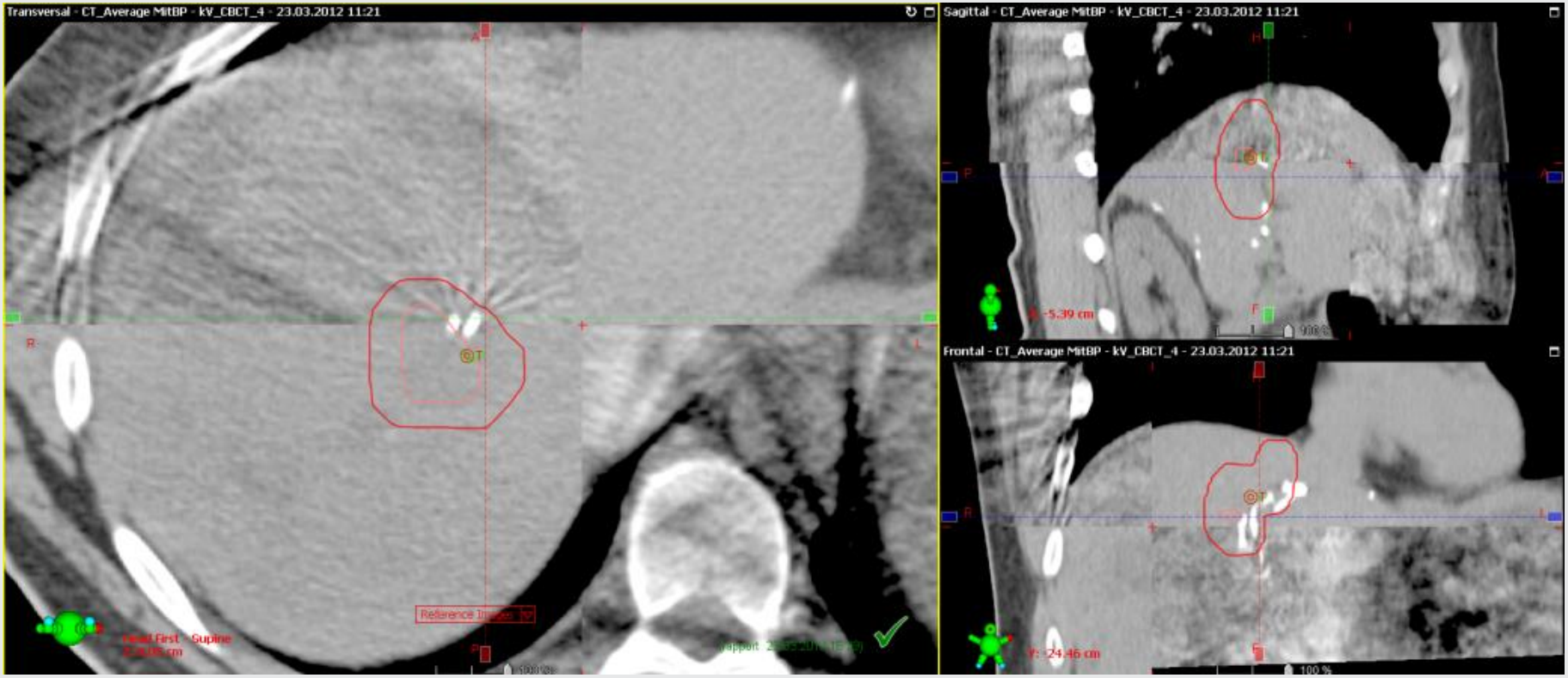
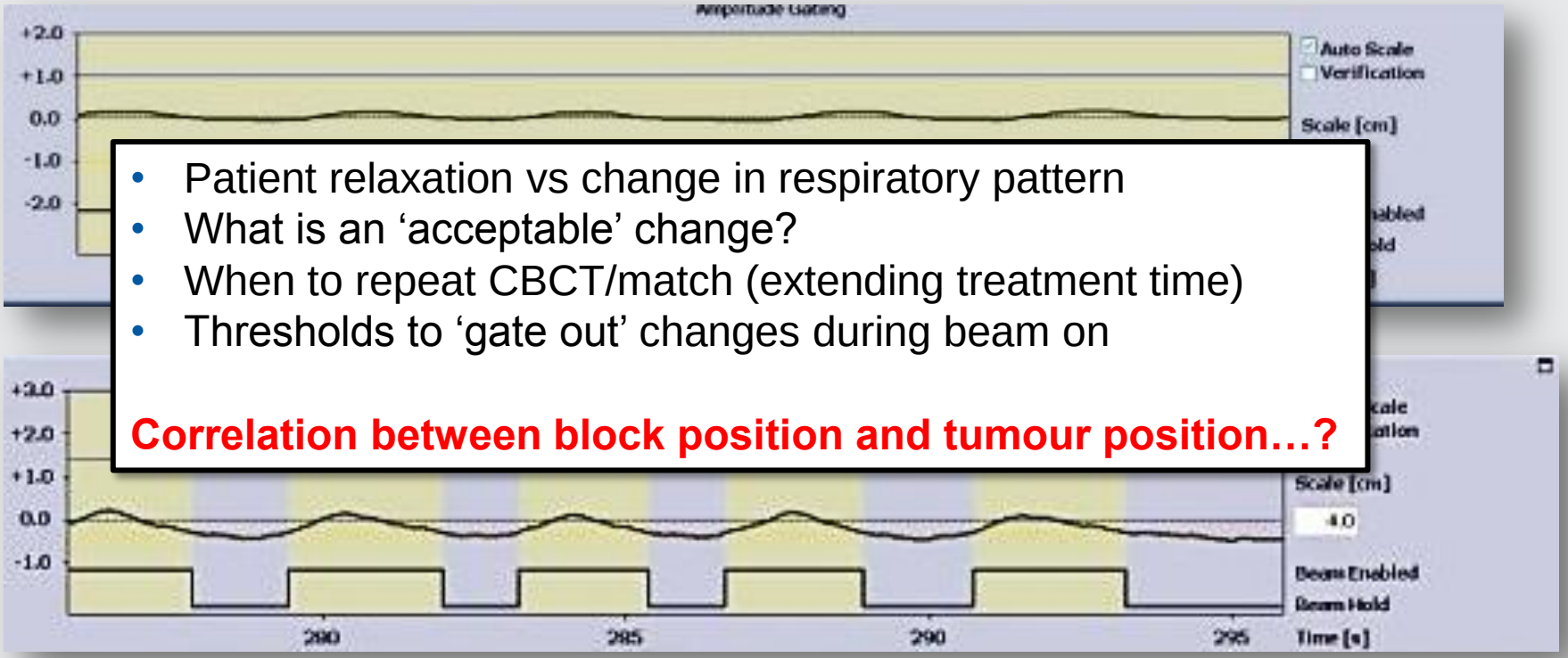


SBRT: Treatment delivery (respiratory tracking)

- After matching...

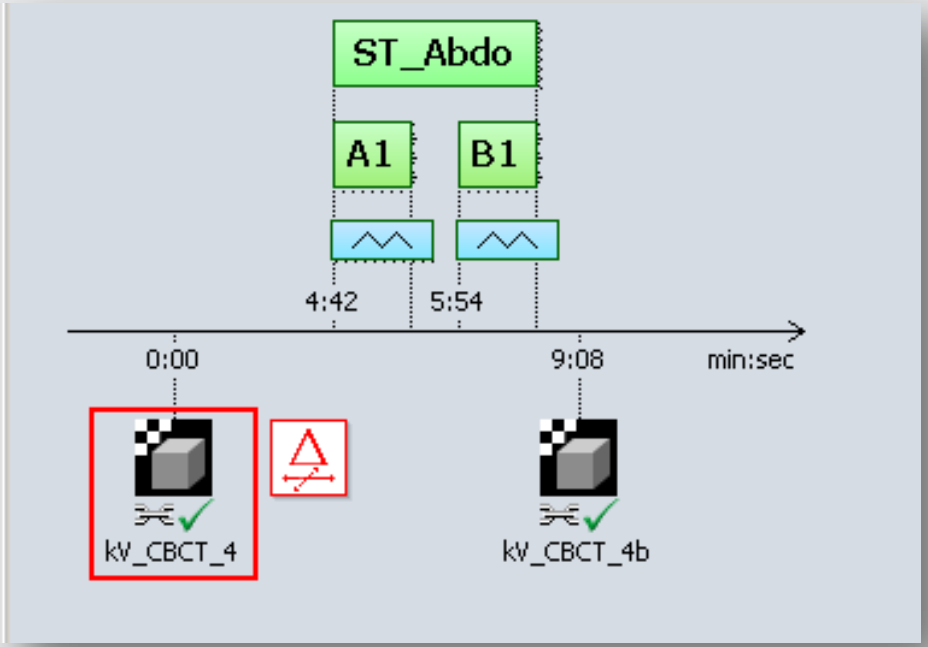


- Patient relaxation vs change in respiratory pattern
- What is an 'acceptable' change?
- When to repeat CBCT/match (extending treatment time)
- Thresholds to 'gate out' changes during beam on

Correlation between block position and tumour position…?

SBRT: Treatment delivery

- 4 x 12Gy
- 2 partial arcs
  - 180.1°-30°
  - A1: 1802MU
  - B1: 1828MU
  - 54 seconds/arc
- Max dose rate: 2400MU/Min
  - 10MV FFF



SBRT: Treatment delivery

Radiotherapy and Oncology 106 (2013) 255–259

Contents lists available at SciVerse ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Stereotactic radiotherapy

Clinical application of flattening filter free beams for extracranial stereotactic radiotherapy

Stephanie Lang, Binaya Shrestha, Shaun Graydon, Frederique Cavelaars, Claudia Linsenmeier, Jan Hrbacek, Stephan Klöck, Gabriela Studer, Oliver Riesterer*

Department of Radiation Oncology, University Hospital Zurich, Switzerland

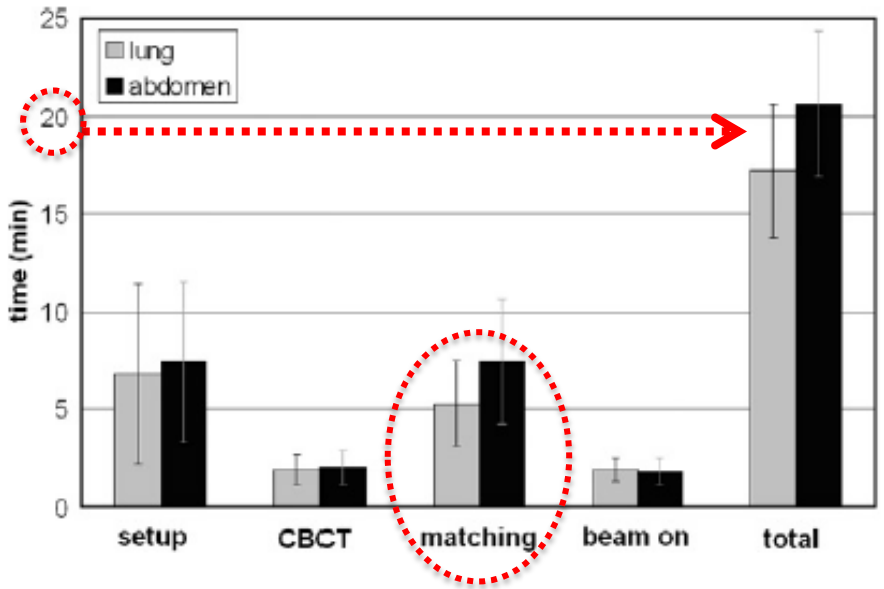


Fig. 1. Total treatment time, separated into patient setup inside the room, CBCT acquisition, matching of the CBCT and actual beam on time.

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SBRT: Treatment delivery

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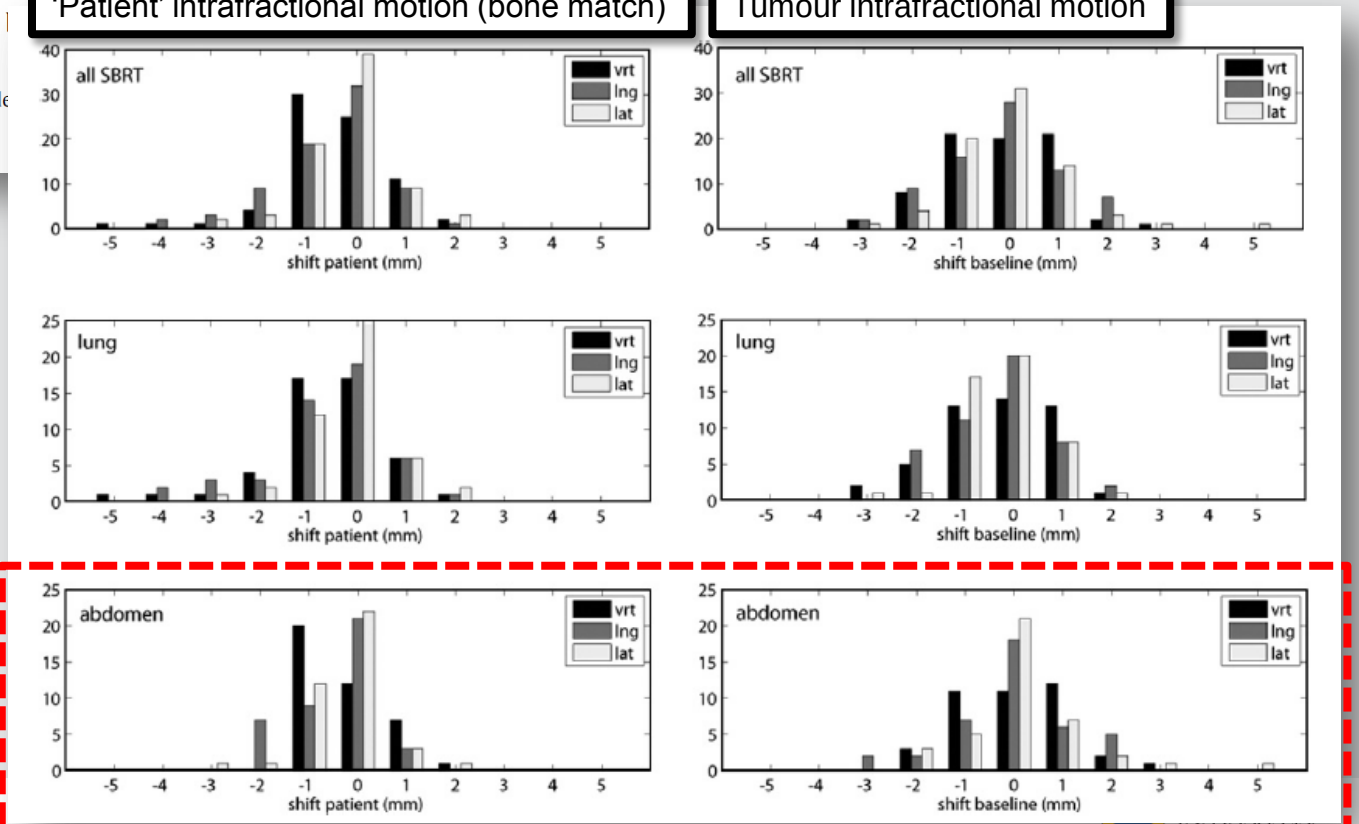
Department of Radiation Oncology, University Hospital Zurich, Switzerland

‘Patient’ intrafractional motion (bone match)

Tumour intrafractional motion



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SBRT: Treatment outcomes

Stieb *et al. Radiation Oncology* (2015) 10:27
DOI 10.1186/s13014-014-0317-0

RADIATION ONCOLOGY

RESEARCH Open Access

Safety of high-dose-rate stereotactic body radiotherapy

Sonja Stieb, Stephanie Lang, Claudia Linsenmeier, Shaun Graydon and Oliver Riesterer*

Table 2 Acute and late lung toxicity in 75 patients with lung lesions

Adverse event	Grade		
	I	II	≥III
Acute toxicity			
Pneumonitis	11%	8%	-
Pleural Effusion	3%	-	-
Atelectasis	8%	-	-
Late toxicity			
Pneumonitis	44%	6%	-
Pleural Effusion	14%	2%	-
Atelectasis	20%	2%	-

If patients were treated at multiple sites, each site was analyzed separately.

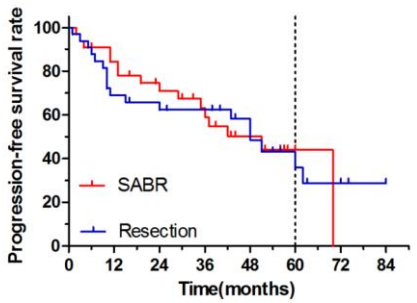
Table 3 Local Control Rate (LCR) 12 months after start of radiotherapy for all lesions and lung lesions

		All (N = 100)		Lung (N = 75)	
LCR – 12 months	All	93.8% (N = 83)		93.5% (N = 61)	
	BED ≤ 100 Gy	90.7% (N = 55)	p = 0.43	89.7% (N = 39)	p = 0.51
	BED > 100 Gy	100% (N = 28)		100% (N = 22)	
	GTV ≤ 14 cm^3	98.1% (N = 58)	p = 0.06	97,9% (N = 51)	p = 0.02
	GTV > 14 cm^3	84.9% (N = 25)		74.1% (N = 10)	
Cox regression	BED	p = 0.36 (0.994)		p = 0.21 (0.986)	
	GTV	p = 0.72 (1.013)		p = 0.16 (0.986)	

p-values indicate significance determined by log-rank test. Cox Regression is shown with p-values and hazard ratio in brackets. (BED: Biologically Effective Dose, GTV: Gross Tumor Volume).

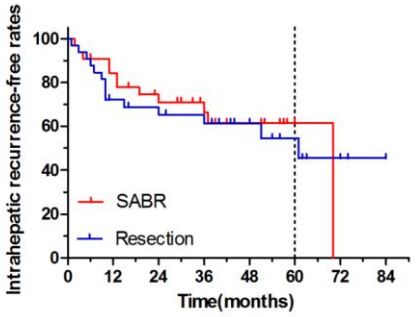
SBRT: Treatment outcomes

Fig 2b



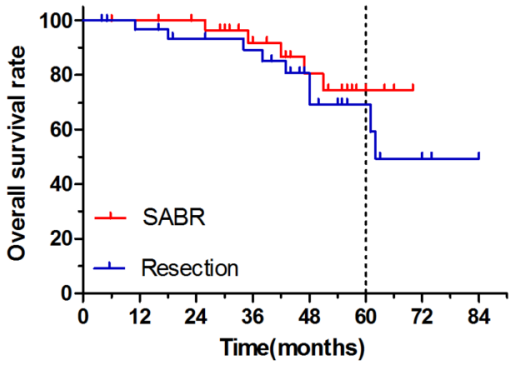
No. at risk	0	12	24	36	48	60	72
SABR	33	26	21	15	8	3	0
Resection	33	19	17	12	6	6	3

Fig 2c



No. at risk	0	12	24	36	48	60	72
SABR	33	26	21	15	8	3	0
Resection	33	19	17	12	6	6	3

Fig 2a



No. at risk	0	12	24	36	48	60	72
SABR	33	31	28	20	14	6	1
Resection	33	30	26	22	14	7	4

Su, T.-S., Liang, P., Liang, J., Lu, H.-Z., Jiang, H.-Y., Cheng, T., Deng, X. (2017). Long-term Survival Analysis of Stereotactic Ablative Radiotherapy Versus Liver Resection for Small Hepatocellular Carcinoma. International Journal of Radiation Oncology*Biology*Physics. http://doi.org/10.1016/j.ijrobp.2017.02.095

Summary

- New treatment possibilities and clinical benefit from modern technology

However…

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- New treatment possibilities and clinical benefit from modern technology

However…

- **Technology is only as good as the application by the user**
- RTs are key in this role:
  - Patient education and positioning at CT
  - Breathing coaching
  - Plan optimisation/evaluation
  - Patient education and positioning at the linac
  - Image matching protocols / intrafractional motion assessment

Thank you.

Acknowledgments:

- Dr Oliver Riesterer
- Prof. Matthias Guckenburger
- Dr Stephanie Lang
- Chris Winter
- Shaun Graydon
- Sarah Verlaan