



CT guided HDR Brachytherapy in Oligometastases

Jens Ricke
Radiology and Nuclear medicine
University of Magdeburg

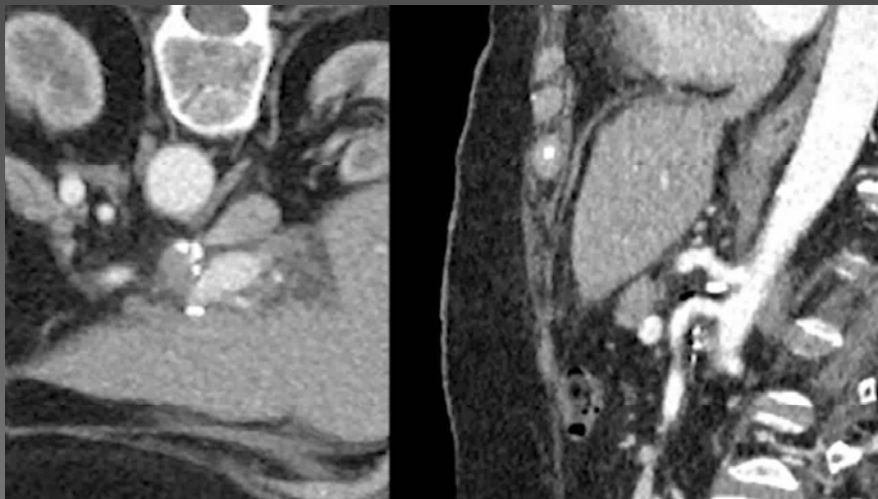
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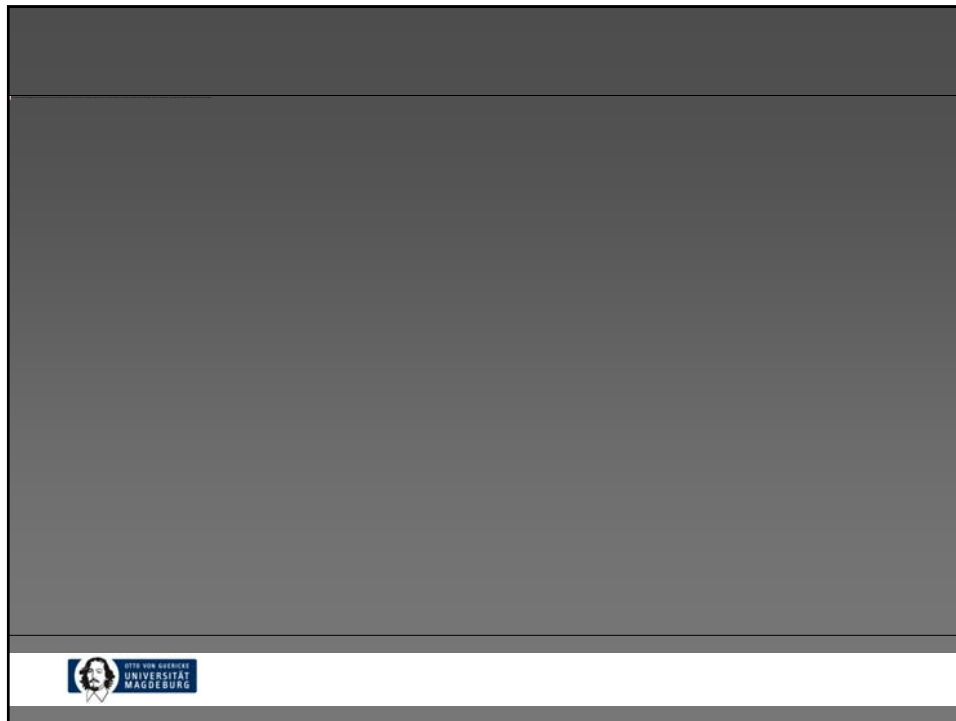
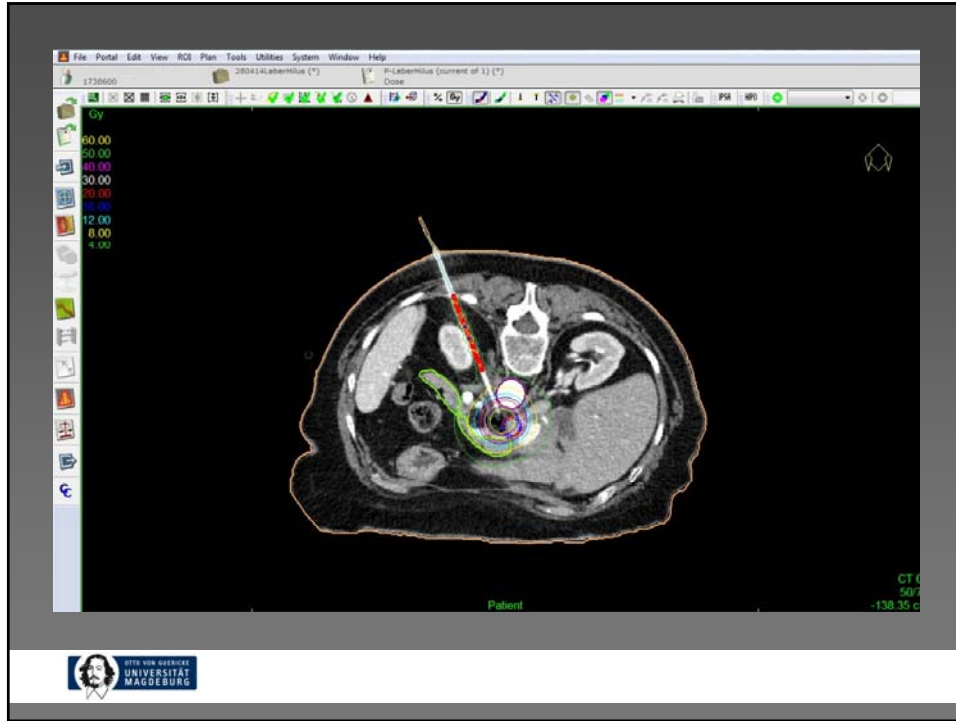
Images: Ricke



Images: Ricke

BrachyNext

Working Together to Shape the Future of
Brachytherapy





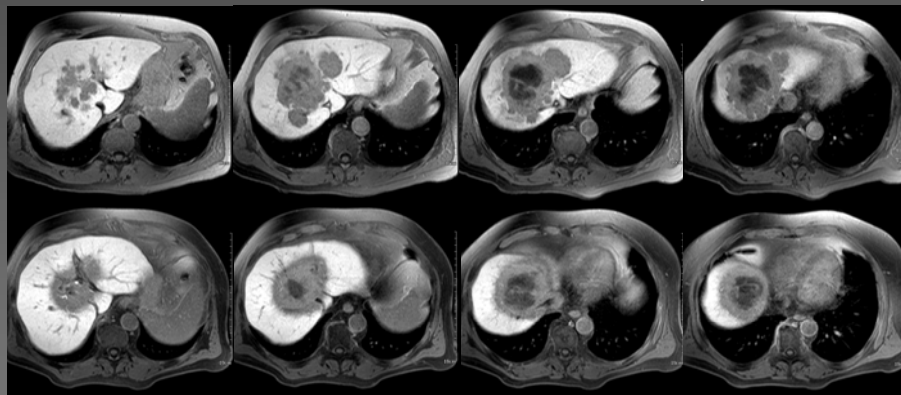
Brachytherapy Workflow



Images: Ricke

mCRC, CT-guided Brachytherapy

pre



3 months post



Images: Ricke



Int. J. Radiation Oncology Biol. Phys., Vol. ■, No. ■, pp. 1-8, 2009
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CLINICAL INVESTIGATION

LOCAL RESPONSE AND IMPACT ON SURVIVAL AFTER LOCAL ABLATION OF LIVER METASTASES FROM COLORECTAL CARCINOMA BY COMPUTED TOMOGRAPHY-GUIDED HIGH-DOSE-RATE BRACHYTHERAPY

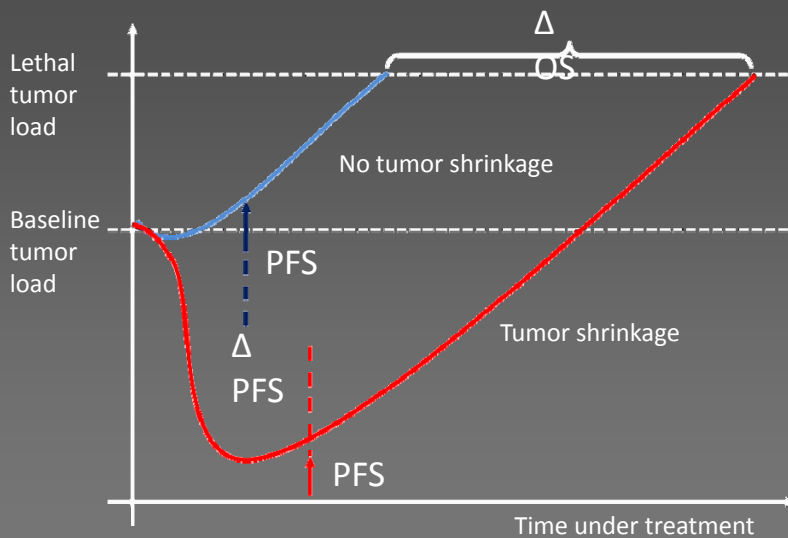
JENS RICKE, M.D.* KONRAD MOHNIKE, M.D.* MACIEJ PECH, M.D.* MAX SEIDENSTICKER, M.D.*
RICARDA RÜHL, M.D.* GERO WIENERS, M.D.* GUNNAR GAFFKE, M.D.* SIEGFRIED KROPP, Ph.D.†
ROLAND FELIX, M.D.‡ AND PETER WUST, M.D.‡

- Prospective randomised dose finding
- Primary endpoint: local control
- Tumors 5 – 15cm
 - FFLP >90% after 12mo (>20Gy single fraction)



Ricke et al. Int J Radiat Oncol Biol Phys 2010

Deepness of response



Mansmann UR, et al. ASCO GI 2013 (Abstract no. 427)



Deepness of response

- Decisive for post-progression-survival in OPUS and CHRYSTAL*
- What is the difference between a volume decrease of 50% with CTx & Cetuximab or complete debulking by ablation?



Mansmann UR, et al. ASCO GI 2013 (Abstract no. 427)

PERSPECTIVES

OPINION

Oligometastases revisited

Ralph R. Weichselbaum and Samuel Hellman

Abstract | We previously proposed a clinical state of metastasis termed 'oligometastases' that refers to restricted tumor metastatic capacity. The implication of this concept is that local cancer treatments are curative in a proportion of patients with metastases. Here we review clinical and laboratory data that support the hypothesis that oligometastasis is a distinct clinical entity. Investigations of the prevalence, mechanism of occurrence, and position in the metastatic cascade, as well as the determination of molecular markers to distinguish oligometastatic from

those of the gastrointestinal (GI) tract.³⁻⁶ This association is partially explained by the venous drainage of the GI tract travelling through the portal vein, although tumor and host genetic factors also have a role in the tropism of GI metastases to the liver. Support for the oligometastatic state of some GI-associated liver metastases comes from data regarding the outcome of patients with colorectal cancer who underwent partial liver resection for metastasis to the liver (Table 1).³⁻⁶ The curative treatment of liver metastasis has been reported for many years; however, each series was relatively small. In

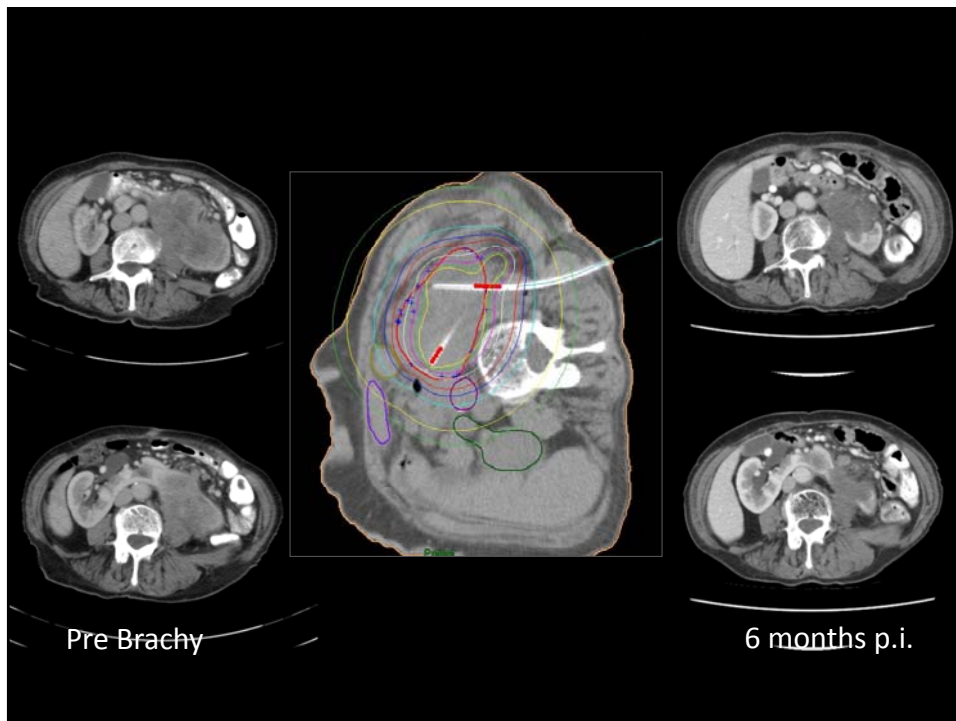


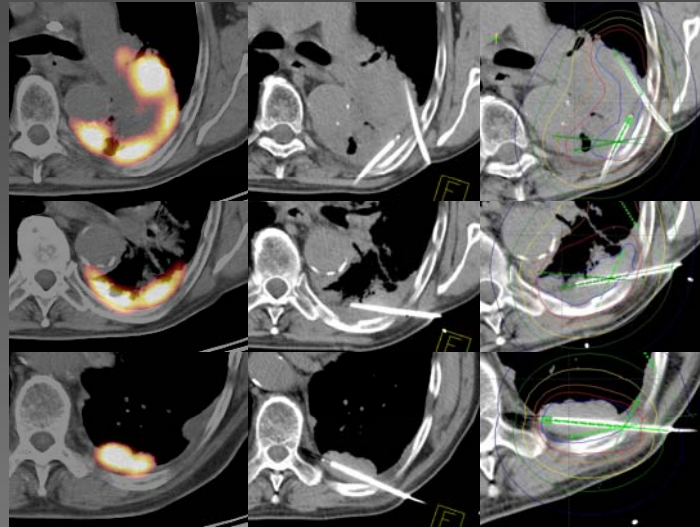
Weichselbaum, R. *Nat. Rev. Clin. Oncol.* 8, 378–382 (2011)



Characteristics of oligometastatic disease

- Number of metastases
- Number of organ systems involved
- Synchronous versus metachrone
 - Residual disease?
- Tumor biology
 - Disease free interval
 - Tumor dynamics
 - Biomarkers





Images: Ricke

Table 5: Variables investigated as potential predictors for progression free survival and overall survival following first local ablation (multivariate analysis)

Variable	PFS p (log rank/Cox)	OS p (log rank/Cox)
Age (<65, 65+)	0,776	0,523
lesion size *	0,188**; 0,025***	0,746
synchronous disease (yes/no)	0,085	0,245
lesion shape (round, oligonodular)	0,036**; 0,228***	0,008**, 0,014***
unilobar or bilobar disease	0,706	0,296
total number of liver lesions	0,907	0,442
Local recurrence	n.a.	0,948

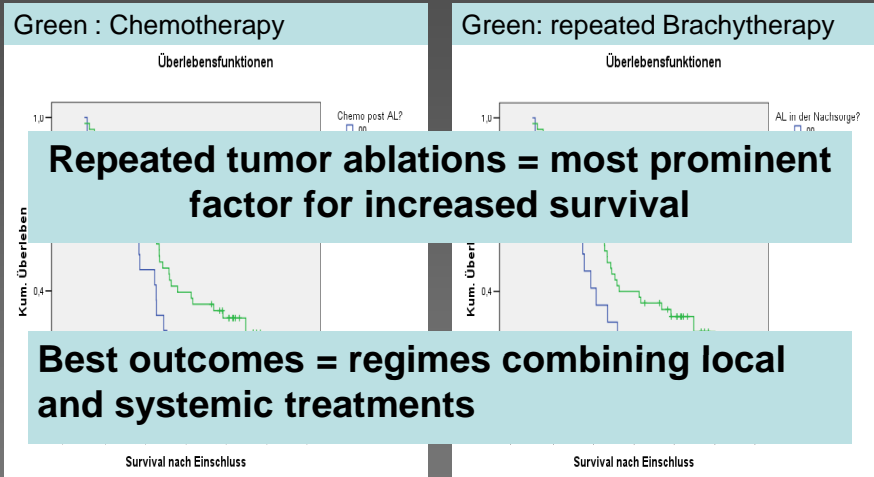
* largest lesion at the time of first local ablation **incl. local recurrence ***excl. local recurrence



Ricke IJROBP 2010



Extensive local ablation in mCRC



Ricke IJROBP 2010

Local control after CT-Brachytherapy

- CRC: 80 - 90% (12 months, 2-15cm) ^{1,2}
- Breast: >95% (12 months, 3-12cm) ^{3,4}
- Cholangiocellular/Adenoca: >80% ^{5,6}
- HCC: >90 (12 months, 5-15) ^{7,8}
- GIST/Sarkoma: 80% ⁹
- Melanoma: >80% ¹⁰

1,2 Colletini 2014, Ricke 2010
 3,4 Colletini 2014, Wieners 2011
 5,6 Kamphues 2012, Schnapauff 2012
 7,8 Colletini 2012, Mohnike 2010
 9 Bretschneider 2014
 10 Bretschneider 2014





Randomized controlled trial

Image-guided Iridium 192-HDR-Brachytherapy (iBT)

versus

Conventional Transarterial chemoembolisation (cTACE)

once or repetitive

until the primary endpoint was reached = TTUP



Mohnike presented at EASL 2013

Key inclusion criteria

- Recruitment from 2006 to 2010
 - Child-Pugh-Stage < 9 points
 - absence of portal vein thrombosis
 - at the affected liver lobe
 - total number of lesions up to 5



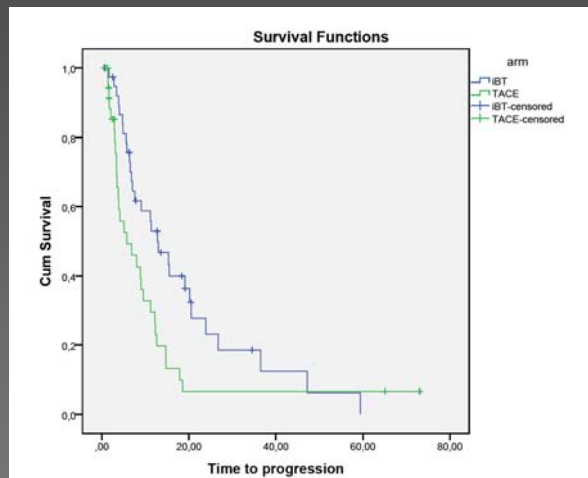
Mohnike presented at EASL 2013



Patient characteristics, mean ± SD or N (%)

		iBT* (N = 39)	cTACE† (N = 38)	p
Age		70 ± 7	67 ± 9	n.s.
Pretreatment AFP5 (ng/ml)		1065 ± 3560	1200 ± 3938	n.s.
Pretreatment Bilirubin (µmol/l)		14.6 ± 7.7	22.6 ± 13.3	n.s.
Number of lesions		2.1 ± 1,3	2.3 ± 1.1	n.s.
Longest diameter (cm)		5.2 ± 3.2; max. 15,5	4.7 ± 3.2; max. 14,7	n.s.
BCLC	A	N = 9 (23%)	N = 11 (29%)	
	B	N = 16 (41%)	N = 19 (50%)	
	C	N = 14 (36%)	N = 8 (21%)	n.s.
Child-Pugh-Score	A	N = 35 (90%)	N = 27 (71%)	
	B	N = 4 (10%)	N = 11 (29%)	0.07

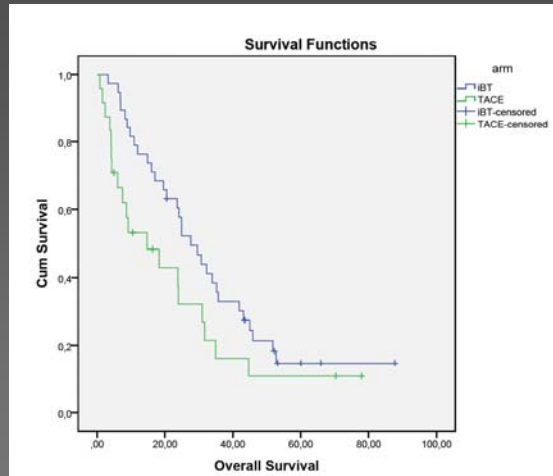
TTP



12.8 v 5.7 months
(iBT and TACE, p<0.05)



OS excluding cross over patients



27.6 v 14.7 months
(iBT and TACE, $p < 0.05$)



Complications of Liver Brachy: n=374

- 4/374 clinically evident pneumothoraces
 - CTCAE I-II, image diagnosis, no chest tube
- 3 III° ascites in 2 patients
 - 1 cirrhosis and 1 PV- thrombosis
- Abscess: 3/343 interventions



Magdeburg group, unpublished data



Gastric/duodenal ulcer

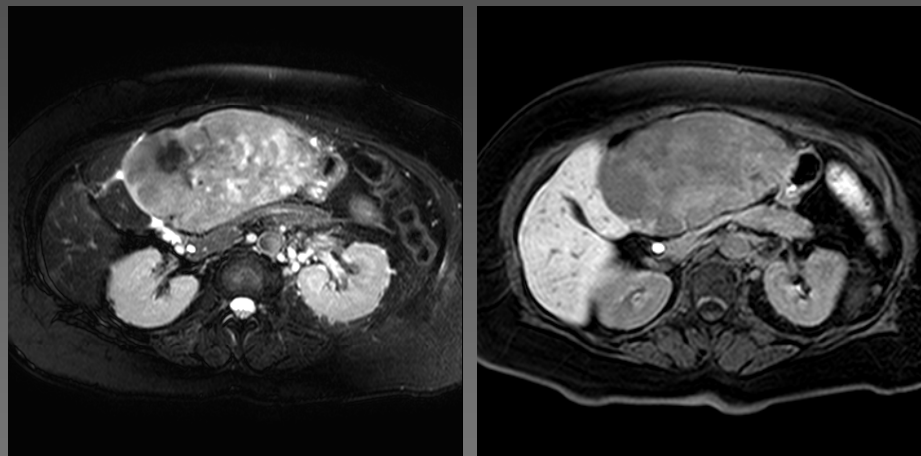
- Ulcerations in 3/343 interventions*
- Stomach organ-at-risk in 59 interventions**
 - w/ ulceration: mean 14.33 Gy/ml
 - w/o ulceration: mean 10.02 Gy/ml (1-19 Gy/ml)
- Prevention: protection (pantoprozol) for ≥ 6 weeks
- Dose treshold: 14Gy/1cc organ surface



*Magdeburg group, unpublished data

**Streitparth IJROBP 2005

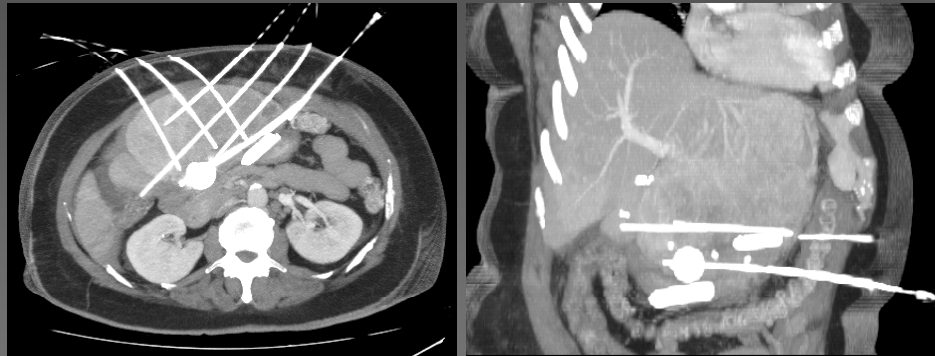
Single fraction treatments of large volumes



Images: Ricke

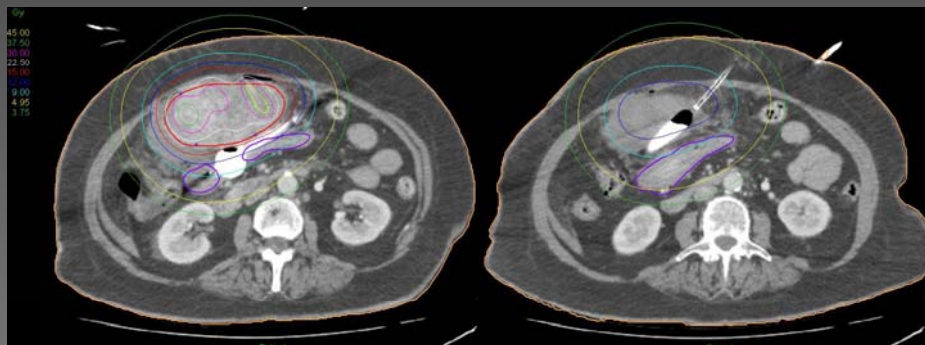


Single fraction treatments of large volumes



Images: Ricke

Single fraction treatments of large volumes



Images: Ricke

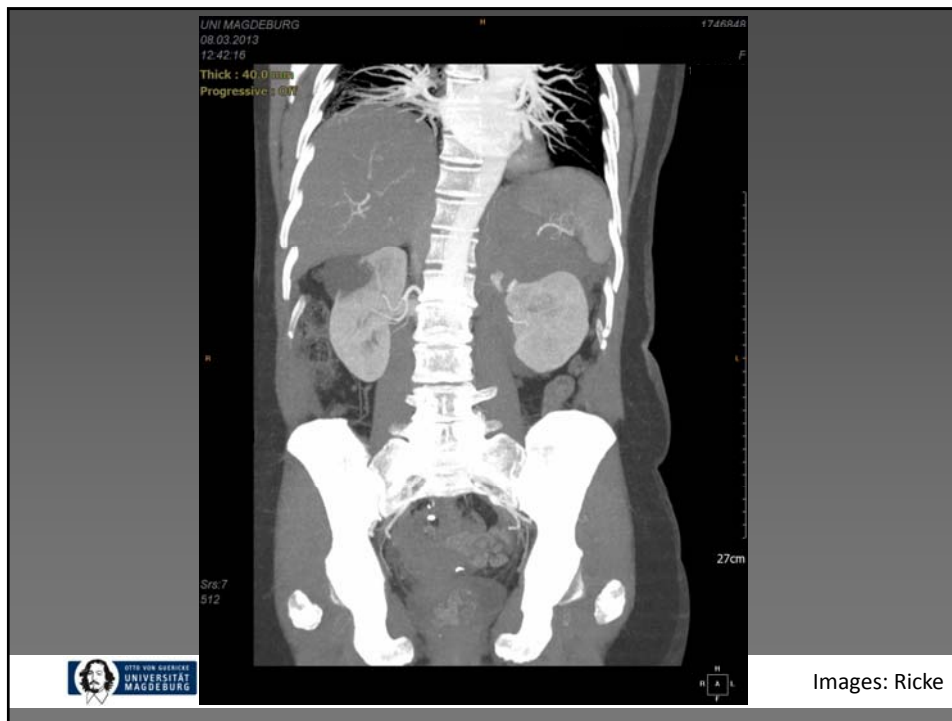


Bleeding after Liver Brachytherapy

- 5 grade III-IV (CTCAE) (1.4%, but only in cirrhotic patients!)
 - All managed by coil embolization
 - 1 death after consecutive liver failure (cirrhotic liver, hb↓ for 3h)
- Child A: 2/74 interventions (2.7%)
- Child B: 3/13 interventions (23%)
 - Relative risk of severe hemorrhage: 22fold higher in \geq Child B



Magdeburg group, unpublished data



Images: Ricke





Take home points

- Not a single one of all interventions shown...
... could have been done by RFA or Microwave
- Team up with your IR!
 - Radiation is highly superior to thermal ablation
 - Your IR is the master of image guidance



Take home points

- Gyn and ENT is only a small fraction of what should be done
- Clinical outcome data is key
 - The concept of oligometastatic disease is for Brachy



BrachyNext

Working Together to Shape the Future of
Brachytherapy



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DFMT
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Welcome

What we stand for

- Exclusive training programs in minimally-invasive treatment techniques
- Teaching in an interdisciplinary context
- Modern hands-on trainings in small groups learning life case scenarios
- Preclinical research



Microtherapy or minimal-invasive medicine opens a perspective of completely new therapeutic dimensions in numerous medical subspecialties. In some fields such as Oncology or vascular diseases it has already or bears potential to change existing treatment paradigms. Technical advances enable treatment of an increasing number of diseases with a minimum of trauma and discomfort to the patient. However, such strategies demand a highly developed sense of interdisciplinary strategies and a culture of teamwork and communication across medical specialties. The same challenges apply for the development of new materials, tools and interventional techniques which can only be successfully implemented in close

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