



HEIDELBERG
UNIVERSITY
HOSPITAL

dkfz.

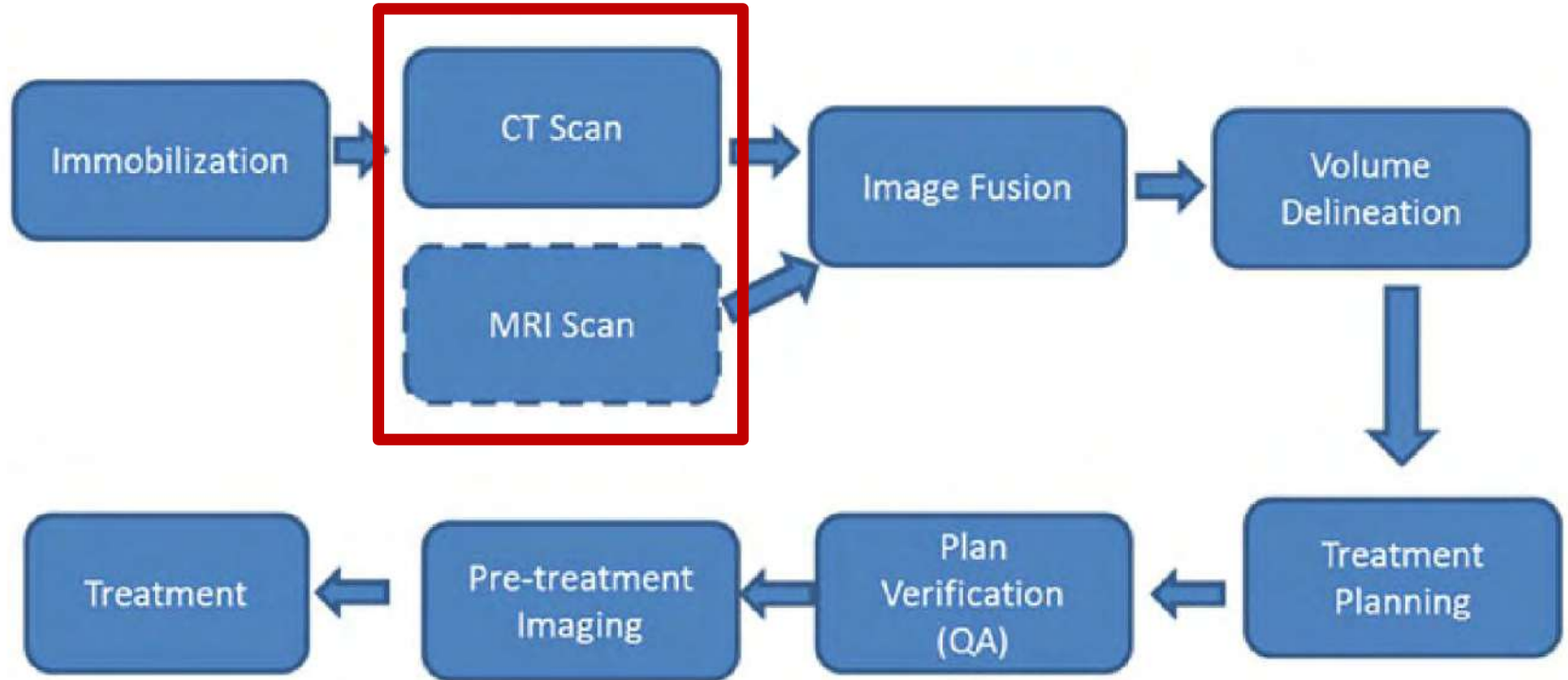
MR-geführte Radiotherapie von Oligometastasen

Dr. Juliane Hörner-Rieber; November 2018

Department of Radiation Oncology, University Hospital Heidelberg and
Clinical Cooperation Unit Radiation Oncology E050, German Cancer Research Center



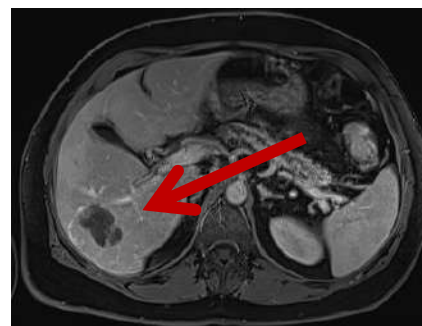
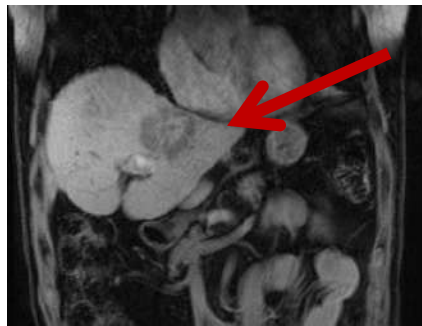
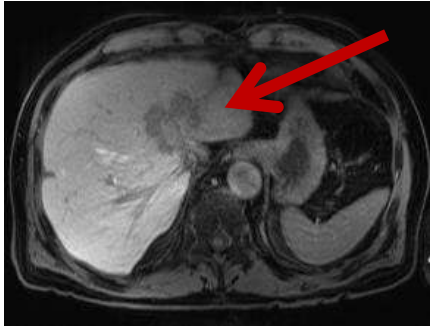
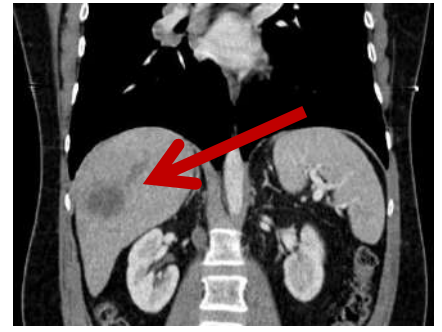
Imaging in radiation oncology



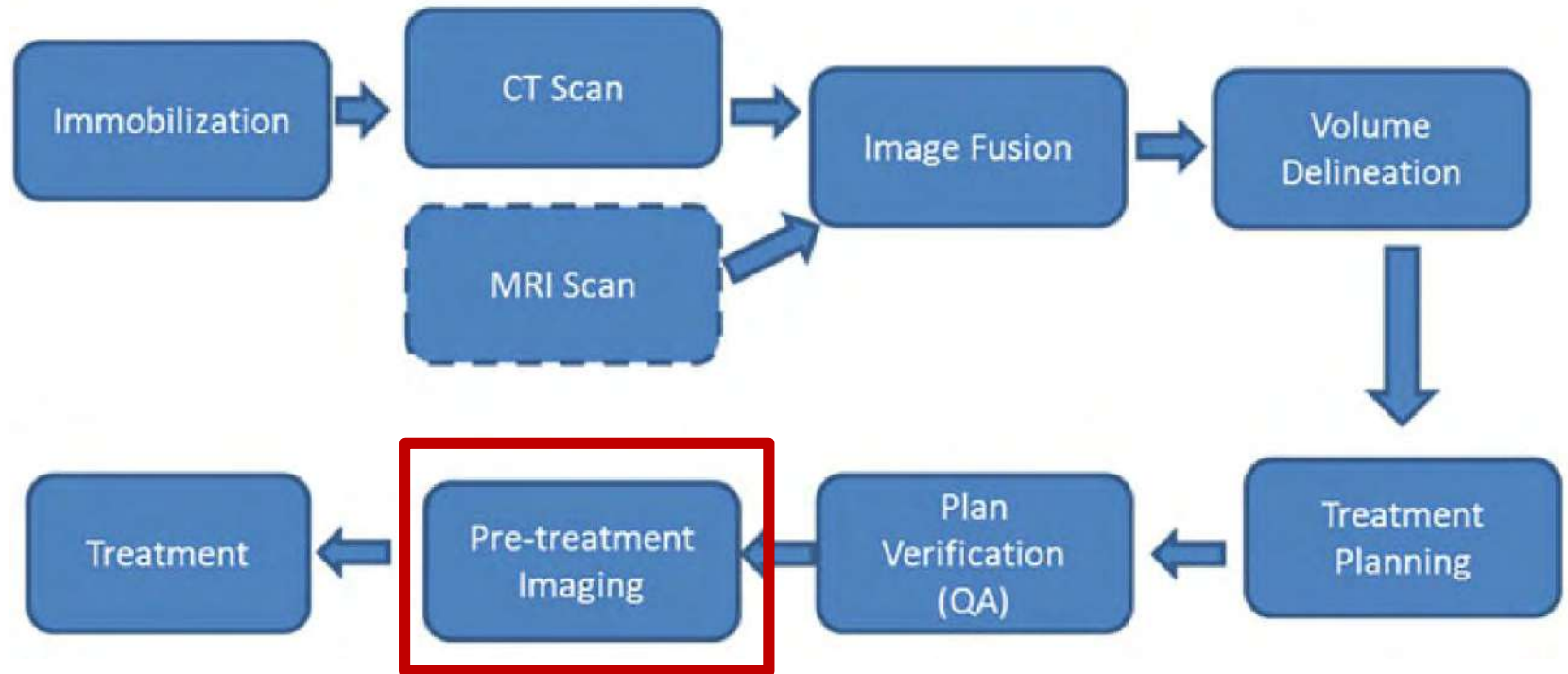
Chandarana, J. et al. Magn. Reson. Imaging 2018

MR-Imaging in radiation oncology for SBRT planning

Liver metastases RT planning



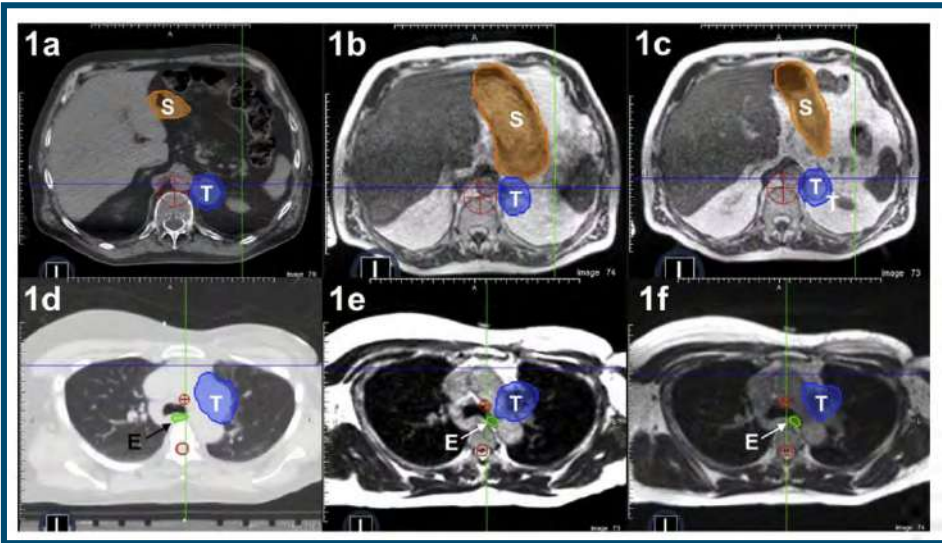
Imaging in radiation oncology



Chandarana, J. et al. Magn. Reson. Imaging 2018

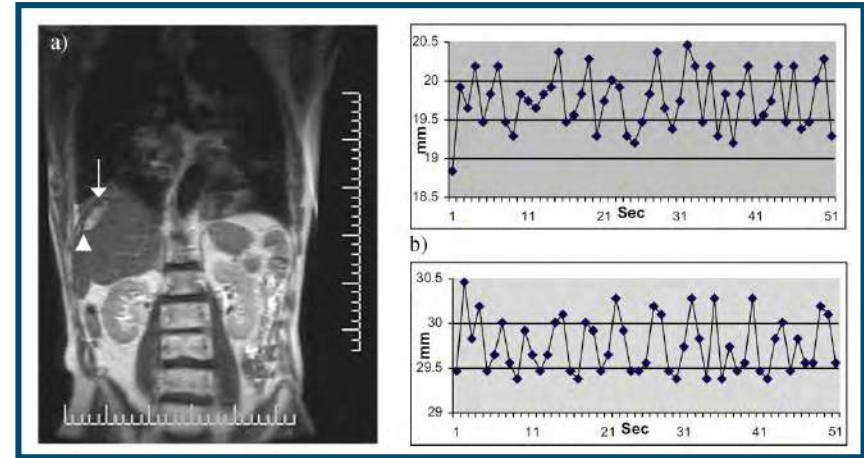
Why do we need image-guided radiotherapy?

Interfractional motion of the stomach
and the esophagus



Henke et al.; IJROBP 2016

Intrafractional motion of the liver



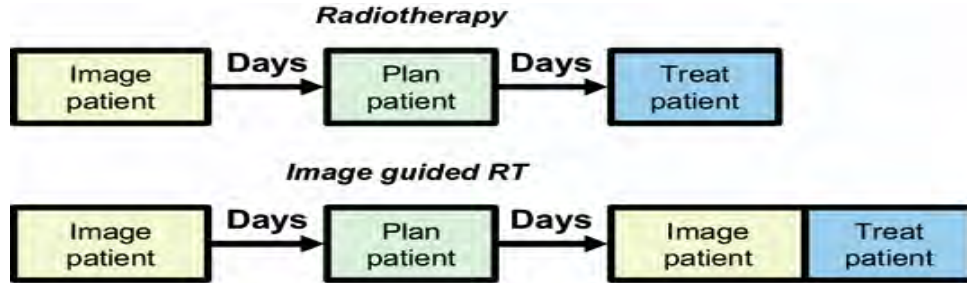
Kirilova et al.; IJROBP 2008

From conventional to image-guided/adaptive radiotherapy



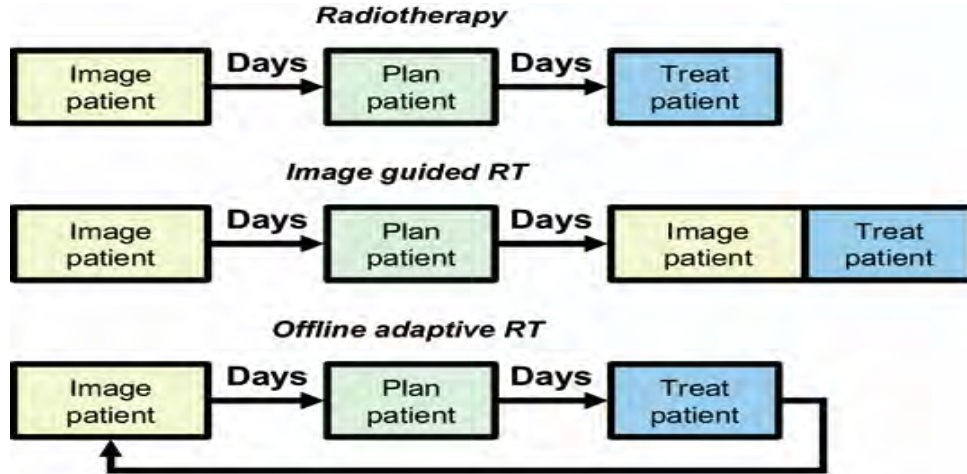
L. Xing, J. Siebers, P. Keall; Semin Radiat Oncol 2007

From conventional to image-guided/adaptive radiotherapy



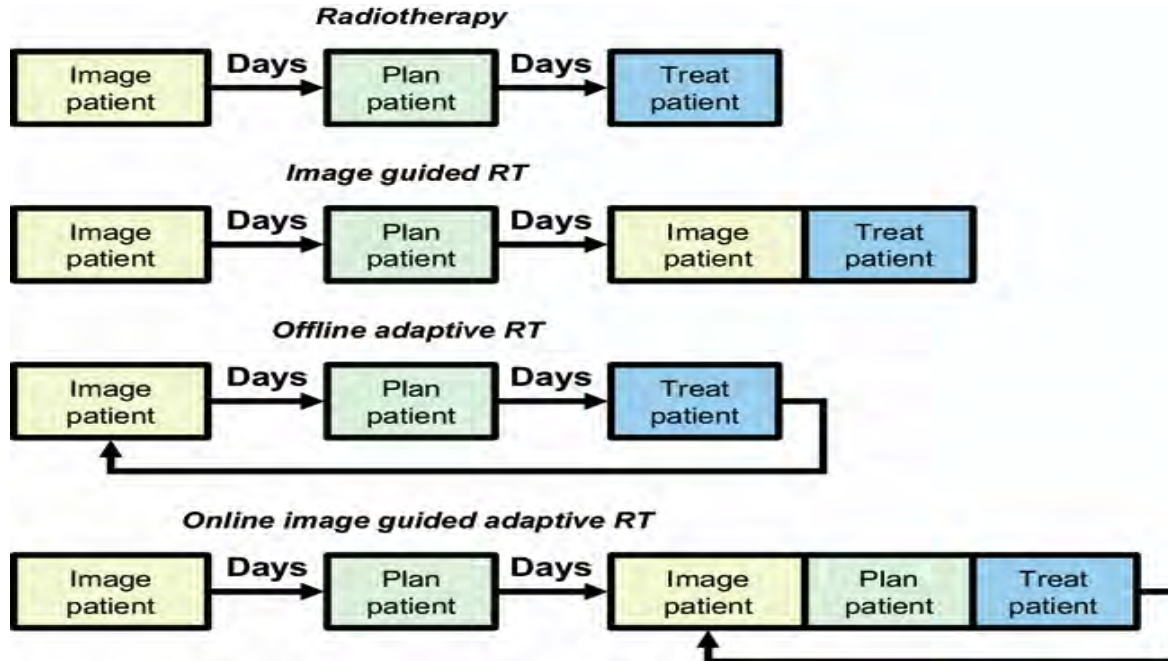
L. Xing, J. Siebers, P. Keall; Semin Radiat Oncol 2007

From conventional to image-guided/adaptive radiotherapy



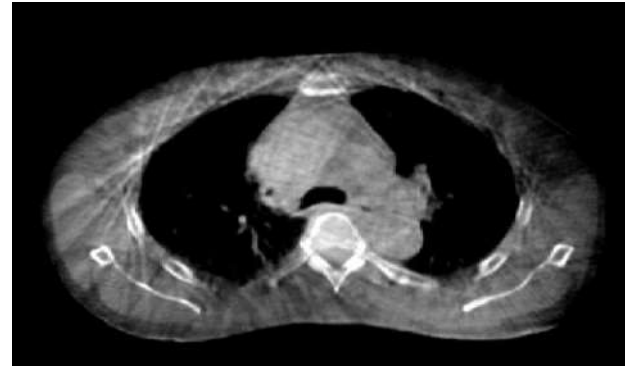
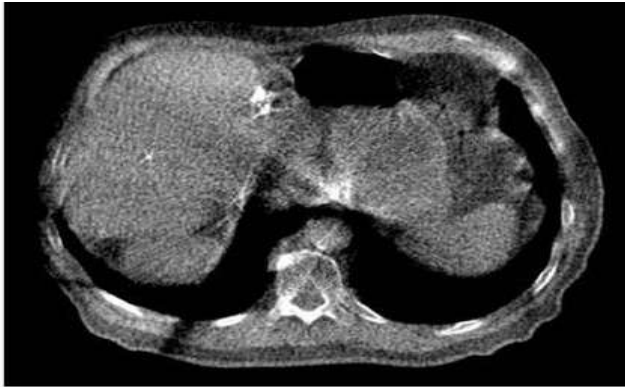
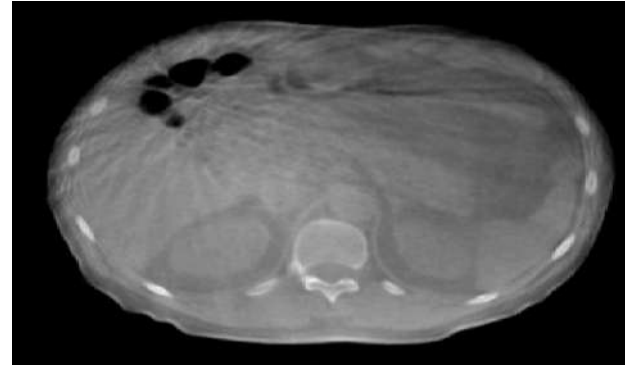
L. Xing, J. Siebers, P. Keall; Semin Radiat Oncol 2007

From conventional to image-guided/adaptive radiotherapy



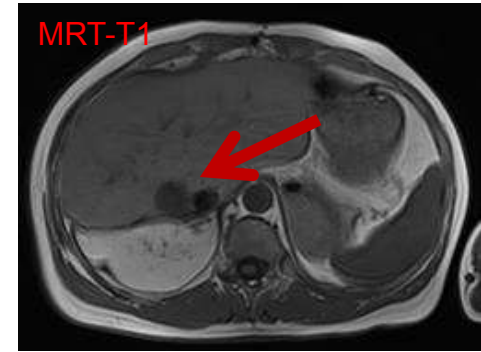
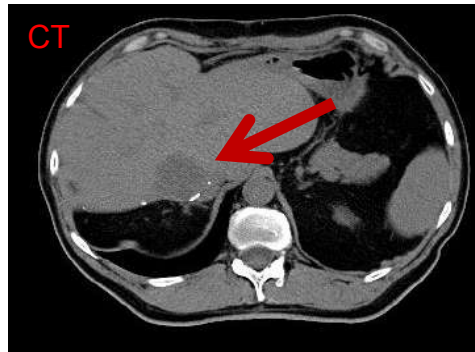
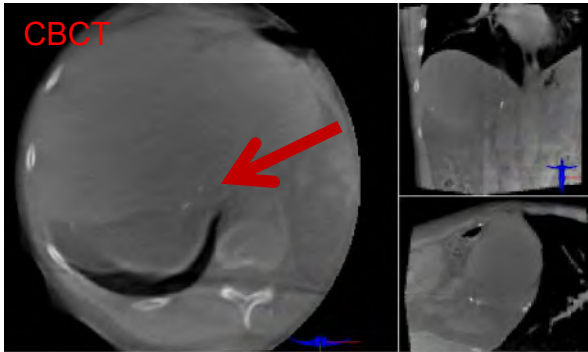
L. Xing, J. Siebers, P. Keall; Semin Radiat Oncol 2007

Image-guided radiotherapy– Limitations....



Advantages of IGRT with MRI

- **better soft tissue contrast**
- **no additional radiation dose for IGRT**



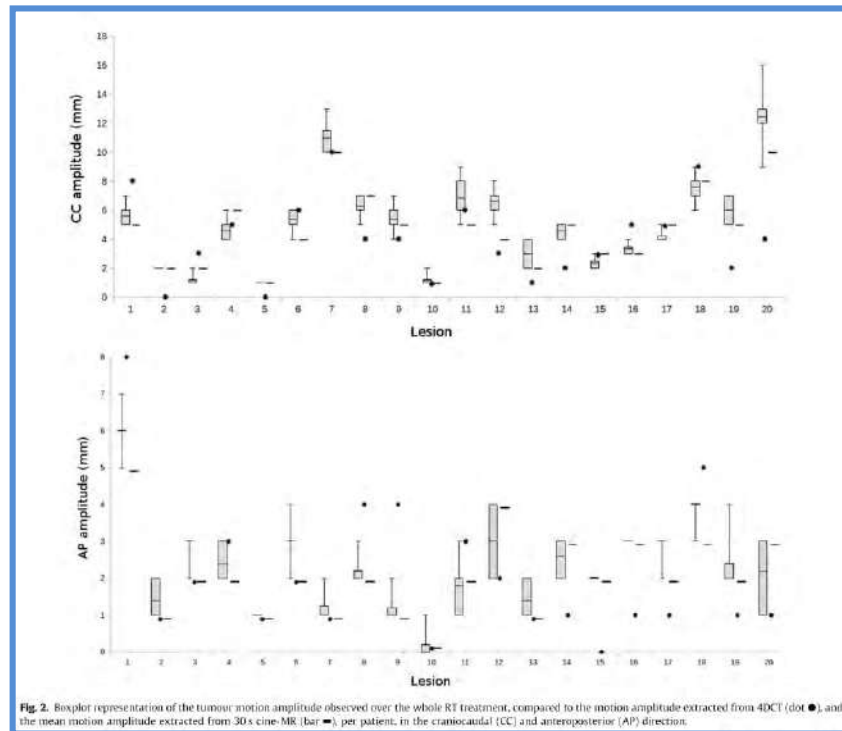
Advantages of IGRT with online MRI

Table 1

The lesion site, number of treatment fractions, average treatment fraction time, 4DCT-based motion amplitude (A_{4DCT}), mean motion amplitude during 30 s simulation (A_{30sMRI}) ± 1 SD, and mean treatment motion amplitude (A_{mean}) ± 1 SD, for all lesions.

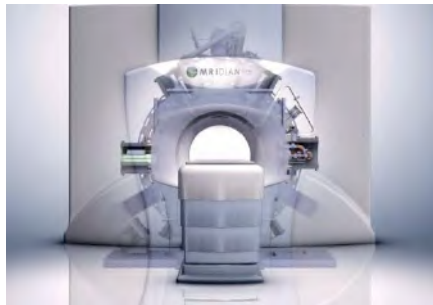
Lesion	Lesion site	Number of fractions	Average treatment fraction time (min)	A_{4DCT} (mm)		$A_{30sMRI} \pm 1$ SD (mm)		$A_{mean} \pm 1$ SD (mm)	
				CC	AP	CC	AP	CC	AP
1	Lung	5	11 $\pm$ 1	8	8	5 $\pm$ 2	5 $\pm$ 2	6 $\pm$ 1	5 $\pm$ 1
2	Lung	10	18 $\pm$ 5	0	1	2 $\pm$ 0	1 $\pm$ 0	2 $\pm$ 0	1 $\pm$ 1
3	Lung	5	6 $\pm$ 0	3	2	2 $\pm$ 0	2 $\pm$ 1	1 $\pm$ 0	2 $\pm$ 0
4	Lung	5	19 $\pm$ 1	5	3	6 $\pm$ 2	2 $\pm$ 1	5 $\pm$ 1	2 $\pm$ 1
5	Lung	5	13 $\pm$ 1	0	1	1 $\pm$ 0	1 $\pm$ 0	1 $\pm$ 0	1 $\pm$ 0
6	Lung	5	20 $\pm$ 0	8	2	4 $\pm$ 1	2 $\pm$ 1	4 $\pm$ 1	2 $\pm$ 1
7	Lung	5	15 $\pm$ 4	10	1	10 $\pm$ 4	1 $\pm$ 1	11 $\pm$ 1	1 $\pm$ 1
8	Pancreas	10	14 $\pm$ 0	4	4	7 $\pm$ 2	2 $\pm$ 1	6 $\pm$ 1	2 $\pm$ 0
9	Pancreas	5	26 $\pm$ 5	4	4	5 $\pm$ 1	1 $\pm$ 1	4 $\pm$ 1	1 $\pm$ 1
10	Pancreas	5	17 $\pm$ 0	1	0	1 $\pm$ 1	0 $\pm$ 0	1 $\pm$ 0	0 $\pm$ 0
11	Pancreas	22	10 $\pm$ 0	6	3	5 $\pm$ 2	2 $\pm$ 1	6 $\pm$ 2	2 $\pm$ 1
12	Pancreas	10	10 $\pm$ 2	3	2	4 $\pm$ 2	4 $\pm$ 1	6 $\pm$ 1	3 $\pm$ 1
13	Pancreas	5	16 $\pm$ 5	1	1	2 $\pm$ 2	1 $\pm$ 1	3 $\pm$ 1	1 $\pm$ 1
14	Liver	5	15 $\pm$ 0	2	1	5 $\pm$ 3	3 $\pm$ 1	5 $\pm$ 1	3 $\pm$ 1
15	Liver	3	19 $\pm$ 3	3	0	3 $\pm$ 1	2 $\pm$ 1	2 $\pm$ 1	2 $\pm$ 0
16	Liver	3	16 $\pm$ 6	5	1	3 $\pm$ 1	3 $\pm$ 1	3 $\pm$ 1	3 $\pm$ 0
17	Kidney	5	36 $\pm$ 8	5	1	5 $\pm$ 1	2 $\pm$ 1	4 $\pm$ 0	2 $\pm$ 1
18	Kidney	5	15 $\pm$ 2	9	5	8 $\pm$ 2	3 $\pm$ 1	7 $\pm$ 1	3 $\pm$ 0
19	Kidney	5	20 $\pm$ 4	2	1	5 $\pm$ 3	2 $\pm$ 1	6 $\pm$ 1	2 $\pm$ 1
20	Kidney	5	7 $\pm$ 1	4	1	10 $\pm$ 6	3 $\pm$ 2	9 $\pm$ 3	2 $\pm$ 1

- Lesions moving with small amplitude show limited amplitude variability
- However, baseline drifts and shifts cause significant geometrical uncertainty



MR-Linac: available systems

ViewRay MRIdian® Linac



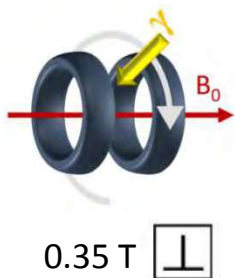
www.viewray.com



Mutic and Dempsey
Sem Rad Onc 2014

Clinical use:

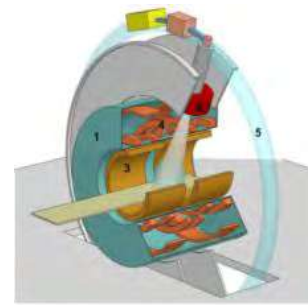
Since 2014 with ^{60}Co
Since 2017 with a linac



Elekta Unity



mrrt.elekta.com

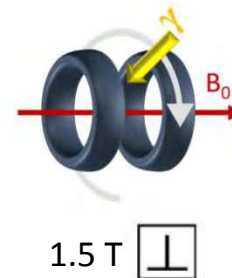


Raaymakers et al.
PMB 2009

CE since 18.06.2018

First patients 2017, UMC
Utrecht

Raaymakers et al. PMB 2017



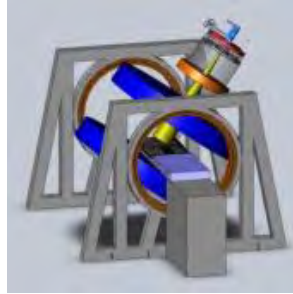
MR-Linac: available systems

MagnetTx Aurora RT™

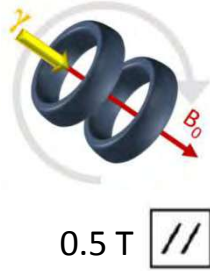


www.magnettx.com

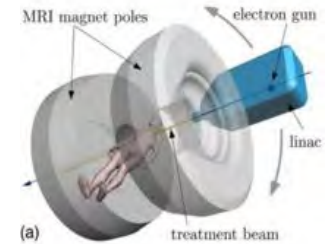
Cross Cancer Institute,
Edmonton
University of Alberta



Fallone et al.
Med Phys 2009

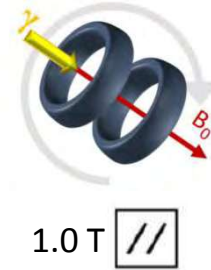


The Australian MRI-Linac

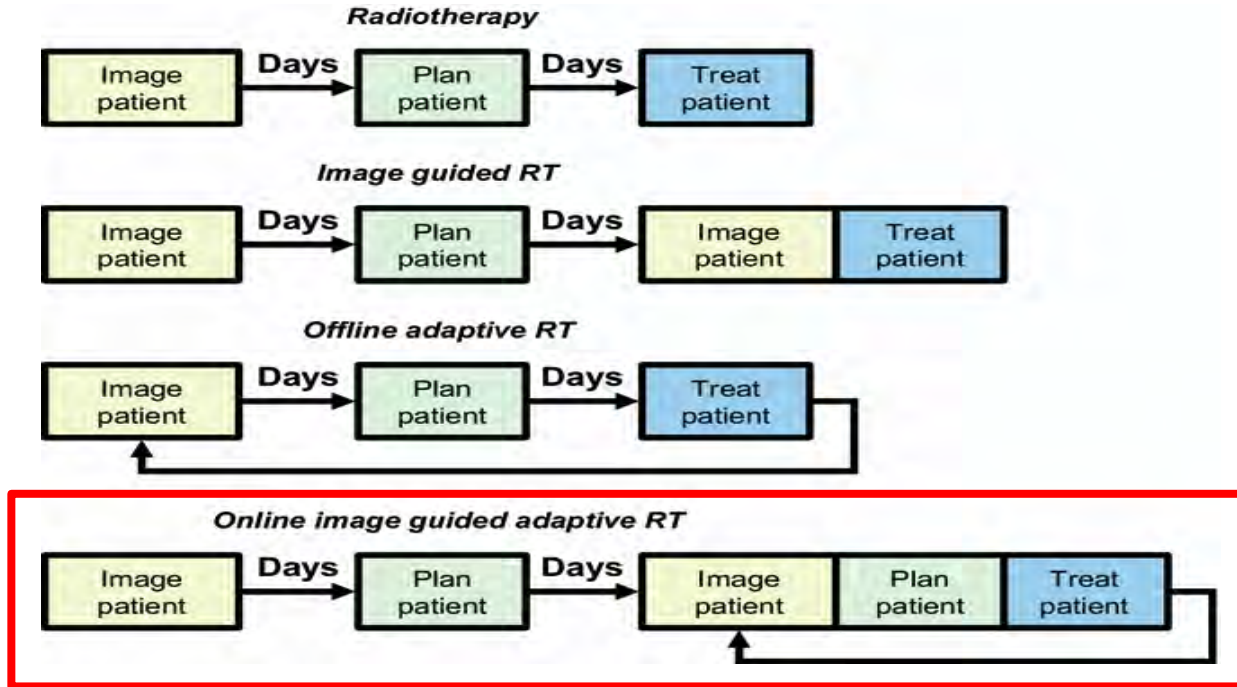


Keall et al.
Sem Rad Onc 2014

Australian
MRI-Linac Program
(collaboration of different
research facilities)

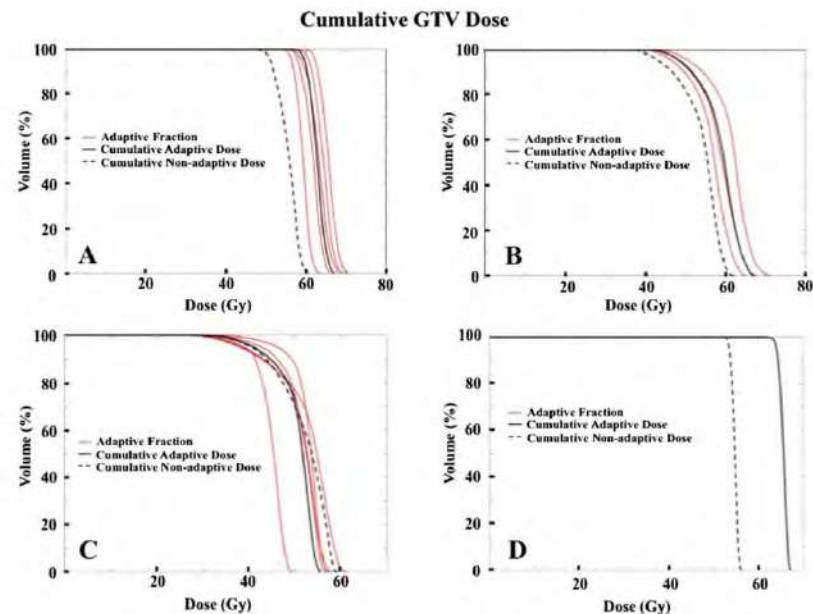
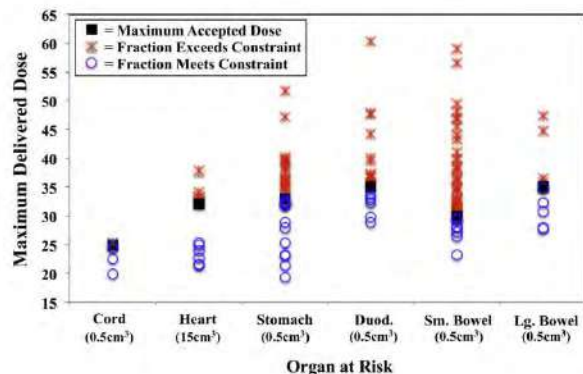
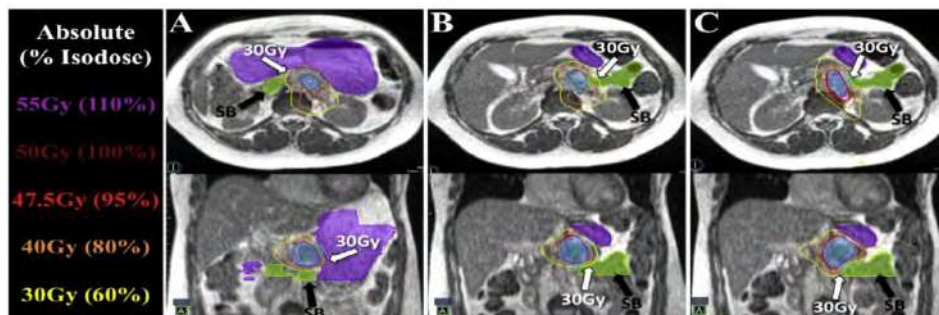


Adaptive treatment



L. Xing, J. Siebers, P. Keall; Semin Radiat Oncol 2007

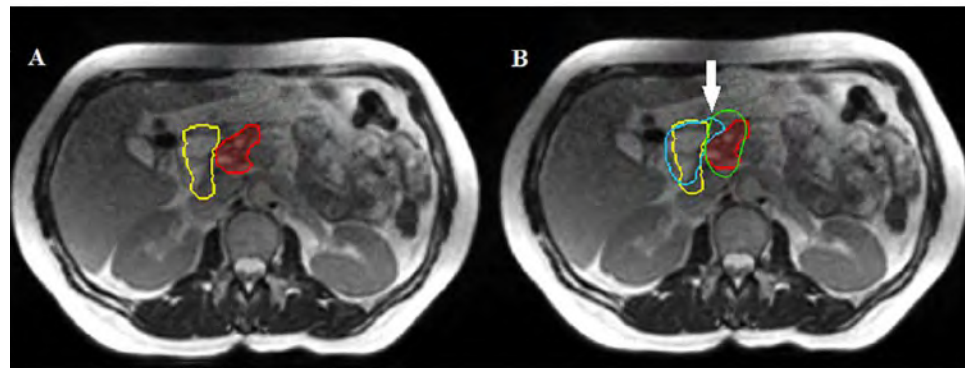
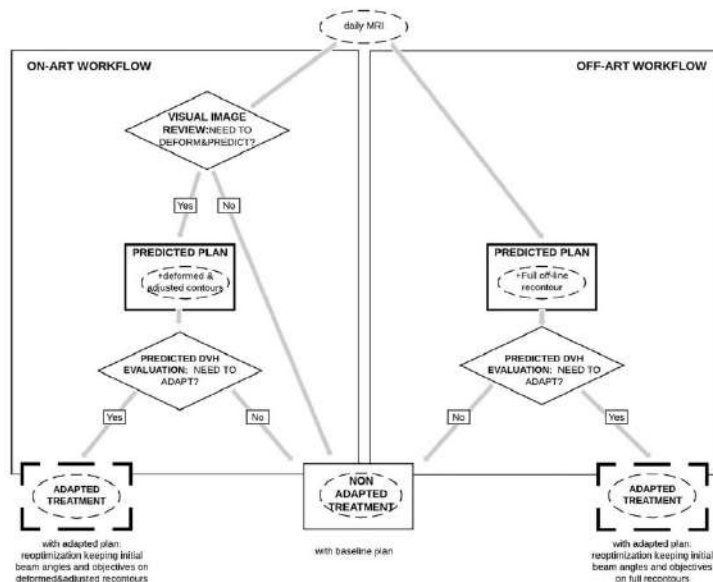
Why do we need adaptation?



- better sparing of OARs
- potential of dose escalation

Henke et al., Radiother Oncol 2018

How do we decide if we need to adapt?



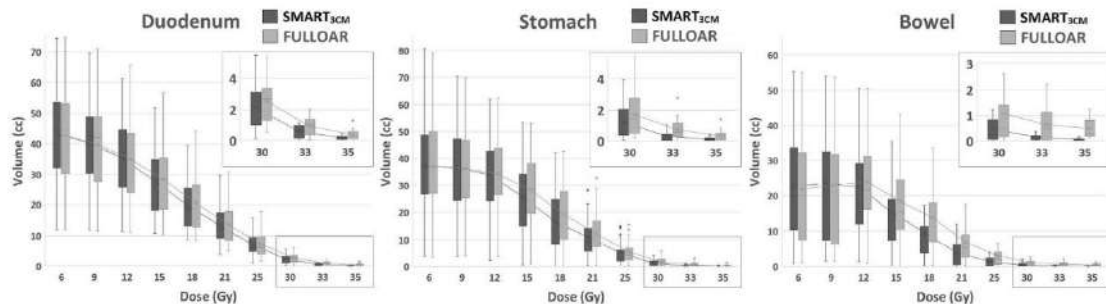
On-ART	Off-ART		Concordance
	25 Yes	10 No	
14 YES	13	1	93%
21 NO	12	9	43%
Total decision mismatch = 37%			

- **Daily-image visual review is not reliable to determine benefit or not for adaptive radiotherapy!**
- **Online predicted plan based on deformed and manually adjusted contours should be generated for every fraction**

Tyran et al, Radiother Oncol 2018

The SMART strategy...

Only OAR re-contouring at 3 cm distance from PTV

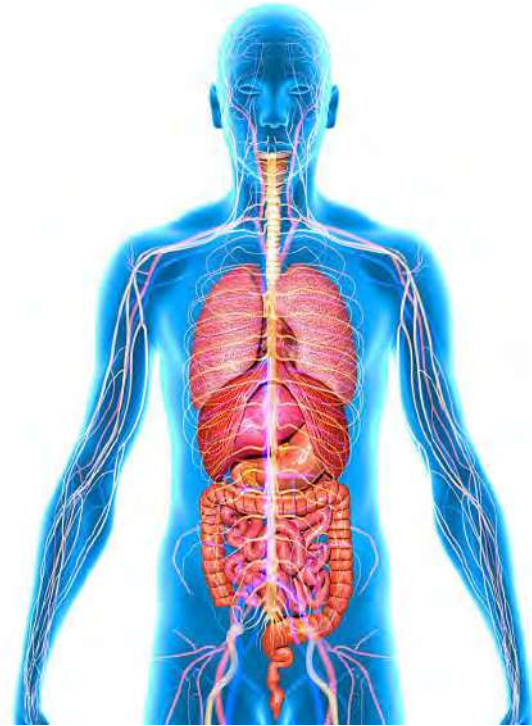


- significant lower number of optimizations
- identical PTV coverage
- significantly lower intermediate and higher doses to OARs

Bohoudi et al, Radiother Oncol 2017

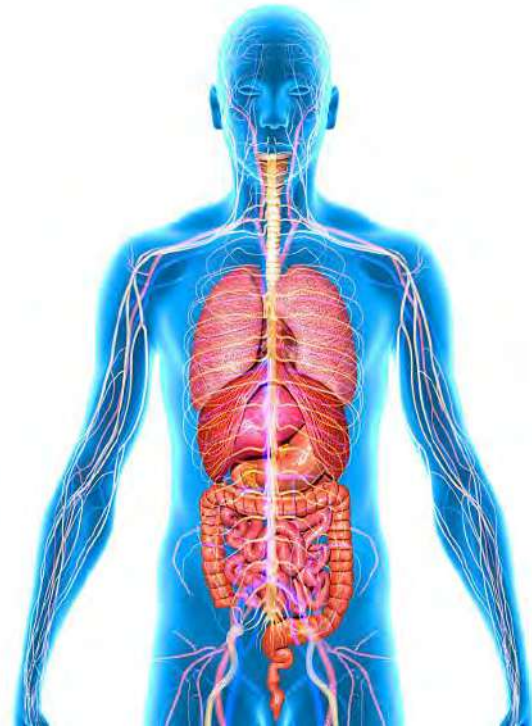
MR-guided SBRT for oligometastases

- Liver metastases
- Central lung metastases
- Adrenal metastases
- Lymph node metastases

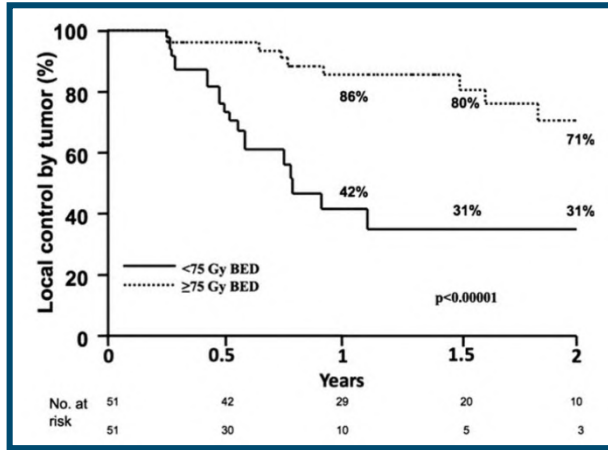


MR-guided SBRT for oligometastases

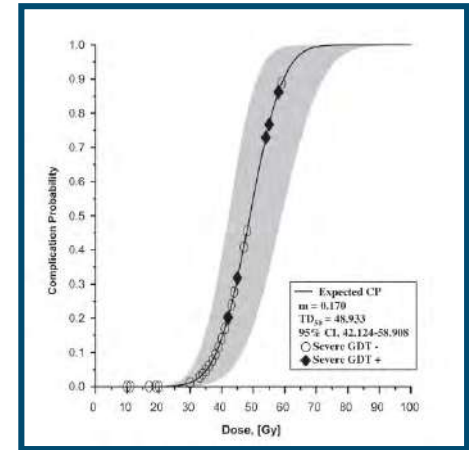
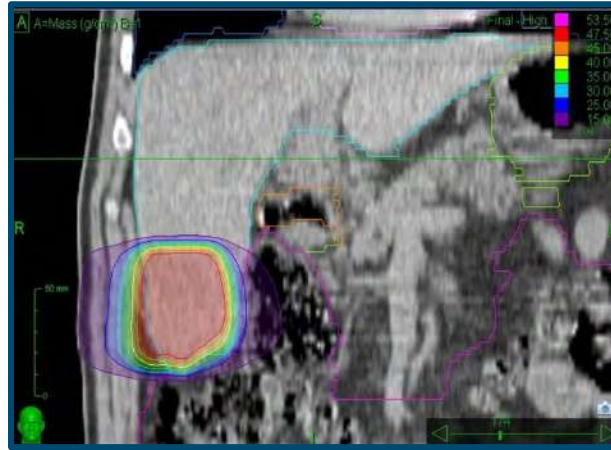
- **Liver metastases**
- Central lung metastases
- Adrenal metastases
- Lymph node metastases



Why do we need MR-guided RT for liver metastases?



Chang et al., Cancer 2011

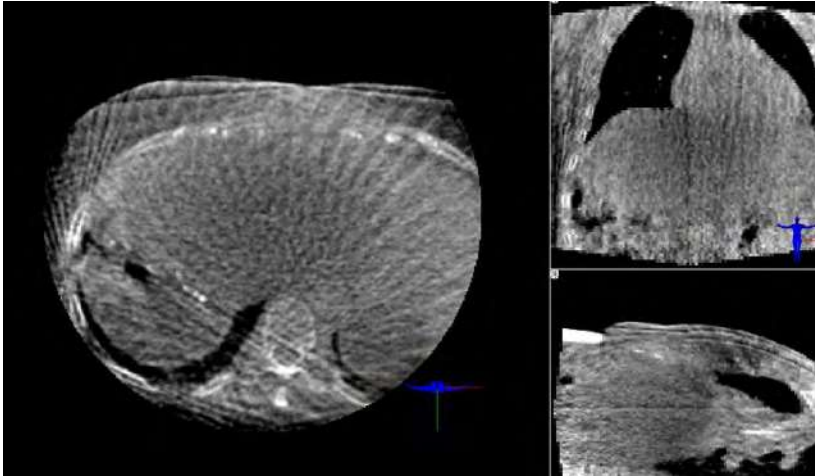


Bae et al., IJROBP 2012

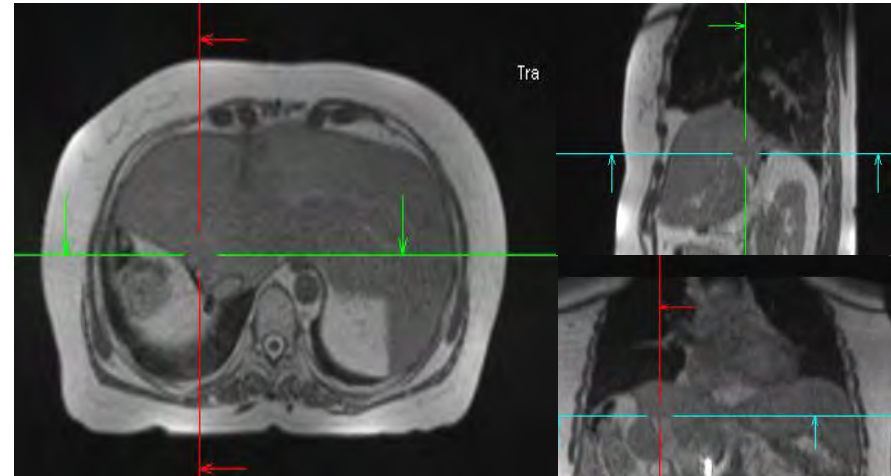
- **Main prognostic factor for LC: BED ≥ 100 Gy**
- **Due to close proximity to OARs (duodenum) SBRT with sufficiently high dose is often not possible!**
- **Significantly improved tissue contrast with MR-guided RT**

Why do we need MR-guided RT for liver metastases?

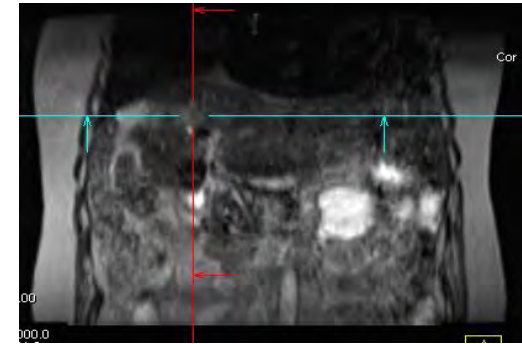
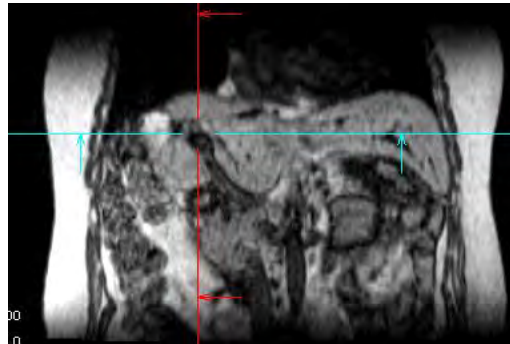
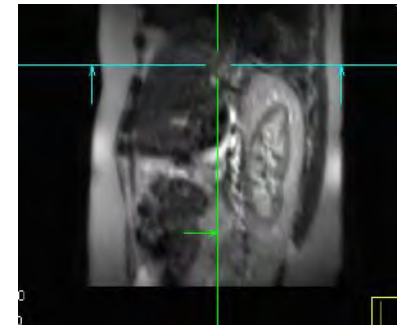
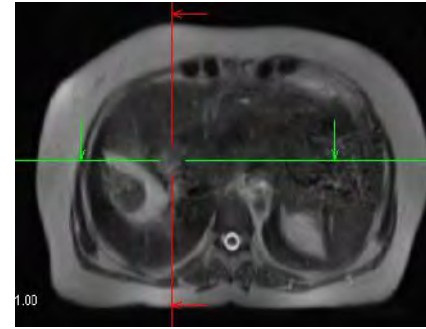
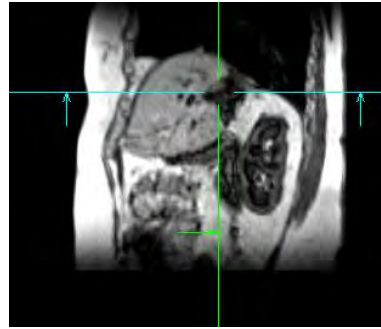
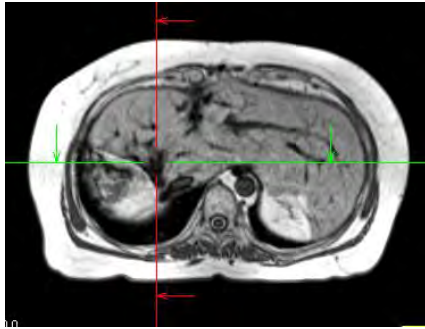
Current standard



TrueFISP at MRLinac



Why do we need MR-guided RT for liver metastases?



Why do we need MR-guided RT for liver metastases?

MR-guided
tumor setup

Adaptive
planning

Online
guidance

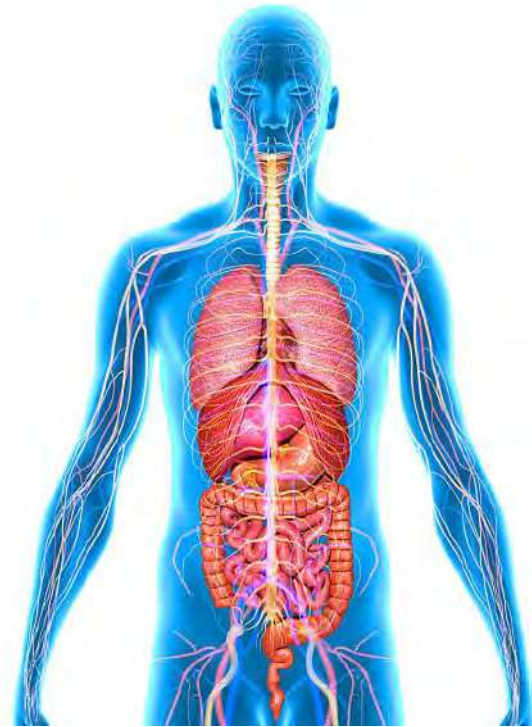
Gated
delivery

- Improved soft tissue contrast (**detection of metastases!**)
- No need for marker implementation
- Adapting to changes in anatomy
- Ensuring target coverage, sparing of OARs (**small bowel!**), **dose escalation?**
- Reduced PTV margins
- Automated delivery shut-off

Adapted from Lagerwaard SBRT Amsterdam 2017

MR-guided SBRT for oligometastases

- Liver metastases
- **Central lung metastases**
- Adrenal metastases
- Lymph node metastases



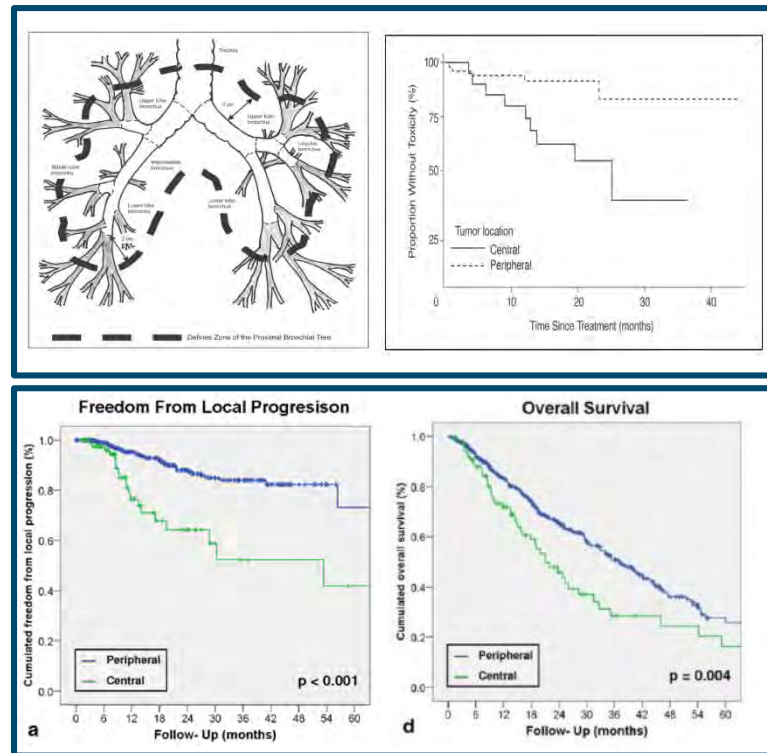
Why do we need MR-guided RT for central lung SBRT?

Excessive Toxicity When Treating Central Tumors in a Phase II Study of Stereotactic Body Radiation Therapy for Medically Inoperable Early-Stage Lung Cancer

Robert Timmerman, Ronald McGarry, Constantin Yiannoutsos, Lech Papiez, Kathy Tudor, Jill DeLuca, Marvene Ewing, Ramzi Abdulrahman, Colleen DesRosiers, Mark Williams, and James Fletcher

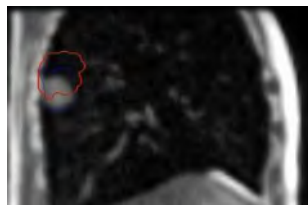
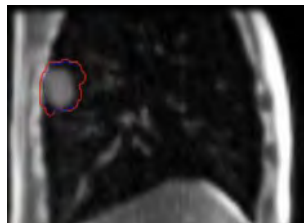
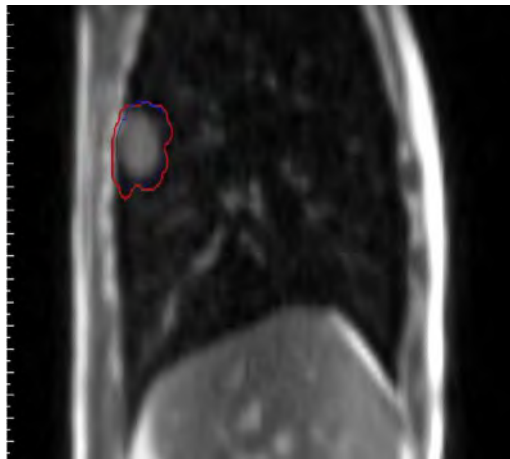
- **SBRT with high ablative doses for central lung tumors leads to strongly increased toxicity (e.g. Haemoptysis, bronchial stricture, oesophagus ulcer...)**
- **Extended fractionation and reduced single doses are applied or total dose is reduced to meet OAR constraints.**

Adaptive MR-guided RT allows dose escalation and simultaneous improvements in OAR sparing!

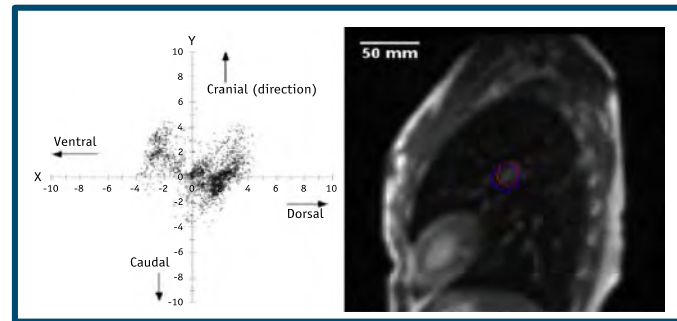


Schanne et al., SUON 2015

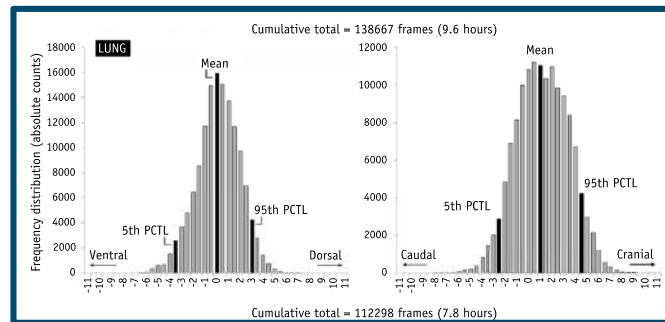
Why do we need MR-guided RT for central lung SBRT?



- Gated SBRT delivered during breath-hold real-time MR-guidance results in at least 95% geometric GTV coverage

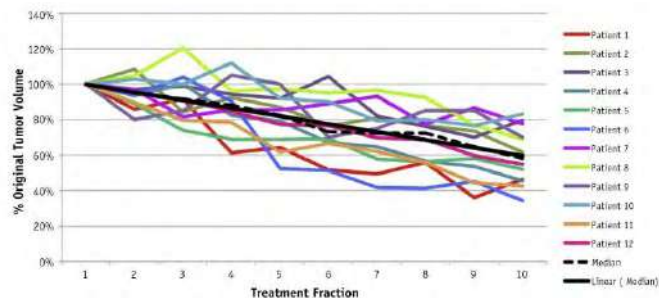


Position of GTV centroid relative to PTV centroid

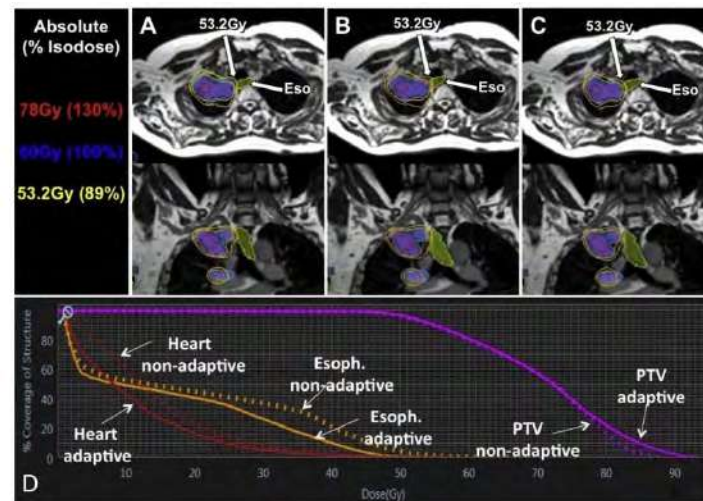
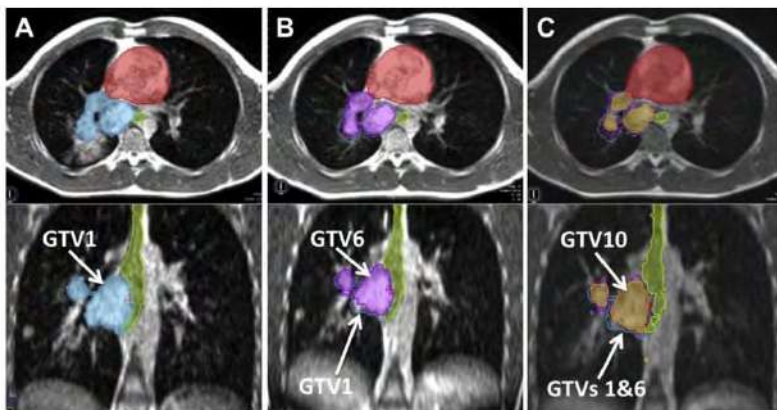


Van Sörssen de Koste et al., IJROBP 2018

Benefit of plan adaptation for central lung SBRT



60 Gy in 12 Fx or 62.5 Gy in 10 Fx

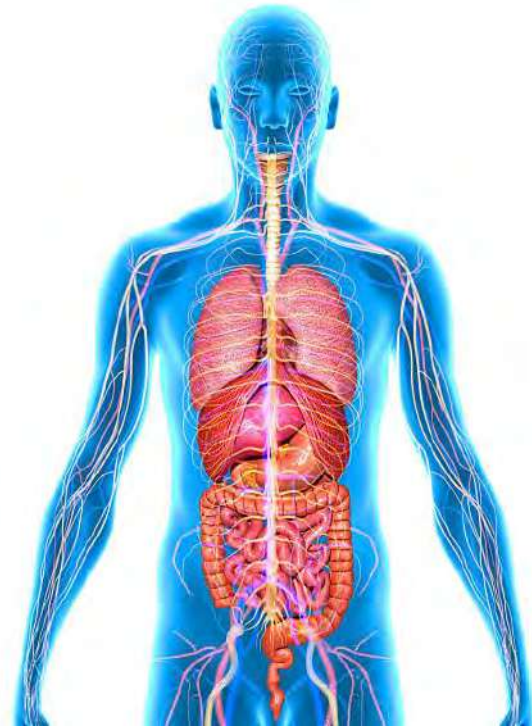


Henke, IJROPB 2018

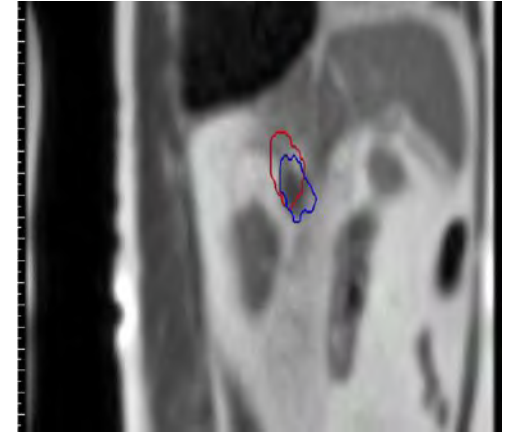
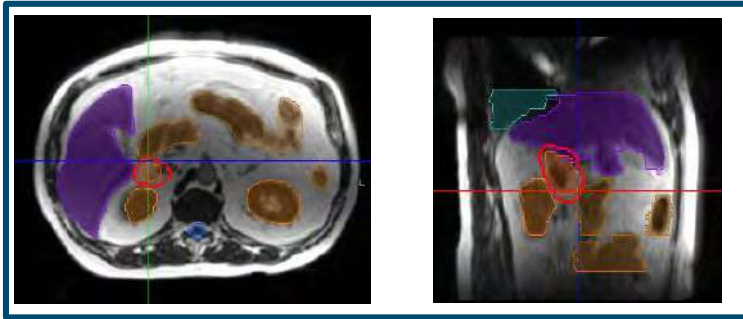
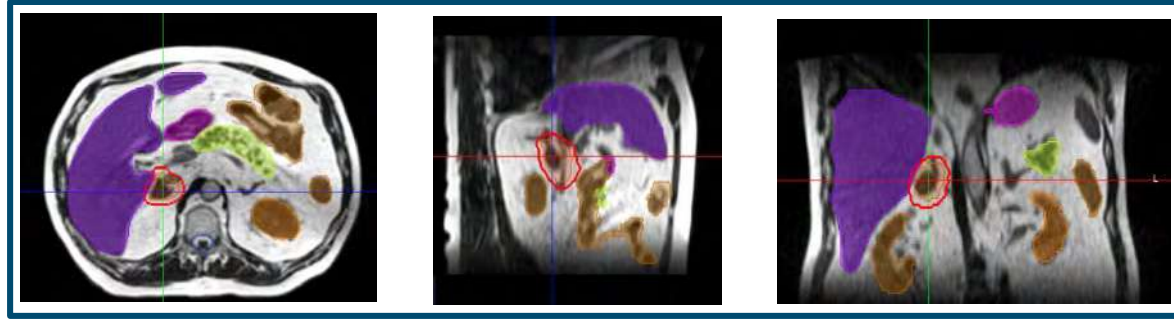
Midtreatment adaptive planning based on tumor response is dosimetrically advantageous for sparing of surrounding critical structures

MR-guided SBRT for oligometastases

- Liver metastases
- Central lung metastases
- **Adrenal metastases**
- Lymph node metastases

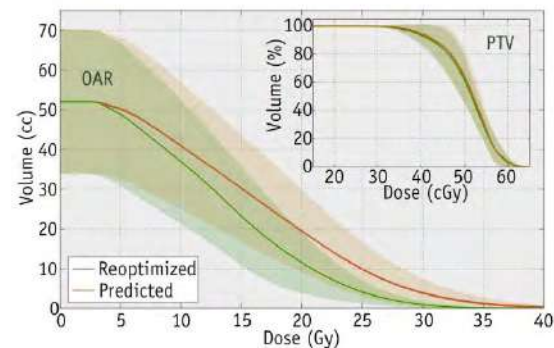
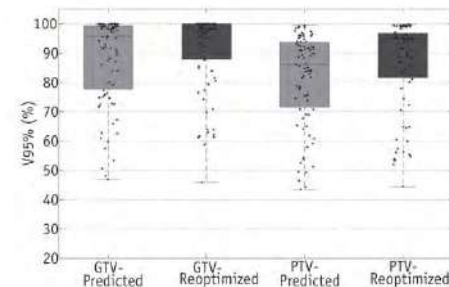
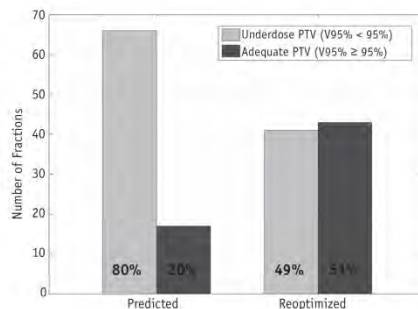
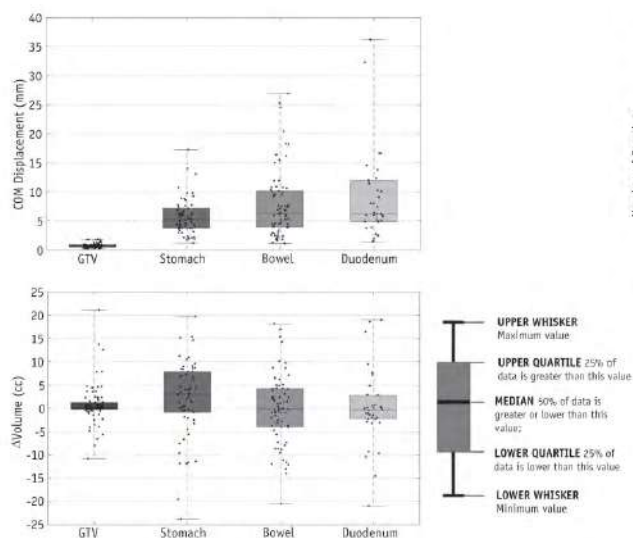


Why do we need MR-guided RT for adrenal SBRT?



**Intra- and intrafractional movement
of tumor and organs at risk...**

Benefit of plan adaptation for adrenal SBRT

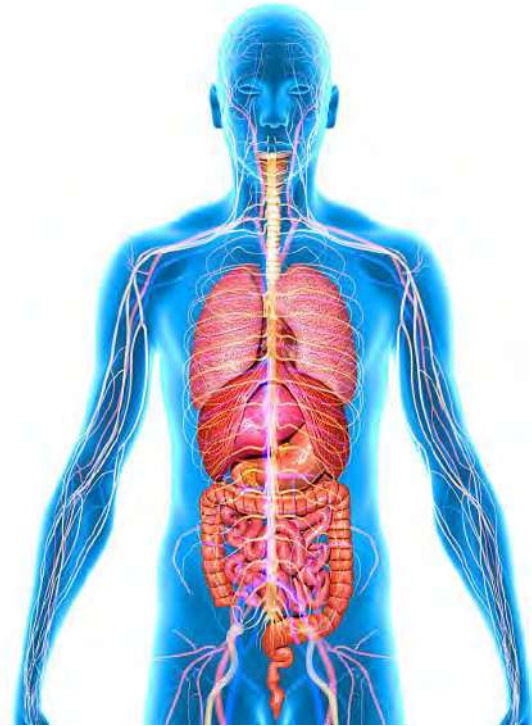


- Online reoptimization of RT plans leads to significantly better target coverage and sparing of OARs

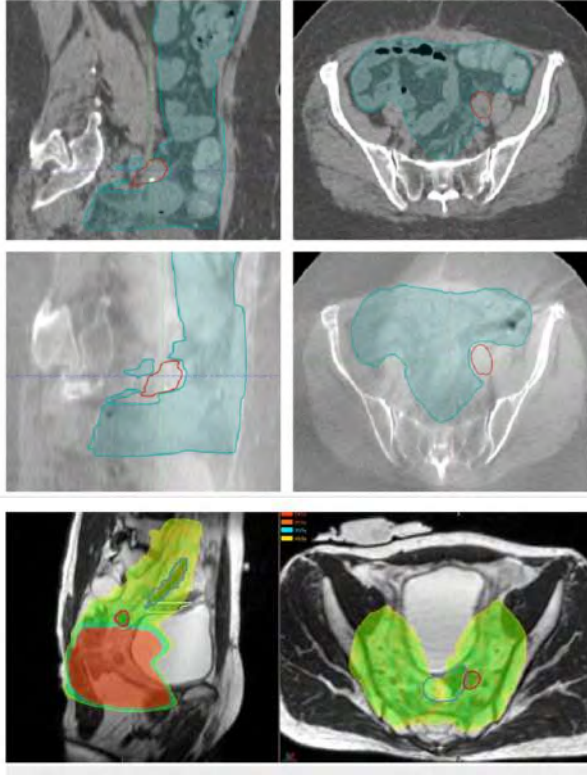
Palacios et al., Radiother Oncol 2018

MR-guided SBRT for oligometastases

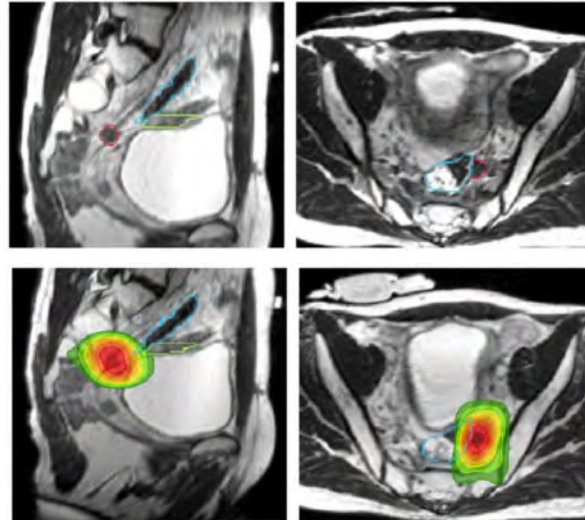
- Liver metastases
- Central lung metastases
- Adrenal metastases
- **Lymph node metastases**



Why do we need MR-guided RT for lymph node SBRT?



- 39-y male patient with **pT4pN1cM1a rectal cancer** (hepatic metastases)
- **Neoadjuvant RCHT with 50.4 Gy** in 1.8 Gy pelvis plus boost to 54.0 Gy to primary tumor, **CHT with capecitabine und trastuzumab** plus **RFA to hepatic metastases**



Local relapse in a left pelvic lymph node metastasis

SBRT with 35 Gy in 5 fractions

Why do we need MR-guided RT for lymph node metastases?

MR-guided
tumor setup

Adaptive
planning

Online
guidance

Gated
delivery

- Improved soft tissue contrast (**detection of lymph node metastases!**)
- No need for marker implementation
- Adapting to changes in anatomy
- Ensuring target coverage, sparing of OARs (**small bowel!**), **dose escalation?**
- Reduced PTV margins
- Automated delivery shut-off

Adapted from Lagerwaard SBRT Amsterdam 2017

MR-guided SBRT for oligometastases...

- Better soft tissue contrast combined with no additional radiation dose due to imaging!
- Due to improve imaging SBRT with smaller safety margins is possible!
- Improved sparing of organs at risk leads to less toxicity and side-effects
- Potential of dose escalation might lead to improved tumor control



MR-Linac in Heidelberg: funded by



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