Associazione Italiana Radioterapia Oncologica

XXIV CONGRESSO NAZIONALE
AIRO
Padova, 8-11 novembre

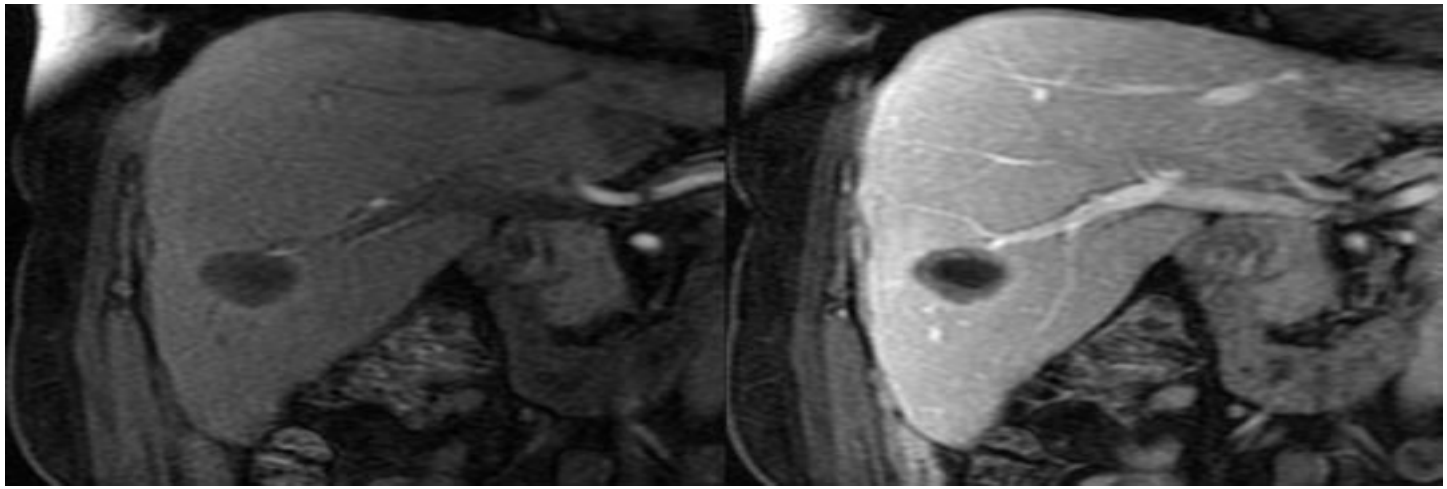
SIMPOSIO AIRO-SIRM

LA MALATTIA METASTATICA EPATICA: IL RUOLO DELLA SBRT

Filippo Alongi MD
Chief, Radiation Oncology

Ospedale
Sacro Cuore - Don Calabria
Negrar (Verona)

LIVER METASTASES :
WHAT IS THE STANDARD OF CARE?



- The most common metastatic lesion in the liver is from **colorectal adenocarcinoma** (50% colon cancer pts with liver metastasis at diagnosis).

- **If untreated**, 3-year survival is 3% with **no survivors at the 5** year time point.
  Choti et al, Ann Surg 2002

- Negative margins liver **resection** resulted in **5 years** survival between **25 and 60%**
  Fong et al, Ann Surg 1999
  Rosen et al, Ann Surg 1992

LIVER METASTASES :
WHAT IS THE STANDARD OF CARE?

•**Liver resection** feasibility is based on:

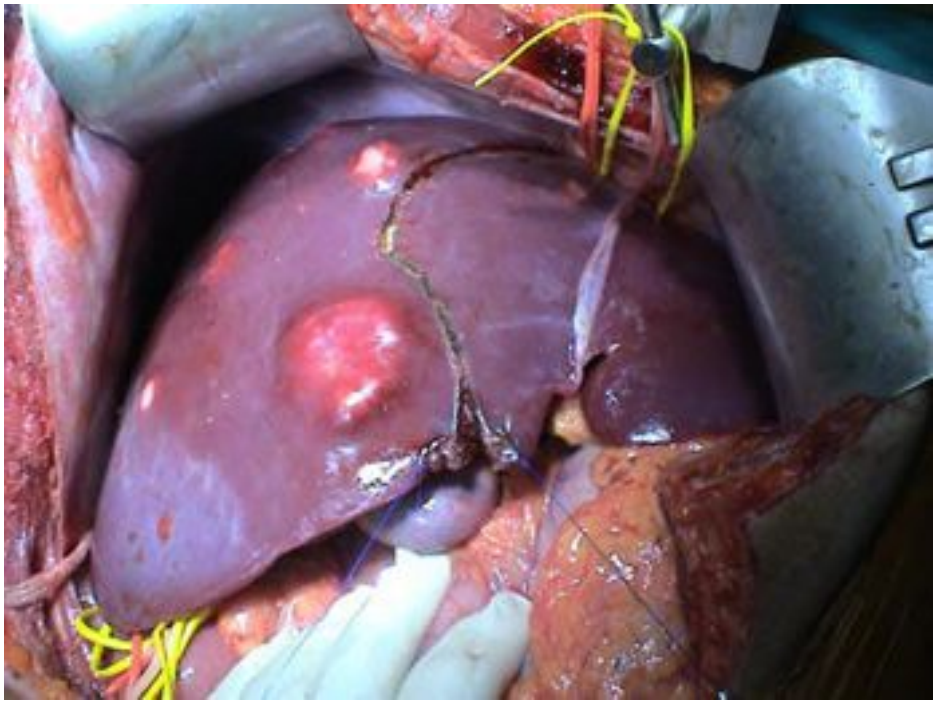
-limited number of lesions,

- intrahepatic locations of lesions,

- lack of major vascular involvement,

-absent or limited extrahepatic disease,

-sufficient functional hepatic reserve



Thus, the patients considered to be resectable are few and selected (20%)

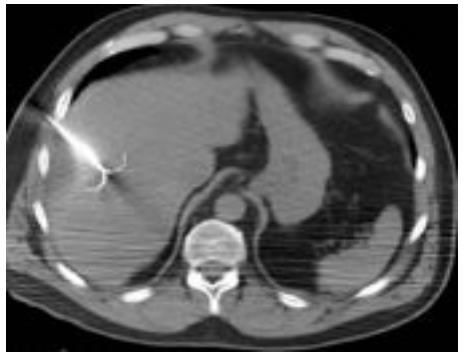
Altendorf-Hofmann et al, Surg Oncol Clin N Am 2003

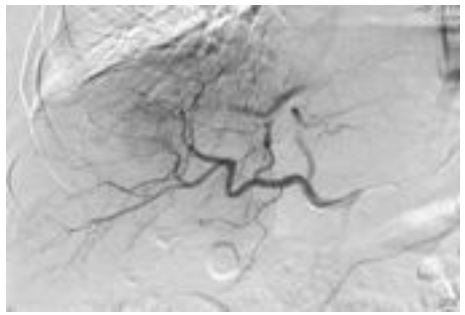
LIVER METASTASES :
WHAT IS THE STANDARD OF CARE?

Local options for patients **(80%)** not resectable or not candidates for liver resection remain**:**

- Radiofrequency ablation (RFA)
- Cryosurgical ablation
- Transasterial chemo-embolization (TACE)
- Percutanoeous Ethanol Injection (PEI)
- High Focused Ultrasound ablation (HIFU)
- Interstitial radiation therapy

Pawlik, et al, Ann Surg onco 2003
Bageacu et al, Eur J Surg Oncol 2007
Garcea G, Eur J Cancer 2003





However, these are (mini) invasive approaches, technically limited by several factors (distance to vessels or OARs, size <3cm, number, etc)

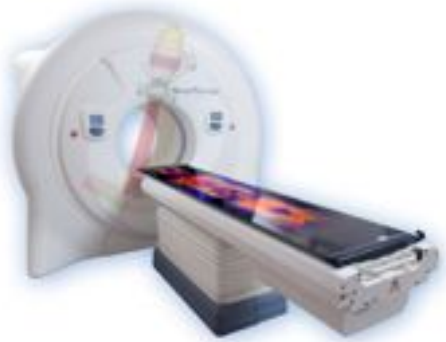
LIVER METASTASES :
WHAT ABOUT RT??

•Historically, hepatic **radiotherapy** has been limited due to the low tolerance of the whole liver to radiation and the potential for radiation induced liver disease (**RILD**).

Park et al, Int J Radiat Oncol Biol Phys 2002
Tai et al, Int J Radiat Oncol Biol Phys 2009

STEREOTACTIC BODY RT(SBRT):
HIGH TECH REVOLUTION

With new technology devices, now is possible to delivery high (ablative) doses to small volumes (SRS and SBRT/SABR)



PRECISION DEVISES TO DELIVERY SBRT/SRS

ABLATIVE (SB)RT:
FROM BRAIN STEREOTAXIS TO NEW INDICATIONS

STEREOTACTIC HIGH DOSE FRACTION RADIATION THERAPY OF EXTRACRANIAL TUMORS USING AN ACCELERATOR

Clinical experience of the first thirty-one patients

HENRIC BLOMGREN, INGMAR LAX, INGEMAR NÄSLUND and RUT SVANSTRÖM

˝Our impression at present is that SRT with high-dose fractions may **not only** be of clinical value **for patients with intracranial metastases** but also for some patients with extracranial lesions˝.

Blomgren H, Acta Oncol 1995; 34(6): 861-70

OLIGOMETASTASES:
THE NEW PARADIGMA FOR ABLATIVE DOSES WITH RT

VOLUME 31 · NUMBER 11 · APRIL 10 2013
JOURNAL OF CLINICAL ONCOLOGY | COMMENTS AND CONTROVERSIES

Extracranial Oligometastases: A Subset of Metastases Curable With Stereotactic Radiotherapy

Kimberly S. Corbin, Samuel Hellman, and Ralph R. Weichselbaum, *University of Chicago Medical Center, Chicago, IL*

The Oncologist | Radiation Oncology

Review and Uses of Stereotactic Body Radiation Therapy for Oligometastases

Filippo Alongi,[a] Stefano Arcangeli,[a] Andrea Riccardo Filippi,[b] Umberto Ricardi,[b] Marta Scorsetti[a]

H. Badakhshi · A. Grün · C. Stromberger · V. Budach · D. Boehmer
Department for Radiation Oncology, Charité University Medicine, Berlin

Oligometastases: the new paradigm and options for radiotherapy

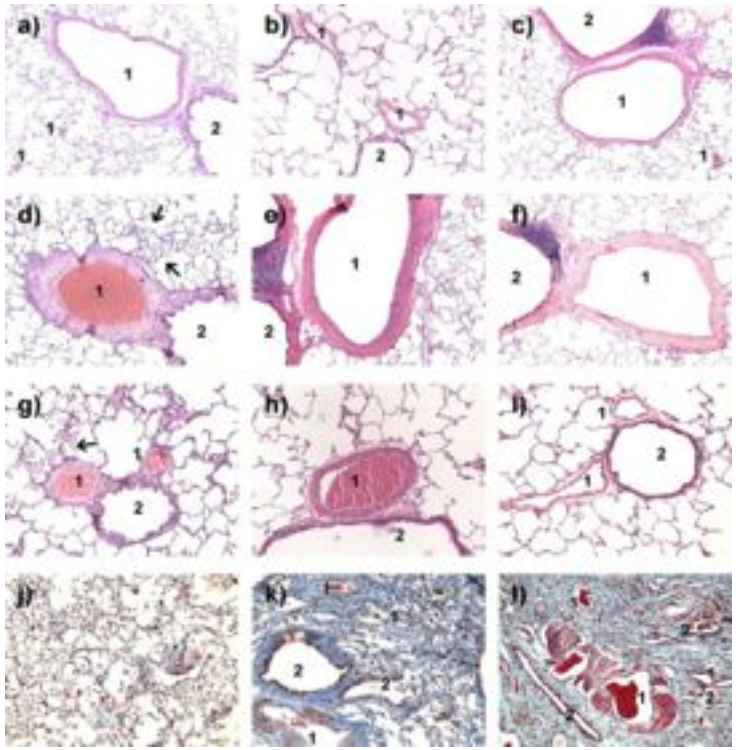
A critical review

VOLUME 32 · NUMBER 26 · SEPTEMBER 10 2014
JOURNAL OF CLINICAL ONCOLOGY | REVIEW ARTICLE

Radical Irradiation of Extracranial Oligometastases

Joseph K. Salama and Michael T. Milano

STEREOTACTIC BODY RT(SBRT):
BIOLOGICAL RATIONALE OF ABLATION



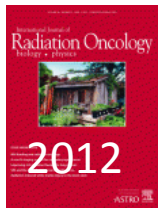
- In terms of ***Radiobiology, SBRT*** **/SABRT** may add a novel mechanism of radiation-induced damage.

- At higher doses per fraction (***ablative doses***), emerging data suggest that a different mechanism involving microvascular damage begins to have a substantial effect on the tumor cell kill.
Garcia - Barros M., et al. Science, 2003

Targeting the tumor vasculature for obliteration with high-dose radiation may be beneficial for tumor control.
Fuks and Kolesnick, Cancer Cell 2005 .

LIVER STEREOTACTIC (ABLATIVE) RT:
WHAT ARE THE RESULTS?

CRITICAL REVIEW



RADIOTHERAPY FOR LIVER METASTASES: A REVIEW OF EVIDENCE

MORTEN HØYER, PH.D.,* ANAND SWAMINATH, M.D.,† SEAN BYDDER, B.H.B., M.B.CH.B.,‡ MICHAEL LOCK, M.D.,§ ALEJANDRA MÉNDEZ ROMERO, PH.D.,‖ BRIAN KAVANAGH, M.P.H.,¶ KARYN A. GOODMAN, M.D.,# PAUL OKUNIEFF, M.D.,** AND LAURA A. DAWSON, M.D.†

CME ASTRO

Local control of liver metastases using SBRT is encouraging, with rates ranging from **70% to 100%** at 1 year and 60% to 90% at 2 years

LIVER STEREOTACTIC (ABLATIVE) RT:
WHAT ARE THE RESULTS?

Which endpoints should be considered for clinical trials of RT for liver metastases?

Primary **endpoints on trials** on ablation of liver metastases include:

-survival,

-progression-free survival,

-and *(not only) local control* of treated tumors.

LIVER STEREOTACTIC (ABLATIVE) RT:
WHAT ARE THE RESULTS? RETROSPECTIVE STUDIES

Table 2. Overview of retrospective studies of SBRT for liver metastases

Primary author	No. of patients	Tumor volume	Type of mets	RT dose	Toxicity	Outcomes
Blomgren (34), 1995	14	3–260 mL	CRC (11) Anal canal (1) Kidney (1) Ovarian (1)	7.7–45 Gy (1–4 frx)	2 cases of hemorrhagic gastritis	50% response rate
Wada (44), 2004	5	NR	NR	45 Gy (3 frx)	No serious toxicity	2-yr LC, 71.2%
Wulf (36), 2006	44 (39 liver mets)	9–355 mL	CRC (23) Breast (11) Ovarian (4) Other (13)	30–37.5 Gy (3 frx) 26 Gy (1 frx)	No Grade 2–4 toxicity	1-yr LC, 92% 2-yr LC, 66% 1-yr OS, 72% 2-yr OS, 32%
Katz (40), 2007	69	0.6–12.5 cm (median, 2.7 cm)	CRC (20) Breast (16) Pancreas (9) Lung (5) Other (19)	30–55 Gy (5–15 frx)	No Grade 3/4 toxicity	10-mo LC, 76% 20-mo LC, 57% Median survival, 14.5 mo
van der Pool (42), 2010	20	0.7–6.2 cm (median, 2.3 cm)	CRC (20)	30–37.5 Gy (3 frx)	2 Grade 3 late liver enzyme changes 1 Grade 2 rib fracture	1-yr LC, 100% 2-yr LC, 74% Median survival, 34 mo

Hoyer et al Int J Radiat Oncol Biol Phys 2012

LIVER STEREOTACTIC (ABLATIVE) RT:
WHAT ARE THE RESULTS? PROSPECTIVE STUDIES

Table 1. Overview of prospective studies of SBRT for liver metastases

Primary author	Design	No. of patients with mets	Tumor volume	Type of mets	RT dose	Toxicity	Outcomes
Herfarth (32), 2004	Phase I–II	35	1–132 mL (median, 10 mL)	Not reported by patient	Dose escalation, 14–26 Gy (1 frx)	No significant toxicity reported	1-yr LC, 71% 18-mo LC, 67% 1-yr OS, 72%
Méndez Romero (30), 2006	Phase I–II (HCC and mets)	25 (17 liver mets)	1.1–322 mL (median, 22.2 mL)	CRC (14) Lung (1) Breast (1) Carcinoid (1)	30–37.5 Gy (3 frx)	2 Grade 3 liver toxicities	2-yr LC, 86% 2-yr OS, 62%
Hoyer (41), 2006	Phase II (CRC oligomets)	64 (44 liver mets)	1–8.8 cm (median, 3.5 cm)	CRC (44)	45 Gy (3 frx)	1 liver failure 2 severe late GI toxicities	2-yr LC, 79% (by tumor) and 64% (by patient)
Rusthoven (37), 2009	Phase I–II	47	0.75–97.98 mL (median, 14.93 mL)	CRC (15) Lung (10) Breast (4) Ovarian (3) Esophageal (3) HCC (2) Other (10)	Dose escalation, 36–60 Gy (3 frx)	No RILD Late Grade 3/4 <2%	1-yr LC, 95% 2-yr LC, 92% Median survival, 20.5 mo
Lee (33), 2009	Phase I–II	68	1.2–3,090 mL (median, 75.9 mL)	CRC (40) Breast (12) Gallbladder (4) Lung (2) Anal canal (2) Melanoma (2) Other (6)	Individualized dose, 27.7–60 Gy (6 frx)	No RILD 10% Grade 3/4 acute toxicity No Grade 3/4 late toxicity	1-yr LC, 71% Median survival, 17.6 mo
Ambrosino (39), 2009	Prospective cohort	27	20–165 mL (median, 69 mL)	CRC (11) Other (16)	25–60 Gy (3 frx)	No serious toxicity	Crude LC rate 74%
Goodman (35), 2010	Phase I (HCC and liver mets)	26 (19 liver mets)	0.8–146.6 mL (median, 32.6 mL)	CRC (6) Pancreatic (3) Gastric (2) Ovarian (2) Other (6)	Dose escalation, 18–30 Gy (1 frx)	No dose–limiting toxicity 4 cases of Grade 2 late toxicity (2 GI, 2 soft tissue/rib)	1-yr local failure, 23% 2-yr OS, 49% (mets only)

Abbreviations: SBRT = stereotactic body radiotherapy; mets = metastases; RT = radiotherapy; LC = local control; OS = overall survival; HCC = hepatocellular carcinoma; CRC = colorectal; RILD = radiation-induced liver disease; frx = fractions; GI = gastrointestinal.

Hoyer et al Int J Radiat Oncol Biol Phys 2012

LIVER STEREOTACTIC (ABLATIVE) RT:
WHAT ARE THE RESULTS?

Which endpoints should be considered for clinical trials of RT for liver metastases?

SURVIVAL

•**2-year overall survival rates:** 30%-83%, with occasional long-term survivors .

•However, out-of-field metastatic progression develops in a substantial proportion of patients;

•Therefore, there is a strong rationale to ***combine SBRT with systemic treatments***.

LIVER STEREOTACTIC (ABLATIVE) RT:
WHO ARE THE CANDIDATES?

•*No randomized* Phase III (SABR vs Surgery) data have been reported.

•There is *significant heterogeneity* concerning:
-patient selection (CRC vs. other primary subtypes),
-tumor volumes,
-total dose, dose per fraction,
-and dosimetric planning criteria.

Ideal candidates for liver metastasis SBRT shoud have:
- a good performance status (Eastern Cooperative Oncology Group 0–1),
-adequate hepatic function,
-no extrahepatic disease,
-an uninvolved liver volume of 700 mL or greater

Hoyer et al Int J Radiat Oncol Biol Phys 2012

LIVER STEREOTACTIC (ABLATIVE) RT:
HOW WE CAN DO IT?

To improve the accuracy of the treatment SBRT involves:

- **high accuracy and precision of highly conformal,**
- **high-dose RT, delivered in a limited number of fractions,**
- **immobilization and motion management**
- **Multimodal imaging, IGRT, advanced planning,**

LIVER STEREOTACTIC (ABLATIVE) RT:
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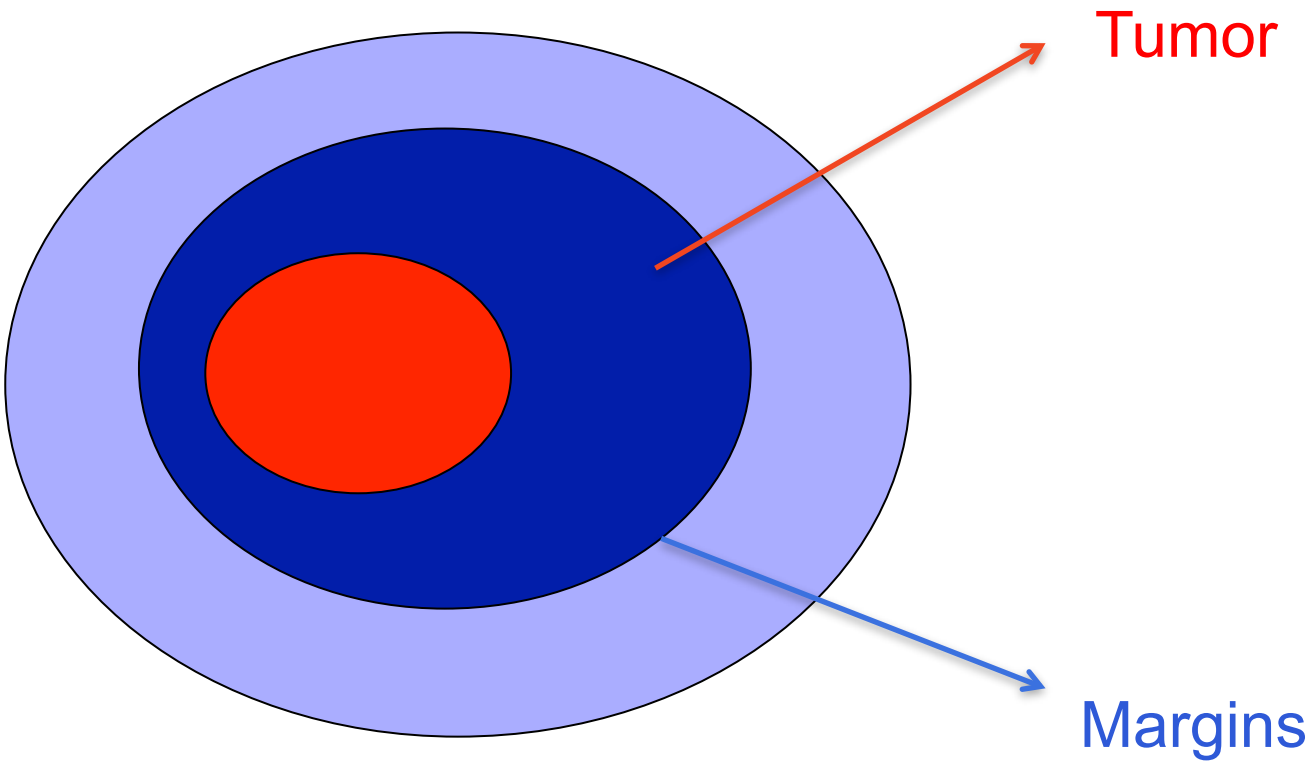
IMOBILIZATION AND MOTION MANAGEMENT

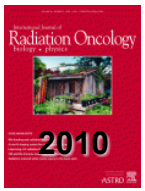
Treatment planning: Treatment volumes



WILD MARGINS INCREASE THE RISK OF TOXIC EFFECTS

IMOBILIZATION AND MOTION MANAGEMENT

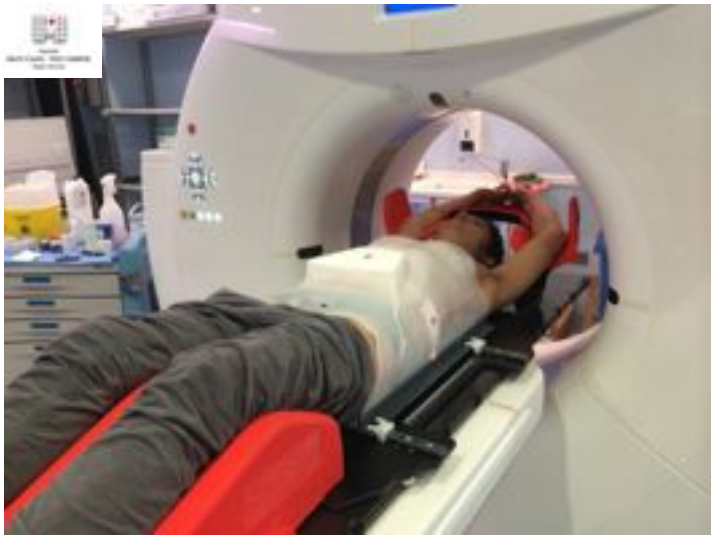
MANAGEMENT BY ABDOMINAL COMPRESSION

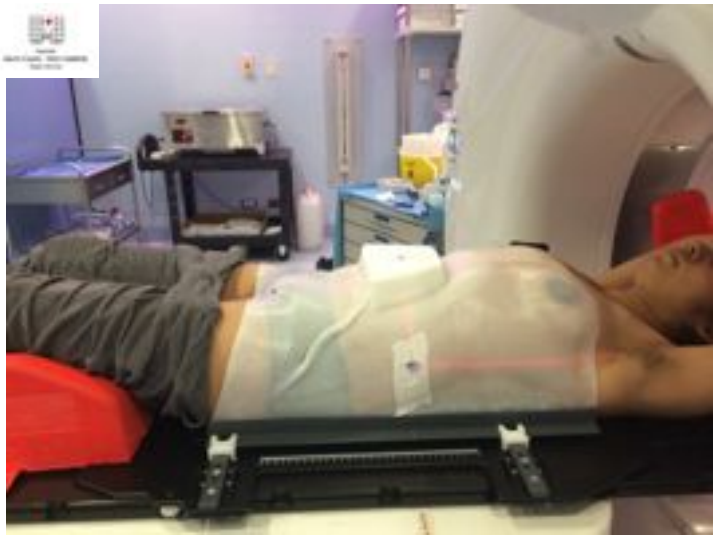


INTERFRACTION LIVER SHAPE VARIABILITY AND IMPACT ON GTV POSITION DURING LIVER STEREOTACTIC RADIOTHERAPY USING ABDOMINAL COMPRESSION

CYNTHIA L. ECCLES, B.SC., LAURA A. DAWSON, M.D., JOANNE L. MOSELEY, PH.D., AND KRISTY K. BROCK, PH.D.

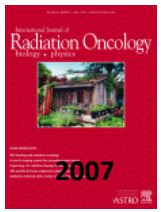
Conclusions: Interfraction liver deformations in patients undergoing SBRT under abdominal compression after rigid liver-to-liver registrations on respiratory sorted CBCT scans were small in most patients (<5 mm).





IMOBILIZATION AND MOTION MANAGEMENT

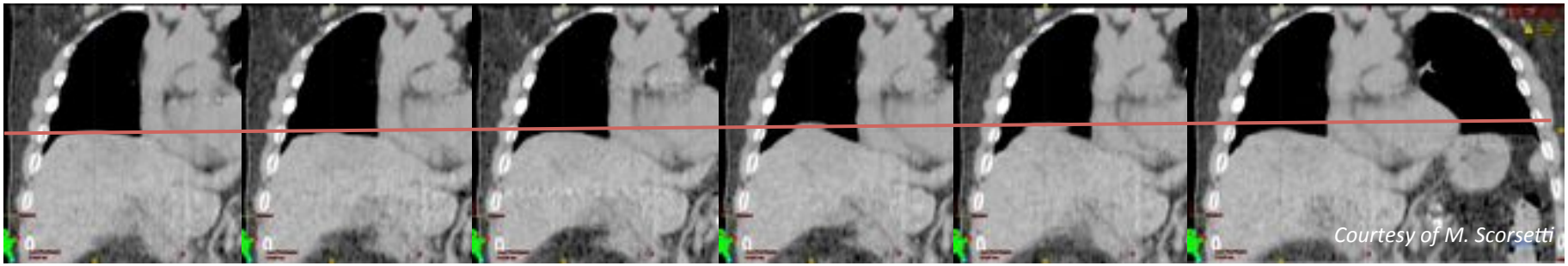
MANAGEMENT BY 4DCT



FOUR-DIMENSIONAL COMPUTED TOMOGRAPHY SCAN ANALYSIS OF TUMOR AND ORGAN MOTION AT VARYING LEVELS OF ABDOMINAL COMPRESSION DURING STEREOTACTIC TREATMENT OF LUNG AND LIVER

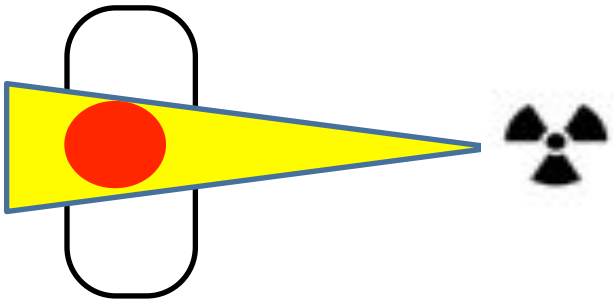
JOHN H. HEINZERLING, M.D.,* JOHN F. ANDERSON, B.S.,* LECH PAPIEZ, PH.D.,* THOMAS BOIKE, M.D.,* STANLEY CHIEN, PH.D.,† GEOFFREY ZHANG, PH.D.,* RAMZI ABDULRAHMAN, M.D.,* AND ROBERT TIMMERMAN, M.D.*

Conclusions: Four-dimensional CT shows significant control of both lower lobe lung and liver tumors using abdominal compression. High levels of compression improve SI tumor motion when compared with MC.

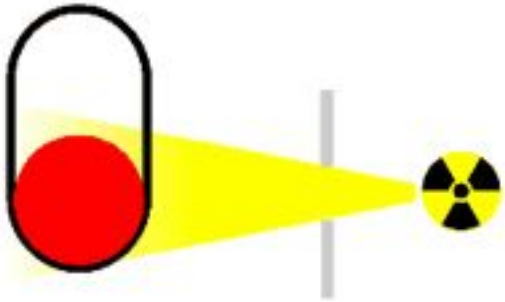


MANAGEMENT BY TRACKING OR GATING

TRACKING



GATING



IMOBILIZATION AND MOTION MANAGEMENT

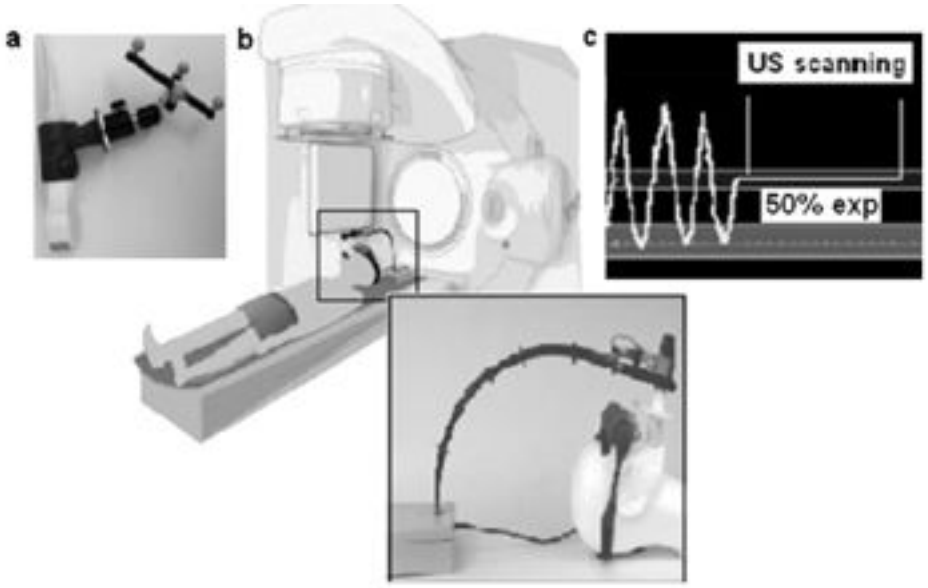
MANAGEMENT BY REAL TIME TUMOR TRACKING

LINAC INTEGRATED DEVICES

DEDICATED ROBOTIC LINAC WITH INTEGRATED TRECKING SYSTEMS

IMOBILIZATION AND MOTION MANAGEMENT

GATING WITH ACTIVE BREATH CONTROL



2006

Strahlentherapie und Onkologie
Original Article

Frameless Stereotactic Radiosurgery of a Solitary Liver Metastasis Using Active Breathing Control and Stereotactic Ultrasound

Judit Boda-Heggemann[1], Cornelia Walter[1], Sabine Mai[1], Barbara Dobler[1], Dietmar Dinter[2], Frederik Wenz[1], Frank Lohr[1]

2012

International Journal of Radiation Oncology biology • physics

Active Breathing Control in Combination With Ultrasound Imaging: A Feasibility Study of Image Guidance in Stereotactic Body Radiation Therapy of Liver Lesions

Esther Bloemen-van Gurp, PhD,* Skadi van der Meer, MSc,* Janet Hendry, MSc,* Jeroen Buijsen, MD,* Peter Visser, MSc,* Davide Fontanarosa, MSc,* Martin Lachaine, PhD,† Guido Lammering, MD, PhD,* and Frank Verhaegen, PhD*,‡

LIVER STEREOTACTIC (ABLATIVE) RT:
HOW WE CAN DO IT?

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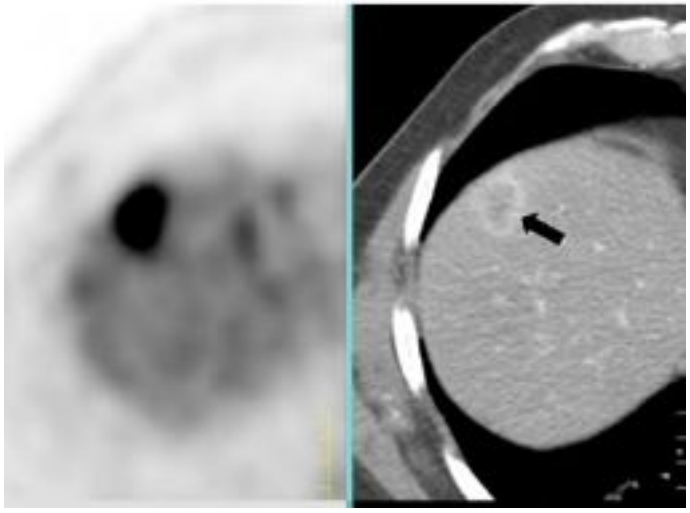
TARGET EVALUATION AND MANAGEMENT BY CT (3 phases) and PET

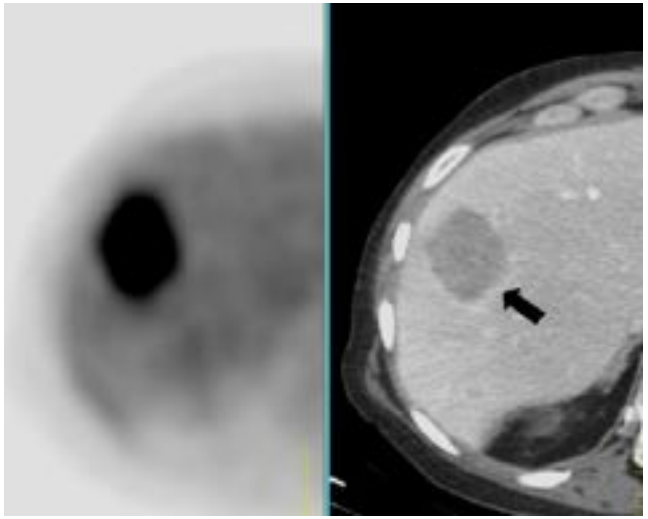
RADIOLOGY 2012

Evaluation of contrast medium enhancement and [^{18}F]-FDG uptake of liver metastasis in PET/CT prior to therapy

Walter Hundt[a,*,1], Christian la Fougère[c,1], Jelena Vogtmann[b], Silke Steinbach[d], Mykhaylo Burbelko[a], Reinhold Tiling[c]



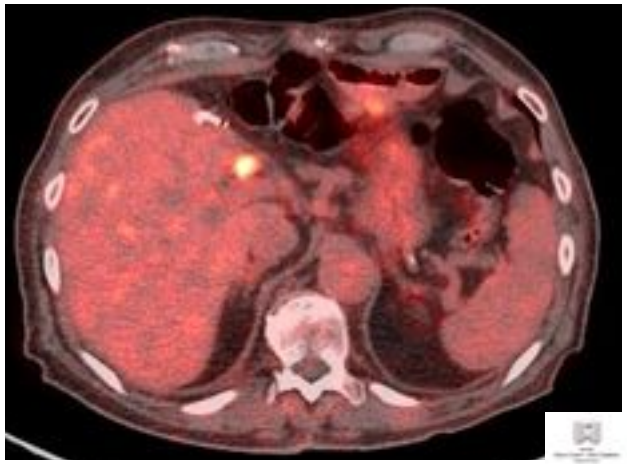
Liver metastases of a colon carcinoma.



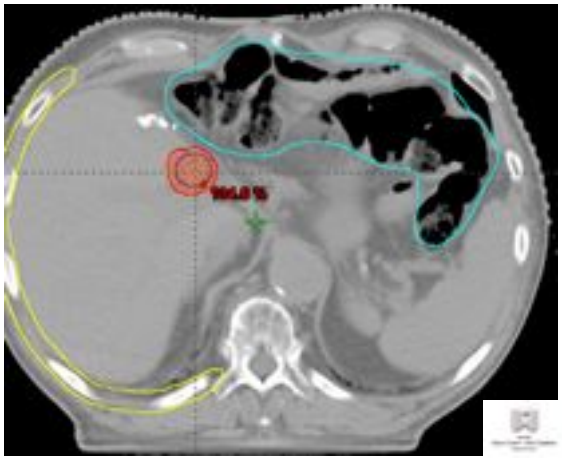
Liver metastases of a breast carcinoma.

MULTIMODAL IMAGING & PRECISION OF HIGHLY CONFORMAL

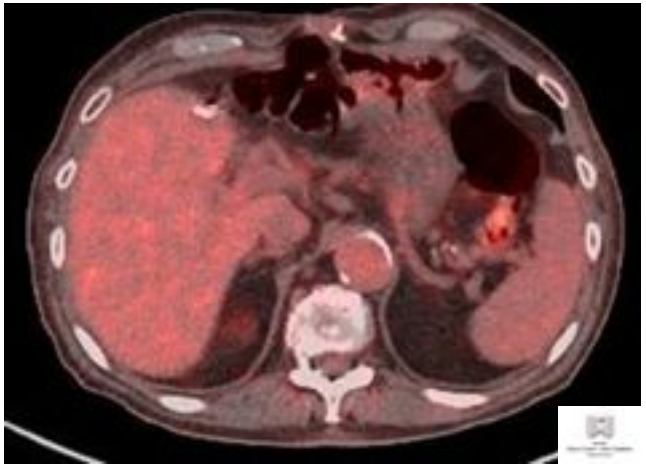
Patient treated with SBRT for isolated M+ (primary colon)



PET–CT pre-treatment,



RapidArc-FFF beams on Truebeam



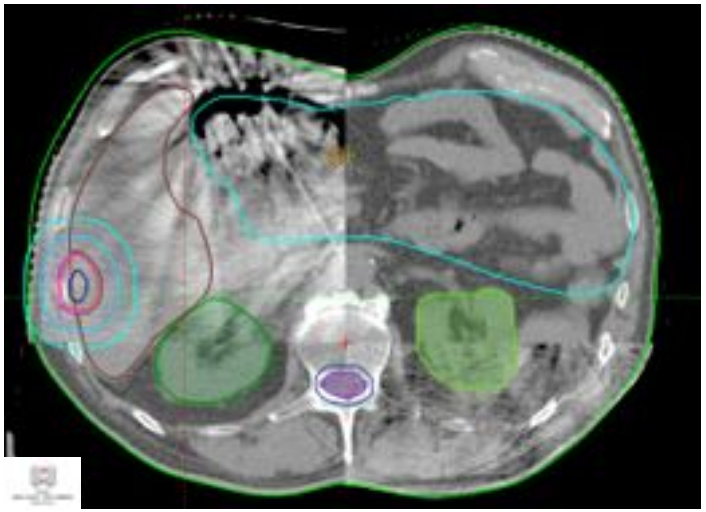
PET–CT post-treatment

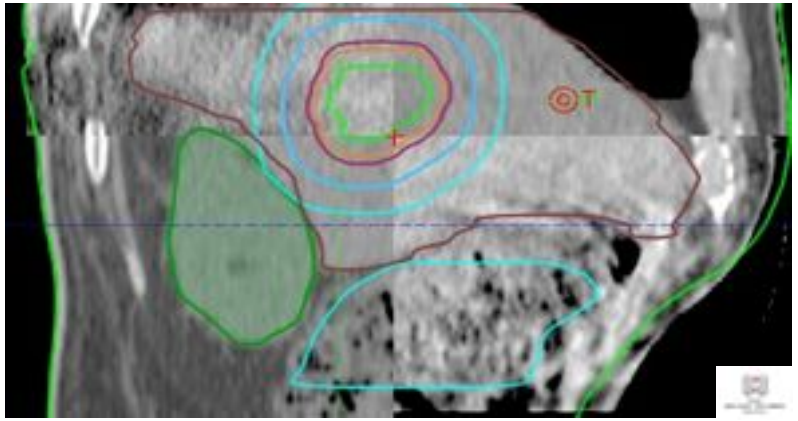
IMAGE GUIDE RADIATION THERAPY

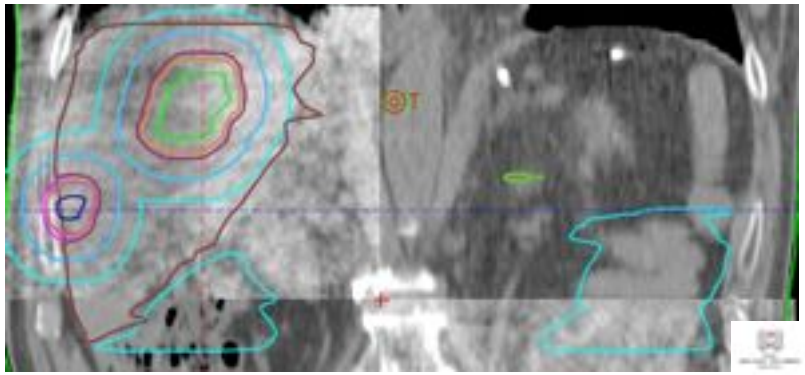
IGRT by CBCT

CBCT strongly suggested for:

- SRS & SBRT/SABR(without cranial/body- frame







CT sim-CBCT matching for liver SBRT

CONTRAINTS AND PLANNING

• Liver obeys the **parallel architecture model of radiobiology**, so the risk of RILD is more dependent on:

-The **mean dose** of radiation delivered to normal liver tissue (threshold 30 Gy, with an incresing risk of 4% per Gy)
-The **critical volume** irradiated (strong "volume effect" estimated by Lyman NTCP model)

Table 3. Constraints proposed for 3-fraction SBRT schedule

Organ at risk	Wulf *et al.* (36)	Rusthoven *et al.* (37)	Hoyer RAS–Trial (www.cirro.dk)	RTOG 0236 SBRT lung (www.rtog.org)	QUANTEC (48)
Liver (CTV excluded)	30% <21 Gy* 50% <15 Gy*	700 mL < 15 Gy	700 mL < 15 Gy	NA	700 mL ≤15 Gy D_{mean} <15 Gy
Stomach	$D_{5\ mL}$ <21 Gy	D_{max} ≤30 Gy	$D_{1\ mL}$ <21 Gy	NA	D_{max} <30 Gy ($D_{5\ mL}$ <22.5 Gy)
Bowel	$D_{5\ mL}$ <21 Gy	D_{max} ≤30 Gy	$D_{1\ mL}$ <21 Gy	NA	D_{max} <30 Gy
Esophagus	$D_{5\ mL}$ <21 Gy	NA	$D_{1\ mL}$ <21 Gy	D_{max} ≤27 Gy	NA
Kidney	NA	Total kidney $D_{35\%}$ <15 Gy	Total kidney $D_{35\%}$ <15 Gy	NA	NA
Spinal cord	NA	D_{max} ≤18 Gy	D_{max} <18 Gy	D_{max} ≤18 Gy	D_{max} ≤20 Gy
Heart	$D_{5\ mL}$ <21 Gy	NA	$D_{1\ mL}$ <30 Gy	D_{max} ≤30 Gy	NA

•It is possible to safely treat small hepatic lesions with high doses of radiation by **using SBRT**, with adequate dose constraints for normal liver (**minimum volume of 700mL should receive a total dose less than 15 Gy)**

Tarita et al , J gastrointest Oncolo 2014

CONSTRAINTS AND PLANNING

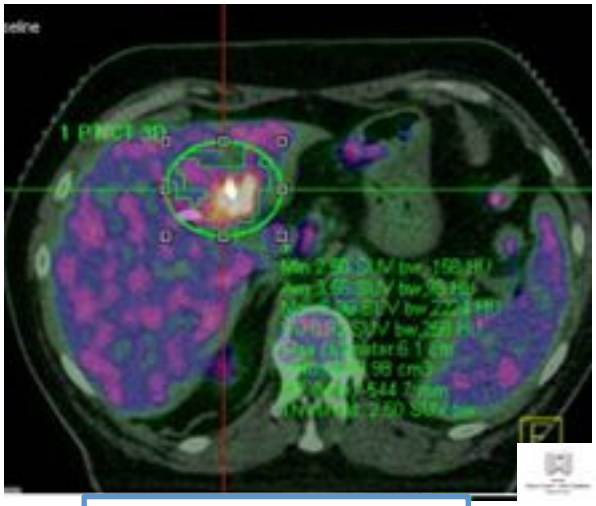
ORGAN	Dose-Volume Limits	Other Conditions
Healthy liver (defined as total liver volume minus cumulative GTV)	> 700 cc at < 15 Gy in 3 F	The volume of healthy liver > 1000 cc
Spinal cord	< 18 Gy in 3 F	
Kidneys (R+L)	V15 Gy < 35%	
Stomach, duodenum, small intestine	< 21 Gy in 3 F (also for minimum volumes)	Patients with GTV < 8 mm from the heart, stomach, duodenum and small intestine to be excluded
Heart	<30 Gy in 3 F	
Rib	V_{30gy}<2cc	

It appears that if is possible to adhere to the "**Liver constraints**" used in the published studies, the anticipated incidence of RILD should be low

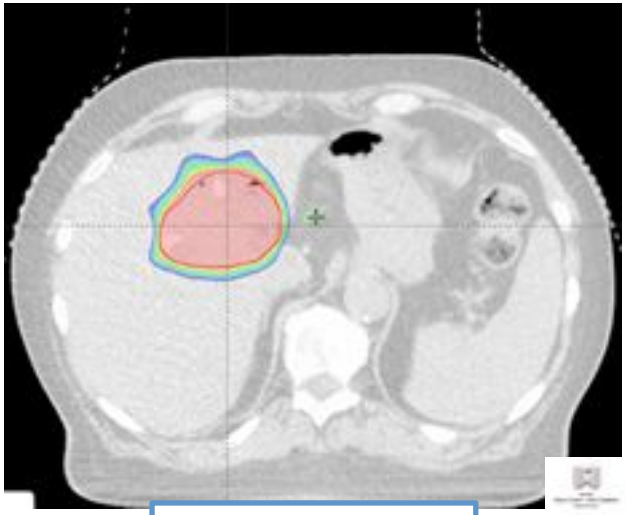
Milano et al, Radiat Oncol 2008
Rusthoven et al, JCO 2009
Scorsetti et al, Int J Radiat Oncol Biol Phys 2013

CONSTRAINTS AND PLANNING

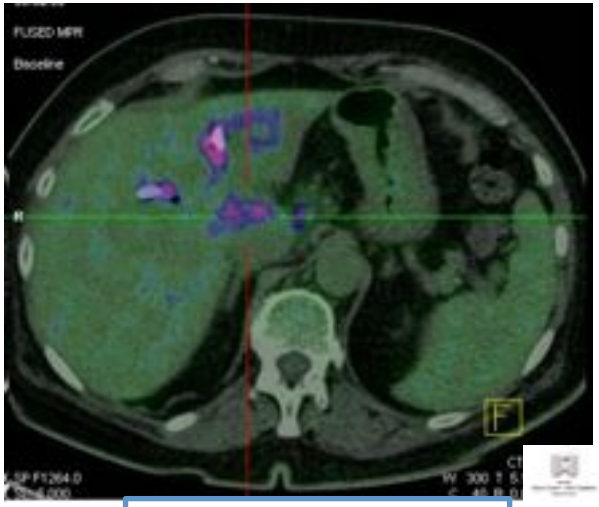
RapidArc(VMAT)-FFF beams on TrueBeam



CT-PET before SBRT



Planning CT



CT-PET after 60 days

LIVER STEREOTACTIC (ABLATIVE) RT:
..THUS, WHAT ABOUT TOXICITIES?

Table 1. Overview of prospective studies of SBRT for liver metastases

Primary author	Design	No. of patients with mets	Tumor volume	Type of mets	RT dose	Toxicity	Outcomes
Herfarth (32), 2004	Phase I–II	35	1–132 mL (median, 10 mL)	Not reported by patient	Dose escalation, 14–26 Gy (1 frx)	No significant toxicity reported	1-yr LC, 71% 18-mo LC, 67% 1-yr OS, 72%
Méndez Romero (30), 2006	Phase I–II (HCC and mets)	25 (17 liver mets)	1.1–322 mL (median, 22.2 mL)	CRC (14) Lung (1) Breast (1) Carcinoid (1)	30–37.5 Gy (3 frx)	2 Grade 3 liver toxicities	2-yr LC, 86% 2-yr OS, 62%
Hoyer (41), 2006	Phase II (CRC oligomets)	64 (44 liver mets)	1–8.8 cm (median, 3.5 cm)	CRC (44)	45 Gy (3 frx)	1 liver failure 2 severe late GI toxicities	2-yr LC, 79% (by tumor) and 64% (by patient)
Rusthoven (37), 2009	Phase I–II	47	0.75–97.98 mL (median, 14.93 mL)	CRC (15) Lung (10) Breast (4) Ovarian (3) Esophageal (3) HCC (2) Other (10)	Dose escalation, 36–60 Gy (3 frx)	No RILD Late Grade 3/4 <2%	1-yr LC, 95% 2-yr LC, 92% Median survival, 20.5 mo
Lee (33), 2009	Phase I–II	68	1.2–3,090 mL (median, 75.9 mL)	CRC (40) Breast (12) Gallbladder (4) Lung (2) Anal canal (2) Melanoma (2) Other (6)	Individualized dose, 27.7–60 Gy (6 frx)	No RILD 10% Grade 3/4 acute toxicity No Grade 3/4 late toxicity	1-yr LC, 71% Median survival, 17.6 mo
Ambrosino (39), 2009	Prospective cohort	27	20–165 mL (median, 69 mL)	CRC (11) Other (16)	25–60 Gy (3 frx)	No serious toxicity	Crude LC rate 74%
Goodman (35), 2010	Phase I (HCC and liver mets)	26 (19 liver mets)	0.8–146.6 mL (median, 32.6 mL)	CRC (6) Pancreatic (3) Gastric (2) Ovarian (2) Other (6)	Dose escalation, 18–30 Gy (1 frx)	No dose-limiting toxicity 4 cases of Grade 2 late toxicity (2 GI, 2 soft tissue/rib)	1-yr local failure, 23% 2-yr OS, 49% (mets only)

•Severe toxicity (**Grade 3 or more**) is uncommon.
•Toxicity is more likely in patients receiving a high dose to the bowel or to large volumes of the liver.

Hoyer et al Int J Radiat Oncol Biol Phys 2012

LIVER STEREOTACTIC (ABLATIVE) RT:
HOW WE CAN DO IT?

To improve the accuracy of the treatment SBRT involves:

- **high accuracy and precision of highly conformal,**
- **high-dose RT, delivered in a limited number of fractions,**
- **immobilization and motion management**
- **Multimodal imaging, IGRT, advanced planning,**

LIVER STEREOTACTIC (ABLATIVE) RT:
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LIVER METASTASES :
DOSE ESCALATION

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•Dose escalation studies with fractionated regimens of ablative radiation have shown that **A DOSE RESPONSE EXIST**.

Park et al, Int J Radiat Oncol Biol Phys 2002
Tai et al, Int J Radiat Oncol Biol Phys 2009

LIVER STEREOTACTIC BODY RT:
RADIOSURGERY(High Single dose)

•1995-1998: The earliest reports are from Stockholm in 50 pts with SRS (14.2 Gy)→80% LC @1.5-38 months

Blomgren H., et al , J Radiosurg 1995

•2001: Phase I-II study from Heidelberg with SRS (14-26Gy) in 33 Pts→98% LC @ 6 months and 81% @ 18 months

Herfarth KK er al JCO 2001

•2006: Experience from Wurzburg 26 Gy in 39 pts → 86%LC @1 year and 58% @ 2 years

Wurf et al, Acta Oncologica 2006

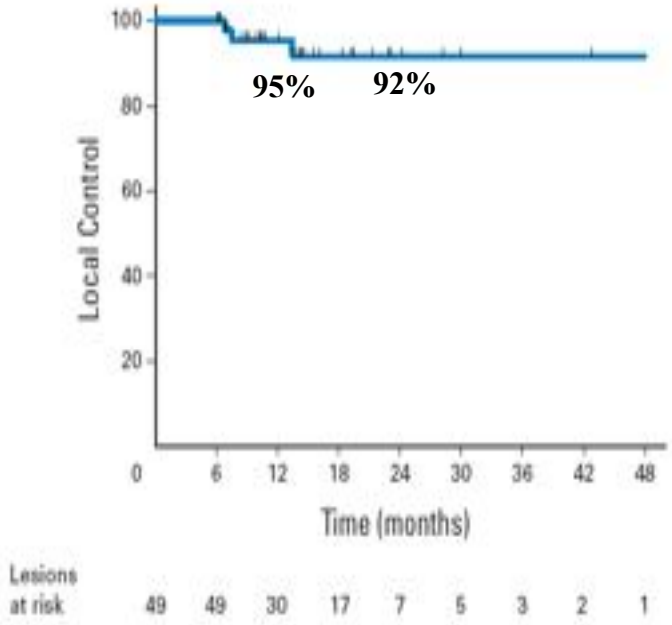
SRS via a **single-dose** is a feasible method for treatment of singular inoperable liver metastases with the potential of a high local tumor control rate and low morbidity

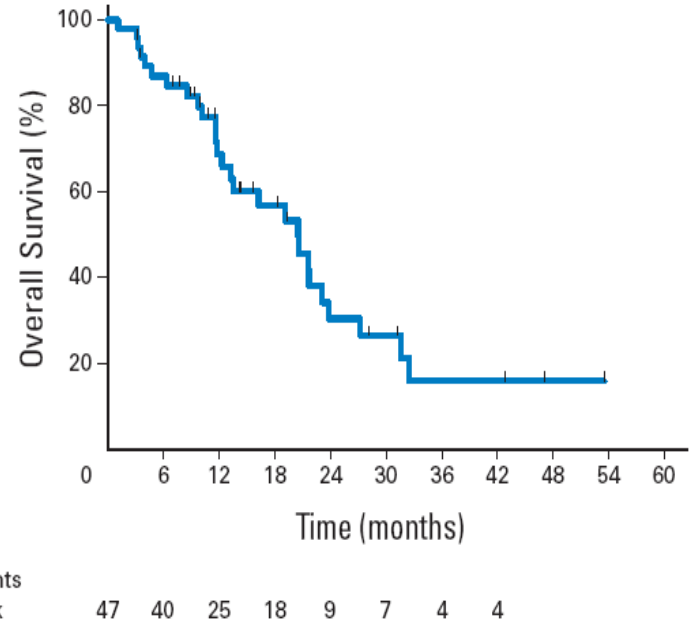
LIVER STEREOTACTIC BODY RT:
DOSE ESCALATION (60 Gy in 3)

Multi-Institutional Phase I/II Trial of Stereotactic Body Radiation Therapy for Liver Metastases

Kyle E. Rusthoven, Brian D. Kavanagh, Higinia Cardenes, Volker W. Stieber, Stuart H. Burri, Steven J. Feigenberg, Mark A. Chidel, Thomas J. Pugh, Wilbur Franklin, Madeleine Kane, Laurie E. Gaspar, and Tracey E. Schefter

2009





Correlation between local control and diameter > 3cm

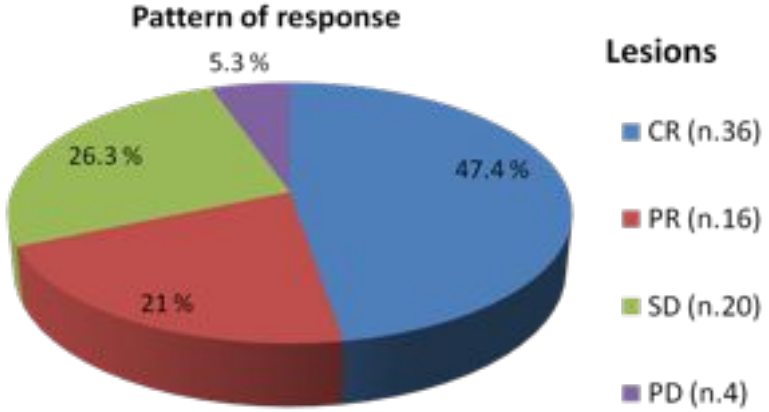
LIVER STEREOTACTIC BODY RT:
DOSE ESCALATION (75 Gy in 3)

International Journal of Radiation Oncology biology • physics
www.redjournal.org

linical Investigation: Gastrointestinal Cancer

Is Stereotactic Body Radiation Therapy an Attractive Option for Unresectable Liver Metastases? A Preliminary Report From a Phase 2 Trial

Marta Scorsetti, MD,* Stefano Arcangeli, MD,* Angelo Tozzi, MD,* Tiziana Comito, MD,* Filippo Alongi, MD,* Pierina Navarria, MD,* Pietro Mancosu, MSc,* Giacomo Reggiori, MSc,* Antonella Fogliata, MSc,† Guido Torzilli, MD,† Stefano Tomatis, MSc,* and Luca Cozzi, PhD†



95% in field response rates

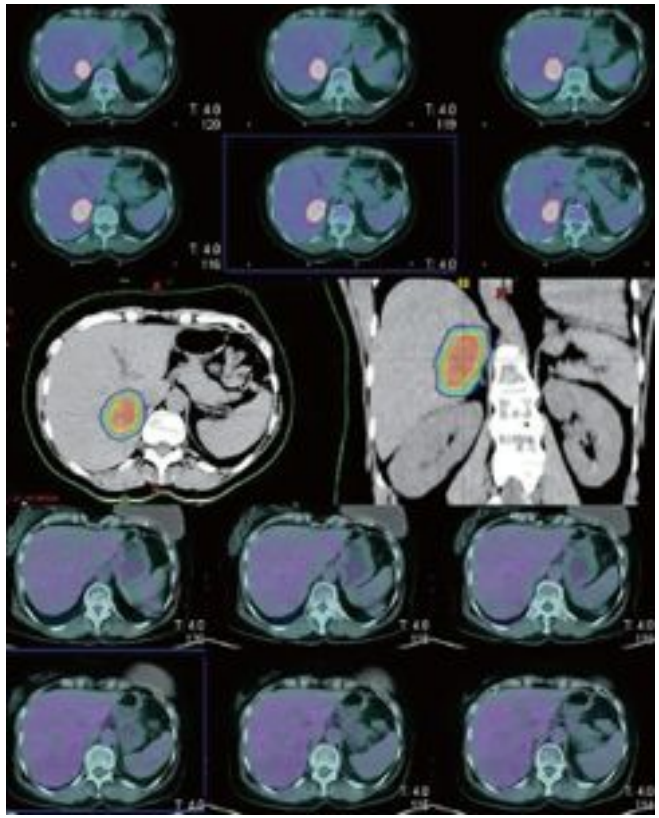
No Correlation between local control and diameter > 3cm

LIVER STEREOTACTIC BODY RT:
DOSE ESCALATION

Practical Indications

Selection criteria	*Patients categories*		
	Suitable	**Cautionary**	**Unsuitable**
Lesion Number	< 3	4	> 4
Lesion Diameter	1-3 cm	>3 and ≤ 6cm	> 6cm
Distance from OARs	>8 mm	5-8 mm	< 5mm
Free Liver Volume	>1000cc	< 1000cc and ≥ 700 cc	<700 cc

Lesion diameter	**Prescription Dose**
≤ 3 cm	48 - 60 Gy
3-6 cm	60 – 75 Gy



Scorsetti et al. SBRT in unresectable liver metastases. J gastointest Oncol 2014

LIVER STEREOTACTIC (ABLATIVE) RT:
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HOW WE CAN DO IT?

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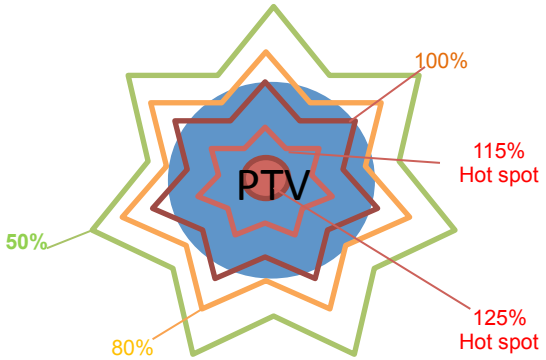
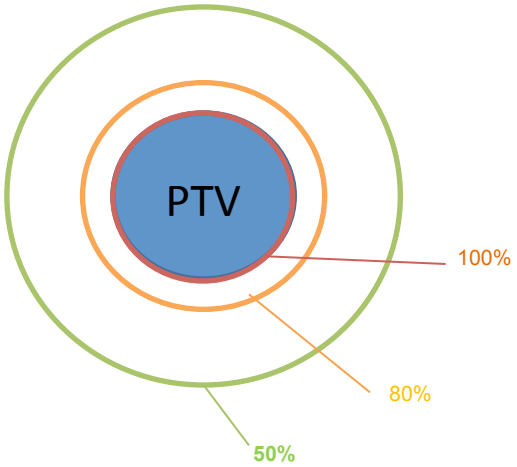
LIVER STEREOTACTIC (ABLATIVE) RT:
HOW WE CAN DO IT?

How to prescribe?? A current controversy..

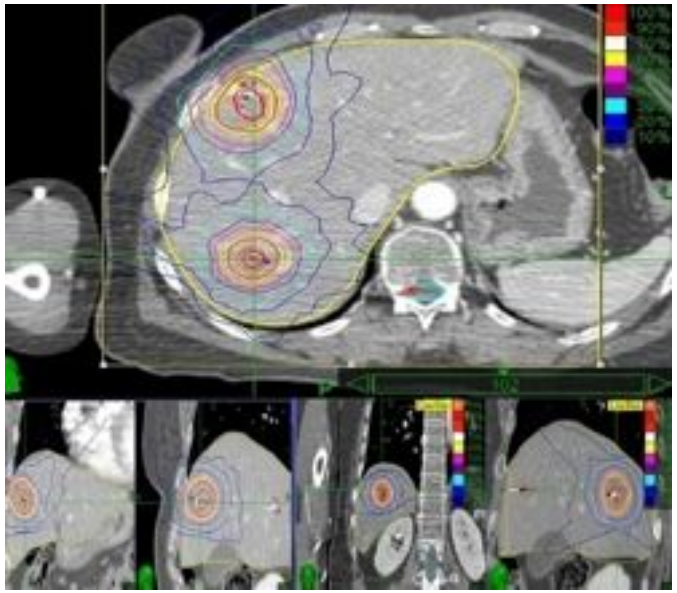
Heterogenous dose distribution inside PTV (**SRS style**):
- Max dose typically 125% or higher
- hot spot risk without motion management/no IGRT
- ripid fall-off



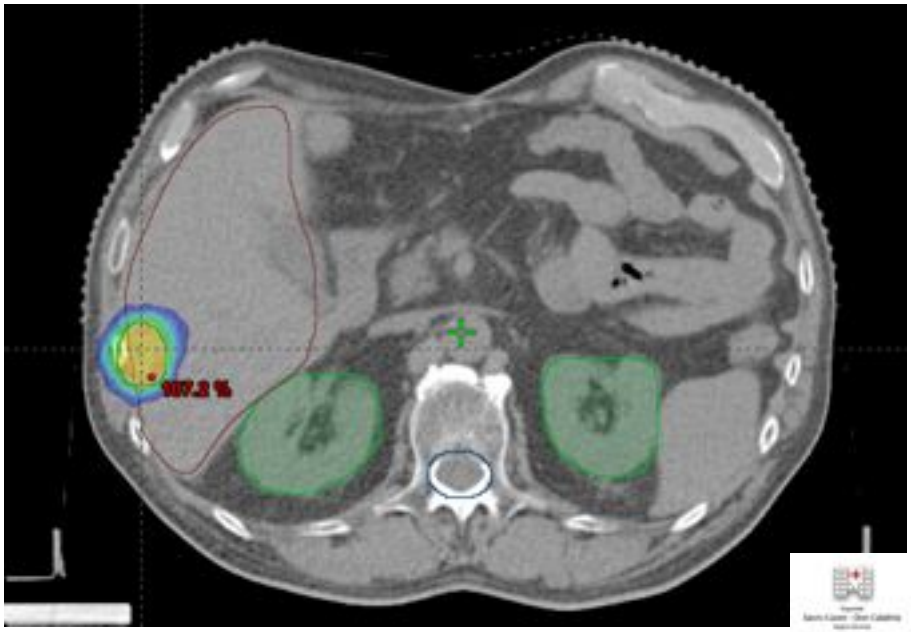
Homogeneous dose distribution inside PTV(**ICRU/IMRT style**):
- max dose typically within 110% or less
- no hot spot risk
- less ripid fall-off



LIVER STEREOTACTIC ABLATIVE RT(SBRT):
HIGHLY CONFORMAL ON DEDICATED MACHINES



LIVER STEREOTACTIC ABLATIVE RT(SBRT):
HIGHLY CONFORMAL ON ADVANCED LINAC



60Gy in 3 fractions

FFF 10 X beams

Dose rate 2400, *BOT 150 sec*

Multiple arc Jaw tracking

LIVER STEREOTACTIC ABLATIVE RT(SBRT):
HIGHLY CONFORMAL …

PROTON THERAPY?HEAVY IONS?

BIOLOGICAL PROFILING BEFORE RT?

LIVER STEREOTACTIC ABLATIVE RT(SBRT):
TAKE HOME MESSAGES

- SBRT is technically feasible *(with dedicated machines but also with Linacs)*
- Toxicity is acceptable *(if contraints are respected..)*
- High doses and dose escalation are effective (IGRT, imobilization, High conformal delivery,..)
- Local control is high(85-100%). Survival is encouraging (30-85%)
- Combination with (new?) systemic therapies is needed in prospective trials

PLEASE, NOT ONLY HIGH TECHNOLOGY
….HIGH EXPERTISE IS NEEDED!!!

Ospedale
Sacro Cuore - Don Calabria

Thanks for your attention