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Advanced Radiotherapy with Versa HD in clinical routine : Physical and medical aspects

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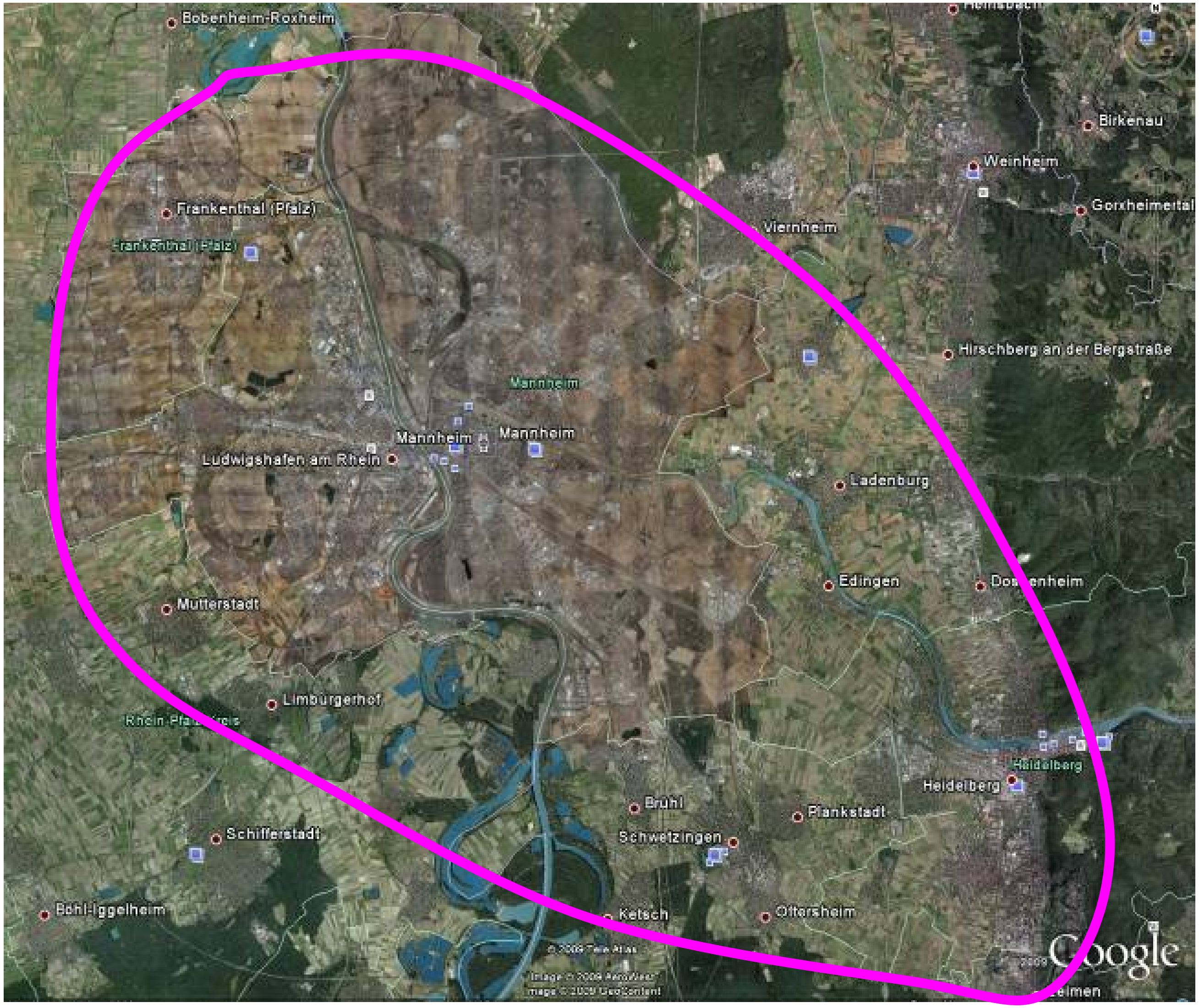
University Medical Center Mannheim, Founded 1701; Employees 4784; Beds 1.400


Mannheim, Germany
Tokyo, Japan



Mannheim clinic	6	Linacs
Heidelberg clinic / DKFZ	9	Linacs
Ludwigshafen	2	Linacs
In a area of 25 km	17	Linacs

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Clinic statistics

Staff

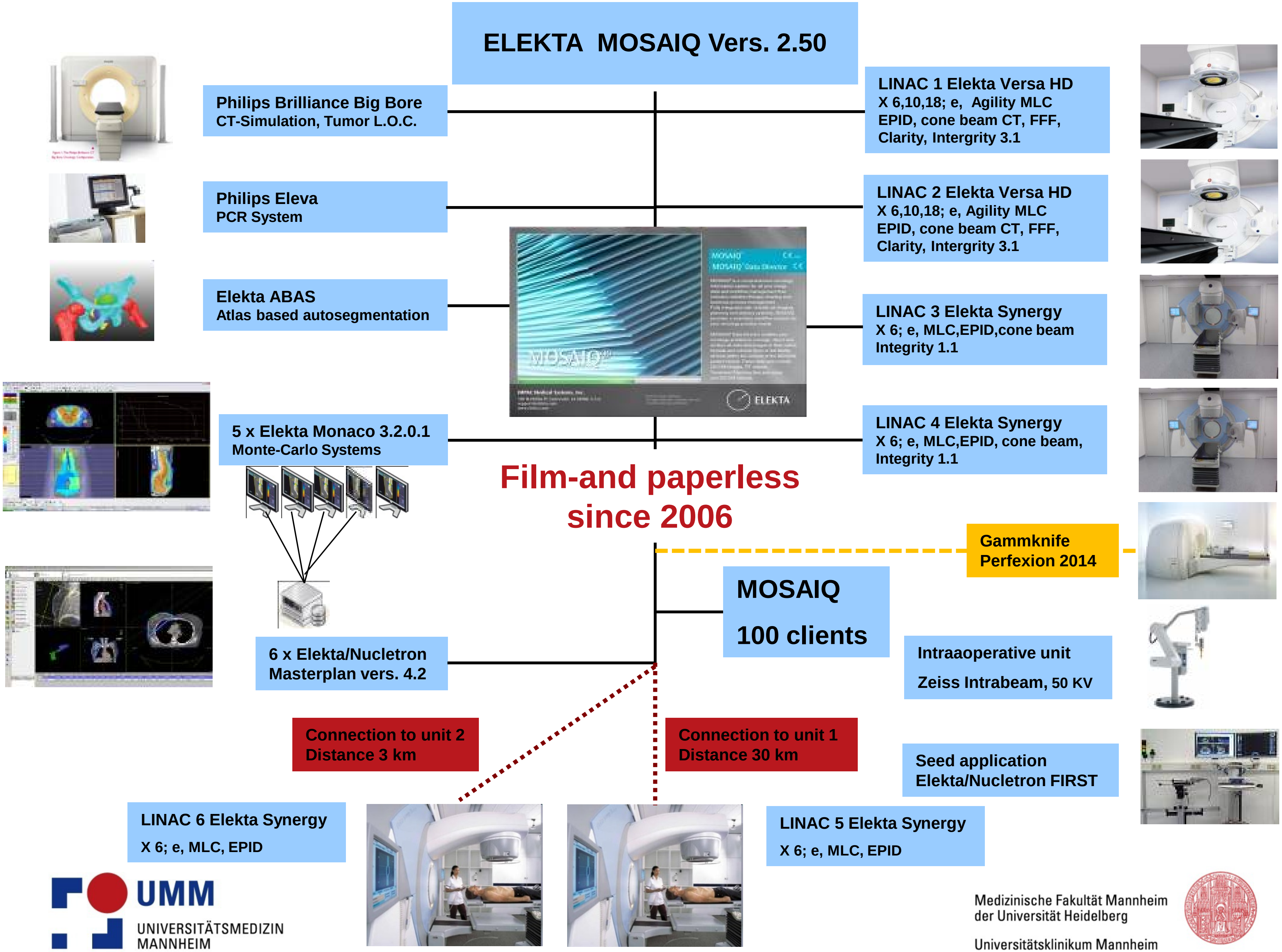
22	MD´s (attending + residents)
12	Full licensed physicist
6	PhD-students
17	Radiographers
35	Researchers at two professorships
	International Master course medical physics

Treatment

2300 patients per year, ~1500 IMRT / VMAT Series per year, trend ⬆

~100 kV cone beam CT´s per day ~30 MV EPIDS per day

Film- and paperless since 2006


ELEKTA MOSAIQ Vers. 2.50
Philips Brilliance Big Bore
CT-Simulation, Tumor L.O.C.
Philips Eleva
PCR System
Elekta ABAS
Atlas based autosegmentation
5 x Elekta Monaco 3.2.0.1
Monte-Carlo Systems
6 x Elekta/Nucletron
Masterplan vers. 4.2
LINAC 1 Elekta Versa HD
X 6,10,18; e, Agility MLC
EPID, cone beam CT, FFF,
Clarity, Intergrity 3.1
LINAC 2 Elekta Versa HD
X 6,10,18; e, Agility MLC
EPID, cone beam CT, FFF,
Clarity, Intergrity 3.1
LINAC 3 Elekta Synergy
X 6; e, MLC,EPID,cone beam
Integrity 1.1
LINAC 4 Elekta Synergy
X 6; e, MLC,EPID, cone beam,
Integrity 1.1
Film-and paperless
since 2006
Gammknife
Perfexion 2014
MOSAIQ
100 clients
Intraaoperative unit
Zeiss Intrabeam, 50 KV
Seed application
Elekta/Nucletron FIRST
Connection to unit 2
Distance 3 km
Connection to unit 1
Distance 30 km
LINAC 6 Elekta Synergy
X 6; e, MLC, EPID
LINAC 5 Elekta Synergy
X 6; e, MLC, EPID
MOSAIQ
ELEKTA
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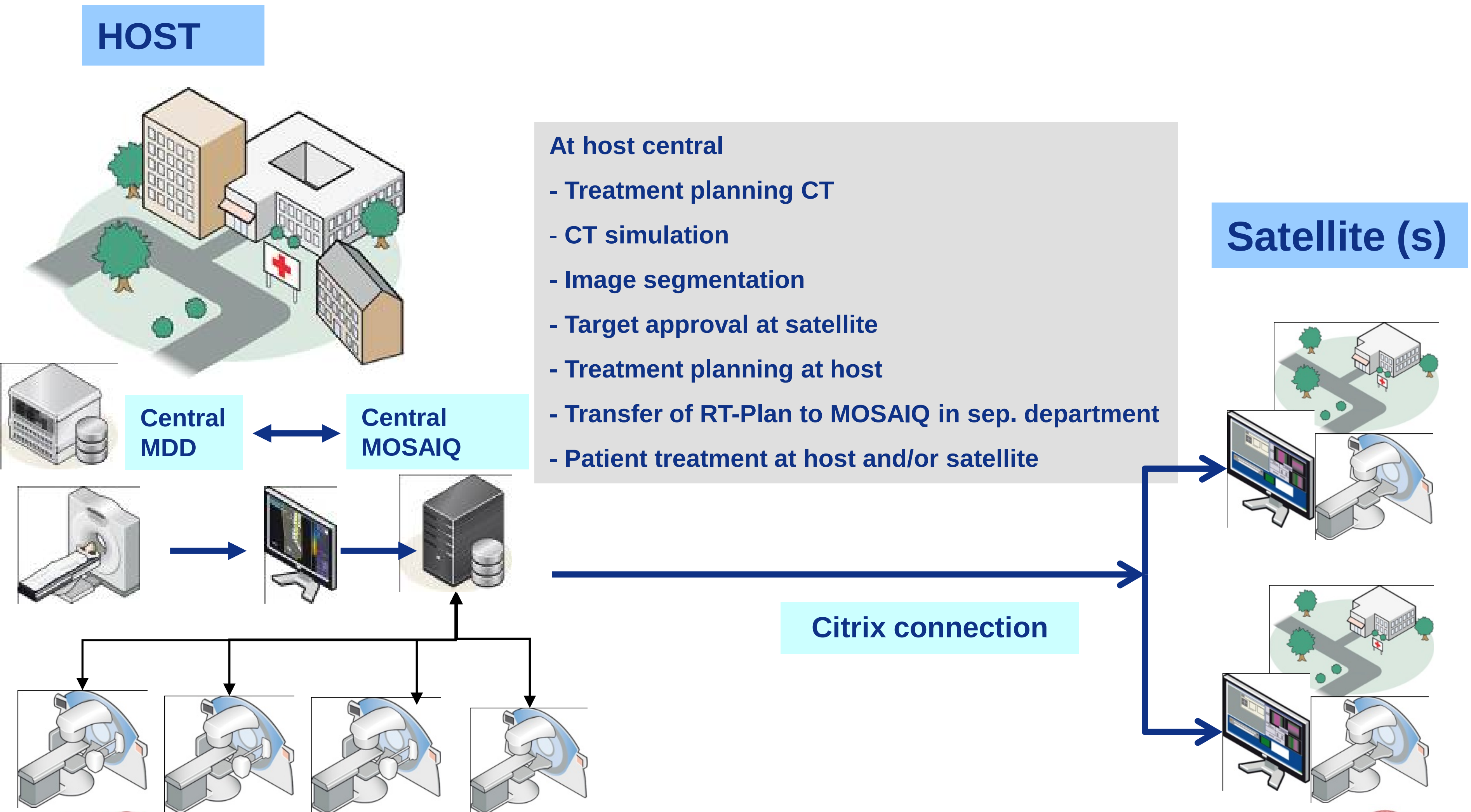
Satellite concept



Clinic backbone Mosaiq/Mosaiq Data Director

Principles being film- and paperless since 2006

- Paperless with MOSAIQ as an Electronic Medical Record (EMR) and
- Filmless with Mosaiq Data Director (MDD)

Paperless regarding information in the EMR

- What is not in Mosaiq does not exist anywhere else in the department
- Central access to these data

Filmless regarding the information in the Dicom-Archive

- All image information should be readable independent from the original application (e.g. treatment planning system)

Efficient data management : Consequences for the archive

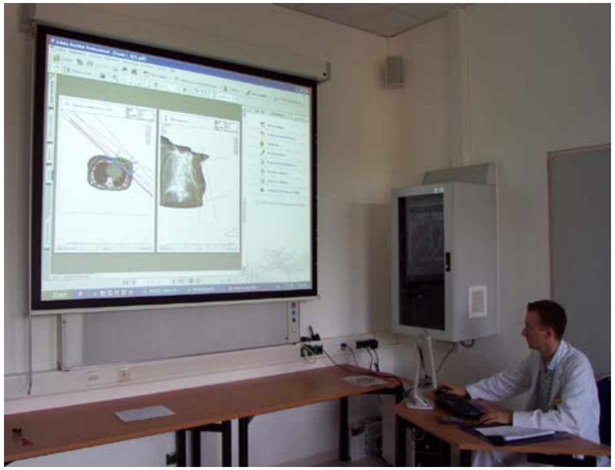
Before

After

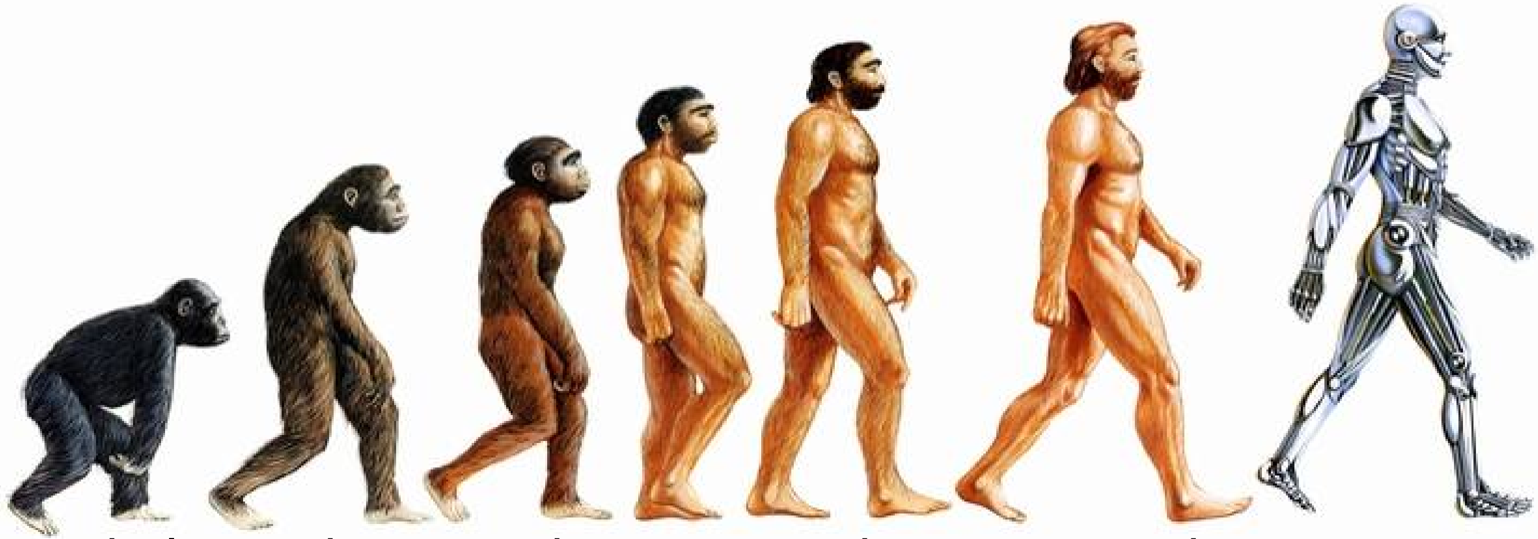
EMR-> electronic morning conference

8:20
Preparation of morning conference by a resident

8:30 – 9:00
Morning conference



The evolution of radiotherapy – the next generation



- Cobalt

- Linac

- Linac
- MLC
- IMRT

- Desktop
- MLC
- IMRT
- IGRT
- Monaco 1.0

- Integrity 1.1
- MLCi2
- IMRT
- IGRT
- VMAT
- Monaco 2.04

- Integrity 3.1
- IGRT
  - XVI 5.0
  - Clarity
  - ABC 2
- VMAT/ dMLC
- Monaco 3.3
- Mosaiq 2.5
- Versa HD

Treatment chain

- **Philips Brillinace CT** Big Bore – 16 stripe
- **Monaco 3.3** to use the full capability of the moving leaf banks
- **Mosaiq 2.5** to deliver FFF
- **Integrity 3.1** to deliver FFF beams

- **Agility MLC** to get high leaf speeds
- **DMLC/ VMAT** to be fast and conformal
- **FFF** to achieve high dose rates

- **IGRT (XVI,Symmetry/Clarity)** to position accurately
- **Patient immobilization (ABC)**
- A fast and reliable **QA** method

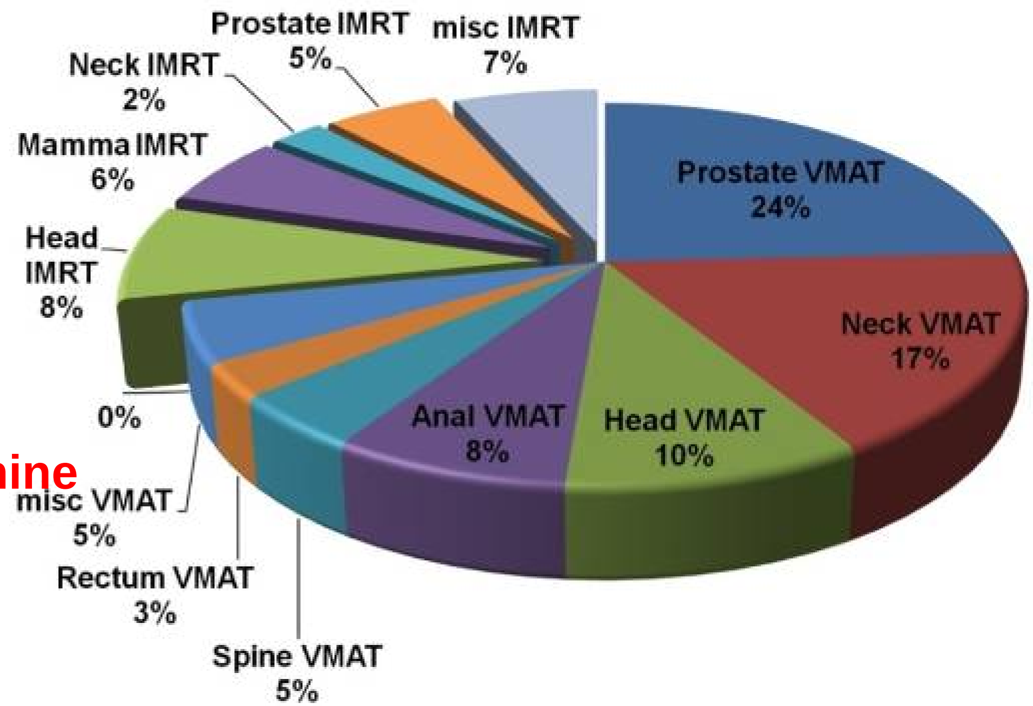
Where are we clinically?

About 80% of all treatments are intensity modulated techniques

- Monaco VMAT since 2010 (versions 1.0.2, 2.0.3, 2.0.4, 3.0, 3.2, 3.3)
- Average number of IMRT/ VMAT treatment plans per week: 40

Equipment Mannheim:

- 2 Elekta Versa HD with Agility MLC, FFF, IGRT
- 2 Elekta Synergy with MLCi 2, IGRT



Calculated slot times per machine

LB1	**14,7 min**
LB2	**15,5 min**
LB3	**14,6 min**
LB4	**15,1 min**

One clinical hour at a Linac

Elekta Synergy Platform + Desktop 7 + MLCi 2

Action	Patient	Time	Description	MU's	Fx Dose	Treatment Time	Total
finish treatment	Patient A	8:08					
finish IGRT	Patient B	8:20	2x MV Images (IView)	4.0 MU			
finish treatment	Patient B	8:29	6X StepNShoot 100CPs	401.4 MU	1.8 Gy	~9 min	
finish treatment	Patient C	8:38	6X StepNShoot 68CPs	637.7 MU	2.0 Gy	~7 min	~34 min
finish treatment	Patient D	8:46	6X StepNShoot 46CPs	531.3 MU	2.0 Gy	~7 min	
finish IGRT	Patient E	8:52	1x MV Images (IView)	2.0 MU			
finish treatment	Patient E	9:03	6X StepNShoot 150CPs	721.0 MU	2.0 Gy	~11 min	

Elekta Synergy + Integrity 1.1 + MLCi 2

Action	Patient	Time	Description	MU's	Fx Dose	Treatment Time	Total
finish treatment	Patient A	11:22					
finish IGRT	Patient B	11:35	cone beam CT (XVI)				
finish treatment	Patient B	11:43	6X StepNShoot 82CPs	614.6 MU	1.8 Gy	~8 min	
finish IGRT	Patient C	11:51	cone beam CT (XVI)				
finish treatment	Patient C	11:56	6X VMAT 205CPs	670.5 MU	2.0 Gy	~5 min	~26 min
finish IGRT	Patient D	12:06	cone beam CT (XVI)				
finish treatment	Patient D	12:13	6X VMAT 181CPs	1357.0 MU	2.0 Gy	~7 min	
finish IGRT	Patient E	12:22	cone beam CT (XVI)				
finish treatment	Patient E	12:26	6X VMAT 191CPs	479.7 MU	1.8 Gy	~6 min	

Elekta Synergy + Integrity 1.1 + MLCi 2

Action	Patient	Time	Description	MU's	Fx Dose	Treatment Time	Total
finish treatment	Patient A	11:22					
finish IGRT	Patient B	11:35	cone beam CT (XVI)				
finish treatment	Patient B	11:43	6X StepNShoot 82CPs	614.6 MU	1.8 Gy	~8 min	
finish IGRT	Patient C	11:51	cone beam CT (XVI)				
finish treatment	Patient C	11:56	6X VMAT 205CPs	670.5 MU	2.0 Gy	~5 min	~26 min
finish IGRT	Patient D	12:06	cone beam CT (XVI)				
finish treatment	Patient D	12:13	6X VMAT 181CPs	1357.0 MU	2.0 Gy	~7 min	
finish IGRT	Patient E	12:22	cone beam CT (XVI)				
finish treatment	Patient E	12:26	6X VMAT 191CPs	479.7 MU	1.8 Gy	~6 min	

Versa HD + Integrity 3.1 + Agility

Action	Patient	Time	Description	MU's	Fx Dose	Treatment Time	Total
finish treatment	Patient A	10:15					
finish treatment	Patient B	10:22	10X VMAT 206CPs	424.8 MU	1.8 Gy	~4 min	
finish IGRT	Patient C	10:30	cone beam CT (XVI)				
finish IGRT	Patient C	10:32	2x MV Images (IView)	4.0 MU			
finish treatment	Patient C	10:37	10X VMAT 128CPs	491.2 MU	1.8 Gy	~5 min	
finish IGRT	Patient D	10:45	cone beam CT (XVI)				~28 min
finish treatment	Patient D	10:48	10X VMAT 189CPs	826.8 MU	2.0 Gy	~7 min	
finish IGRT	Patient E	10:55	cone beam CT (XVI)				
finish treatment	Patient E	11:00	10X DMLC 96CPs	670.2 MU	2.0 Gy	~5 min	
finish IGRT	Patient F	11:09	cone beam CT (XVI)				
finish treatment	Patient F	11:16	6X DMLC 165CPs	597.2 MU	2.0 Gy	~7 min	

Versa HD + Integrity 3.1 + Agility

Action	Patient	Time	Description	MU's		Fx Dose	Treatment Time	Total
finish treatment	Patient A	10:15						~28 min
finish treatment	Patient B	10:22	10X VMAT 206CPs	424.8	MU	1.8 Gy	~4 min	
finish IGRT	Patient C	10:30	cone beam CT (XVI)					
finish IGRT	Patient C	10:32	2x MV Images (IView)	4.0	MU			
finish treatment	Patient C	10:37	10X VMAT 128CPs	491.2	MU	1.8 Gy	~5 min	
finish IGRT	Patient D	10:45	cone beam CT (XVI)					
finish treatment	Patient D	10:48	10X VMAT 189CPs	826.8	MU	2.0 Gy	~7 min	
finish IGRT	Patient E	10:55	cone beam CT (XVI)					
finish treatment	Patient E	11:00	10X DMLC 96CPs	670.2	MU	2.0 Gy	~5 min	
finish IGRT	Patient F	11:09	cone beam CT (XVI)					
finish treatment	Patient F	11:16	6X DMLC 165CPs	597.2	MU	2.0 Gy	~7 min	

Versa HD + Integrity 3.1 + Agility + FFF

Action	Patient	Time	Description	MU's		Fx Dose	Treatment Time	Total
finish treatment	Patient A	12:18						~29 min
finish IGRT	Patient B	12:25	cone beam CT (XVI)					
finish treatment	Patient B	12:33	10X FFF DMLC 40CPs ABC	2,260.1	MU	12.0 Gy	~8 min	
finish IGRT	Patient C	12:42	cone beam CT (XVI)					
finish treatment	Patient C	12:51	6X FFF DMLC 37CPs	757.6	MU	5.0 Gy	~9 min	
finish IGRT	Patient D	13:04	cone beam CT (XVI)					
finish treatment	Patient D	13:07	10X VMAT 219CPs	644.6	MU	2.0 Gy	~3 min	
finish IGRT	Patient E	13:17	cone beam CT (XVI)					
finish IGRT	Patient E	13:19	2x MV Images (IView)	4.0	MU			
finish treatment	Patient E	13:28	6X DMLC 149CPs	584.4	MU	1.8 Gy	~9 min	

Current status Versa HD in Mannheim

- Nov. 2012: machine commissioning finished, validation report received
- Mar. 13th: first patient treated with FFF
- Jul. 22-26: matching second Versa HD
- Until Oct. 2013 : 60 patients treated with FFF
- Hypo-fractionated (> 5 Gy/fx) treatments performed:
  - Brain metastases,
  - Lung,
  - Liver,
  - Adrenal glands

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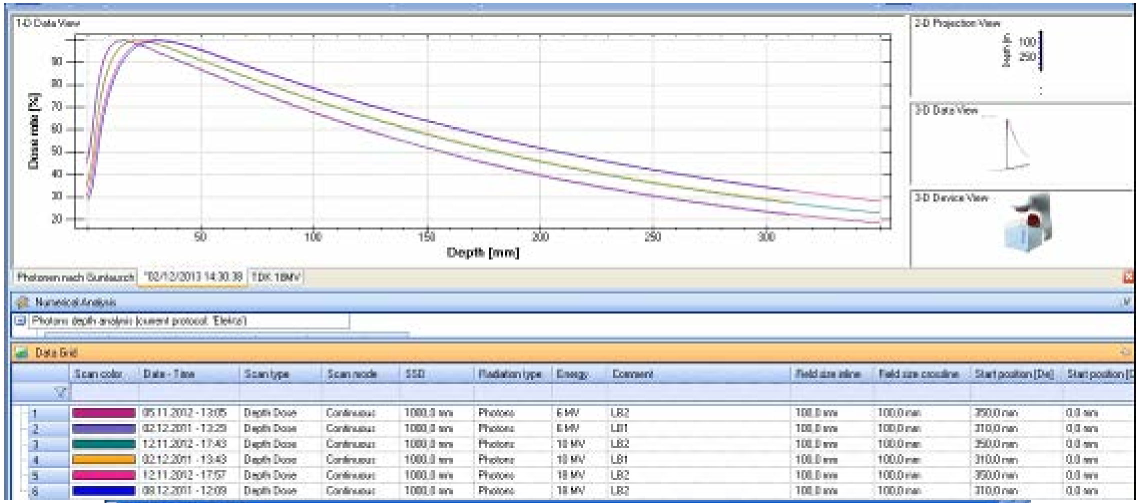
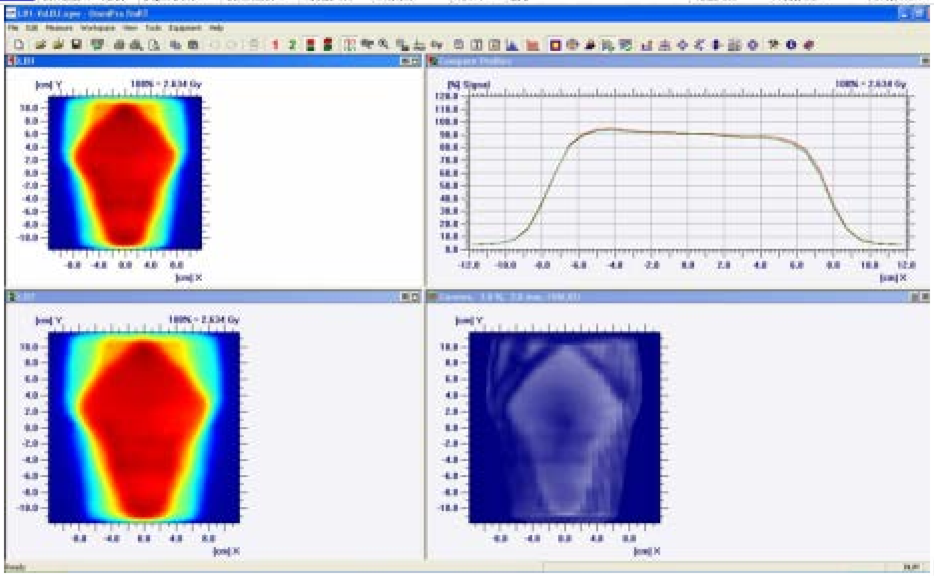
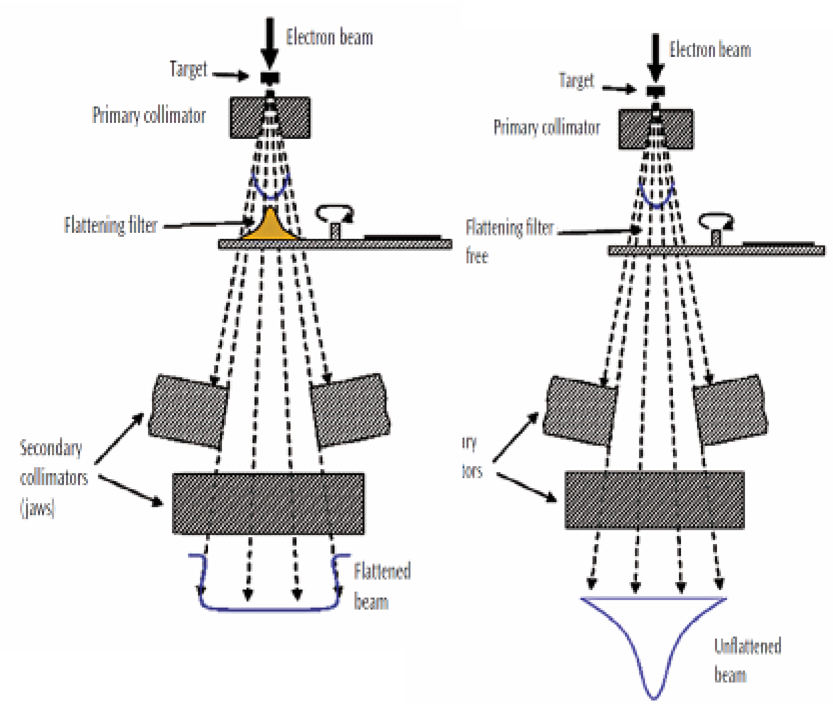
UMM Versa HD twins
LINAC1 vers. LINAC2





Versa HD FFF beam

Flattening filter free (FFF) mode

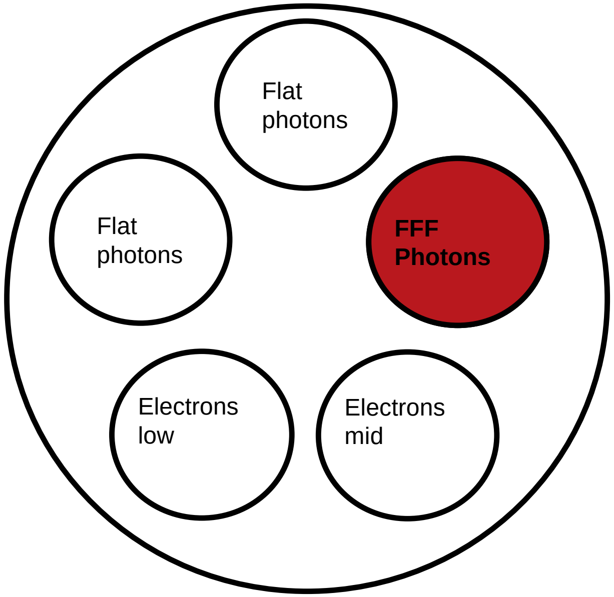


*By courtesy of, Elekta Crawley

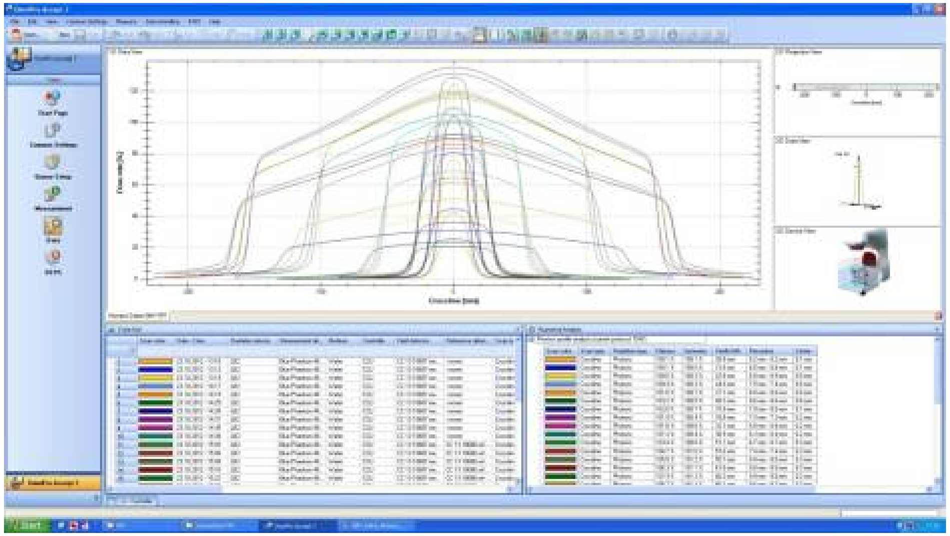
- FFF increases the dose rate for 6MV ~16 Gy/min, 10 MV ~22 Gy/min
- FFF beams have less variation of off-axis beam hardening
- FFF has less photon head scatter
- FFF has less leakage outside of beam collimation

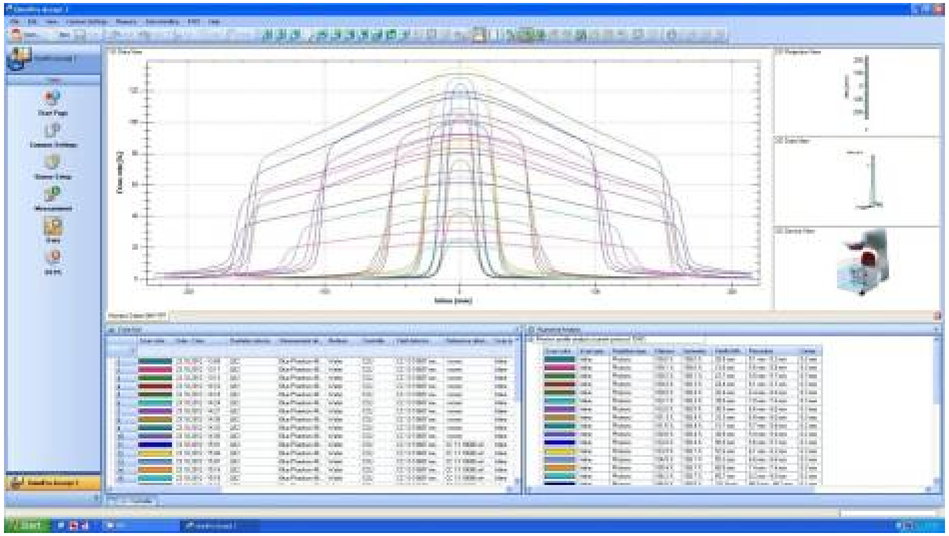
FFF machine setup

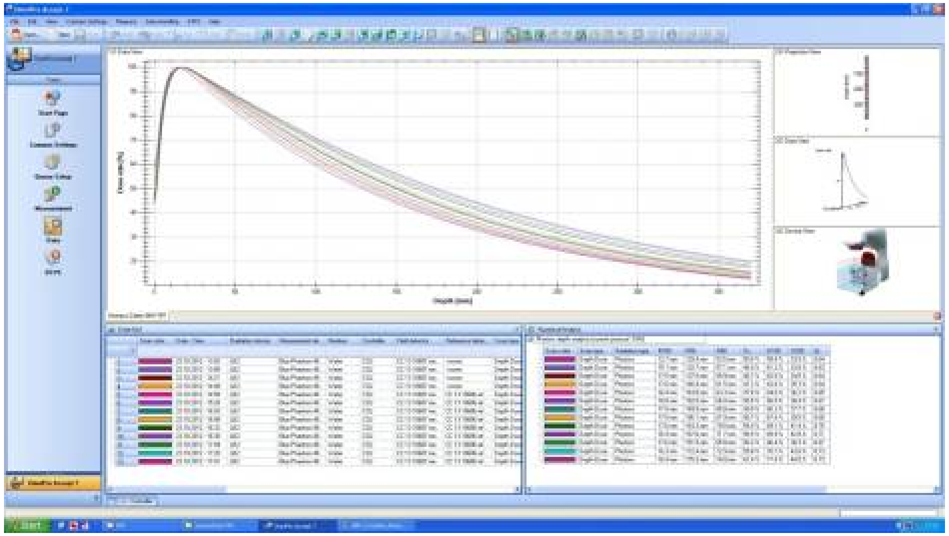
Photonen (MV)	FF	FFF
X06	√	√
X10	√	√
X18	√	ø
Elektronen (MeV)		
Low 04,06,08	√	√
Mid 10,12,15	√	√
High 18,20,22	ø	ø



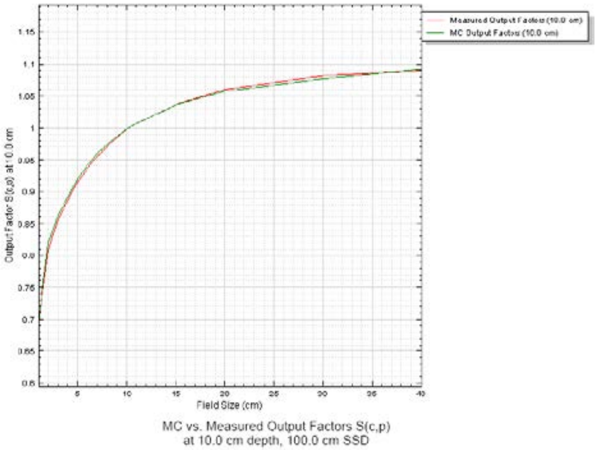
FFF – Basic data for Monaco 3.3, e.g.6 MV

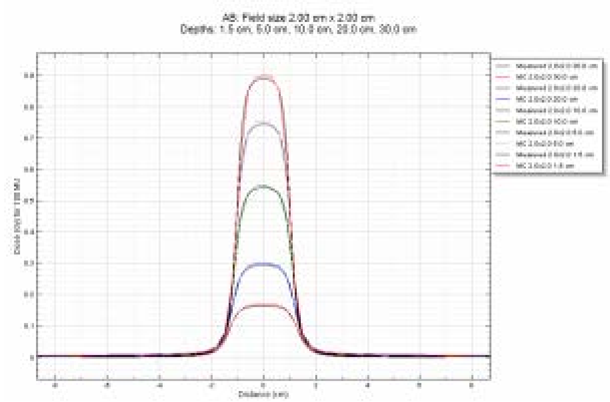


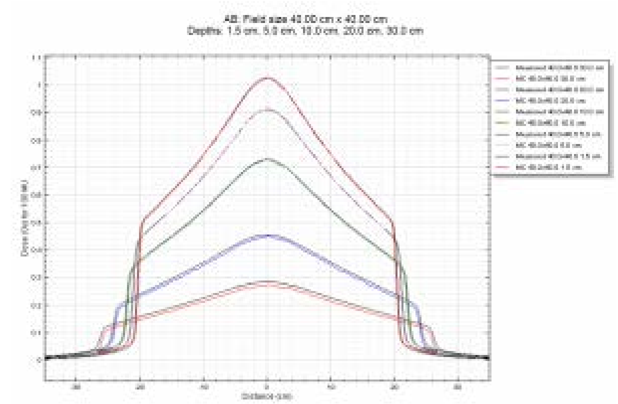


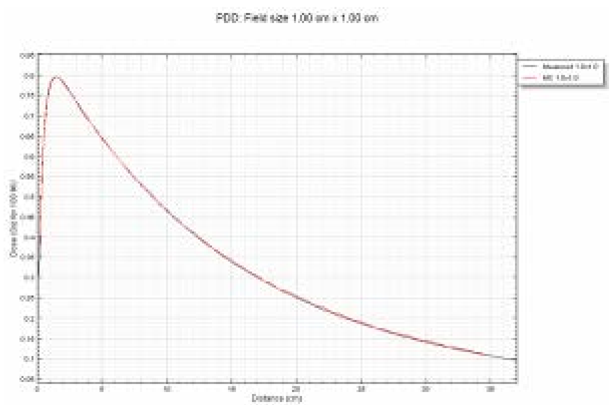


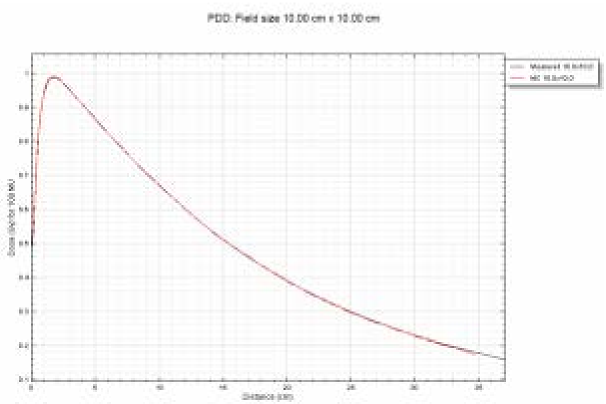
FFF – Validation measured vers. calculated data e.g. 6 MV

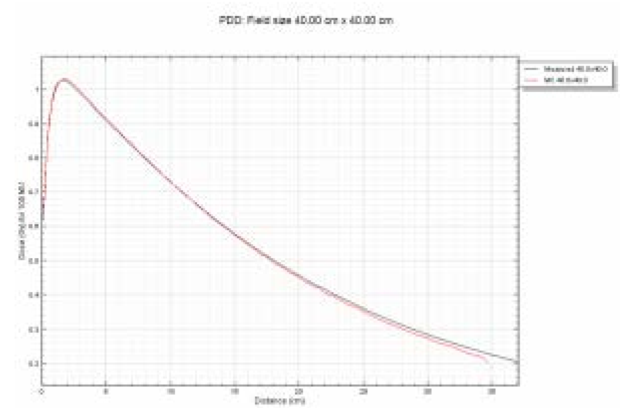












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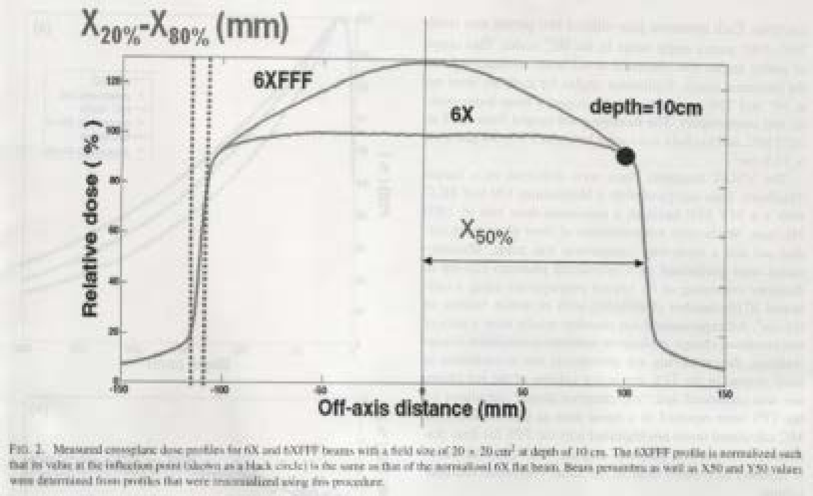
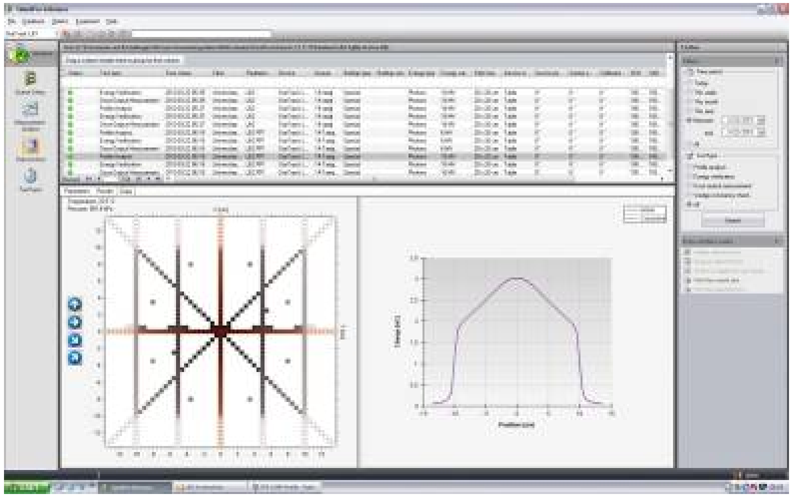
FFF QA aspects



Gete et.al.:MonteCarlo validation of FFF VMAT treatment plans
Medical Physics, Vol.40, No.2 February 2013



QA profiles IBA StarTrack

Actual FFF QA discussion :

- Dosimetry Kq factor (changes in the x-ray spectrum without the flattening filter)
- Penumbra and field size definition of FFF beams
- Definition of measuring point at the FFF crossprofiles for QA

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Commissioning FFF for Monaco 3.3 and Agility

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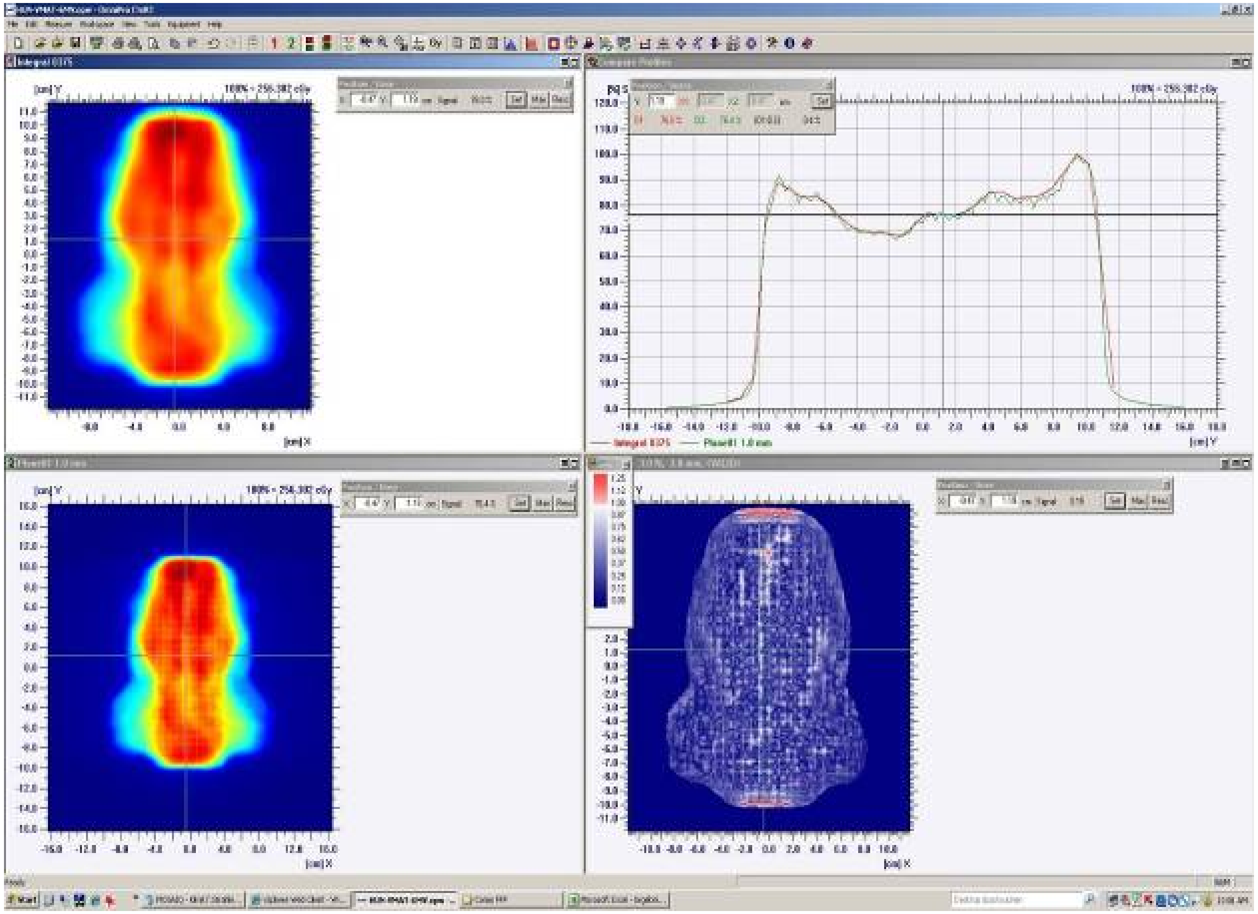
Larger volume
Head & Neck 6MV FFF – VMAT 2 Arcs – 2Gy

Gamma 33:
98,99%

Gamma 55:
99,91%

collapsed

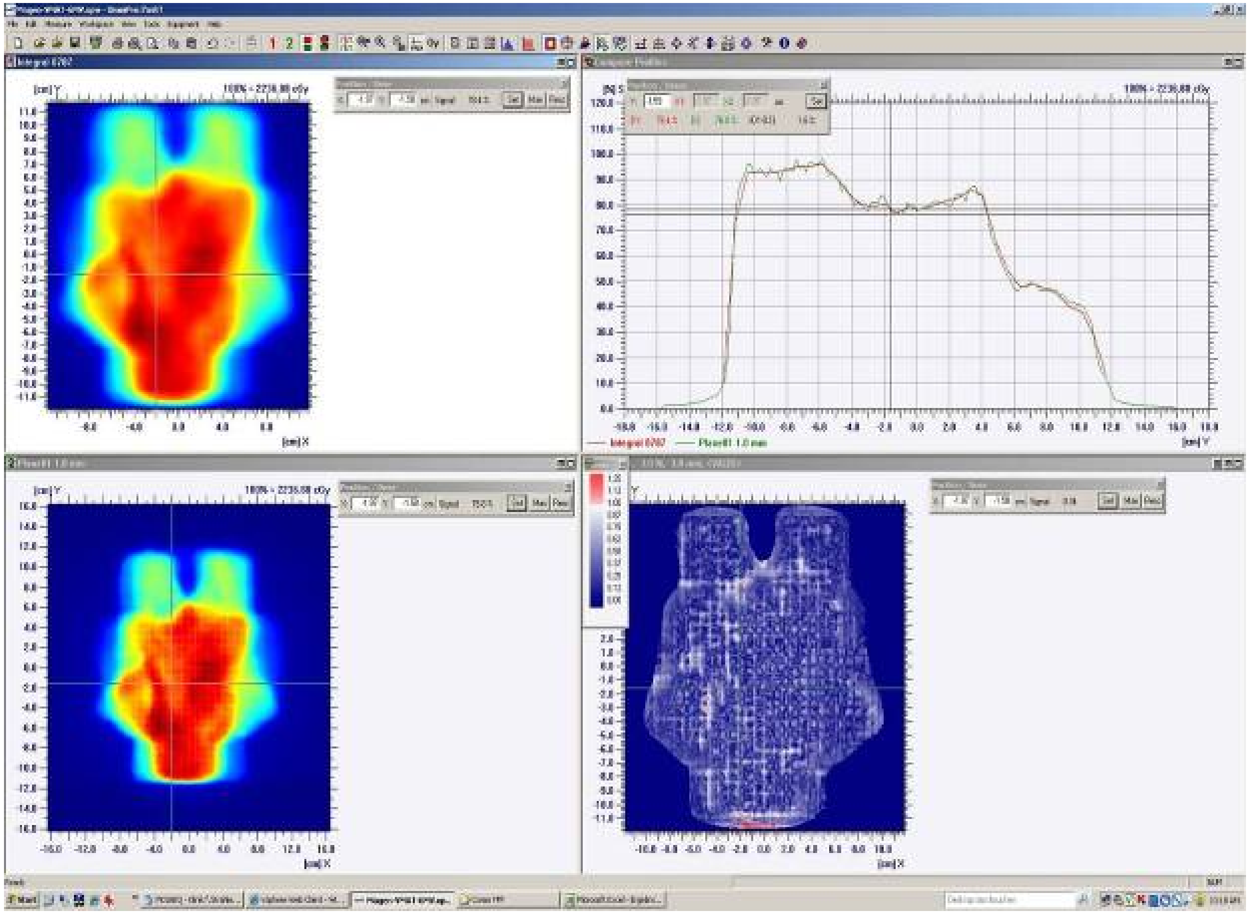


Larger volume stomach
6 MV FFF – VMAT 2Arcs – 15Gy

Gamma 33:
99,48%

Gamma 55:
100%

collapsed

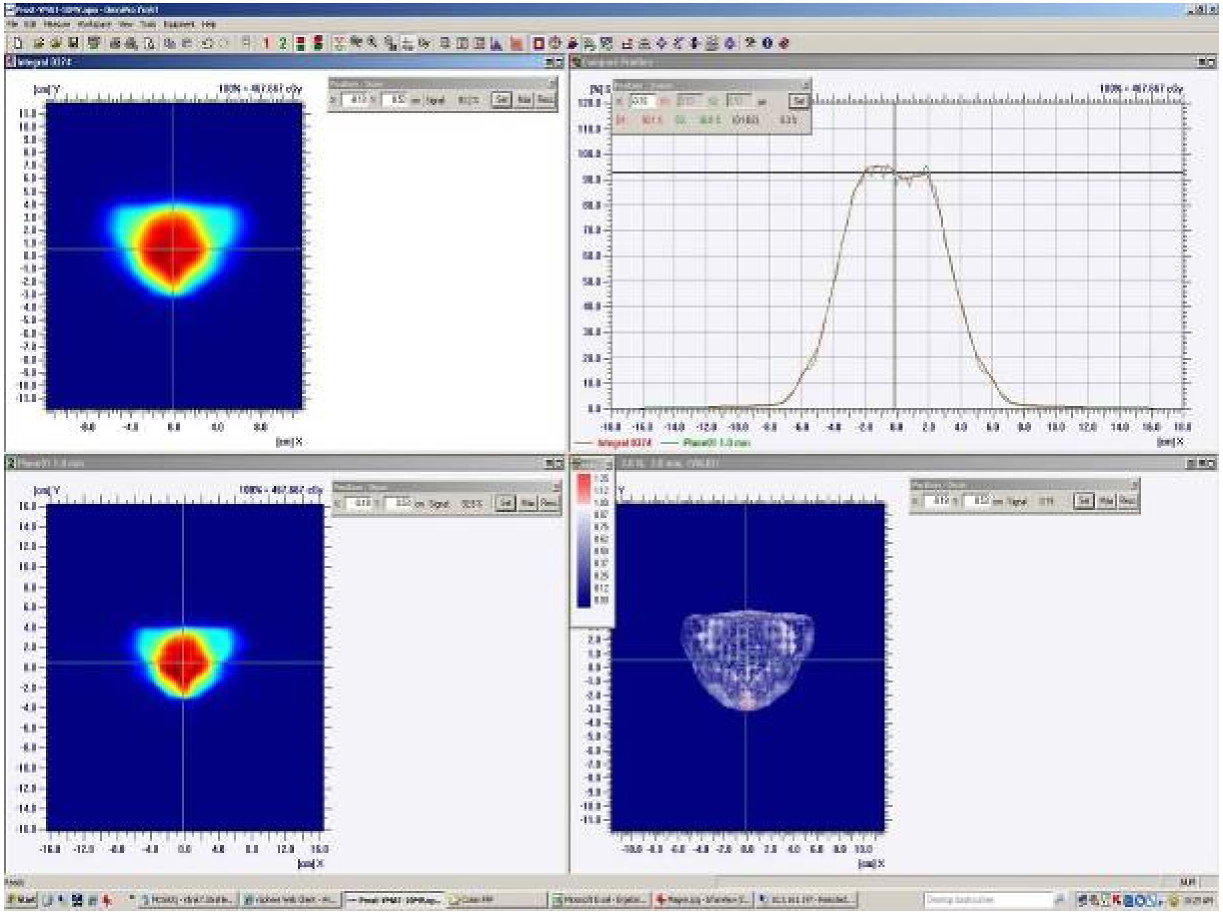


Midsize volume Prostate with integrated boost 10MV FFF – VMAT 2Arcs -2,5Gy

Gamma 33:
99,17%

Gamma 55:
100%

collapsed



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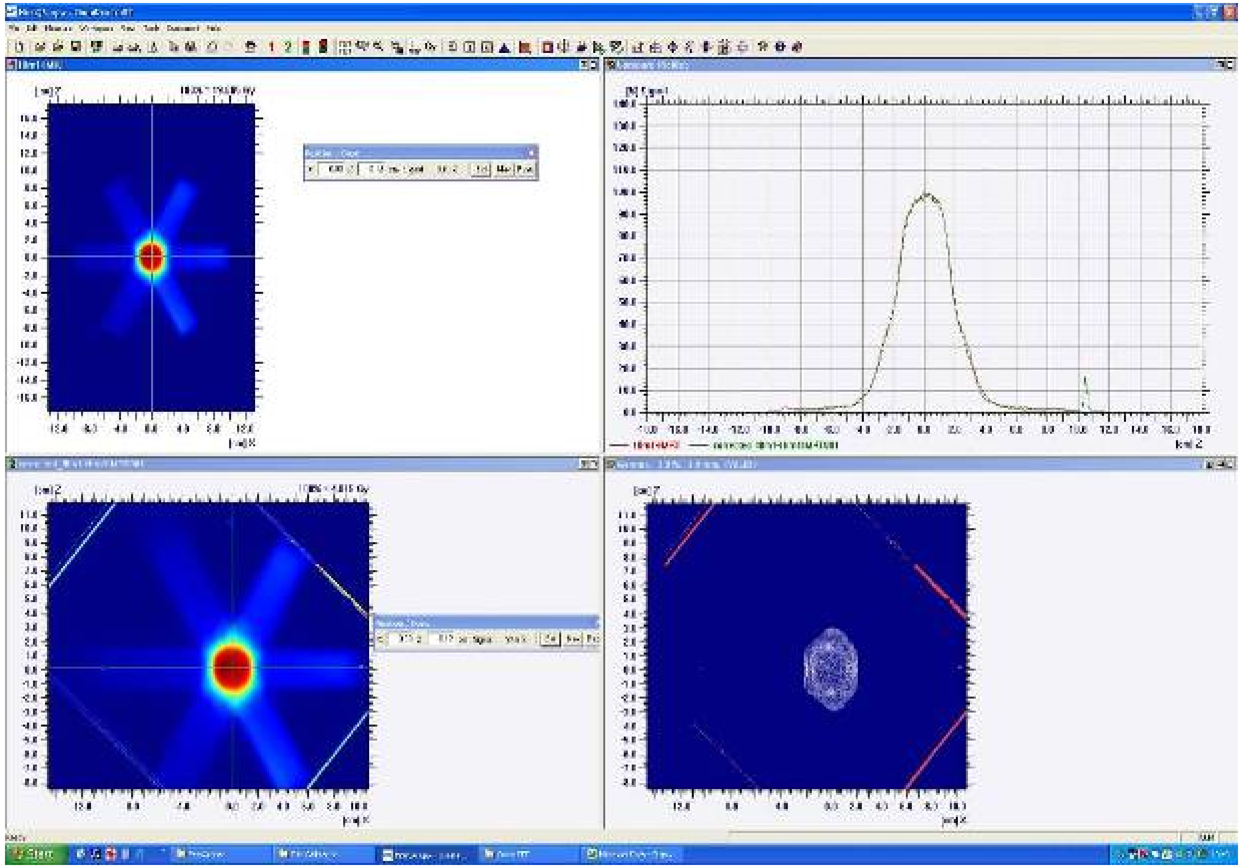
Small volume Brain 1 – 6 MV FFF – IMRT vs VMAT (non coplanar)

Stieler et al., Radiother Oncol, 2013

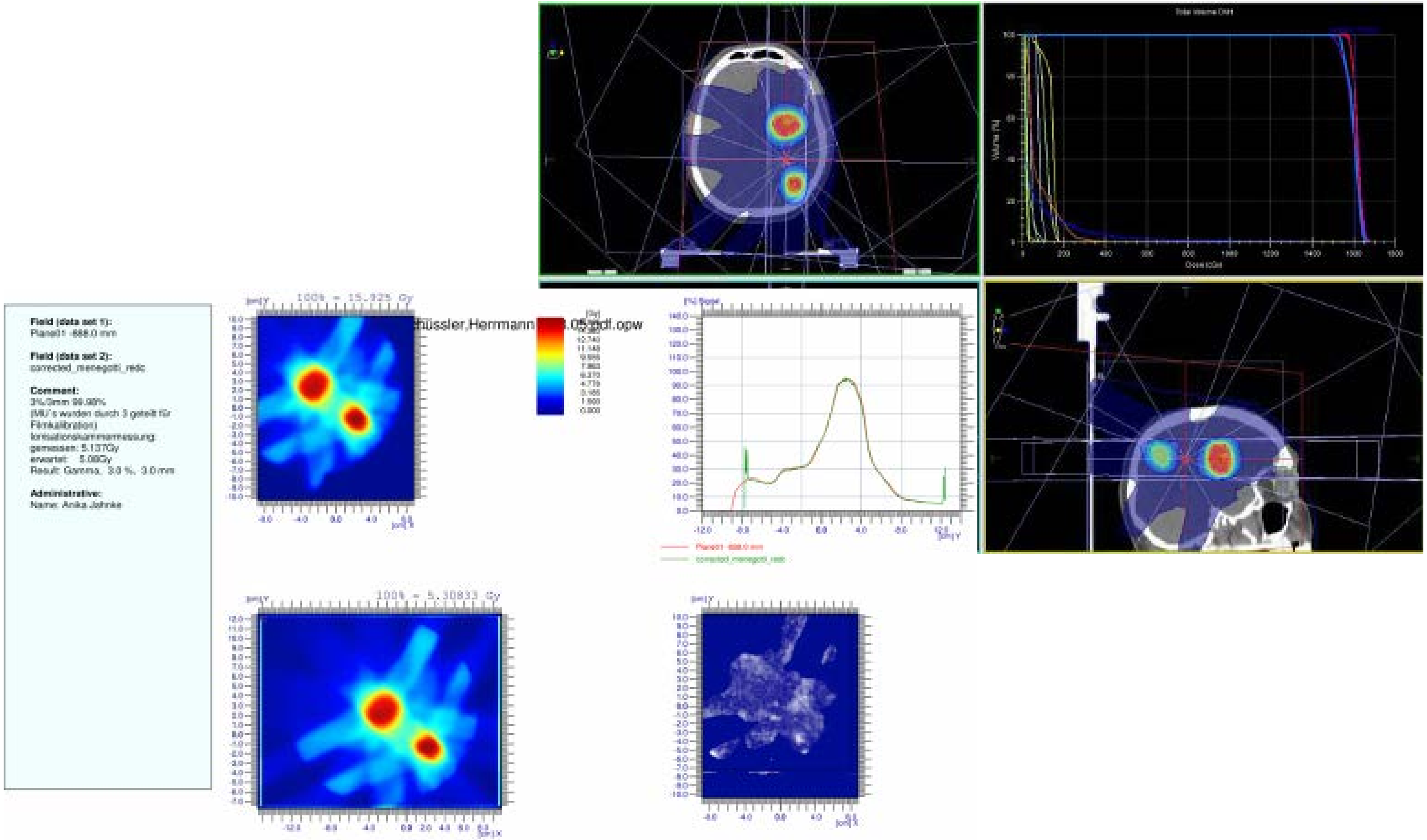
Gamma 33:
99,86%
Gamma 55:
100%
Kammer:
-1.1%



Our first FFF treatment

Stieler et al., Radiother Oncol, 2013

2 metastases 16 Gy each, one fraction



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Our first FFF treatment

Stieler et al., Radiother Oncol, 2013

Plan Information

Studyset ID: CT3   # of Slices: 163   Pixel Size: 0.07   Scan Orientation: HFS

Treatment Position: HEAD IN

Setup Information

Scan Reference Coordinates (cm): No Scan Reference Point has been selected

Beam #	Description	Machine ID	Energy	Gantry	Coll.	Couch	Isocenter X	Isocenter Y	Isocenter Z	# of Segs	MU/fx
1	G12A	Agility_6MV_FFF	6 (FFF)	181.0	0.0	0.0	2.75	-46.90	-2.00	11	296.79
2	G10A	Agility_6MV_FFF	6 (FFF)	220.0	0.0	0.0	2.75	-46.90	-2.00	19	522.46
3	G11A	Agility_6MV_FFF	6 (FFF)	288.0	0.0	0.0	2.75	-46.90	-2.00	21	621.86
4	G13A	Agility_6MV_FFF	6 (FFF)	72.0	0.0	0.0	2.75	-46.90	-2.00	28	676.61
5	G14A	Agility_6MV_FFF	6 (FFF)	144.0	0.0	0.0	2.75	-46.90	-2.00	23	491.76
6	G15A	Agility_6MV_FFF	6 (FFF)	30.0	0.0	90.0	2.75	-46.90	-2.00	22	461.56
7	G16A	Agility_6MV_FFF	6 (FFF)	70.0	0.0	90.0	2.75	-46.90	-2.00	24	688.53
8	G17A	Agility_6MV_FFF	6 (FFF)	160.0	0.0	90.0	2.75	-46.90	-2.00	24	441.39
9	VER3A	Agility_6MV_Int	6	0.0	0.0	0.0	2.75	-46.90	-2.00	0	0.00
10	Ver4A	Agility_6MV_Int	6	270.0	0.0	0.0	2.75	-46.90	-2.00	0	0.00
									Total:	172	4200.98

Normalization

Prescription (cGy): 1600.0   # of Fractions: 1 (1,600.00 cGy/fx)

100.00 % of 1600.0 cGy to cover 50.00 % of PTV.1

Dose Calculation

Grid Spacing (cm): 0.20

# of Calculation Points: 5906752

Assigned CTtoED File: DICOM3.BrillianceBigC

Algorithm: Monte Carlo Photon

Calculate Dose to: Medium

MC Std Dev per Plan: 1.00

Max Dose in Plan (cGy): 1674.7

Max Dose Location (cm): X = 1.95   Y = -46.90   Z = 1.40

Delivery Mode: Step & Shoot IMRT

Whole procedure

Incl.CBCT and verification 19 min.

treatment time (beam on) 7 min.

							p / Field Meterset	Dose	Machine	Notes T S P F D C	Sts	By	Rx:GH Fx	ED	Dly	Cum	Rx:Einzeit Fx	ED	Dly	Cum
									LB3											
									LB3											
									LB3											
									LB4											
									LB4											
									LB3											
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									LB3											
									LB2				1		300 cGy	300 cGy				
									LB2											
									LB2				2	1	300 cGy	600 cGy				
QA		18:02	2Flds						LB2											
36	08.03.2013	10:54	2Flds						LB2				3	2	300 cGy	900 cGy				
37	11.03.2013	14:18	2Flds						LB2				4	5	300 cGy	1.200 cGy				
38	12.03.2013	14:59	2Flds						LB2				5	6	300 cGy	1.500 cGy				
39	13.03.2013	11:22	4Flds			1Pl			LB2								1		1.600 cGy	1.600 cGy
		11:22	CT			CT			LB2			AZ								
		11:23	VER4	1			2,0 MU		LB2		^ *	AZ								
		11:24	VER3	1			2,0 MU		LB2		^ *	AZ								
		11:34	G12A	1			2609,6 MU	800 cGy	LB2		^ *	AZ							800 cGy	
		11:41	G13A	1			1591,5 MU	800 cGy	LB2		^ *	AZ							800 cGy	
40	14.03.2013	7:44	2Flds						LB2				6	8	300 cGy	1.800 cGy				
QA		9:46	1Fld						LB2											
41	15.03.2013	7:44	2Flds						LB2				7	9	300 cGy	2.100 cGy				
42	18.03.2013	7:44	2Flds						LB2				8	12	300 cGy	2.400 cGy				

Most important indications and treatment philosophy

1. **Head and Neck Cancer**

   CNS

   Paranasal Sinus Tumors / Integrated Boost
   (Better Tumor coverage and shortening of overall treatment time)

   NPC and other ENT Tumors
   (Parotid sparing when possible, better tumor coverage for NPC)

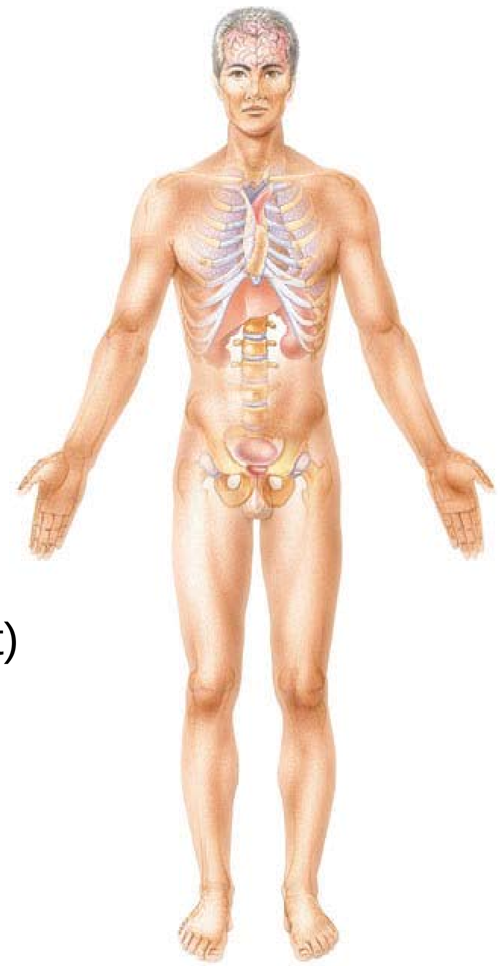
2. **Prostate / Integrated boost**
   (Potentially hypofractionation)

3. **Gastric cancer**
   (Better kidney sparing while treating the whole of the target)

4. **Breast Cancer**

5. **Lung Cancer**

6. **Metastases**



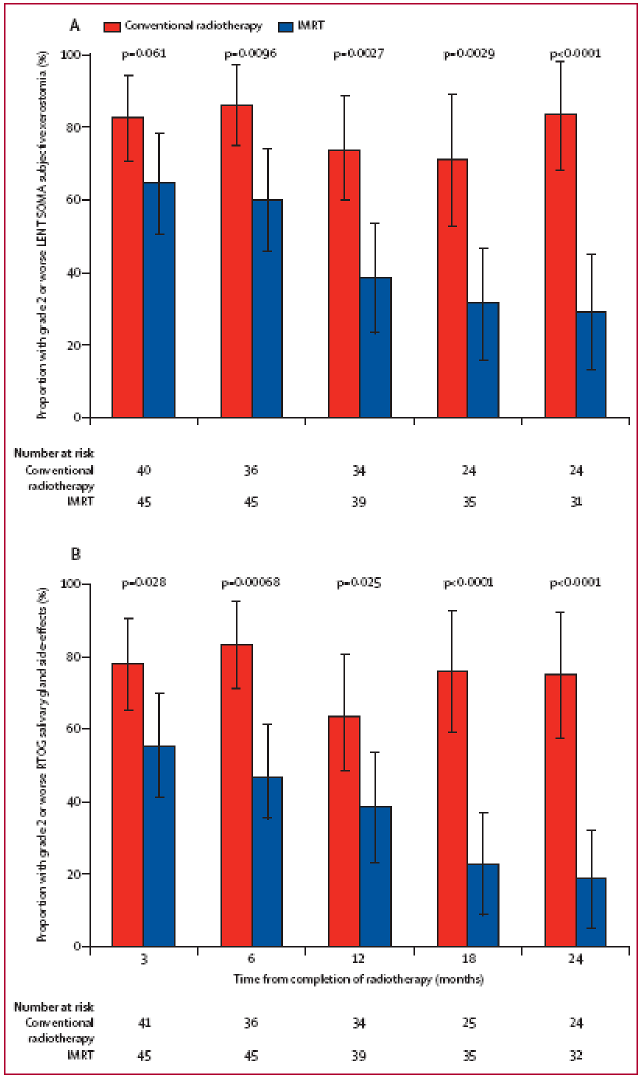


Figure 2: **Proportion of patients reporting grade 2 or worse LENT SOMA subjective xerostomia and RTOG salivary gland side-effects**
p values quoted compare proportions with grade 2 or worse side-effects in each group with a χ^2 test. Error bars represent 95% CIs. IMRT=intensity-modulated radiotherapy. LENT SOMA=Late Effects of Normal Tissues Subjective-Objective Management Analytic. RTOG=Radiation Therapy Oncology Group.

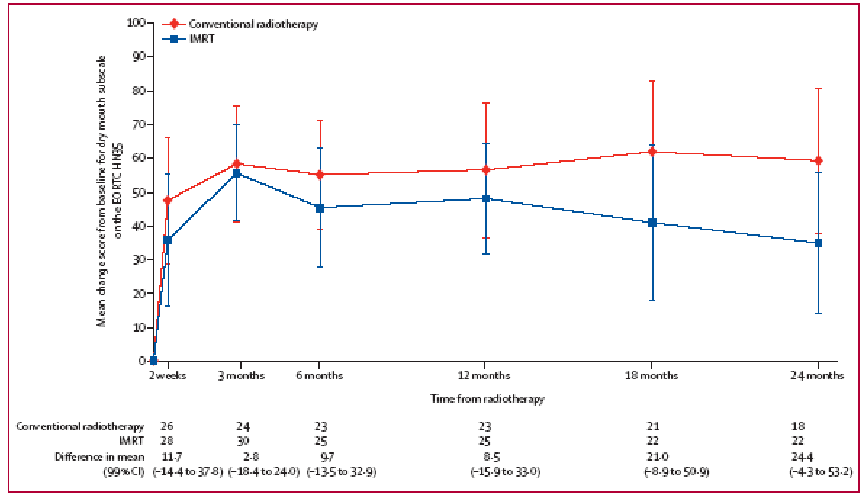


Figure 3: **Mean EORTC HN35 dry mouth subscale score changes from baseline**
IMRT=intensity-modulated radiotherapy. EORTC HN35=European Organization for Research and Treatment of Cancer head and neck specific module HN35.

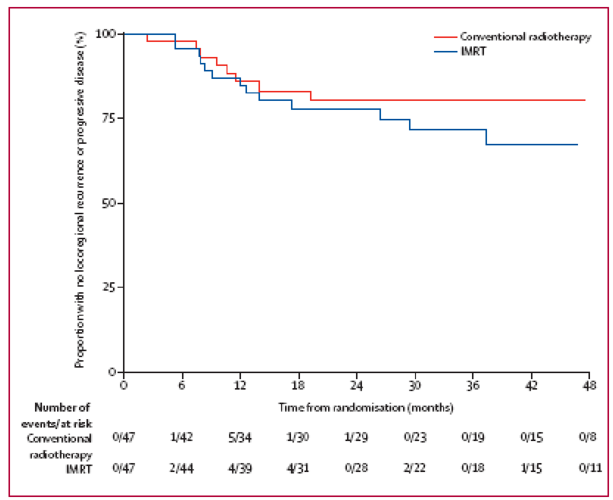


Figure 4: **Kaplan-Meier plot of locoregional progression-free survival by treatment group**
Hazard ratio 1·53 (95% CI 0·63 to 3·70). Log-rank test p=0·34. 2-year locoregional progression-free survival estimates for conventional radiotherapy 80% (95% CI 65 to 90) and for IMRT 78% (62 to 87); absolute difference 3% (–15 to 20). IMRT=intensity-modulated radiotherapy.

„Unexpectedly, acute fatigue was greater in patients treated with IMRT, which could be due to the greater radiation dose to non-tumour tissues. In an unplanned dosimetry review in a subset of patients, mean radiation doses to the posterior fossa were 20–30 Gy in the patients treated with IMRT compared with about 6 Gy in patients treated with conventional RT“

Nutting et al., Lancet Oncol, 2011

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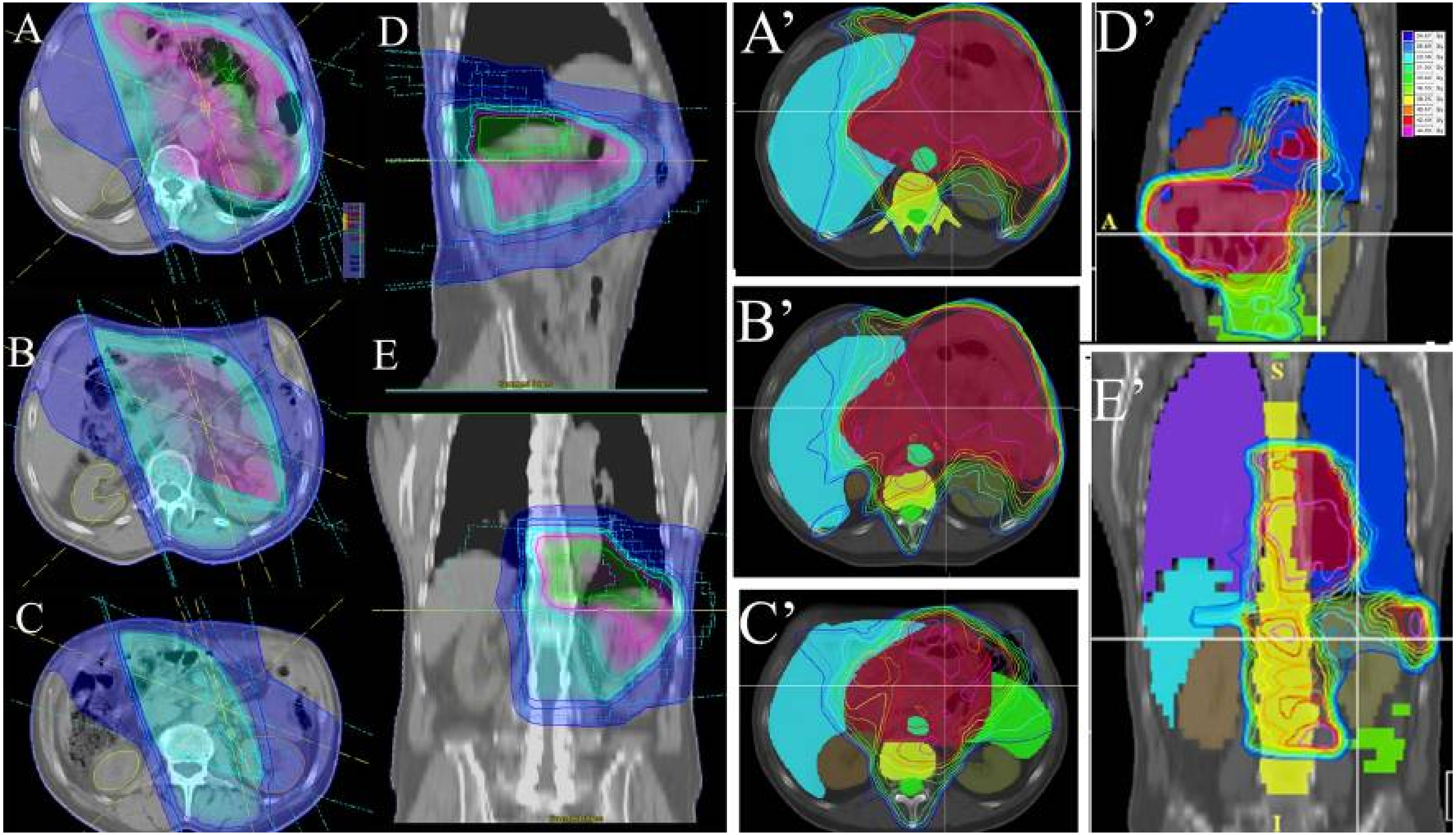
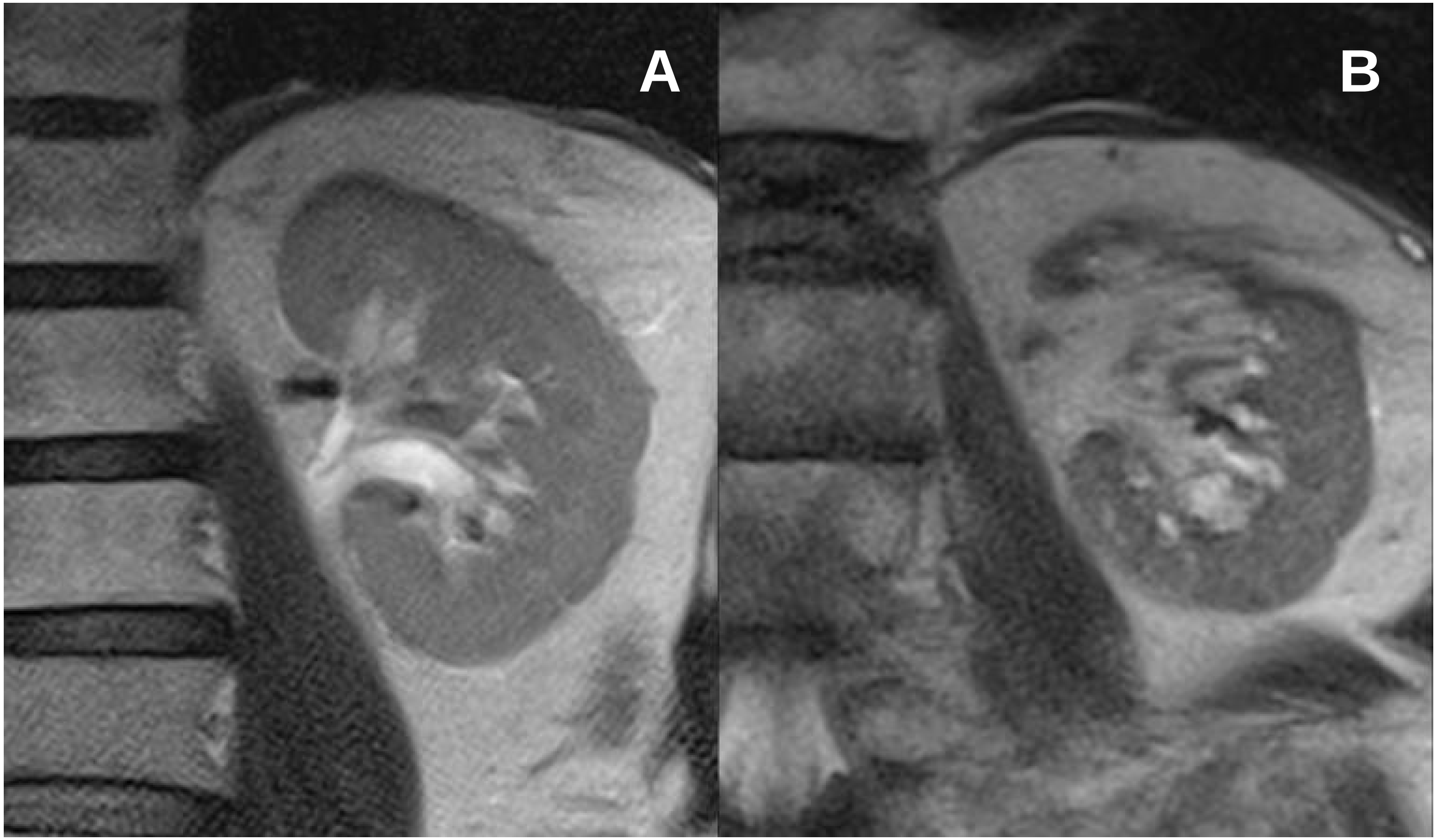
3DCRT IMRT



	Right Kidney (Gy)							Left Kidney (Gy)						
	Median	Mean	D30	D60	Cranial part	Middle part	Caudal part	Median	Mean	D30	D60	Cranial part	Middle part	Caudal part
3DCRT-1	2.52	3.18	3.3	2.4	5	<5	<5	41.07	36.9	46.3	38.4	47.8	45.3	25.2
3DCRT-2	3.2	7.76	8.1	2.7	22.5	4.5	<4.5	25.8	22.95	27	18	45	42.7	36
IMRT-1	1.49	1.61	1.77	1.39	11	5	0	20.25	22.18	26.68	18.15	29	26	9
IMRT-2	14.77	16.12	17.4	13.8	13	8	4	23.84	23.28	27.7	21.2	26.8	18.5	13.5

T2w: (A) IMRT vs. (B) 3D

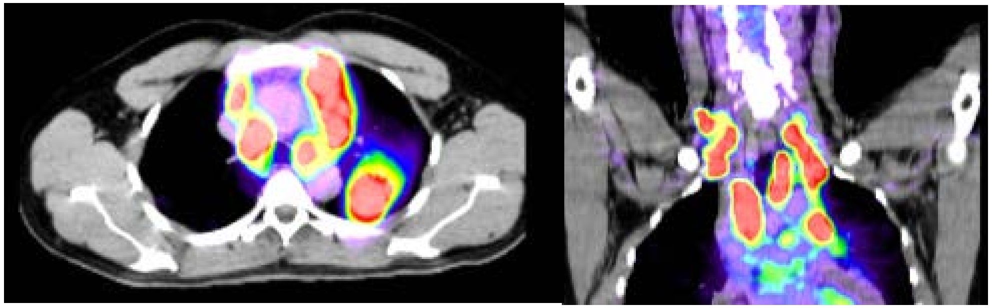


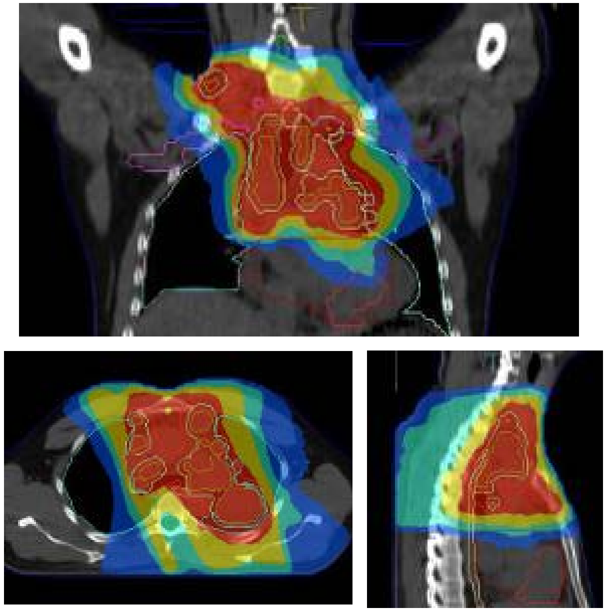
Haneder et al., SUON, 2012

Image Guided, PET-assisted Radiotherapy of Lung Cancer

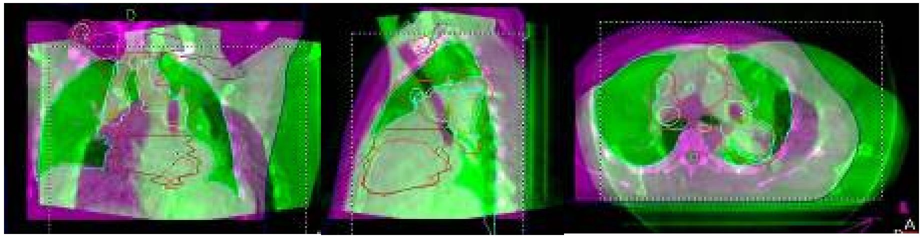
Target Volume Reduction and RT-Optimization for critical Tumor-to-Lung Ratio

1. CTV-Definition/Minimimization based on functional Imaging (PET-CT)

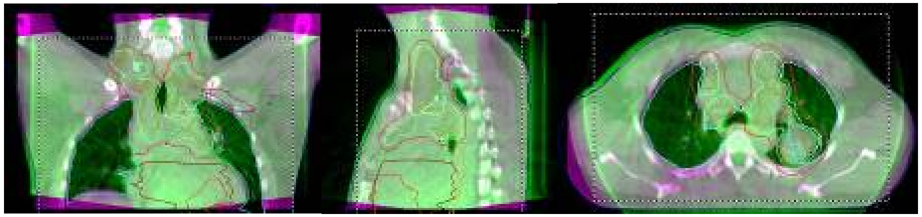




2. Treatment Planning as IMRT based on Monte-Carlo Dose calculation



Suboptimal Positioning



Optimal Positioning

3. Image Guided Radiotherapy Treatment with Cone-Beam-CT at Linac

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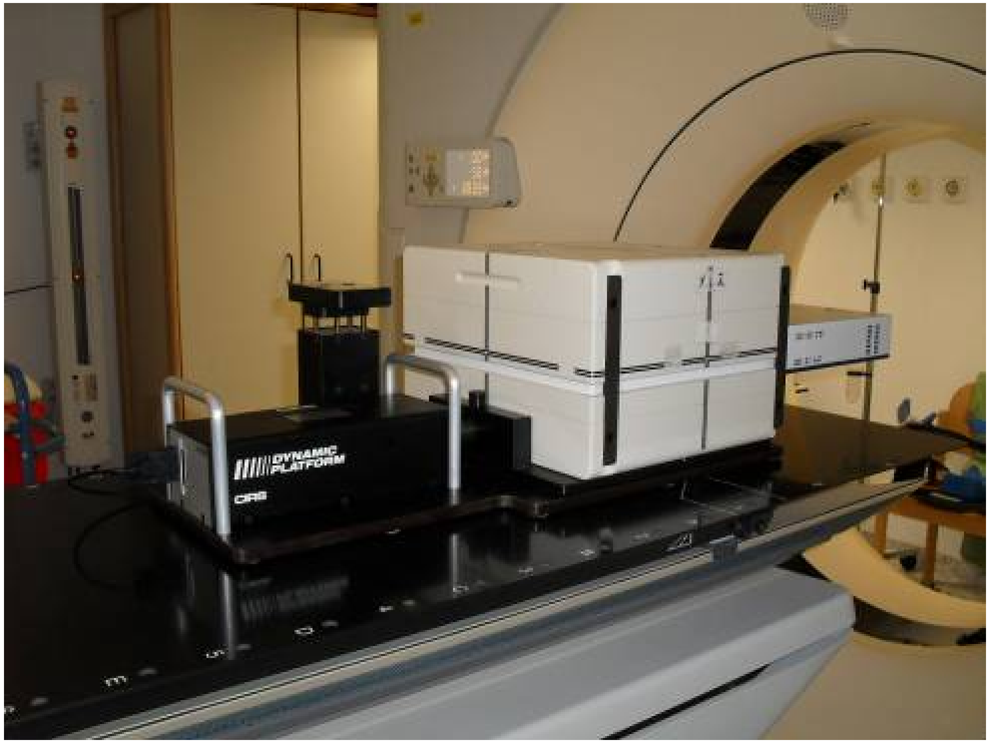
Fleckenstein et al., submitted

Measurement setup

- IBA Matrixx Evolution
- IBA Multicube
- CIRS dynamic platform model 008PL (accuracy 0.05mm)

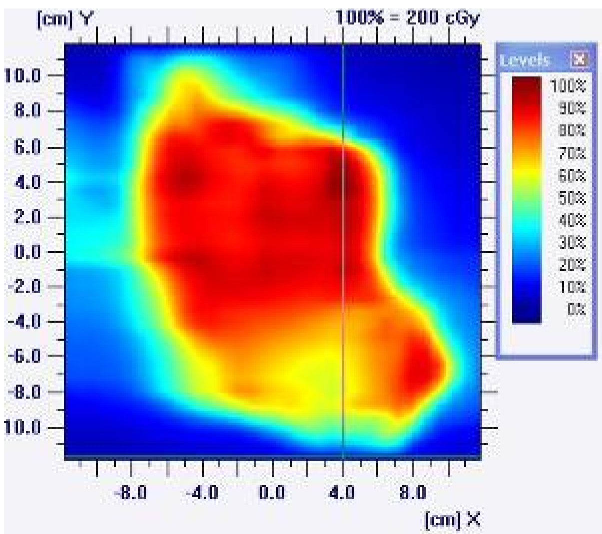
- VMAT plan generated in Monaco 2.0.3.beta



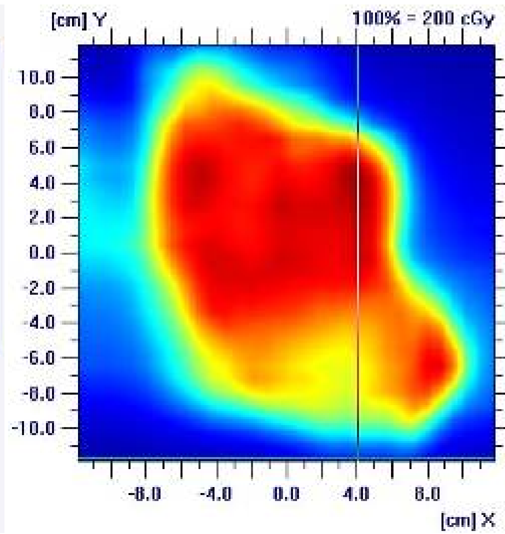
Fleckenstein et al., submitted

A=10mm, T=3.6s, cos4-motion trajectory

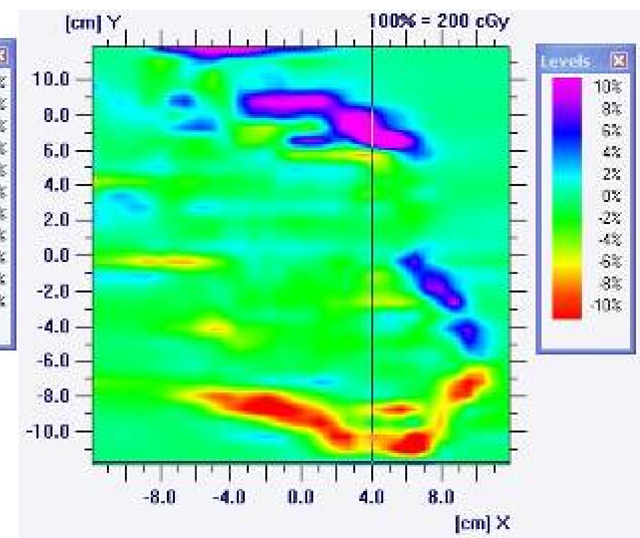
static case



with motion



difference map



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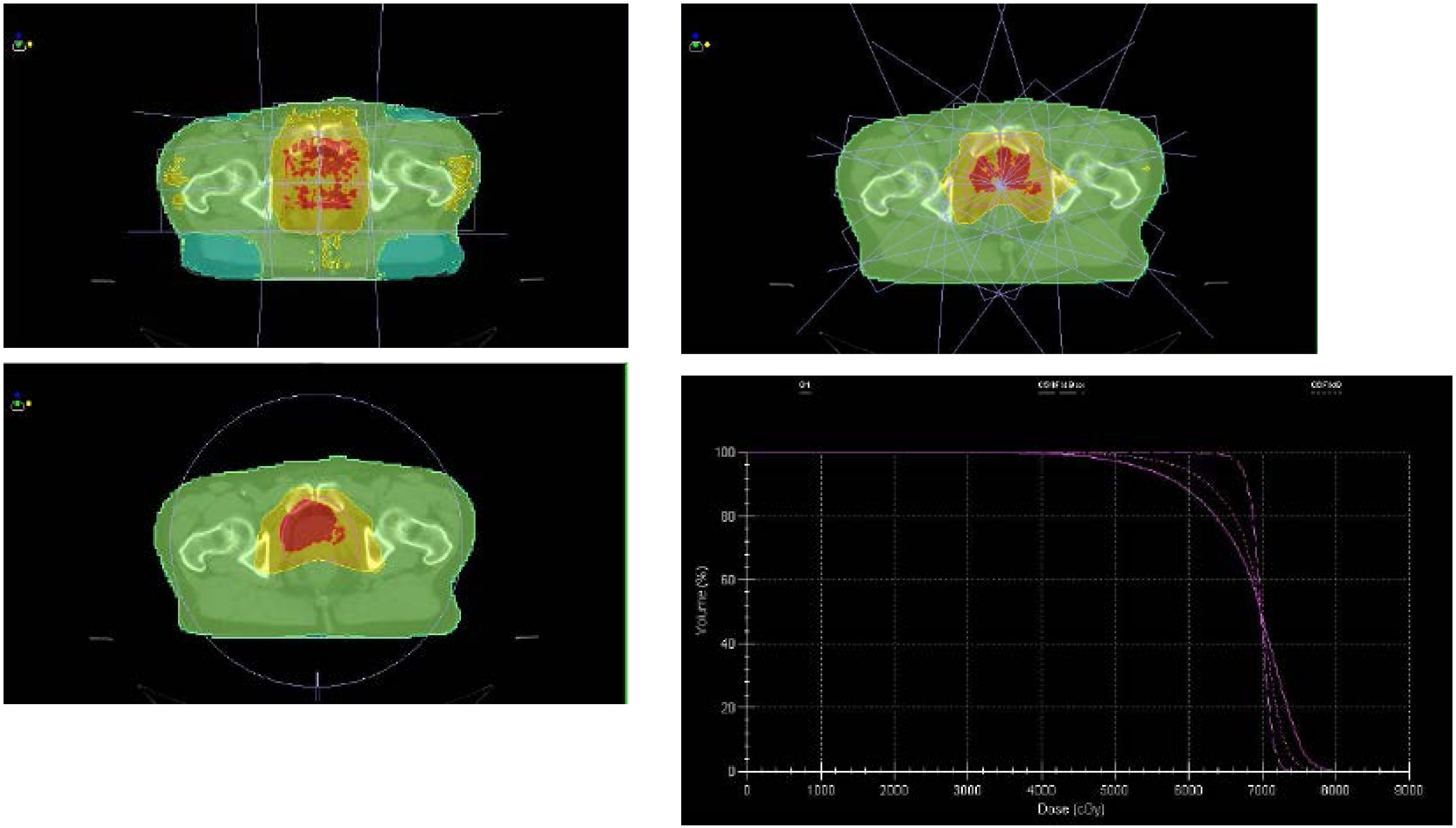
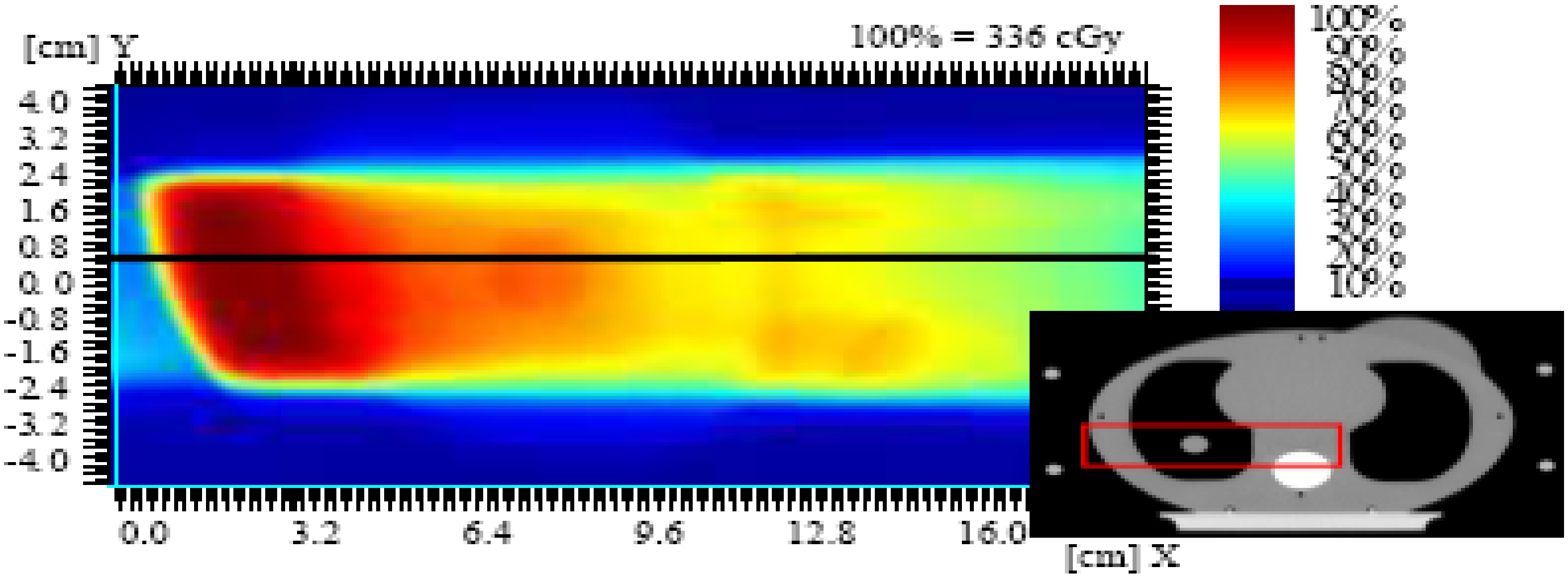
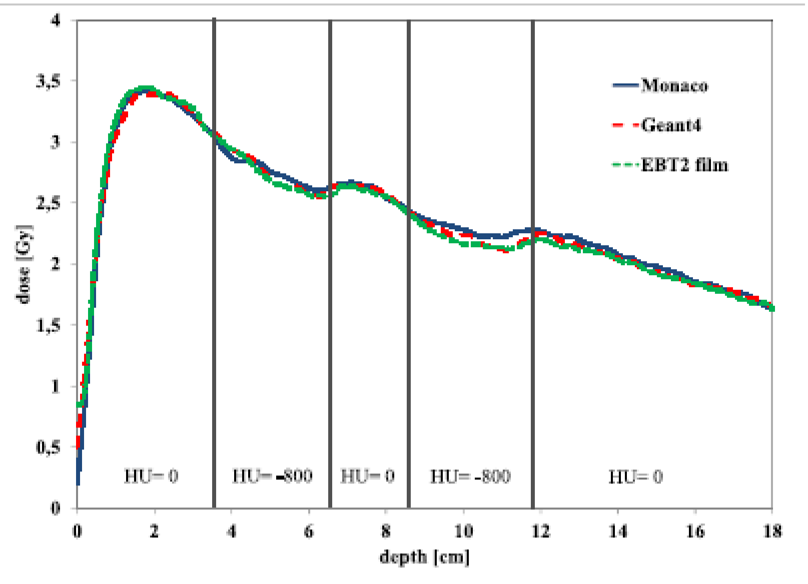


1 Gy (blue), 5 Gy (green), 45 Gy (yellow) and 70 Gy (red)

Fleckenstein et al., Z Med Phys, 2013





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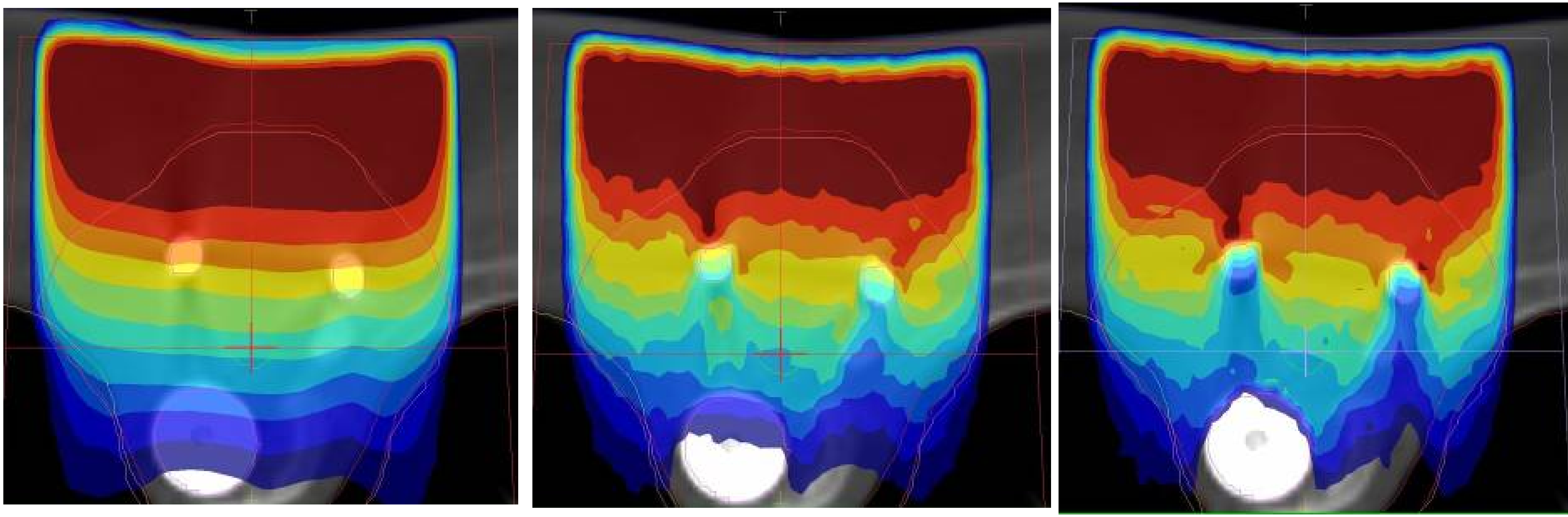
Hounsfield Unit conversion: metallic implants



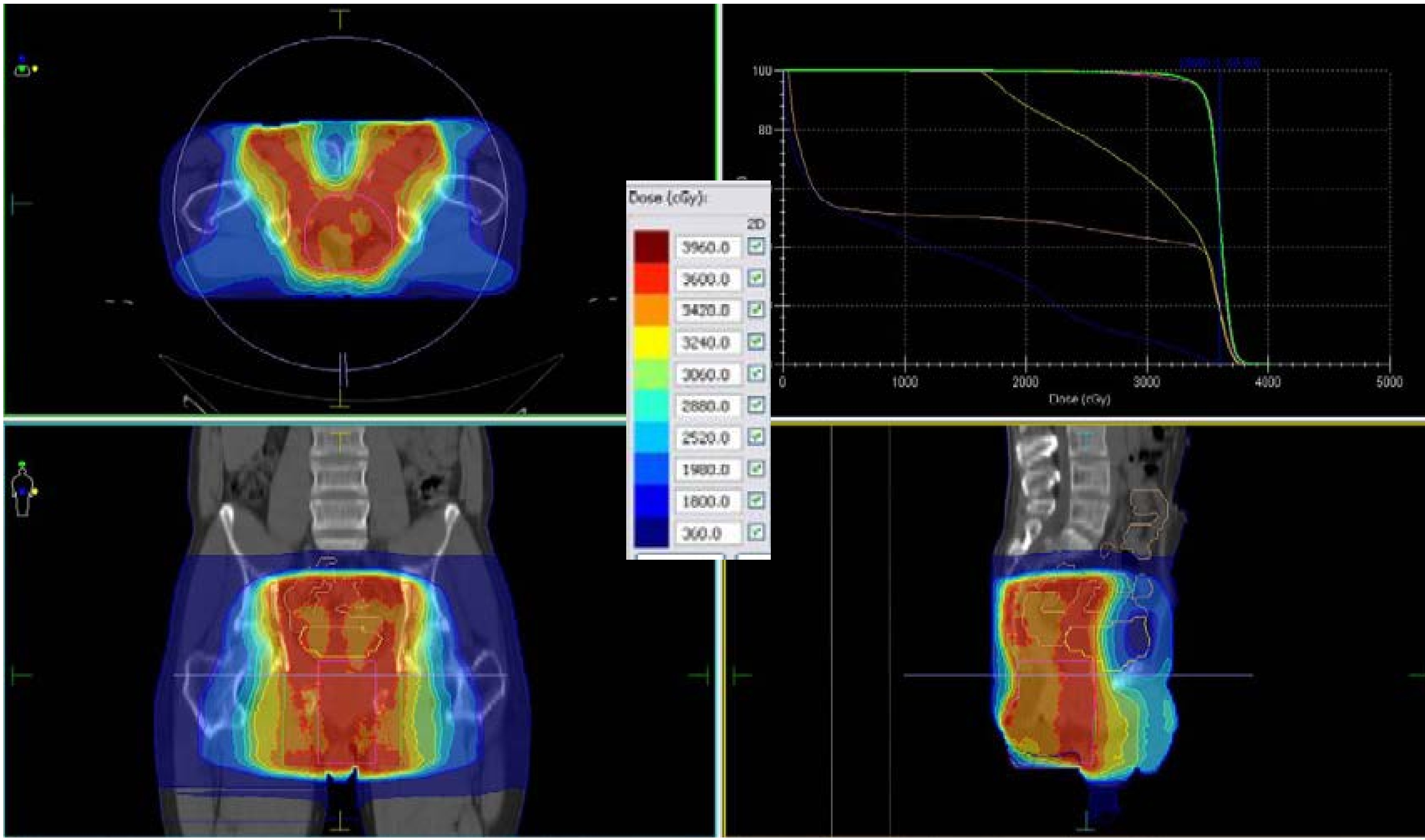
pencil beam

Monte Carlo: variance 0.5%, grid: 2mm

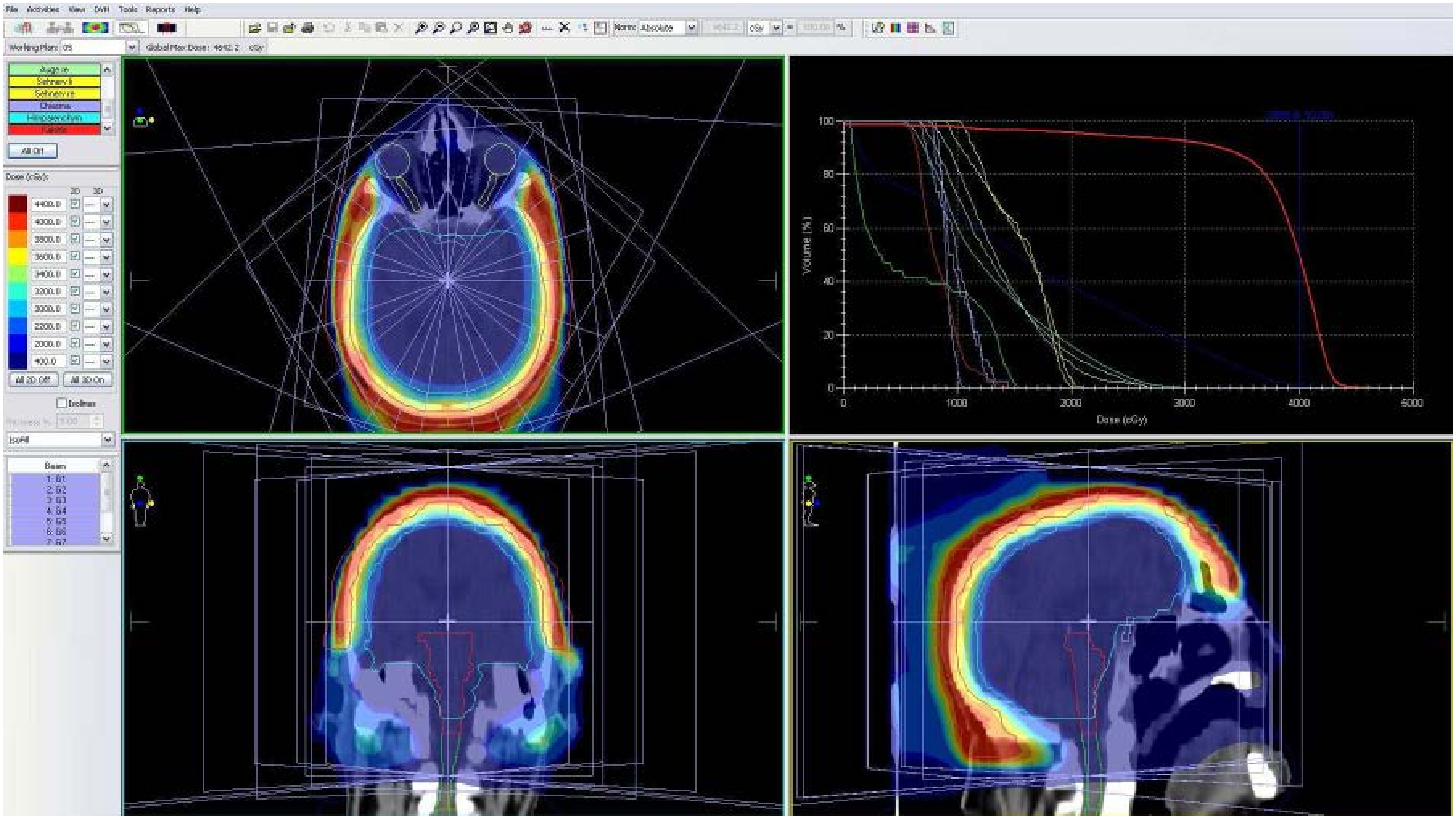
isolines 2.5%

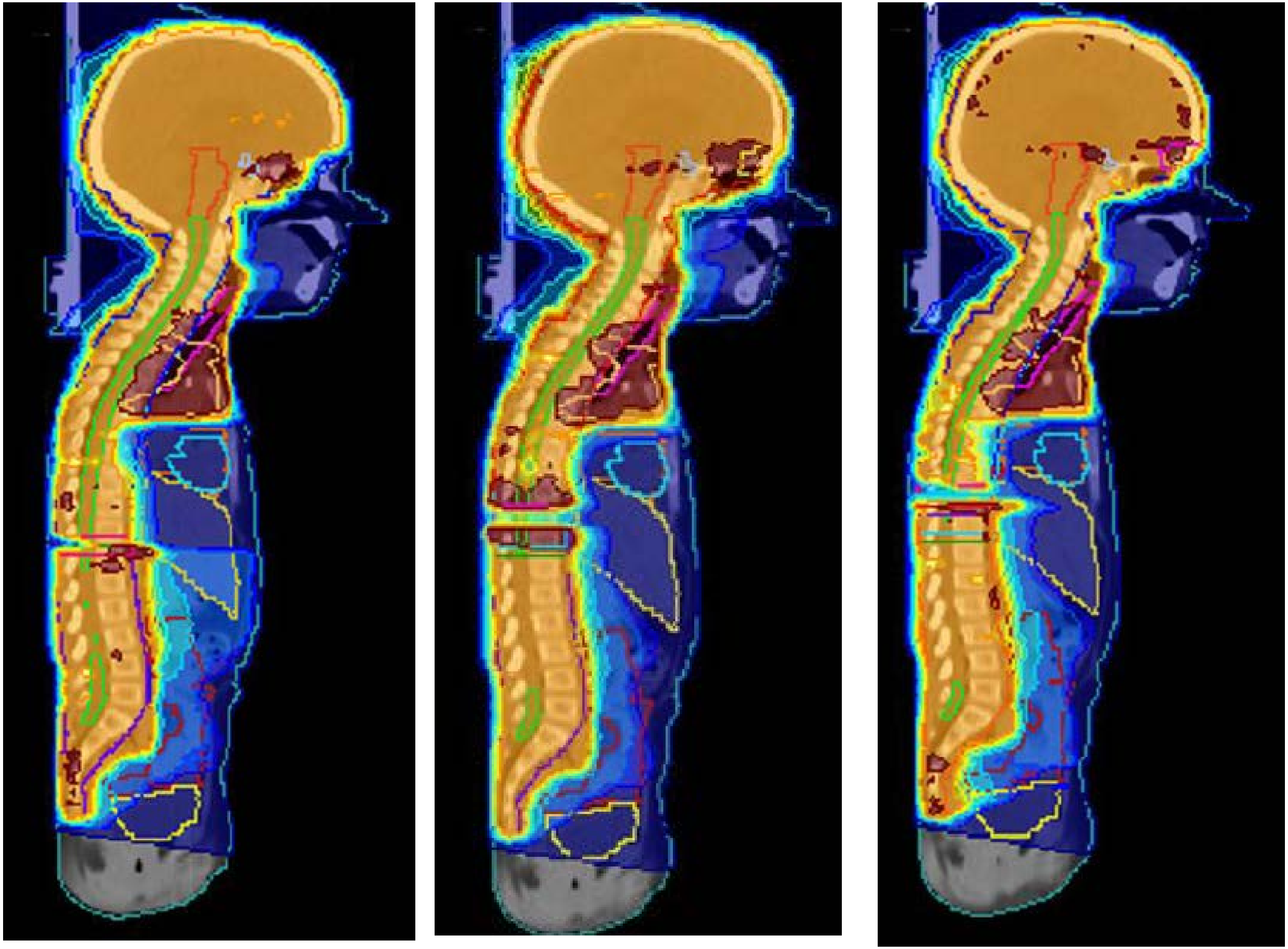
- contouring implants, which are in the PTV, improves the target DVH and enhances the optimization convergence probability
- relative electron density of titanium implants: 3.73
- use clear and fill options for CT reconstruction artifacts

Anal Cancer



640 MU
BOT 8 min





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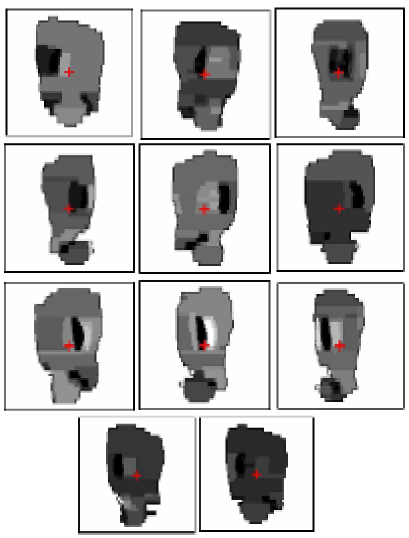
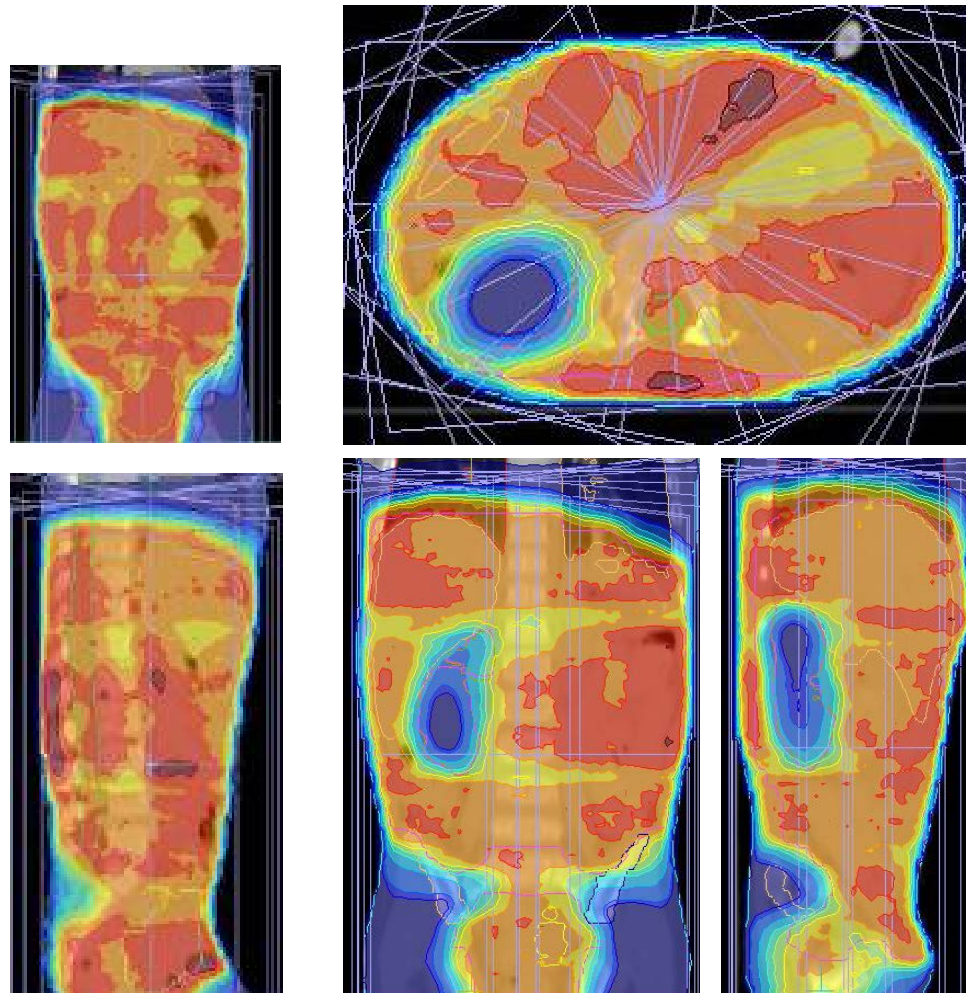
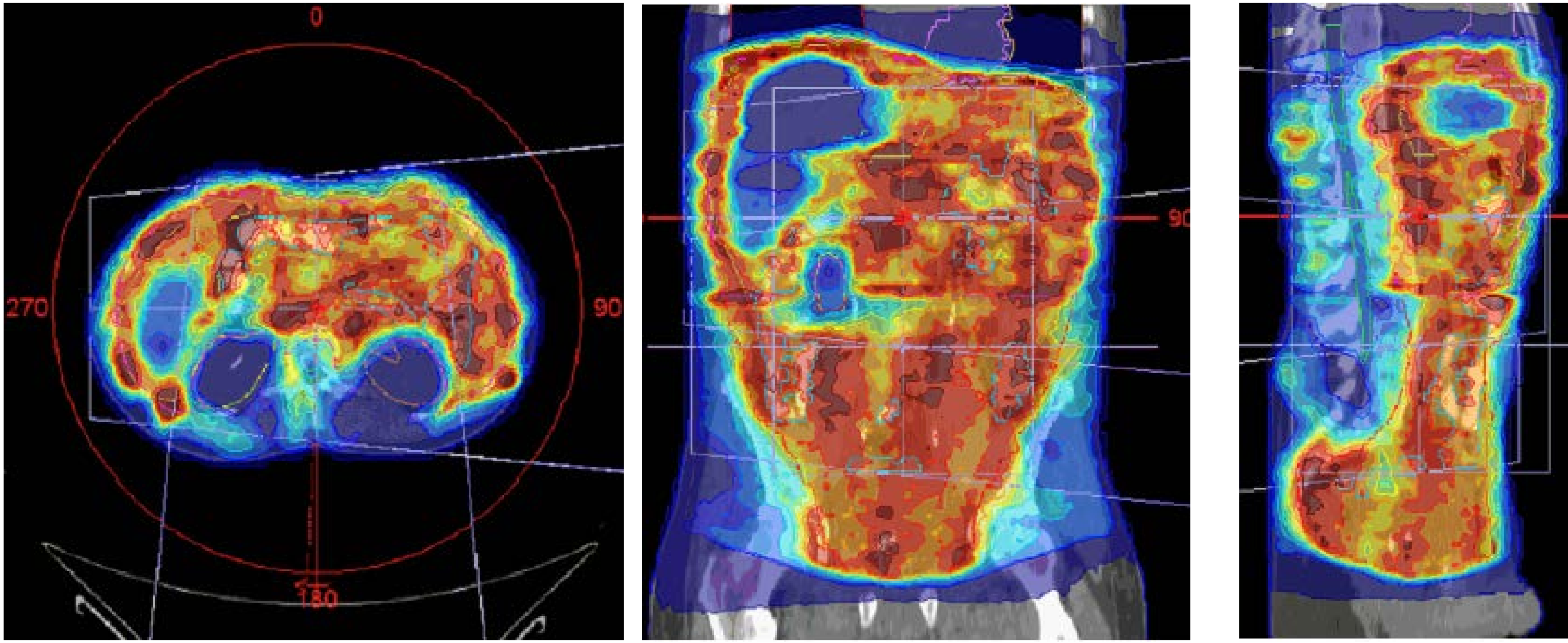
Step-and-Shoot IMRT





695 MU/1.5 Gy
92 Segments
T= 13 min



Peritoneal PNET

Two arcs, Two isocenters, 2740 MU/1.5 Gy

First CT to last beam off: ~20 min (2 CTs, 2 Arcs)

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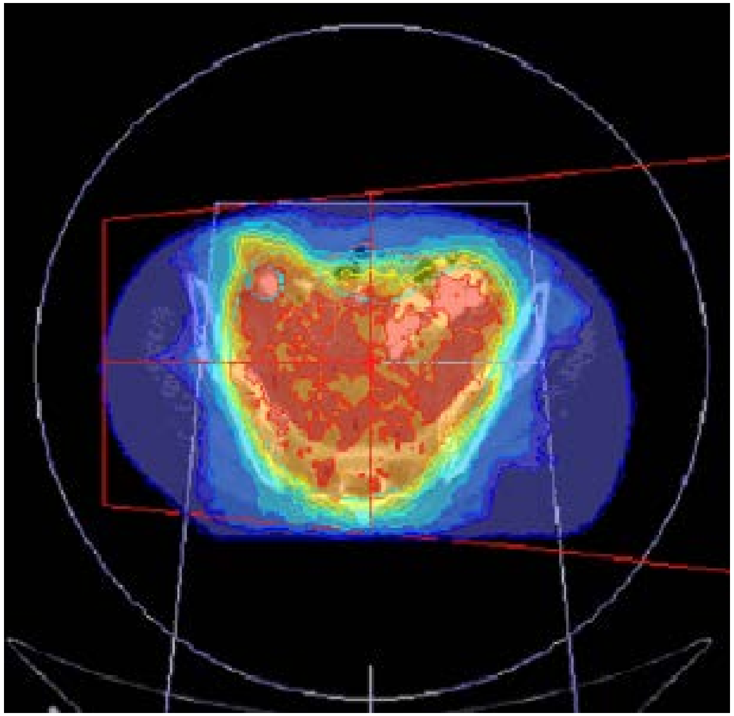

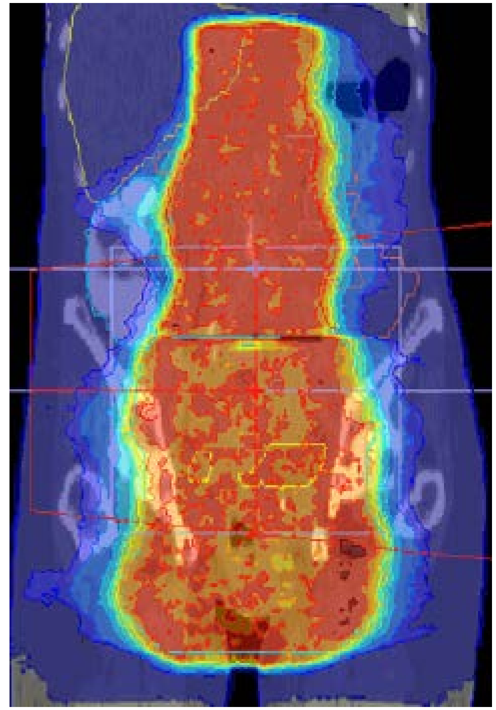

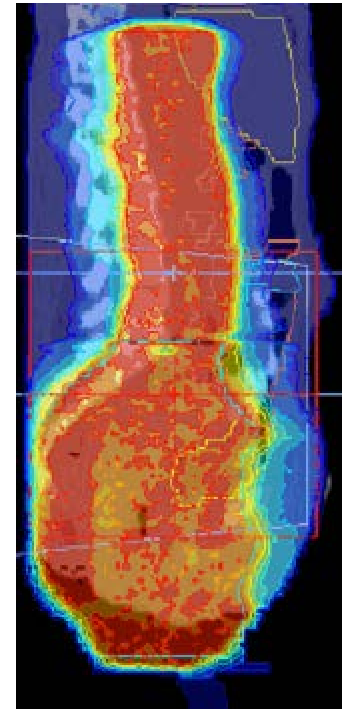

Anal Cancer

Two arcs, Two isocenters, 1403 MU/1.8 Gy

First CT to last beam off: <20 min (2 CTs, 2 Arcs)

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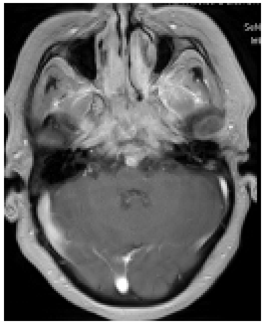
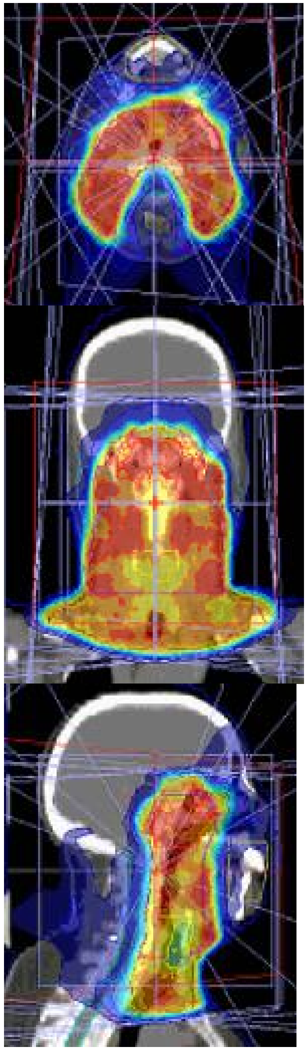
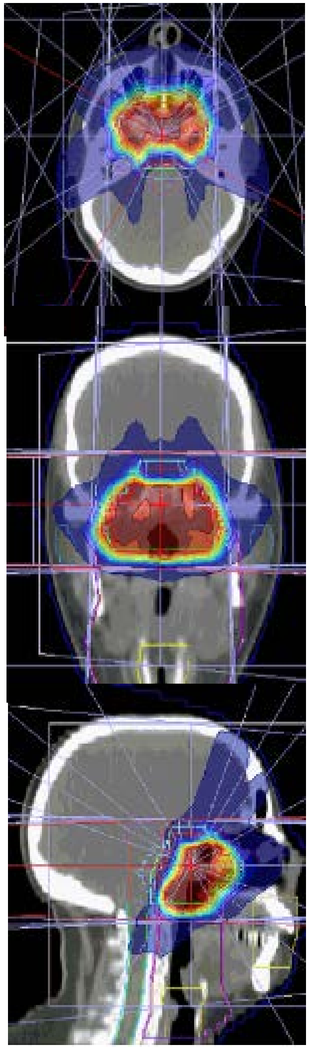
NPC

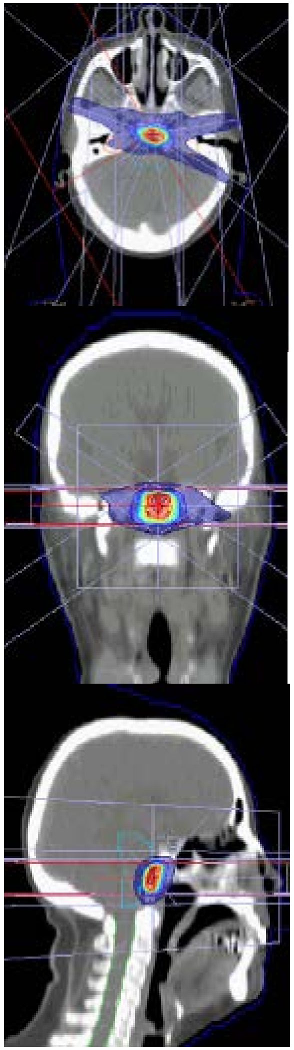
Treatment Sequence

before

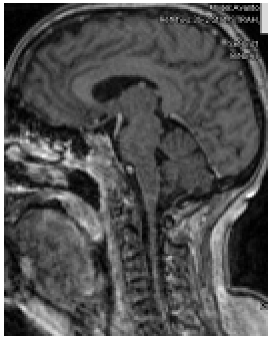






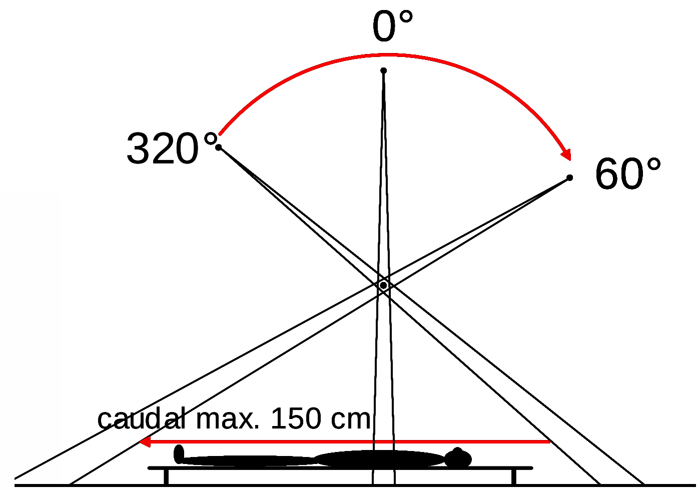


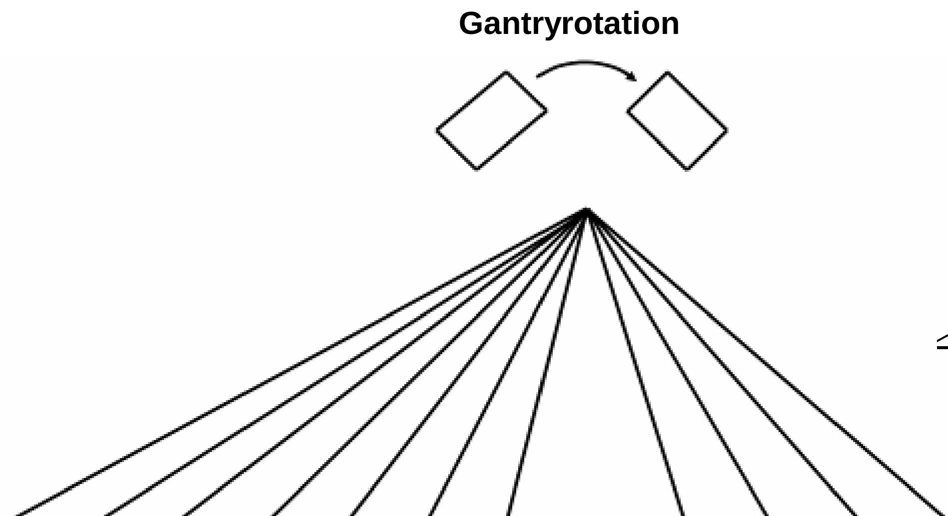
after



VMAT-TBI

Unterteilung eines kontinuierlichen Bestrahlungsbogens von 320° bis 60° mit 10 Kontrollpunkten (Feldgröße 10x40cm)





Einstrahlwinkel	55°-60°	50°-55°	40°-50°	30°-40°	20°-30°	10°-20°	10°-350°	340°-350°	330°-340°	320°-330°
Rel. MU's	358%	276%	185%	144%	117%	108%	100%	108%	117%	144%

Phantom:

RW3 Plattenphantom
auf einer Kohlefaserplatte
parallel zu der Gantrybewegung
SSD von ca. 200cm
Spoiler aus Plexiglass

Messungen:

Linac Elekta Synergy mit 6MV
Stabionisationskammer
Flime (EBT Gafchromic)
Profillänge
- 300 cm (Kammer)
- 180 cm (Film)

Messpunktauflösung
- 5cm und 10cm (Kammer)

Tiefer
- 8 und 10 cm (Kammer)
- 7,12,13 cm (Film)

Dosis:

1Gy pro Bogen in der Mitte
des Phamtondickes

Clinical experiences with FFF treatment delivery

Jens Fleckenstein, Ph.D.
University Medicine Mannheim, Germany

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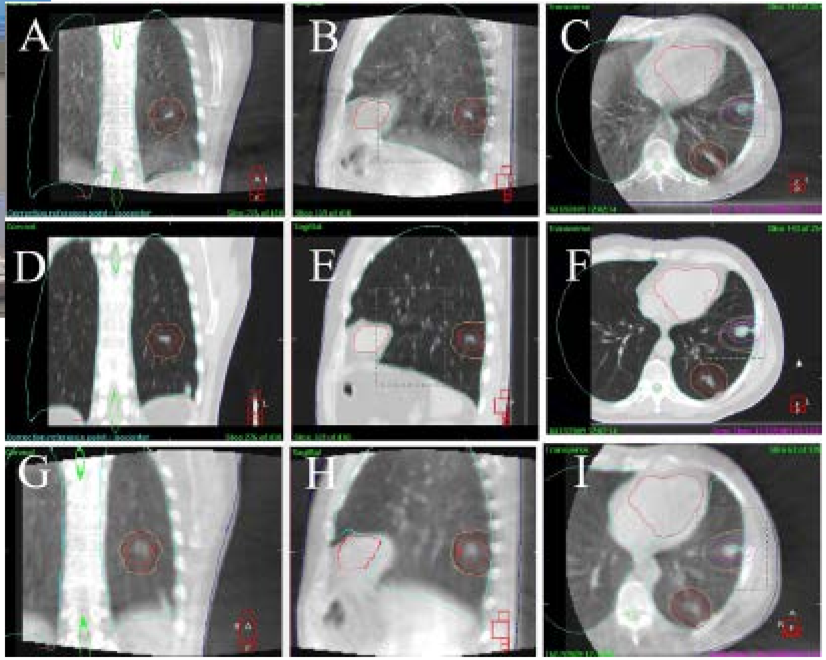
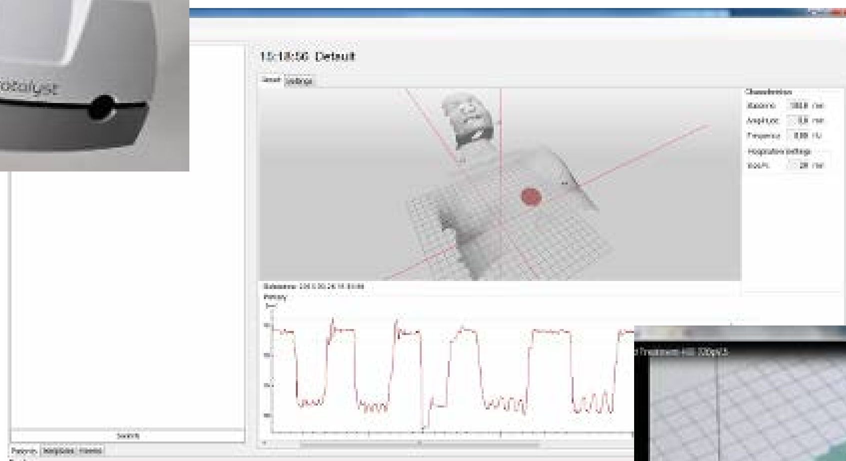
(VI.b)
Lung treatments

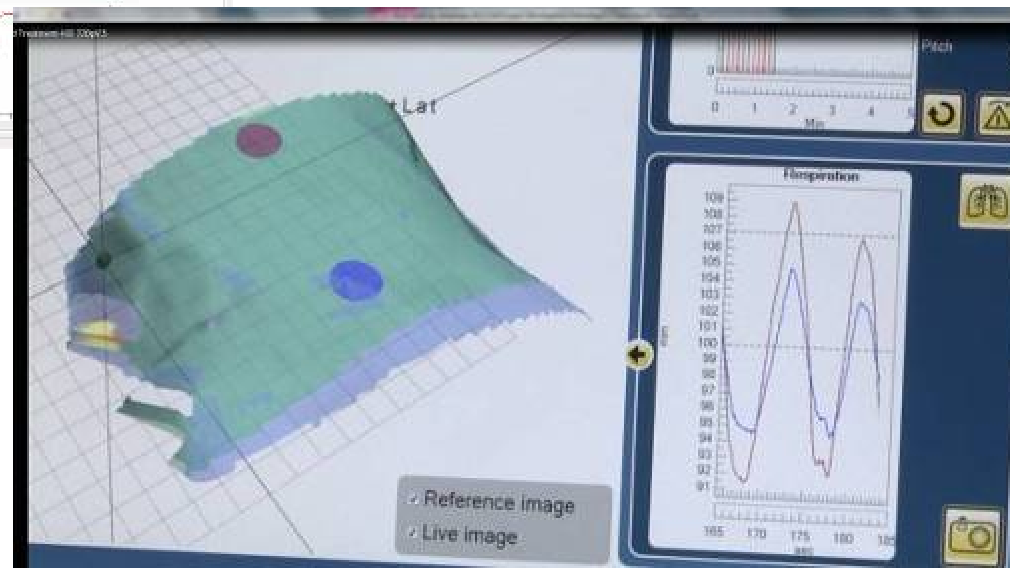
Clinical Setup:
1. Flow-Based Breath Hold Triggering



Boda-Heggemann et al, Radiother Oncol, 2011
Boda-Heggemann et al., Radiother Oncol, 2013

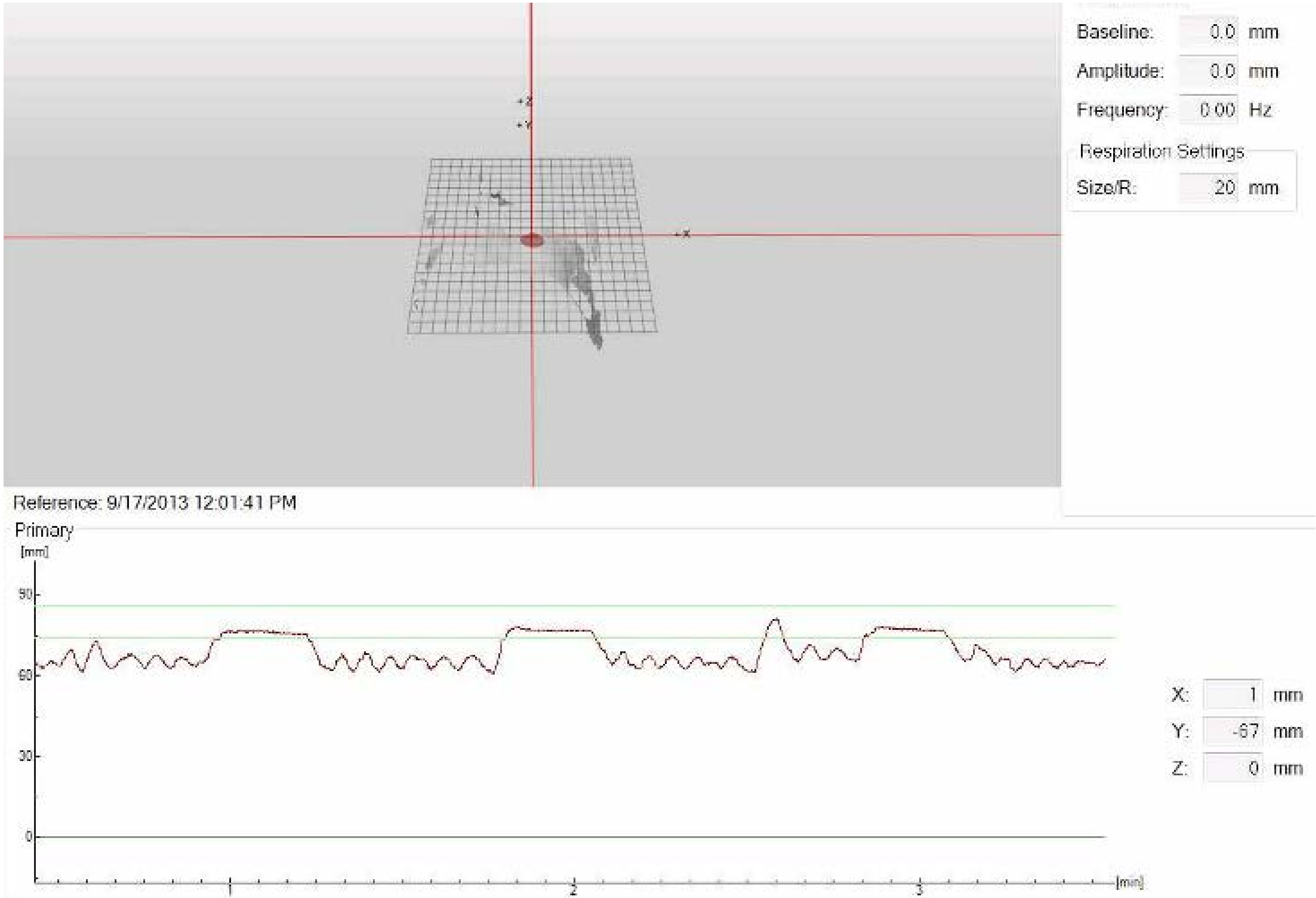
Clinical Setup:
2. Surface-based Surveillance



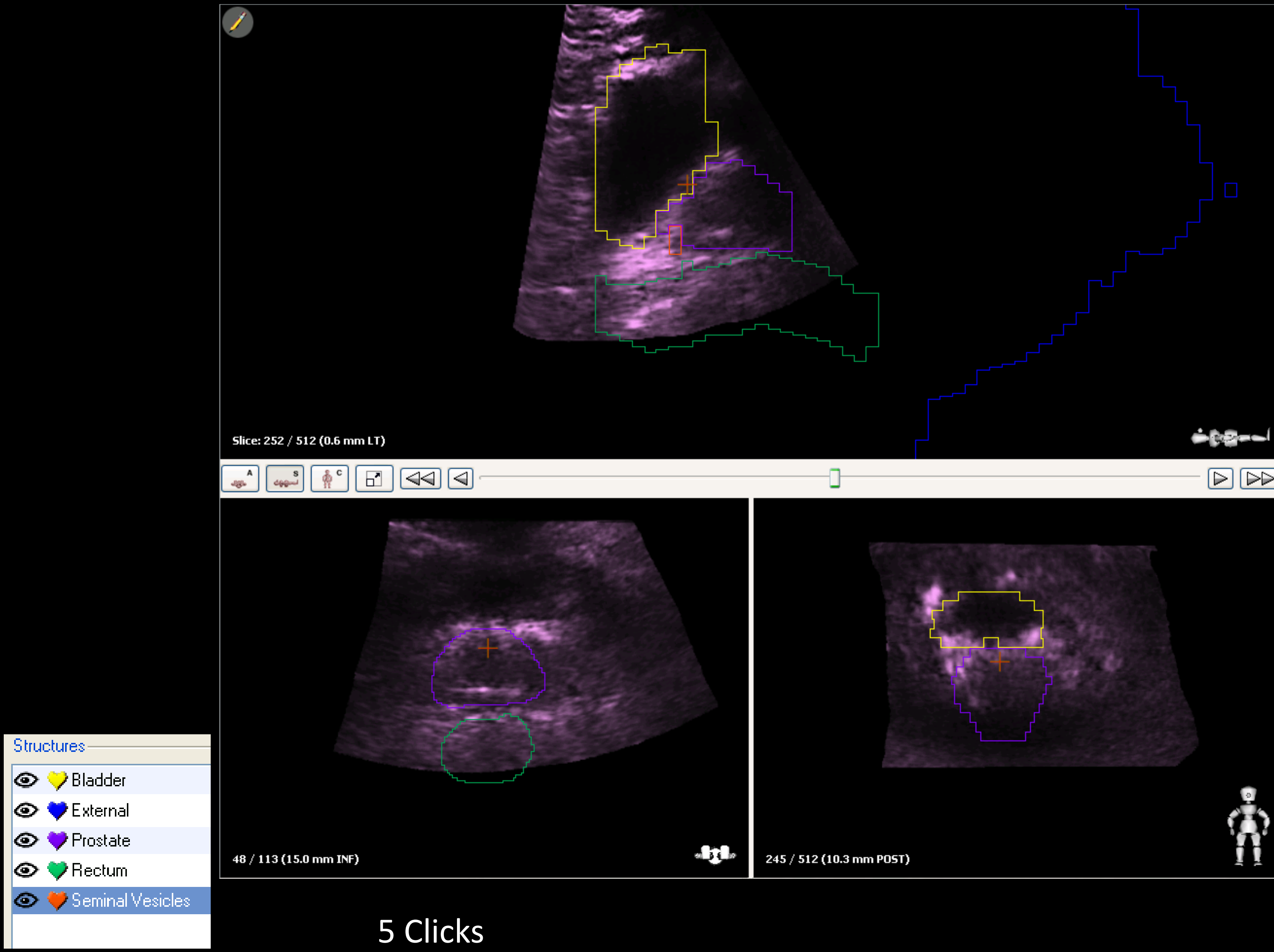


Stieler et al., SUON, 2012
Stieler et al., SUON, 2013

Breath hold surveillance

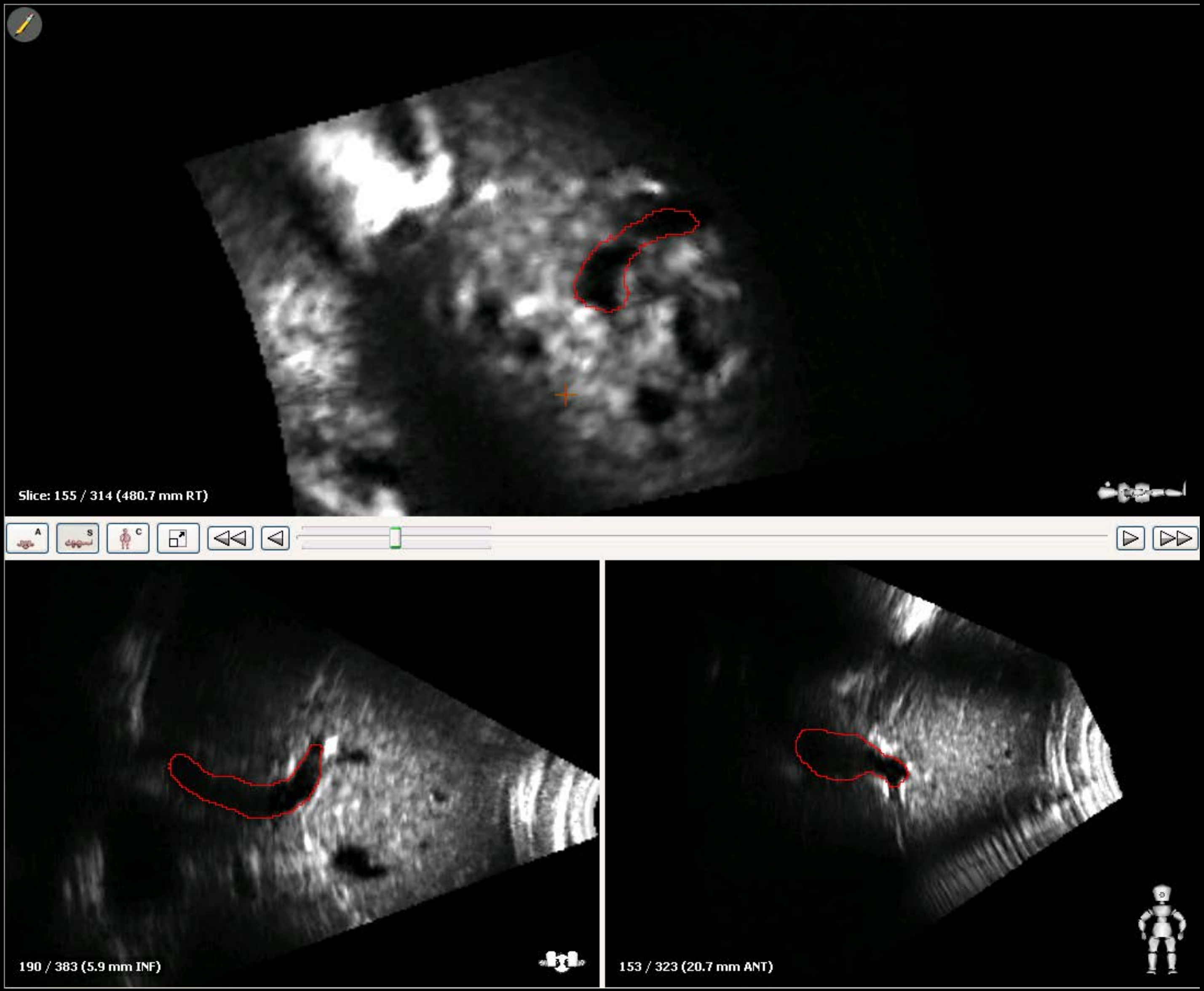


TPUS & TAUS Fused with CT

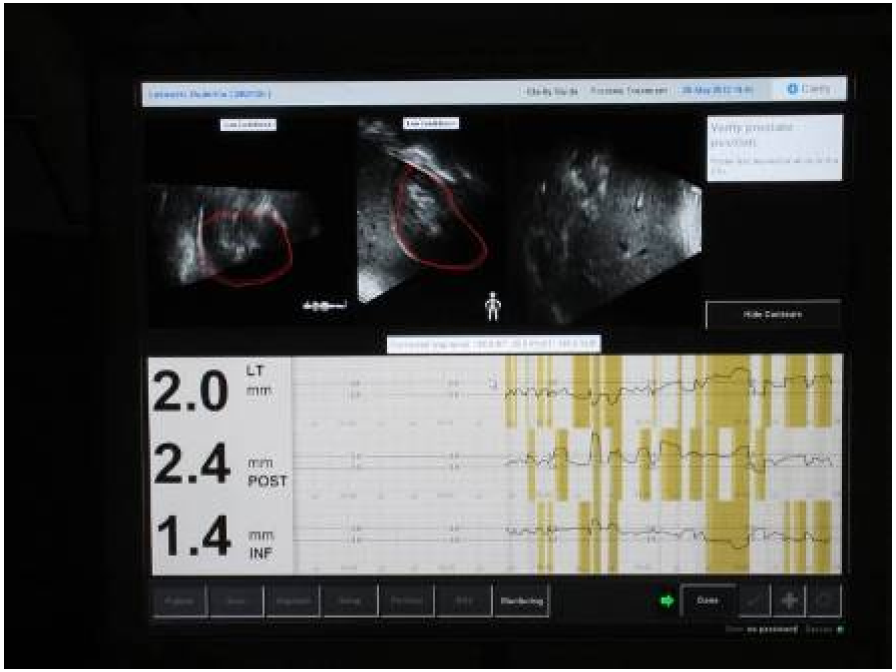


5 Clicks

Tracking Possibilities with the Portal Vein



Clinical Setup:
3. Direct Liver Tracking



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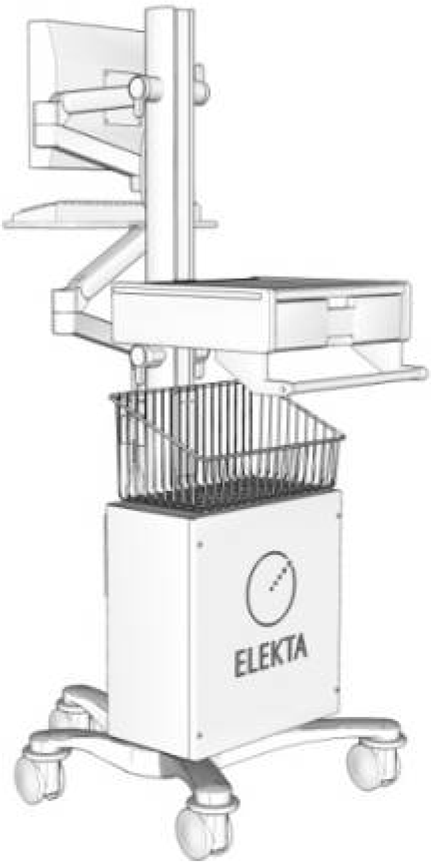
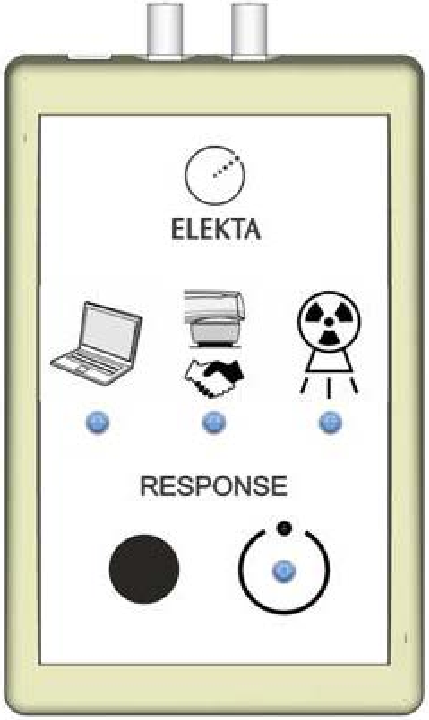
Clinical Setup: Flow-Based Breath Hold Triggering

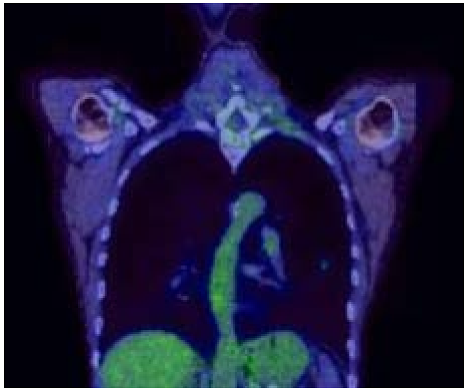




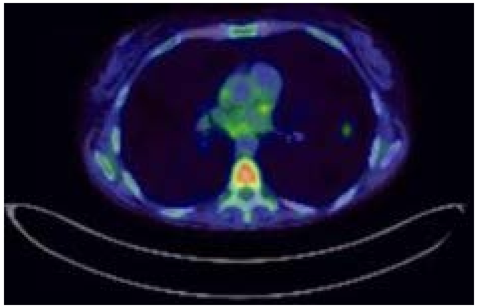
SABR (Stereotactic Ablative Radiotherapy) can be applied in a standard treatment slot

Boda-Heggeman et al.,
Radiother Oncol, 2013

- Flattening-filter-free FFF 10 MV Versa HD
- intensity modulated Monaco dMLC plan
- Active breathing coordinator ABC
- image-guidance XVI, EPID



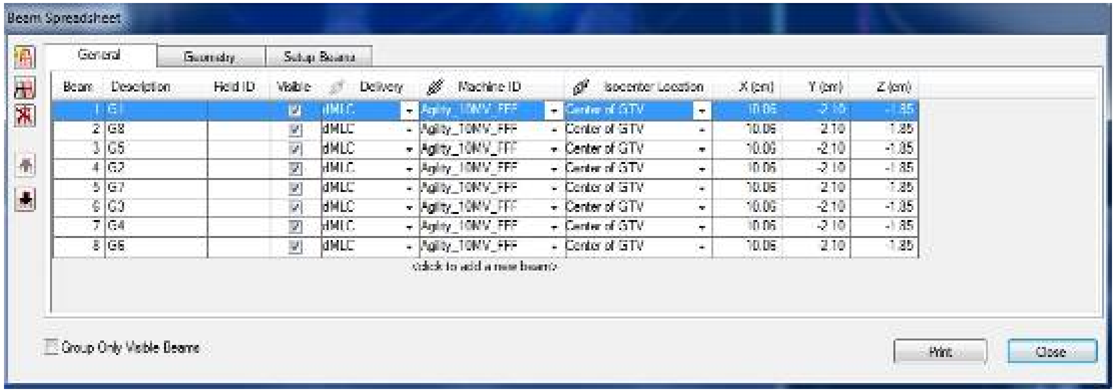
Transversal and coronal PET-CT images of the patient

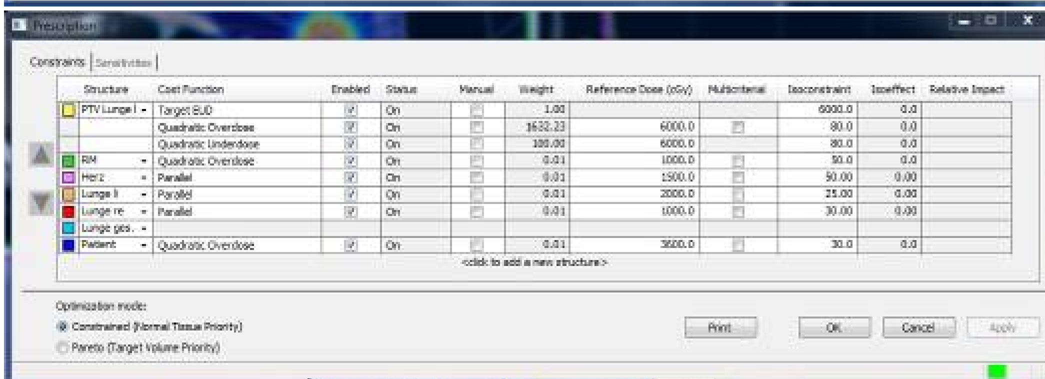


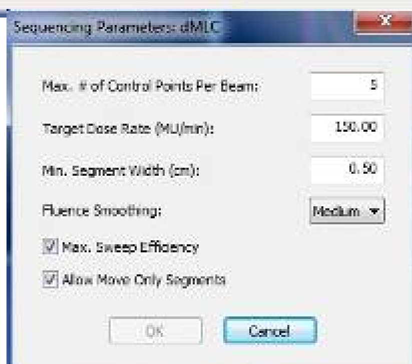
Boda-Heggemann et al., Radiother Oncol, 2013

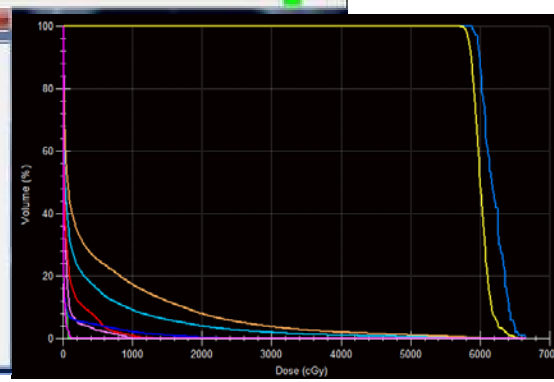
SABR (Stereotactic Ablative Radiotherapy)

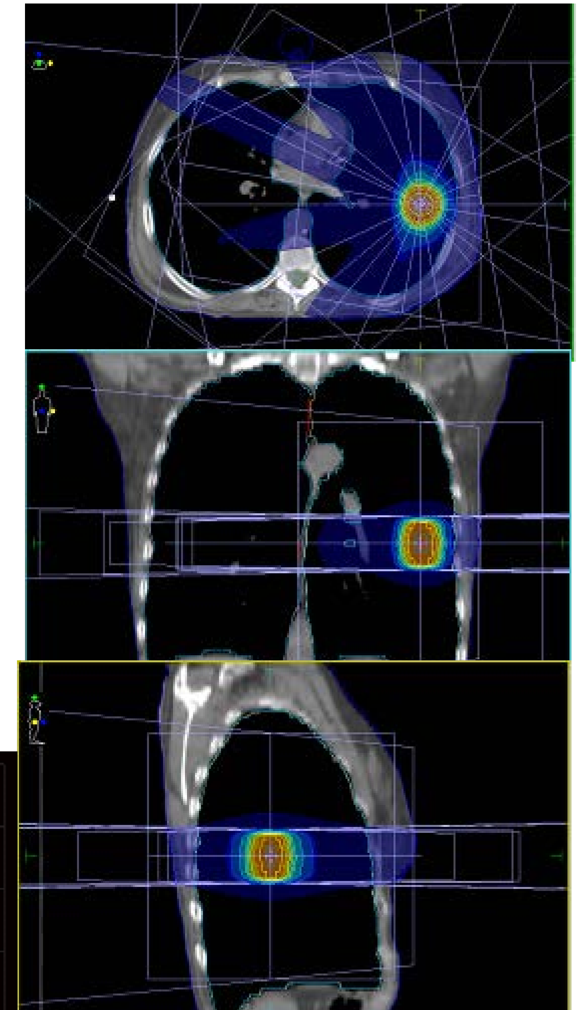
Treatment planning











SABR (Stereotactic Ablative Radiotherapy)

documentation

First fraction setup time incl. ABC/ CBCT and EPID: T= 30 min
treatment time: T= 8 min (8 beams, 2.3k MU)

Plan Information

Studyset ID: CT1 **# of Slices:** 88 **Pixel Size:** 0.12 **Scan Orientation:** HFS

Treatment Position: HEAD IN

Setup Information

Scan Reference Coordinates (cm): No Scan Reference Point has been selected

Beam #	Description	Machine ID	Energy	Gantry	Coll.	Couch	Isocenter X	Isocenter Y	Isocenter Z	# of Segs	MU/fx
1	G1	Agility_10MV_FFF	10 (FFF)	190.0	0.0	0.0	10.06	-2.10	-1.85	4	325.68
2	G8	Agility_10MV_FFF	10 (FFF)	220.0	0.0	0.0	10.06	-2.10	-1.85	4	286.03
3	G5	Agility_10MV_FFF	10 (FFF)	295.0	0.0	0.0	10.06	-2.10	-1.85	4	253.22
4	G2	Agility_10MV_FFF	10 (FFF)	335.0	0.0	0.0	10.06	-2.10	-1.85	4	236.79
5	G7	Agility_10MV_FFF	10 (FFF)	0.0	0.0	0.0	10.06	-2.10	-1.85	4	280.43
6	G3	Agility_10MV_FFF	10 (FFF)	30.0	0.0	0.0	10.06	-2.10	-1.85	4	237.69
7	G4	Agility_10MV_FFF	10 (FFF)	80.0	0.0	0.0	10.06	-2.10	-1.85	4	341.93
8	G6	Agility_10MV_FFF	10 (FFF)	140.0	0.0	0.0	10.06	-2.10	-1.85	4	298.01
9	VER1	Agility_6MV_Int	6	0.0	0.0	0.0	10.06	-2.10	-1.85	0	0.00
10	VER2	Agility_6MV_Int	6	90.0	0.0	0.0	10.06	-2.10	-1.85	0	0.00
									Total:	32	2259.77

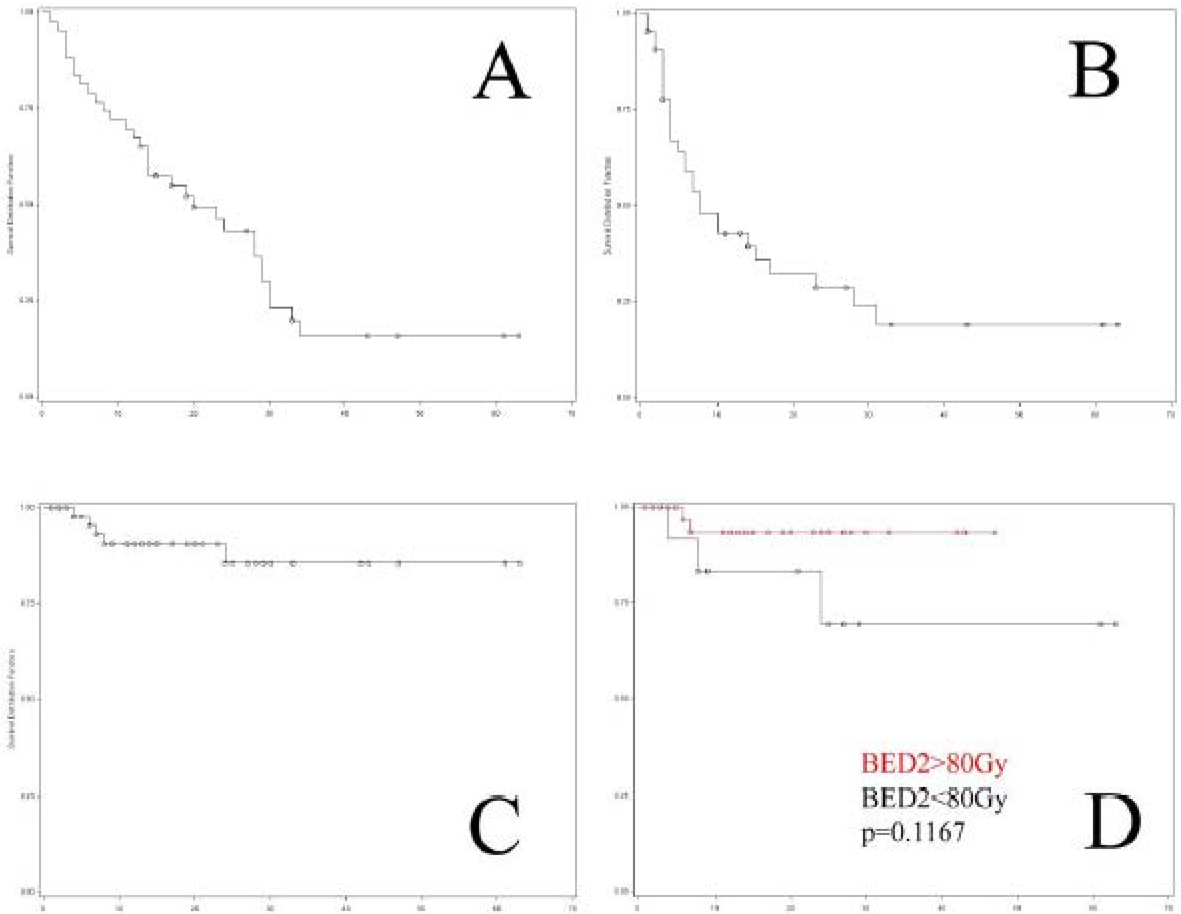
Normalization

Prescription (cGy): 6000.0 # of Fractions: 5 (1,200.00 cGy/fx)

Rad Rx: Lungenmetastase FFF - IMRT Plan - Xrays Dose: 6.000 cGy @ 1.200 cGy		A 26.3.2013 SM
Site Setup		AE 22.3.2013 KS
Treatment Fields		
G1 - 190° Lunge ABC FFF - 10 X FFF DMLC 5 Control Points	26.03.2013	A 26.3.2013 SM
G8 - 220° Lunge ABC FFF - 10 X FFF DMLC 5 Control Points	26.03.2013	A 26.3.2013 SM
G5 - 295° Lunge ABC FFF - 10 X FFF DMLC 5 Control Points	26.03.2013	A 26.3.2013 SM
G2 - 335° Lunge ABC FFF - 10 X FFF DMLC 5 Control Points	26.03.2013	A 26.3.2013 SM
G7 - 0° Lunge ABC FFF - 10 X FFF DMLC 5 Control Points	26.03.2013	A 26.3.2013 SM
G3 - 30° Lunge ABC FFF - 10 X FFF DMLC 5 Control Points	26.03.2013	A 26.3.2013 SM
G4 - 80° Lunge ABC FFF - 10 X FFF DMLC 5 Control Points	26.03.2013	A 26.3.2013 SM
G6 - 140° Lunge ABC FFF - 10 X FFF DMLC 5 Control Points	26.03.2013	A 26.3.2013 SM
VER1 - 0° Lunge ABC FFF - 6 X MLC	26.03.2013	A 26.3.2013 SM
VER2 - 90° Lunge ABC FFF - 6 X MLC	26.03.2013	A 26.3.2013 SM
CT1 - FFF - CT		A 25.3.2013 KH
EPID - 0° - 10 X FFF	26.03.2013	A 26.3.2013 SM

62	26.03.2013	11:46	11Fld			1PI			LB2					1	1.200 cGy	1.200 cGy
		11:46	CT1			CT			LB2		+	Sv/Sv				
		11:53	VER2	1			2,0 MU		LB2		^	Sv				
		11:54	VER1	2			4,0 MU		LB2		^ +	Sv				
		12:01	EPID	2			10,1 MU		LB2		^ +	Sv/Sv				
		12:05	G7	1			280,4 MU	150 cGy	LB2		^	Sv			150 cGy	
		12:06	G3	1			237,7 MU	150 cGy	LB2		^	Sv			150 cGy	
		12:07	G4	1			341,9 MU	150 cGy	LB2		^	Sv			150 cGy	
		12:08	G6	1			298,0 MU	150 cGy	LB2		^	Sv			150 cGy	
		12:10	G1	1			325,7 MU	150 cGy	LB2		^	Sv			150 cGy	
		12:11	G8	1			286,0 MU	150 cGy	LB2		^	Sv			150 cGy	
		12:12	G5	1			253,3 MU	150 cGy	LB2		^	Sv			150 cGy	
		12:13	G2	1			236,8 MU	150 cGy	LB2		^	Sv			150 cGy	

Clinical Results Image Guided BH-Lung SABR



Boda-Heggemann et al., submitted

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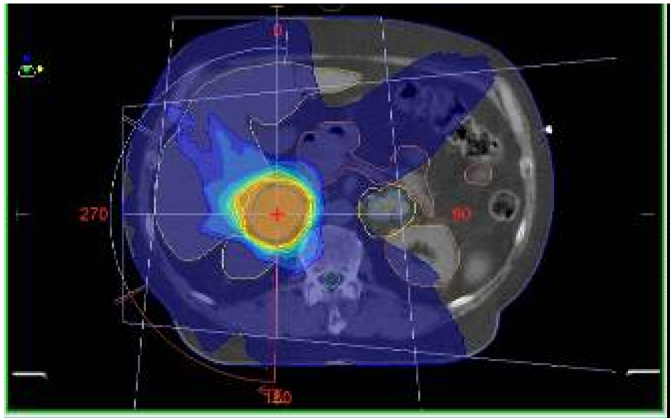
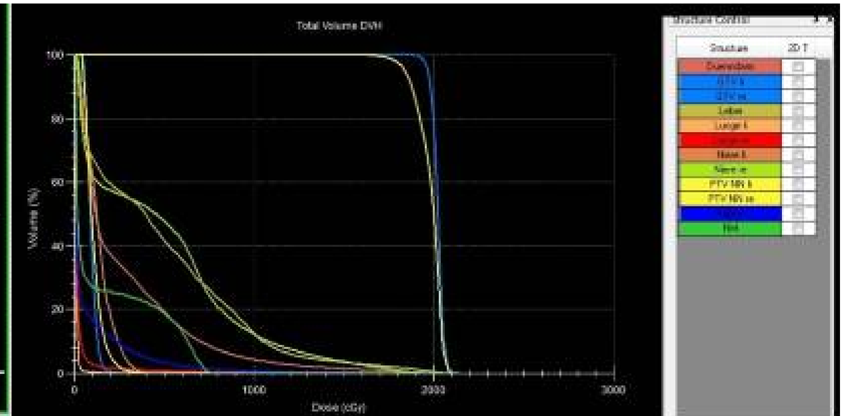
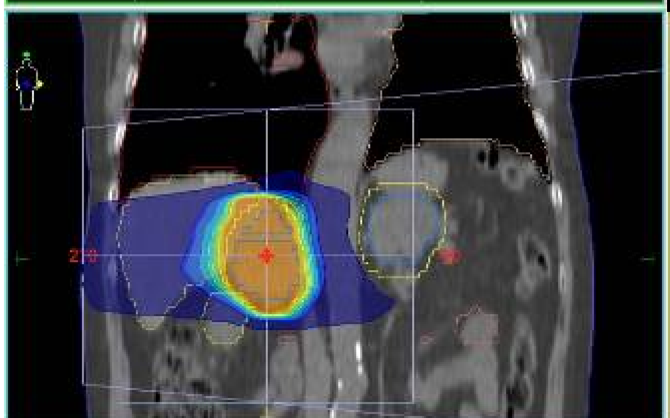
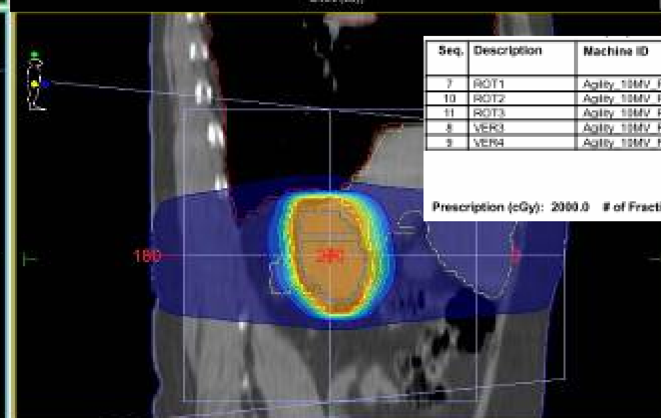
(VI.c)
Treatment of adrenal glands

Right adrenal gland
3 × 60° partial VMAT arcs, D= (4 × 5) Gy





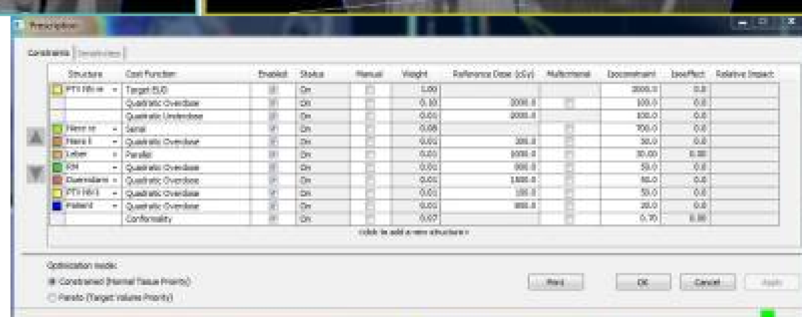




Seq.	Description	Machine ID	Energy	Gantry	Coll.	Couch	Isocenter X	Y	Z	# of Segs	MU/fx
7	ROT1	Agility_10MV_FFF	10 (FFF)	181.0/60.0	0.0	0.0	-4.68	-140.70	-0.85	13	295.37
10	ROT2	Agility_10MV_FFF	10 (FFF)	242.0/60.0	0.0	0.0	-4.68	-140.70	-0.85	14	287.95
11	ROT3	Agility_10MV_FFF	10 (FFF)	303.0/60.0	0.0	0.0	-4.68	-140.70	-0.85	15	356.32
8	VER3	Agility_10MV_FFF	10 (FFF)	0.0	0.0	0.0	-4.68	-140.70	-0.85	0	0.00
9	VER4	Agility_10MV_FFF	10 (FFF)	270.0	0.0	0.0	-4.68	-140.70	-0.85	0	0.00
									Total:	42	939.64

Normalization

Prescription (cGy): 2000.0 # of Fractions: 4 (500.00 cGy/fx)



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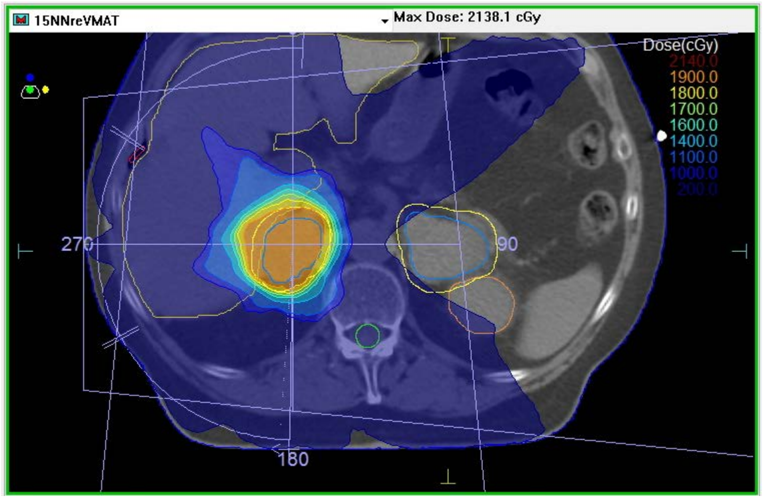
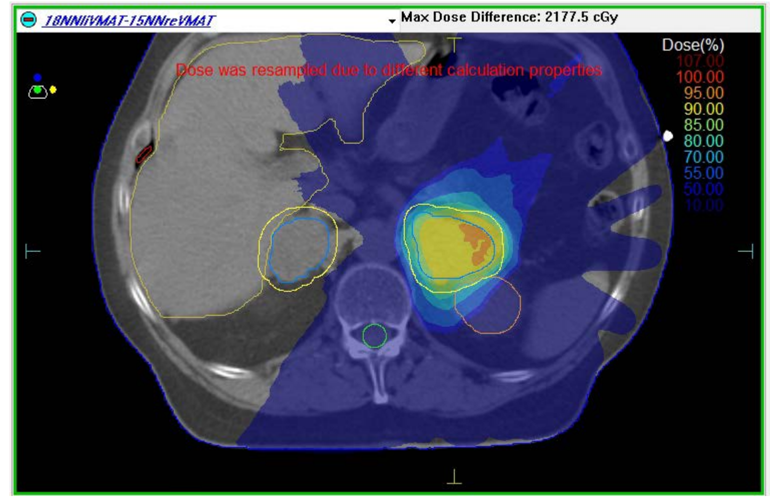
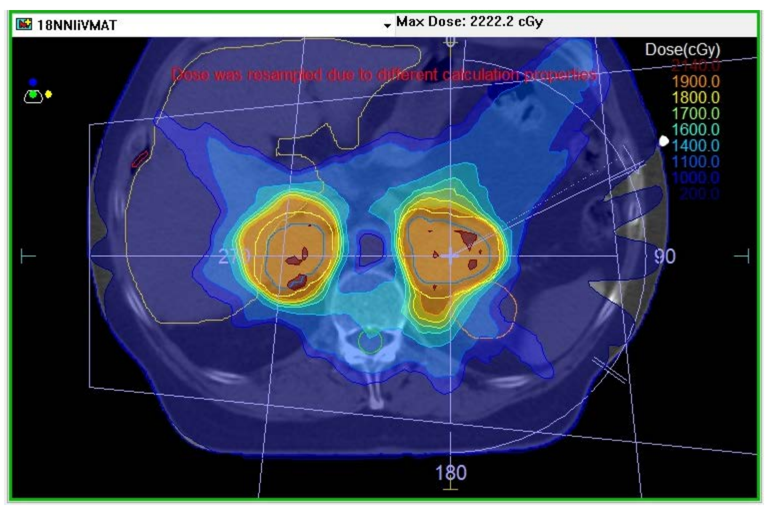
Sum plan adrenal glands
D= (4 × 5) Gy, T= 3 min







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(VI.d)
Liver treatment

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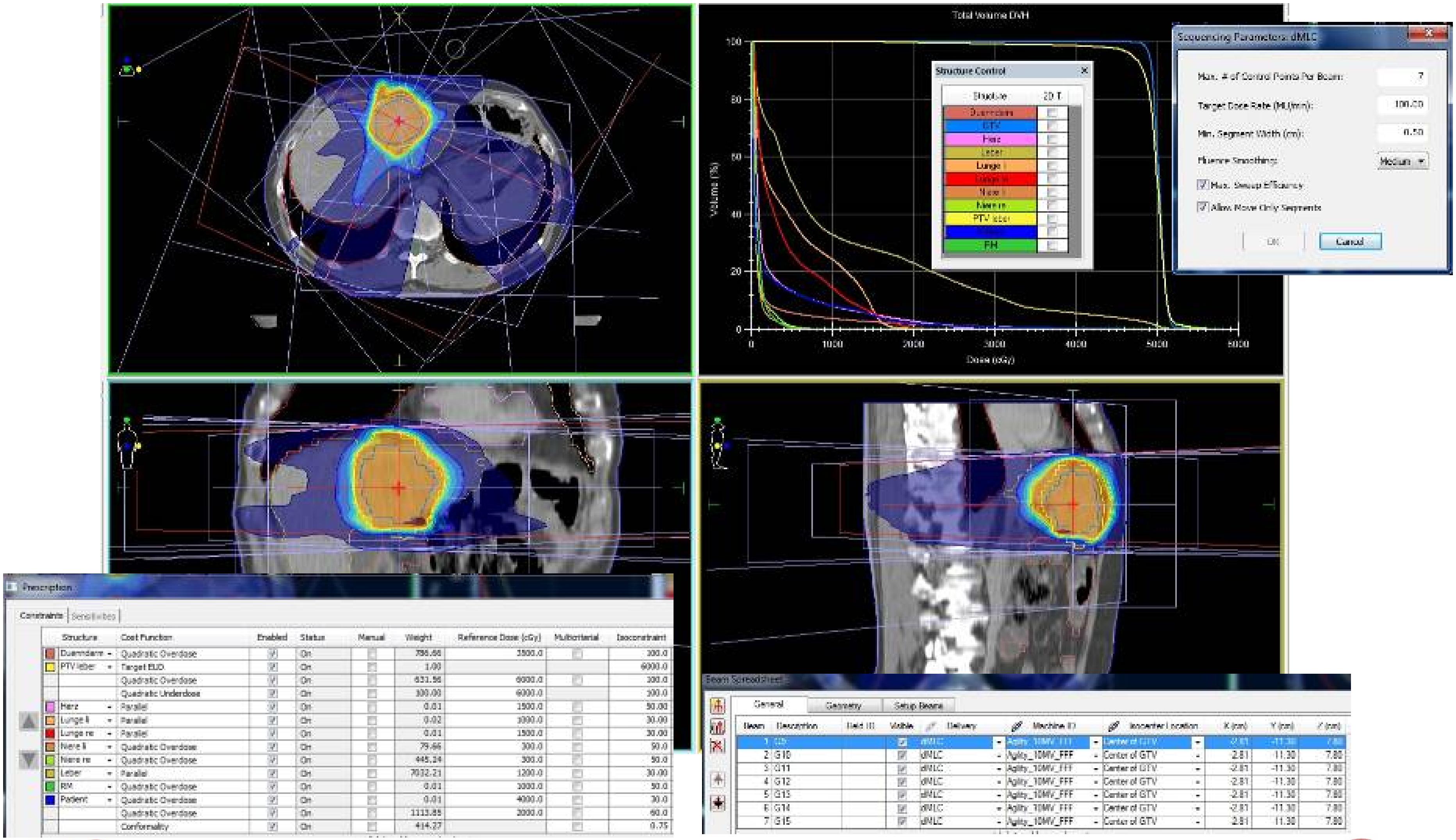
7 fields dMLC, 10 MV
T= 6 min, D= (10 × 5) Gy



Clinical Results Liver

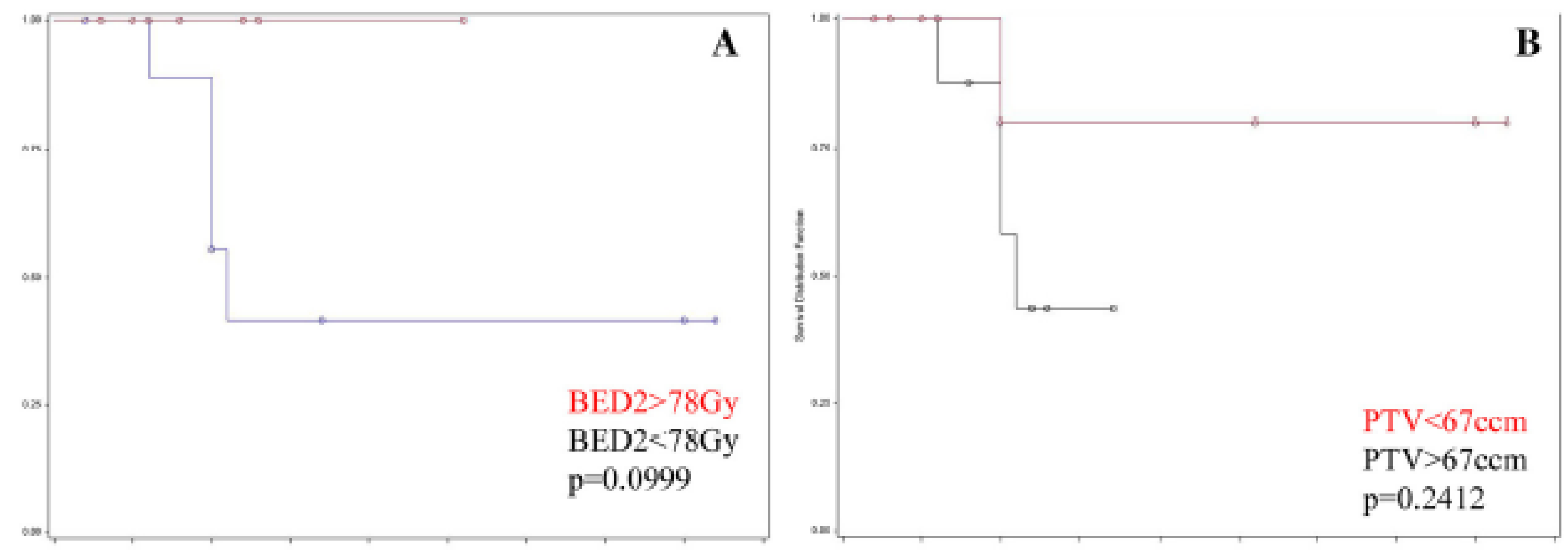
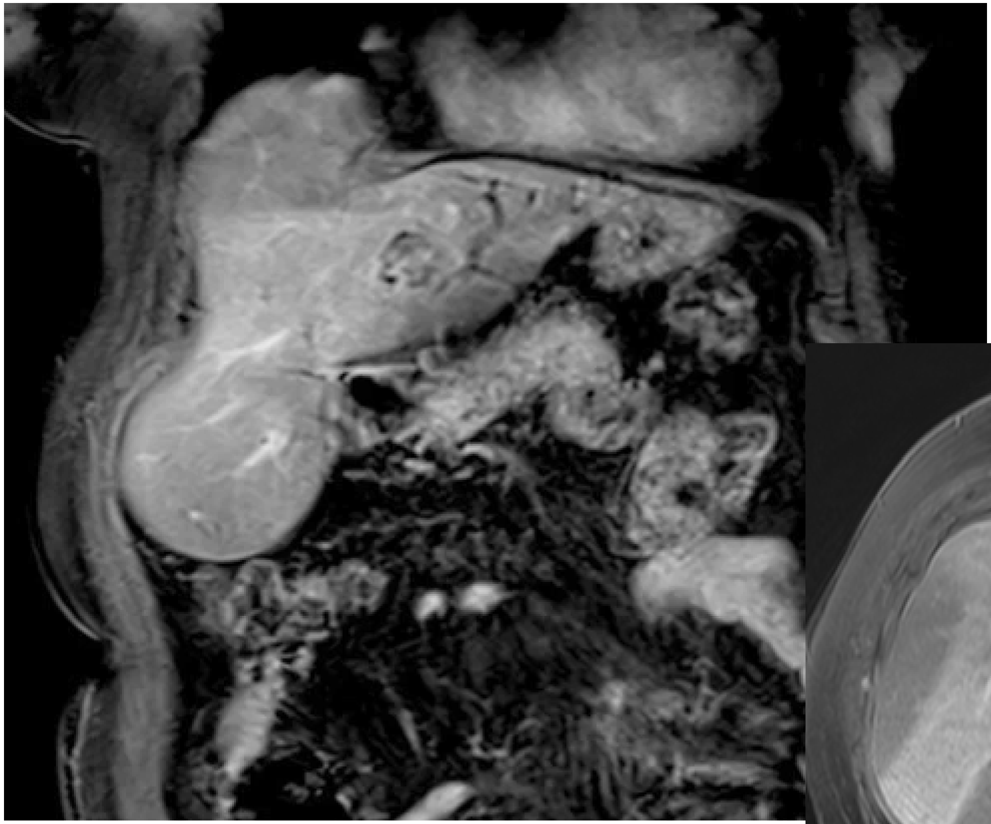
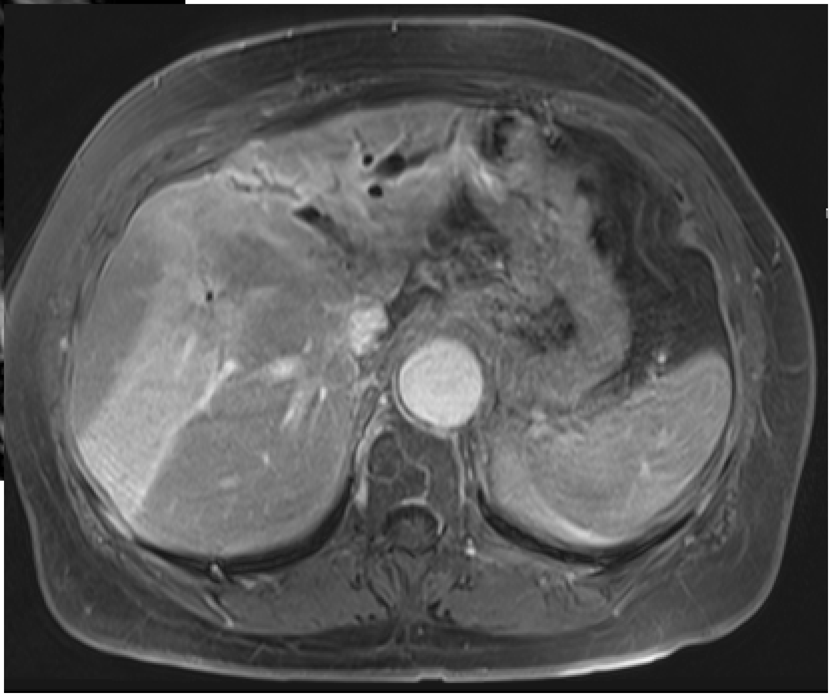


Figure 3 A) Local control of patients with BED2 ≥ 78 Gy (red) and <78 Gy (black), p = 0.0999 (trend to significance; Kaplan-Meier log-rank test). B) Local control of patients with PTV < 67 cm^3 (red) and ≥67 cm^3 (black), p = 0.2412, not significant.

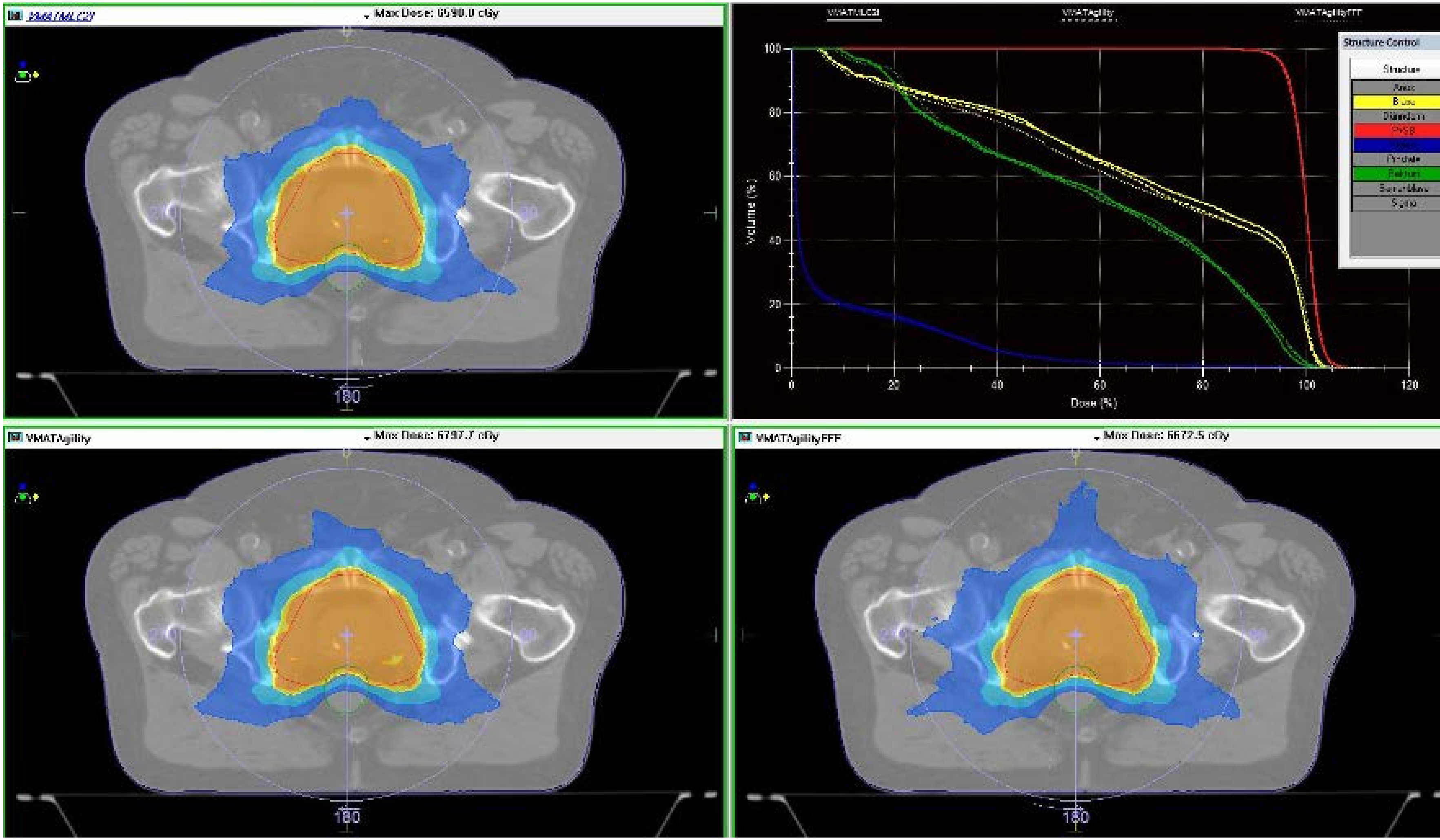
Boda-Heggemann et al., Rad Onc, 2012





(VII)
Comparison of
MLCi2 – Agility - Versa HD
treatment times

Prostate
moderately complex, D= (30 × 2) Gy, 1 VMAT arc



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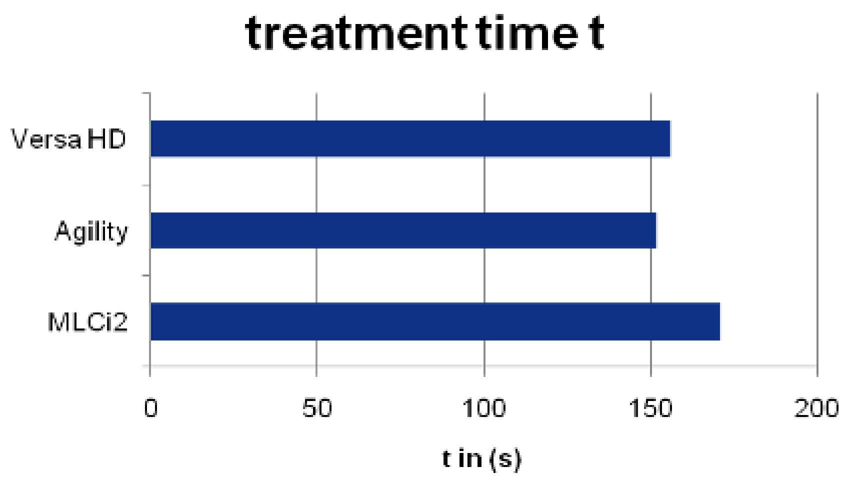
Prostate
moderately complex, D= (30 × 2) Gy, 1 VMAT arc

PROSTATE	MLCi2 Monaco 3.3	Agility Monaco 3.3	Versa HD Monaco 3.3
Homogenity index	1.09	1.09	1.09
OAR Rectum, mean dose	35.8Gy	35.6	35.96 Gy
OAR Bladder, mean dose	42.3 Gy	41.7	40.95 Gy
beam-on time per fraction	171 s	152 sec	156 s
number of MU's delivered	789	762	915



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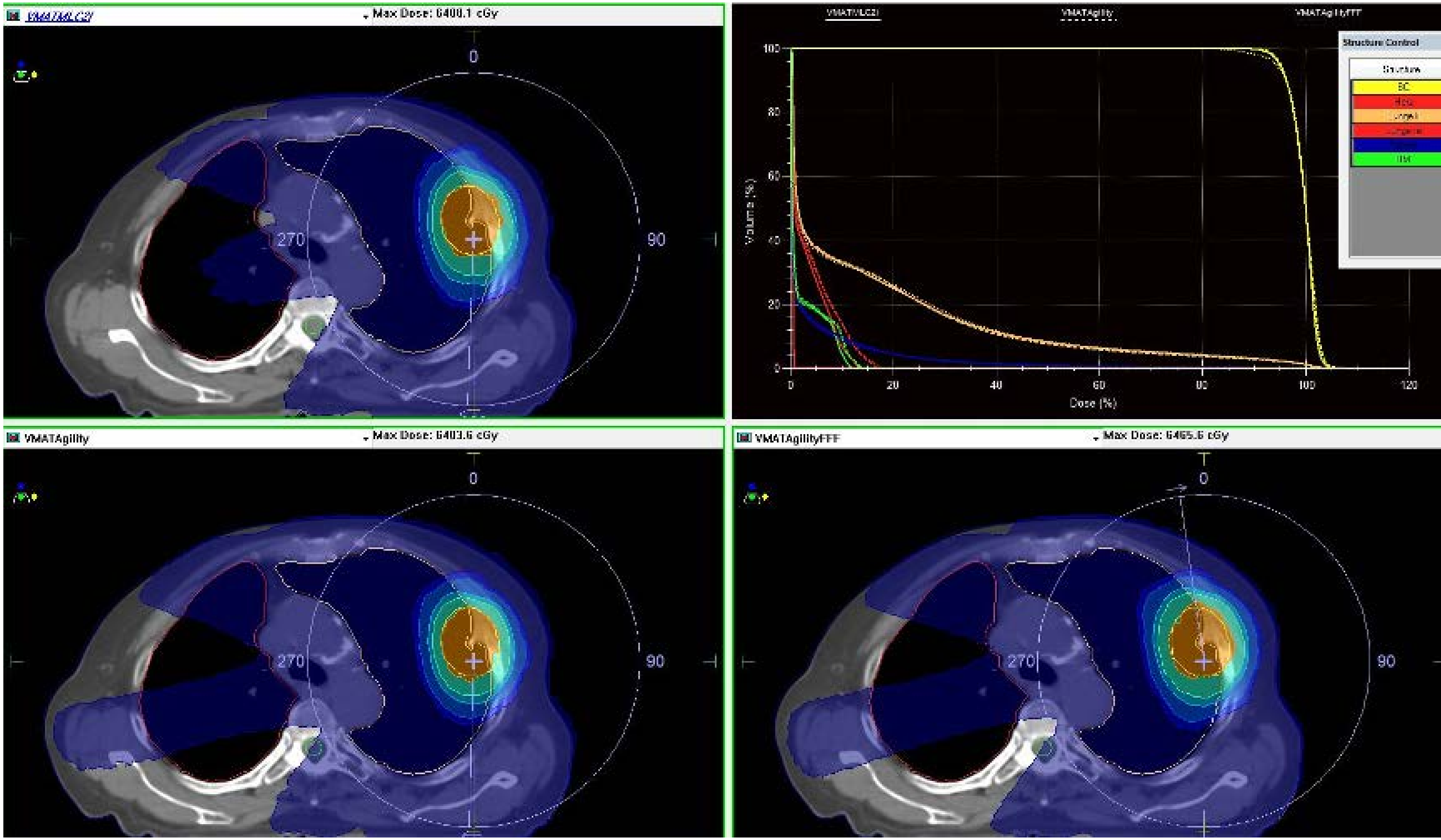
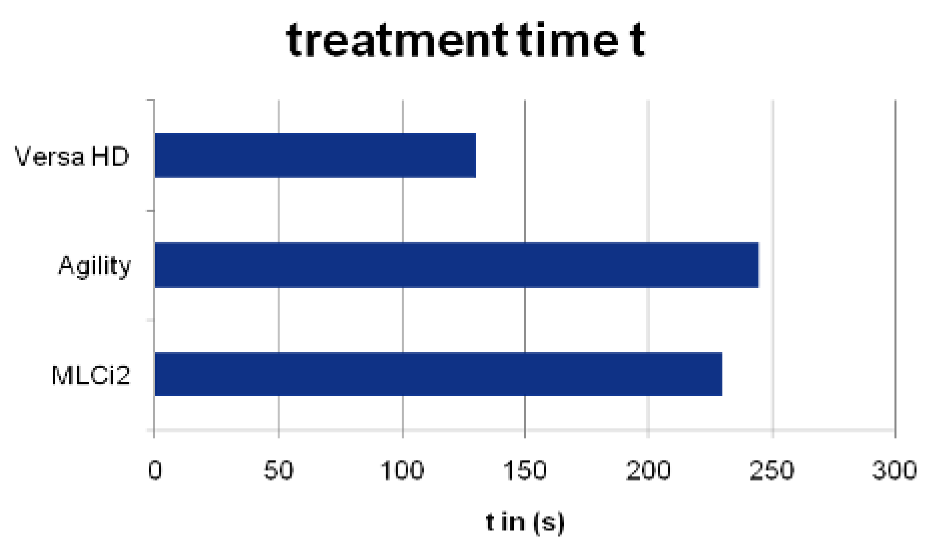
Lung
moderately complex, D= (5 × 12) Gy, 1 VMAT arc

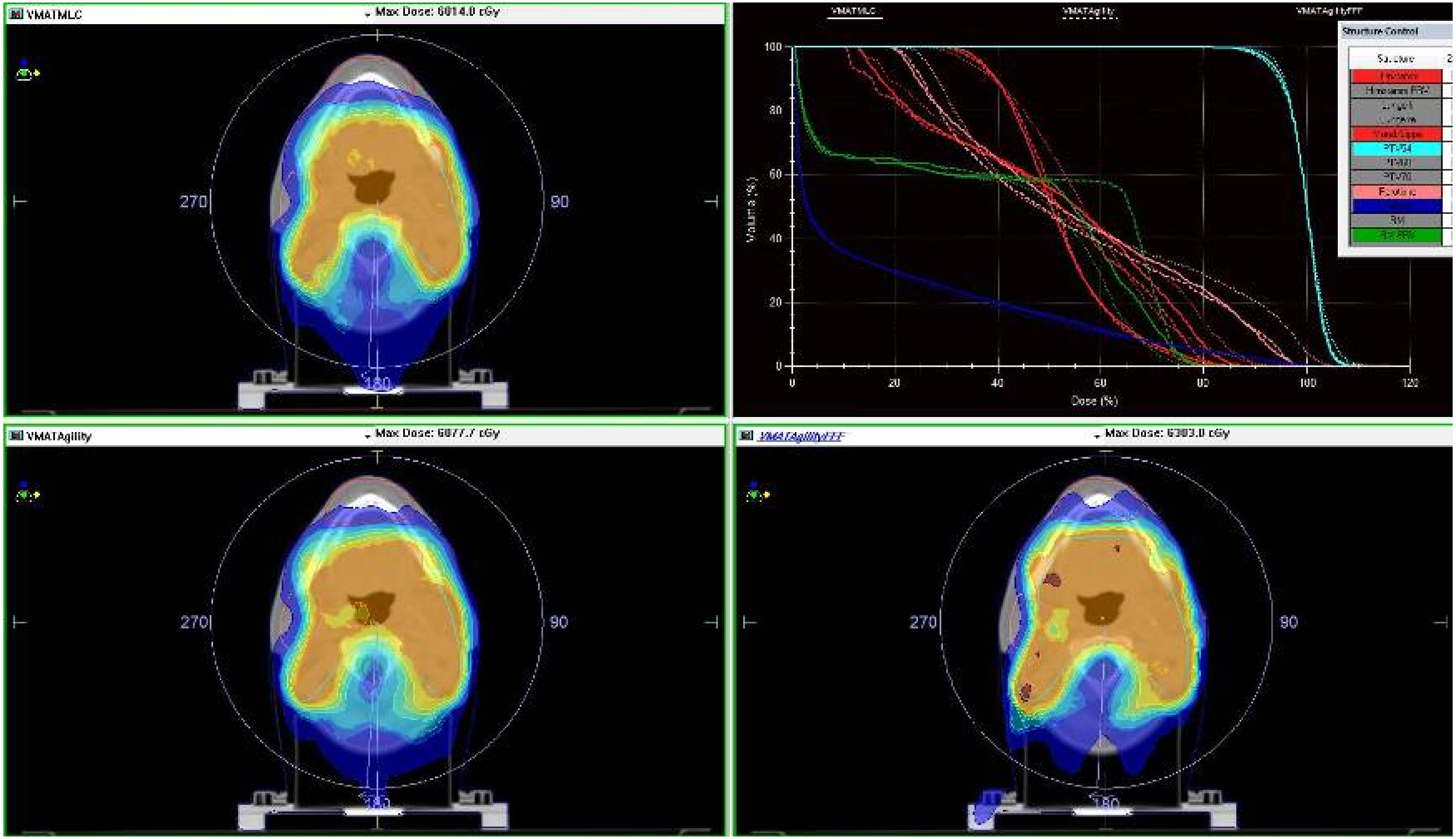


Lung
moderately complex, D= (5 × 12) Gy, 1 VMAT arc

LUNG	MLCi2 Monaco 3.3	Agility Monaco 3.3	Versa HD Monaco 3.3
Homogeneity Index	1.09	1.09	1.09
OAR Lung left, mean dose	8.25 Gy	8.13 Gy	8.35 Gy
OAR Lung right, mean dose	1.80 Gy	2.2 Gy	2.15 Gy
OAR Heart, Mean dose	0.18 Gy	0.17 Gy	0.17 Gy
beam-on time per fraction	230 s	245 s	130 s
number of MU's delivered	2014	1997	2281



Head & Neck
complex segmentation, D= (30 × 1.8) Gy, 2 VMAT arcs



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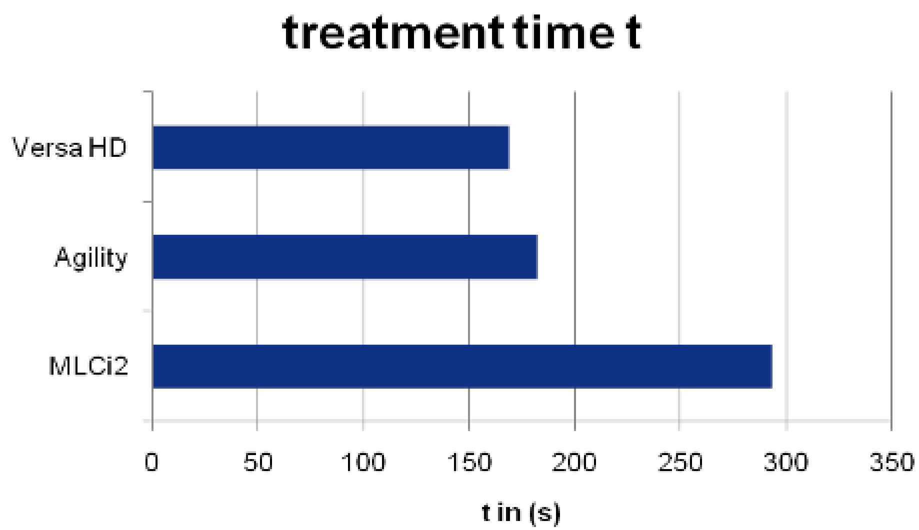
Head & Neck
highly complex, D= (30 × 1.8) Gy, 2 VMAT arcs

Head and neck	MLCi2 Monaco 3.3	Agility Monaco 3.3	Versa HD Monaco 3.3
Homogeneity Index	1.12	1.14	1.13
OAR Parotis, mean dose	29.79 Gy	28.86 Gy	30.91 Gy
OAR Spinal Cord, max dose	44.33 Gy	42.40 Gy	44.62 Gy
OAR Lips, Mean dose	27.99 Gy	28.01 Gy	30.82 Gy
OAR Brain stem, mean dose	28.32 Gy	26.94 Gy	29.46 Gy
beam-on time per fraction	293 s	182 s	169 s
number of MU's delivered	635	633	1123



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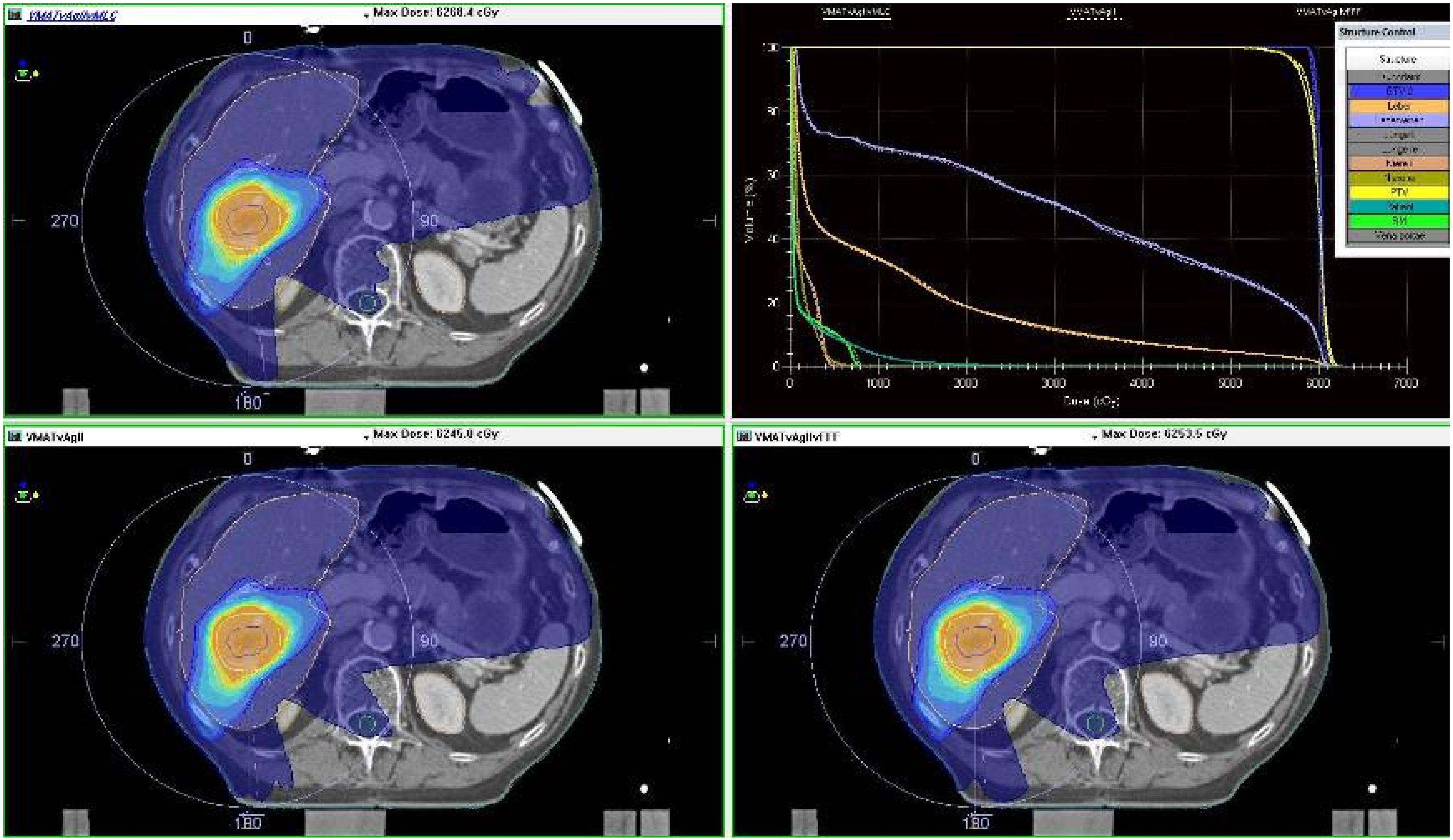
Liver
moderately complex, D= (5 × 12) Gy, 1 VMAT arc



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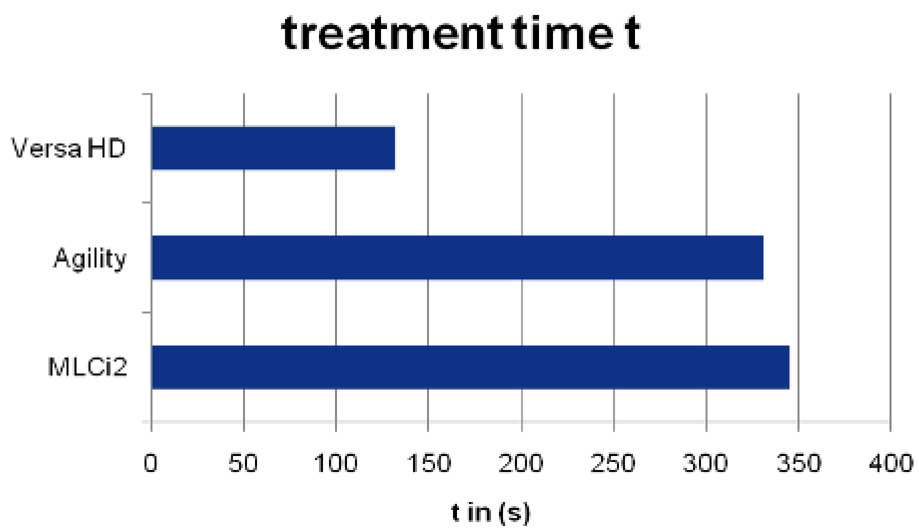
Liver
moderately complex, D= (5 × 12) Gy, 1 VMAT arc

LIVER	MLCi2 Monaco 3.3	Agility Monaco 3.3	Versa HD Monaco 3.3
Homogeneity index	1.07	1.06	1.06
OAR Liver, mean dose	10.57 Gy	10.46 Gy	10.44 Gy
OAR Kidney, max dose	8.63 Gy	8.15 Gy	8.13 Gy
OAR Spinal Cord, max dose	7.82 Gy	7.91 Gy	8.20 Gy
beam-on time per fraction	345 s	331 s	132 s
number of MU's delivered	2494	2710	2733



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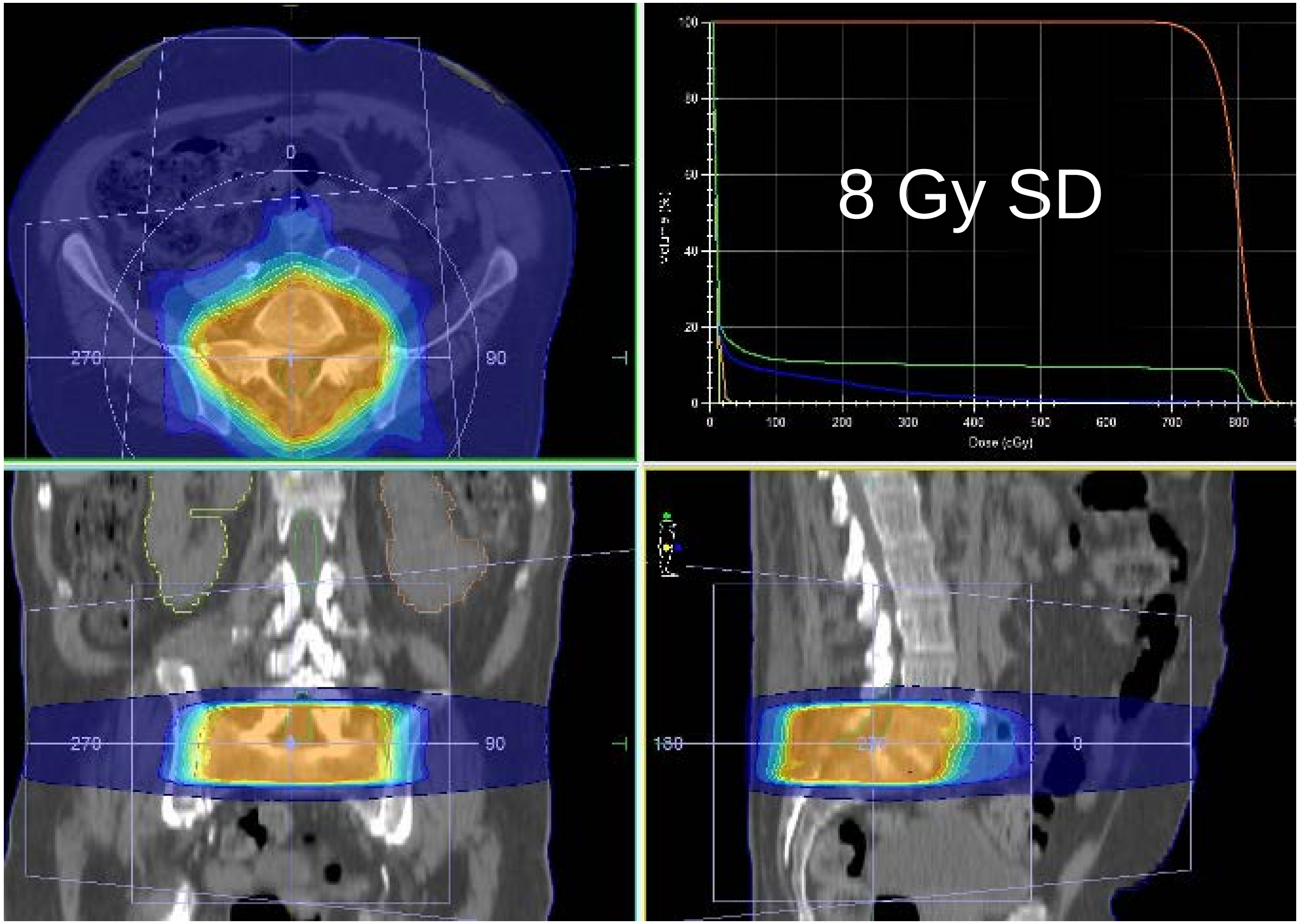
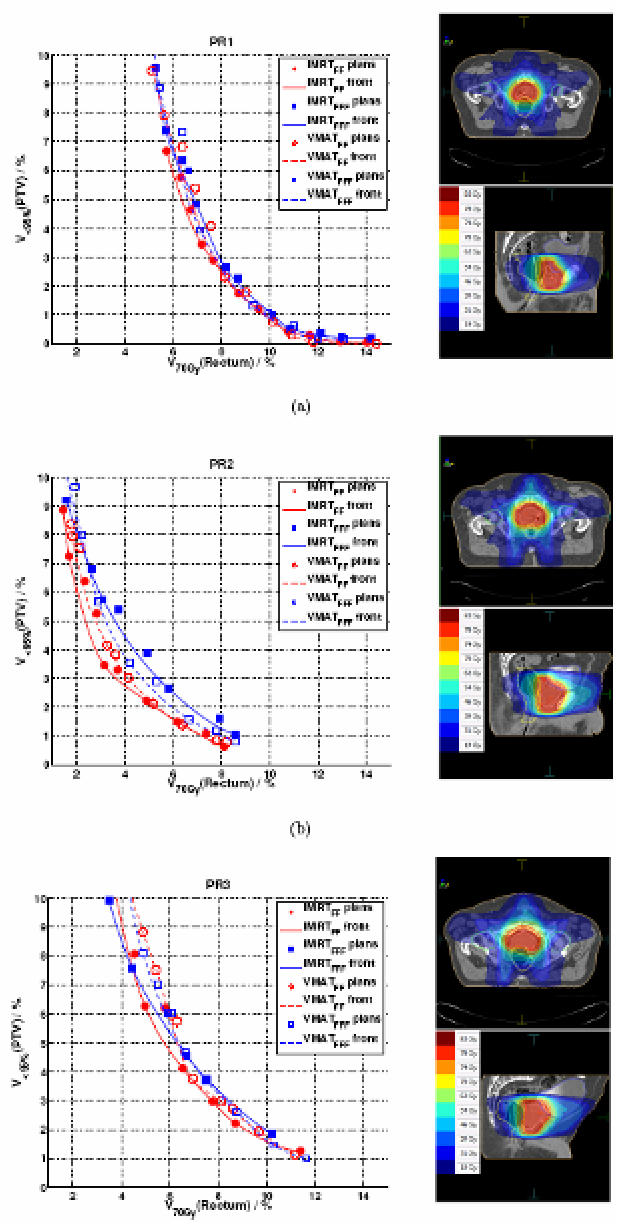
Palliative Spinal RT – Hypofractionated FFF

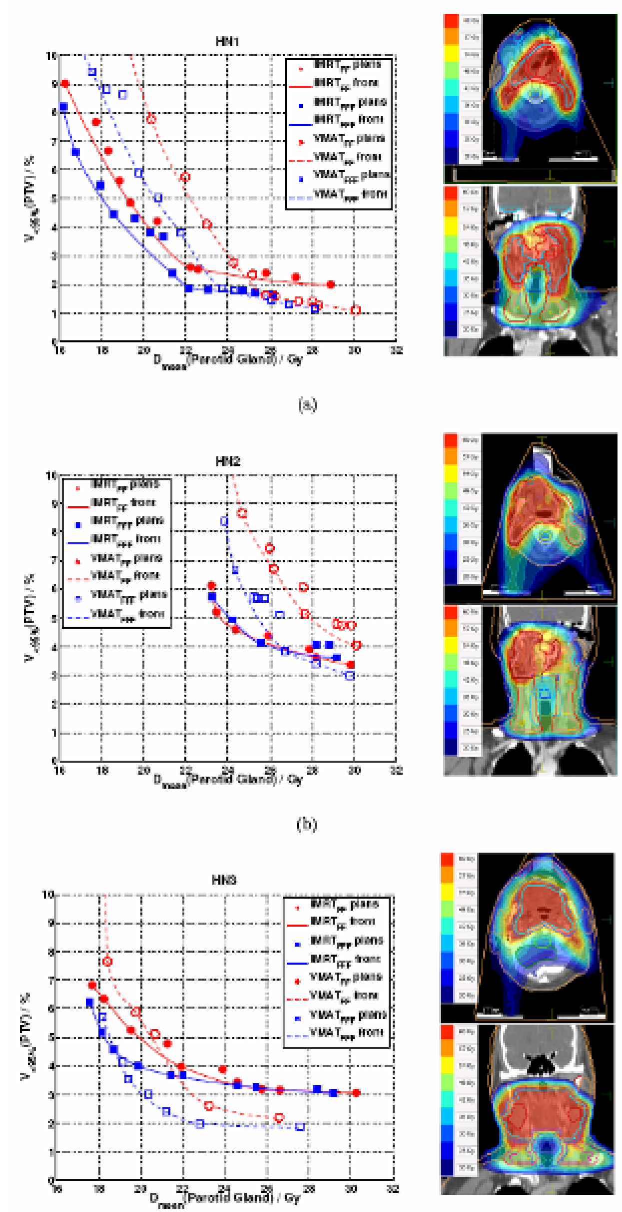


Evaluation of treatment plan quality of IMRT and VMAT with and without flattening filter using Pareto optimal fronts

Lechner et al., submitted

Courtesy AKH Vienna





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Dose Rate effects in Photon and Particle treatments - Are high dose rates problematic?

Dose Rate? Pulse Rate??? Dose per Pulse????

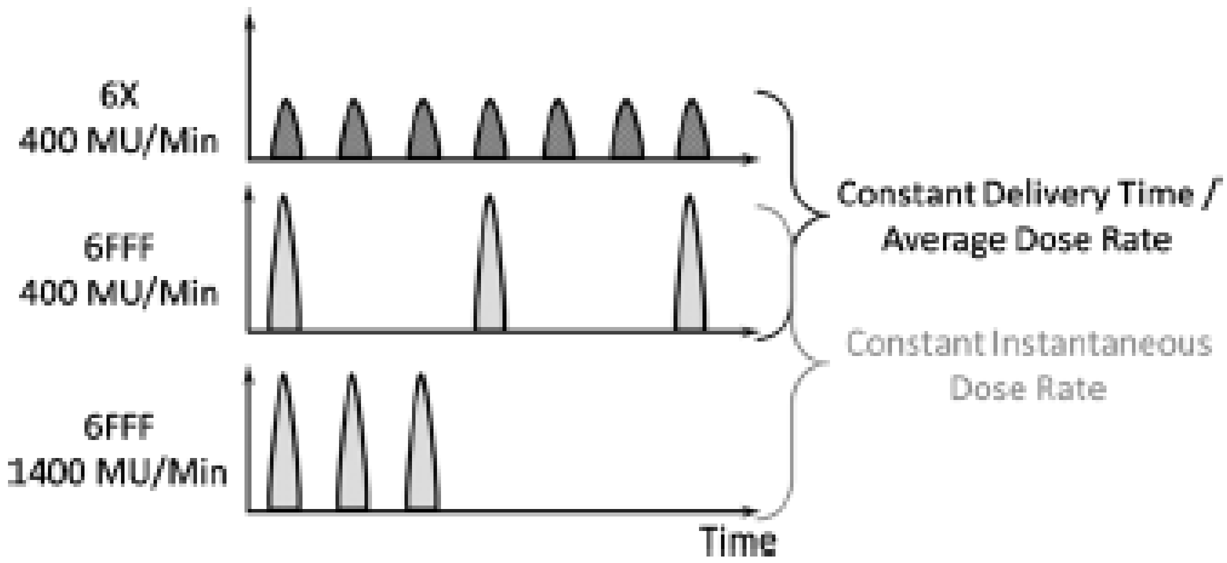


Figure 1. Schematic illustrating the different dose-per-pulse and pulse repetition frequencies of the x-ray fields used in this study.

King et al., PMB, 2013

Negative Studies

Michaels, Rad Res, 1978 (OER, field emitting device)
Ling, IJROBP, 1985 (OER)
Steel et al., 1990 (cell lines, 0,25-90 cGy/min)
“There was little evidence of a dose-rate effect above 2 cGy/min but significant sparing was seen at lower dose rates”

Zackrisson, Acta Oncol, 1991 (cell lines, HDR e-, 24000Gy/min)
Soerensen, R&O, 2011 (cell lines, diff. DR/pulse)
Verbakel, Acta Oncol, 2013 (cell lines, moving strip)
King, PMB, 2013 (cell lines, mesh buildup)

Reviews bei
Ling, R&O, 2010
Wilson, Br J Radiol, 2012 (Oxygen depletion)

Positive Studies

Lohse, R&O, 2011

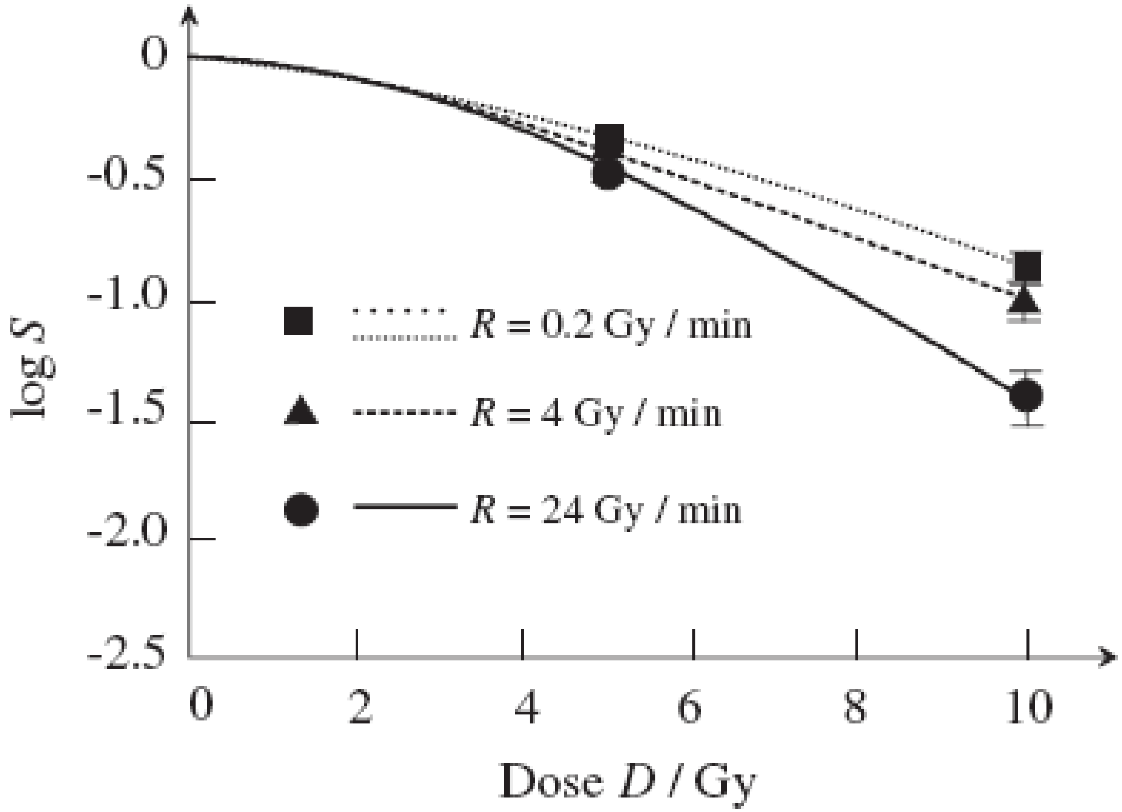
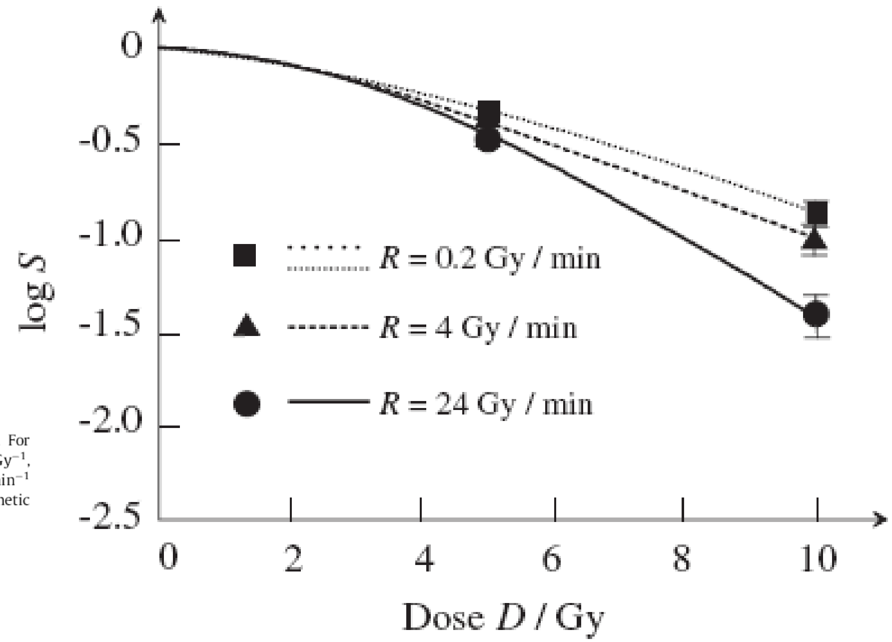


Fig. 4. Surviving fraction of T98G-glioblastoma cells at different dose rates. For 24 Gy/min, the Γ-LQ-model can fit the experimental data with $\alpha = 0.03\ Gy^{-1}$, $\beta = 0.04\ Gy^{-2}$ and $\gamma = 0.556\ min^{-1}$; for 4 Gy/min, γ has to be adapted to $0.361\ min^{-1}$ and for $R = 0.2$ Gy/min,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

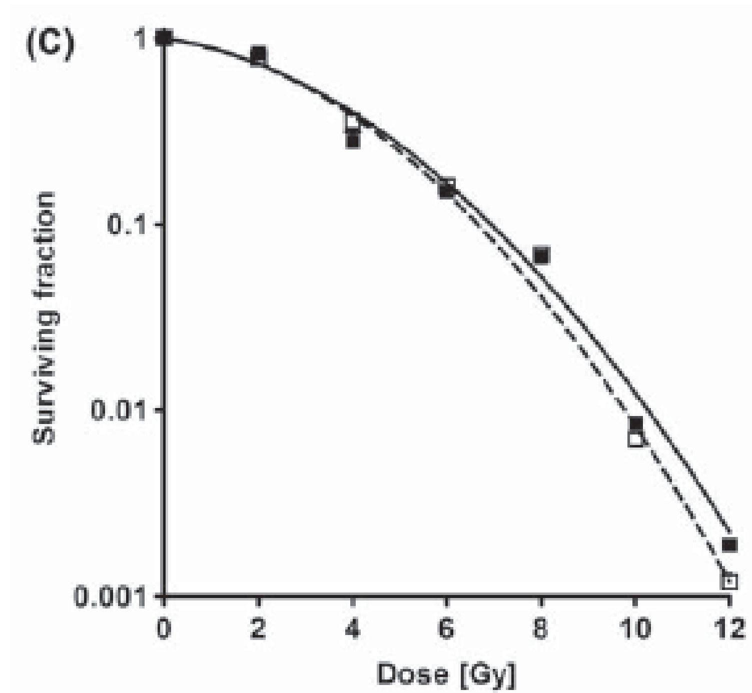
But: Disparate Results for same cell line (T98 Glioma)



Lohse, R&O, 2011

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 $\gamma = 0.0313\ \mathrm{min}^{-1}$.

VS.



Verbakel, Acta Oncol, 2013

Figure 3. Normalized cell survival curves for SW 1573 (A), D384 (B) and T98 (C) cells. Error bars represent the standard error of the
mean (n 3). Open squares FF, Closed squares FFF.

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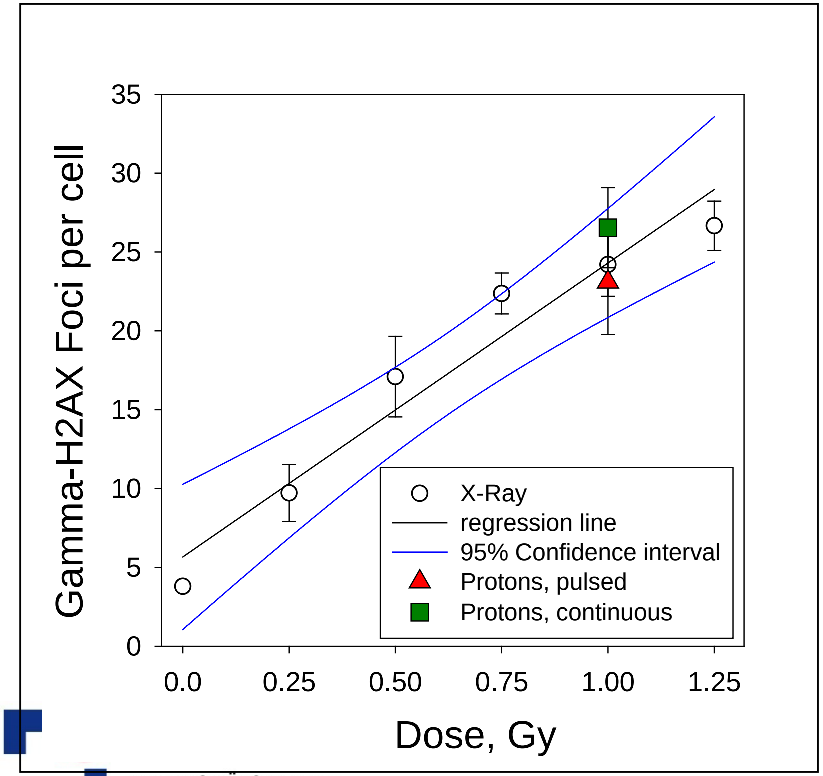
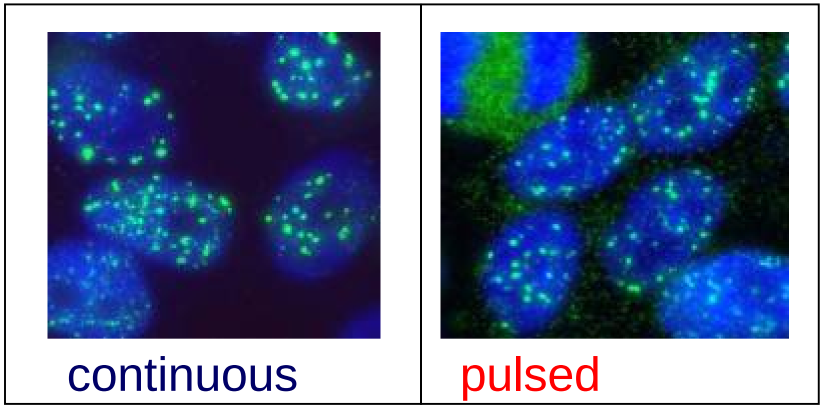
γ-H2AX-foci in HeLa cells / repair of DNA DSBs

20 MeV protons (tandem accelerator)
1 Gy (single dose)





	continuous (1 Gy in 100 ms)	**pulsed** (1 Gy in 1 ns)
Foci per cell	26.54 ± 2.54	23.29 ± 2.04
RBE	1.13 ± 0.21	0.96 ± 0.18

Synopsis

Low dose rates

-> Loss of effect

Intermediate dose rates (covering the spectrum of what is currently possible with FFF Linacs (overall and per pulse)

->No effect

Ultra-high Dose rates

(not relevant for photons, possibly for laser pulsed particles)

-> Oxygen Depletion

Take home messages - Versa HD

- Better modulation in shorter treatment times
  - higher conformity/ homogeneity – 160 MLC leaves
  - higher leaf speed
  - higher dose rates can be achieved with FFF
- Where do we see this clinically
  - Agility speed improvements can be seen for many treatment sites and fractionation schemes
  - The advantage of higher dose rates from FFF can mainly be seen for moderately complex plans with fraction doses D> 5 Gy
- Quality assurance
  - An extensive measuring/ validation of base data and commissioning phase is necessary
  - individual pre-treatment plan verification recommended