

# Radioterapija oligometastatske bolesti

VESNA PLEŠINAC KARAPANDŽIĆ  
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# Metastaze

- neizlečiva bolest
- sistemска терапија



they are also blood borne, extensive, and widespread.

From considerations of these theories of cancer dissemination, in the light of the emerging information on the multistep nature of cancer progression, we propose the existence of a clinical significant state of **oligometastases**. For certain tumors, the anatomy and physiology may limit or concentrate these metastases to a single or a limited number of organs. The likelihood of the oligometastatic state should correlate with the biology of tumor progression, rough clinical surrogates of which, for many tumors, might be primary tumor size and grade. Metastasizing cells may seed specific organs as a function of the seeding site. Tumors early in the chain of progression may have metastases limited in number and location because the facility for metastatic growth has not been fully developed and the site for such growth is restricted (this is in contrast to micrometastases, which, although small in size, are extensive in number). With further progression the tumor seeding efficiency increases and be-

## Oligometastaze

### DEFINICIJA

## Oligometastases

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*Journal of Clinical Oncology*, Vol 13, No 1 (January), 1995: pp 8-10

# NEGDE IZMEĐU!!!

a heterogeneous disease that can be thought of as a spectrum of proclivities extending from a disease that remains local throughout its course to one that is systemic when first detectable. This hypothesis suggests that metastases are a function of tumor growth and progression. Lymph

Osnova—biologija kancera

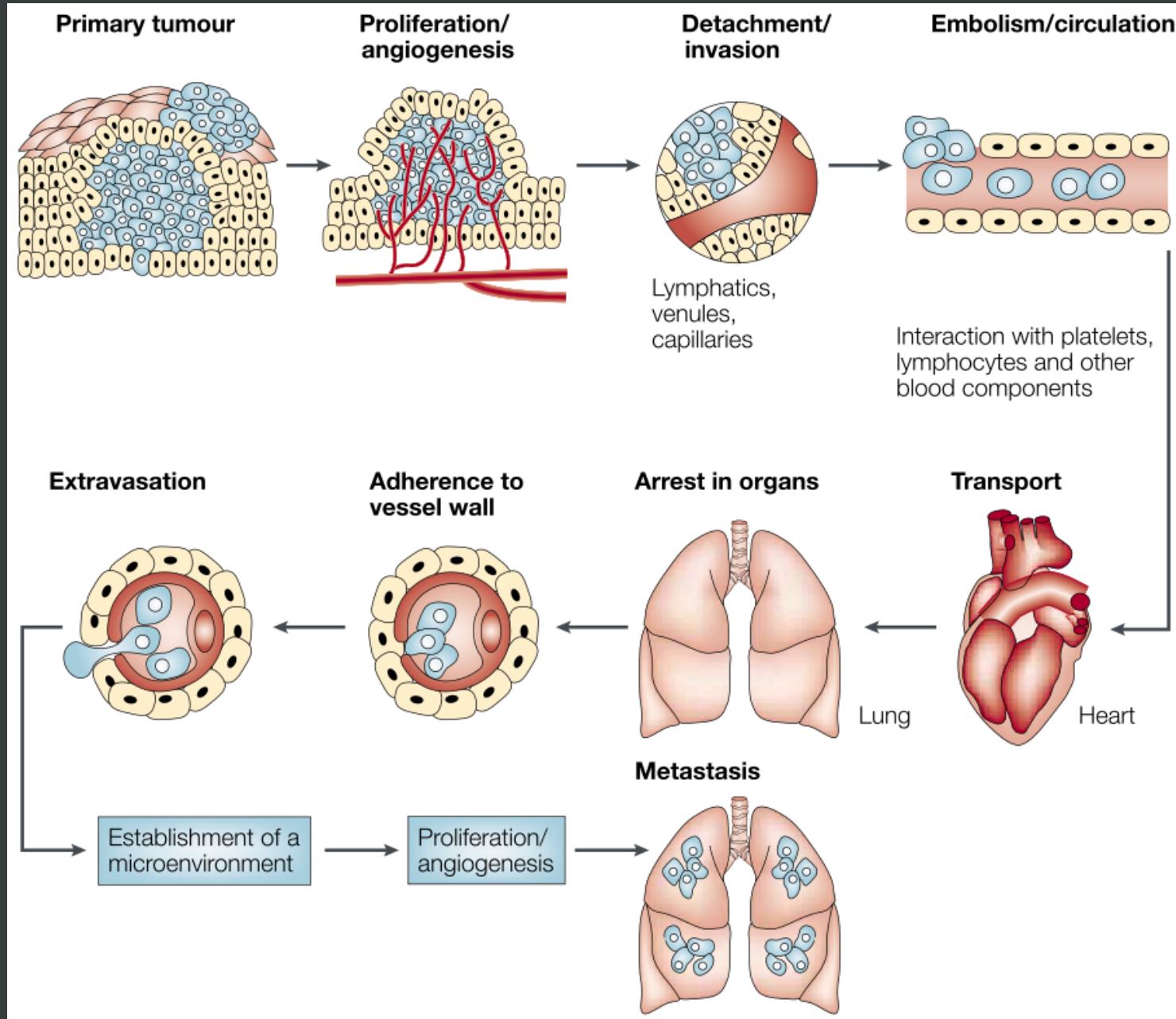
- KONTINUALNA TEORIJA
- SPEKTRALNA TEORIJA
- SISTEMSKA TEORIJA

## KARNOFSKY MEMORIAL LECTURE

### **Natural History of Small Breast Cancers**

By Samuel Hellman

*Journal of Clinical Oncology, Vol 12, No 10 (October), 1994: pp 2229-2234*



# KAPACITET!!!

## Osnova—biologija tumora

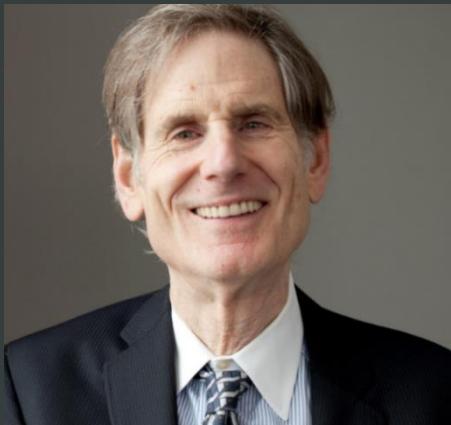
- VIŠESTENPENI PROCES
- EVOLUCIJA
- OGRANIČENE GENETSKE PROMENE

The pathogenesis of cancer metastasis: the ‘seed and soil’ hypothesis revisited

Isaiah J. Fidler

NATURE REVIEWS | CANCER VOLUME 3 | JUNE 2003

Samuel Hellman



Ralph Weichselbaum

Based on the spectrum hypothesis describing the natural history of breast cancer [10], a clinically significant disease state of *oligometastases* has been proposed [11]. In this paradigm, a disease state between locoregionally confined and widely metastatic cancer may exist where tumors early in the evolution of metastatic progression produce metastases limited in number and location. Such limited metastases are termed de novo *oligometastases*. In patients who

## Oligometastaze

NEGDE IZMEĐU

# OGRANIČEN METASTATSKI KAPACITET!!!

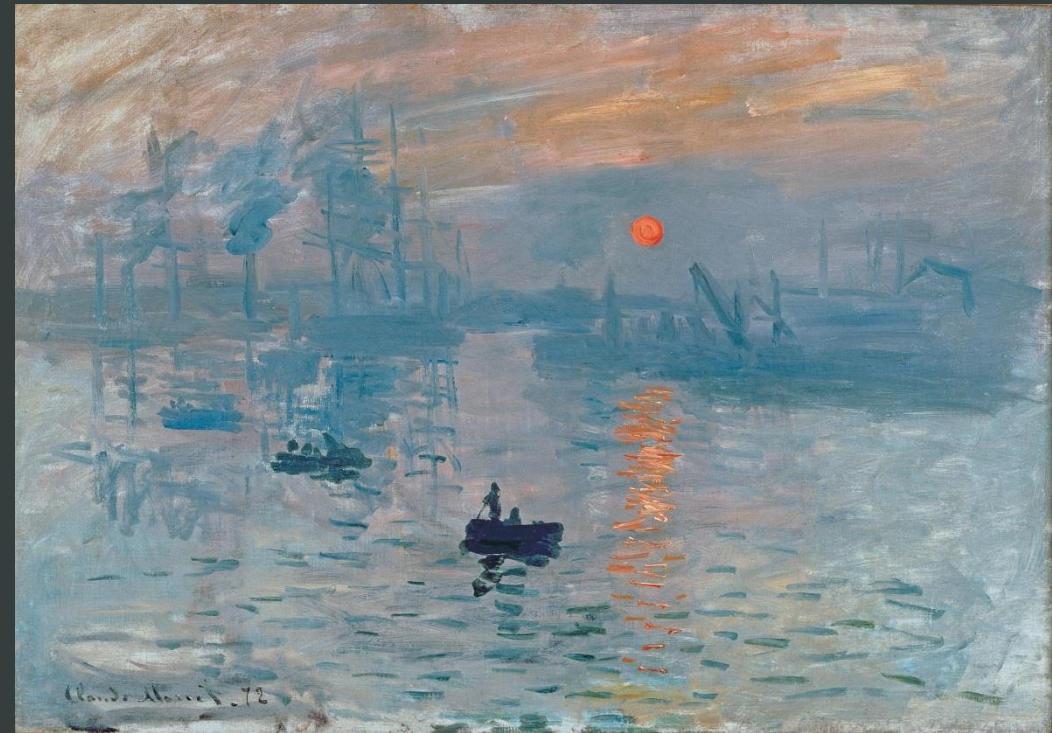
### A Rationale for the Targeted Treatment of Oligometastases With Radiotherapy

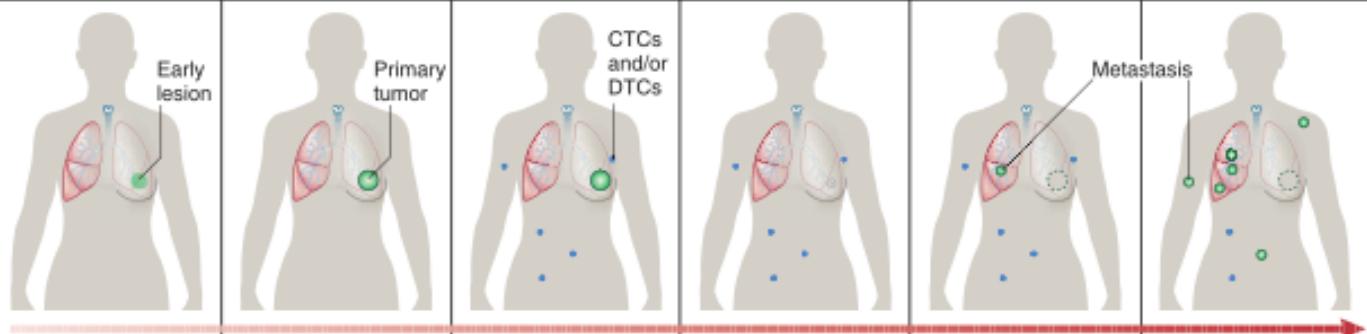
DHARA M. MacDERMED, MD,<sup>1</sup> RALPH R. WEICHSELBAUM, MD,<sup>1,2,3</sup> AND JOSEPH K. SALAMA, MD<sup>1,2,3\*</sup>

Journal of Surgical Oncology 2008;98:202–206

# Posledice i značaj oligometastaza

- lokalna terapija—benefit
- „window of opportunity“
- kurativni pristup!?
- prevalenca
- dijagnosticke metode
- rana detekcija





| Status                        | Pre-neoplasm<br>Subclinical                                   | Primary (-)<br>CTCs and/or DTCs   | Primary (+)<br>CTCs and/or DTCs  | Dormancy  | Oligometastases   | Systemic<br>metastases |  |  |
|-------------------------------|---|---|--|---|---|------------------------|--|--|
| Focus                         | Management of primary tumor                                   |   | Prevention of metastasis   |   | Treatment of metastasis   |                        |  |  |
| Challenge                     | Early detection and prevention<br>Identify high-risk patients |   | Prevent local and distant relapse<br>Drug resistance of DTCs   |   | Early detection of relapse<br>Heterogeneity and drug resistance   |                        |  |  |
| New tools                     | Diagnostic<br>markers   | Prognostic<br>markers   | Profiling of primary tumor, metastases, CTCs and/or DTCs for accurate targeting<br>Biomarkers and imaging technologies for disease monitoring<br>Biomarkers for therapeutic efficacy   |   |   |                        |  |  |
| Possible treatment strategies | Prophylactic<br>treatment<br>Vaccination                      | Surgery, radiotherapy<br>(+) Systemic therapy   |  | Targeted therapy against driver oncogenes and their<br>pathways tailored by genetic makeup of tumor cells |   |                        |  |  |
|                               |   |   | Long-term adjuvant treatment (for high-risk patients):<br>• Metronomic chemotherapy and anti-angiogenesis<br>• Targeting common driver oncogenes and pathways<br>• Immunotherapy<br>• Targeting dormancy-related survival and CSC signaling and niche components |   | Systemic therapy<br>Immunotherapy<br>Stroma-targeting treatments<br>Palliative radiation and/or surgery |                        |  |  |
|                               |   |   |  | Surgery<br>stereotactic<br>radiotherapy   |   |                        |  |  |
| Possible new targets          |   | DTC and/or CTC survival pathways; stem cell features; tumor-stroma crosstalk and Activation of metastasis-suppressive signaling |  |   |   |                        |  |  |

## Evolucija kancera

### TERAPIJSKE OPCIJE

- HIRURGIJA—RESEKCIJA METASTAZA
- RADIOTERAPIJA—STEREOTAKSIČNA RADIOTERAPIJA

Tumor metastasis: moving new biological insights into the clinic

Liling Wan<sup>1</sup>, Klaus Pantel<sup>2</sup> & Yibin Kang<sup>1,3</sup>

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**Table 3** | Selected series of resection for colorectal cancer liver metastases

| Study                                    | n                | Mean number<br>of lesions,<br>size (cm) | Outcomes   |
|--|------------------|---|--|
| Hughes et al. (1986) <sup>53</sup>       | 607              | NA                                      | 5-year OS 33%  |
| Rosen et al. (1992) <sup>135</sup>       | 280              | NA                                      | 3-year OS: 47%; 5-year OS 25%                                |
| Scheele et al.<br>(1995) <sup>84</sup>   | 434              | NA                                      | Median survival: 40 months;<br>3-year OS: 45%; 5-year OS 33% |
| Jamison et al.<br>(1997) <sup>136</sup>  | 280              | NA                                      | Median survival: 33 months;<br>5-year OS 27%                 |
| Fong et al. (1999) <sup>7</sup>          | 1,001            | NA                                      | Median survival: 42 months;<br>3-year OS: 57%; 5-year OS 36% |
| Minagawa et al.<br>(2000) <sup>137</sup> | 235              | NA                                      | 3-year OS: 51%; 5-year OS 38%                                |
| Choti et al. (2002) <sup>8</sup>         | 226              | NA                                      | Median survival: 46 months;<br>3-year OS: 57%; 5-year OS 40% |
| Abdalla et al.<br>(2004) <sup>122</sup>  | 190              | NA                                      | 5-year OS 58%  |
| Pawlik et al. (2005) <sup>10</sup>       | 557              | NA                                      | 3-year OS: 74%; 5-year OS 58%                                |
| Wei et al. (2006) <sup>138</sup>         | 423              | NA                                      | Median survival: 53 months;<br>3-year OS: 64%; 5-year OS 47% |
| Shah et al. (2007) <sup>139,*</sup>      | 841              | 1 in 78%,<br><5 cm in 68%               | Median survival: 48 months;<br>3-year OS: 59%; 5-year OS 43% |
| Rees et al. (2008) <sup>81</sup>         | 929              | NA                                      | 5-year OS 36%  |
| de Jong et al.<br>(2009) <sup>83,‡</sup> | 1,506            | 1 (median),<br>3.4 cm                   | 3-year RFS: 38%; 5-year RFS: 30%                             |
| Adam et al. (2009) <sup>68</sup>         | 184 <sup>§</sup> | 5.3, 5 cm                               | 5-year OS 33%  |

\*43 center population data. <sup>\*</sup>Multi-institutional trial from 1982 to 2008. Intrahepatic recurrence occurred in 43% of patients; combined recurrence occurred in 21% of patients. <sup>§</sup>Initially unresectable disease.

Abbreviations: NA, not available; OS, overall survival; RFS, recurrence-free survival.

# Hirurgija—rezultati lokalne terapije

## RESEKCIJA METASTAZA KOLOREKTALNOG KARCINOMA U JETRI

### The role of local therapy in the management of lung and liver oligometastases

Simon S. Lo, Susan D. Moffatt-Bruce, Laura A. Dawson, Roderich E. Schwarz, Bin S. Teh, Nina A. Mayr, Jiade J. Lu, John C. Grecula, Thomas E. Olencki and Robert D. Timmerman

Lo, S. S. et al. *Nat. Rev. Clin. Oncol.* 8, 405–416 (2011); published online 24 May 2011; doi:10.1038/nrclinonc.2011.75

**Table 1** | Pulmonary metastasectomy for different histological types

| Study                                | Histological type     | n     | Type of resection       | Risk factors for decreased survival  | Overall survival (%)                               |
|--------------------------------------|-----------------------|-------|-------------------------|--|--|
| Onaitis et al. (2009) <sup>4</sup>   | CRC                   | 378   | WR 72%; AR 28%; PN 0.2% | Age <65; female sex; DFI <12 months  | 78 (3-year)  |
| Riquet et al. (2010) <sup>32</sup>   | CRC                   | 127   | WR 23%; AR 64%; PN 13%  | Incomplete resection; single metastasis  | 41 (5-year)<br>27 (10-year)                        |
| Suri et al. (2005) <sup>34</sup>     | Sarcoma               | 103   | WR 84%; AR 6%; PN 2%    | Extrapulmonary disease; >4 nodules resected; incomplete resection                          | 21 (5-year)  |
| Blackmon et al. (2009) <sup>35</sup> | Sarcoma               | 234   | WR 85%; AR 14%; PN 1%   | >3 nodules; synchronous disease; prior metastasectomy                                      | 35 (5-year; ≤2 nodules)<br>25 (5-year; >2 nodules) |
| Murthy et al. (2005) <sup>37</sup>   | RCC                   | 417   | WR 70%; AR 26%; PN 4%   | Incomplete resection; larger nodule size; involved lymph nodes; decreased FEV <sub>1</sub> | 45 (5-year)  |
| Assouad et al. (2007) <sup>36</sup>  | RCC                   | 65    | WR 56%; AR 40%; PN 4%   | Size of metastases; lymph-node involvement   | 37 (5-year)  |
| Petersen et al. (2007) <sup>5</sup>  | Melanoma              | 1,720 | WR 66%; AR 33%; PN 1%   | Nodular histology; DFI <12 months; extrathoracic metastases                                | 21 (5-year)  |
| Clavero et al. (2006) <sup>39</sup>  | Gynecologic cancers   | 103   | WR 63%; AR 36%; PN 1%   | DFI <24 months; cervical primary site  | 47 (5-year)<br>34 (10-year)                        |
| Shiono et al. (2009) <sup>40</sup>   | Head and neck cancers | 237   | WR 33%; AR 63%; PN 4%   | Male sex; oral cavity cancers; lymph-node metastases; DFI <24 months                       | 26 (5-year)  |
| Winter et al. (2008) <sup>41</sup>   | Head and neck cancers | 332   | WR 78%; AR 21%; PN 1%   | Incomplete resection; surgical complications; adjuvant therapy                             | 24 (5-year)  |

Abbreviations: AR, anatomic resection (including lobectomy, segmentectomy, bilobectomy); CRC, colorectal carcinoma; DFI, disease-free interval; FEV<sub>1</sub>, forced expiratory volume; PN, pneumonectomy; RCC, renal cell carcinoma; WR, wedge resection.

# Hirurgija—rezultati lokalne terapije

## RESEKCIJA METASTAZA U PLUĆIMA

### The role of local therapy in the management of lung and liver oligometastases

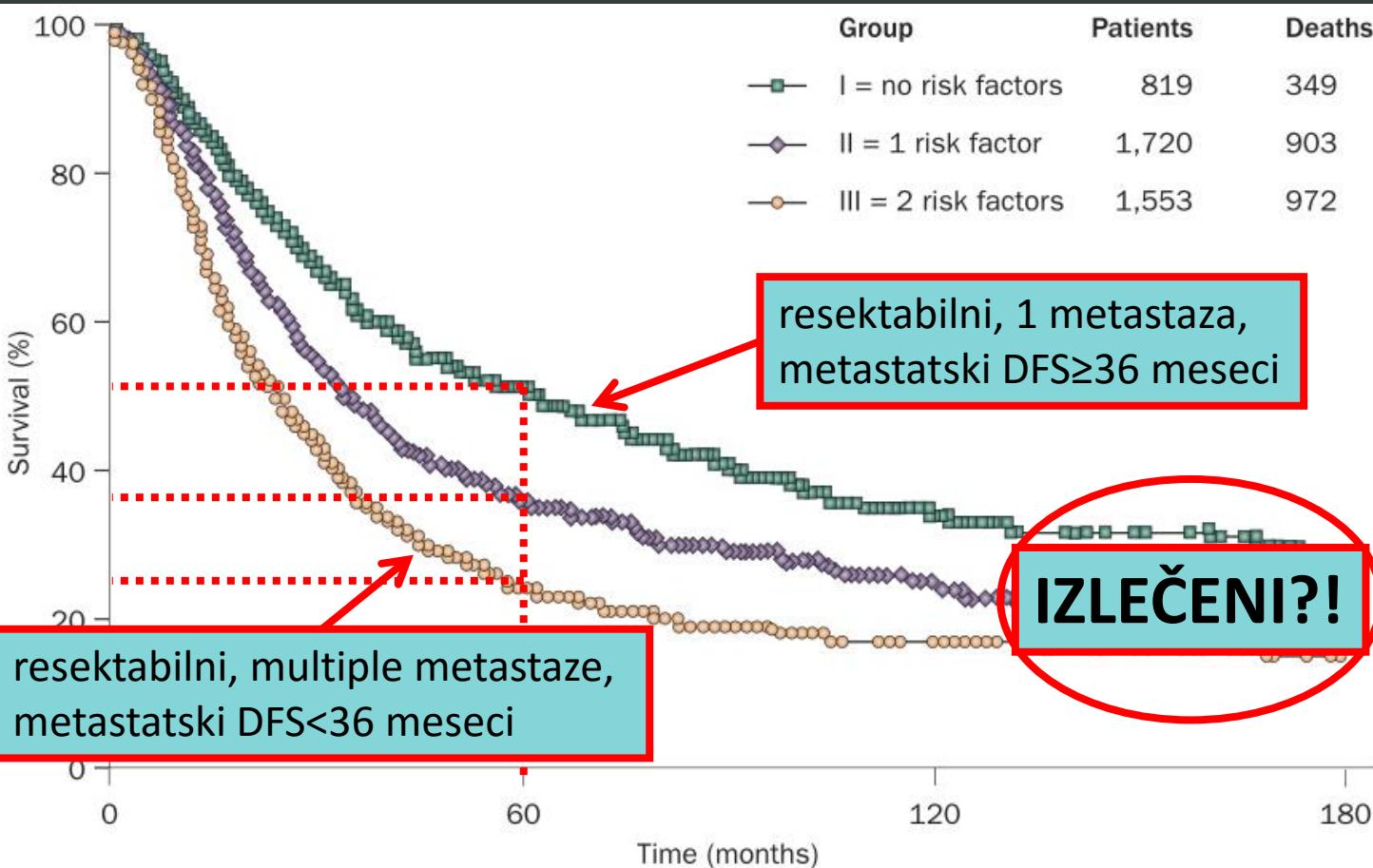
Simon S. Lo, Susan D. Moffatt-Bruce, Laura A. Dawson, Roderich E. Schwarz, Bin S. Teh, Nina A. Mayr, Jiade J. Lu, John C. Grecula, Thomas E. Olencki and Robert D. Timmerman

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# Hirurgija—selekcija pacijenata

- broj i veličina metastaza
- broj metastatskih mesta
- metastatic disease-free interval
- adekvatnost resekcije
- histologija
- faktori vezani za pacijenta





**Figure 1** | Survival of patients undergoing pulmonary resection of metastatic tumors. Each curve represents the survival of patients with an increasing number of risk factors for recurrence as determined by a retrospective review of the data.<sup>7</sup> These categories are: group I, a single resectable metastasis with a disease-free interval from primary tumor to metastasis of  $\geq$ 36 months; group II, multiple metastases or a disease-free interval <36 months; group III, multiple metastases and a disease-free interval <36 months. The size, number and tumor type are risk factors for recurrence. Permission obtained from Elsevier © Pastorino, U. et al. *J. Thorac. Cardiovasc. Surg.* **113**, 37–49 (1997).

# Hirurgija— prognostički faktori

## RESEKCIJA METASTAZA U PLUĆIMA

### OPINION

## Oligometastases revisited

Ralph R. Weichselbaum and Samuel Hellman

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

# Stereotaksična radioterapija

- SRS—stereotactic radiosurgery
- SBRT—stereotactic body radiotherapy



Stereotactic body radiation therapy (SBRT) is an external beam radiation therapy method used to very precisely deliver a high dose of radiation to an extracranial target within the body, using either a single dose or a small number of fractions. Specialized treatment planning results in high target dose and steep dose gradients beyond the target. The ability to deliver a single or a few fractions of high-dose ionizing radiation with high targeting accuracy and rapid dose falloff gradients encompassing tumors within a patient provides the basis for the development of SBRT.

## SBRT

### DEFINICIJA

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

LOUIS POTTERS, M.D.,\* BRIAN KAVANAGH, M.D.,† JAMES M. GALVIN, D.Sc.,‡ JAMES M. HEVEZI, Ph.D.,§  
NORA A. JANJAN, M.D.,¶ DAVID A. LARSON, M.D., Ph.D.,\*\* MINESH P. MEHTA, M.D.,||  
SAMUEL RYU, M.D.,|| MICHAEL STEINBERG, M.D.,||§§ ROBERT TIMMERMAN, M.D.,||  
JAMES S. WELSH, M.D.,\*\*\* AND SETH A. ROSENTHAL, M.D.||††

Activate Windows

Int. J. Radiation Oncology Biol. Phys., Vol. 76, No. 2, pp. 326–332, 2010

# SBRT—radiobiologija

- LQ 
- DNK
- mikrovaskulatura
- imunologija
- generalized LQ
- universal survival curve—USC



**Table 2** | SBRT for lung metastasis from selected studies

| Study                                     | Study type               | n   | Number of lesions | Dose   | Median follow up (months)   | Outcomes  |
|---|--------------------------|-----|-------------------|--|-----------------------------|---|
| Okunieff et al. (2006) <sup>19</sup>      | Retrospective            | 42  | 125               | 5 Gy × 10 fractions prescribed to 80% isodose line   | 18.7                        | 3-year LC: 91%; 1 and 2 year PFS: 25% and 16%; grade 3 toxic effects: 4%  |
| Norihisa et al. (2008) <sup>49</sup>      | Retrospective            | 34  | 43                | 12 Gy × 4–5 fractions prescribed to isocenter  | 27                          | 2-year LRF: 90%; 2-year OS: 84.3%; 2-year PFS: 34.8%; grade 2 and 3 toxic effects: 12% and 3%                               |
| Guckenberger et al. (2009) <sup>134</sup> | Retrospective            | 84  | 118               | 6–7 Gy × 4–8 fractions, 10–12.5 Gy × 3 fractions and 26 Gy × 1 fraction prescribed to 65% isodose line | 14                          | 3-year LC: 82%; 3-year OS: 16%; grade 3 or higher toxic effects: 1.2%   |
| Ernst-Stecken et al. (2006) <sup>46</sup> | Prospective (phase I-II) | 18  | 36                | 7–8 Gy × 5 fractions (90% coverage of 90% of PTV required)   | NA                          | CR: 51%; PR: 33%; SD: 3% (including 3 patients with primary lung tumors); grade 4 or higher toxic effects: 0                |
| Le et al. (2006) <sup>18</sup>            | Prospective (phase I-II) | 11* | 11                | 15–30 Gy × 1 fraction  | NA                          | 1-year FFP: <20 Gy 54%, >20 Gy 91% ( $P=0.03$ )*; grade 2/3 pneumonitis: 4 patients*; treatment-related deaths: 3 patients* |
| Rusthoven et al. (2009) <sup>14</sup>     | Prospective (phase I-II) | 38  | 63                | 16–20 Gy × 3 fractions prescribed to isodose line covering PTV   | 15.4 for assessable lesions | LC: 100% and 96% at 1 and 2 years; OS: 39% at 2 years; grade 4 or higher toxic effects: 0                                   |

\*Data for whole group of 32 patients (21 with primary lung cancer and 11 with lung metastasis). Abbreviations: CR, complete response; FFP, free-from-progression; LC, local control; LRF, local relapse-free; NA, not available; OS, overall survival; PFS, progression-free survival; PR, partial response; PTV, planning treatment volume; SBRT, stereotactic body radiation therapy; SD, stable disease.

## SBRT—rezultati

### METASTAZE U PLUĆIMA

### The role of local therapy in the management of lung and liver oligometastases

Simon S. Lo, Susan D. Moffatt-Bruce, Laura A. Dawson, Roderich E. Schwarz, Bin S. Teh, Nina A. Mayr, Jiade J. Lu, John C. Grecula, Thomas E. Olencki and Robert D. Timmerman

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# SBRT—rezultati

## METASTAZE U JETRI

**Table 4 |** Results of SBRT for liver metastasis from selected studies

| Study                                      | Type                                    | n  | Number of lesions            | Dose  | Median follow up (months)       | Outcomes   | Toxic effects   |
|--|---|----|------------------------------|---|---------------------------------|--|---|
| Katz et al. (2007) <sup>20</sup>           | Retrospective                           | 69 | 174                          | 30–55 Gy in fractions of 2–6 Gy prescribed to 80%                                   | 14.5                            | 10-month and 20-month LC: 76% and 57%; 6-month and 12-month OS: 46% and 24%  | Grade 3 or higher toxic effects: 0  |
| Van der Pool et al. (2010) <sup>116</sup>  | Retrospective (colorectal primary only) | 20 | 31                           | 12.5–15 Gy × 3 fractions prescribed to PTV  | 26                              | 2-year LC: 74%<br>83%<br>2-year OS:  | Grade 3 or higher liver toxic effects: 2 patients   |
| Ambrosino et al. (2009) <sup>140</sup>     | Prospective                             | 27 | 1–3 lesions for each patient | 25–60 Gy in 3 fractions prescribed to 80%   | 13                              | LC (crude): 74%  | Mild to moderate transient hepatic dysfunction: 9 patients; minor complications: 4 patients; progressive disease with liver failure: 2 patients |
| Herfarth et al. (2001) <sup>21</sup>       | Prospective (phase I-II)                | 33 | 56                           | 14–26 Gy × 1 fraction prescribed to 80%   | 5.7                             | 6-month, 12-month, and 18-month LC: 75%, 71% and 67%; 1-year OS: 72% (analysis including 4 patients with primary liver tumors) | RILD: 0   |
| Méndez-Romero et al. (2006) <sup>117</sup> | Prospective (phase I-II)                | 14 | 34                           | 12.5 Gy × 3 fractions prescribed to 65%   | 12.9                            | 1-year and 2-year LC: 100% and 86%<br>1-year and 2-year OS: 85% and 62%  | Grade 3 toxic effects: acute (n=3) and late (n=1); grade 4 or higher toxic effects: 0   |
| Rusthoven et al. (2009) <sup>15</sup>      | Prospective (phase I-II)                | 47 | 63                           | 12–20 Gy × 3 fractions prescribed to isodose line covering PTV                      | 16 for assessable lesions       | 1-year and 2-year LC: 95% and 92%<br>2-year OS: 30%  | Grade 4 toxic effects: 0  |
| Lee et al. (2009) <sup>16</sup>            | Prospective (phase I)                   | 70 | 143                          | 27.7–60 Gy in 6 fractions prescribed to isodose line covering PTV (median: 41.4 Gy) | 10.8 for 68 assessable patients | 1-year LC: 71%; 18-month OS: 47%; median PFS: 3.7 months   | Acute grade 3 toxicities: 10%; late grade 4 and 5 toxicities: 2.9% and 1.5%   |
| Rule et al. (2011) <sup>17</sup>           | Prospective (phase I)                   | 27 | 37                           | 10 Gy × 3–5 fractions to 12 Gy × 5 fractions prescribed to 70–85%                   | 20                              | 24-month LC: (30 Gy) 56%; (50 Gy) 89%; (60 Gy) 100%  | Maximum-tolerated dose not reached  |

Abbreviations: LC, local control; OS, overall survival; PFS, progression-free survival; PTV, planning treatment volume; RILD, radiation-induced liver disease.

## The role of local therapy in the management of lung and liver oligometastases

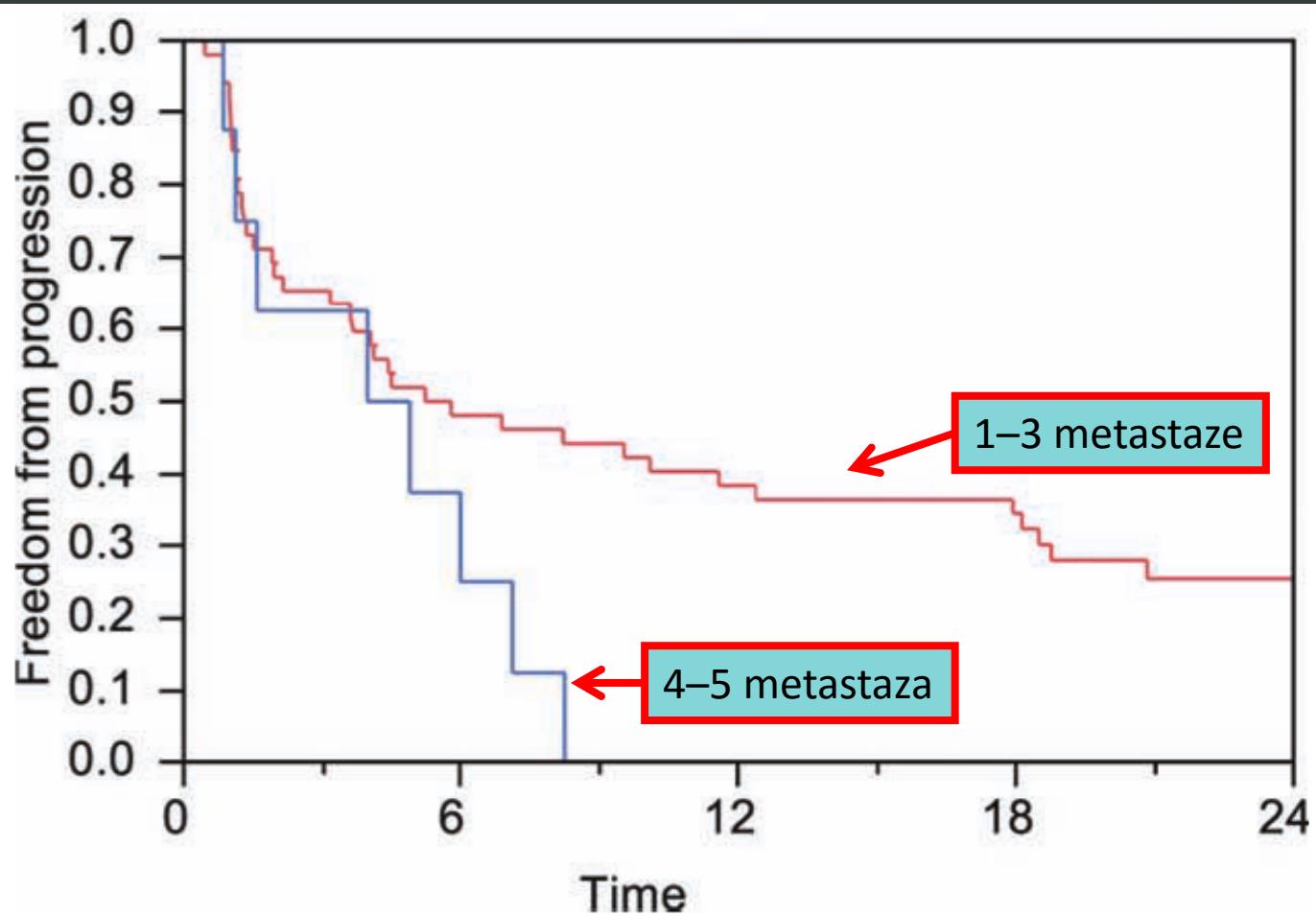
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# SBRT—selekcija pacijenata

- koga lečiti?
- sličnosti hirurgije i radioterapije
- opterećenost bolešću
- karakteristike pacijenta





**Figure 1.**

(Bottom) Freedom from progression is shown for patients with 1 to 3 metastases (red line) versus 4 to 5 metastases (blue line) at protocol enrollment,  $P=.07$  by log-rank test. Dashed lines represent 95% confidence intervals.

## SBRT—prognostički faktori

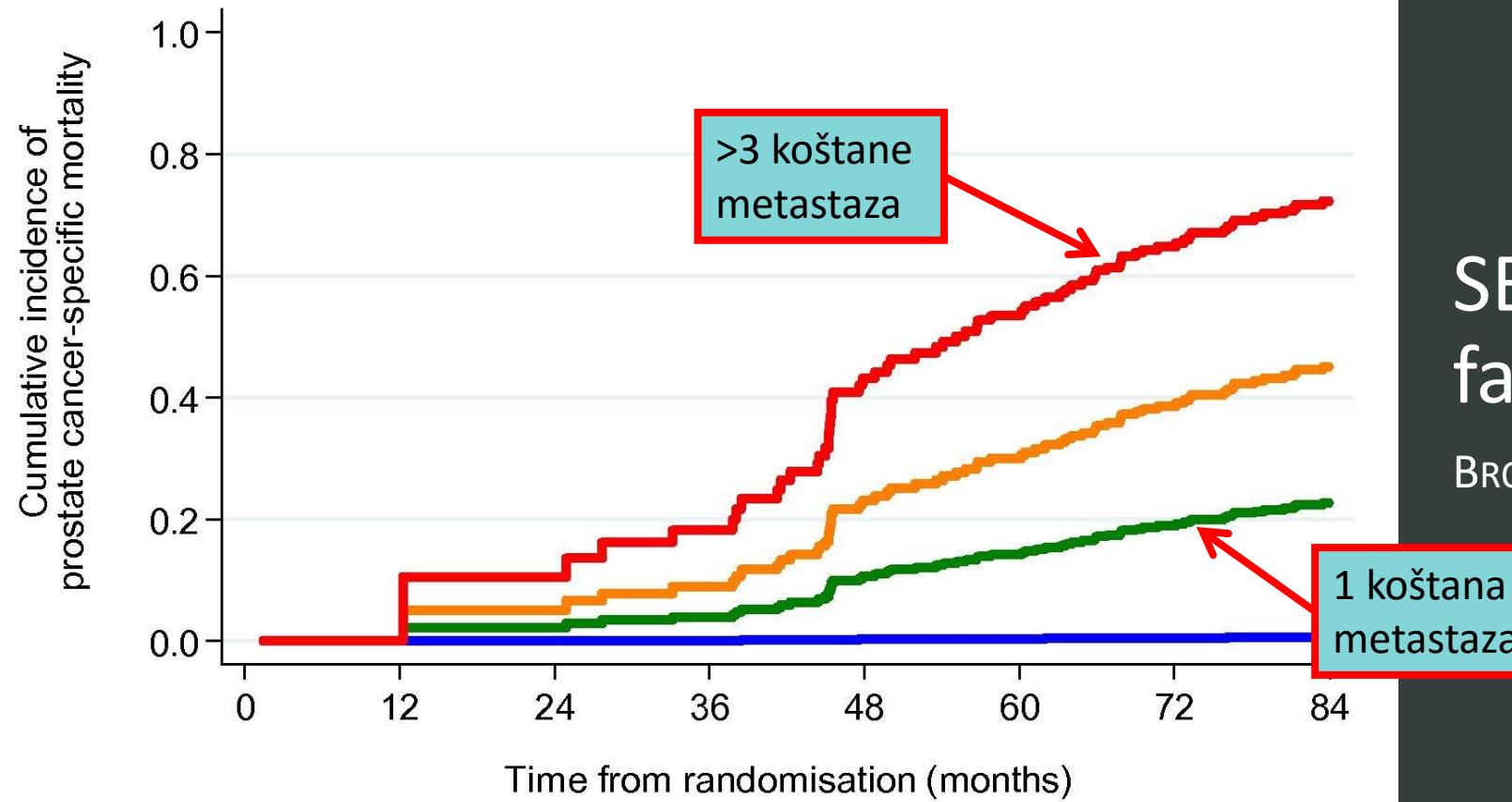
### BROJ METASTAZA

## Stereotactic Body Radiotherapy for Multisite Extracranial Oligometastases

Final Report of a Dose Escalation Trial in Patients With 1 to 5 Sites of Metastatic Disease

Joseph K. Salama, MD<sup>1</sup>; Michael D. Hasselle, MD<sup>2</sup>; Steven J. Chmura, MD, PhD<sup>2,3</sup>; Renuka Malik, MD<sup>2</sup>; Neil Mehta, MD<sup>2</sup>; Kamil M. Yenice, MD<sup>2</sup>; Victoria M. Villaflor, MD<sup>3,4</sup>; Walter M. Stadler, MD<sup>3,4</sup>; Philip C. Hoffman, MD<sup>3,4</sup>; Ezra E. W. Cohen, MD<sup>3,4</sup>; Philip P. Connell, MD<sup>2,3</sup>; Daniel J. Haraf, MD<sup>2,3</sup>; Everett E. Vokes, MD<sup>2,3,4</sup>; Samuel Hellman, MD<sup>2</sup>; and Ralph R. Weichselbaum, MD<sup>2,3,5</sup>

Cancer 2012;118:2962-70

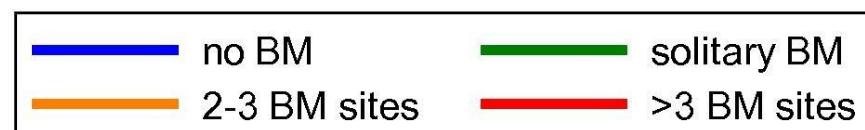


## SBRT—prognostički faktori

BROJ METASTAZA

Number at risk

1071    1052    1034    1004    961    933    877    690

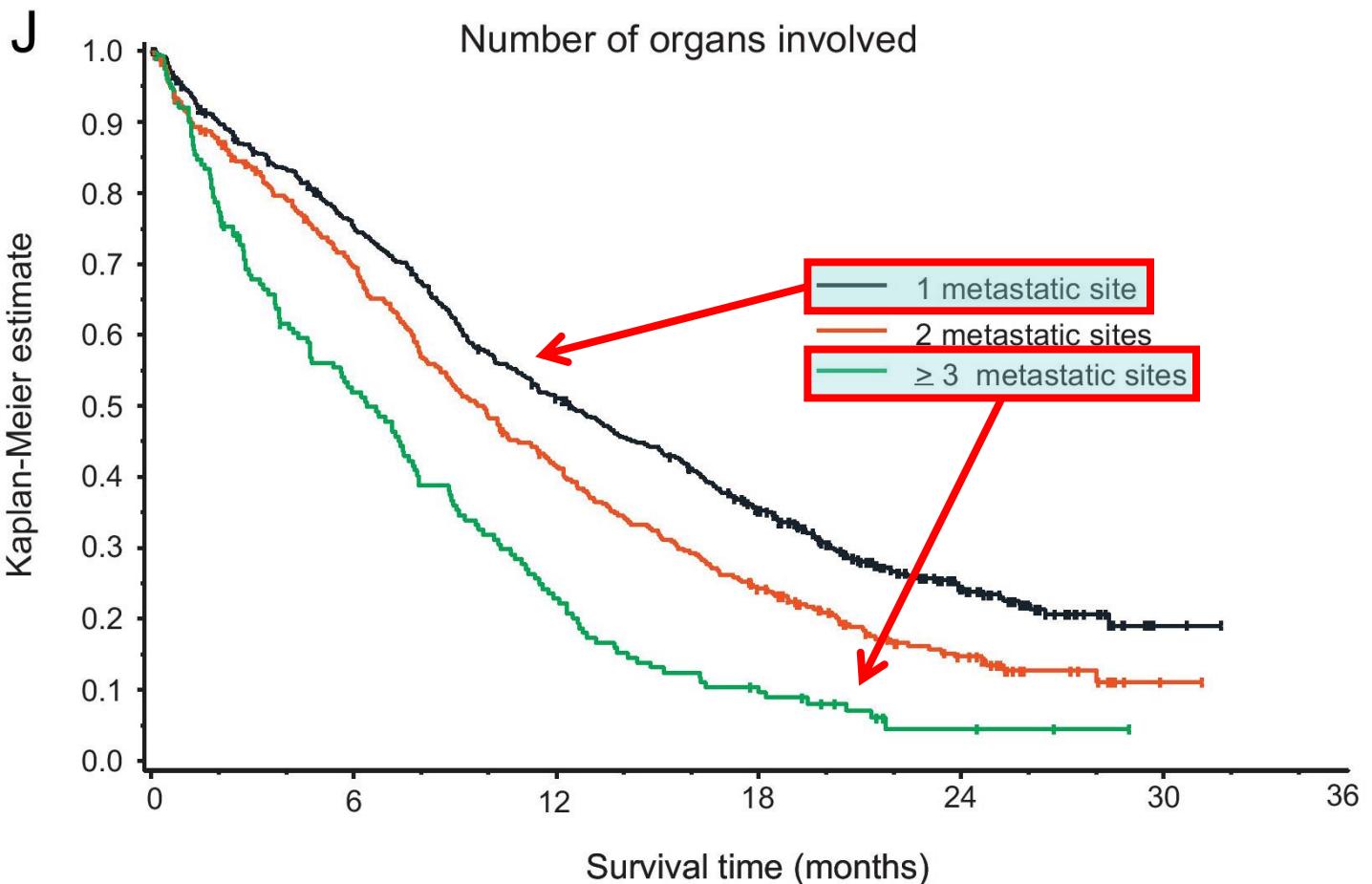


Oligometastatic bone disease in prostate cancer patients treated on the TROG 03.04 RADAR trial



Swetha Sridharan <sup>a</sup>, Allison Steigler <sup>b</sup>, Nigel A. Spry <sup>c</sup>, David Joseph <sup>c</sup>, David S. Lamb <sup>d</sup>, John H. Matthews <sup>e</sup>, Chris Atkinson <sup>f</sup>, Keen-Hun Tai <sup>g</sup>, Gillian Duchesne <sup>g</sup>, David Christie <sup>h</sup>, John Attia <sup>b,i</sup>, Elizabeth G. Holliday <sup>b,i</sup>, James W. Denham <sup>b,\*</sup>

S. Sridharan et al./Radiotherapy and Oncology 121 (2016) 98–102



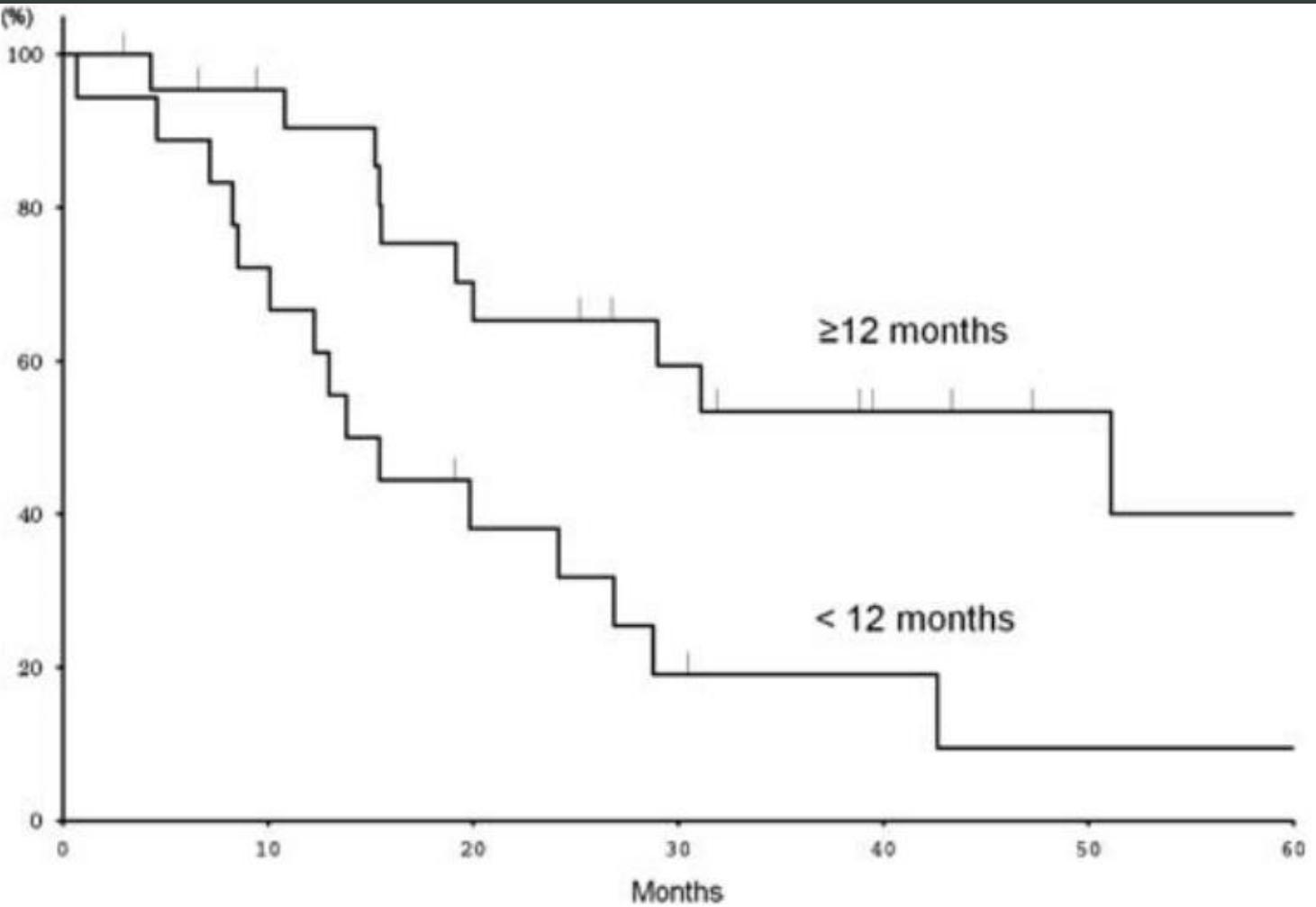
## SBRT—prognostički faktori

### BROJ METASTATSKIH MESTA

1 Prognostic factors in patients with advanced non-small cell lung cancer: Data from the phase III FLEX study  
 0

R. Pirker<sup>a,\*</sup>, J.R. Pereira<sup>b</sup>, A. Szczesna<sup>c</sup>, J. von Pawel<sup>d</sup>, M. Krzakowski<sup>e</sup>, R. Ramlau<sup>f</sup>, I. Vynnychenko<sup>g</sup>, K. Park<sup>h</sup>, W.E.E. Eberhardt<sup>i</sup>, F. de Marinis<sup>j</sup>, S. Heeger<sup>k</sup>, T. Goddemeier<sup>l</sup>, K.J. O'Byrne<sup>m</sup>, U. Gatzemeier<sup>n</sup>

R. Pirker et al. / Lung Cancer 77 (2012) 376–382



**Figure 3.** Kaplan–Meier curve of OS rates for patients with interval to recurrence of <12 months ( $n = 18$ ) and  $\geq 12$  months ( $n = 23$ ). Significant statistical difference was found ( $P = 0.006$ ) between the two groups.

## SBRT—prognostički faktori

### DISEASE FREE INTERVAL

**JJCO** Japanese Journal of Clinical Oncology

Clinical Outcomes of Stereotactic Brain and/or Body Radiotherapy for Patients with Oligometastatic Lesions

Tetsuya Inoue<sup>1,\*</sup>, Norio Katoh<sup>1</sup>, Hidefumi Aoyama<sup>1</sup>, Rikiya Onimaru<sup>1</sup>, Hiroshi Taguchi<sup>1</sup>, Shunsuke Onodera<sup>1</sup>, Satoshi Yamaguchi<sup>2</sup> and Hiroki Shirato<sup>1</sup>

*Jpn J Clin Oncol* 2010;40(8):788–794  
doi:10.1093/jjco/hyq044

Advance Access Publication 20 April 2010

**Table 3**

Multivariate analysis of survival of the total cohort.

| Covariate                         | HR (95% CI)      | p-Value |
|-----------------------------------|------------------|---------|
| <b>Performance status</b>         |                  |         |
| 0–1                               | 0.49 (0.32–0.74) | <0.001  |
| 2–3                               |                  |         |
| <b>Number of metastasis</b>       |                  |         |
| 1                                 | 0.75 (0.57–0.99) | 0.049   |
| 2–6                               |                  |         |
| <b>Size of largest metastasis</b> |                  |         |
| ≤30 mm                            | 0.53 (0.40–0.69) | <0.001  |
| >30 mm                            |                  |         |
| <b>Timing of metastasis</b>       |                  |         |
| Synchronous                       | 0.71 (0.54–0.95) | 0.02    |
| Metachronous                      |                  |         |
| <b>Pre-SBRT chemotherapy</b>      |                  |         |
| Yes                               | 0.59 (0.44–0.78) | <0.001  |
| No                                |                  |         |

## SBRT—prognostički faktori

### PROGNOSTIČKI MODEL

SBRT of oligometastases

Survival and prognostic factors in 321 patients treated with stereotactic body radiotherapy for oligo-metastases

Mette Marie Fode \*, Morten Høyer \*

M.M. Fode, M. Høyer / Radiotherapy and Oncology 114 (2015) 155–160



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## SBRT—prognostički faktori

ZAKLJUČAK

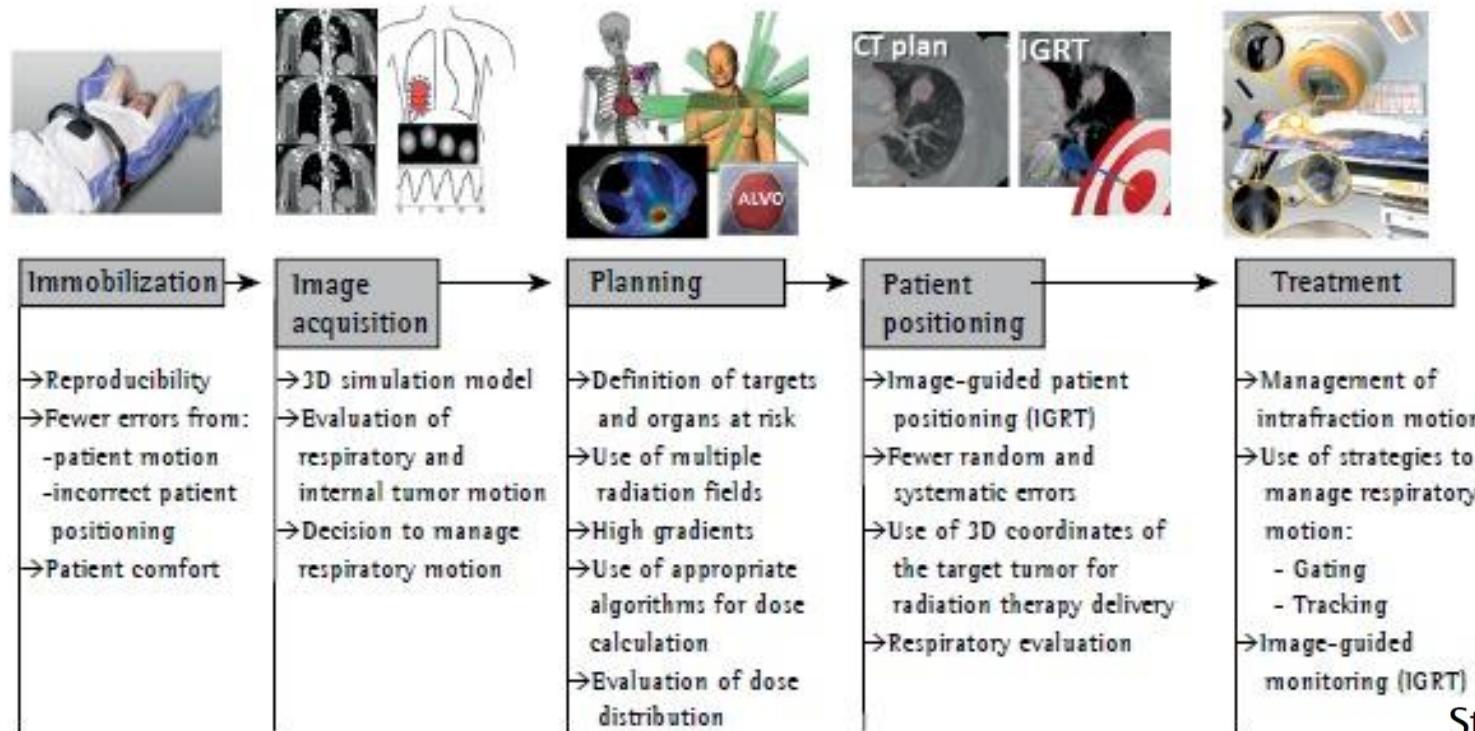
**Table 2.** Major prognostic factors for patients with oligometastatic cancers evident across multiple studies, colloquially termed the "four aces"

| Prognostic factor      | Common definitions  |
|------------------------|---|
| Young age              | Usually defined as <65 or <70, or analyzed as a continuous variable   |
| Patient fitness        | Karnofsky performance status $\geq 70$  |
| Slow-growing cancers   | Metachronous presentation of oligometastases<br>Longer disease-free interval between original tumor and development of metastases |
| Minimal disease burden | Presence of fewer metastatic sites<br>Single-organ oligometastases<br>Lack of extracranial disease                                |

### New Strategies in Stereotactic Radiotherapy for Oligometastases CME

David A. Palma, Alexander V. Louie, and George B. Rodrigues  
Clin Cancer Res; 21(23) December 1, 2015

# SBRT PROCES



## Stereotactic body radiotherapy in lung cancer: an update\*

Radioterapia estereotáxica extracraniana  
em câncer de pulmão: atualização

Carlos Eduardo Cintra Vita Abreu<sup>1</sup>, Paula Pratti Rodrigues Ferreira<sup>1</sup>,  
Fabio Ynoe de Moraes<sup>1</sup>, Wellington Furtado Pimenta Neves Jr<sup>1</sup>,  
Rafael Gadia<sup>2</sup>, Heloisa de Andrade Carvalho<sup>1,3</sup>

J Bras Pneumol. 2015;41(4):376-387



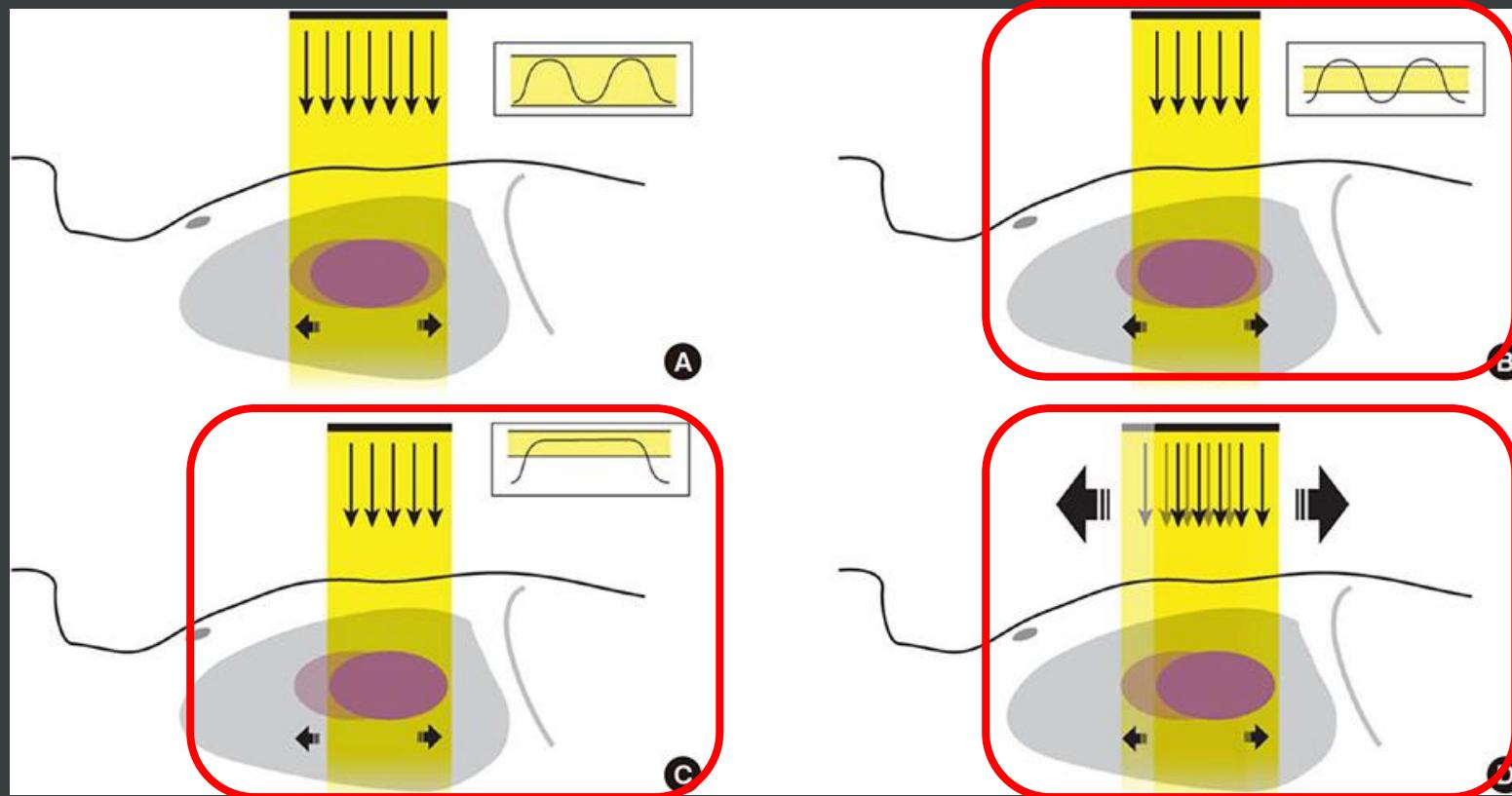
## SBRT—pozicioniranje

STEREOTAKSIČNI RAM

**The impact of abdominal compression on outcome in patients treated with stereotactic body radiotherapy for primary lung cancer**

Wambaka Ange MAMPUYA, Yukinori MATSUO\*, Nami UEKI, Mitsuhiro NAKAMURA,  
Nobutaka MUKUMOTO, Akira NAKAMURA, Yusuke IIZUKA, Takahiro KISHI,  
Takashi MIZOWAKI and Masahiro HIRAKAWA

**Journal of Radiation Research, 2014, 55, 934–939**



## SBRT—imidžing

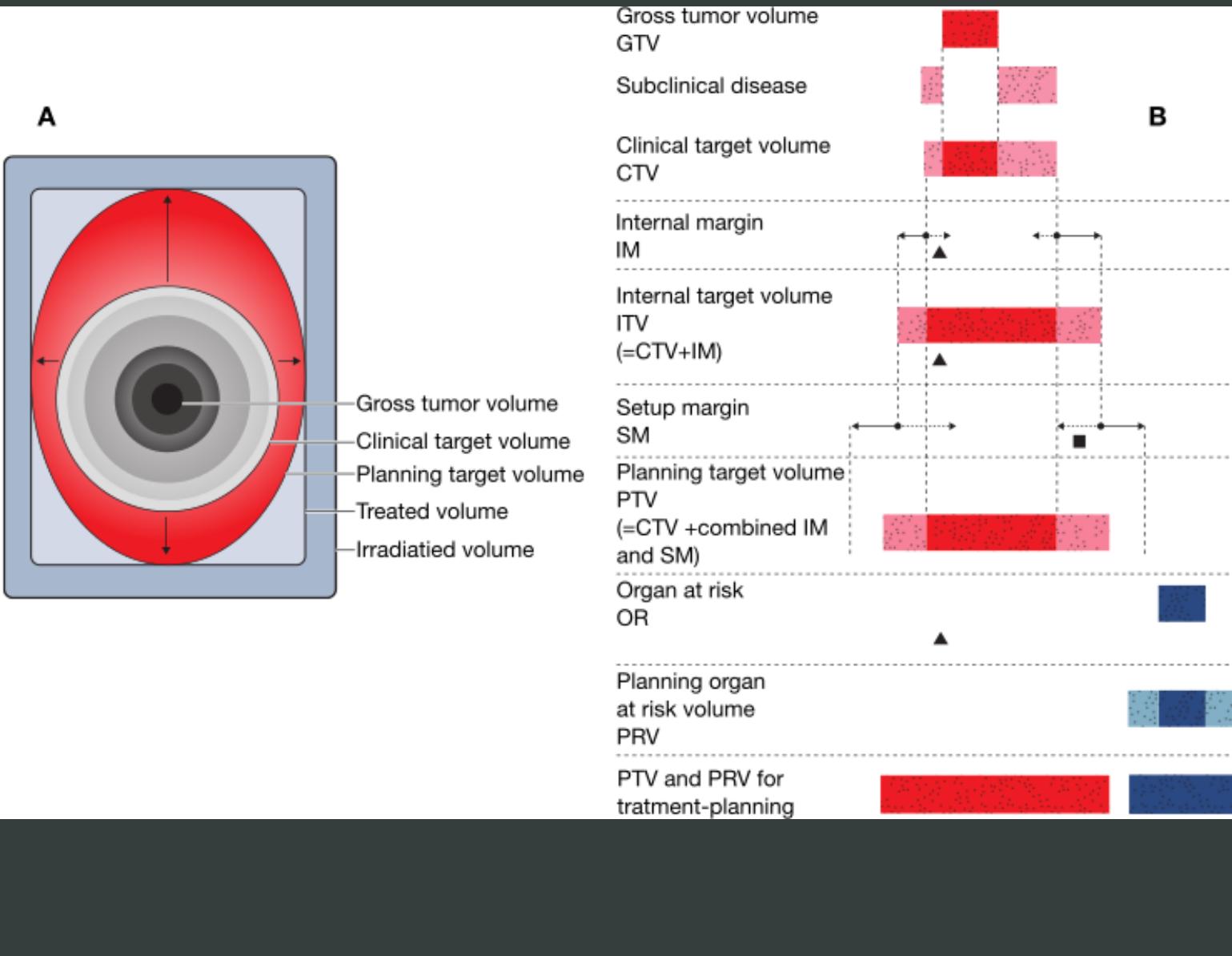
### PROBLEM POMERANJA TUMORA

- GATING
- TRACKING
- DAMPENING

Evolving Clinical Cancer Radiotherapy: Concerns Regarding Normal Tissue Protection and Quality Assurance

Won Hoon Choi and Jaeho Cho

*J Korean Med Sci 2016; 31: S75-87*

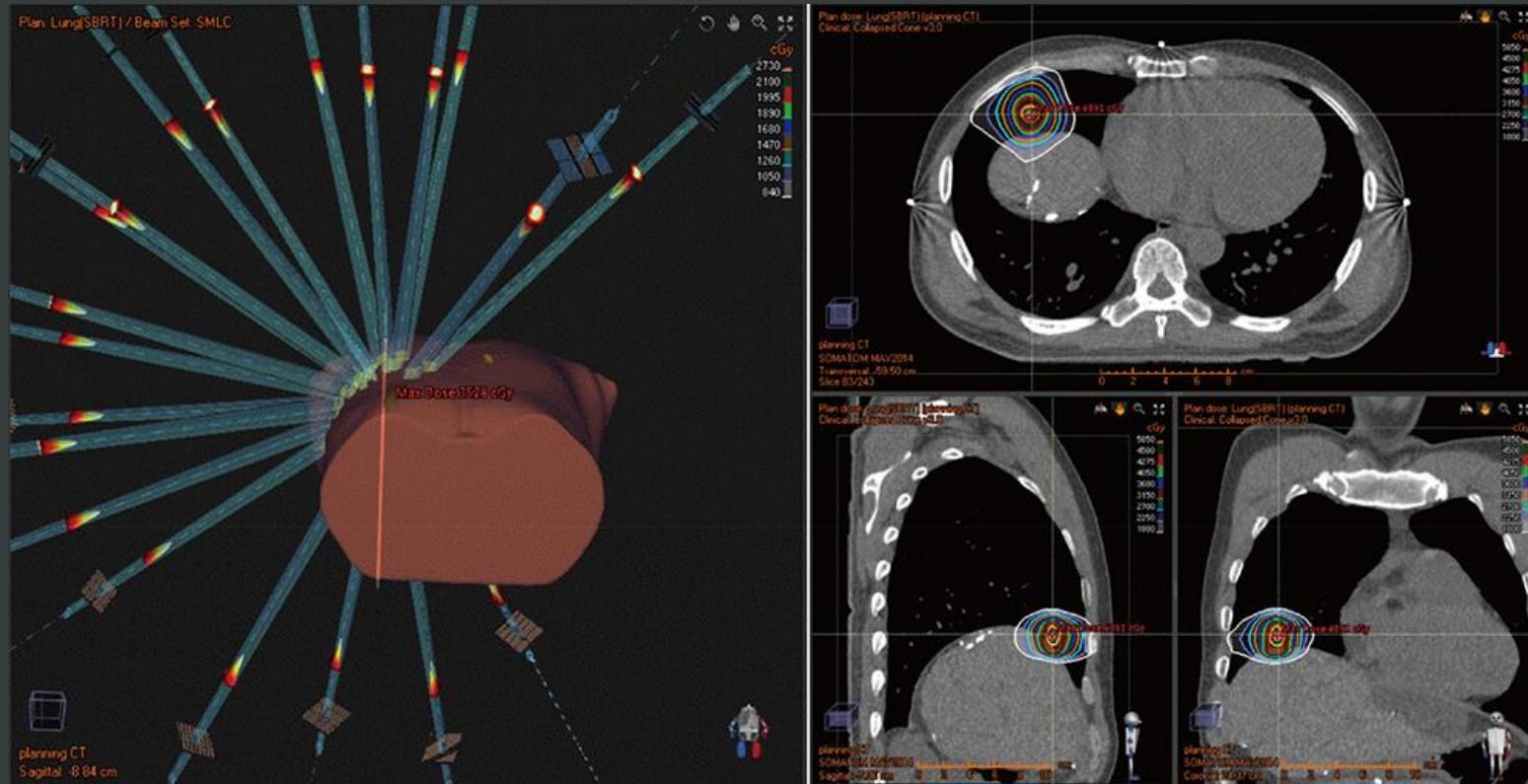


## SBRT—delineacija

- ICRU 50 i 62
- $\text{GTV} \approx \text{CTV}$
- ITV
- PTV

KHAN'S

# Treatment Planning in Radiation Oncology



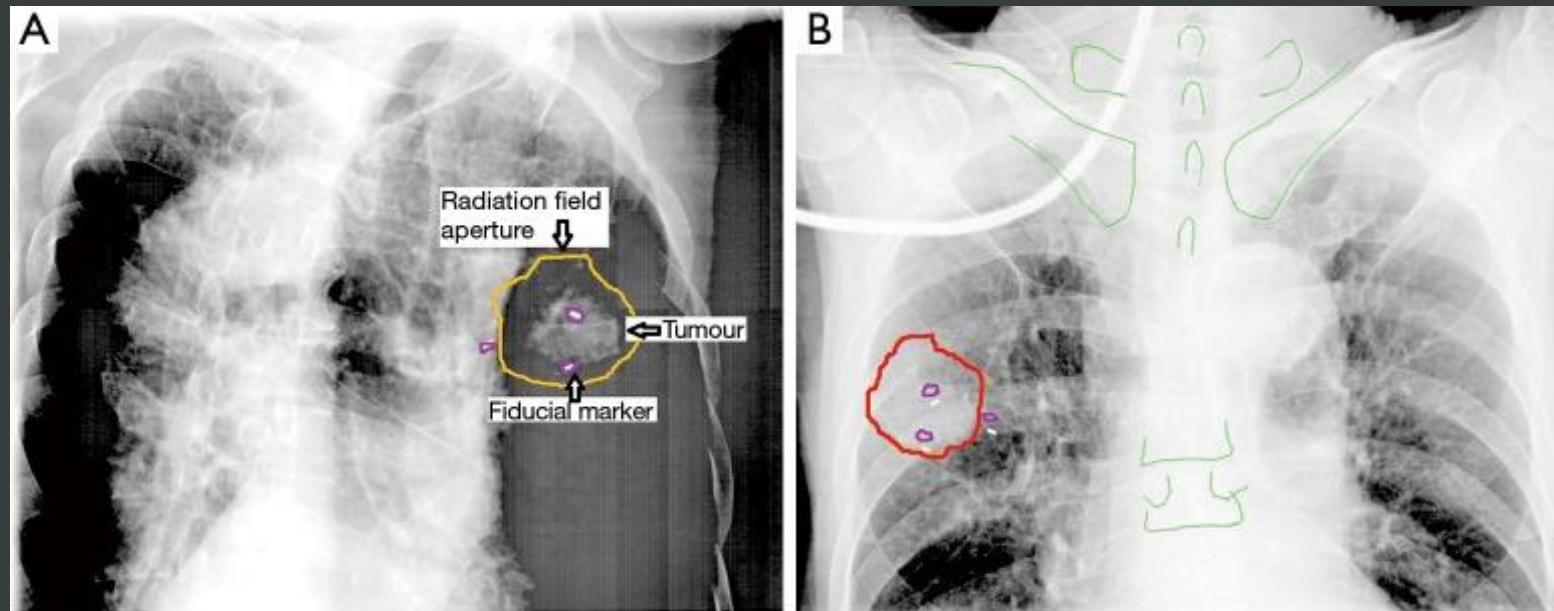
## SBRT—aranžman polja

- VEĆI BROJ POLJA
- NEKOPLANARNA
- BRZ PAD DOZE

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*J Korean Med Sci 2016; 31: S75-87*



## SBRT—tretman

- POZICIONIRANJE NA APARATU
- PROVERA I KOREKCIJA POZICIJE

**Stereotactic body radiotherapy: current strategies and future development**

Maverick W. K. Tsang

*J Thorac Dis* 2016;8(Suppl 6):S517-S527

# Oligometastaze—zaključak

- ograničen metastatski kapacitet
- karakteristika mnogih tumora
- benefit od lokalne terapije
- pravilna selekcija pacijenata
- SBRT
- ISTRAŽIVANJA!



# Hvala na pažnji!