# Integrating liver directed therapies as embolization and radiotherapy into systemic treatment

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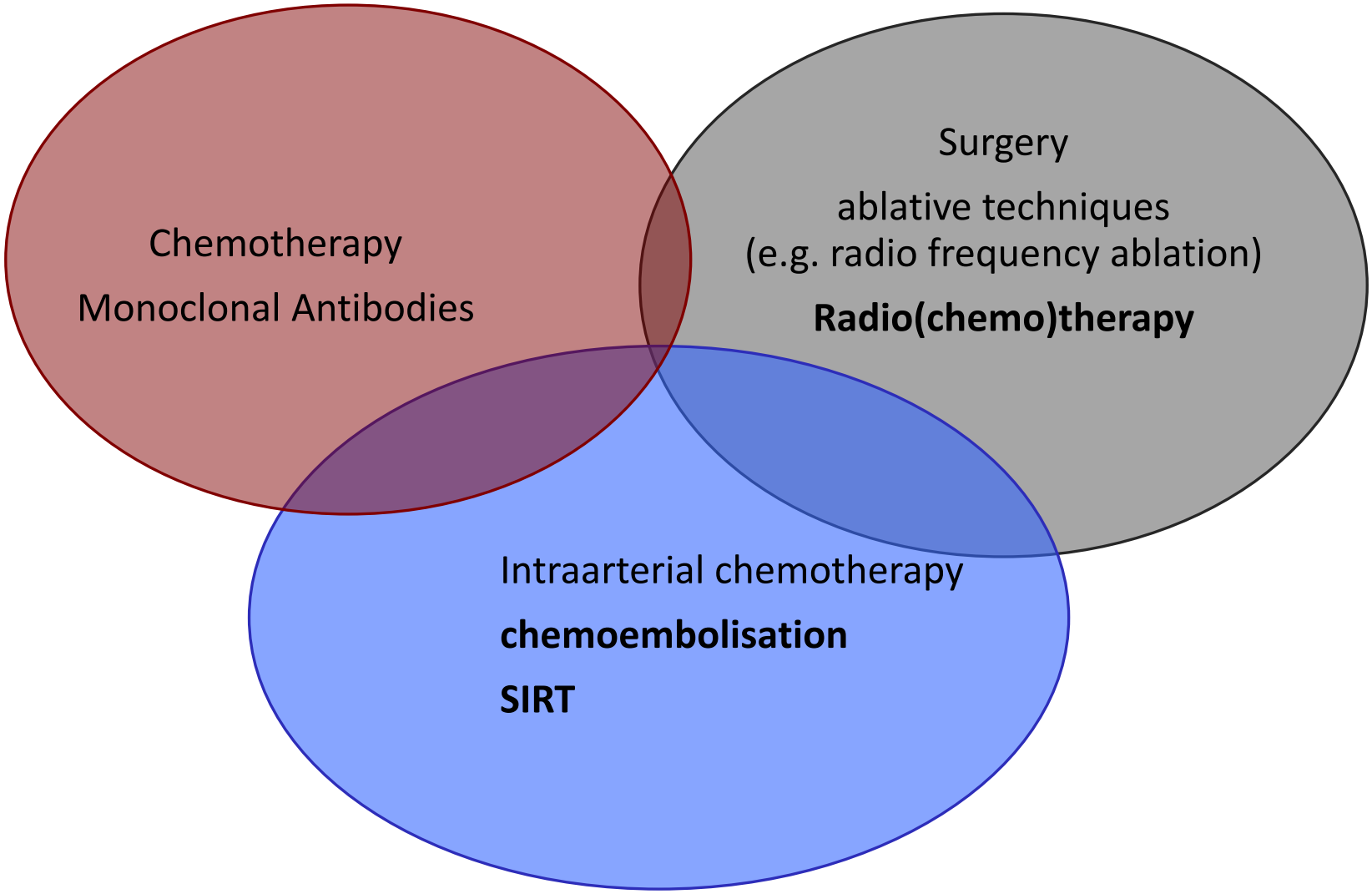
Deutsche Krebshilfe
HELFEN. FORSCHEN. INFORMIEREN.

# Multimodal Therapy of mCRC: Armamentarium



# Embolization techniques: What we know today

- Physiological rationale is good
- Chemoembolization is active
  - Thousands of patients in treatment series with more or less refractory disease
  - Few case control series
  - very few reports of randomized trials
- Significant, but manageable toxicity
- Key factors: selection...selection...selection

# ...and questions - from today´s perspective

- How about a **defined therapeutic situation**?
  - e.g. 1st/2nd line...
- How about a **defined strategy**?
  - e.g. „conversion“ to resectability, defined treatment aim
- How about **integration** in a modern multimodal management?
  - Combination with i.v. chemotherapy and monoclonal antibodies?
  - before/after resection or other ablation?
- How **compared to i.v**. therapy?

# Irinotecan-loaded beads: Salvage treatment

- 55 mCRC patients
  - 17 2nd line,
  - 14 3rd line,
  - 24 4th line
- 17 patients with liver involvement > 50%
- 99 DEBIRI treatments (median 2, range 1-5)

**TABLE 4** Response rates for all 55 patients evaluated

| Response ($n = 55$) | 3 months | 6 months | 12 months |
|---|---|---|---|
| Complete response | 7 (12%) | 7 (12%) | 8 (15%) |
| Partial response | 28 (53%) | 21 (38%) | 14 (25%) |
| Stable disease | 15 (30%) | 19 (34%) | 23 (42%) |
| Progression of disease | 3 (5%) | 8 (15%) | 10 (18%) |
| Dead of disease | 0 | 5 | 9 |
| Death of other cause | 2 | 0 | 0 |

**TABLE 5** Progression-free, hepatic-specific, and overall survival

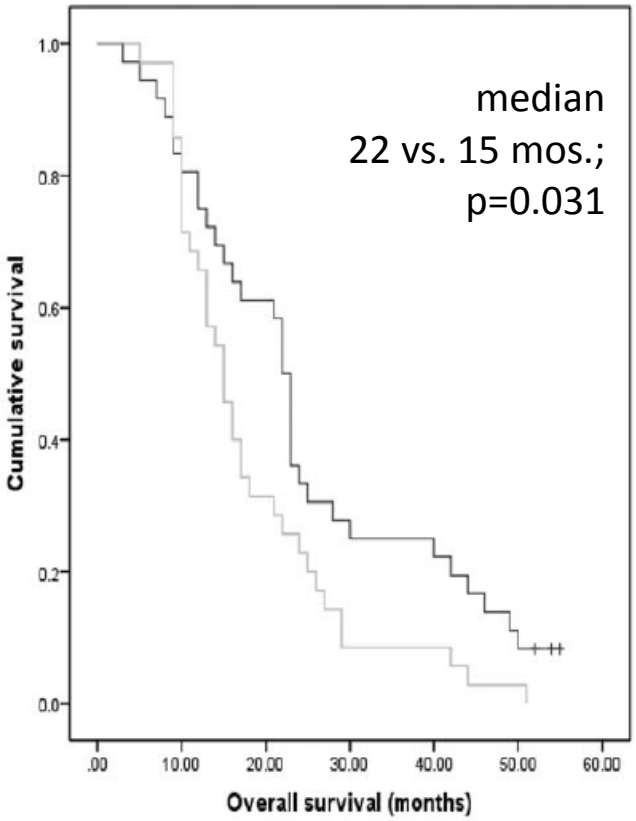
| Survival | Median (months) | At 1 year (%) |
|---|---|---|
| PFS | 11 | 55 |
| Hepatic | 15 | 75 |
| Extrahepatic | 13 | 45 |
| Overall survival | 19 | 75 |

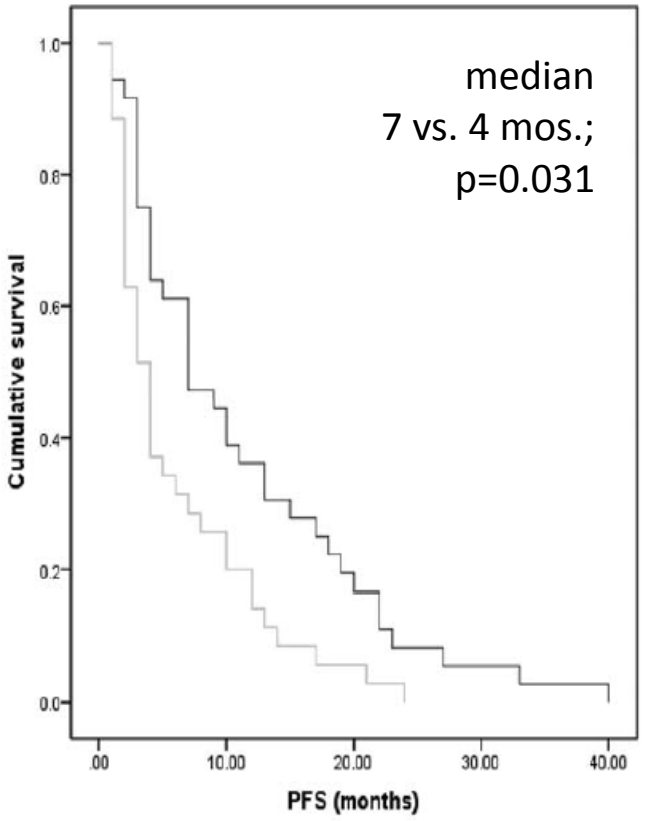
*PFS* progression-free survival

Martin et al Ann Surg Oncol 2011

# DEBIRI versus FOLFIRI in nonresectable CRC liver metastases

- Phase III, prospective randomized; > 45% pretreated
- Primary endpoint: increase median survival by 40% at 2-years




Fiorentini et al., Anticancer Res 2012

# DEBIRI versus FOLFIRI in nonresectable CRC liver metastases

- Objective response 68% vs. 20%
- Time to extrahepatic progression (occuring in all patients): 13 vs. 9 mos.
- Toxicity remarkable

Table III. *Toxicity observed during therapy.*

| Toxicity (Grade 2 and 3) | DEBIRI (% out of 70 cycles delivered) | FOLFIRI (% out of 277 cycles delivered) |
|---|---|---|
| Pain | 30% | 0% |
| Vomiting | 25% | 25% |
| Diarrhea | 2% | 35% |
| Asthenia | 20% | 50% |
| Leukopenia | 5% | 35% |
| Anaemia | 5% | 35% |
| Fever | 15% | 3% |
| Alopecia | 5% | 35% |

Fiorentini et al., Anticancer Res 2012

# FOLFOX-Bevacizumab plus DEBIRI: 1st line mCRC Phase I/II Study

- Concurrent full dose: mFOLFOX6 +/- Avastin
  - Oxaliplatin 85mg/m$^2$
  - with 2 LC Bead™ treatments (100mg irinotecan)
- Schema:

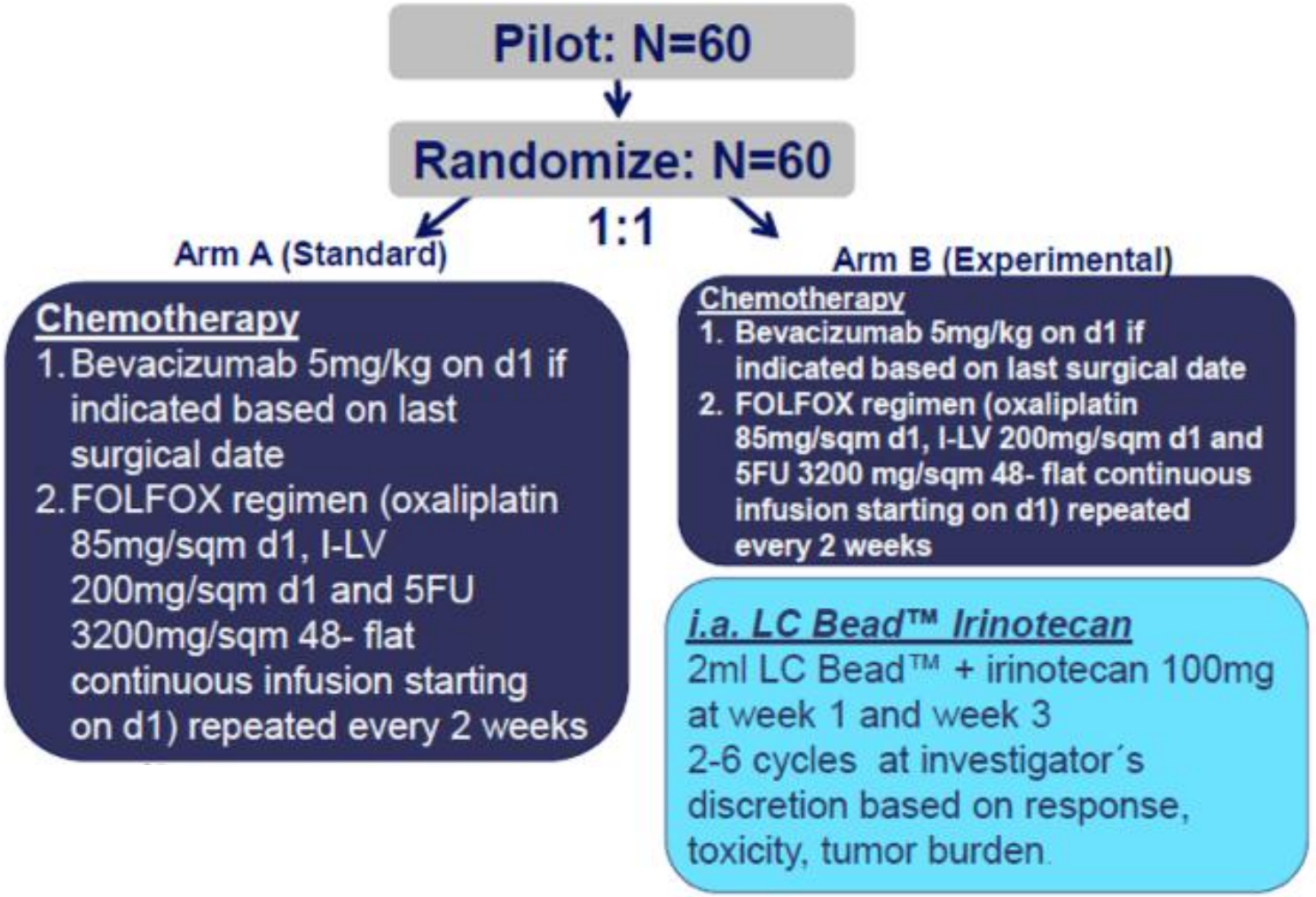
| Week 1 | Week 2 | Week 3 | Week 4 | Week 5 | Week 6 | Week 7 |
|---|---|---|---|---|---|---|
| FOLFOX + Avastin | LC Bead 100mg Irinotecan | FOLFOX +Avastin | LC Bead 100mg Irinotecan | FOLFOX + Avastin | Break | FOLFOX + Avastin |

Then repeat CT to evaluate initial response

- 10 pts: at least 12 cycles FOLFOX+bev and at least 2 DEBIRI Tx
- 12-month response rates: 100 % (2 CR, 8 PR).
- Four patients were successfully downstaged to resection and/or ablation with a median overall survival of 15.2 months.

Martin et al J Gastrointest Surg 2012

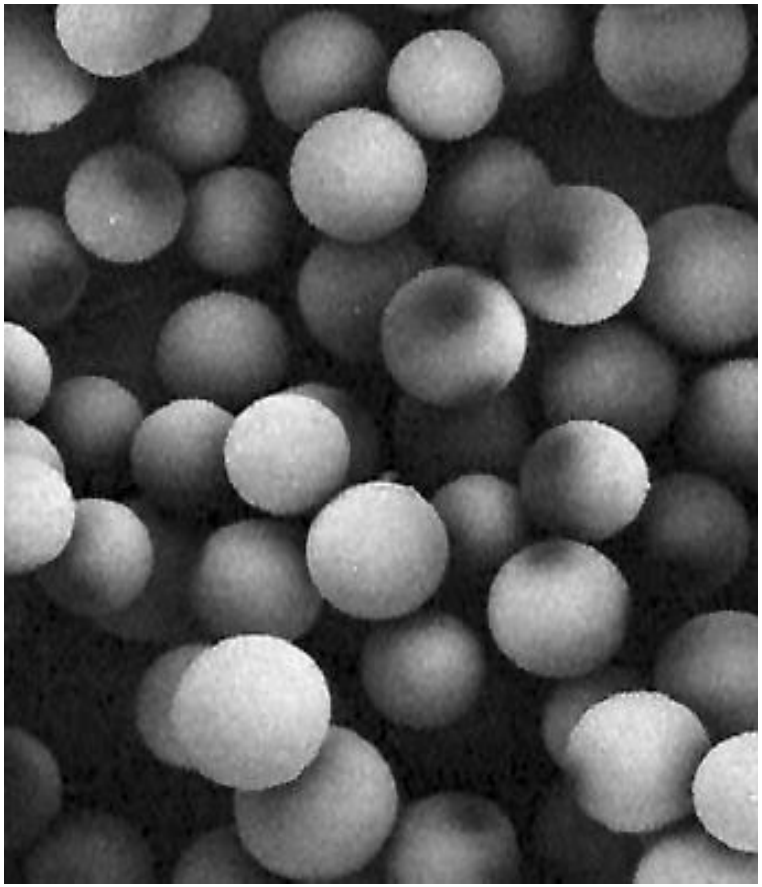
# US randomized phase II (just opened)




PI: Robert Martin, Louisville

# SIRT: Radioembolisation

Mikrospheres (20-40 μm) loaded with Yttrium-90



Y-90: Beta emitter

- mean range: 3,9 mm
- max range: 11 mm
- max energy: 2,27 MeV
- Half life: 64 h

# SIRT: Potential adverse events

| SAE | Incidence |
|---|---|
| Radiation gastritis or duodenitis | ~5–10%<br>1–2% grade 3–4 |
| Radiation pancreatitis | <1% |
| Radiation cholecystitis | <1% |
| Radiation Induced Liver Disease (RILD) | <1% |
| Radiation pneumonitis | no cases since lung-shunt study |

# Risk factors for REILD

**Risk Factors for REILD Among Patients Receiving Whole-Liver RE on Multivariate Analysis**

| Variable | *P* | OR | 95% CI |
|---|---|---|---|
| Age <55 y | .003 | 1.9 | 1.24–2.91 |
| Activity relative to targeted liver volume >0.8 GBq/L | .03 | 1.6 | 1.17–2.18 |
| Capecitabine administered within the last month | .07 | 5.5 | 0.74–40.8 |
| Leukocyte count <4000/pL | .16 | 3.5 | 0.55–22.0 |



Sangro, Eur J Cancer 2008

**British Journal of Cancer (2010) 103,** 324 – 331
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**www.bjcancer.com**

# Multi-centre phase II clinical trial of yttrium-90 resin microspheres alone in unresectable, chemotherapy refractory colorectal liver metastases

**M Cosimelli*[,1], R Golfieri[2], PP Cagol[3], L Carpanese[1], R Sciuto[1], CL Maini[1], R Mancini[1], I Sperduti[1], G Pizzi[1], MG Diodoro[1], M Perrone[1], E Giampalma[2], B Angelelli[2], F Fiore[4], S Lastoria[4], S Bacchetti[3], D Gasperini[3], O Geatti[3] and F Izzo[4] for the Italian Society of Locoregional Therapies in Oncology (SITILO)**

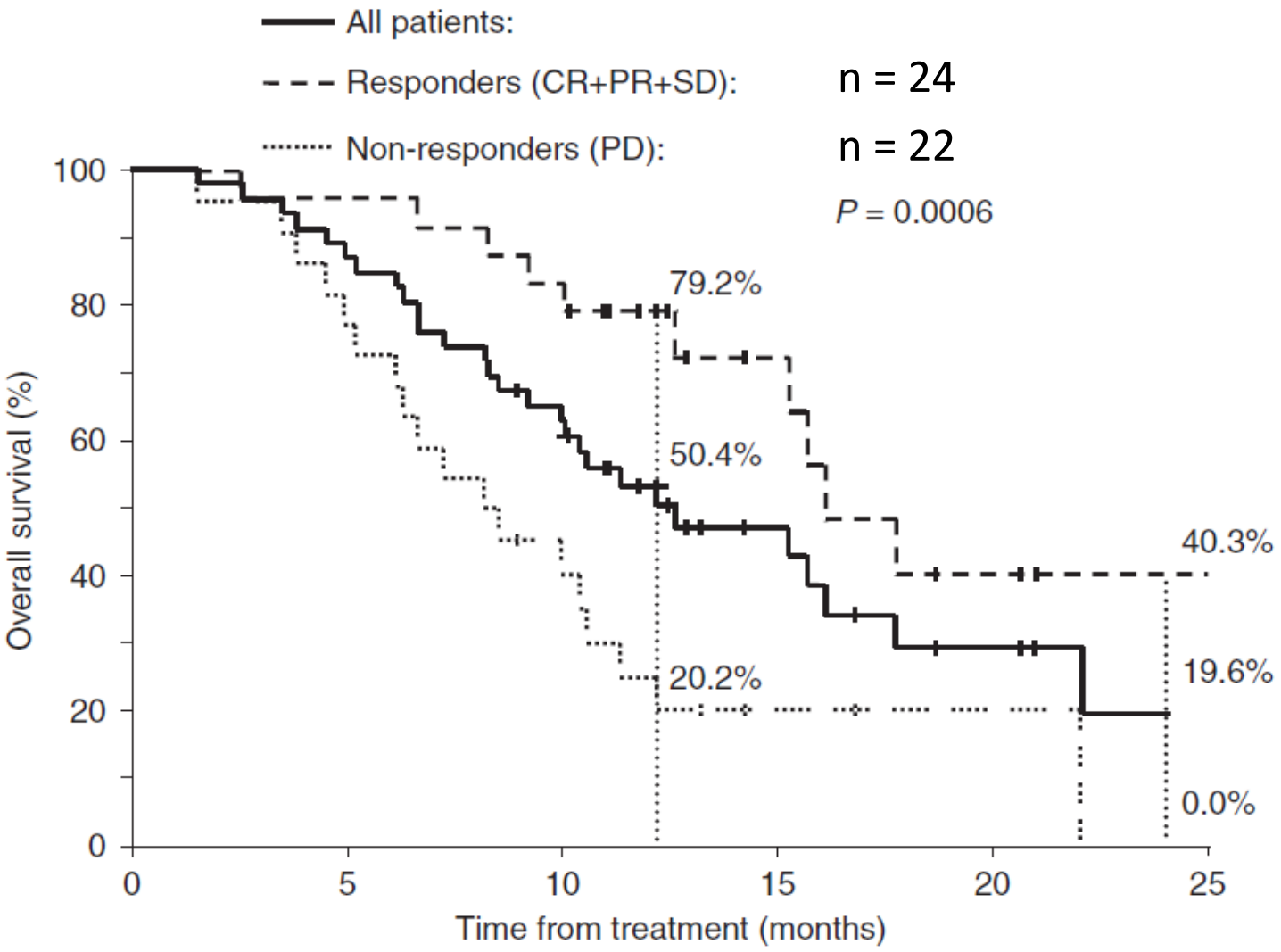
*[1]Regina Elena National Cancer Institute, Via Elio Chianesi, 53, 00144 Rome, Italy; [2]S Orsola-Malpighi University Hospital, Bologna, Italy; [3]University of Udine, Udine, Italy; [4]Fondazione Pascale Cancer Institute of Naples, Naples, Italy*

# Multicenter phase II study in refractory CRC

| | |
|---|---|
| *Prior resection:* n *(%)* | |
| Extra-hepatic | 11 (22) |
| Hepatic | 12 (24) |
| *Prior chemotherapy lines:* n *(%)* | |
| Three | 12 (24) |
| Four | 25 (50) |
| Five | 13 (26) |
| Prior bevacizumab: *n* (%) | 11 (22) |
| Prior cetuximab: *n* (%) | 5 (10) |
| *Liver involvement:* n *(%)* | |
| <25% | 20 (40) |
| 25–50% | 30 (60) |
| *Number of metastases:* n *(%)* | |
| ⩽4 | 21 (42) |
| >4 | 29 (58) |
| Bilobar/unilobar: *n* (%) | 35/15 (70/30) |
| Synchronous/metachronous: *n* (%) | 36/14 (72/28) |
| Median size of metastases: mm (range) | 50 (8–120) |



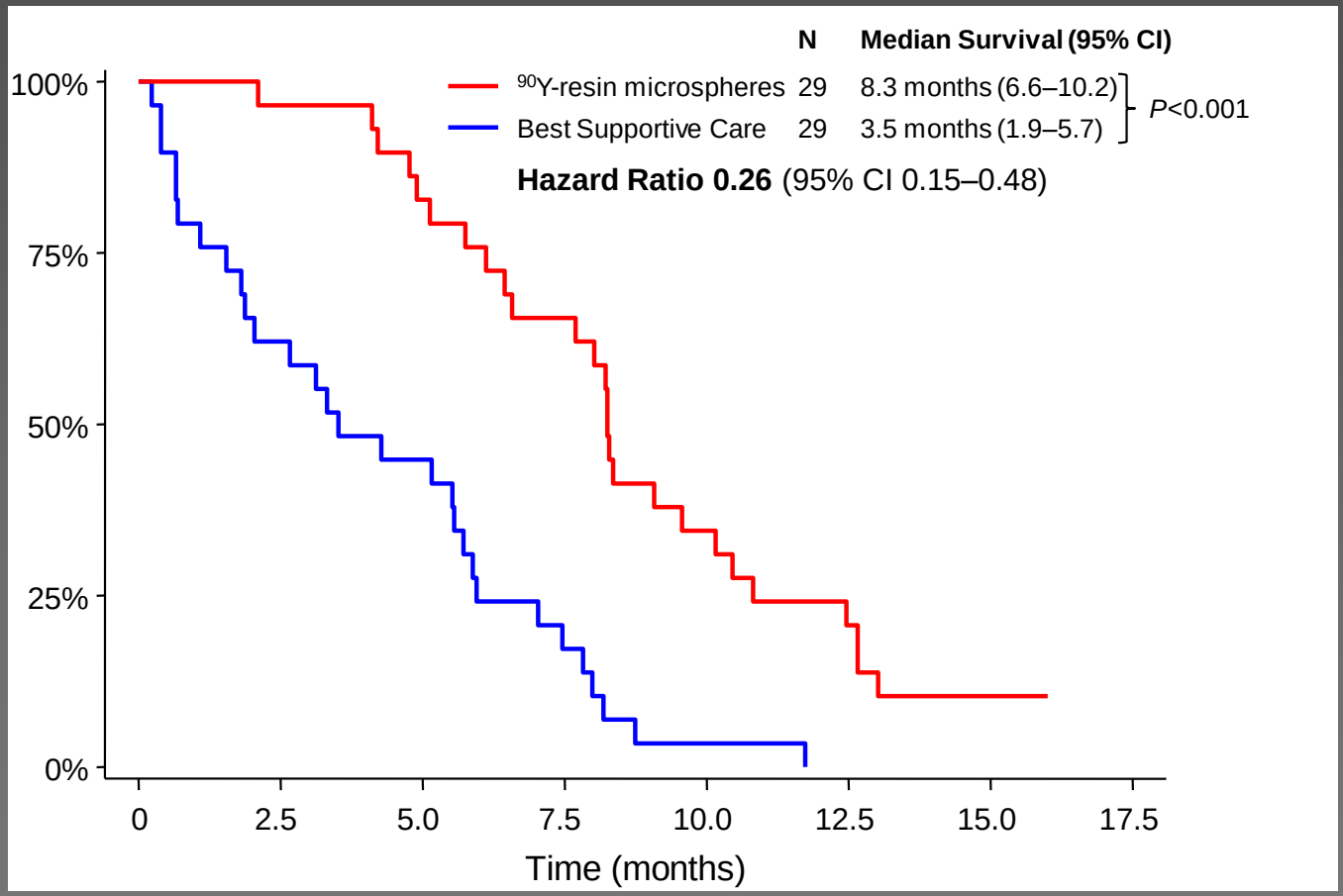
Cosimelli et al., Br J Cancer 2010



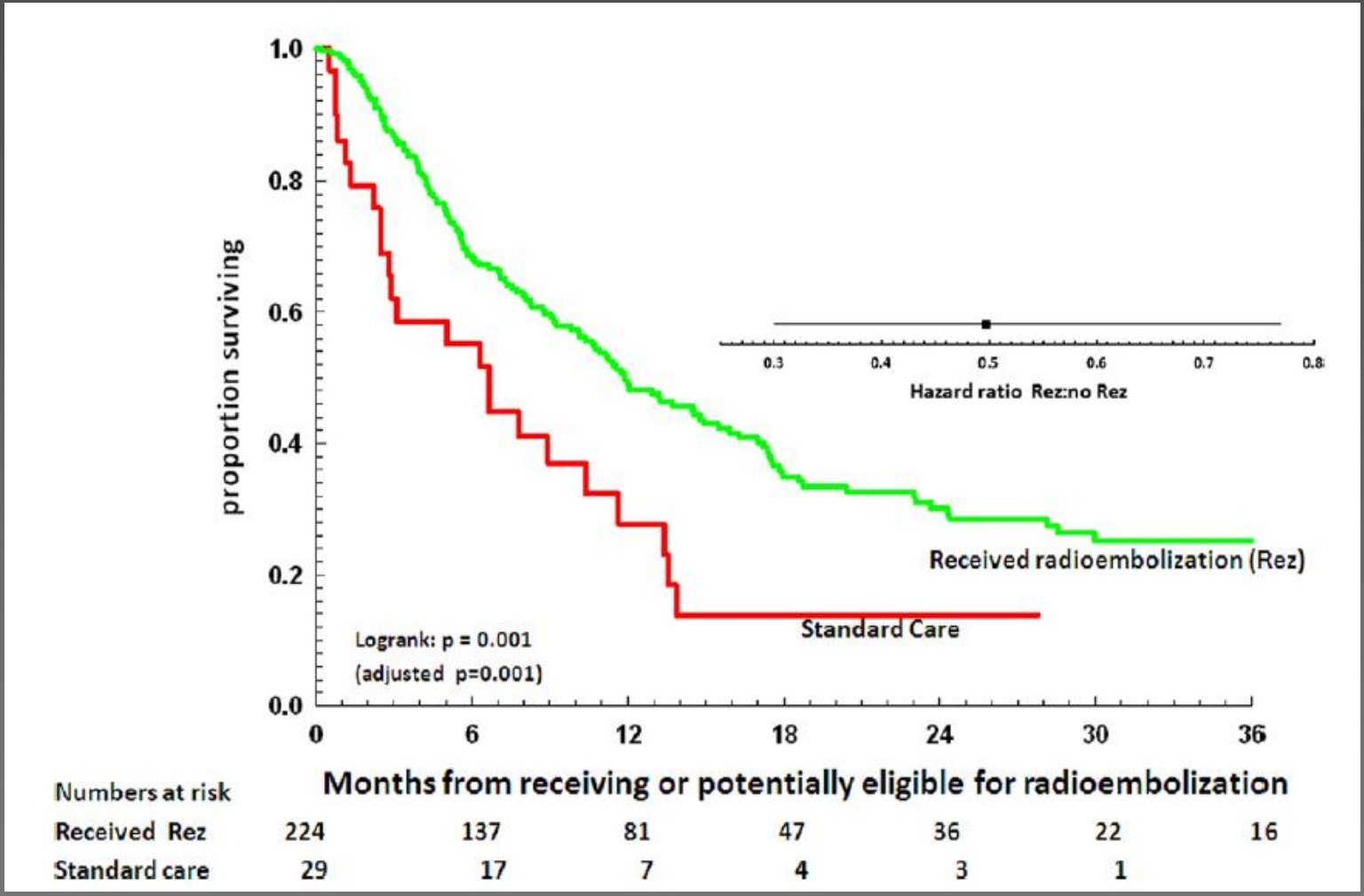



Cosimelli et al., Br J Cancer 2010

# German Matched Pair Analysis in Refractory Patients: Overall Survival



# Matched-pair for standard care, n=224






Bester et al., J Vasc Interv Radiol 2012

VOLUME 28 · NUMBER 23 · AUGUST 10 2010

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

# Phase III Trial Comparing Protracted Intravenous Fluorouracil Infusion Alone or With Yttrium-90 Resin Microspheres Radioembolization for Liver-Limited Metastatic Colorectal Cancer Refractory to Standard Chemotherapy

*Alain Hendlisz, Marc Van den Eynde, Marc Peeters, Geert Maleux, Bieke Lambert, Jaarke Vannoote, Katrien De Keukeleire, Chris Verslype, Luc Defreyne, Eric Van Cutsem, Philippe Delatte, Thierry Delaunoit, Nicola Personeni, Marianne Paesmans, Jean-Luc Van Laethem, and Patrick Flamen*

# Baseline demographics

| | 5-FU | | 5-FU&Y90 | |
|---|---|---|---|---|
| Time since diagnosis, months | | % | | % |
| Median | 22 | | 22 | |
| Range | 12-44 | | 7-52 | |
| Missing | 0 | 0 | 1 | 5 |
| Time since last chemotherapy, weeks | | | | |
| Median | 14 | | 8 | |
| Range | 2-60 | | 2-57 | |
| Missing | 0 | 0 | 2 | 10 |
| Previous chemotherapy regimen* | | | | |
| Irinotecan based | 20 | 87 | 13 | 62 |
| Oxaliplatin based | 2 | 9 | 4 | 19 |
| Other based | 1 | 4 | 4 | 19 |
| No. of liver metastases measured | | | | |
| 1 lesion | 1 | 4 | 2 | 10 |
| 2-4 lesions | 10 | 44 | 10 | 48 |
| ≥ 5 lesions | 10 | 44 | 8 | 38 |
| Not measurable† | 2 | 9 | 1 | 5 |
| Presence of nontarget lesions | | | | |
| Yes | 6 | 26 | 5 | 24 |
| Missing | 1 | 4 | 1 | 5 |
| Sum of the lesions diameters, mm | | | | |
| Median | 216 | | 176.5 | |
| Range | 51-416 | | 31-324 | |
| Missing | 2 | 9 | 1 | 5 |



Hendlisz et al., J Clin Oncol 2010

**Table 3.** Time to Liver Progression, Time to Progression Overall, and Overall Survival

| Time to Progression and OS | FU Alone (n = 23) | Radioembolization + FU (n = 21) | Hazard Ratio | 95% CI | *P* |
|---|---|---|---|---|---|
| TTLP, median, months | | | | | |
| All progressions considered as events | 2.1 | 5.5 | 0.38 | 0.20 to 0.72 | .003 |
| Patients with treatment change censored at the time of change | 2.1 | 5.6 | 0.35 | 0.18 to 0.69 | .002 |
| TTP, median, months | 2.1 | 4.5 | 0.51 | 0.28 to 0.94 | .03 |
| OS, median, months | 7.3 | 10.0 | 0.92 | 0.47 to 1.78 | .80 |

Abbreviations: TTLP, time to liver progression; TTP, time to progression overall; OS, overall survival; FU, fluorouracil.



Hendlisz et al., J Clin Oncol 2010

# “SIRFLOX” first-line FOLFOX +/- SIRT

ClinicalTrials.gov
A service of the U.S. National Institutes of Health

Home Search Study Topics

Study 1 of 1 for search of: sirflox

Previous Study | Return to Search Results | Next Study

Full Text View | Tabular View | No Study Results Posted | Related Studies

## FOLFOX Plus SIR-SPHERES MICROSPHERES Versus FOLFOX Alone in Patients With Liver Mets From Primary Colorectal Cancer (SIRFLOX)

**This study is currently recruiting participants.**
Verified May 2012 by Sirtex Medical

First Received on July 25, 2008. Last Updated on May 23, 2012 History of Changes

| | |
|---|---|
| **Sponsor:** | Sirtex Medical |
| **Information provided by (Responsible Party):** | Sirtex Medical |
| **ClinicalTrials.gov Identifier:** | NCT00724503 |

### Purpose

This study is a randomized multi-center trial that will assess the effect of adding SIRT, using SIR-Spheres microspheres, to a standard chemotherapy regimen of FOLFOX as first line therapy in patients with non-resectable liver metastases from primary colorectal adenocarcinoma.

Treatment with the biologic agent bevacizumab, if part of the standard of care at participating institutions, is allowed within this study at the discretion of the treating Investigator.

| Condition | Intervention |
|---|---|
| Colorectal Cancer<br>Colorectal Carcinoma<br>Liver Metastases | Drug: Systemic chemotherapy (FOLFOX)<br>Device: SIR-Spheres yttrium-90 microspheres |

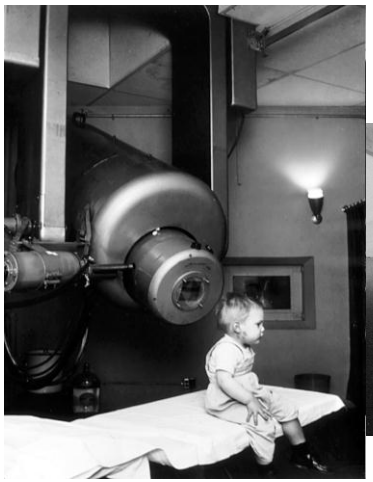
Study Type: Interventional
Study Design: Allocation: Randomized
Endpoint Classification: Safety/Efficacy Study
Intervention Model: Parallel Assignment
Masking: Open Label
Primary Purpose: Treatment

Official Title: Randomised Comparative Study Of Folfox6m Plus Sir-Spheres® Microspheres Versus Folfox6m Alone As First Line Treatment In Patients With Nonresectable Liver Metastases From Primary Colorectal Carcinoma

# Evolution of Radiation Oncology

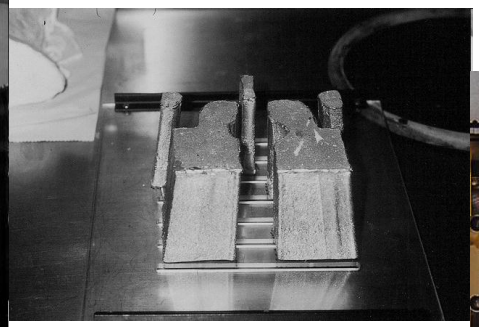
## 1960`s to Now

1960s
The first Clinac



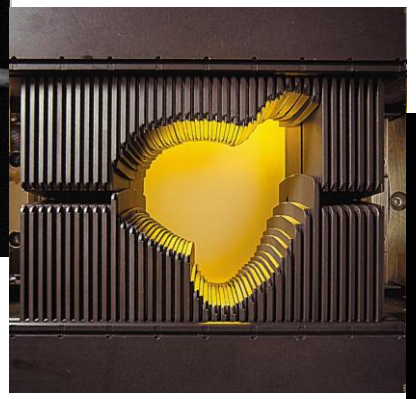
RT of Retinoblastom

1970
Cerrobend Blocking

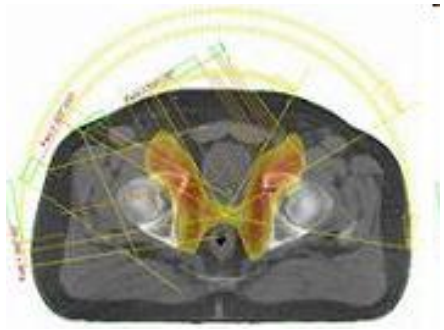


1980

Multileaf Collimator

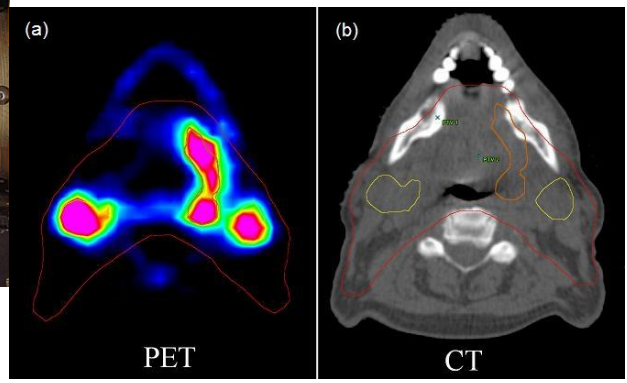


1990
PET/CT
Dose-painting

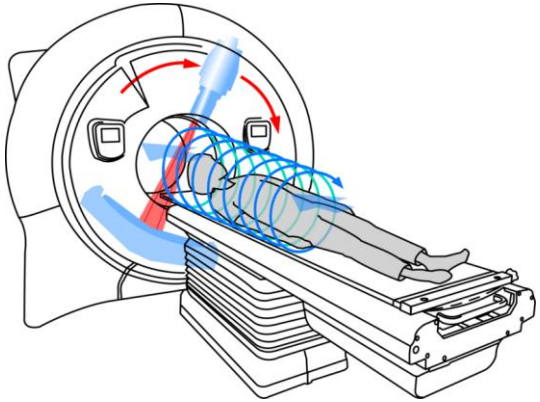


IMRT

2000







2011
Protons
Heavy ions

REVIEW

# A Rationale for the Targeted Treatment of Oligometastases With Radiotherapy

DHARA M. MacDERMED, MD,[1] RALPH R. WEICHSELBAUM, MD,[1,2,3] AND JOSEPH K. SALAMA, MD[1,2,3]*

[1]Department of Radiation and Cellular Oncology, University of Chicago, Chicago, Illinois
[2]Cancer Research Center, University of Chicago, Chicago, Illinois
[3]Ludwig Center for Metastasis Research, University of Chicago, Chicago, Illinois

An oligometastatic state has been proposed wherein patients with metastases limited in number and location may benefit from local therapy directed at all known sites of metastases. We describe here the clinical and biological basis for the oligometastatic state. We present evidence for a potentially curative approach to patients with oligometastases using stereotactic body radiotherapy (SBRT) and we review the literature for SBRT directed at specific metastatic sites in the lungs, liver and multiple organs.
*J. Surg. Oncol. 2008;98:202–206.* © 2008 Wiley-Liss, Inc.

KEY WORDS: oligometastatic; stereotactic body radiotherapy; biology of metastases

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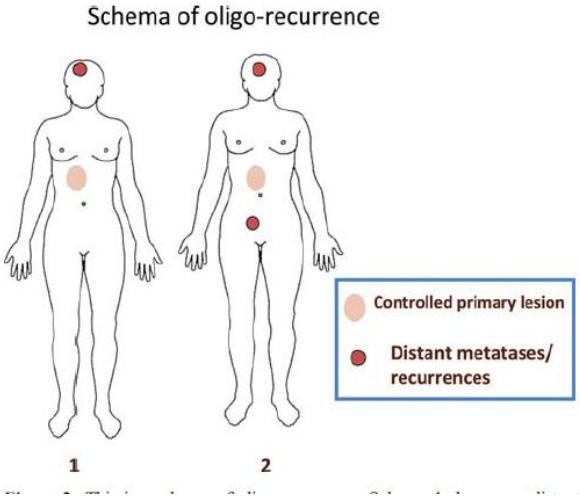
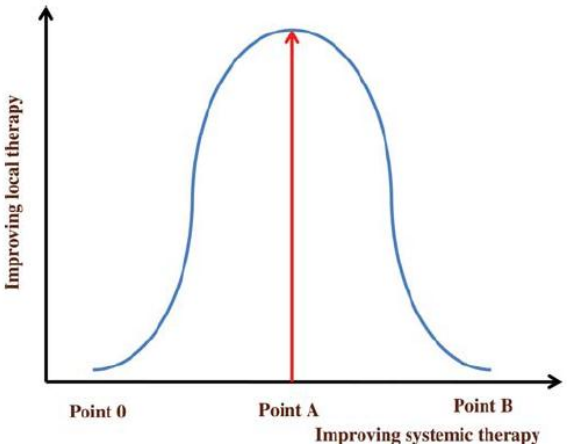


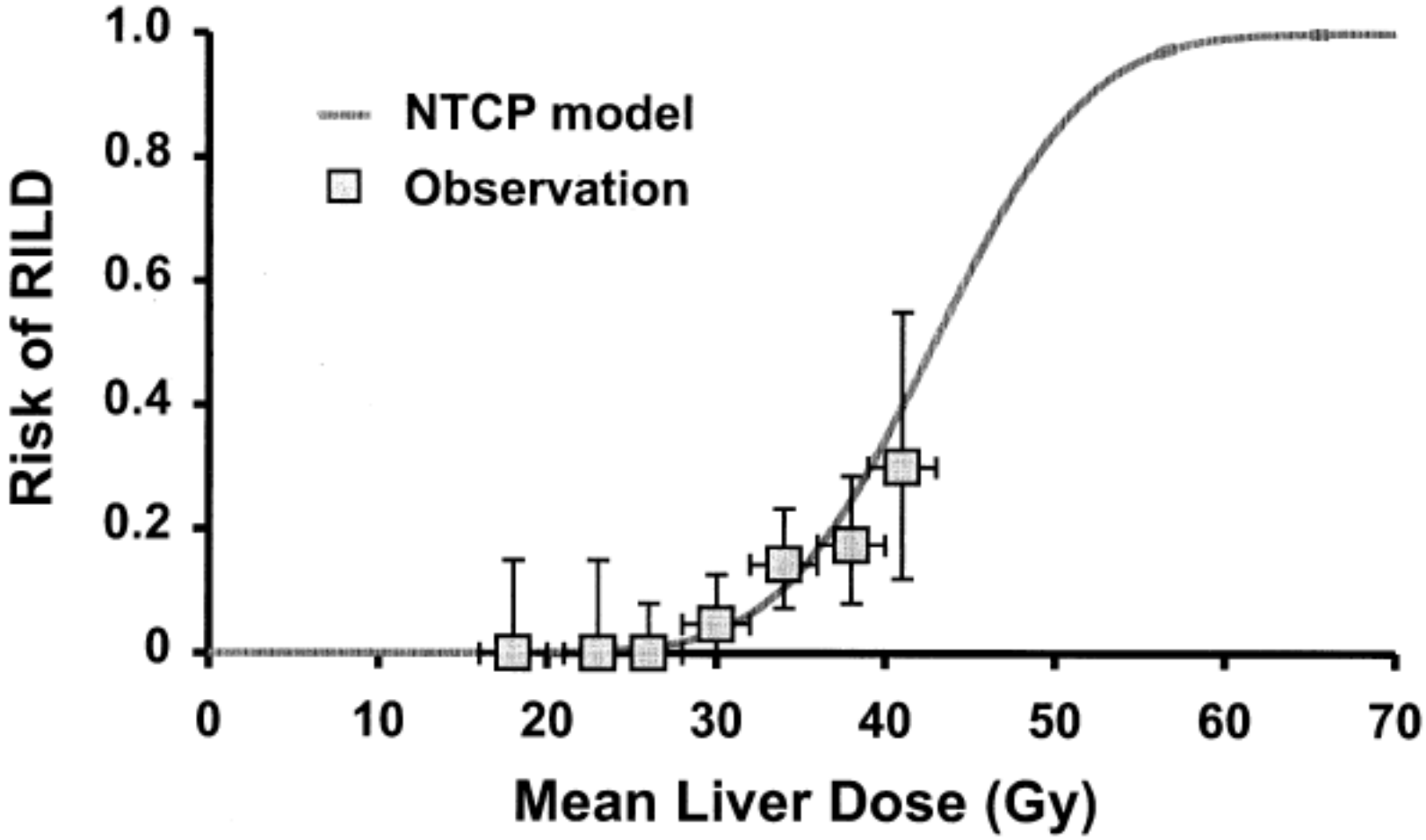




REPORT

# AMERICAN SOCIETY FOR THERAPEUTIC RADIOLOGY AND ONCOLOGY (ASTRO) AND AMERICAN COLLEGE OF RADIOLOGY (ACR) PRACTICE GUIDELINE FOR THE PERFORMANCE OF STEREOTACTIC BODY RADIATION THERAPY

Stereotactic body radiation therapy (SBRT):

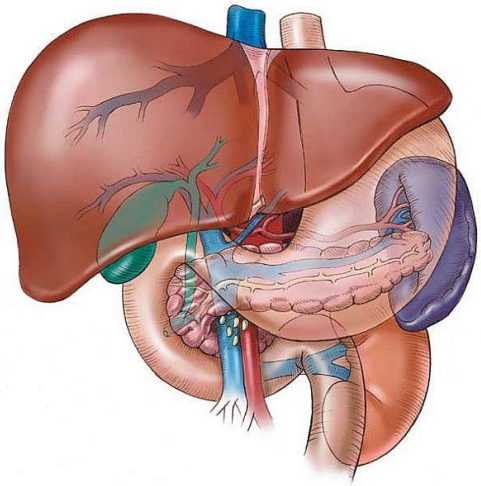
- **Very precise and accurate delivery of a high dose of radiation** to an extracranial target within the body
- **Non invasive** treatment
- **High target dose and steep dose gradients** beyond the target
- **A single or few fractions** of high-dose ionizing radiation



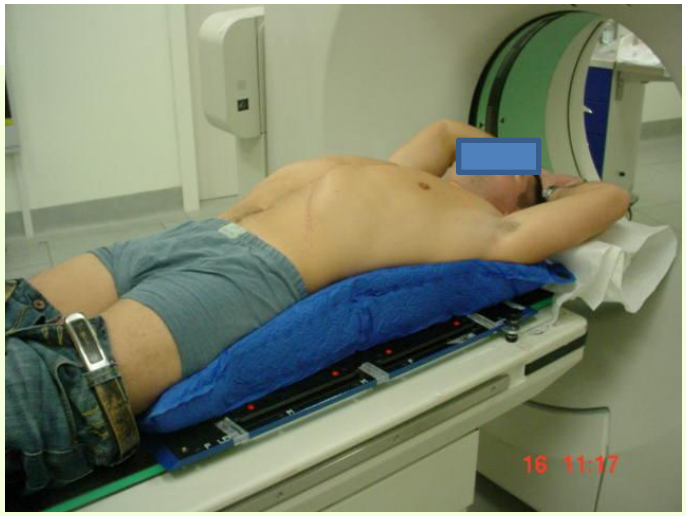

Dawson et al., Cancer 2010

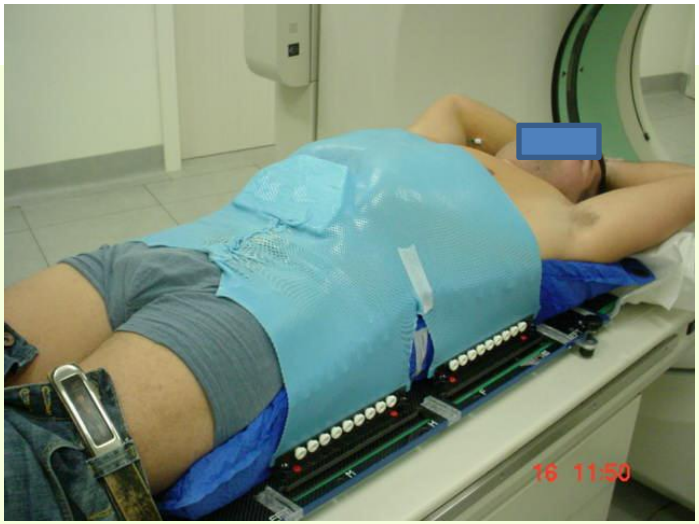
# SBRT to liver metastases: Constraints

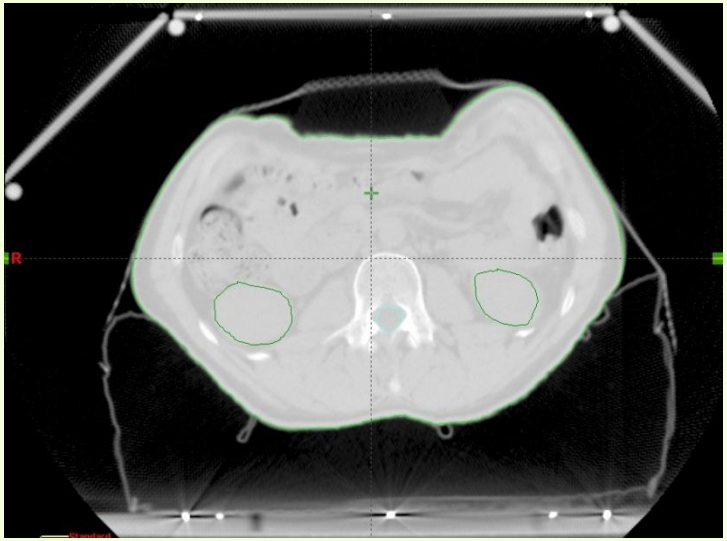
| ORGAN | Dose-Volume Limits | Other Conditions |
|---|---|---|
| Healthy liver (defined as total liver volume minus cumulative GTV) | > 700 cc at < 15 Gy in 3 F | The volume of healthy liver > 1000 cc |
| Spinal cord | < 18 Gy in 3 F | |
| Kidneys (R+L) | V15 Gy < 35% | |
| Stomach, duodenum, small 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 | |

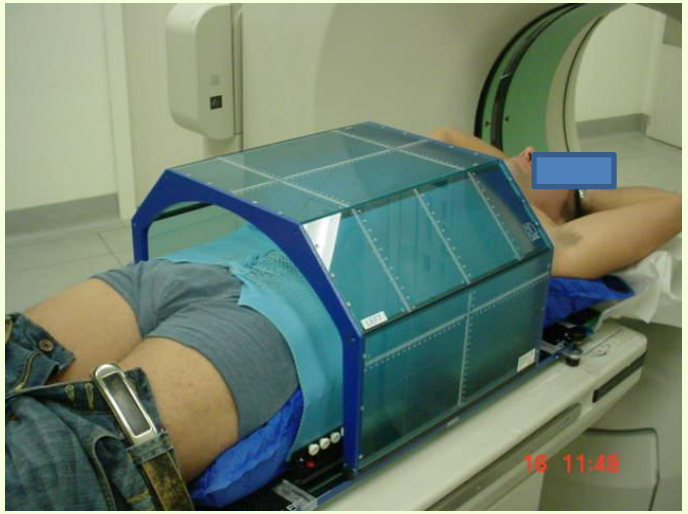


# Prerequisites: Positioning



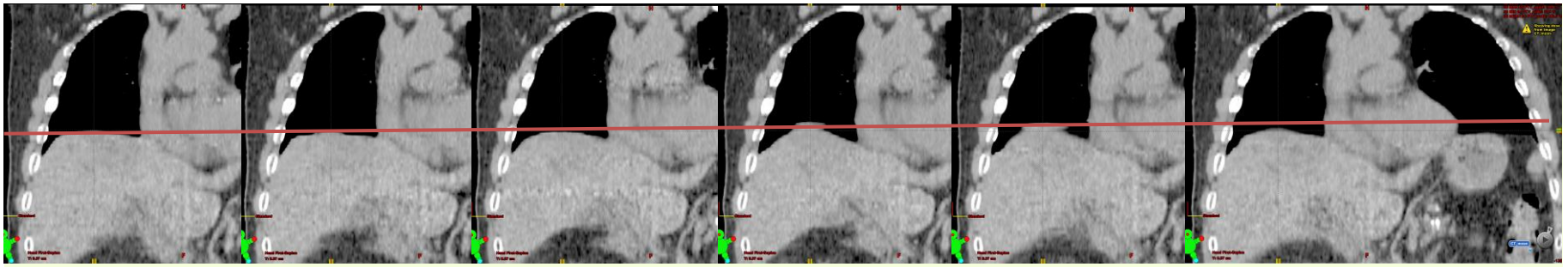






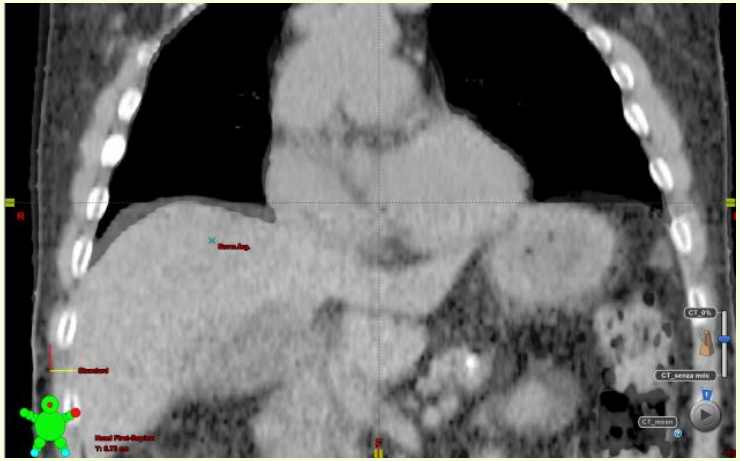
Eccles et al, Int J Rad Onc Biol Phys 2010

# Prerequisites: 4D CT

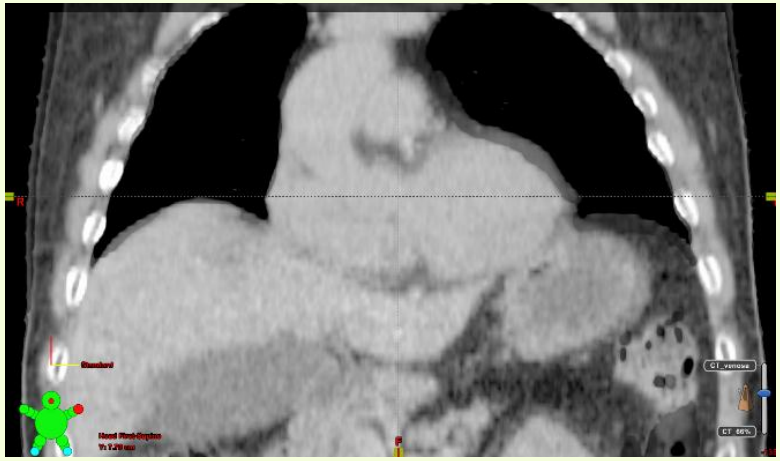


Min

Max



4D-CT min

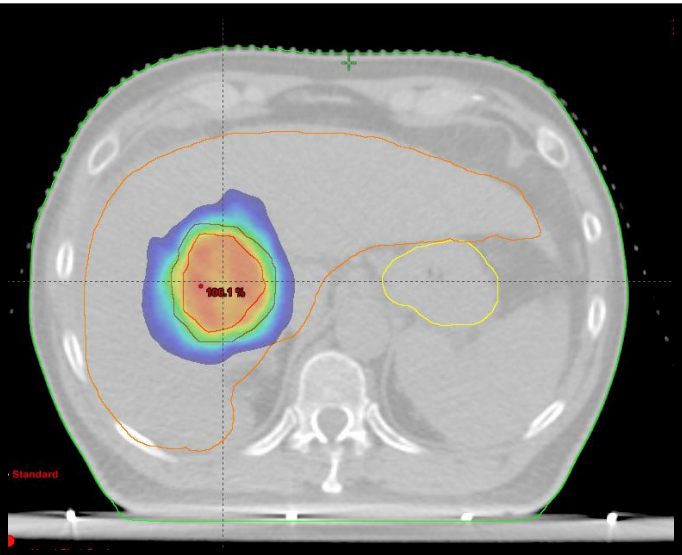


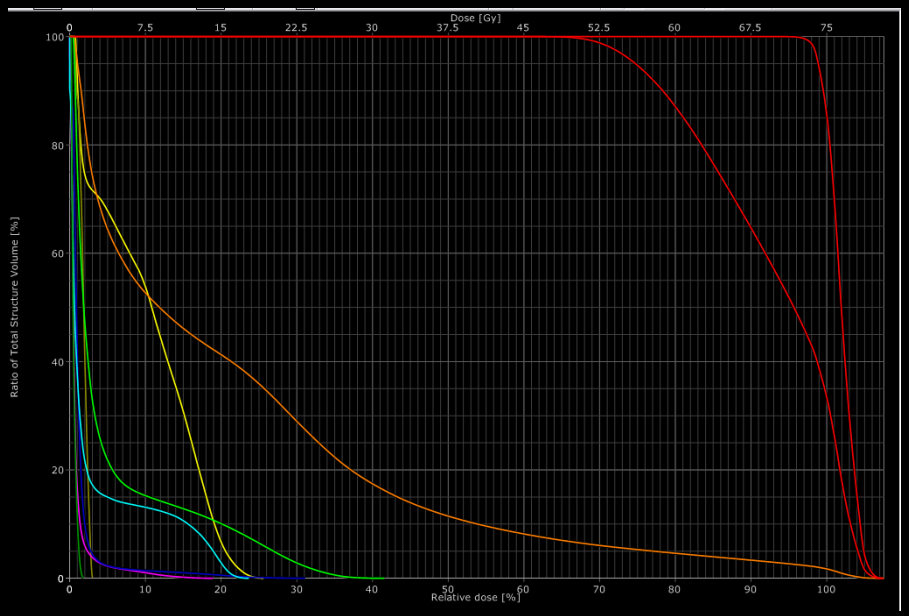
4D-CT max

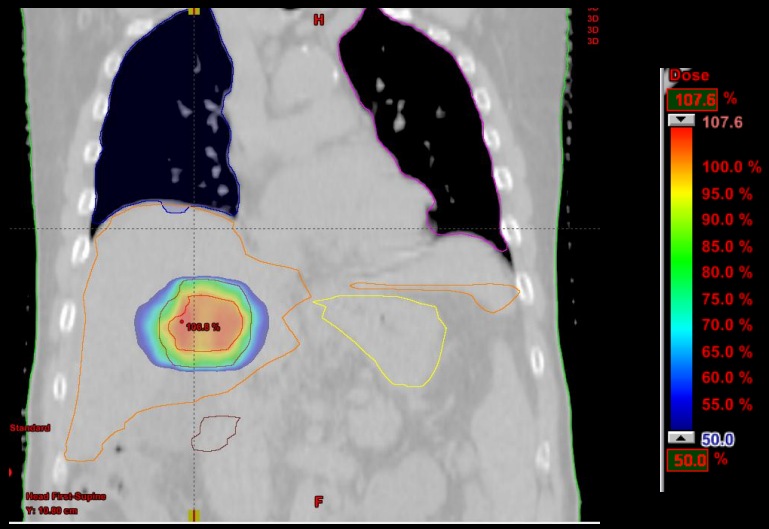
Case et al, Int J Rad Onc Biol Phys 2010

# SBRT liver: 25Gy x 3

Hubertus Wald Tumorzentrum
Universitäres Cancer Center Hamburg



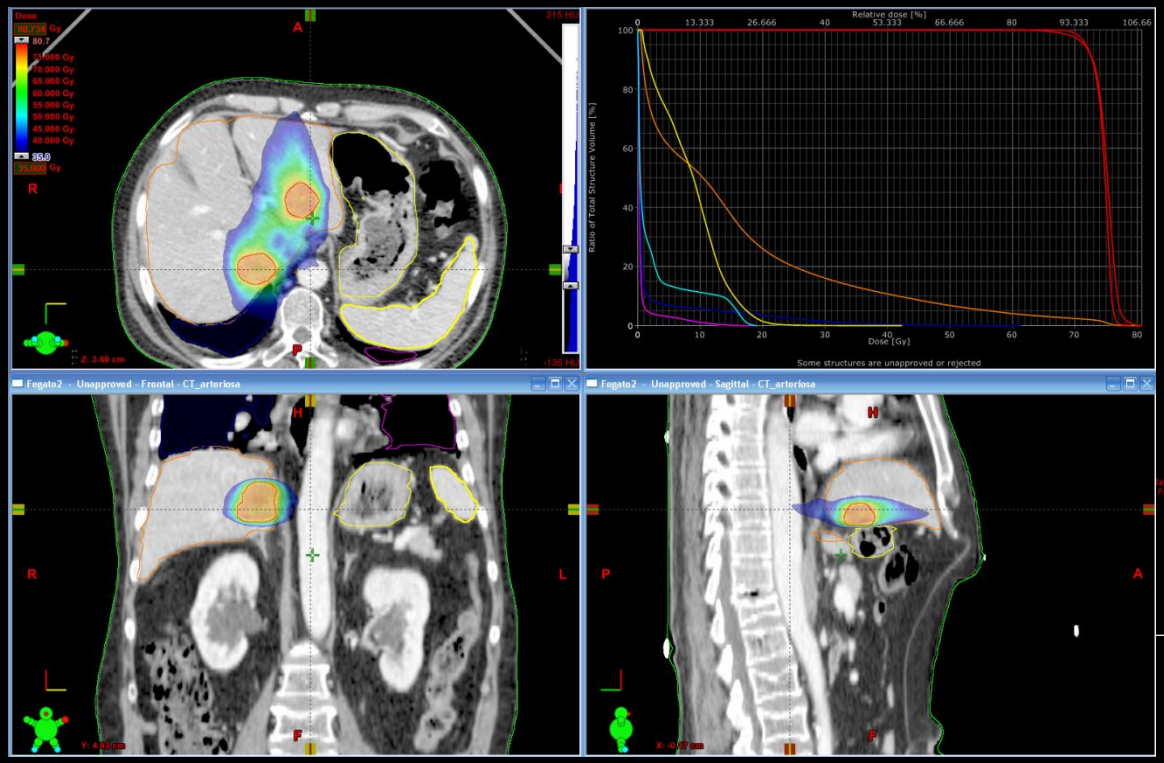

1 isocentre, 1 arc
Jaw tracking

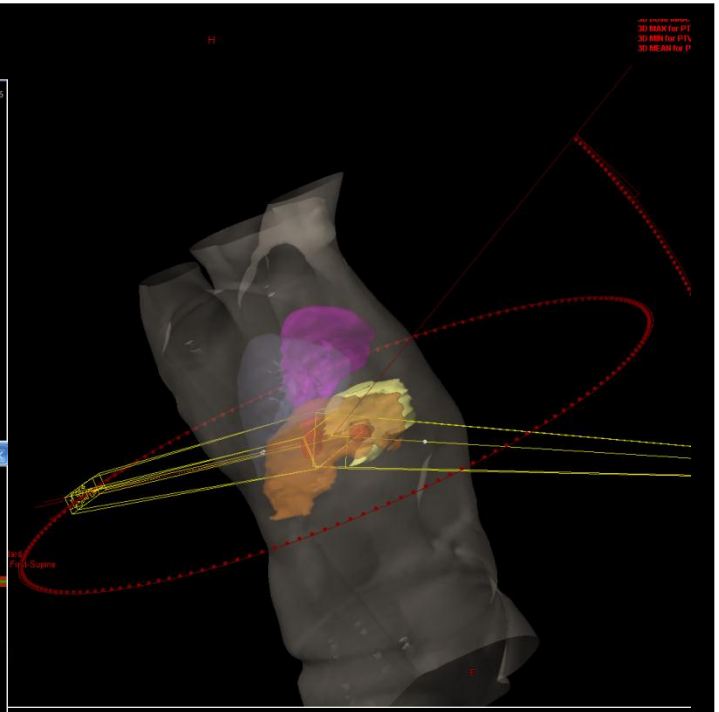
MU: 5642
BOT: 137s

Spinal cord max dose = 17.3 Gy
Right kidney mean dose = 3.9 Gy
Liver mean dose = 15.7 Gy
Stomach mean dose = 19.3 Gy

# SBRT liver: 25Gy x 3

Hubertus Wald Tumorzentrum
Universitäres Cancer Center Hamburg



PTV1&PTV2: V95%=99.5%
Spinal cord: Max dose=17.3 Gy
Stomach: Max=21.0Gy, Mean=9.5 Gy
Liver: Mean=15.5 Gy, D15Gyfree=2811cc

1 isocentre, 3 arcs
Jaw tracking

MU:3216+3527+563
BOT: 174s(80+82+14s)

# Follow-up 25Gy x 3; 10FFF

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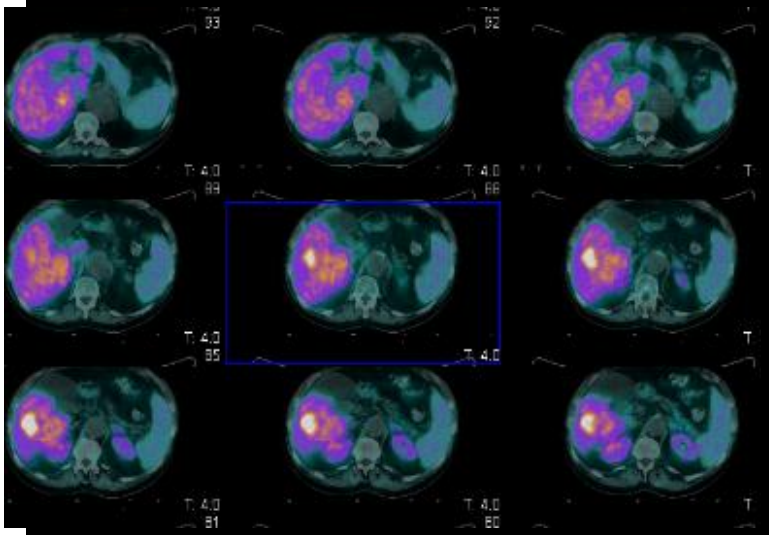
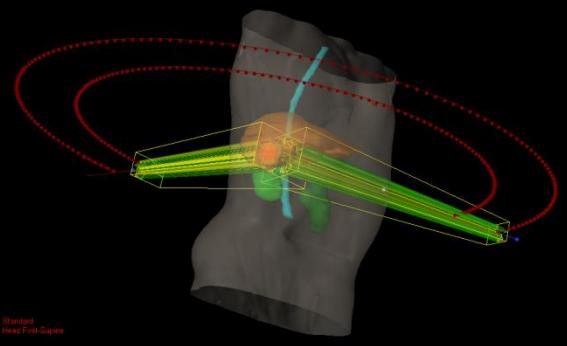
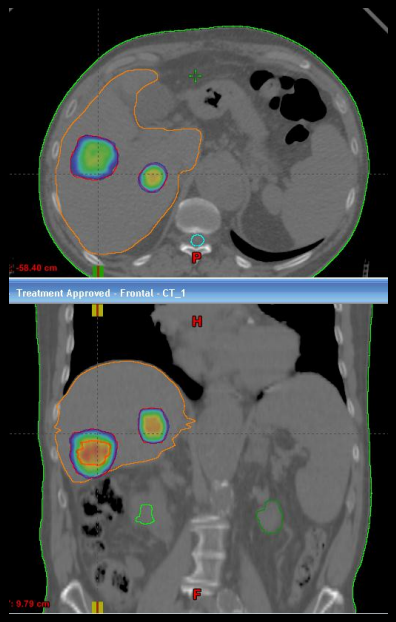
PET pre



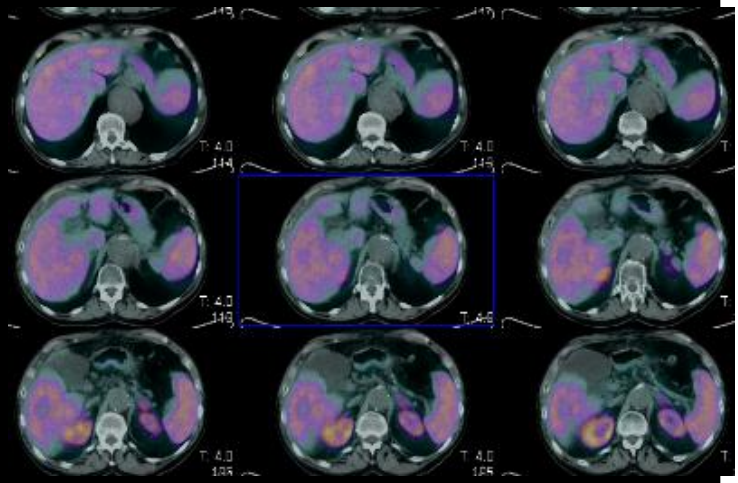


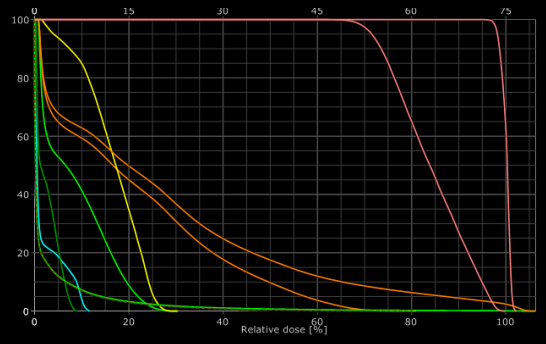
RapidArc
1 isocentre
2 arcs
Jaw tracking




MU:3174+3004
BOT:170s

PET post; 3 months





# SBRT of liver metastases: Dosing schedules

**Table 3.** Prospective Trials of Stereotactic Body Radiation Therapy for Hepatic Metastases

| Study | No. of Lesions | Fractionation | Median Follow-Up | Actuarial Local Control | |
|---|---|---|---|---|---|
| | | | | Time | % |
| Herfarth et al[6] | 55 | 1 × 14 Gy to 1 × 26 Gy | 6 months | 18 months | 67 |
| Hoyer et al[24] | 141* | 3 × 15 Gy | 4.3 years | 2 years | 79 |
| Milano et al[21] | 293† | 10 × 5 Gy | 41 months‡ | 2 years | 67 |
| Mendez-Romero et al[25] | 45 | 3 × 12.5 Gy§ | 13 months | 2 years | 82 |
| Rusthoven et al (this study) | 49 | 3 × 20 Gy | 16 months | 2 years | 92 |

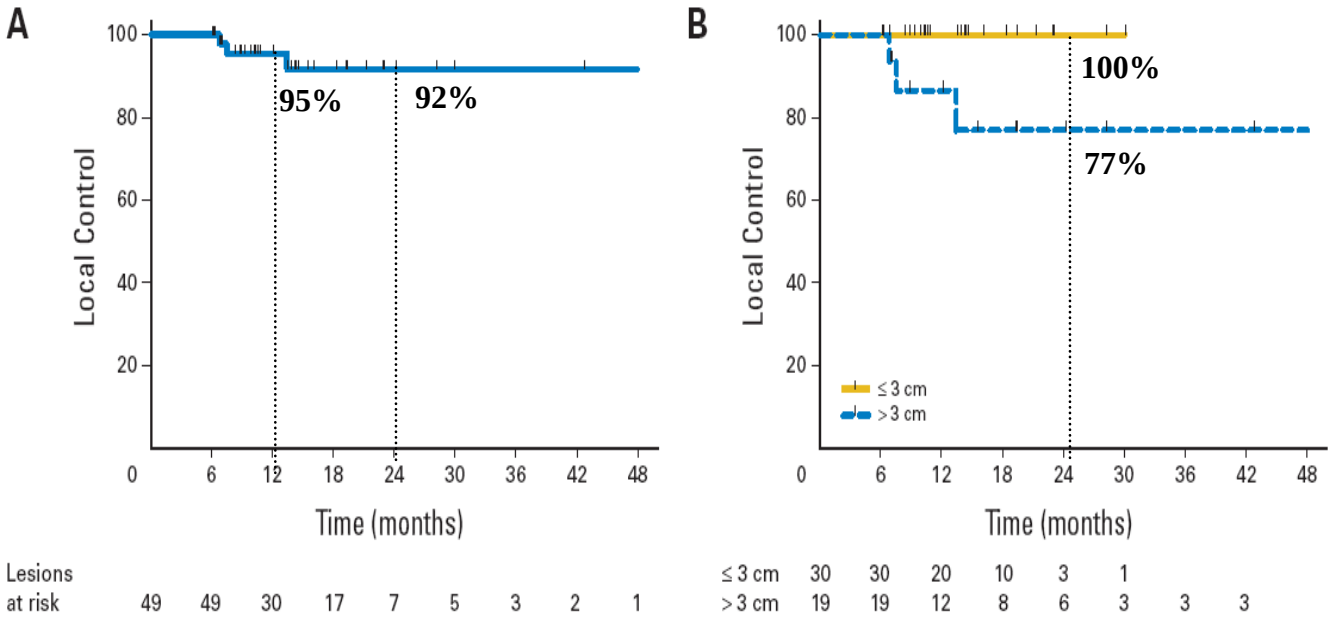
*Total number of colorectal cancer metastases; 44 liver metastases.
†Total number of lesions treated; 45% of patients were treated for hepatic metastases.
‡In surviving patients.
§Different fractionation (3 × 10 Gy or 5 × 5 Gy) used for patients with hepatocellular carcinoma or with lesions ≥ 4 cm.

Rusthoven et al, JCO 2009

- The primary end point was in field local control defined as no growth of the treated lesion in patients with at least 6 months of FU imaging post- SBRT
- The secondary end points were toxicity (CTCAE3), progression-free survival and overall survival

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

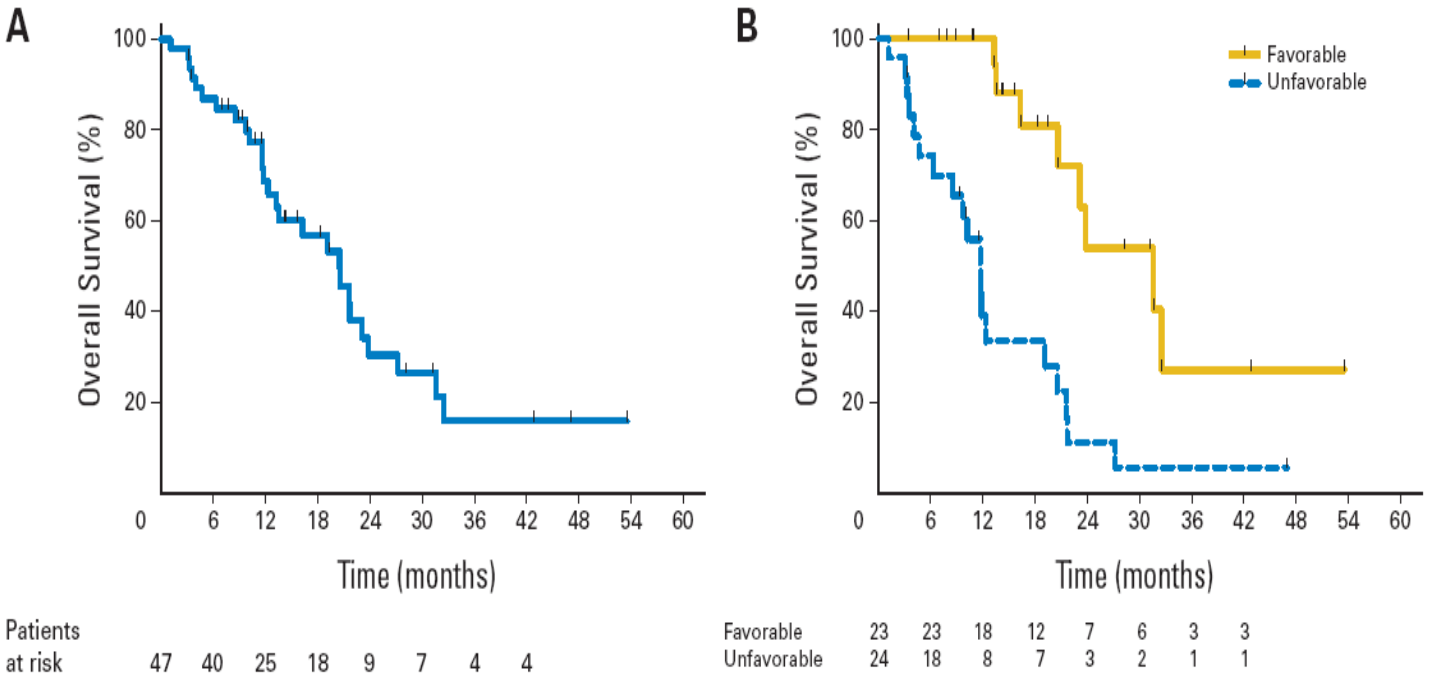
*Kyle E. Rusthoven, Brian D. Kavanagh, Higinia Cardenes, Volker W. Stieber, Stuart H. Burri, Steven J. Feigenberg, Mark A. Chidel, Thomas J. Pugh, Wilbur Franklin, Madeleine Kane, Laurie E. Gaspar, and Tracey E. Schefter*




Actuarial local control for (A) all lesions and (B) lesions according to maximal tumor diameter.

Rusthoven et al., J Clin Oncol 2009

# SBRT Liver Metastases: CRC vs. others




Actuarial survival for (A) all patients and (B) patients according to primary site.

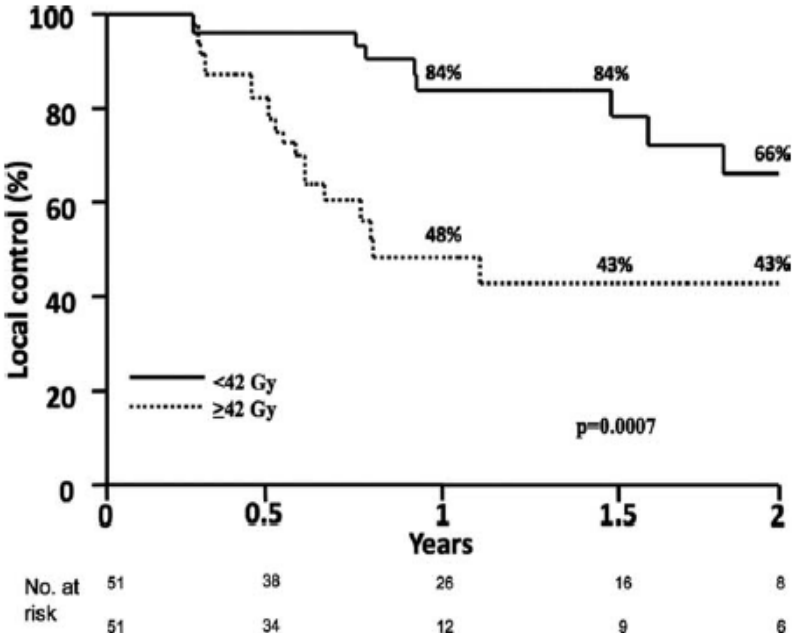
Primary tumors of the lung, ovary, and non CRC gastrointestinal malignancies (ie, unfavorable primary sites) were associated with worse survival

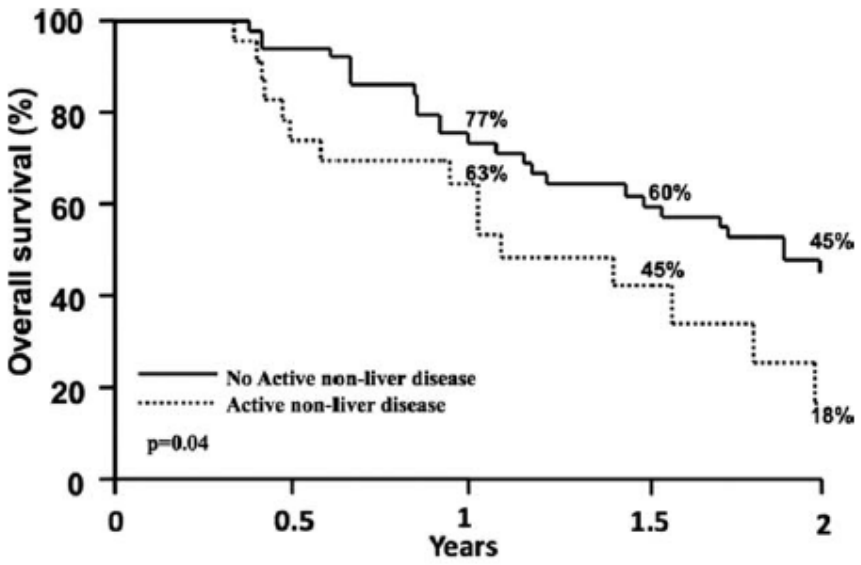
Rusthoven et al., J Clin Oncol 2009

# Stereotactic Body Radiotherapy for Colorectal Liver Metastases

## A Pooled Analysis

Daniel T. Chang, MD[1]; Anand Swaminath, MD[2]; Margaret Kozak, BA[1]; Julie Weintraub, MD[3]; Albert C. Koong, MD, PhD[1]; John Kim, MD[2]; Rob Dinniwell, MD[2]; James Brierley, MD[2]; Brian D. Kavanagh, MD, MPh[3]; Laura A. Dawson, MD[2]; and Tracey E. Schefter, MD[3]




Chang et al., Cancer 2011

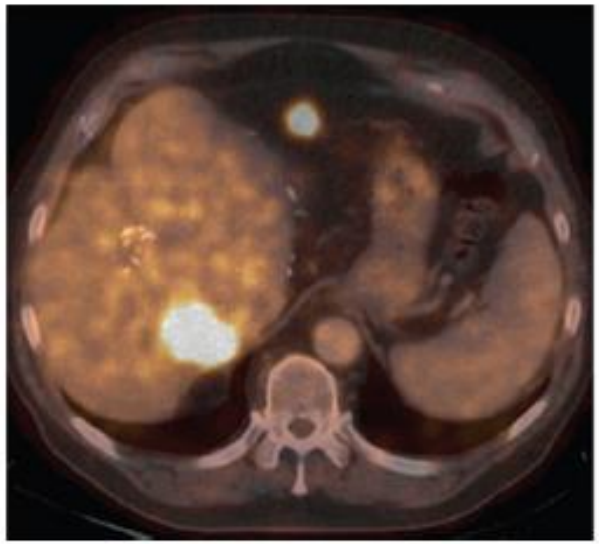
original article

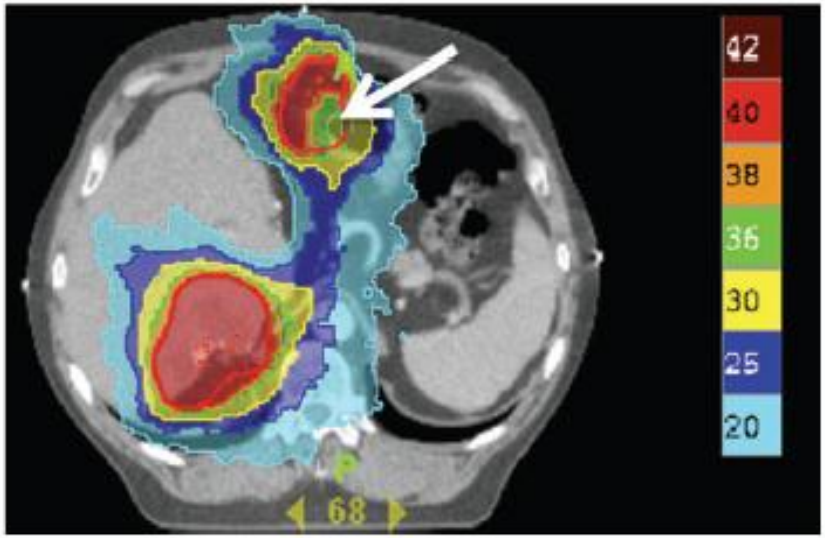
*Annals of Oncology* 22: 362–368, 2011
doi:10.1093/annonc/mdq385
Published online 4 August 2010

# Phase II study of helical tomotherapy for oligometastatic colorectal cancer

B. Engels[1], H. Everaert[2], T. Gevaert[1], M. Duchateau[1], B. Neyns[3], A. Sermeus[4], K. Tournel[1], D. Verellen[1], G. Storme[1] & M. De Ridder[1]*

*Departments of [1]Radiation Oncology; [2]Nuclear Medicine; [3]Medical Oncology; [4]Gastroenterology, UZ Brussel, Vrije Universiteit Brussel, Brussels, Belgium*





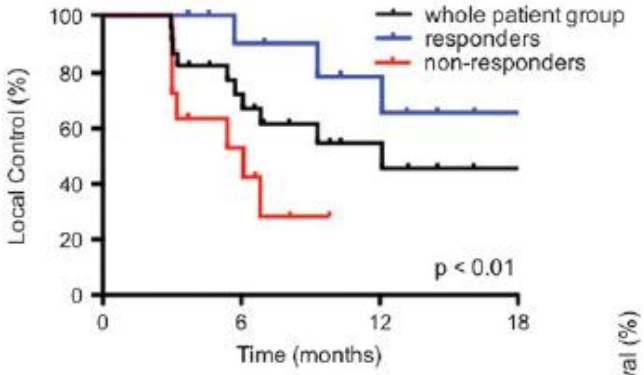
# SBRT for metastases: Questions

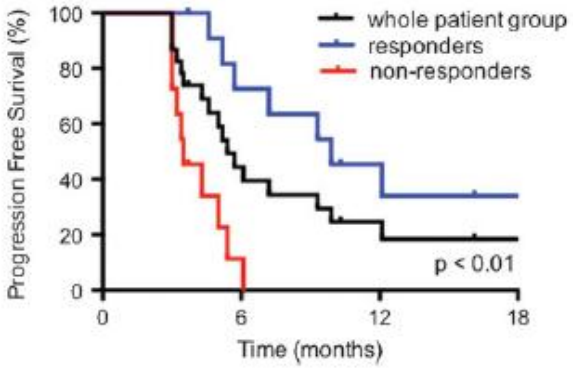
- Other sites (lung, bones...?)
- Patient selection
- Integration into clinical setting

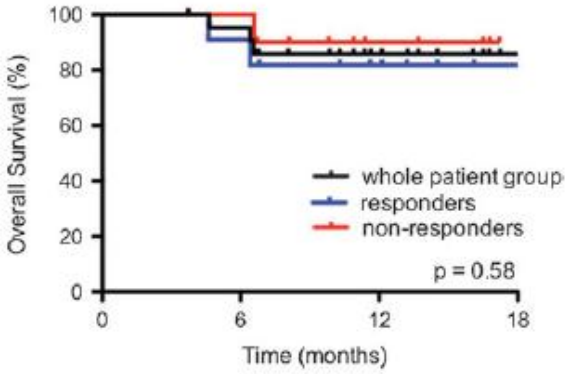
# Stereotactic RT: Lung metastases of CRC

| Study and year | Lesions/ patients, n | Method | Median follow-up[1], months | Local control % | Overall survival % |
|---|---|---|---|---|---|
| Higashiyama et al. [31] (2003) | 100/100 | resection (R0 or R1) | 30.3 | NR | 49.4 (5 years) |
| Pfannschmidt et al. [8] (2003) | 215/167 | resection (R0) | 56.5 (0.5–183.9) | NR | 32.4 (5 years) |
| Saito et al. [9] (2002) | 267 more/165 | resection (R0) | 56.5 (5–135) | NR | 39.6 (5 years) |
| Kanemitsu et al. [32] (2004) | NR/313 | resection (R0 or R1/2) | 29 (1–168) | NR | 38.3 (5 years) |
| Welter et al. [33] (2006) | 266/169 | resection (R0 or R1/2) | NR | NR | 39.1 (5 years) |
| Nakagawa et al. [18] (2000) | 10/5 | SBRT (3-D)<br>20–25 Gy/1 fraction | 10.1 (2–20.5) | 100 crude (1 year) | 60 crude (1 year) |
| Wulf et al. [17] (2004) | 51/41 | SBRT (3-D)<br>26 Gy/1 fraction<br>12–12.5 Gy/3 fractions | 9 (2–37) | 100 (1 year)<br>80 (2 years) | 85 (1 year)<br>33 (2 years)<br>11 (3 years) |
| Le et al. [19] (2006) | 12/12 | SBRT (Robotic)<br>15–25 Gy/1 fraction | 18 | 58 (1 year) | 56 (1 year) |
| Collins et al. [34] (2007) | 12/9 | SBRT (motion tracking)<br>45–60 Gy/3 fractions | 12 (6–30) | 78 crude (1 year) | 78 crude (1 year) |
| Present data | 18/13 | SBRT (Robotic)<br>39–51 Gy/3 fractions | 28 (15–57) | 86.9 (1 year)<br>52.7 (2 years)<br>52.7 (3 years) | 100 (1 year)<br>75.5 (2 years)<br>64.7 (3 years) |
| King et al. [35] (2004) | 44/19 | RFA | 23.9 (4.9–30.3) | 80 crude (1 year) | NR |
| Steinke et al. [36] (2004) | 52/23 | RFA | 14 (5.7–27) | 57 (2 years) | 78 crude (1 year) |
| Yan et al. [22] (2006) | NR/55 | RFA | 24 (6–40) | 65 (1 year) | 85 (1 year)<br>64 (2 years)<br>46 (3 years) |
| Hiraki et al. [23] (2007) | 49/27 | RFA | 20.1 (11.2–47.7) | 74 (1 year)<br>56 (2 years) | 96 (1 year)<br>54 (2 years)<br>48 (3 years) |

# Pre-RT, after CT response by PET/CT

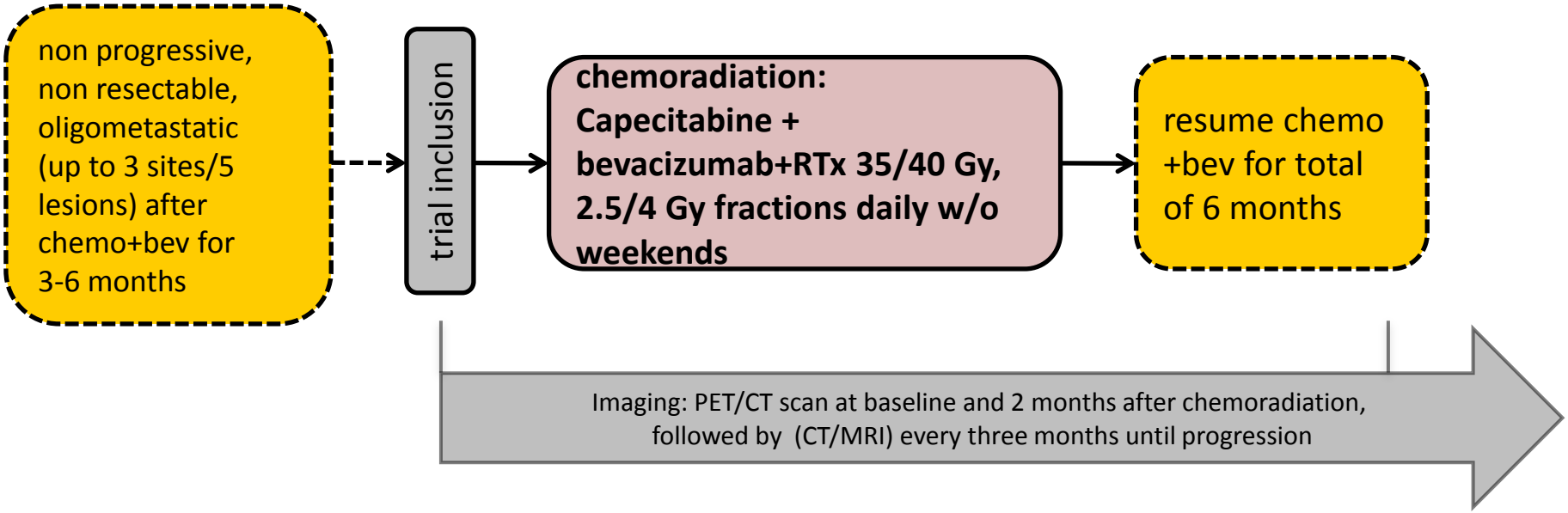



| Variable | Distribution | No. of patients | % |
|---|---|---|---|
| Sex | Male | 14 | 61 |
| | Female | 9 | 39 |
| Age (years) | Median | 64 | |
| | Range | 47–90 | |
| Karnofsky performance status | Median | 80 | |
| | Range | 60–90 | |
| Previous chemotherapy (number of lines) | 0 | 7 | 31 |
| | 1 | 7 | 31 |
| | 2 | 7 | 31 |
| | 3 | 1 | 4 |
| | 4 | 1 | 4 |
| Previous local therapy for metastases | No | 13 | 57 |
| | Yes | 10 | 43 |
| Number of metastases | 1 | 6 | 26 |
| | 2 | 9 | 39 |
| | 3 | 5 | 22 |
| | 4 | 2 | 9 |
| | 5 | 1 | 4 |
| Gross tumor volume (cc) | Median | 22 | |
| | Range | 2–274 | |
| Number of involved sites | 1 | 14 | 61 |
| | 2 | 8 | 35 |
| | 3 | 1 | 4 |
| Localization | Liver | 7 | 31 |
| | Lymph node | 10 | 43 |
| | Lung | 7 | 31 |
| | Soft tissue | 3 | 13 |
| | Bone | 3 | 13 |
| | Peritoneum | 2 | 9 |
| Follow-up (months) | Median | 12 | |
| | Range | 3–18 | |

# AIO multicenter phase II trial: OLGA




n=72

Statistics: PFSR@12 months from start of chemotherapy from 40%→53%
(alpha 10%, beta 20%)

PI: Dirk Arnold

Hubertus Wald Tumorzentrum
Universitäres Cancer Center Hamburg

# Chemoembolization, SIRT and external RT to liver metastases

- SBRT is a non-invasive alternative to other local ablation
- SIRT and CE are feasible  in more disseminated disease
- Safe - but not without specific toxicity
- Efficacious - but not without limitations
  - Sustained local control proven
- Integration and selection are the most relevant issues
- Multidisciplinary team and quality assurance mandatory
- Clinical trials in this field:
  - Need to focus on integration (more than on comparison)
  - Need to define best endpoints

# Multimodal treatment of oligometastatic disease

Resection

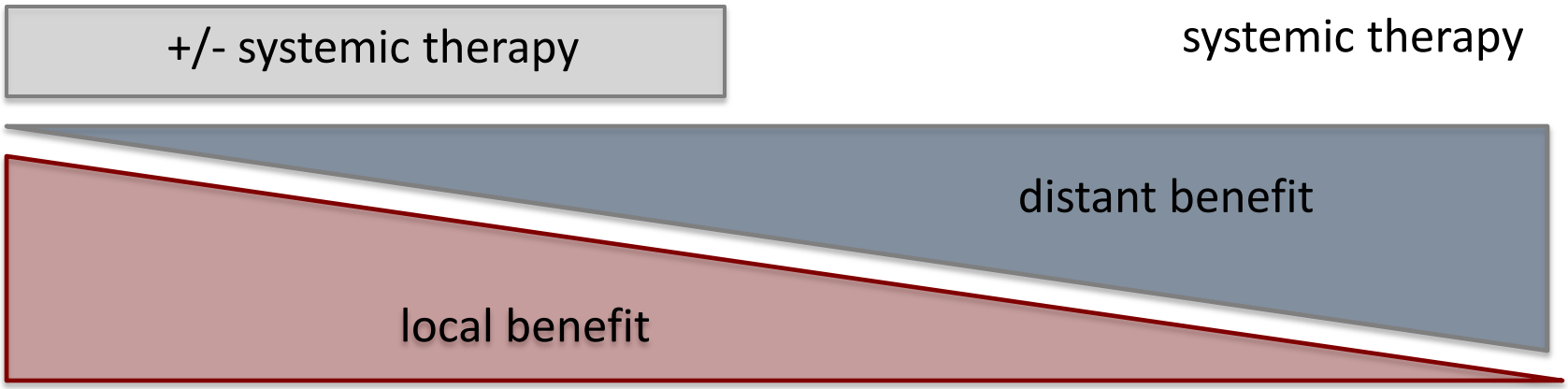
Radiofrequency ablation / LITT

Chemorad of metastases

SIRT

Chemoembolization

Intraarterial chemotherapy



# AIO Concept: Situation dependent optimization of post-inducion treatment

AIO KRK 0207 trial

**FOLFOX or XELOX**

**Bevacizumab**

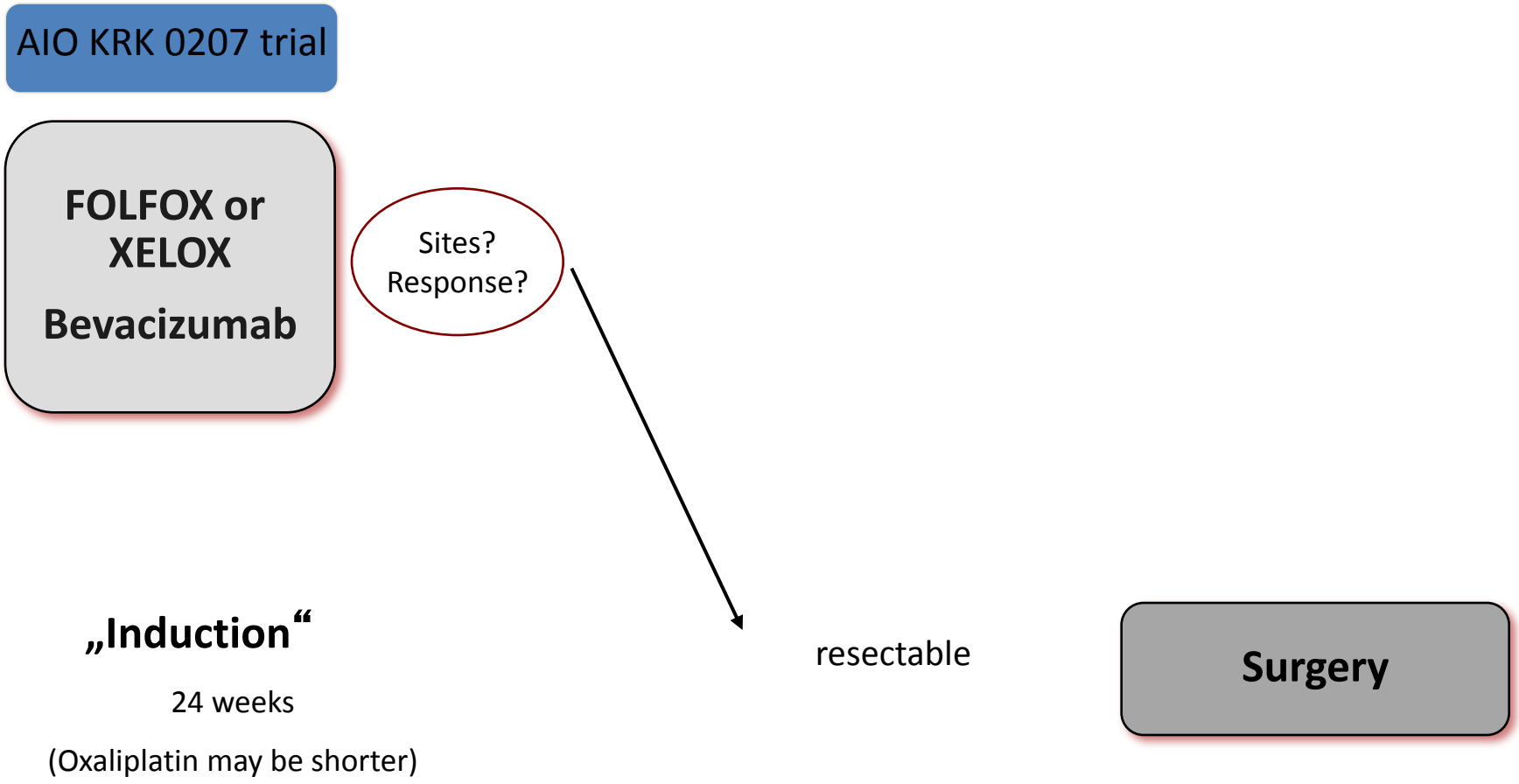
Sites?
Response?

**„Induction“**

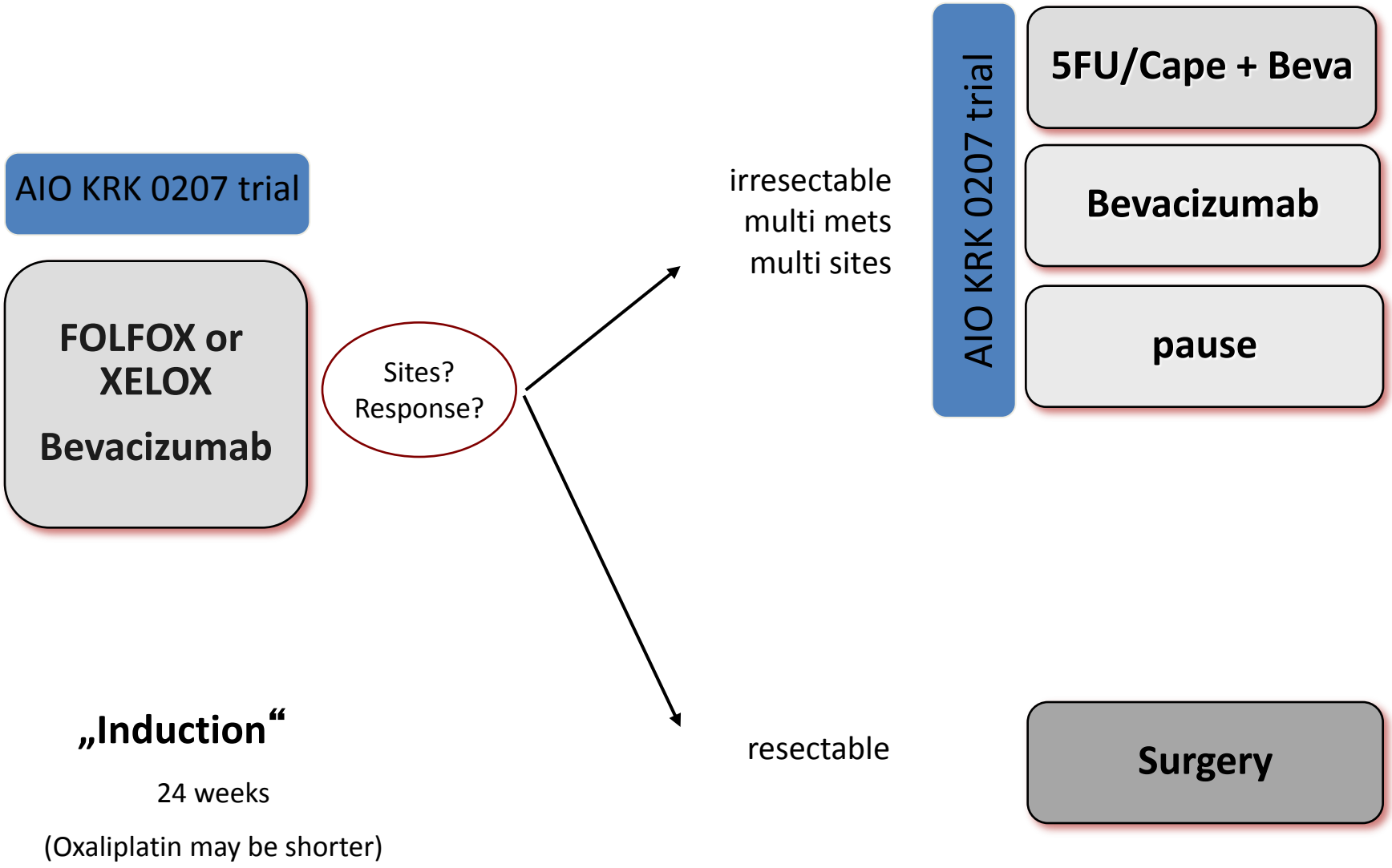
24 weeks

(Oxaliplatin may be shorter)

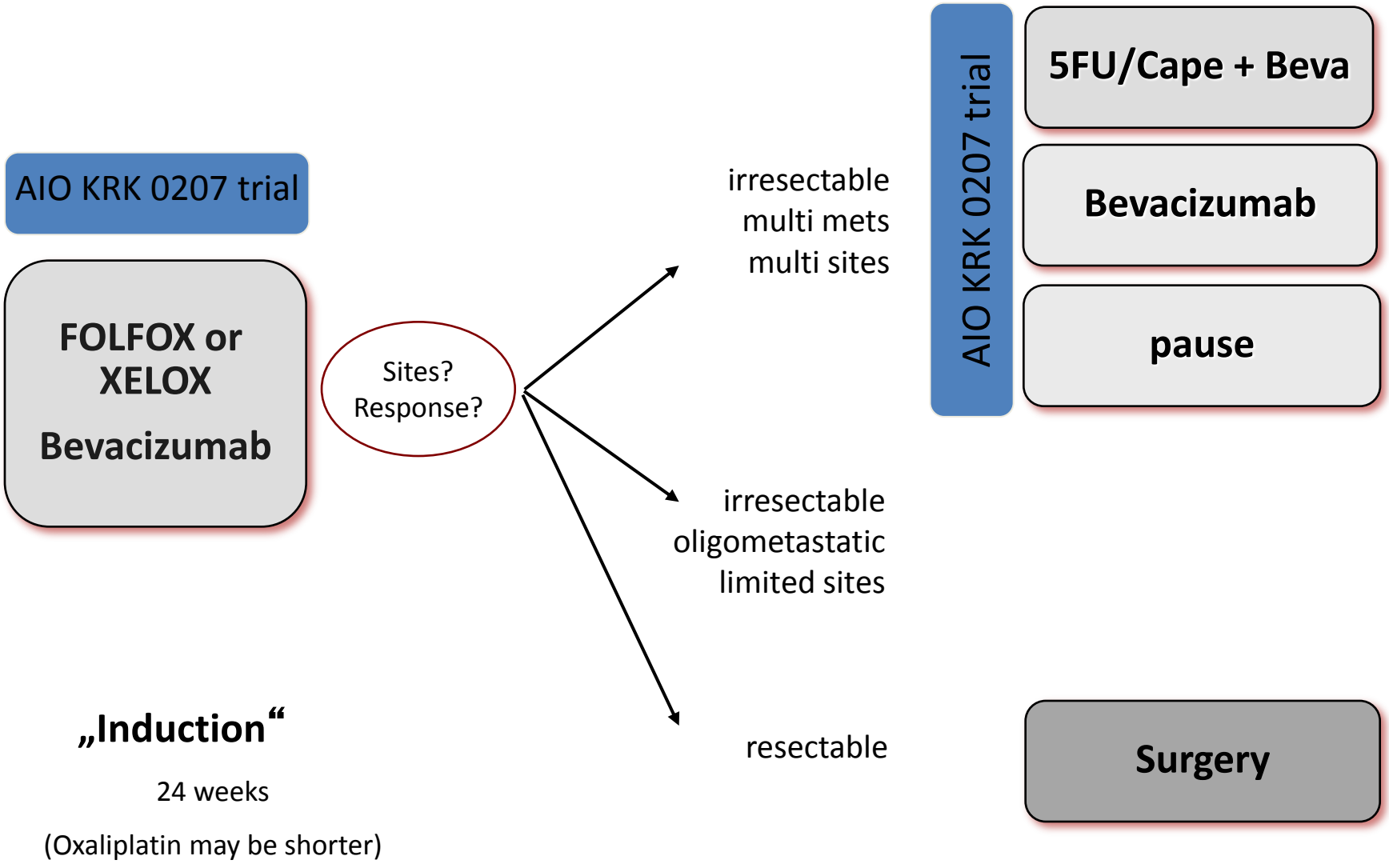
# AIO Concept: Situation dependent optimization of post-inducion treatment



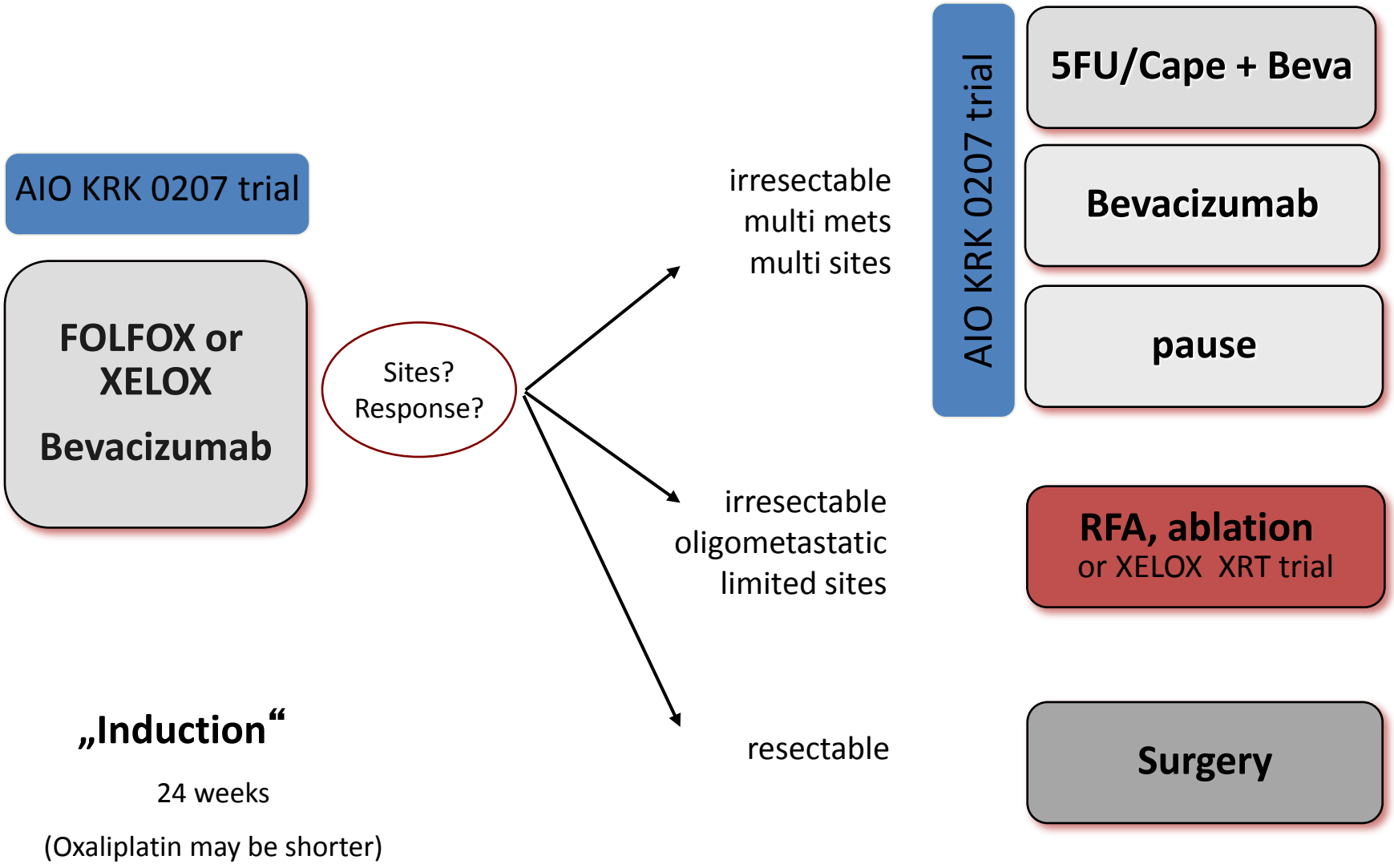
# AIO Concept: Situation dependent optimization of post-inducion treatment



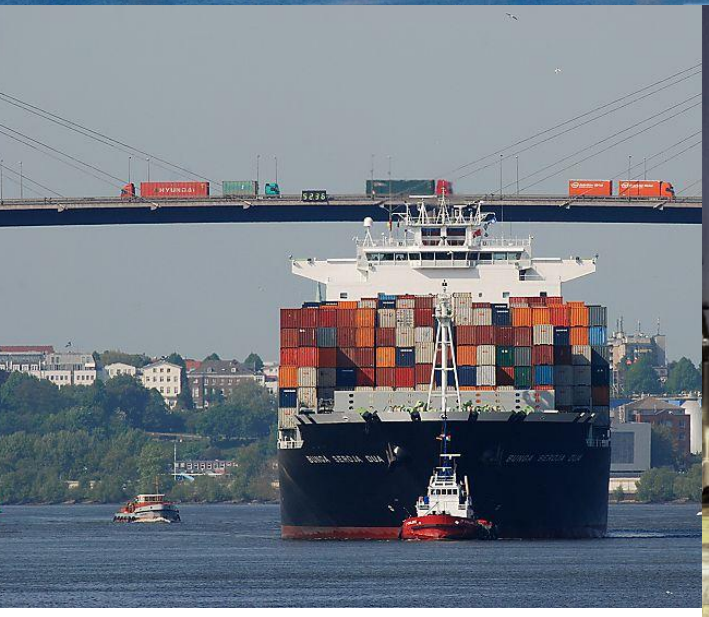
# AIO Concept: Situation dependent optimization of post-inducion treatment



# AIO Concept: Situation dependent optimization of post-inducion treatment



# Thank you for your attention



# Improvement of prognosis and quality of life by IRINO beads?

Italian phase II DEBIRI trial,
N=62 refractory patients

- 55 / 62 pts (90%): general improvement of QoL
- Median time with **freedom from symptoms** 5.3 mos. (5-20)
- Median **Time to further chemotherapy**: 6.3 mos. (5-22)