Oligometastasis : Radiation Oncologist's perspective

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Apollo Multispeciality Hospital, Kolkata

47th ICRO, NRSMC&H Kolkata, 12th -13th April 2025

- What is Oligometastasis?
- How this state happens??

- Definitions related to Oligomets

- Rationale for RT in Oligomets

- Sites where oligomets is being treated with RT

- Is treating Oligometastasis beneficial for patients??

SEED AND SOIL THEORY :1889 AD

STEPHEN PAGET, M.A., F.R.C.S.
(Founder of the Research Defence Society).

- Stephen Paget proposed his "seed and soil" theory of cancer.
- He analyzed over 1000 autopsy records of women who had breast cancer and found that the patterns of metastasis were not random.
- Thus, he proposed that tumor cells (the seeds) have a specific affinity for specific organs (the soil), and metastasis would only result if the seed and soil were compatible.

SPECTRUM THEORY

Journal of Clinical Oncology®
An American Society of Clinical Oncology Journal

EDITORIAL

Oligometastases

Authors: S Hellman and R R Weichselbaum | AUTHORS INFO & AFFILIATIONS

1995

- Cancer spread is orderly, extending in a contiguous fashion from the primary tumor through the lymphatics to the lymph nodes and then to distant sites.
- There are tumor states intermediate between purely localized lesions and those widely metastatic., existence of a clinical significant state of oligometastases.

Micro-RNA THEORY

2011

OPEN ACCESS Freely available online

PLoS one

MicroRNA Expression Characterizes Oligometastasis(es)

Yves A. Lussier[1,2,3,4*], H. Rosie Xing[1,2,5,6☯], Joseph K. Salama[8☯], Nikolai N. Khodarev[1,5☯], Yong Huang[1,3☯],

Abstract

Background: Cancer staging and treatment presumes a division into localized or metastatic disease. We proposed an intermediate state defined by ≤5 cumulative metastasis(es), termed oligometastases. In contrast to widespread polymetastases, oligometastatic patients may benefit from metastasis-directed local treatments. However, many patients who initially present with oligometastases progress to polymetastases. Predictors of progression could improve patient selection for metastasis-directed therapy.

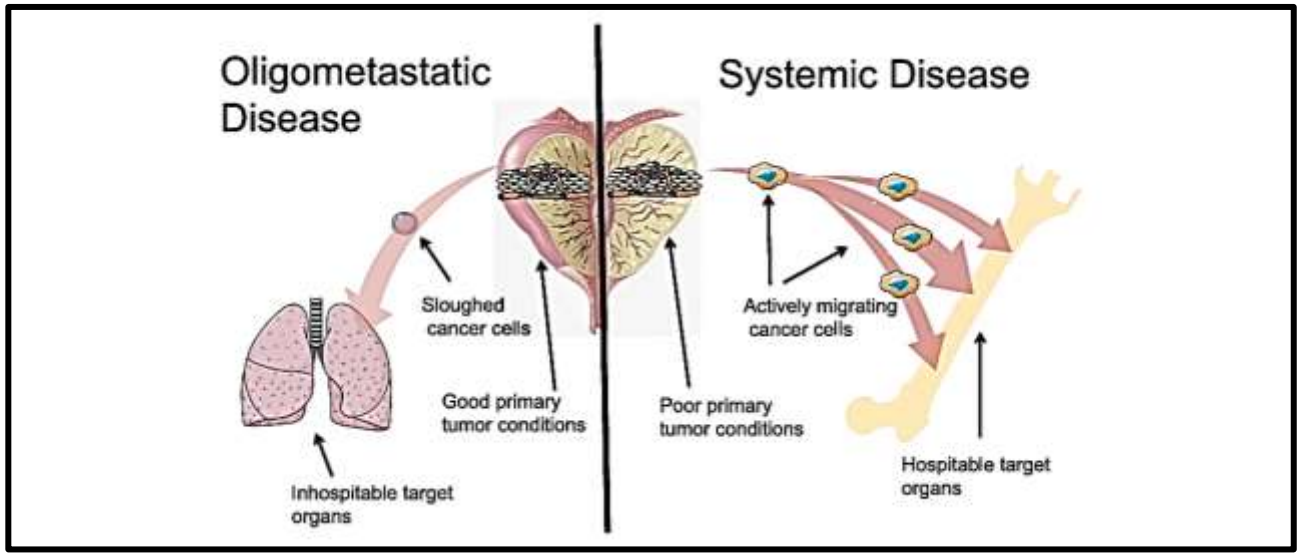
Methods: Here, we identified patterns of microRNA expression of tumor samples from oligometastatic patients treated with high-dose radiotherapy.

Results: Patients who failed to develop polymetastases are characterized by unique prioritized features of a microRNA classifier that includes the microRNA-200 family. We created an oligometastatic-polymetastatic xenograft model in which the patient-derived microRNAs discriminated between the two metastatic outcomes. MicroRNA-200c enhancement in an oligometastatic cell line resulted in polymetastatic progression.

Conclusions: These results demonstrate a biological basis for oligometastases and a potential for using microRNA expression to identify patients most likely to remain oligometastatic after metastasis-directed treatment.

CLONAL THEROY

2015



Oligometastatic disease versus systemic disease

Oligometastatic

Metastatic **growth potential is limited**, secondary to:

- **environmental conditions** in the primary tumor forestalling evolutionary clonal pressure,
- cancer cells that slough out of the primary tumor that **do not have the properties necessary to survive the circulation and invade into target organ sites**
- Cancer cells land in **inhospitable target organs**.

Systemic

Widespread metastatic growth potential is unlimited, secondary to:

- due to **environmental conditions in the primary tumor** creating many **undifferentiated, aggressive clones**
- cancer cells that actively migrate out of the primary tumor that have the **properties necessary to survive the circulation and invade into target organ sites**
- Cancer cells land in **hospitable target organs**

www.impactjournals.com/oncotarget/ Oncotarget, Vol. 6, No. 11

2015

The biology and treatment of oligometastatic cancer

Diane K. Reyes[1], Kenneth J. Pienta[1,2]

- A disease state that exists in a transitional zone between localized and widespread systemic disease, termed oligometastasis.
- Change in treatment paradigm, i.e. if primary cancer site (if still present) is controlled, or resected, and metastatic sites are ablated (surgically or with radiation), a prolonged DFS , and perhaps even cure, may be achieved

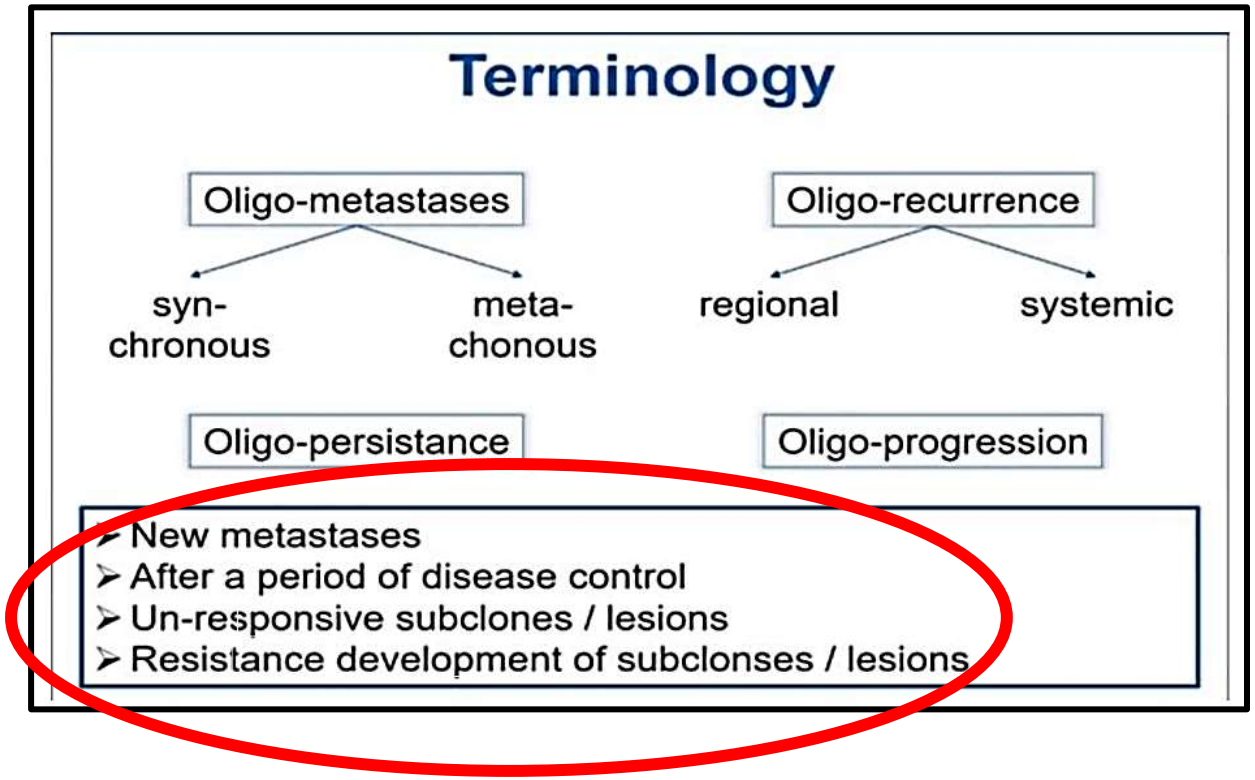
Table 3: Definitions of Oligometastasis

Terms	Definition
Oligometastasis	"…metastases (from tumors early in the chain of progression) limited in number and location because the facility for metastatic growth has not been fully developed and the site for growth is restricted…"
Oligometastatic disease	Solitary or few detectable metastatic lesions that are usually confined to a single organ
Oligometastases	Due to limited metastatic competence and does not occur following otherwise successful systemic treatment. New metastases in this situation, albeit even limited, is likely to have more extensive malignant capabilities that were somehow spared from eradication by therapeutic means, or from the development of resistant clones
Induced oligometastases	Occurs when widespread micrometastatic disease is mostly eradicated by systemic chemotherapy but drug resistant clones are left behind, or tumor foci is located in a site not accessed by chemotherapy
Oligorecurrence	Limited metastases in the presence of a controlled primary lesion
Sync-oligometastases	≤5 metastatic or recurrent lesions in the presence of active primary lesions
Synchronous oligometastasis	Oligometastatic disease is detected at the time of diagnosis of the primary tumor, therefore there is an active primary tumor
Metachronous oligometastasis	Development of oligometastatic disease after treatment of the primary tumor; interval for classification of metachronous versus synchronous is not standardized; between Controlled primary lesion except for concomitant primary and distant recurrence
Oligoprogression	Progression of a limited number of metastatic deposits, while remaining metastases are controlled with systemic therapy
Oligometastasis (specific to prostate cancer)	Rising PSA following primary therapy, with oligometastasis on imaging, in whom local treatment (surgical metastasectomy (usually LN dissection), or SBRT for bony mets or LN recurrence) is required to defer initiation of ADT
Oligometastasis (specific to	Castrate resistant prostate cancer with a rising PSA and oligometastasis on imaging, in whom local treatment (surgical metastasectomy (usually LN bony mets or LN recurrence) may allow deferral of

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

Matthias Guckenberger, Yolande Lievens, Angelique B Bouma, Laurence Collette, Andre Dekker, Nandita M deSouza, Anne-Marie C Dingemans,



Intermediate state between localised and systemically metastasised disease.

- **Oligometastases is the state in which the patient shows distant relapse in only a limited number of regions**
- **Oligo-recurrence has a primary site of the cancer controlled, meaning that all gross recurrent or metastatic sites could be treated using local therapy**

Synchronous oligometastatsis :

- De-novo presentation of oligo-metastases
- ≤5 metastatic or recurrent lesions in the presence of active primary lesions
- Oligometastatic disease is detected at the time of diagnosis of the primary tumor, therefore there is an active primary tumor

Oligoprogressive disease :

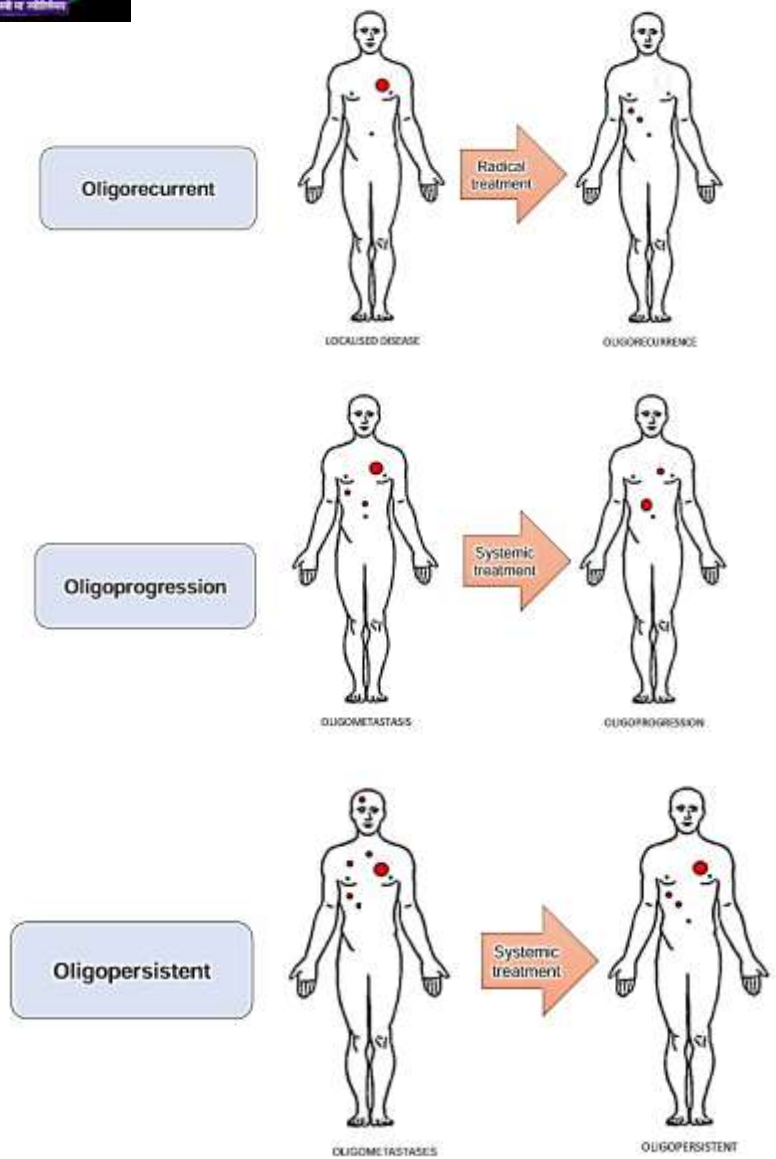
- Majority of metastatic disease controlled by systemic treatment, a few 'resistant' clones progress

Metachronous oligometastasis

- After period initial disease-free interval, new presentation of oligo-metastases

Induced Oligometastasis/Oligopersistance

- Induced oligometastasis occurs when widespread micrometastatic disease is mostly eradicated by systemic chemotherapy but drug resistant clones are left behind, or tumor foci is located in a site not accessed by chemotherapy



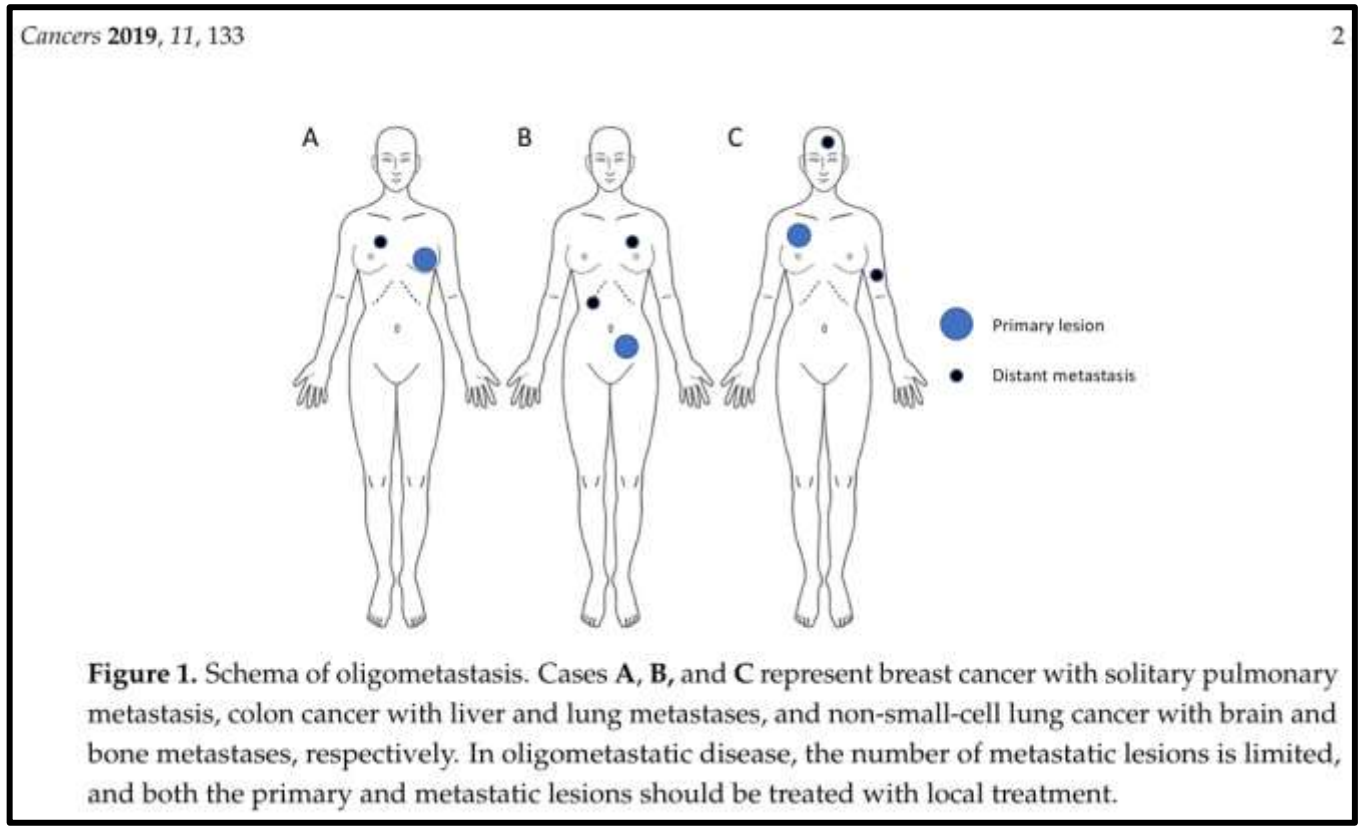


Figure 1. Schema of oligometastasis. Cases **A**, **B**, and **C** represent breast cancer with solitary pulmonary metastasis, colon cancer with liver and lung metastases, and non-small-cell lung cancer with brain and bone metastases, respectively. In oligometastatic disease, the number of metastatic lesions is limited, and both the primary and metastatic lesions should be treated with local treatment.

Cancers 2019, 11, 133; doi:10.3390/cancers11020133

Oligemets with favourable prognosis:

2013

Editorial

Oligometastases/Oligo-Recurrence of Lung Cancer

Yuzuru Niibe,[1] Joe Y. Chang,[2] Hiroshi Onishi,[3] Joseph Salama,[4]

TABLE 1: Niibe-Onishi-Chang classification.

Favorable	Intermediate		Unfavorable
	Relatively favorable	Relatively unfavorable	
Oligorecurrence Site no. 1-2 NSCLC (brain and adrenal gland) Colon and rectum cancer (lung and liver) Renal cell cancer	*oligo-recurrence* site no. 1-2 breast cancer (bone, lung, and liver) SCLC (brain) site no. 3–5 NSCLC (brain and adrenal gland) colon and rectum cancer (lung and liver) renal cell cancer	*oligo-recurrence* site no. 3–5 breast cancer (bone, lung, and liver) SCLC (brain)	*Oligometastases* and *oligo-recurrence* pancreatic cancer (any site) melanoma (any site) sarcoma (any site)
	sync-oligometastases site no. 1-2 NSCLC (brain and adrenal gland) colon and rectum cancer (lung and liver) renal cell cancer	*sync-oligometastases* site no. 3–5 NSCLC (brain and adrenal gland) colon and rectum cancer (lung and liver) breast cancer (bone, lung, and liver)	*polymetastases*

PRIMARY	METASTATIC SITE
LUNG-NSCLC	ADRENAL, BRAIN
LUNG-SCLC	BRAIN
PROSTATE	BONE
COLORECTAL	LIVER
CERVIX	BONE

FAVORABLE PRIMARY

- Hormone Receptor Positive Breast Ca
- ALK/EGFR/ ROS Positive Lung Ca
- Prostate Ca
- Thyroid Ca
- RCC

Treatment options for Oligometastatic diseases

- **SBRT**
- **RFA**
- **SURGERY**
- **BRACHYTHERAPY**
- **INTRA ARTERIAL EMBOLIZATION**
- **COMBINING WITH IMMUNOTHERAPY**

REVIEW

Journal of Surgical Oncology 2008;98:202–206

2008

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]*

- In patients with widespread metastases, a state of induced oligometastases may be generated with effective systemic therapy to eradicates the majority of metastatic deposits.
- Residual tumor foci in such patients are attributable to the presence of cells that are resistant to cytotoxic agents, hormonal deprivation and/or targeted agents.
- Oligometastatic state is a window of opportunity where focal therapy to known sites of gross disease may be beneficial.
- Patients who develop metachronous and synchronous pulmonary and hepatic metastases have shown good outcomes following resection .

- Targets tumors with minimal margins
- High ablative dose per fraction delivering 6–10 times the standard daily amount of radiotherapy (5–22 Gy) in each dose
- Significantly shortens course of RT from 7 weeks of daily treatments to 3–10 treatments over 1–3 weeks,
- No delay in Systemic therapy
- Better technology
- Good number of studies

- **SBRT refers to an emerging radiotherapy procedure that is highly effective in controlling early stage primary and oligometastatic cancers at locations throughout the abdominopelvic and thoracic cavities, and at spinal and paraspinal sites.**

- **The major feature that separates SBRT from conventional radiation treatment is the delivery of large doses in a few fractions, which results in a high biological effective dose BED**

Radiobiology of SBRT

2017

Repair

LONGER TIME RADIATION EXPOSURE HINDERS THE REPAIR MECHANISM

Repopulation

SHORTER DURATION TREATMENT RULES OUT REPOPULATION

Vascular Damage/ Reoxygenation Massive vascular destruction no/minimal perfusion

Re-distribution No cells exist to migrate from one phase to other

Abscopal Effect

Two mechanistic explanations have been proposed to account for the abscopal effect: the induction of cytokines, eliciting augmented tumor surveillance, tumor growth inhibition and tumoricidal effects and/or the activation of the immune system.
Evidence in experimental models suggests that the abscopal effect is tumor specific and is in part immune mediated and that T cells are required to mediate distant tumor inhibition induced by radiation

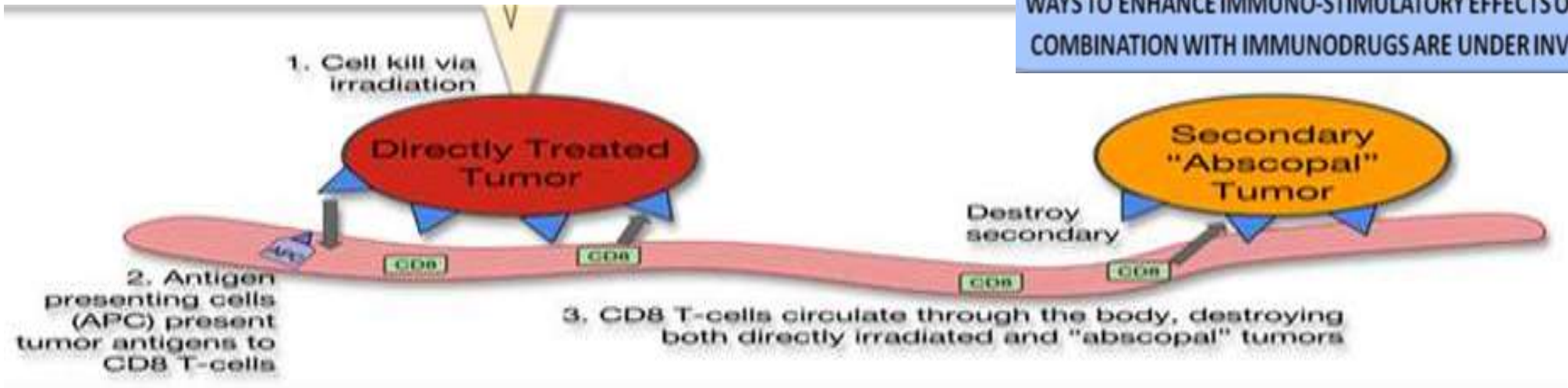
SBRT INDUCES IMMUNOGENIC REACTION
THAT IS NOT SEEN IN CONVENTIONAL FRACTIONATION.

VERY HIGH DOSE CAUSES MASSIVE DAMAGE OF CANCER CELLS
THAT LEADS TO MASSIVE RELEASE OF ANTIGENS BY CANCER CELLS.

RELEASED MASSIVE ANTIGENS LEADS TO 'T' CELL SENSITIZATION
EFFECTOR T CELLS KILL TUMOR CELLS AFTER RECOGNITION.

INCREASE IN T-CELL PRIMING IN DRAINING LYMPH NODES
LEADING TO ERADICATION OF THE PRIMARY & METASTATIC TUMORS.

WAYS TO ENHANCE IMMUNO-STIMULATORY EFFECTS OF RADIATION
COMBINATION WITH IMMUNODRUGS ARE UNDER INVESTIGATION.



Oligometastases: Patient selection for local treatment

Patient-related factors

- **Age**
- **Performance status**
- **Organ function**
- **Patient preferences**

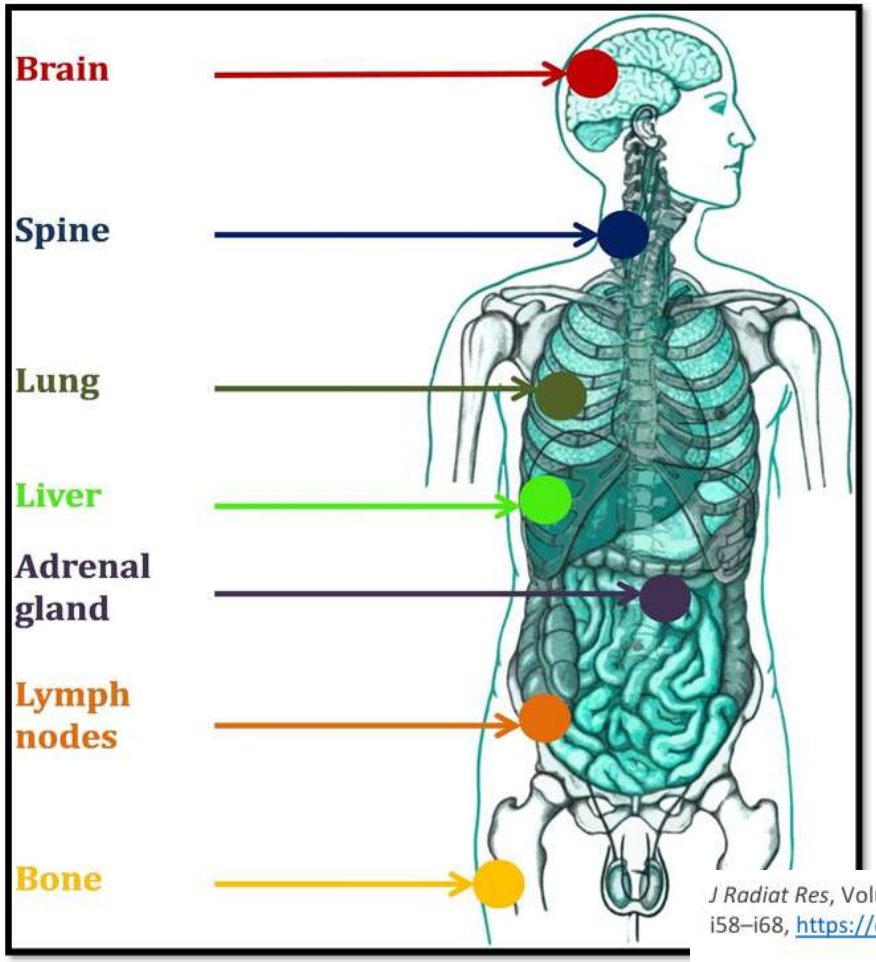
Tumour-related factors

- **Location**
- **Size**
- **Proximity to vessels/critical organs**

Treatment-related factors

- **Availability of expertise**
- **Cost**
- **Waiting list**

Metastatic sites addressed with stereotactic RT



J Radiat Res, Volume 57, Issue S1, August 2016, Pages i58–i68, https://doi.org/10.1093/jrr/rrw006.

OXFORD UNIVERSITY PRESS

Factors to keep in mind while treating Oligo metastatic disease:

- **Treatment of both Primary and Metastatic site**
- **Treatment of only Metastatic site**

Primary Sites from where Oligometastasis happens:

- **Breast**
- **Lung**
- **Prostate**
- **Colorectal**

Sites where Oligimetastasis happens :

- **Brain**
- **Spine**
- **Adrenal**
- **Liver**

Oligometastatic Breast cancer

- **Local Therapy**
- **Ablative/Sx treatment of metastatic disease**

JOURNAL OF CLINICAL ONCOLOGY | ORIGINAL REPORT

2009

Breast Cancer With Synchronous Metastases: Survival Impact of Exclusive Locoregional Radiotherapy

Romuald Le Scodan, Denise Stevens, Etienne Brain, Jean Louis Floiras, Christine Cohen-Solal,

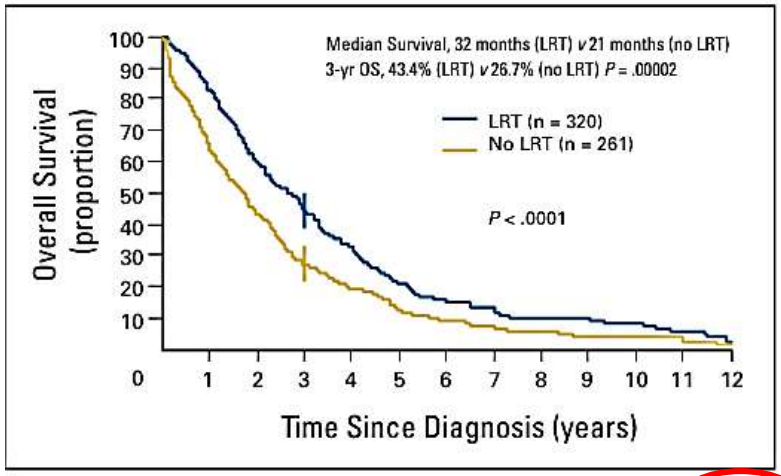


Fig 1. Survival curves according to locoregional treatment (LRT) in the entire population. OS, overall survival.

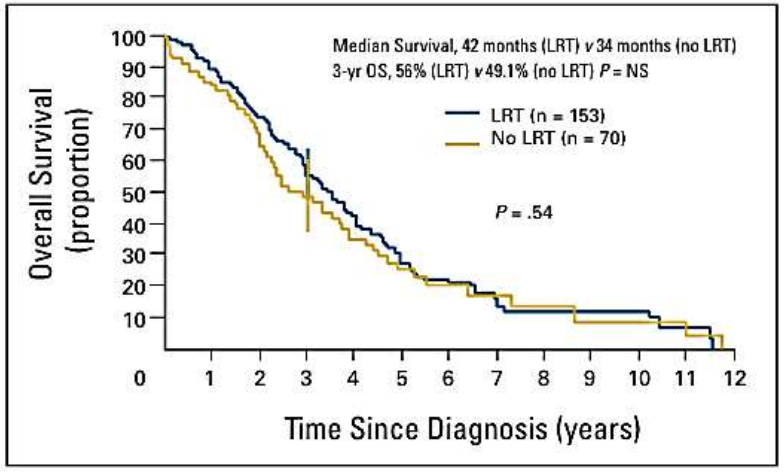


Fig 3. Survival curves according to locoregional treatment (LRT) for patients with bone metastases alone. OS, overall survival.

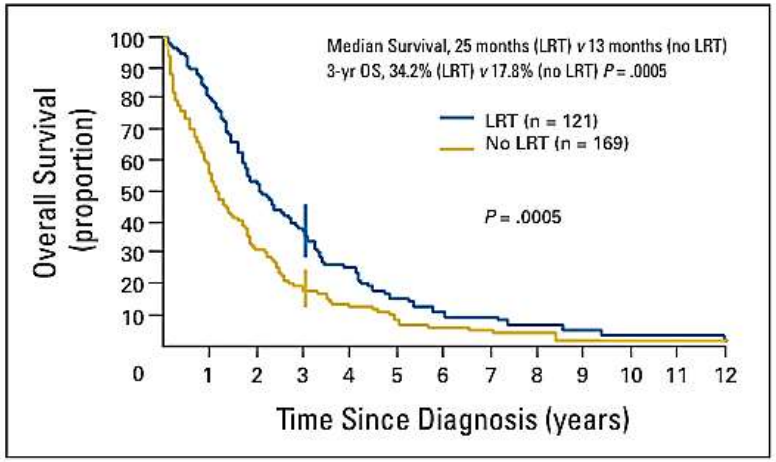


Fig 2. Survival curves according to locoregional treatment (LRT) for patients with visceral metastases. OS, overall survival.

- **Locoregional treatment (LRT), mainly Locoregional Radiation (LRR), associated with improved survival in breast ca with synchronous metastases.**
- **Exclusive LRR represent an active alternative to surgery.**

2021

REVIEW

IJC

Oligometastatic breast cancer: Are we there yet?

Maha AlSendi[1] | David O'Reilly[1] | Youssef H. Zeidan[2] | Catherine M. Kelly[1]

- Patients with de novo OMBC and (1-3) bone-only lesions consider SBRT
- Patients with de novo OMBC with visceral involvement, initial Systemic Therapy is more appropriate to assess disease biology.
- Surgical resection or RFA can be considered for single lesions if the goal is to achieve local control.
- For induced OMD after ST, SBRT can be considered in patients with long disease-free interval, small (≤3 cm) and few lesions (1-3) where complete ablation is possible and toxicity is low.

Treatment Strategies for Oligometastatic Breast Cancer

Breast Cancer (WJ Gradishar, Section Editor) | Published: 23 August 2021

Volume 22, article number 94, (2021) Cite this article

Currently, selection criteria to consider for ablative therapy include

1. longer disease-free interval from diagnosis to metastasis (>2 years),
2. fewer metastases,
3. fewer involved organs.

TABLE 2 List of Prospective trials evaluating the role of SBRT in OMBC

Reference	Setting	Intervention	Radiotherapy dose/volumes	Primary endpoints
CLEAR, Jeong J, NCT03750396	Oligometastatic breast cancer recurrence (>12 months). All sites of metastases	Surgery or radiotherapy or radiofrequency on metastasis	Total radiation dose and fractions are various according to metastatic lesions (57-97.5 Gy/6-10 fractions)	PFS
NRG Oncology, NCT02364557	Limited MBC	SBRT ± surgery	Radiosurgery in 1, 3 or 5 fractions (according to discretion of physician)	PFS, OS
STEREO-SEIN, NCT02089100	De novo oligometastatic breast cancer, excluding triple negative subtype	SBRT	SBRT with radical intent to all sites of metastases	PFS
MSKCC, NCT03808337	Metastatic NSCLC or TNBC	SBRT concurrently to systemic therapy	SBRT with a minimum BED of 48 Gy to all sites	PFS
NCI, NCT00182793	Stage IIIb-IV BC	RT on primary site or site of metastasis (oligometastatic), high dose chemotherapy autologous stem cells transplant	Tomotherapy on site of disease with standard fractionation	5-year RFS, 5-year OS
CIMER, NCT04220476	Oligometastatic, luminal BC	SBRT (Immune-SBRT every 48 hours)	SBRT every 48 hours to all sites of metastases, 50 Gy in five fractions	ORR, PFS, OS
MSKCC, NCT03808662	Oligoprogressive NSCLC or TNBC	SBRT	SBRT 9-10 Gy × 3 or 10 Gy × 5 fractions given every other day to all sites	PFS

REVIEW ARTICLE

2022

Oligometastasis in breast cancer—current status and treatment options from a radiation oncology perspective

Marc D. Piroth[1] · David Krug[2] · Petra Feyer[3] · René Baumann[4] · Stephanie Combs[5] · Marciana-Nona Duma[6] ·

Table 2 Randomized controlled trials of local treatment in patients with oligometastatic breast cancer

–	OLIGOMA (NCT04495309)	NRG-BR002 (NCT02364557)	STEREO-SEIN (NCT02089100)	OMIT (NCT04413409)	Chinese Academy of Sciences (NCT04646564)	LARA NCT04698252
Sample size	564 patients	402 patients (phase II/III)	280 patients	172 patients	170 patients	74 patients
Maximum number of metastatic lesions	5	4	5 (≤ 10 cm/≤ 30 ml)	3 (only lung or liver metastases, < 5 cm)	5 (≤ 5 cm)	4 (bone/lung/liver), ipsilateral cervical or contralateral axillary metastases
Setting	Any treatment line	First-line setting, maximum of 1 year after diagnosis of MBC	First-line metastatic setting, HR positive	First-line setting	Metachronous recurrence > 3 months after surgery	Stable disease after 6 months of systemic therapy; HR positive, HER2 negative
Type of local therapy	Radiotherapy	Radiotherapy, surgery	Radiotherapy	Surgery	Radiotherapy	Radiotherapy, surgery, radiofrequency ablation
Primary endpoint	PFS + QoL	PFS/OS	PFS	OS	PFS	PFS

Predictors for a good prognosis after SBRT

- favorable biological subtype (hormone receptor positive, HER2 negative),
- solitary metastasis,
- bone-only metastasis,
- long metastasis-free interval.

Oligometastatic Ca Lung

Contents lists available at ScienceDirect

Lung Cancer

journal homepage: www.elsevier.com/locate/lungcan

2013

Radical treatment of synchronous oligometastatic non-small cell lung carcinoma (NSCLC): Patient outcomes and prognostic factors

Gwendolyn H.M.J. Griffioen[a,*], Daniel Toguri[b], Max Dahele[a], Andrew Warner[b],

- Radical treatment of selected NSCLC patients with 1–3 synchronous metastases can result in favorable 2-year survivals.
- Favorable outcomes associated with : small radiotherapy treatment volumes or resected disease had the best OS

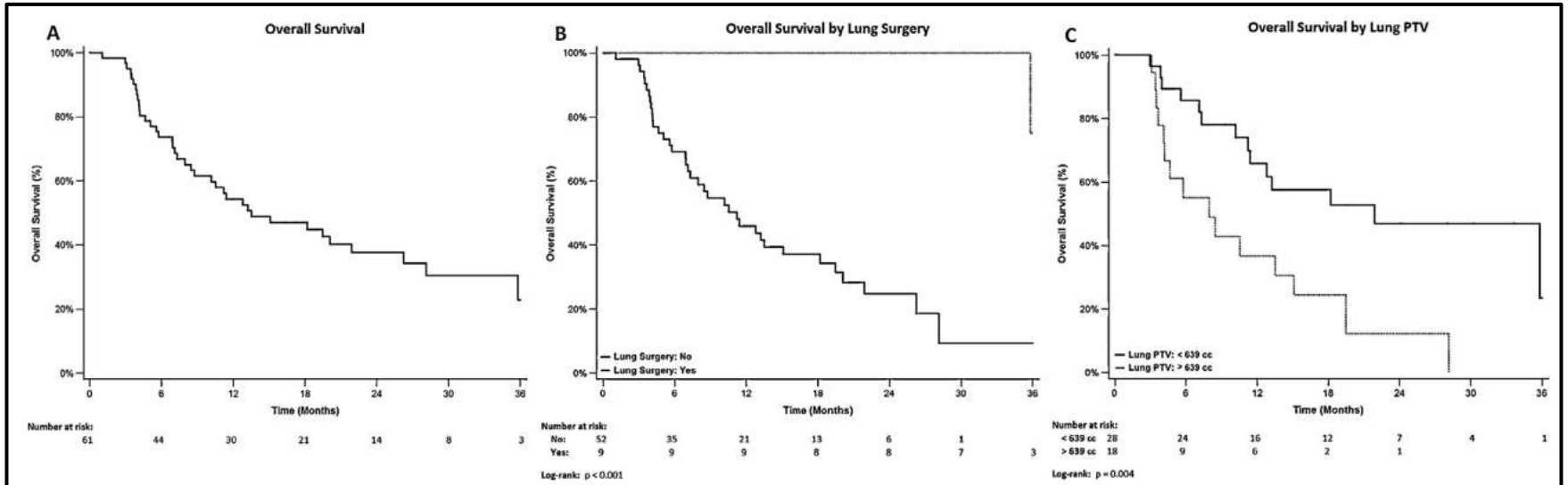


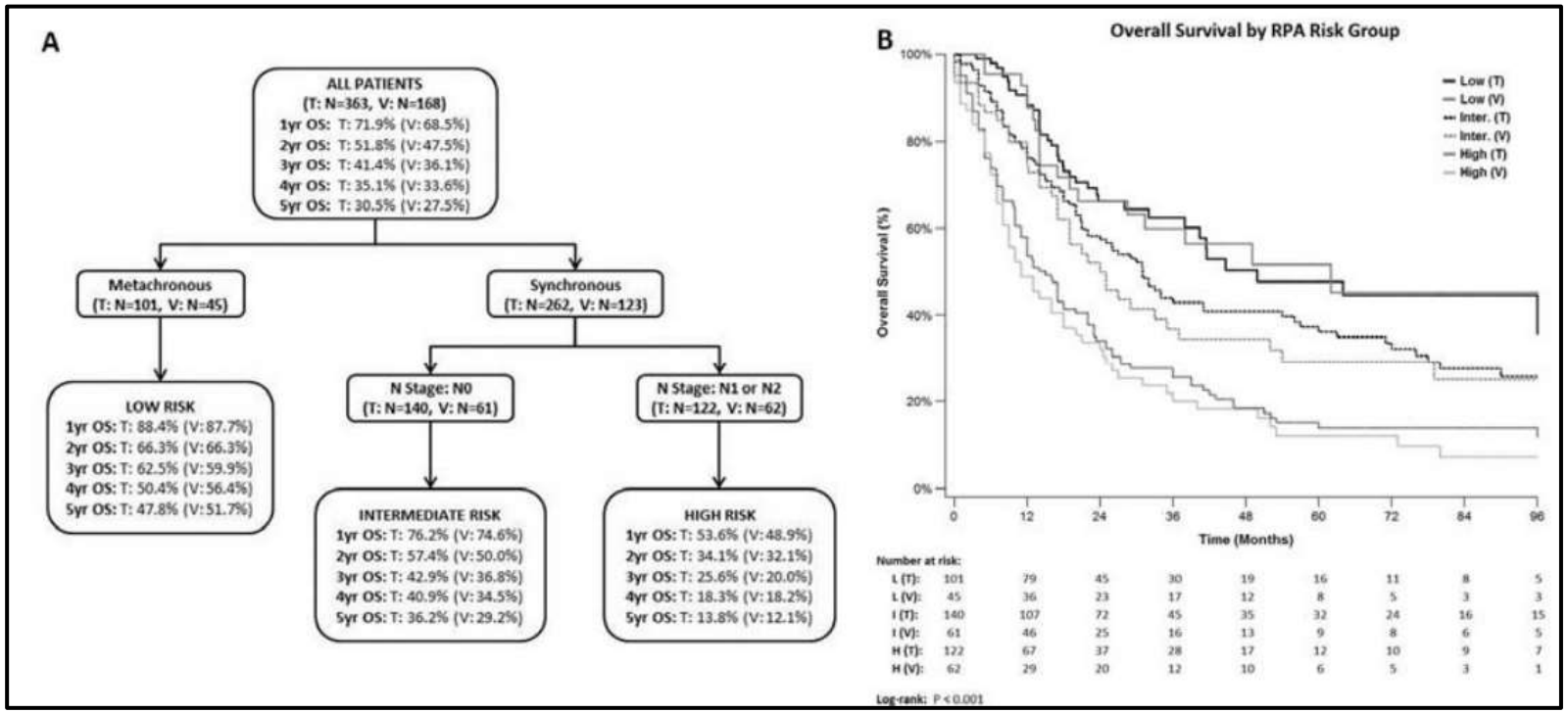
Fig. 1. Kaplan–Meier curves of overall survival of all patients (A), those undergoing lung surgery (B), and by planning target volume (PTV) of the intrathoracic tumor (C).

2014

Accepted Manuscript

An Individual Patient Data Meta-Analysis of Outcomes and Prognostic Factors after Treatment of Oligometastatic Non-Small Cell Lung Cancer

Allison B. Ashworth , Suresh Senan , David A. Palma , Marc Riquet , Yong Chan



Factors predictive of OS :

- **synchronous versus metachronous metastases (*P* < .001), N-stage (*P* = .002), and adenocarcinoma histology (*P* = .036)**

In RPA, 3 risk groups identified:

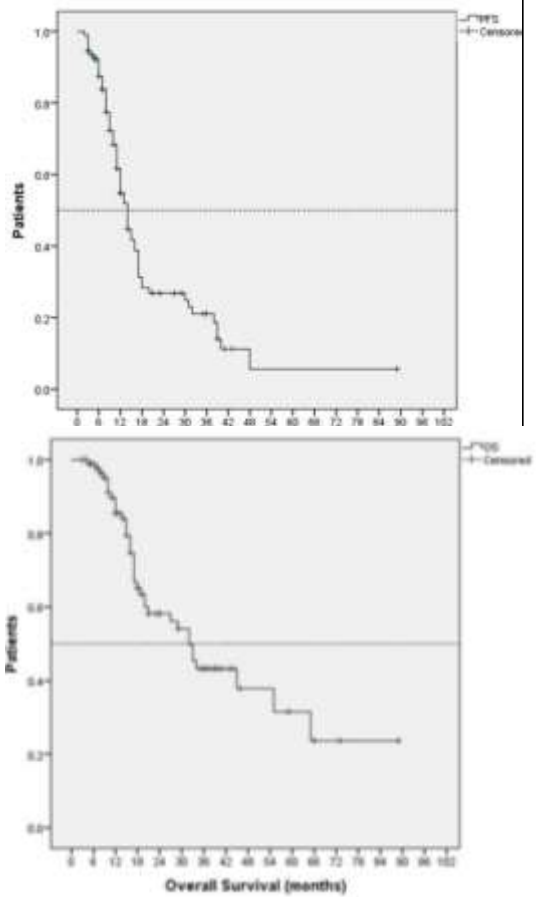
- **low-risk, metachronous metastases (5-year OS, 47.8%);**
- **intermediate risk, synchronous metastases and N0 disease (5-year OS, 36.2%)**
- **high risk, synchronous metastases and N1/N2 disease (5-year OS, 13.8%).**

2017

Lung Cancer
Volume 112, October 2017, Pages 134-139

Outcome of radical local treatment of non-small cell lung cancer patients with synchronous oligometastases

Margriet Kwint [a], Iris Walraven [a], Sjaak Burgers [b], Koen Hartemink [c], Houke Klomp [c]



- median follow-up 35 months.
- Median PFS 14 months , median OS 32 months
- 1- and 2-year OS rates 85% and 58% and the 1- and 2-year PFS rates 55% and 27%, respectively.
- Radical local treatment of a selected group of NSCLC patients with good performance status presenting with synchronous oligometastatic disease resulted in favorable long-term PFS and OS

2022

International Journal of Radiation Oncology*Biology*Physics
Volume 112, Issue 2, 1 February 2022, Pages 361-375

Clinical Investigation

American Radium Society Appropriate Use Criteria for Radiation Therapy in Oligometastatic or Oligoprogressive Non-Small Cell Lung Cancer

Arya Amini MD *, Vivek Verma MD †, Charles B. Simone II MD ‡ §, Indrin J. Chetty PhD ‖,

Consolidative RT is appropriate for patients with oligometastatic disease:

- (3 or fewer sites, after first-line systemic therapy)
- not progressed after 2 to 3 months, or 2 to 3 cycles of chemotherapy,
- all sites are amenable to radiation.

Summary of studies of radiation therapy

Trial (yr and design)	Patients (Mets per patient)	RT technique	Definitive thoracic therapy / Systemic therapy	Median progression free survival (months)	Overall survival (OS)	Toxicity
Gomez et al (2016) P	49 (≤3)	Various	Yes /All received induction chemo	11.9 (LCT) vs 3.9 (no LCT)	Median OS not reached	20vs 8.3% G3
Iyengar et al. (2014) P	24 (≤6)	SBRT	NA / All progressed through 1st line chemo, all received erlotinib	14.7	Median 20.4 months	2 G3 RT-related toxicities
Griffioen et al. (2013) R	61 (≤3)	Various	Yes / 84% chemo	6.6	2 years 38%	6.6% G3
Cheruvu et al. (2011) R	96 (≤8)	SBRT	NA /70% chemo	NA	2 years 25% (oligorecurrence) vs 43% (de novo oligometastases)	NA
Hasselle et al. (2012) R	25 (≤5)	SRS/ SBRT	NA / 76% prior to SBRT	7.6	1 year 81.1%	8% G3
SABR COMET trial: (2020) P	99 (≤5)	Standard-of-care:(arm 1),SOC plus SABR (arm 2)		5-year PFS rate was not reached in arm 1 and 17.3% in arm 2	5-year OS :17.7% -arm 1 versus 42.3% - arm 2	no Gr 2-5 adverse events, no differences in QOL between arms

Oligometastatic NSCLC: Ongoing trials

Trial	Arms	Primary outcome
OMEGA (Phase 3)	Standard treatment plus local ablative therapy (surgery and/ or radiotherapy) or to standard treatment alone	Overall survival
SARON (Phase 3)	Efficacy and safety of SABR in addition to chemotherapy compared to standard treatment alone	OS/PFS/QOL/Toxicity/ Local control
HALT (Phase 3)	SBRT plus TKI compared to TKI alone beyond oligo-progression in patients with oncogene-driven NSCLC	PFS/OS/toxicity/pattern of disease progression
OITROLC (Phase 3) optimal timing for radiation therapy	Upfront chemo plus concurrent radiotherapy to the primary and all metastatic sites versus a consolidative approach after two cycles of induction chemotherapy	Response rate / toxicity / QOL

Oligometastatic Ca Prostate

47th ICRO, NRSMC&H Kolkata, 12th -13th April 2025

2013

frontiers in ONCOLOGY

ORIGINAL RESEARCH ARTICLE
published: 22 January 2013
doi: 10.3389/fonc.2012.00215

Stereotactic body radiation therapy in the treatment of oligometastatic prostate cancer

*Kamran A. Ahmed[1†], Brandon M. Barney[2†], Brian J. Davis[2], Sean S. Park[2], Eugene D. Kwon[3] and Kenneth R. Olivier[2]**

Purpose/objective(s): To report outcomes and toxicity for patients with oligometastatic (≤5 lesions) prostate cancer (PCa) treated with stereotactic body radiation therapy (SBRT). **Materials/methods:** Seventeen men with 21 PCa lesions were treated with SBRT between February 2009 and November 2011. All patients had a detectable prostate-specific antigen (PSA) at the time of SBRT, and 11 patients (65%) had hormone-refractory (HR) disease. Treatment sites included bone ($n = 19$), lymph nodes ($n = 1$), and liver ($n = 1$). For patients with bone lesions, the median dose was 20 Gy (range, 8–24 Gy) in a single fraction (range, 1–3). All but two patients received some form of anti-androgen therapy after completing SBRT. **Results:** Local control (LC) was 100%, and the PSA nadir was undetectable in nine patients (53%). The first post-SBRT PSA was lower than pre-treatment levels in 15 patients (88%), and continued to decline or remain undetectable in 12 patients (71%) at a median follow-up of 6 months (range, 2–24 months). Median PSA measurements before SBRT and at last follow-up were 2.1 ng/dl (range, 0.13–36.4) and 0.17 ng/dl (range, <0.1–140), respectively. Six (55%) of the 11 patients with HR PCa achieved either undetectable or declining PSA at a median follow-up of 4.8 months (range, 2.2–6.0 months). Reported toxicities included one case each of grade 2 dyspnea and back pain, there were no cases of grade ≥3 toxicity following treatment. **Conclusion:** We report excellent LC with SBRT in oligometastatic PCa. More importantly, over half the patients achieved an undetectable PSA after SBRT. Further follow-up is necessary to assess the long-term impact of SBRT on LC, toxicity, PSA response, and clinical outcomes.

2017

Habl *et al. BMC Cancer* (2017) 17:361
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BMC Cancer

RESEARCH ARTICLE Open Access

Oligometastases from prostate cancer: local treatment with stereotactic body radiotherapy (SBRT)

Gregor Habl[1,2*], Christoph Straube[1,2], Kilian Schiller[1,2], Marciana Nona Duma[1,2], Markus Oechsner[1,2]

Conclusion :

- **SBRT of bone metastases is a highly effective therapy with an excellent risk-benefit profile.**
- **PFS limited due to high distant failure rate,**
- **Biomarkers besides PSA for identifying purely oligometastasized patients**
- **SBRT offers high local cancer control rates in bone oligometastases of PC and can delay modification of systemic treatment.**

SYSTEMATIC REVIEW **2020**

Stereotactic body radiotherapy (SBRT) in metachronous oligometastatic prostate cancer: a systematic review and meta-analysis on the current prospective evidence

[1]MICHAEL YAN, [1]NIKITHA MOIDEEN, [2]VANESSA FREITAS BRATTI and [1]FABIO YNOE DE MORAES

Table 2. Study Outcomes

First Author	Local Control	Local Recurrence-Free Survival		Androgen Deprivation-Free Survival		Biochemical Recurrence-Free Survival		Progression-Free Survival		Treatment Escalation-Free Survival		Grade ≥ 3 Toxicity (%)
	Overall (%)	2 year (%)	Median (mo)	2 year (%)	Median (mo)	2 year (%)	Median (mo)	2 year (%)	Median (mo)	2 year (%)	Median (mo)	
Muacevic (14)	97	96	NR									0
Decaestecker (13)	100			60	25			35	19			0
Kneebone (16)						16	11					0
Jereczek-Fossa (15)	90	84	NR					30	17			0
Ost* (3)	100			44	21	28	10					0
Siva†(19)		93	NR	48								3 -VCF
Gomez-Iturriaga (17)	89											0
Bowden†(20)										52	27	0
Pasqualetti (18)	96				29							0
Philips* (4)	99					57	NR	58	NR			0
Quantitative Synthesis (95% CI)	**97 (94–100)**	**88.7 (5.4) ‡**		**52 (41–62)**	**24.7 (20.1–29.2)**	**33 (11–55)**		**39 (24–54)**				

CONCLUSION :
SBRT is effective in controlling

- **local disease burden in metachronous OMPC**
- **delaying clinical progression**
- **initiation of ADT.**

Associated with minimal significant toxicities.

Oligometastatic Colorectal ca

2018

SBRT for LC (local control) in CRC liver and lung oligometastases

- **For liver LC rates : 50% - 100% after 1 year and 32% - 91% after 2 years.**
- **BED range 40.5–262.5 Gy .**

- **For lung LC rates : 62% - 92% after 1 one year and from 53% - 92% after 2 years.**
- **BED range 51.3–262.5 Gy.**

Conclusions: SBRT of oligometastatic CRC offers high LC with low morbidity and toxicity

2018

- **1- and 5-year local recurrence rates 13.6% and 44.3, respectively.**
- **2-and 5-year OS rates 76.1% and 35.9%, respectively.**

- **A biological equivalent dose of ≥120 Gy led to an improvement in local recurrence.**

- **Lung metastasis was associated with improved local recurrence.**

- **Larger total PTV size (≥17.5 cc) associated with worse OS, PFS, and Widespread progression.**

Brain Metastasis

- **Most common intracranial neoplasm.**
- **Most common intracranial metastatic site is brain parenchyma.**
- **Advances in systemic cancer management has lead to higher incidence of brain metastasis.**
- **Advanced imaging techniques and early suspicion has made it possible to detect oligo brain metastasis.**

Brain Metastasis

Primaries metastasizing to Brain:

- Lung 39-56%
- Breast 13-30%
- Melanoma 6-11%
- Renal 2-6%
- Colorectal 3-4%

Conventional Management of Brain Metastases

- Medical decompression -Steroids, Mannitol, Glycerol
- 1-3 lesions, resectable - Surgical resection + Whole Brain Radiotherapy
- Multiple/unresectable lesions - Whole Brain Radiotherapy

Decision of Management depends upon:

- Performance status
- Nature of metastasis
- Primary site
- Extracranial disease status
- Expected survival

	KPS	Age	No. of Brain Mets	Extracranial Mets	Tumor Subtype
Lung	Y	Y	Y	Y	-
Breast	Y	Y	-	-	Y
Melanoma	Y	-	Y	-	-
RCC	Y	-	Y	-	-
GI	Y	-	-	-	-

Brain Metastasis

Evolving end points

- Survival
- Brain tumour control
- Quality of life
- Cognitive function

WBRT

Pros:

- Most chemotherapy drugs do not cross BBB
- Metastases to CNS can be multifocal
- Reduced steroid dependence

Cons:

- Cognitive decline
- Lack of survival benefit

Surgery + RT vs. RT alone

Trial	N	Endpoint	Surgery +RT	RT Alone	p value	Ref
Patchell et al	48	OS Local failure	40weeks 20%	15weeks 52%	<0.02 <0.02	NEJM, 1990
Noordjik et al	63	OS FIS	10months 7.5 months	6months 3.5 months	0.04 0.06	IJROBP, 1994
Mintz et al	84	OS FIS %	5.6% 32%	6.3months 32%	NS NS	Cancer, 1996

For single brain metastases, 2 out of 3 trials have shown surgical resection+ RT has OS & LC advantage over RT alone.

Surgery vs SRS

- **No randomized trials**
- **Similar LC rates 80-90% (when either one is combined with WBRT)**

Brain Metastasis

Surgery + SRS vs Surgery alone

Lancet Oncol 2017

Post-operative stereotactic radiosurgery versus observation for completely resected brain metastases: a single-centre, randomised, controlled, phase 3 trial

Anita Mahajan, Salmaan Ahmed, Mary Frances McAleer, Jeffrey S Weinberg, Jing Li, Paul Brown, Stephen Settle, Sujit S Prabhu, Frederick F Lang,

- 1-3 metastases;
- resection cavity =<4cm
- SRS done within 30 days of resection; dose=12 - 16Gy
- Median FU =11.1 months
- Median 12-month freedom from local recurrence significantly better for SRS (72%) vs observation (43%)

SURGERY + SRS vs SURGERY + WBRT

Postoperative stereotactic radiosurgery compared with whole brain radiotherapy for resected metastatic brain disease (NCCTG N107C/CEC·3): a multicentre, randomised, controlled, phase 3 trial

Lancet Oncol 2017

Paul D Brown, Karla V Ballman, Jane H Cerhan, S Keith Anderson, Xiomara W Carrero, Anthony C Whitton, Jeffrey Greenspoon, Ian F Parney,

- One resected brain metastases
- Resection cavity <= 5cm
- SRS (12-20Gy) vs. WBRT(30Gy/10#/2weeks or 37.5Gy/15#/3 weeks)
- Significantly longer cognitive –deterioration free survival with SRS (median 3.7 vs 3 months)
- Significantly poorer surgical bed control at 6 months with SRS (80.4%) vs WBRT (87.1%)
- Median OS similar :12.2 months (SRS) vs 11.6 months (WBRT)

SRS + WBRT vs WBRT

Whole brain radiation therapy with or without stereotactic radiosurgery boost for patients with one to three brain metastases: phase III results of the RTOG 9508 randomised trial

- OS benefit for single unresectable brain met (no breast cancer patients analysed in this subgroup),
- LC benefit for 2-3 brain mets,
- steroid-usage lowered with SRS.
- Subset analysis shows OS benefit for single brain met, NSCLC, RPA class I, tumor < 2cm
- For breast cancer patients with 1-3 brain metastases, presence of extracranial disease, TNBC & having >1 brain metastasis predicts for worse OS.

SRS + WBRT vs SRS

Phase 3 Trials of Stereotactic Radiosurgery With or Without Whole-Brain Radiation Therapy for 1 to 4 Brain Metastases: Individual Patient Data Meta-Analysis

Arjun Sahgal, MD,* Hidefumi Aoyama, MD, PhD,† Martin Kocher, MD,‡

- Meta-analysis of 3 randomised trials
- SRS alone 51%; SRS+WBRT 49%
- For patients <50 years age, 1-4 brain mets, SRS has OS advantage over SRS + WBRT
- Patients with single metastases had significantly better OS than with 2-4 metastases.
- Local control significantly better with WBRT in all age groups

Immediate vs delayed RT for asymptomatic oligo brain mets

A randomized phase III trial of stereotactic radiosurgery (SRS) versus observation for patients with asymptomatic cerebral oligo-metastases in non-small-cell lung cancer

S. H. Lim[1], J. Y. Lee[1], M.-Y. Lee[1], H. S. Kim[1], J. Lee[1], J.-M. Sun[1], J. S. Ahn[1], S.-W. Um[2], H. Kim[2],

- **Metastatic NSCLC;**
- **1-4 asymptomatic brain metastases**
- **SRS (N=49) followed by chemotherapy vs upfront chemotherapy (N=49)**
-
- **No difference in OS / time to CNS progression**

Dose protocols-Brain Metastases

SRS: (RTOG 90-05)

- **<2cm – 24Gy**
- **2.1- 3 cm – 18Gy**
- **3.1-4 cm – 15 Gy**

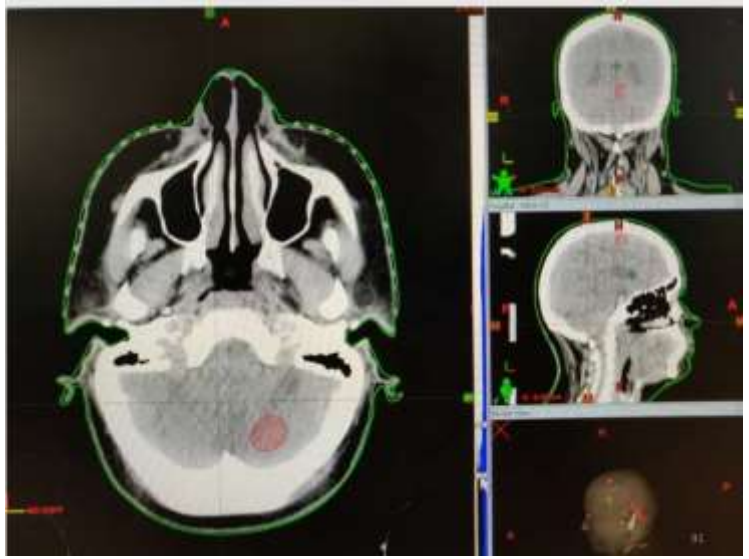
FSRT:

- **30Gy/5#**
- **40Gy/10#**

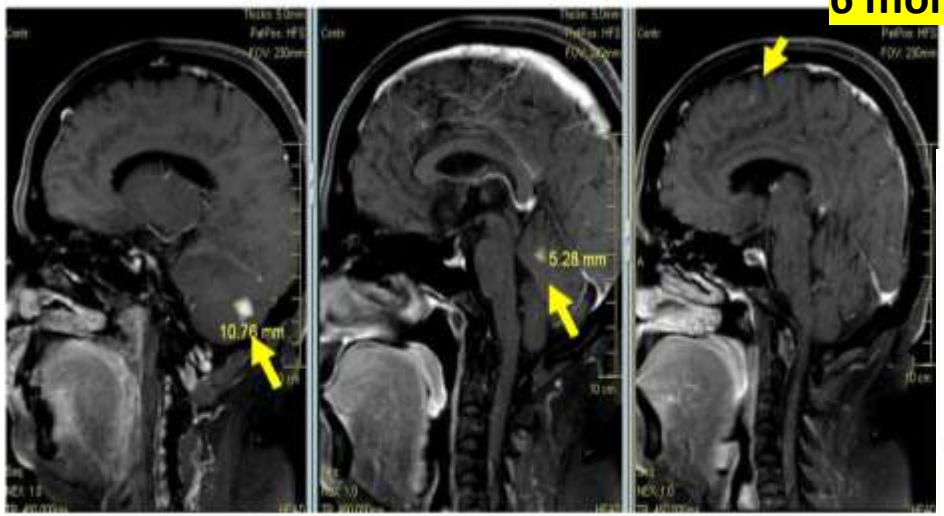
- **Target=tumour+ small margin (1-2 mm)**
- **Unlike conventional RT, dose distribution is deliberately made inhomogeneous, by covering periphery of tumor by 50-80%, rather than 95%.**
- **This ensures high dose at the centre of the tumour as well as rapid fall off of dose beyond the periphery of the tumour.**

Brain Metastases

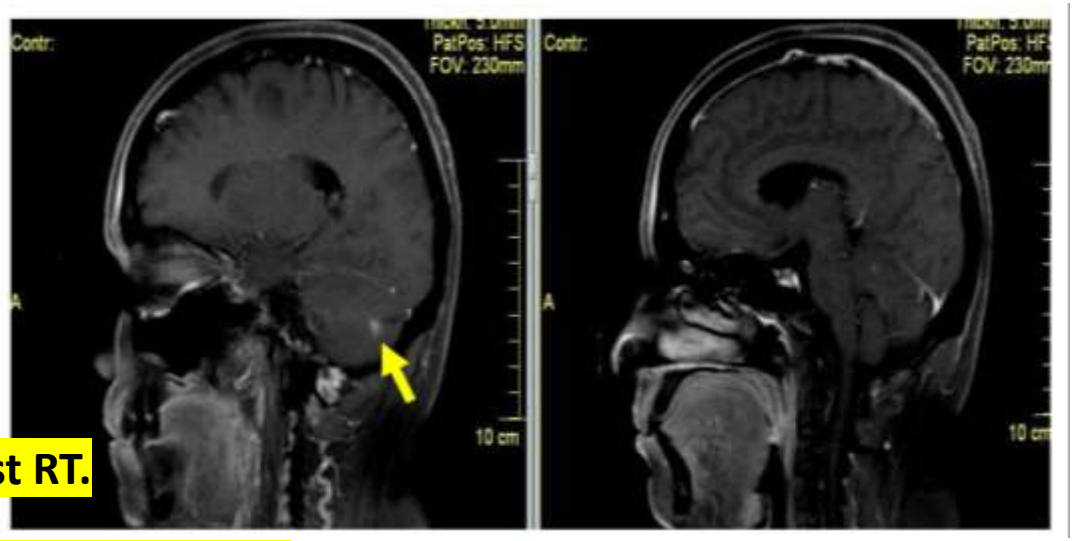
At presentation



6 months post RT



24 months post RT.



Summary of trials

	Outcome	Level of evidence
SRS+WBRT Vs WBRT alone	Improve survival in single metastatic disease with KPS>=70	Level I
	Improve local control	Level II
	Improve survival in multiple metastatic disease	Level III
SRS Vs WBRT+SRS	Equivalent survival	Level II
	improves cognitive function	Level II
	Higher out of field metastatic potential	Level II
Surgery+WBRT Vs SRS+/- WBRT	Equivalent survival in <3cm	Level II
SRS Vs WBRT	Better than WBRT up to 3 mets in survival	Level III
WBRT with hippocampal sparing +memantine	Delayed cognitive decline	Level II+

SBRT for Oligomets to Spine

2012

CME ASTRO

International Journal of Radiation Oncology biology • physics

www.redjournal.org

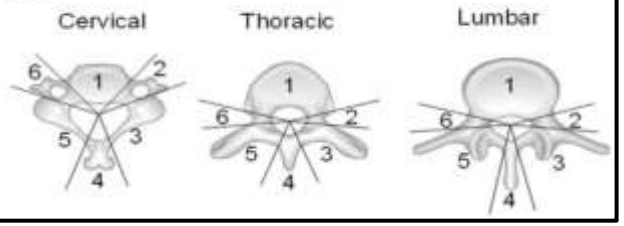
Clinical Investigation: Central Nervous System Tumor

International Spine Radiosurgery Consortium Consensus Guidelines for Target Volume Definition in Spinal Stereotactic Radiosurgery

Brett W. Cox, MD,*,1 Daniel E. Spratt, MD,*,1 Michael Lovelock, PhD,†

Vertebra divided into 6 sectors:

- 1- Vertebral body
- 2- L pedicle
- 3- L transverse process
- 4- Spinous process
- 5- R transverse process
- 6- R pedicle



General Principles - Criteria for SBRT

- Inclusion:
  - Spinal or paraspinal metastasis
    - Radioresistant histology
    - Failure of prior EBRT
    - Oligometastatic or bone-only metastatic disease
  - 3 or fewer involved spine segments
  - Stable spinal column
    - Calculate Spinal Instability Neoplastic Score (SINS score)
  - Low grade epidural disease
    - Utilize Bilsky grade
  - Limited extra-spinal systemic disease
  - Life expectancy >3 months
  - KPS > 40-50
- Exclusion:
  - Unstable spine requiring stabilization
  - Previous SBRT to lesion
  - EBRT within 90 days
  - Worsening neurologic deficit
  - Inability to lie flat on table
  - <3-month life expectancy
  - Spinal canal compromise >25%
  - Inability to have MRI
  - Receiving radiosensitizing chemotherapy

Bilsky Grade	Details
0	Absence of epidural disease
1a	Impingement without deformation of thecal sac
1b	Impingement and deformation of the thecal sac
1c	Deformation of the thecal sac with abutment of the spinal cord
2	Epidural spinal cord compression with visible cerebrospinal fluid (CSF)
3	Epidural spinal cord compression without visible CSF

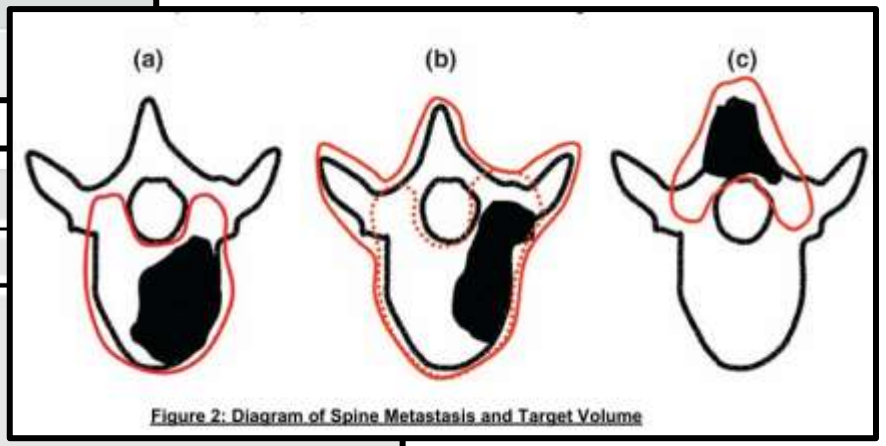


Figure 2: Diagram of Spine Metastasis and Target Volume

Table 4 Summary of contouring guidelines for GTV, CTV, and PTV in spinal stereotactic radiosurgery

Target volume	Guidelines
GTV	• Contour gross tumor using all available imaging • Include epidural and paraspinal components of tumor
CTV	• Include abnormal marrow signal suspicious for microscopic invasion • Include bony CTV expansion to account for subclinical spread • Should contain GTV • Circumferential CTVs encircling the cord should be avoided except in rare instances where the vertebral body, bilateral pedicles/lamina, and spinous process are all involved or when there is extensive metastatic disease along the circumference of the epidural space without spinal cord compression
PTV	• Uniform expansion around CTV • CTV to PTV margin ≤3 mm • Modified at dural margin and adjacent critical structures to allow spacing at discretion of the treating physician unless GTV compromised • Never overlaps with cord • Should contain entire GTV and CTV

Oligomets to Adrenal

Stereotactic body radiation therapy for adrenal metastases: a retrospective review of a noninvasive therapeutic strategy

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Table 1. Patient and disease characteristics.

Patient number	Lesion number	Primary	Time to metastases (months)	Additional sites of disease	Size of adrenal lesion (cm³)	Rx dose (Gy)/fraction number	Prior surgery
1	1	HCC	8	None	123.6	16.0/1	No
	2	HCC	8	–	115	16.0/1	No
2	1[†]	HCC	22	None	85.9	0.1/1	Yes
3	1	NSCLC	4	Brain	46.8	15.0/1	No
4	1[†]	NSCLC	28	Brain, lung	5	22.0/1	Yes
5	1[†]	NSCLC	12	None	15.9	18.0/1	Yes
6	1[†]	NSCLC	0	Brain	6.4	36.0/3	No
	2[†‡]	NSCLC	0	–	68.8	24.0/3	No
7	1[†]	SCLC	0	Brain	63.8	27.0/3	No

[†]Pathology proved metastatic lesions.
[‡]Patient received previous external beam radiotherapy to a dose of 40 Gy, 16 months prior to SBRT.
HCC: Hepatocellular carcinoma; NSCLC: Non-small-cell lung cancer; SBRT: Stereotactic body radiation therapy; SCLC: Small-cell lung cancer.

Executive summary

Adrenal metastases

- Detection is on the rise with advanced imaging techniques in routine follow-up of primary malignancies.
- The majority of metastases are adenocarcinomas, with the lung as the most common primary site.
- Adrenal metastases often occur in the setting of widespread metastatic disease, but up to 25% represent the only site of metastasis.

Local therapy

- Both open and laparoscopic adrenalectomy, in the setting of solitary adrenal gland metastases, can result in long-term disease-free survival.
- Radiofrequency ablation is an additional treatment option shown to induce local control, but long-term studies are lacking.

Stereotactic body radiation therapy for the treatment of adrenal metastases

- Stereotactic body radiation therapy can be safely delivered in single fraction (16 Gy) or hypofractionated treatment regimens (27 Gy over three fractions).
- A radiographic response was observed in nearly half of the treated lesions, although the majority of lesions eventually failed locally within 1 year.
- Median overall survival from stereotactic body radiation therapy was 8 months.

2020

König et al. Radiation Oncology (2020) 15:30
https://doi.org/10.1186/s13014-020-1480-0

Radiation Oncology

RESEARCH Open Access

Stereotactic body radiotherapy (SBRT) for adrenal metastases of oligometastatic or oligoprogressive tumor patients

Laila König[1,2,3*], Matthias F. Häfner[1,2,3], Sonja Katayama[1,2,3], Stefan A. Koerber[1,2,3], Eric Tonndorf-Martini[1,2,3,4]

Table 1 Patient, tumor and treatment characteristics *(Continued)*

	Total number of patients (%)
Yes	9 (32.1%)
Chemotherapy	6 (66.7%)
Targeted therapy	2 (22.2%)
Immunotherapy	1 (11.1%)
	Mean
Total dose (Gy)	47.3
Fractions (n)	9
Single dose (Gy)	5.6
BED_{10} (Gy)	73.5
Prescribed isodose line (%)	89
Median GTV volume (range) in cm^3	27
Median PTV volume (range) in cm^3	111

SBRT for adrenal metastases resulted in promising local control with only mild toxicity

2022

Contents lists available at ScienceDirect

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Outcomes and toxicities in oligometastatic patients treated with stereotactic body radiotherapy for adrenal gland metastases: A multi-institutional retrospective study

A. Baydoun [a], H. Chen [b], I. Poon [b], S. Badellino [

Number	47
Primary Site (nb (%))	
• Colorectal	3 (6.4)
• Hepatocellular	1 (2.1)
• Kidney	4 (8.5)
• Melanome	1 (2.1)
• NSCLC	30 (63.8)
• Prostate	1 (2.1)
• Sarcoma	2 (4.3)
• SCLC	4 (8.5)
• Stomach	1 (2.1)
Histology (nb (%))	
• Adenocarcinoma	26 (55.3)
	4 (8.5)
	4 (8.5)
	6 (12.8)
	7 (14.9)
ent (nb (%))	
	26 (55.3)
	14 (29.8)
	5 (10.6)
	0 (0)
	2 (4.2)
Metastasis Timing	
• Synchronous	21 (44.7)
• Early metachronous (6–24 months)	5 (10.6)
• Late metachronous (>24 months)	21 (44.7)
Guckenberger et al. Classification	
• Synchronous Oligometastatic	21 (44.7)
• Metachronous	16 (34.0)
• Oligorecurrence	
• Metachronous oligoprogression	8 (17.0)
• Repeat Oligorecurrence	2 (4.3)

Dose (Gy) / Number of fractions	(nb of lesions(%))
• 24–28/3–5	3 (5.3)
• 30–35/3–5	27 (47.4)
• 40–45/4–5	10 (17.5)
• 50/5	9 (15.8)
• 50/10	8 (14.0)

Oligometastasis to Liver

2018


Mahadevan et al. Radiation Oncology (2018) 13:26
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Radiation Oncology

RESEARCH Open Access

Stereotactic Body Radiotherapy (SBRT) for liver metastasis – clinical outcomes from the international multi-institutional RSSearch® Patient Registry

Anand Mahadevan[1*], Oliver Blanck[2,3], Rachelle Lanciano[4], Anuj Peddada[5], Srinath Sundararaman[6]

- Median tumor volume 40 cm3
- median SBRT dose 45 Gy (12–60 Gy) delivered in a median of 3 fractions [1–5].
- Median OS greater for patients with CRC (27 mo), breast (21 mo) and gynecological (25 mo) metastases compared to lung (10 mo), other gastro-intestinal (GI) (18 mo) and pancreatic (6 mo) primaries ($p < 0.0001$).
- Smaller tumor volumes (< 40 cm3) correlated with improved OS (25 months vs 15 months $p = 0.0014$).
- BED10 ≥ 100 Gy was also associated with improved OS (27 months vs 15 months $p < 0.0001$).
- No difference in LC based on histology of primary tumor

Table 2 – Dose prescription for SBRT in 3 fractions recommended according to lesion size.

Lesion size	Prescription dose
≤3 cm	48–60 Gy
>3–6 cm	60–75 Gy

Table 3 – Recommended OARs dose constraints for SBRT of liver metastasis in 3 fractions.

OAR	Dose-volume limits
Healthy liver (total liver volume minus cumulative GTV)	>700 cm^3 at <15 Gy[a]
Stomach, duodenum, small intestine	D 3 cm^3 at <21 Gy[b]
Both kidneys	V 15 Gy at <35%
Spinal cord	D 1 cm^3 at <18 Gy
Heart	D 1 cm^3 at <30 Gy
Rib	D 30 cm^3 at <30 Gy

[a] Volume of healthy liver >1000 cm^3.
[b] Distance by GTV >8 mm.

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Why discussion about Oligometstatic disease is necessary??

- **Improved imaging (PET-CT)**
- **Increased availability of locoregional treatments (radiofrequency, stereotactic radiotherapy, vertebroplasty, minimally invasive surgery)**
- **Availability of more efficacious systemic treatments (targeted therapies for oncogene addicted NSCLC, immunotherapy)**
- **Multidisciplinary approach**

2019

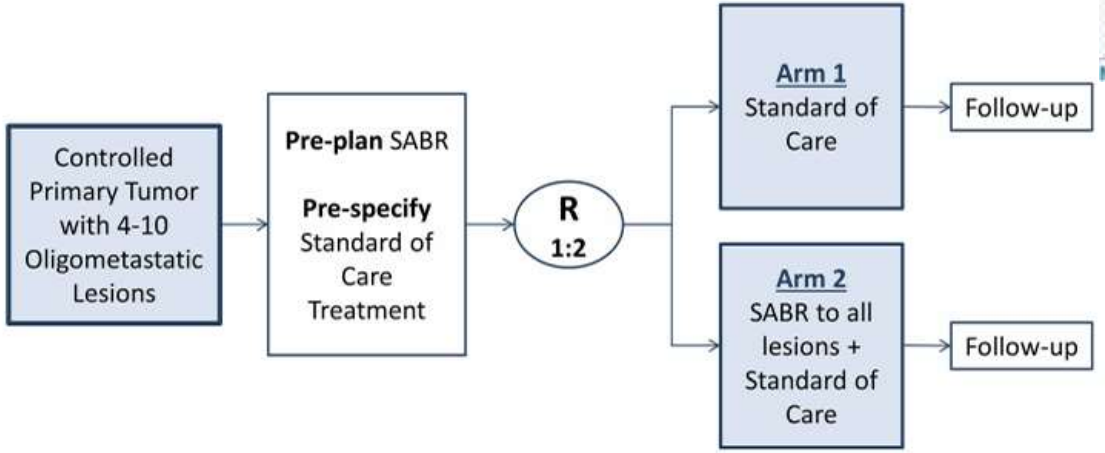
Palma et al. BMC Cancer (2019) 19:816
https://doi.org/10.1186/s12885-019-5977-6

BMC Cancer

STUDY PROTOCOL Open Access

Stereotactic ablative radiotherapy for the comprehensive treatment of 4–10 oligometastatic tumors (SABR-COMET-10): study protocol for a randomized phase III trial

David A. Palma[1*], Robert Olson[2], Stephen Harrow[2], Rohann J. M. Correa[1], Famke Schneiden[3]



Primary endpoint:

- **Overall Survival** Defined as time from randomization to death from any cause

Secondary endpoints

- **Progression-free survival** Defined as time from randomization to disease progression at any site or death Time to development of new metastatic lesions
- **Quality of life** : Assessed with the Functional Assessment of Cancer Therapy
- **Toxicity**: Assessed by the National Cancer Institute Common Toxicity Criteria (NCI-CTC) version 4 **for each organ treated (e.g. liver, lung, bone)**

Table 1 Allowable doses and fractionations*

Number of Fractions	Preferred Dose	Acceptable Doses	Major Deviation
1	20 Gy	16–24 Gy	< 16 Gy or > 24 Gy
3	30 Gy	24–33 Gy	< 24 Gy or > 33 Gy
5	35 Gy	25–40 Gy	< 25 Gy or > 40 Gy

*Note that centres should use doses that standard at their institutions based on the specific clinical situation, within these guidelines. For example, if the standard dose for a 2.5 cm brain metastasis is 24 Gy in 3 fractions, which is an 'acceptable dose', that should be used instead of the 'preferred dose'

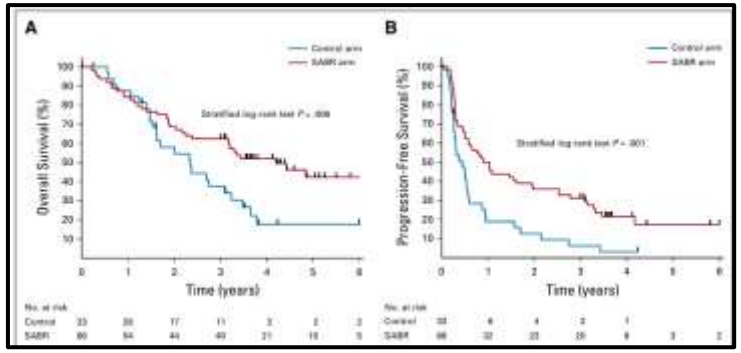
Stereotactic Ablative Radiotherapy for the Comprehensive Treatment of Oligometastatic Cancers: Long-Term Results of the SABR-COMET Phase II Randomized Trial

David A. Palma, MD, PhD[1]; Robert Olson, MD, MSc[2]; Stephen Harrow, MBChB, PhD[3]; Stewart Gaede, PhD[1];

2020

Characteristic	Arm, No. (%) Control (n = 33)	SABR (n = 66)
Median age, years (IQR)	69 (64-75)	67 (59-74)
Sex		
Male	19 (58)	40 (61)
Female	14 (42)	26 (39)
Site of original primary tumor		
Breast	5 (15)	13 (20)
Colorectal	9 (27)	9 (14)
Lung	6 (18)	12 (18)
Prostate	2 (6)	14 (21)
Other	11 (33)	18 (27)

Characteristic	Arm, No. (%) Control (n = 33)	SABR (n = 66)
No. of metastases		
1	12 (36)	30 (46)
2	13 (40)	19 (29)
3	6 (18)	12 (18)
4	2 (6)	2 (3)
5	0 (0)	3 (5)
Location of metastases (n = 191 lesions)		
Adrenal	2 (3)	7 (6)
Bone	20 (31)	45 (35)
Liver	3 (5)	16 (13)
Lung	34 (53)	55 (43)
Other[a]	5 (8)	4 (3)



Conclusion:

- with longer-term follow-up, SABR achieved a **22-month median OS benefit** in patients with a controlled primary tumor and 1-5 oligometastases
- Even with SABR, many patients **progress with new metastases**, likely be cause of the presence of occult micrometastatic disease at presentation, but some can receive **salvage therapy with repeat SABR**.

Randomized evidence of ablative therapy

Study	Primary	Number	Protocol	Results
MDACC/ Colorado Trial: Phase 2 (Gomez, Lancet Oncology 2016)	NSCLC	49	Local consolidation Vs maintenance therapy or observation	PFS better in SABR + mChemo arm. (p=0.0054)
UT Southwestern Trial, Phase 2 (Iyenger et al JAMA Oncol 2018)	NSCLC	29	mChemo Vs SABR+ mChemo	PFS better in SABR+ mChemo (p=0.01)
STOMP Trial Phase 2 (Ost et al J Clin Oncology 2018)	Prostate	62	Surveillance vs metastatic directed therapy	PFS better in LCT arm (p=0.0054)
ORIOLE (Radwan et al BMC Cancer 2017)	Prostate	54	Observation Vs SABR	PFS better in SABR arm (p=0.03)

Selection of favourable candidates

- **Tumour Biology and growth kinetics.**
-
- **Clinical scenario:**

I. **Oligometastasis at presentation.**

II. **Residual oligometastasis after systemic therapy.**

I. **Relapsed oligometastases after curative locoregional therapy.**

RTOG SBRT Protocol

RADIATION THERAPY ONCOLOGY GROUP

RTOG 0631

PHASE II/III STUDY OF IMAGE-GUIDED RADIOSURGERY/SBRT FOR LOCALIZED SPINE METASTASIS

RADIATION THERAPY ONCOLOGY GROUP

RTOG 0438

A PHASE I TRIAL OF HIGHLY CONFORMAL RADIATION THERAPY FOR PATIENTS WITH LIVER METASTASES

original report

Safety and Efficacy of a Five-Fraction Stereotactic Body Radiotherapy Schedule for Centrally Located Non–Small-Cell Lung Cancer: NRG Oncology/RTOG 0813 Trial

- **Dose Prescription**
- **Target coverage**
- **OAR Dose constraints.**

Published in final edited form as:

Int J Radiat Oncol Biol Phys. 2015 November 15; 93(4): 757–764. doi:10.1016/j.ijrobp.2015.07.2260.

NRG Oncology RTOG 0915 (NCCTG N0927): A Randomized Phase II Study Comparing 2 Stereotactic Body Radiation Therapy (SBRT) Schedules for Medically Inoperable Patients with Stage I Peripheral Non-Small Cell Lung Cancer

2018

NRG-BR001 Protocol

- **3-4 mets or 2 mets within 5 cm amenable to SBRT from breast, lung, or prostate cancer**
- **ECOG performance 0-2**

- **Mets categorized into 7 anatomic locations with initial starting dose:**

1. **Bone/Osseous (BO)- 30Gy/10#**
2. **Spinal/Paraspinal (S/P)- 30Gy/10#**
3. **Peripheral Lung (Pl)-45Gy/3#**
4. **Central Lung (CL)- 50Gy/5#**
5. **Abdominal/Pelvic (AP)- 45Gy/3#**
6. **Mediastinal/Cervical (MC)- 50Gy/5#**
7. **Liver (L))- 45Gy/3#**

Table 1 Selection of currently recruiting prospective clinical trials on oligometastasis

Name/type	Primary	Intervention	Prior treatment	Endpoint	# of met	Status/expected completion
STOP-NSCLC RCT II	NSCLC	1:2 SOC *vs.* SBRT to all oligo-progressive lesions	CHT ≤6 weeks prior	PFS	≤5	Recruiting/04/2020
SABR-COMET (15) RCT II	NSCLC	1:2 SOC *vs.* SOC + SABR to all sites	CHT ≥4 weeks prior	OS	≤5	Active, not recruiting/11/2020
SARON-trial RCT III	NSCLC	Platinum-based doublet CHT *vs.* SOC + conventional RT + SABR	None	OS	≤3	Recruiting/08/2022
HALT-trial RCT II/III	NSCLC	2:1 continued TKI + SBRT *vs.* continued TKI only	TKI	PFS	≤3	Recruiting/03/2021
SABR for oligometastases non-randomized II	Any	SABR to all sites for all patients	CHT ≥2 days prior	Tox, QoL	≤5	Recruiting/10/2022
STOMP-trial (16) RCT II	Prostate	1:1 active surveillance *vs.* surgery/SBRT	Surgery/RT or both	ADT-free survival	≤3	Ongoing/05/2017
CORE-trial RCT II/III	NSCLC, prostate, breast	1:1 SOC *vs.* SOC + SBRT	CHT ≥4–6 months prior	PFS	≤3	Recruiting/10/2021
NRG BR002-trial RCT II/III	Breast	1:1 SOC *vs.* SOC + SBRT or surgery	≤6 months first line CHT	PFS - OS	≤2	Recruiting/12/2022
SABR-SCAN-trial RCT II	CRC	1:1 immediate *vs.* delayed SABR of pulmonary metastases	No prior RT allowed	PFS	≤3	Recruiting/06/2019

#, number. NSCLC, non-small cell lung cancer; RCT, randomized controlled trial; SOC, standard of care; SBRT, stereotactic body radiation therapy; PFS, progression free survival; OS, overall survival; SABR, stereotactic ablative radiotherapy; CRC, colorectal cancer; TKI, tyrosine-kinase-inhibitor.

Oligometastasis : take home messages for a Rad Onc:

- Patients with Oligo metastatic disease represents a heterogonous group.
- Effective systemic and supportive therapies has increased life expectancy of metastatic patients requiring better QoL.
- Local High Dose RT can give durable Local control in patients with
  - Good PS
  - Longer Disease free interval
  - Smaller size mets and lesser no. of organ involvement
- Statistically significant Survival benefit with treatment of oligometastatic disease is still not proven for many subsites.
- Choice of treatment should be personalized, determined by various factors including patient preferences and clinical scenario .

Thank You.....