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UNIVERSITÀ DEGLI STUDI DI PERUGIA

Regione Umbria

AZIENDA OSPEDALIERA SANTA MARIA TERNI

ROPI
RETE ONCOLOGICA PAZIENTI ITALIA

LE GIORNATE SCIENTIFICHE - 1ª edizione

LA SALUTE DELL'OSSO

Dalla letteratura scientifica, alle linee guida, ai modelli gestionali per il paziente oncologico

9-10 settembre 2022

ROMA - Hotel Quirinale
Via Nazionale 7

Metastasi ossee: ruolo del radioterapista

Ernesto Maranzano
Prof. Straordinario Radioterapia
Università degli Studi Perugia

Radiotherapy symptoms control in bone metastases

Pain

The most common complaint in patients with bone metastases are pain and/or impaired mobility

Bone metastases:

HOW RADIOTHERAPY WORKS

- **Pain-relieving effect *by***
  - → *direct cytocide effect and reduction of tumor burden, or*
    - → *diminution of the activation of osteoblasts*
  - → *modulation of pain mediators,*
  - → *disruption of neurons involved in the transmission of pain*

- **Pathological fractures prevention *by***
  - → *bone recalcification*

- **Prevention and treatment of spinal cord/ radicular compression *by***
  - → *stopping/slowing the tumor grow into the spinal cord*

Which radiotherapy is best in bone metastases?

- ✓ *Conventional RT (3D-CRT) or*
- ✓ *Stereotactic Ablative Body RT (SABR or SBRT)*

3D-CRT

Review Article

Advances in radiotherapy in bone metastases in the context of new target therapies and ablative alternatives: A critical review

André G. Gouveia [a,b], Dominic C.W. Chan [c], Peter J. Hoskin [d,e], Gustavo N. Marta [b,f], Fabio Trippa [g], Ernesto Maranzano [g], Edward Chow [h], Mauricio F. Silva [b,i,j,*]

Radiotherapy and Oncology 163 (2021) 55–67

Uncomplicated BM *(~2/3)*

Despite guidelines on using 8 single-dose RT in uncomplicated BM, its use remains relatively low. In uncomplicated BM, single-fraction RT produces similar overall and complete response rates to RT with multiple fractions, although it is associated with a higher retreatment rate of 20% versus 8%.

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impending or existing pathologic fracture
a major soft tissue component
spinal cord or cauda equina compression
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Clinical Oncology
Volume 24, Issue 2, March 2012, Pages 112–124
2012

Update on the Systematic Review of Palliative Radiotherapy Trials for Bone Metastases

E. Chow[I], L. Zeng[I], N. Salvo[I], K. Dennis[I], M. Tsao[I], S. Lutz[†]

- **25** randomized trials
- **5617** patients
- **Overall response rate:**
  - **60%** (1696/2818) in single fraction arms
  - **61%** (1711/2799) in multiple fraction arms
- **Complete response rate:**
  - **23%** (620/2641) in single fraction arms
  - **24%** (634/2622) in multiple fraction arms

The only thru difference: higher re-treatment rates in single fraction RT

Contemporary Practice Patterns for Palliative Radiation Therapy of Bone Metastases: Impact of a Quality Improvement Project on Extended Fractionation

Elizabeth M. Jaworski, MD, MS,[a] Huiying Yin, MS, MA,[a] Kent A. Griffith,

Michigan *Radiation Oncology Quality Consortium*

Practical Radiation Oncology® (2021) **11**, e498–e505

practical radiation oncology pro

www.practicalradonc.org

Table 1 Clinical, facility, and physician characteristics

Clinical characteristics at plan level	All; n (%)*	Plans ≤ 10 fractions; n (%)*	Plans > 10 fractions (EF); n (%)*
n	1934	1868	66
Anatomic site treated			
Spine	881 (46%)	854 (46%)	27 (41%)
Hip/pelvis	360 (19%)	349 (19%)	11 (17%)

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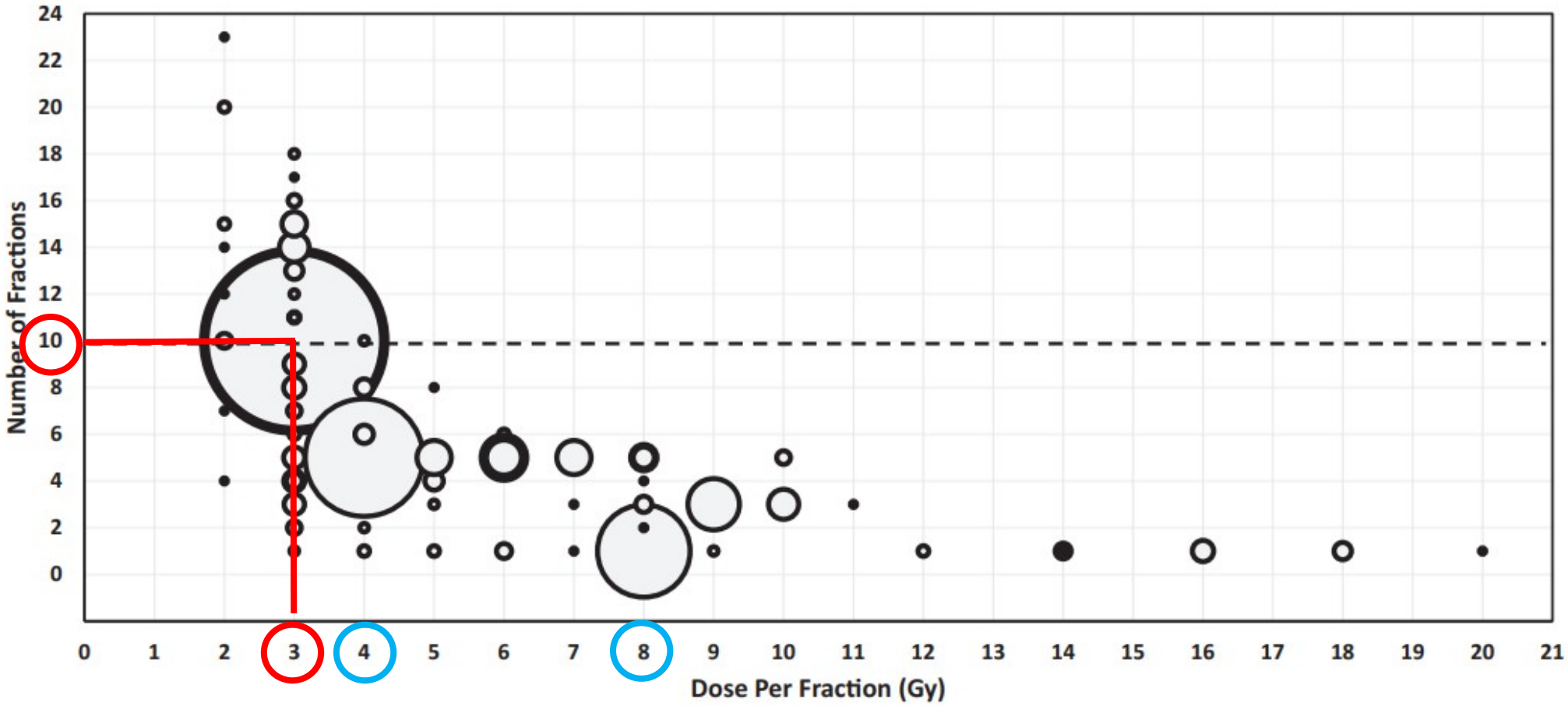

Fig. 1 Heterogeneity in fractionation by plan. Bubble plot of 1934 plans delivered using 60 different fractionation schemes. Circle size corresponds to the relative frequency of use for each fractionation scheme. Circles centered above the dashed line represent plans using extended fractionation.

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- ***A major soft tissue component***
- ***Neuropathic pain***

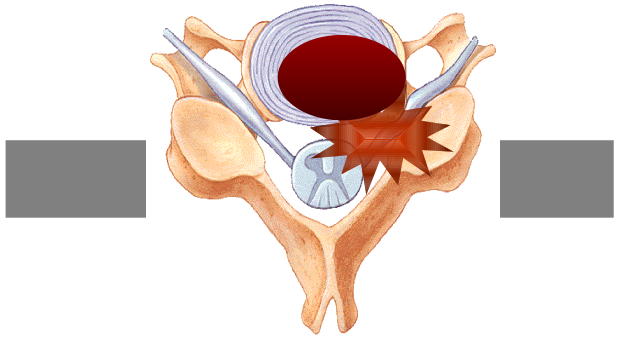
Metastatic spinal cord compression (MSCC)

Definition

The Princess Margaret Hospital of Toronto, Canada, definition:

*"Compression of the dural sac and its contents (*spinal cord and/or cauda equina*) by an* **extradural tumor mass**. *The minimum radiologic evidence for cord compression is* **indentation of the theca at the level of clinical features**. *Clinical features include any or all of the following:* **pain** *(local or radicular),* **weakness**, **sensory disturbance**, *and/or evidence of* **sphincter dysfunction***".*

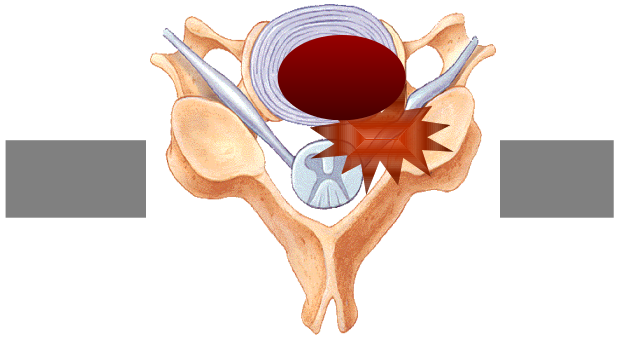
Loblaw, JCO '98



Metastatic spinal cord compression (MSCC)

Prognostic factors

- **EARLY DIAGNOSIS**
- **EARLY THERAPY** ***(within 24/48 h from radiologic diagnosis)***



Roy A Patchell,

Lancet 2005; 366: 643–48

Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial

Interpretation

Direct decompressive **surgery is superior to RT alone** for pts with spinal cord compression caused by metastatic cancer

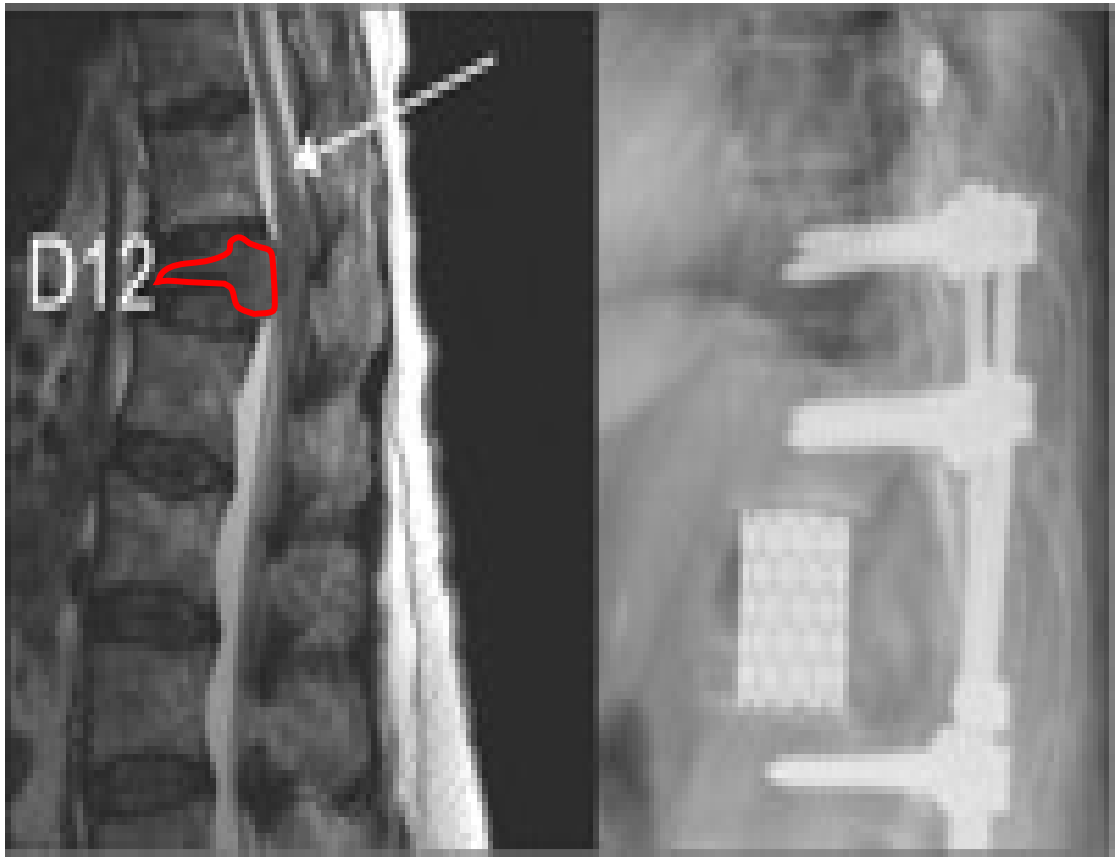
Surgery + RT *vs.* RT alone (cont.)

Patchel's randomized trial → **Surgery is more effective**

SURGICAL APPROACH AND PATIENT SELECTION

Tailored surgery!

1. **posterior, anterior, and/or lateral approach**
2. **plus stabilization of the spine (i.e., no laminectomy)**



Surgery + RT *vs.* RT alone (cont.)

Patchel's randomized trial → **Surgery is more effective**

SURGICAL APPROACH AND PATIENT SELECTION

Selected patients!

1. **Single site**
2. **Good medical status**
3. **Histology not lymphoma or myeloma**
4. **Absence of paraplegia**
5. **Expected survival > 3 months**

Surgery + RT *vs.* RT alone (cont.)

Patchel's randomized trial → **Surgery is more effective**

…….. *CRITICISMS*:

- Recruitment lasted > 10 years! **(in 7 USA Hospitals: 1, 1, 1, 2, 12, 14 e 70 patients, respectively)**
- Not all eligible patients were entered into the study **(high probability of selection bias)**
- 101 valuable patients of 123 recruited! **(18% cases not valuable)**
- 37% patients who underwent RT alone had a spinal instability (**condition in which surgery is considered mandatory)**

JOURNAL OF CLINICAL ONCOLOGY VOLUME 23 · NUMBER 32 · NOVEMBER 10 2005

Radiotherapy Alone or Surgery in Spinal Cord Compression? The Choice Depends on Accurate Patient Selection

Ernesto Maranzano
Radiation Oncology Center, Azienda Ospedaliera, Terni, Italy

Selection criteria for surgery

- good PS and an expected survival of at least 6 months,
- spinal cord compression restricted to a single area,
- non-radiosensitive tumors,
- diagnostic doubts,
- spinal instability,
- bony compression causing spinal cord compression.

About 10% of cases

JOURNAL OF CLINICAL ONCOLOGY | VOLUME 23 · NUMBER 15 · MAY 2005

Short-Course Versus Split-Course Radiotherapy in Metastatic Spinal Cord Compression: Results of a Phase III, Randomized, Multicenter Trial

E. Maranzano et al

Contents lists available at ScienceDirect

Radiotherapy and Oncology 2009

journal homepage: www.thegreenjournal.com

Phase III randomised trial

8 Gy single-dose radiotherapy is effective in metastatic spinal cord compression: Results of a phase III randomized multicentre Italian trial

Ernesto Maranzano [a,*], Fabio Trippa [a], Michelina Casale [a], Sara Costantini [a], Marco Lupattelli [b], Rita Bellavita [b], Luigi Marafioti [c], Stefano Pergolizzi [d], Anna Santacaterina [d], Marcello Mignogna [e], Giovanni Silvano [f], Vincenzo Fusco [g]

TREATMENT SCHEDULES OF RADIOTHERAPY

There are 2 published RCTs (both by the RT Italian Group):

1. short course (8 Gy x 2) *vs.* split-course (30 Gy in 8 fraction) RT
2. short course (8 Gy x 2) *vs.* single fraction (8 Gy) RT

No difference in outcome and toxicity

Results after Radiotherapy
in metastatic spinal cord compression (MSCC)

- **Back pain relief**: 5O-58% (30-35% complete response)

- **Walking capacity**
  - function maintained: 85-90%
  - function recovered: from paresis: 30-35%
    from plegia: 0-10%
- **Bladder function**
  - function maintained: 85-90%
  - function recovered: 10-15%

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Hypofractionated radiotherapy for complicated bone metastases in patients with poor performance status: a phase II international trial

TJ ISSN 0300-8916 | 2017

Mauricio F. Silva[1,2], Gustavo N. Marta[3,4], Felipe P.C. Lisboa[2], Guilherme Watte[5], Fabio Trippa[6], Ernesto Maranzano[6], Neiro W. da Motta[2], Marko Popovic[7], Tuan Ha[8], Bryan Burmeister[9], Edward Chow[7]

Safety & efficacy of hypofractionated RT (2x8Gy) were evaluated in **50** pts with complicated bone metastases

Pain control:

- 12.5% of CR
- 37.5 of PR

} 50% of responders

TABLE I - Baseline characteristics

	No. (%) or median (range) (n = 50)
Sex	
Male	23 (46)
Female	27 (54)
Age, y	58 (26-86)
Type of complicated bone metastases (mixed features can be present)	
Soft tissue component	38 (76)
Postsurgery	18 (36)
Neuropathic pain	3 (6)
Risk of fracture with contraindication to surgery	3 (6)
Primary tumor	
Breast	14 (28)
Lung	9 (18)
Prostate	8 (16)
Other[a]	19 (38)
Place of radiation	
Spine	29 (58)
Pelvis	11 (22)
Ribs	4 (8)
Other[b]	6 (12)

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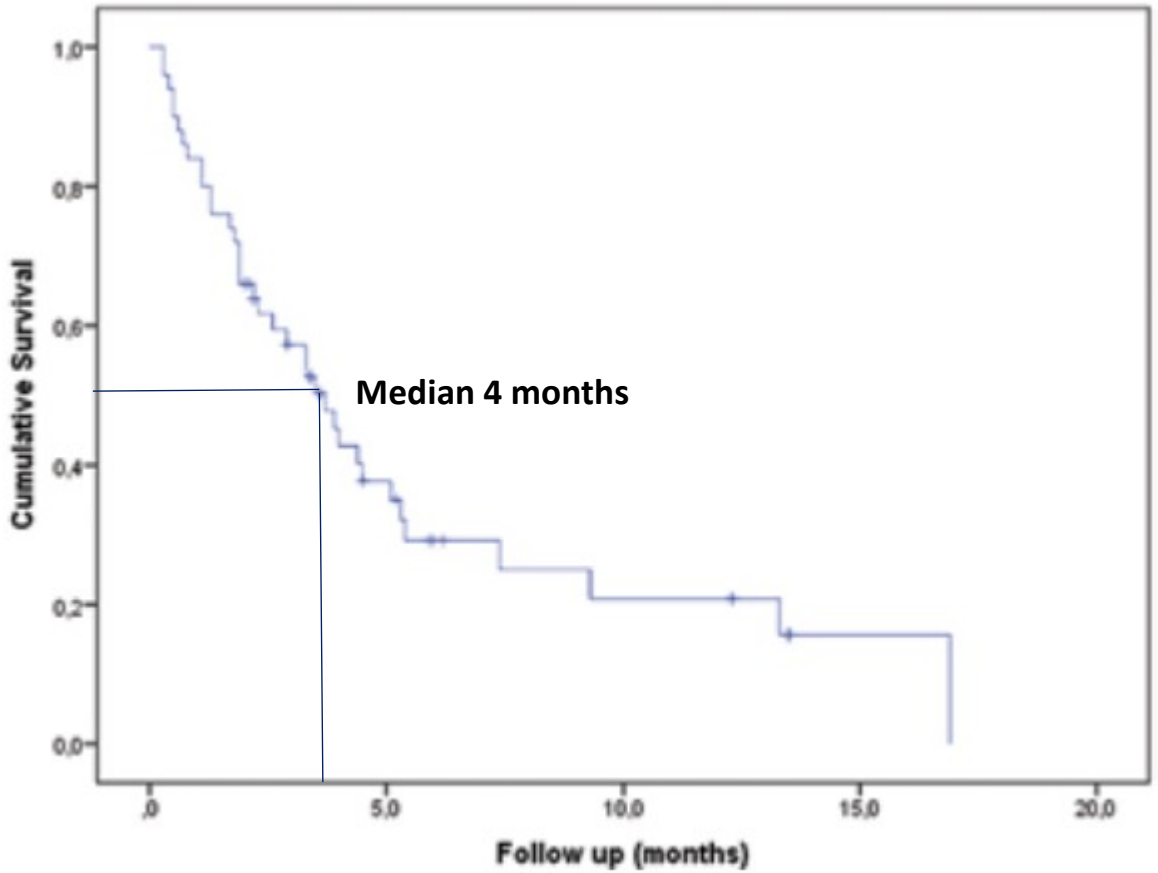

Fig. 1 - Overall survival at 2, 6, and 12 months.

TABLE III - Analysis of the QLQ-BM22 and QLQ-C15-PAL scales: baseline and 2-month follow-up

Scale	Baseline (n = 50)	2nd month (n = 21)	p value
QLQ-BM22			
Painful sites	52.2 ± 23.9	65.9 ± 25.9	0.109
Painful characteristics	47.0 ± 22.3	59.6 ± 23.5	0.145
Functional interference	37.6 ± 25.9	57.7 ± 25.2	0.010
Psychosocial aspects	45.2 ± 22.2	57.4 ± 24.4	0.033

RE-IRRADIATION of Bone Metastases

Contemporary Practice Patterns for Palliative Radiation Therapy of Bone Metastases: Impact of a Quality Improvement Project on Extended Fractionation

Elizabeth M. Jaworski, MD, MS,[a] Huiying Yin, MS, MA,[a] Kent A. Griffith,

Practical Radiation Oncology® (2021) **11**, e498–e505

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n	1934	1868	66
Retreatment			
Yes	172 (9%)	164 (9%)	8 (12%)
No	1762 (91%)	1704 (91%)	58 (88%)

Re-irradiation for painful bone metastases – A systematic review

Erin Wong [a], Peter Hoskin [b], Gillian Bedard [a], Michael Poon [a], Liang Zeng [a], Henry Lam

Radiotherapy and Oncology 110 (2014) 61–70

- Systematic review on conventional external beam palliative re-irradiation

- Reluctance from radiation oncologists to prescribe re-irradiation

- ***Three possible scenarios***:

(1) no pain relief after first time radiation

(2) partial response to first time radiation and those in whom a better response is desired

(3) pain relapse after either partial or complete response to the first time radiation.

- Evaluable population: **645** patients in 15 studies

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Radiotherapy and Oncology 110 (2014) 61–70

- **OR** rate was **68%** (**20% of CR**)
- **No** serious **complications**
- Although both previous responders and non-responder can improve with a re-irradiation, responders have a higher probability to benefit from re-irradiation
- Same efficacy with single and multiple fractions re-irradiation
- Generally primary cancer site was not associated with response to retreatment. Only in the Dutch trial, prostate cancer pts were found to have the lowest response rate to re-irradiation and breast cancer pts the highest
- Patient factors associated with re-irradiation response:
  - a single area of bone metastasis,
  - a high PS,
  - ≥ 4 months between initial treatment and retreatment

Which radiotherapy is best in bone metastases?

- ✓ *Conventional RT (3D-CRT) or*
- ✓ ***Stereotactic Ablative Body RT (SABR or SBRT)***

Radiosurgery (SABR/ SBRT)
&
Oligometastases

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*

OLIGOMETASTASES

Definition

An intermediate state of cancer spread between localized disease and wide spread mets

the implication is that oligometastatic disease may be cured with metastasis-directed therapy

VOLUME 31 · NUMBER 11 · APRIL 10 2013

JOURNAL OF CLINICAL ONCOLOGY

(SBRT)

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

OLIGOMETASTASES

Stereotactic Body Radiotherapy (SBRT)

Published studies on Radiotherapy and Oligometastases by year

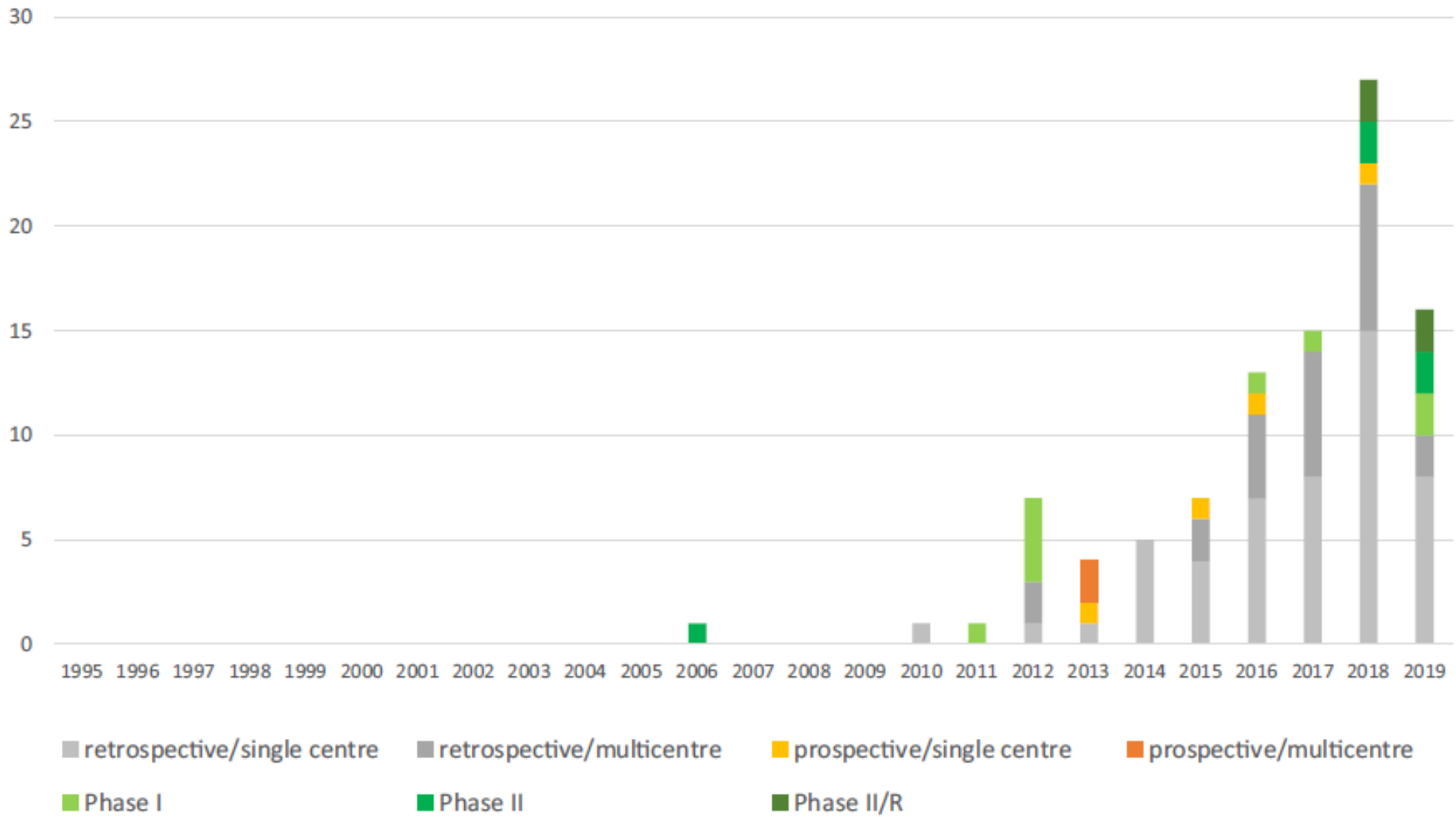

Fig. 1. Number of publications per year and per type, selected in both SLR searches, since the publication of Hellman and Weichselbaum in 1995 [6]. Note: Reports on interim results were not included.

How to define oligometastatic disease?

SunKrist Publishing
Accelerate Scientific Knowledge in Open Access

Universal Journal of Radiology and Nuclear Medicine

Commentary *Volume: 2, Issue: 1* *Scientific Knowledge*

Oligometastatic Disease and Metastasis-Directed Radiotherapy: A Partnership for an Innovative Palliative Approach

Ernesto Maranzano*[1,2], Fabio Trippa[1], Paola Anselmo[1], Fabio Arcidiacono[1], Stefano Pergolizzi[3,4]

[1]Radiotherapy Oncology Centre, "S. Maria" Hospital, Terni, Italy

[2]Full Professor in Radiation Oncology, Department of Medicine and Surgery, University of Perugia, Perugia, Italy

[3]Department of Biomedical, Dental Science and Morphological and Functional Images, University of Messina, Messina, Italy

[4]Radiation Oncology Unit, Azienda Ospedaliera Universitaria, University Hospital Policlinico "G. Martino", Messina, Italy

As in the Virgilio's poetry verse (***fama vires acquirit eundo***) regarding the fame which grows the more it walks (i.e., it spreads), also the ***partnership between Oligometastatic Disease and Metastasis-Directed Radiotherapy can grow over time*** as an innovative approach for cancer patient palliation

How to define oligometastatic disease?

Radiotherapy and Oncology 148 (2020) 157–166

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Original Article

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ESTRO-EORTC

Characterisation and classification of oligometastatic disease: a European Society for Radiotherapy and Oncology and European Organisation for Research and Treatment of Cancer consensus recommendation

Lancet Oncol 2020; 21: e18–28

Matthias Guckenberger, Yolande Lievens, Angelique B Bouma, Laurence Collette, Andre Dekker, Nandita M deSouza, Anne-Marie C Dingemans, Beatrice Fournier, Coen Hurkmans, Frédéric E Lecouvet, Icro Meattini, Alejandra Méndez Romero, Umberto Ricardi, Nicola S Russell, Daniel H Schanne, Marta Scorsetti, Bertrand Tombal, Dirk Verellen, Christine Verfaillie, Piet Ost

- "Oligometastatic" disease (OMD) has been proposed as an intermediate state between localised and widespread systemic disease

- In OMD patients with different tumor types/histologies, early published studies show improved clinical outcome with radical local therapy as surgery or **metastasis-directed radiotherapy** (**MDRT**)

- Unfortunately, neither OMD specific biomarkers nor prospectively validated prognostic scoring systems yet exist so it remains impossible to identify patients with truly limited metastatic capacity, who might really benefit from such a radical approach.

- The current definition of oligometastatic status is based solely on the number of metastases and number of involved organs on high resolution imaging findings and PET/CT, contrast enhanced chest/abdominal and pelvis CT scans, and/or MRI of brain or spine are necessary for case by case diagnostic evaluation

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Regarding definition of OMD with respect to the ***INTERVAL*** between primary cancer diagnosis and development of OMD, the panel suggested following classification:

"Synchronous" OMD arises at the time of initial diagnosis, that is, primary tumor and limited number of metastases are detected simultaneously.

"Metachronous" OMD or "oligorecurrence" occur during the course of disease at least 3 (6?) months after the initial diagnosis, in other words, metastases detected while the primary tumor is controlled and that can be treated with directed local therapy. A metachronous OMD can be:

"Oligoprogression"

"Oligopersistence"

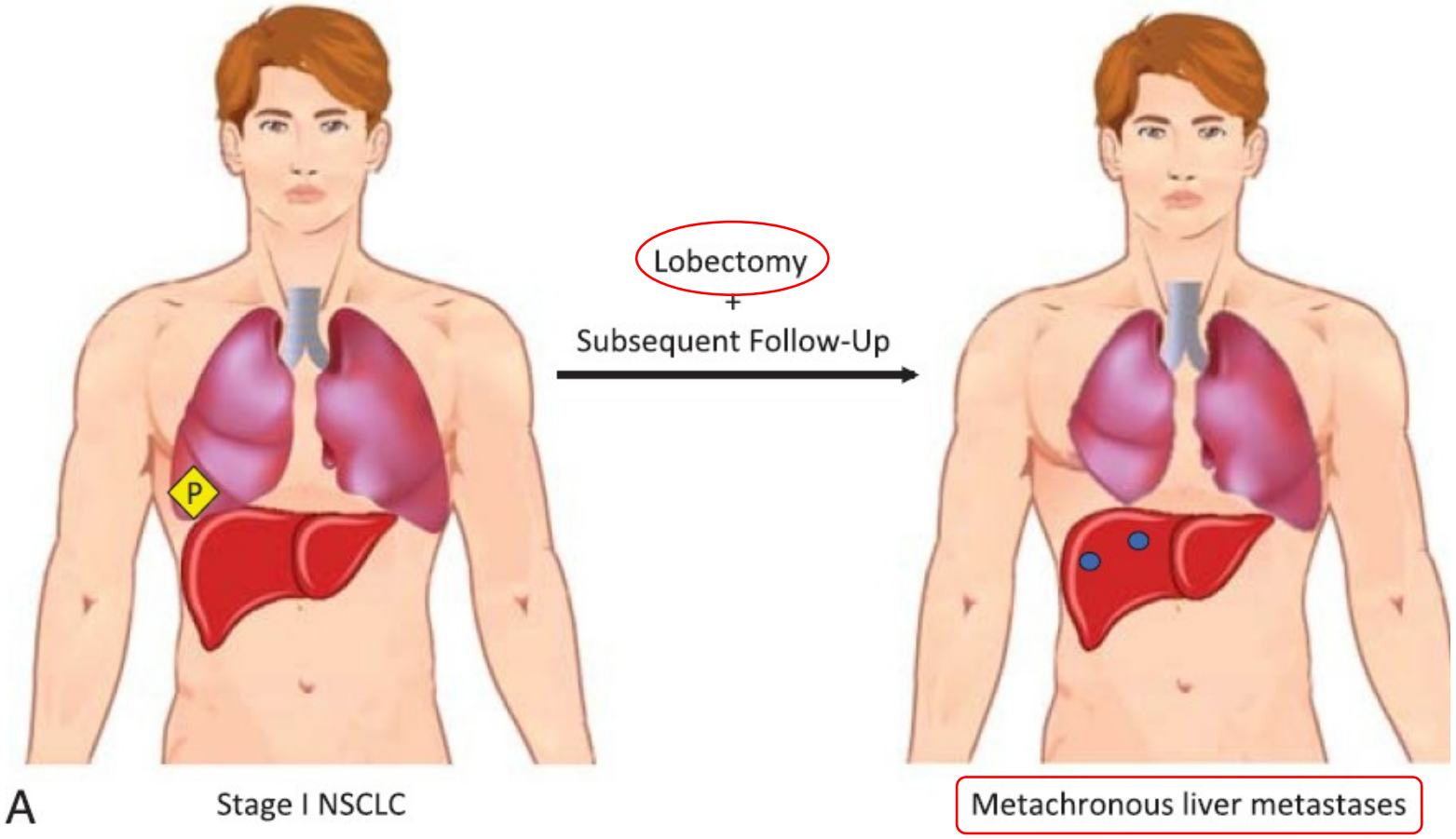
Stereotactic Body Radiotherapy for Oligometastasis

Opportunities for Biology to Guide Clinical Management

(*Cancer J* 2016;22: 247–256)

Rohann J.M. Correa, MD, PhD, Joseph K. Salama, MD,†*
*Michael T. Milano, MD, PhD,‡ and David A. Palma, MD, MSc, PhD, FRCPC**

Oligoprogression → oligometastasis in the setting of a <u>controlled primary tumor</u>



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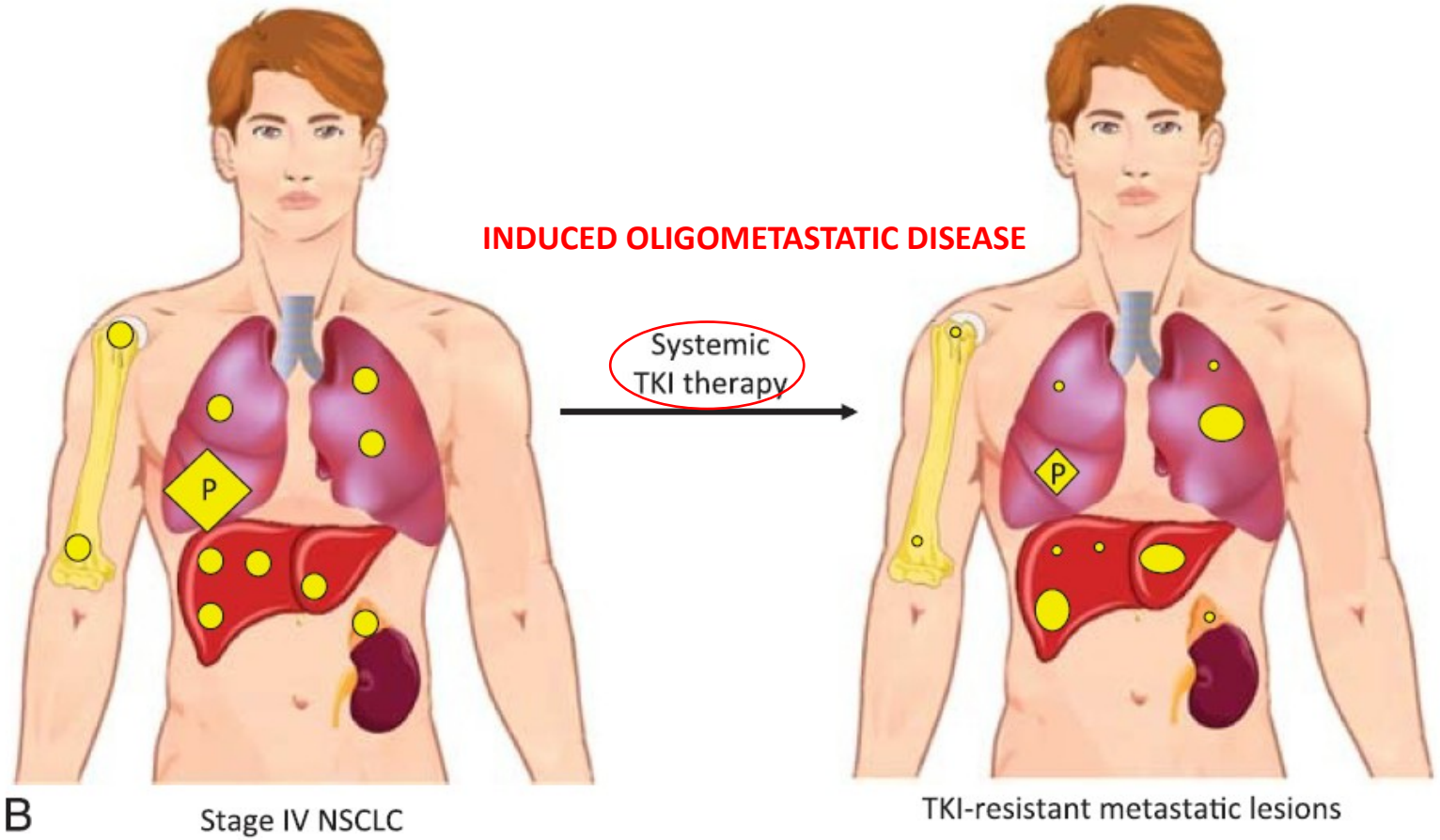
(*Cancer J* 2016;22: 247–256)

Rohann J.M. Correa, MD, PhD, Joseph K. Salama, MD,†*
*Michael T. Milano, MD, PhD,‡ and David A. Palma, MD, MSc, PhD, FRCPC**

Oligopersistence → oligometastasis in the setting where a <u>few metastases progress on **systemic therapy**</u> while the majority are stable



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- The metastasis-directed radiotherapy- MDRT is generally administered with 3 to 5 fractions of high-dose stereotactic body radiotherapy (**SBRT/SABR**) or with high single dose (e.g., brain radiosurgery - **SRS**).

- Both SBRT and SRS allow to administer a so called ablative external beam doses to the tumor sparing the surrounding healthy tissues by a rapid fall of dose outside the target.

- The "***ablative effect***" associated to the high-dose of radiation delivered (at least **8-10Gy**) overcome the possible intrinsic few tumor cell radiosensitivity because ablates tumor directly and induces indirect effects, including vascular endothelial injury and immune activation.

- This approach is performed with the help of high resolution image-guided procedures which can either visualize and locate the target itself and anatomical structures that are closely correlated to the target.

- There are various possible modalities to give this special radiotherapy technique with most of the available modern radiotherapy machines

HyTEC Biology

Biological Principles of Stereotactic Body Radiation Therapy (SBRT) and Stereotactic Radiation Surgery (SRS): Indirect Cell Death

Chang W. Song, PhD,* Eli Glatstein, MD,† Lawrence B. Marks, MD,‡
Bahman Emami, MD,§ Jimm Grimm, PhD,‖ Paul W. Sperduto, MD,¶
Mi-Sook Kim, MD, PhD,# Susanta Hui, PhD,*
Kathryn E. Dusenbery, MD,* and L. Chinsoo Cho, MD*

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

Vol. 110, No. 1, pp. 21e34, 2021

- Irradiation with ≥ **10 Gy/fraction** causes significant ***vascular injury*** in tumors, leading to ***Secondary tumor cell death*** (***radio-ablation***)
- Irradiation with ≥ **10 Gy/fraction** has also been reported to ***increase the antitumor immunity*** (***Abscopal & Bystander effects***)
- The mechanism of normal tissue damage by high-dose irradiation needs to be further investigated.

HyTEC = Hypofractionated Treatment Effects in the Clinic

- There was a total agreement between experts on the concept that MDRT of OMD is **independent** of primary tumor type, histology and metastatic site.

- Diagnostic imaging (such as **CT** scan, **MRI**, **PET/CT**) should be performed using whichever modalities are most adequate to image sites of common metastases and to detect small lesions for that histology.

- The maximal **number** of metastases, the maximal lesion **size** and number of involved **organs** to consider a patient oligometastatic are yet ***unknown***. However, the consensus agreed that ***5 lesions***, a maximum cut-off ***size of 5 cm*** and ***single/limited number of organs*** should be considered an upper bound off-protocol.

- The metastasis-directed radiotherapy- MDRT is generally administered with 3 to 5 fractions of high-dose stereotactic body radiotherapy (**SBRT/SABR**) or with high single dose brain radiosurgery (**SRS**).

- Both SBRT and SRS allow to administer a so called ablative external beam doses to the tumor sparing the surrounding healthy tissues by a rapid fall of dose outside the target.

- The "ablative effect" associated to the high-dose of radiation delivered (at least 8-10Gy) overcome the possible intrinsic few tumor cell radiosensitivity because ablates tumor directly and induces indirect effects, including vascular endothelial injury and immune activation.

- This approach is performed with the help of high resolution ***image-guided procedures*** which can either visualize and locate the target itself and anatomical structures that are closely correlated to the target.

- There are various possible modalities to give this special radiotherapy technique with most of the available modern radiotherapy machines

Image-guided RT-IGRT: *micro multi-leaf collimators &* ***cone beam CT***

SBRT for SPINE

Stereotactic Ablative Radiotherapy for the Management of Spinal Metastases

A Review

JAMA Oncol. doi:10.1001/jamaoncol.2019.5351
Published online January 2, 2020.

Rachel M. Glicksman, MD; Michael C. Tjong, MD; Wellington F. P. Neves-Junior, BSc; Daniel E. Spratt,

- 51 publications with **5655 pts** who underwent SABR for spinal metastases included
- Spinal SABR was associated with **1-year local control rates** by settings of:
  - ~ ***80%*** to 90% in the de novo
  - > ***80%*** in the postoperative
    - > ***65%*** in the reirradiation
- The most commonly discussed adverse effect was development of a vertebral compression fracture with variable rates, most commonly reported as approximately 10% to 15%.

Clinical Trial > Lancet Oncol. 2021 Jul;22(7):1023-1033. doi: 10.1016/S1470-2045(21)00196-0.
Epub 2021 Jun 11.

Stereotactic body radiotherapy versus conventional external beam radiotherapy in patients with painful spinal metastases: an open-label, multicentre, randomised, controlled, phase 2/3 trial

Arjun Sahgal [1], Sten D Myrehaug [2], Shankar Siva [3], Giuseppina L Masucci [4], Pejman J Maralani [5],

- In the palliative setting for symptom control
- For selected patients with painful spinal metastases,
- Stereotactic body radiotherapy at a dose of ***24 Gy in 2*** fractions was superior to conventional external beam radiotherapy at a dose of ***20 Gy in 5*** fractions
- in **improving the complete response rate for pain**.

Mature Local Control and Reirradiation Rates Comparing Spine Stereotactic Body Radiation Therapy With Conventional Palliative External Beam Radiation Therapy

*Int J Radiation Oncol Biol Phys, Vol. 114, No. 2, pp. 293–300, **2022***

Arjun Sahgal et al

Risk of ***local failure and reirradiation is lower with SBRT*** compared with cEBRT for spinal metastases

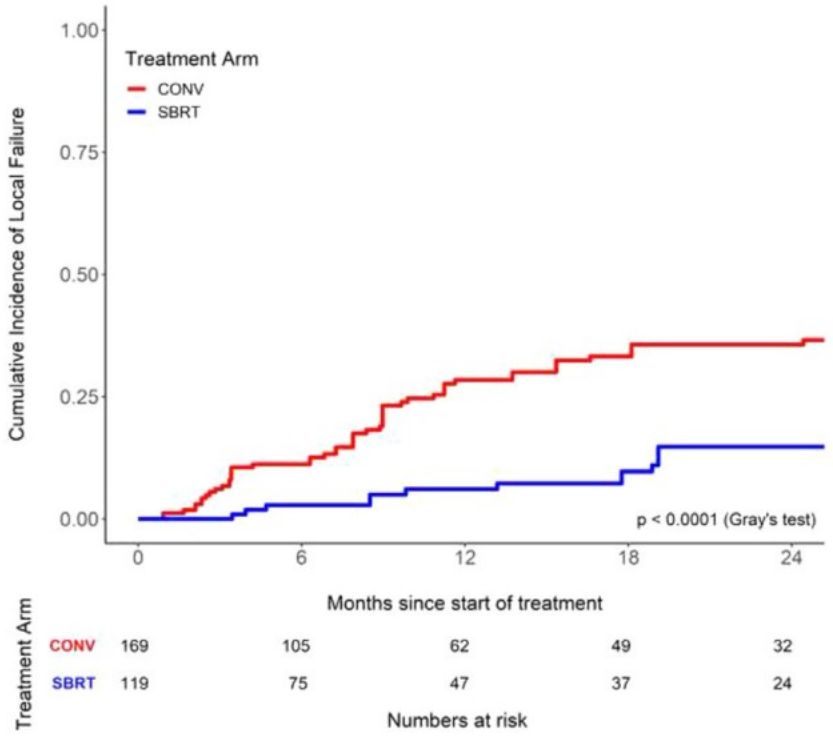


Fig. 1. Cumulative incidence of local failure in the stereotactic body radiation therapy (SBRT) and conventional external beam radiation therapy (cEBRT) cohorts demonstrating statistically significant increase in risk of local failure in the latter. *Abbreviation*: CCTG = Canadian Cancer Trials Group.

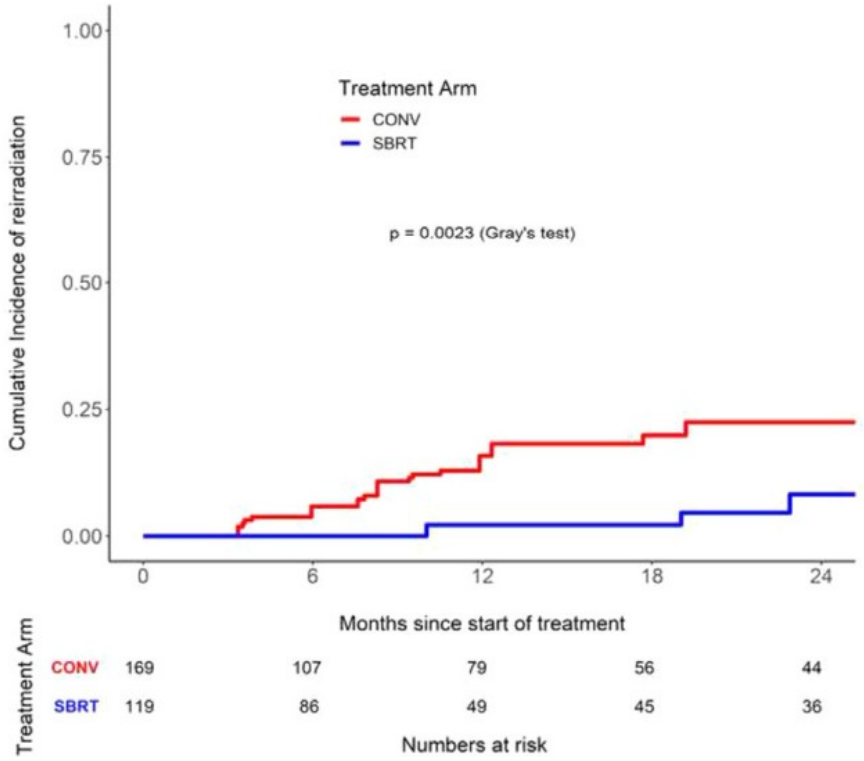


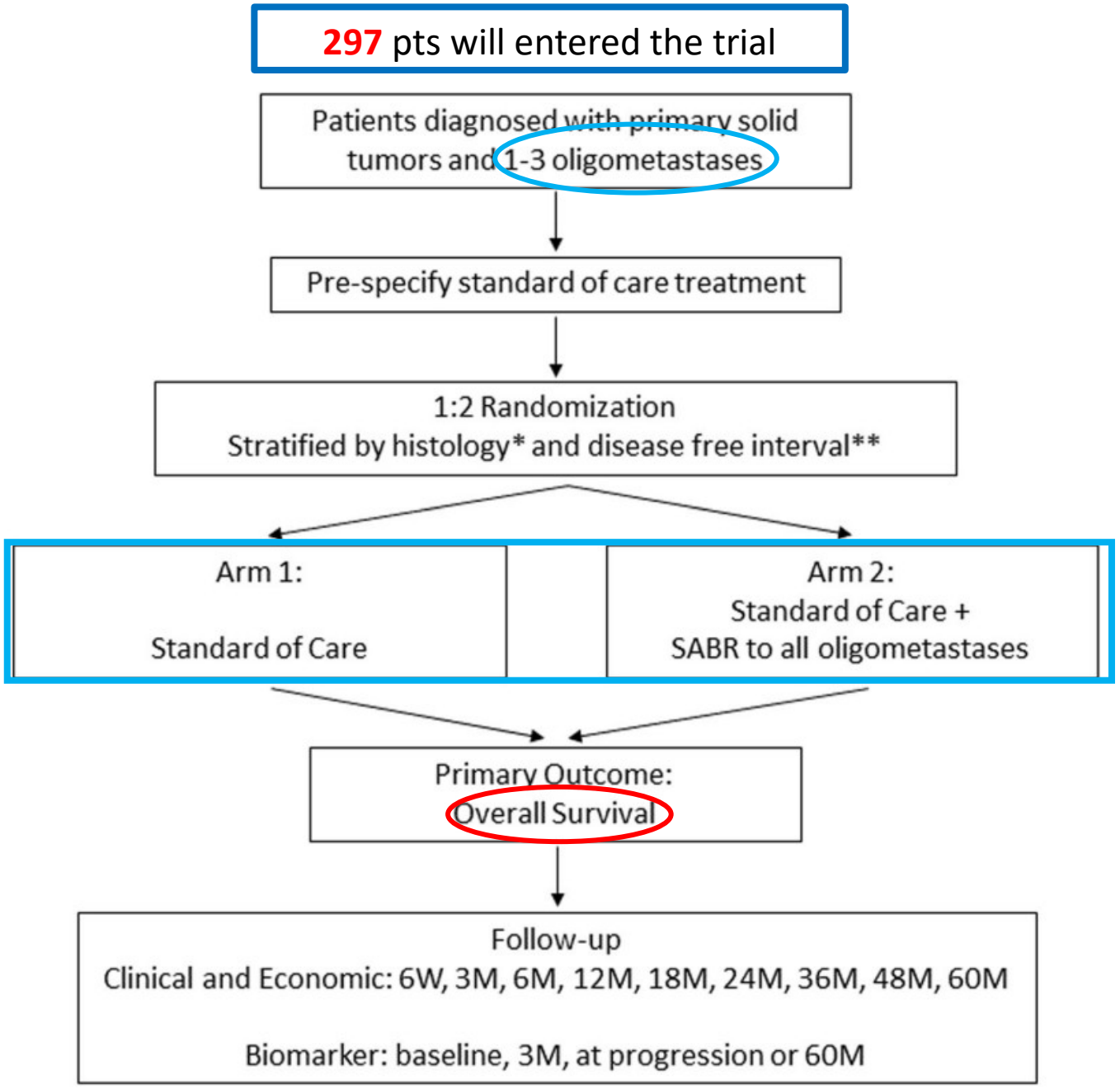
Fig. 3. Cumulative incidence of reirradiation according to the stereotactic body radiation therapy (SBRT) and conventional external beam radiation therapy (cEBRT) cohorts demonstrating significant increase in the need for reirradiation after the latter compared with SBRT.

STUDY PROTOCOL

Stereotactic ablative radiotherapy for the comprehensive treatment of 1–3 Oligometastatic tumors (SABR-COMET-3): study protocol for a randomized phase III trial

Olson *et al. BMC Cancer* (2020) 20:380
https://doi.org/10.1186/s12885-020-06876-4

On going trial



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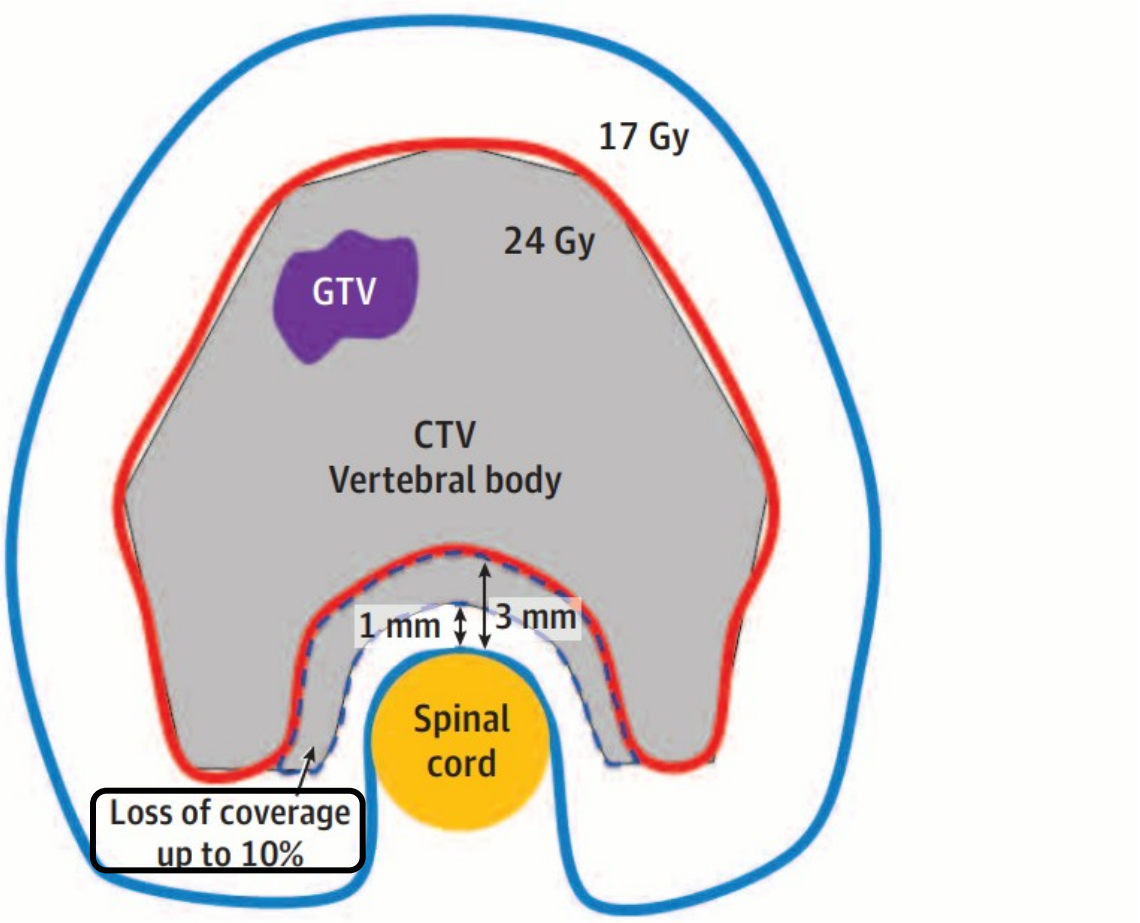
SPINE OLIGOMETASTASES

Figure 1. Planning for Stereotactic Ablative Radiotherapy



Stereotactic Ablative Radiotherapy for the Management of Spinal Metastases

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JAMA Oncol. doi:10.1001/jamaoncol.2019.5351
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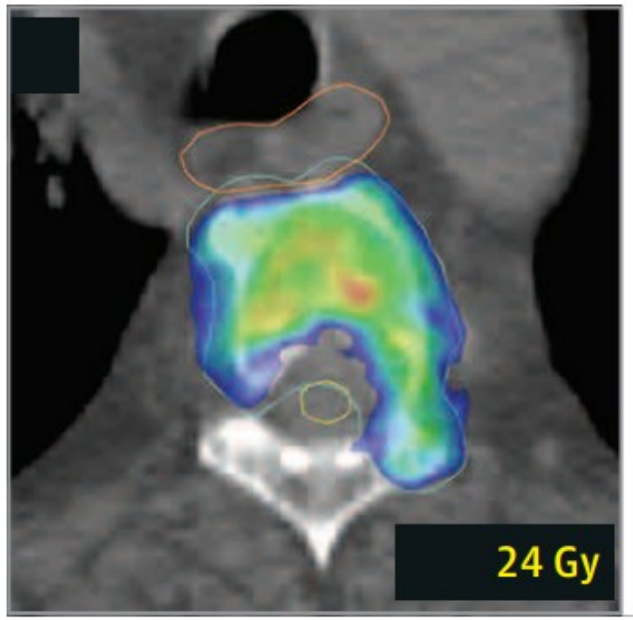
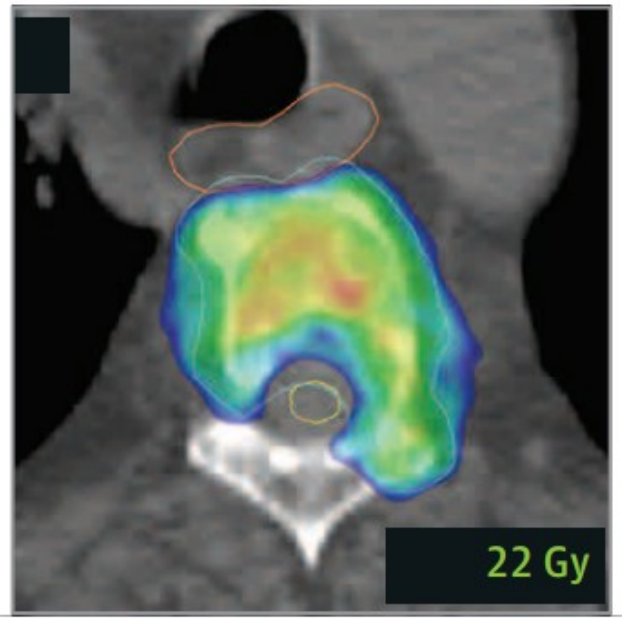
Rachel M. Glicksman, MD; Michael C. Tjong, MD; Wellington F. P. Neves-Junior, BSc; Daniel E. Spratt,

SPINE OLIGOMETASTASES

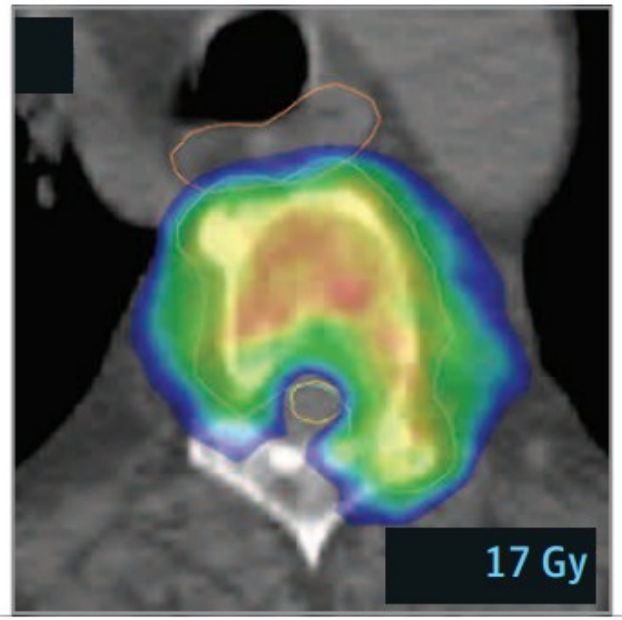
E Dose area receiving 24 Gy on axial plane



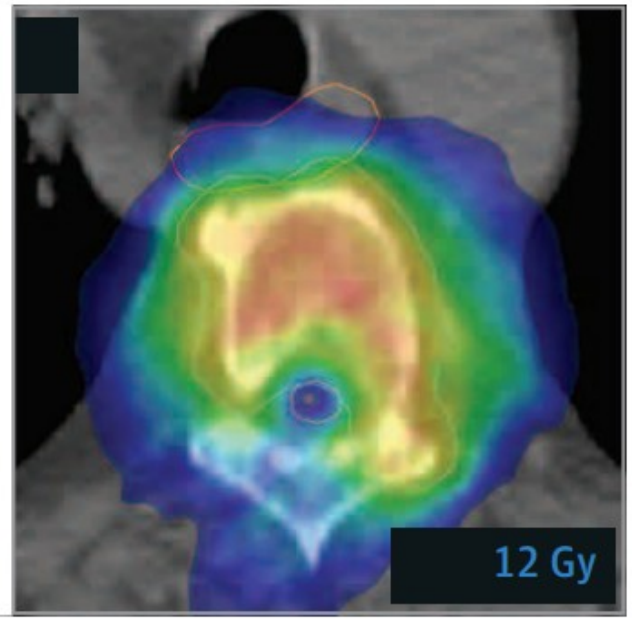
F Dose area receiving 22 Gy on axial plane



G Dose area receiving 17 Gy on axial plane



H Dose area receiving 12 Gy on axial plane

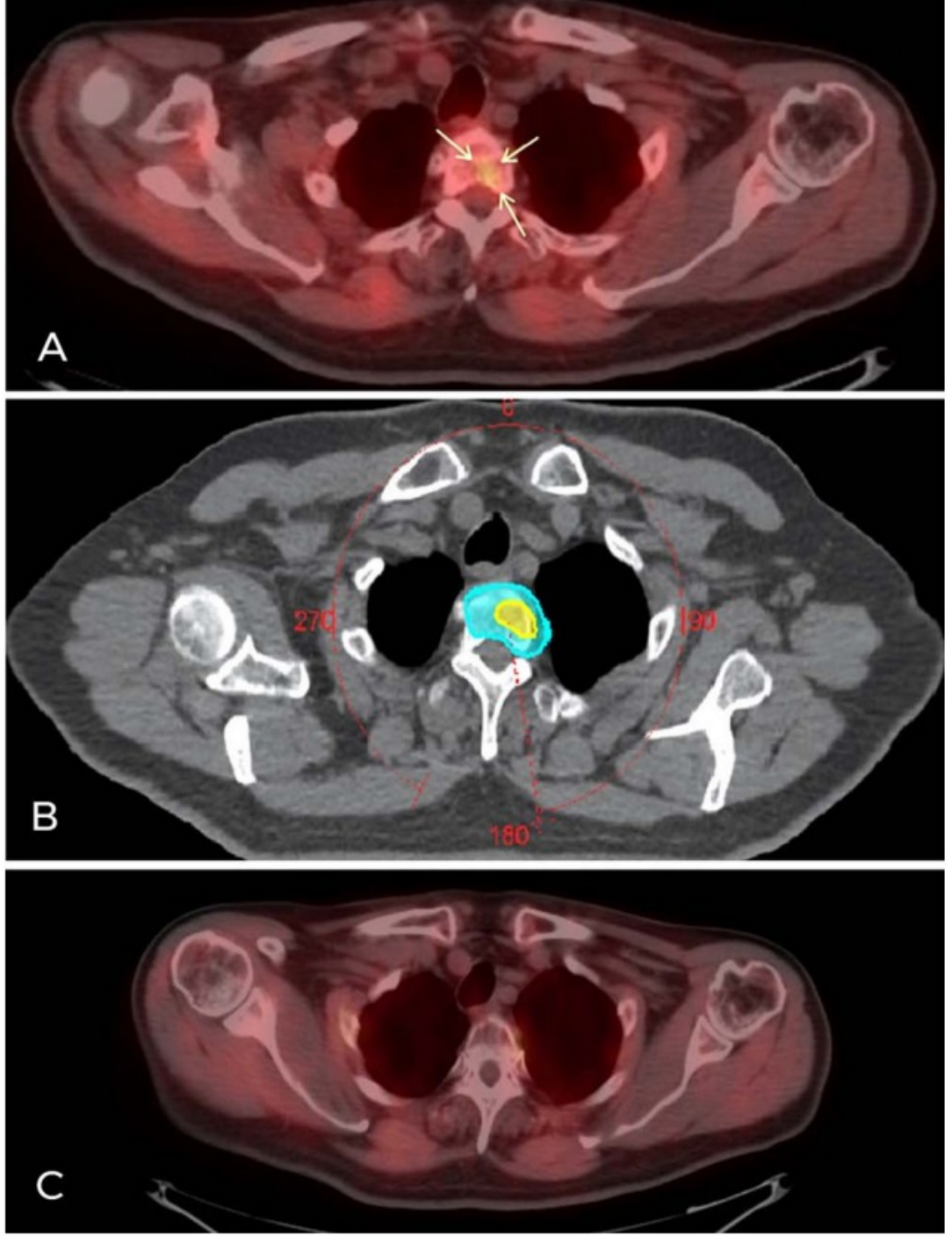


A case of oligometastatic prostate met submitted to concomitant boost- SBRT

A. Pretreatment PET-CT

B. Concomitant boost SBRT isodoses

C. Post-treatment PET-CT → CR

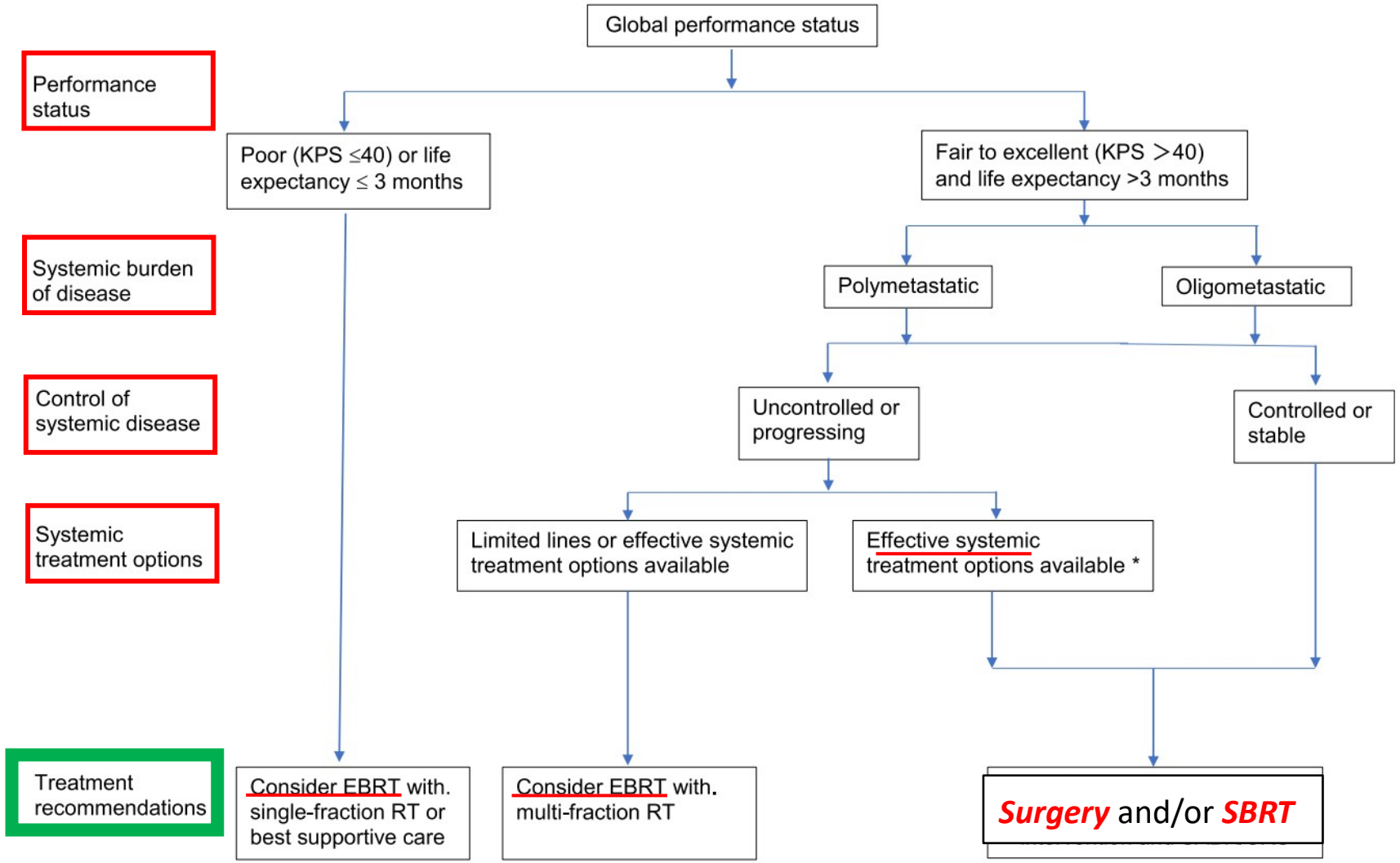


An integrated multidisciplinary algorithm for the management of spinal metastases: an International Spine Oncology Consortium report

Lancet Oncol 2017; 18: e720–30

Daniel E Spratt, Whitney H Beeler, Fabio Y de Moraes, Laurence D Rhines, Joseph J Gemmete, Neeraj Chaudhary, David B Shultz, Sean R Smith,

Algorithm by the International Spine Oncology Consortium report



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Daniel E Spratt, Whitney H Beeler, Fabio Y de Moraes, Laurence D Rhines, Joseph J Gemmete, Neeraj Chaudhary, David B Shultz, Sean R Smith,

Mechanical

Neurological

Oncological

Preferred treatment

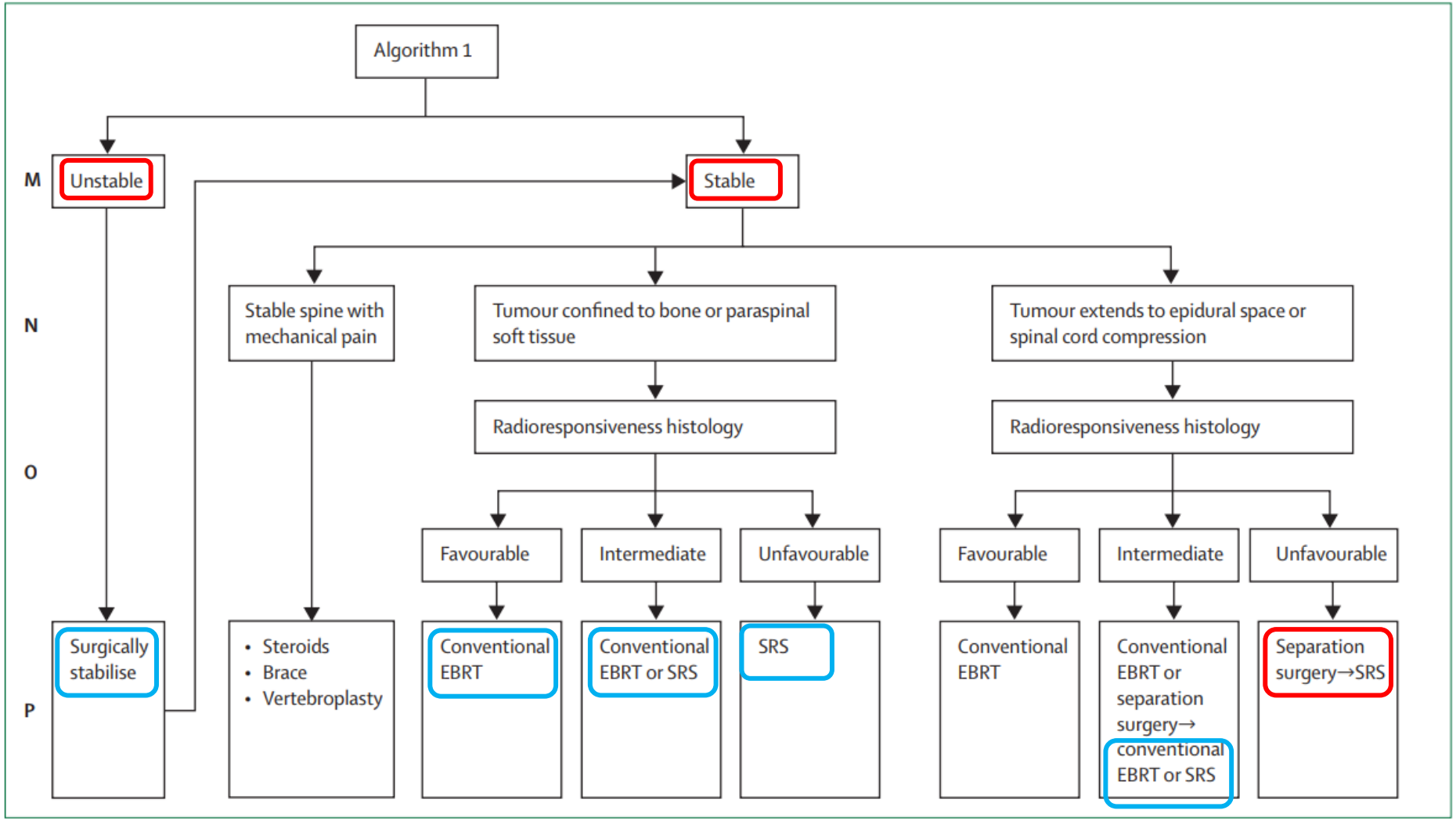
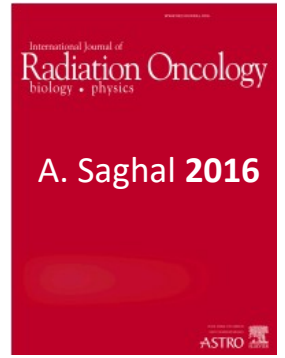


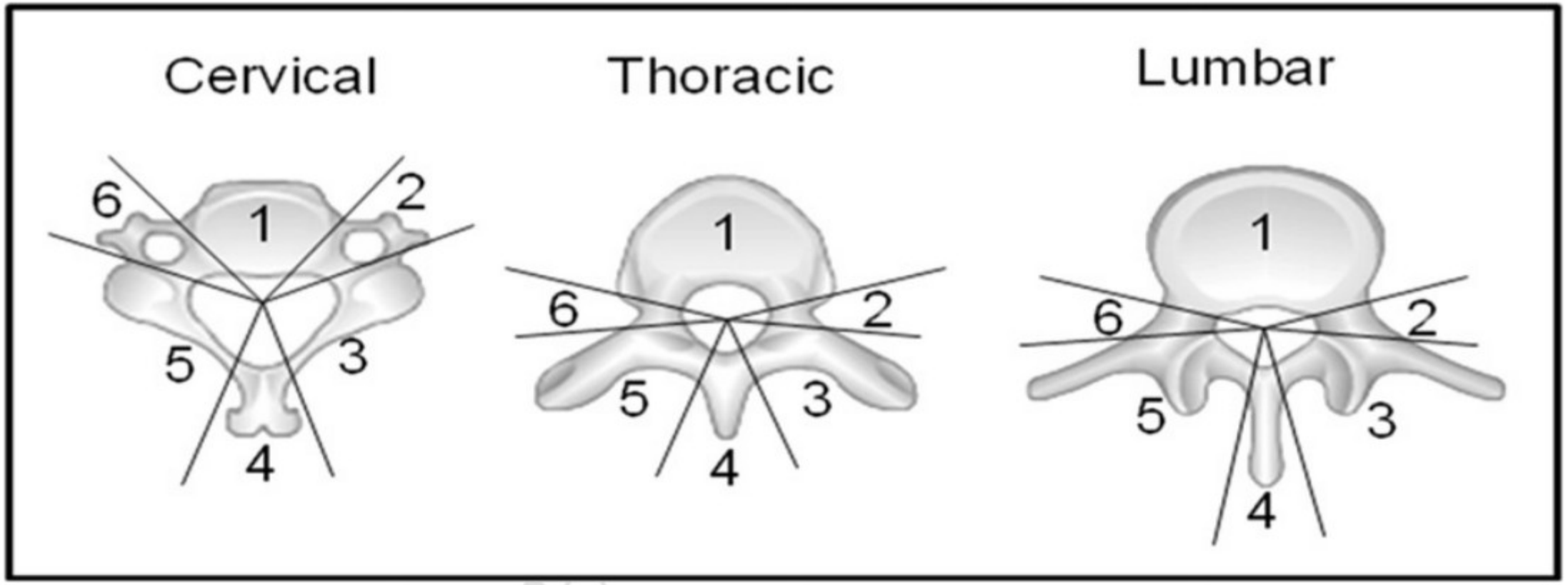
***Figure* 3: MNOP algorithm for spinal metastasis management**

MNOP=mechanical, neurological, oncological, preferred treatment. EBRT=external-beam radiotherapy. SRS=stereotactic radiosurgery.

Consensus Contouring Guidelines for Post-Operative Stereotactic Body Radiation Therapy (SBRT) for Metastatic Solid Tumor Malignancies to the Spine



***Post-Op SBRT** for spinal metastasis*



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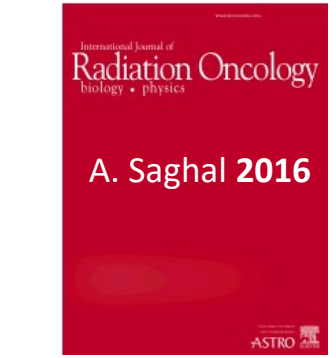
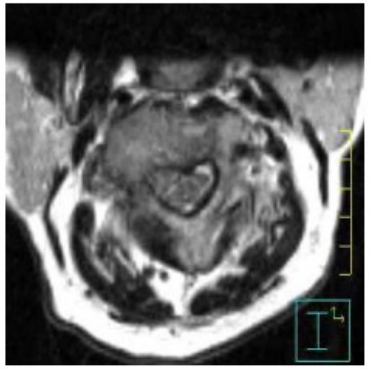
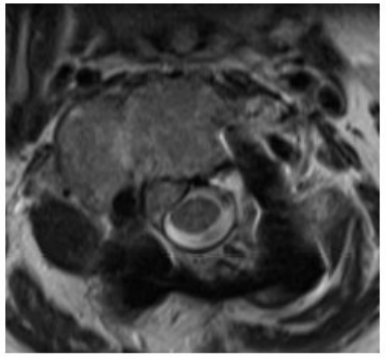
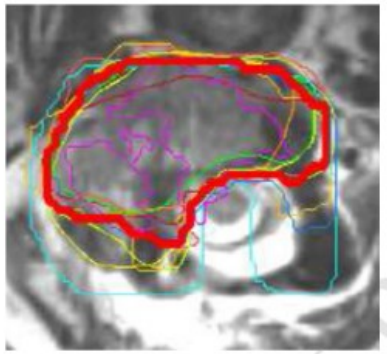
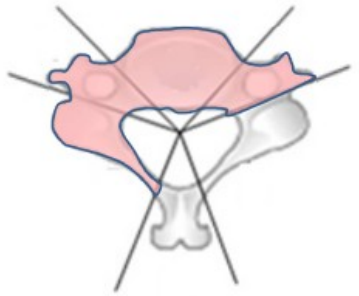
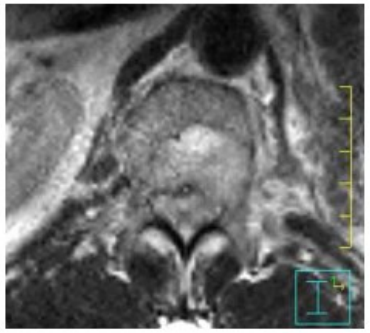
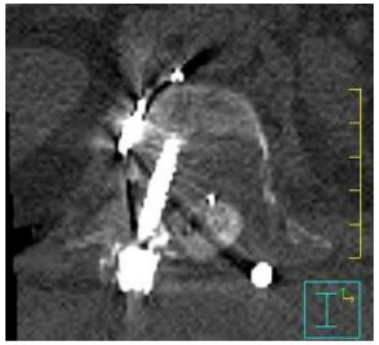
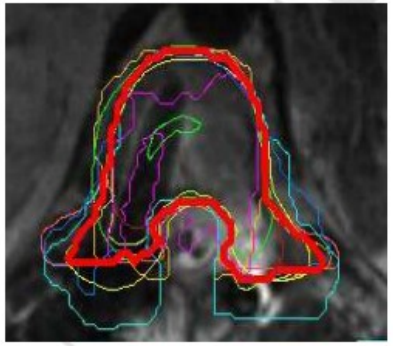
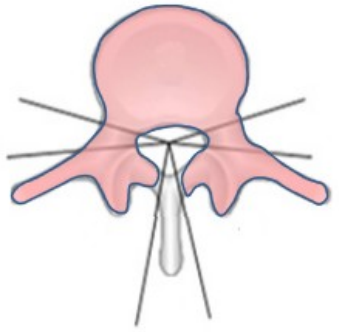
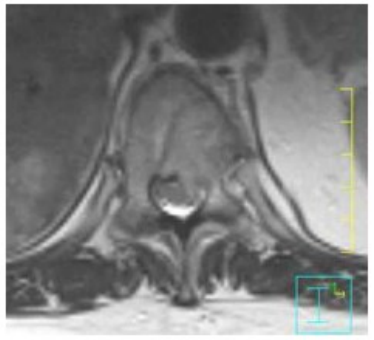
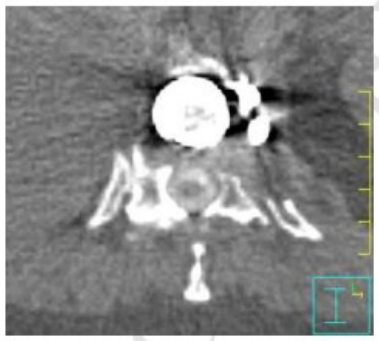
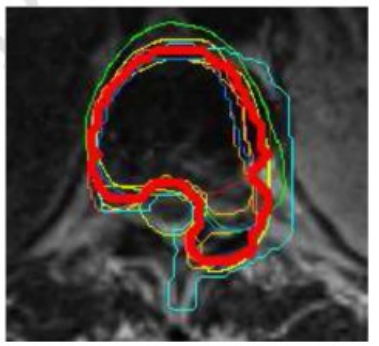
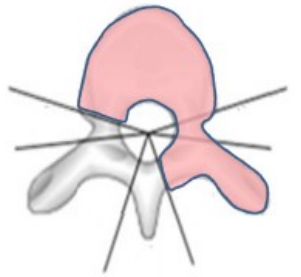
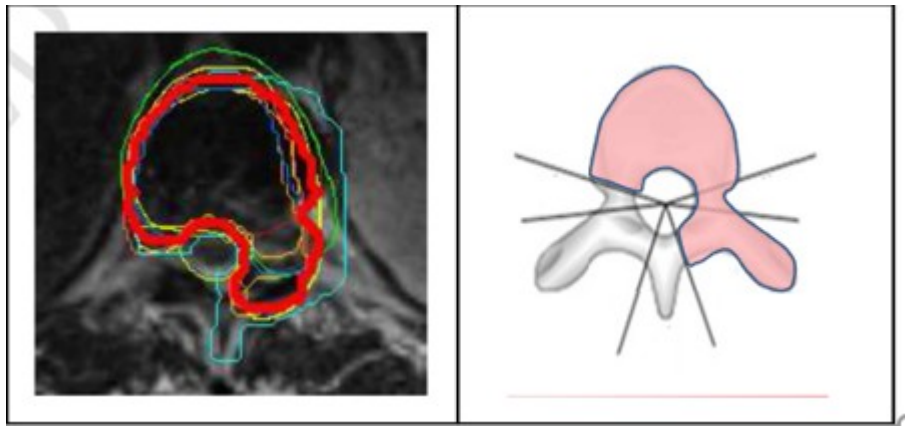
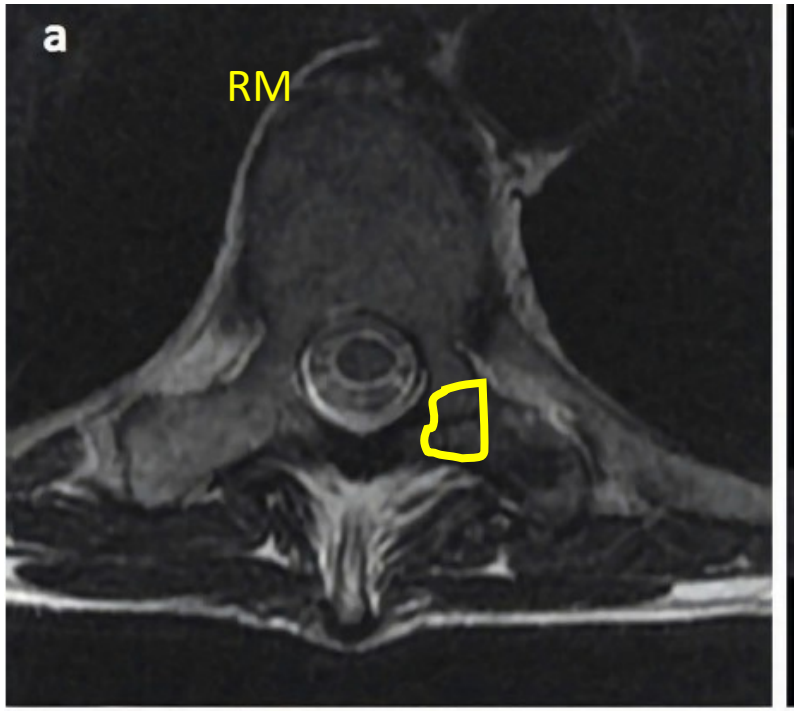


4				
5				
6				

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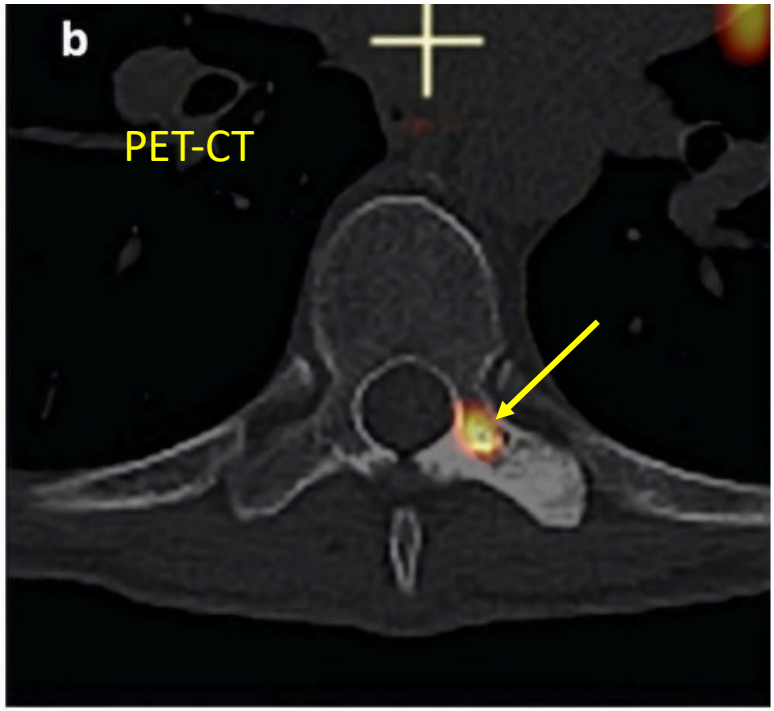
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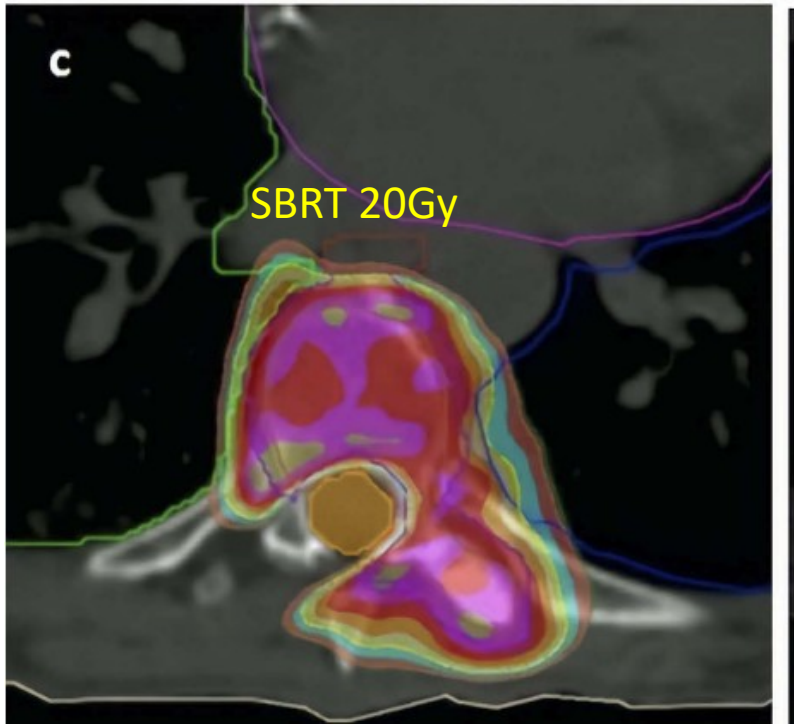
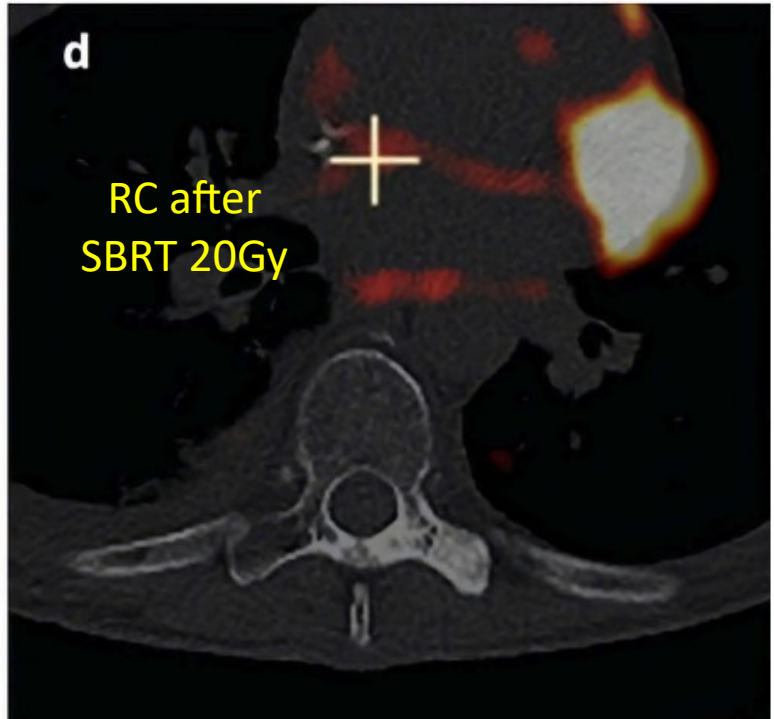
PET-CT


c
SBRT 20Gy


d
RC after
SBRT 20Gy

Stereotactic Radiosurgery for Postoperative Spine Malignancy: A Systematic Review and International Stereotactic Radiosurgery Society Practice Guidelines

Practical Radiation Oncology® (2022) **12**, e65–e78

Salman Faruqi, MD,[a,*] Hanbo Chen, MD,[b] Laura Fariselli, MD,[c]

Table 4 ISRS recommendations for the use of postoperative spine SBRT

Key recommendations
Patient selection - Patients with oligometastatic disease. - Patients with radioresistant histologies and/or those with mass-type tumors with paraspinal extension. - If prior cEBRT or SBRT has been given to the affected spinal segment then salvage postoperative SBRT can be considered.
Follow-up - In addition to history and physical examination, a spine MRI should be considered every 2-3 months post-SBRT for the first year and then every 3-6 months thereafter.

Please note that SBRT must be delivered within 4 weeks of the surgery

Stereotactic Radiosurgery for Postoperative Spine Malignancy: A Systematic Review and International Stereotactic Radiosurgery Society Practice Guidelines Practical Radiation Oncology® (2022) **12**, e65–e78

Salman Faruqi, MD,[a,*] Hanbo Chen, MD,[b] Laura Fariselli, MD,[c]

- ***20 studies*** were identified reporting outcomes for a total of **461** patients based on strict inclusion and exclusion criteria.
- The ***1-year local control*** rate ranged from 70% to 100%.
- Serious toxicities were registered in few patients:
  - ***myelopathy*** in 1 patient (who was previously treated with carbon-ion beam of 70.4 GyE (photon gray equivalent) and 7 years later underwent decompression surgery and SBRT)
  - Postoperative spine SBRT, ***vertebral compression fracture*** was reported in 26 patients (5.6%),
  - 1 patient developed an ***esophageal fistula*** requiring surgical repair

SBRT for NON-SPINE

Outcomes and toxicities of stereotactic body radiation therapy for non-spine bone oligometastases

Dawn Owen MD, PhD [a], Nadia N. Laack MD, MSc [a], Charles S. Mayo PhD [a],

Practical Radiation Oncology (2014) 4, e143–e149

practical radiation oncology
pro

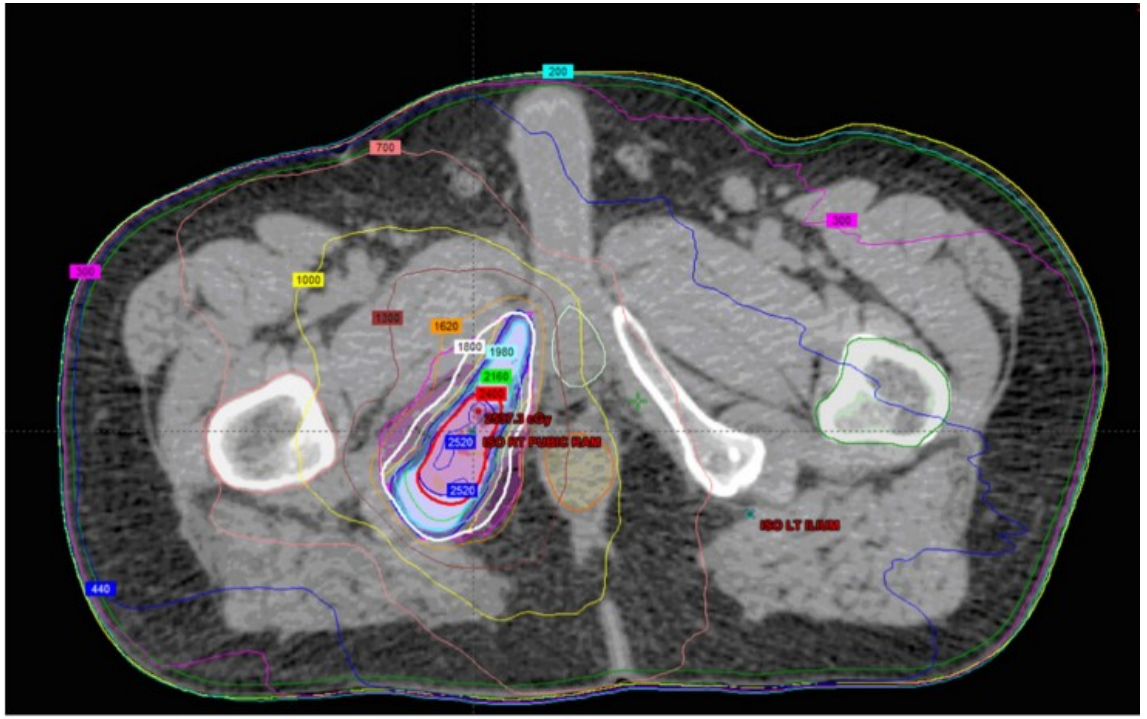
- **74** pts with oligometastatic non-spine bony metastases of varying histologies

- Dose and fractionation varied but the most common prescription was **24 Gy/1 fraction**.

- Local recurrence occurred in 7 patients with a median time to failure of 2.8 months.
- Local control was 91.8% at 1 year

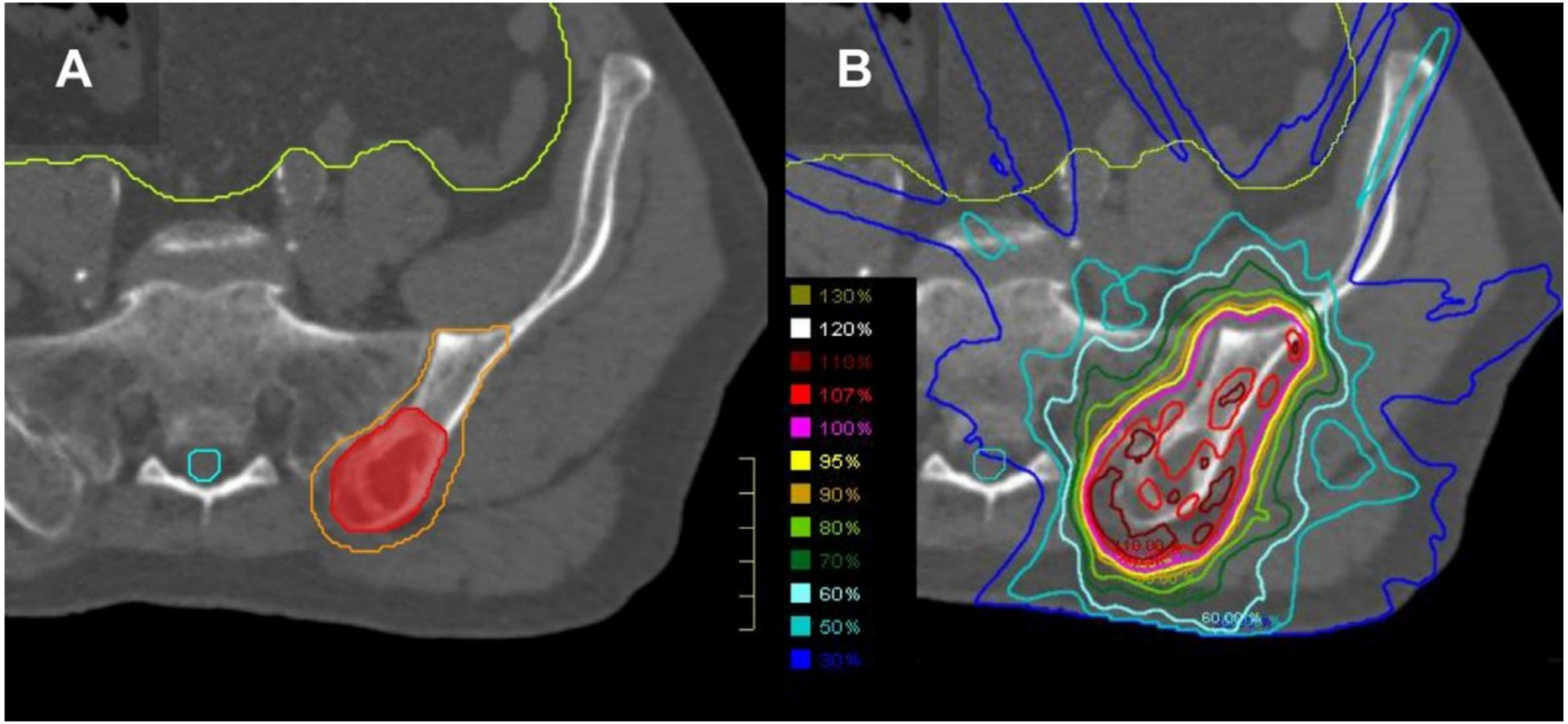
- There were no late grade 3 or 4 toxicities

- SBRT is a feasible and tolerable treatment for non-spine bony metastases. Longer follow-up will be needed to accurately determine late effects



Phase 2 Clinical Trial of Stereotactic Body Radiation Therapy for Painful Nonspine Bone Metastases

Practical Radiation Oncology® (2021) **11**, e139–e145



Single-Fraction Stereotactic vs Conventional Multifraction Radiotherapy for Pain Relief in Patients With Predominantly Nonspine Bone Metastases
A Randomized Phase 2 Trial

JAMA Oncol. doi:10.1001/jamaoncol.2019.0192
Published online April 25, 2019.

Quynh-Nhu Nguyen, MD; Stephen G. Chun, MD; Edward Chow, MBBS, PhD; Ritsuko Komaki,

In this phase 2 non inferiority trial **81** pts received single-fraction **SBRT** and **79** pts **MFRT**

single-fraction SBRT (12 Gy for 4-cm lesions or 16 Gy for <4-cm lesions**)**

vs

Multi-fractions RT (30 Gy in 10 fractions)

Conclusion:

Pain response rates were higher for high-dose, single-fraction **SBRT**,
which should be considered for patients with bone metastases and long estimated survival times.

Phase 2 Clinical Trial of Stereotactic Body Radiation Therapy for Painful Nonspine Bone Metastases

Practical Radiation Oncology® (2021) **11**, e139–e145

Methods and materials:

- **38** patients with painful (2 points on a 0-to-10 scale) **NON-SPINE** bone metastases from a solid tumor were enrolled.
- The prescribed dose was 35 Gy in 5 fractions of **SBRT**.
- The primary endpoint was overall pain response rate (CR and PR 6 months after SBRT)

Outcome:

- 41 mets in **38** pts were registered
- lung cancer (22%), prostate cancer (15%), uterus cancer(15%), and renal cell carcinoma (12%).
- Bone metastases were most commonly located in coxal bones (56%).
- 6-month pain response was 75%.
- The local control rate at 6 months was 92%.

Toxicity:

- 7 pts (17%) experienced bone fracture after irradiation, and 3 pts (7%) experienced grade 2 limb edema.
- One pts had soft tissue abscess around the tumor and osteonecrosis of coxal bones:

  → pts died of infection 4 months after SBRT (a possible treatment-related death).

Phase 2 Clinical Trial of Stereotactic Body Radiation Therapy for Painful Nonspine Bone Metastases

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Review Article

Advances in radiotherapy in bone metastases in the context of new target therapies and ablative alternatives: A critical review

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CONCLUSIONS

- Additional data are needed to determine the value of **SBRT for selected patients** identified by clinical characteristics and/or extent and timing of oligometastatic disease
- Future prospective studies should consider **stratifying patients** into different categories (e.g., synchronous, metachronous, etc)
- For the moment, based on the available evidence, **indications for curative intent RT** of oligometastases can be defined as

→ **1 to 5** metastatic lesions

→ with a **controlled primary** tumor being optional

→ but where all **metastatic sites** must be safely treatable

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SURGERY
in bone metastases

Comparative analysis of risk factors for pathological fracture with femoral metastases

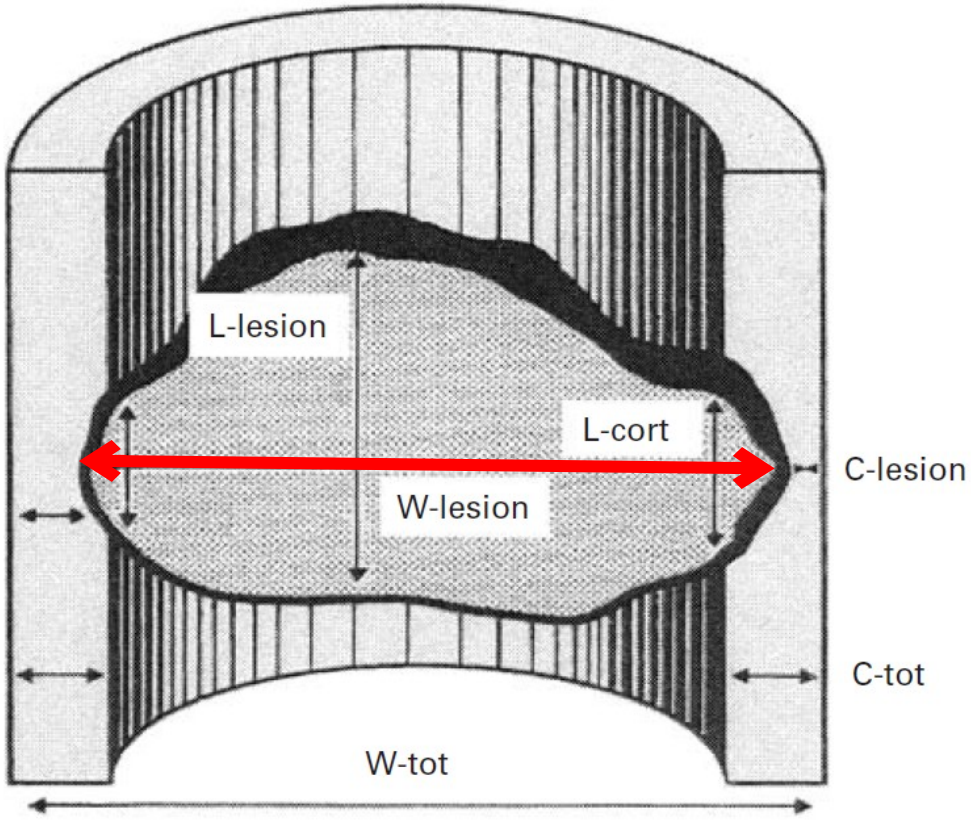
RESULTS BASED ON A RANDOMISED TRIAL OF RADIOTHERAPY

Dutch bone metastasis study: 110 femoral metastases **Y. van der Linden et al. 2004**

The risk factors studied were:

1. **increasing pain,**
2. **the size of the lesion,**
3. **radiographic appearance,**
4. **localization,**
5. **transverse/axial/circumferential involvement of the cortex**
6. **the scoring system of Mirels.**

- **Axial cortical involvement >30 mm (p = 0.01) &**
- **Circumferential cortical involvement >50% (p = 0.03) were predictive of fracture.**



Measurements of metastatic lesions in the femur (mm): largest axial length of the entire lesion *(L-lesion)*, largest transverse extension of the lesion *(W-lesion)*, largest axial cortical involvement *(L-cort)*. Measurement of the femur (mm): largest transverse width of the bone *(W-tot)*, maximal thickness of cortex without lesional involvement *(C-tot)* and minimal thickness of cortex with lesional involvement *(C-lesion)*.

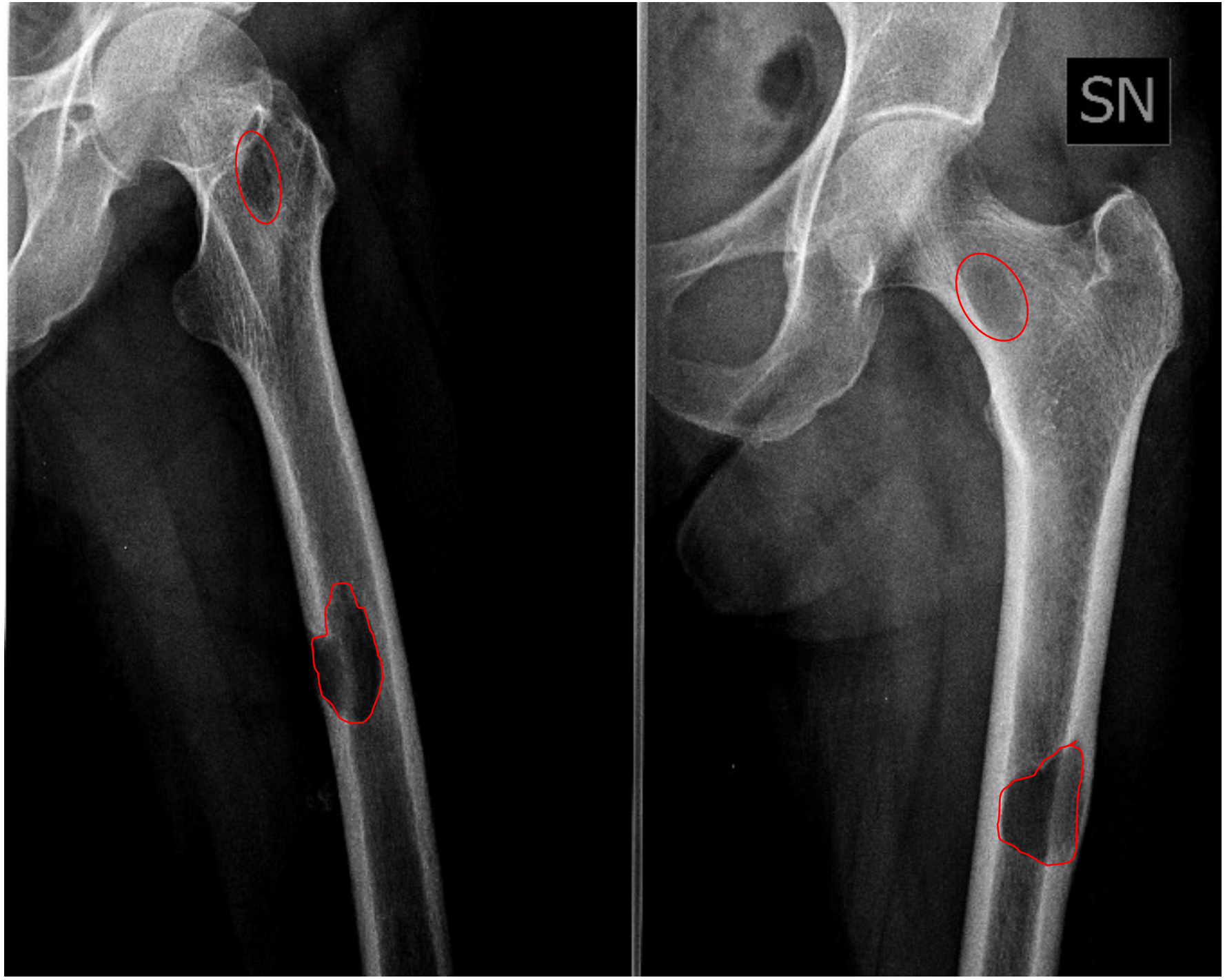

SN

Table 1 Spinal instability neoplastic score

SINS components	Score
Location	
Junctional (occiput-C2, C7-T2, T11-L1, L5-S1)	3
Mobile spine (C3-C6, L2-L4)	2
Semi rigid (T3-T10)	1
Pain	
Mechanical	3
Occasional pain but not mechanical	1
None	0
Bone lesion type	
Lytic	2
Mixed (lytic and blastic)	1
Blastic	0

Table 1 Spinal instability neoplastic score

SINS components	Score
Radiographic spinal alignment	
Subluxation/translation	4
Kyphosis/scoliosis	2
Normal alignment	0
Vertebral body collapse	
>50% collapse	3
<50% collapse	2
No collapse with >50% of body involved by tumor	1
None of the above	0
Posterolateral involvement of spinal elements	
Bilateral	3
Unilateral	1
None of the above	0

Abbreviation: SINS = Spinal Instability Neoplastic Score.

Final score: 0 to 6, stable; 7 to 12, potentially unstable; 13 to 18, unstable.

SPINAL INSTABILITY NEOPLASTIC SCORE (SINS)

JOURNAL OF CLINICAL ONCOLOGY

Fourney et al 2011;29(22):3072-3077

Score:

0-6 ***stable***

7-12 ***potentially unstable***

13-18 ***unstable***

Spine Location

Pain

Type of bone lesion

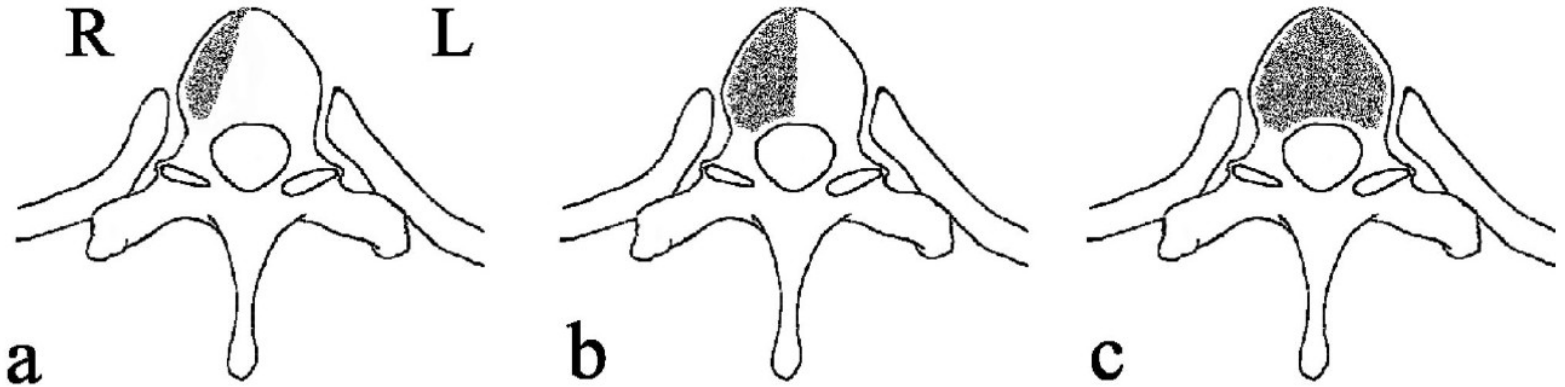
Rx alignment

Body collapse

Posterolateral body involvement

The sensitivity and specificity of SINS for **potentially unstable** or **unstable** lesions were **95.7%** and **79.5%,** respectively.

Impending or pathologic fractures in SPINE



Defect ratio : 0.25 0.40 0.75

- DR= Ø max of lesion (lytic or blastic) / Ø max of vertebral body
- DR ≥ 0.5 → high risk of patological fracture

Ebihara et al Spine 2004;29(9):994-999

Fisher *et al. Radiation Oncology* 2014, **9**:69
http://www.ro-journal.com/content/9/1/69

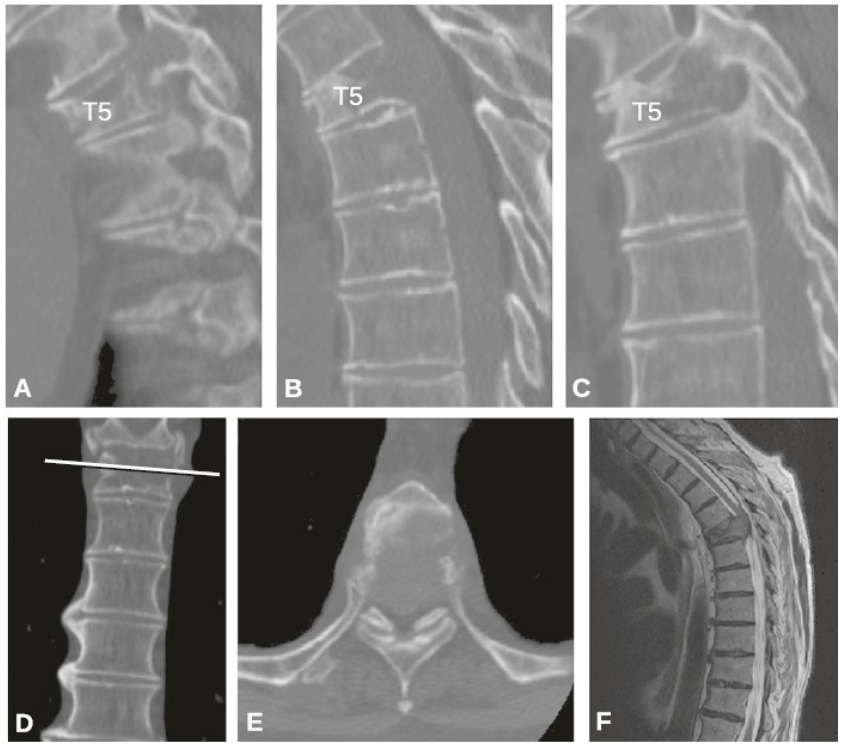
SPINAL INSTABILITY

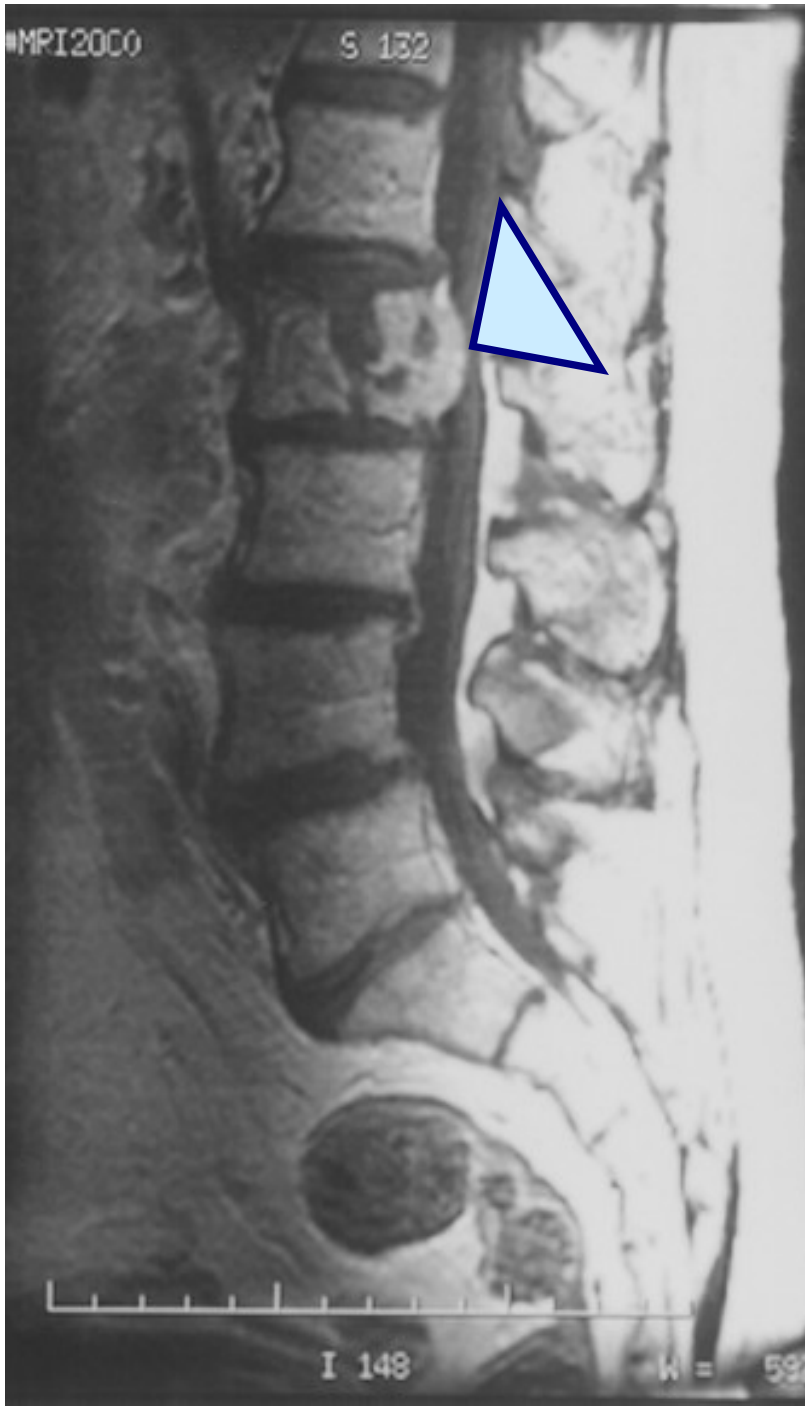
RADIATION ONCOLOGY

RESEARCH Open Access

Reliability of the Spinal Instability Neoplastic Score (SINS) among radiation oncologists: an assessment of instability secondary to spinal metastases

Charles G Fisher[1,16*], Rowan Schouten[2], Anne L Versteeg[3], Stefano Boriani[4], Peter Pal Varga[5], Laurence D Rhines[6],





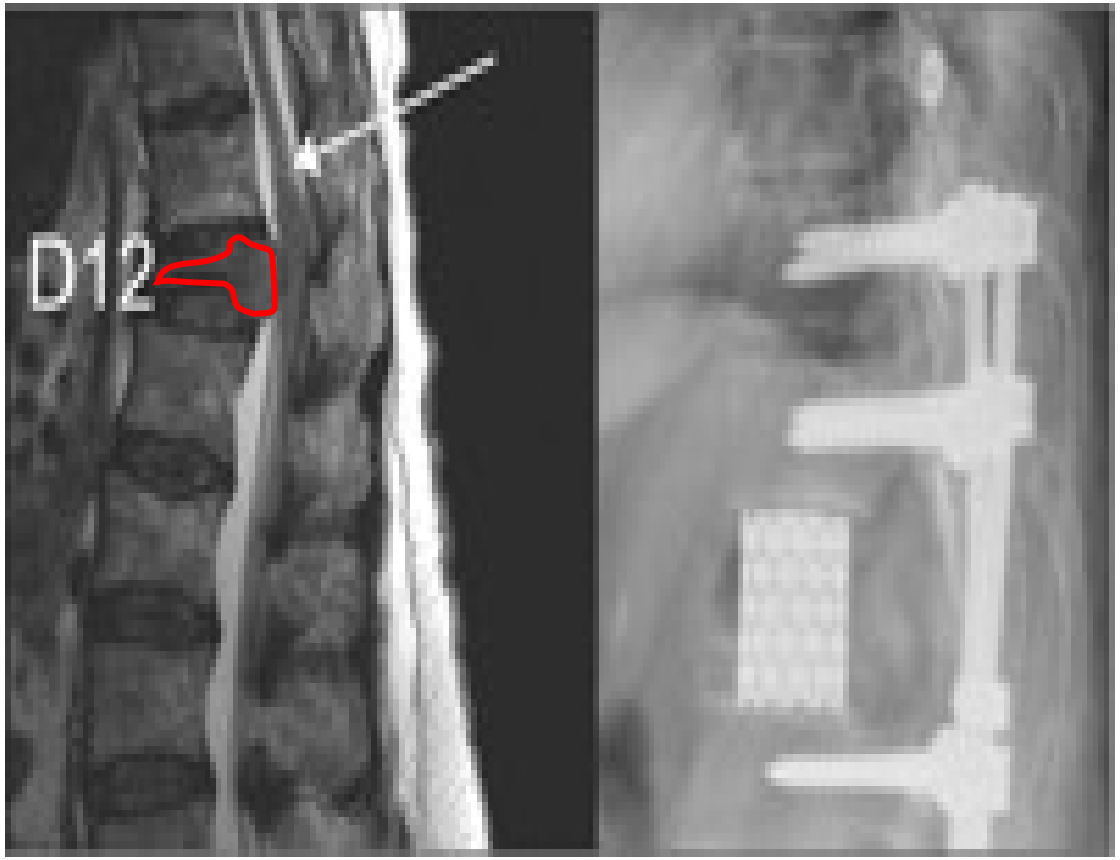
Example of metastatic spinal cord compression due to pathologic fracture and posterior dislocation of vertebral body

Surgery + RT

SURGICAL APPROACH AND PATIENT SELECTION

Tailored surgery!

1. **posterior, anterior, and/or lateral approach**
2. **plus stabilization of the spine (i.e., no laminectomy)**



Surgery + RT

SURGICAL APPROACH AND PATIENT SELECTION

Selected patients!

1. **Single site**
2. **Good medical status**
3. **Histology not lymphoma or myeloma**
4. **Absence of paraplegia**
5. **Expected survival > 3 months**

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Radiotherapy Alone or Surgery in Spinal Cord Compression? The Choice Depends on Accurate Patient Selection

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Selection criteria for surgery

- good PS and an expected survival of at least 6 months,
- spinal cord compression restricted to a single area,
- non-radiosensitive tumors,
- diagnostic doubts,
- spinal instability,
- bony compression causing spinal cord compression.

About 10% of cases

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