Patient Selection for advanced and complex techniques

Stereotactic Treatments

Re-Irradiation

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Radiation Oncologist

Objectives

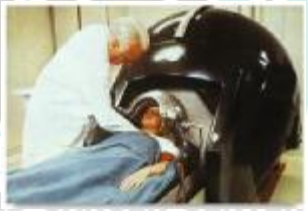
- Hopefully at the end of this session we will be able to have a rough idea on:
  - When to think about SRS or SBRT
  - When to decide to treat a patient who is re-treated
- Quick review on nature and radiobiology of stereotactic treatments
- Indications on SRS and SBRT
  - What evidences say

SRS – root word!

- Stereotactic Radio-Surgery
  - Stereo: Solid
    - Stare – Strong - سترگ
  - Taxis: Arrangement
    - Ataxia – taxidermy
    - Originated from tag – tac (touch)
      - Tag - Tactile

SRS - history

- 1951; Lars Leksell invented the term
  - Goal which is beautifully achieved was: “a method for a non invasive destruction of intra cranial lesions, inaccessible or unsuitable for open surgery”
  - GK
  - 179 Co sources
- 1974; CT scan

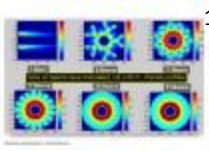


First GK-SRS acoustic neuroma
Localization anatomy based using 2D images
Physics calculation by hand

FIGURE 1-1. Lars Leksell and his physicist colleague, Bonje Larsson, preparing a patient for SRS with a particle beam accelerator in 1958. (Photo courtesy of L. Dade Lunsford, MD.)

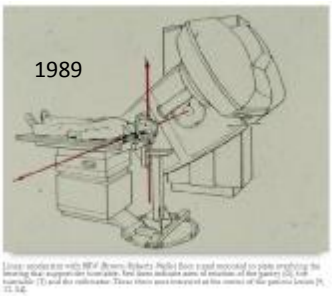
1930
60% Mortality rate of neurosurgery operations

- Advances in CT Scan
- Advances in LINAC based SRS
- Advances in MRI
- Advances in computer systems
- Creastion of 3D treatment planning algorithm



1988
ADVANCES IN RADIATION THERAPY

- 2000 Introduction of micro MLC
- 2002 First patient treated on Tomotherapy system



1989

1999

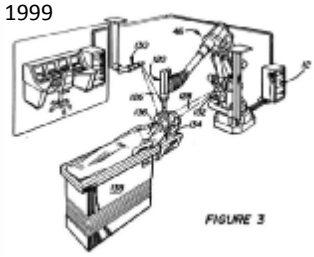


FIGURE 3

Stereotactic Radiation Treatment

- Highly localized
- High dose per fraction
  - >= 6Gy/fr (relatively conservative)
- Small number of fractions
- Potentially ablative
  - Chance of long term response ~ >80%

15/1
18/1
24/1
27/3
30/5

50/5
60/8

RADIOSURGERY FUNDAMENTAL CONCEPT

A touch on radiobiology of SRS - SBRT

- Very rapid reduction in blood flow over the first 24 hours.
  - Vessels length reduction
- Substantial vascular damage —> tumoricidal effect
  - Endothelial damage

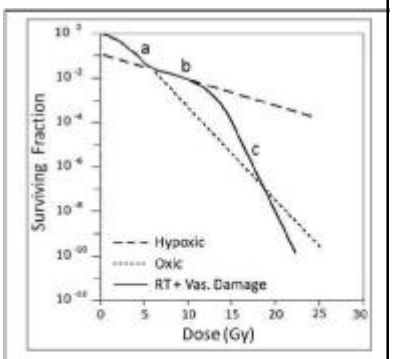


Figure 4
An illustration of how indirect death due to vascular damage could contribute to total clonogenic cell kill in tumors irradiated with large single doses of radiation

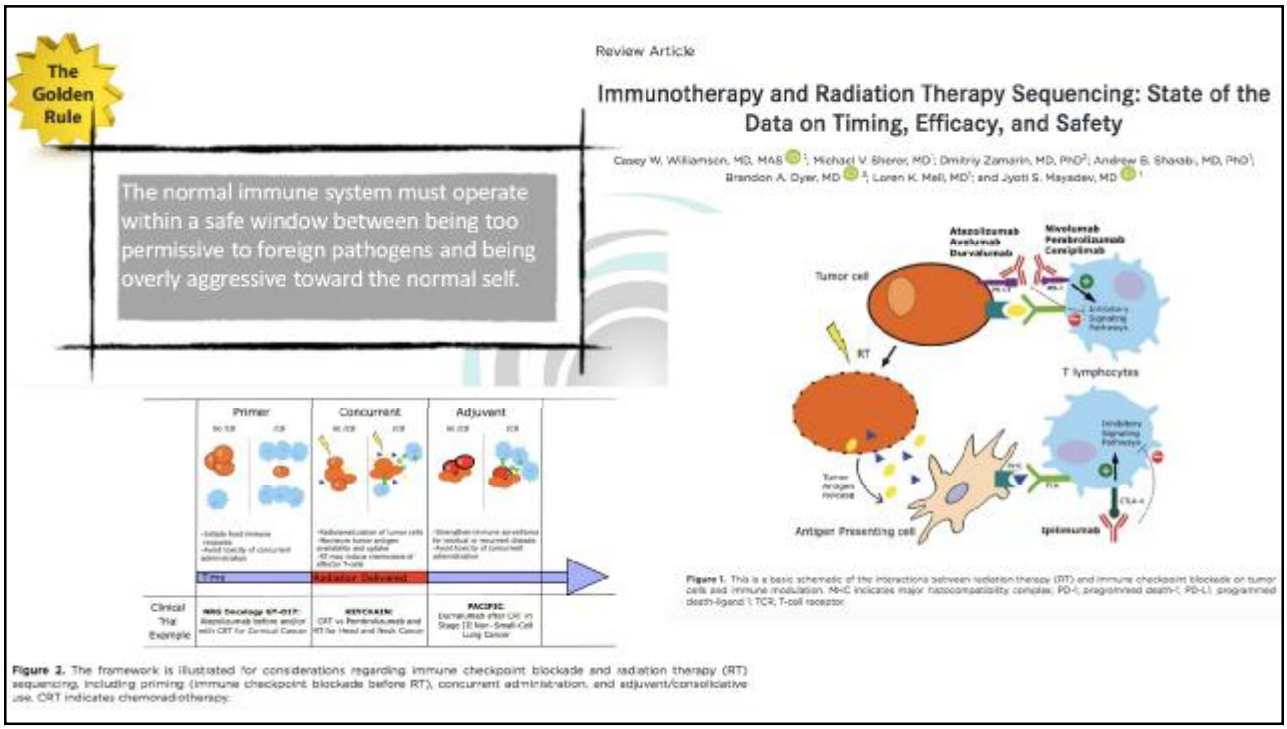
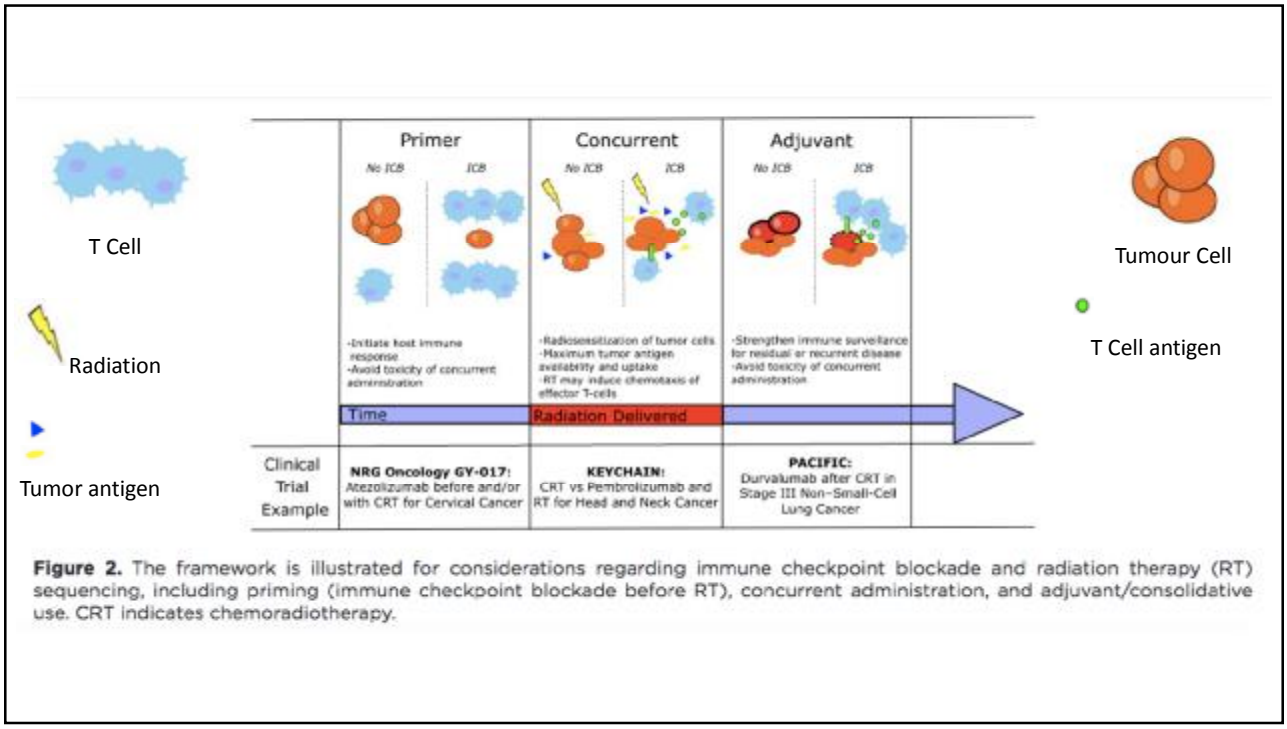


Figure 2. The framework is illustrated for considerations regarding immune checkpoint blockade and radiation therapy (RT) sequencing, including priming (immune checkpoint blockade before RT), concurrent administration, and adjuvant/consolidative use. CRT indicates chemoradiotherapy.



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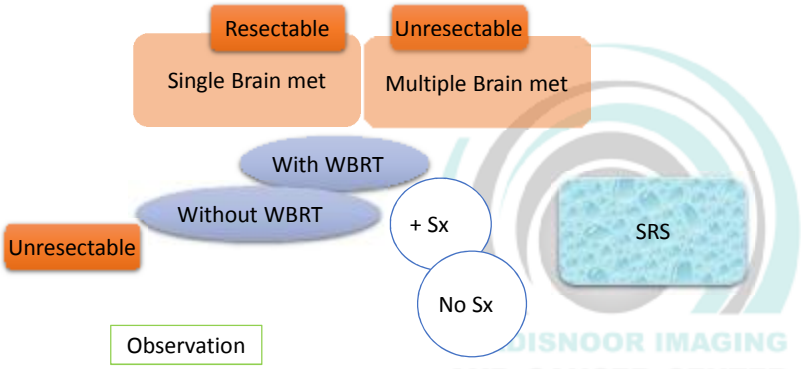
Topics on SRS



Surgery +/- RT

Adjuvant WBRT s/p surgery:
- Decreased the rate of intracranial progression
- Reduced the rate of neurological death
- Did not show a survival benefit

	Patchell et al (1990)	Patchell et al (1998)	EORTC 22952
Patients	48 patients with 1 BM and KPS ≥ 70	95 patients with 1 BM and KPS ≥ 70	359 patients with 1-3 BM and WHO PS ≤ 2
Treatment arms	Surgery + WBRT (36/12) Biopsy + WBRT (36/12)	Surgery + WBRT (50/28) Surgery + observation	Surgery + WBRT (30/10) Surgery + observation SRS* + WBRT SRS* + observation
Results	Surgery improved OS (40w vs 15w) and decreased LR (20% vs 52%)	WBRT did not prolong OS (48w vs 43w) WBRT decreased LR (10% vs 46%) and distant failure (18% vs 70%) WBRT had a lower rate of neurologic death (14% vs 44%)	WBRT did not prolong OS (10.7 mo. vs 10.9 mo.) WBRT decreased overall rate of intracranial progression (48% vs 78 %) and rate of neurologic death
Significance	Adjuvant WBRT improves OS, LR, and QOL	Adjuvant WBRT after surgery does not improve OS but decreases rate of intracranial progression	Same as Patchell 1998, but validated SRS in this setting

20-25/1

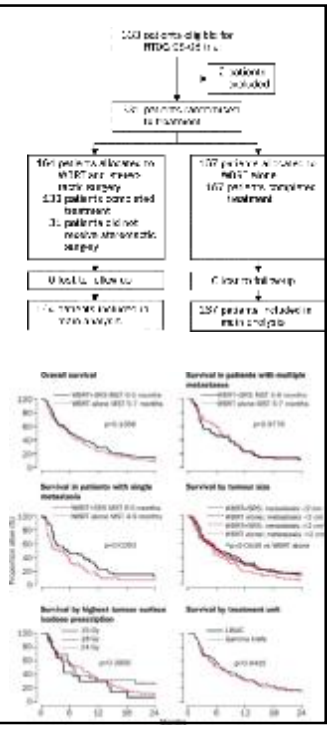
Sx+RT → SOC

Key study: RTOG 9508

WBRT: 37.5 Gy in 15 Fx
SRS: 15-24 Gy per RTOG 9005 protocol

- Randomized to WBRT + observation vs. WBRT + SRS
  - No significant difference in OS (6.5 mo. vs 5.7 mo)
  - SRS improved survival in patients with 1 BM (6.5 mo. vs 4.9 mo.) but not with multiple BM
  - SRS had better LC at 1 year (82% vs 71%) and KPS (43% vs 27%) but did not decrease the rate of neurological death or overall time to progression
  - Established LINAC and GKS as generally equivalent

Take-home point: SRS boost improved LC, KPS, but not OS. Survival benefit noted with single BM.



Multiple brain mets → SRS alone

	JROSG 99-1	Chang et al (2009)	Yamamoto et al (2014)
Patients	132 patients with 1-4 BM and KPS ≥ 70	58 patients with 1-3 BM and KPS ≥ 70	1814 patients total Group A (2-9 BM): 1254 patients Group B (≥10 BM): 560 patients)
Treatment arms	SRS (≤ 2 cm 22-25 Gy; 2-3 cm 18-20 Gy) + observation WBRT (30/10) + SRS*	SRS + observation SRS + WBRT (30/12) SRS dose per RTOG 9005	All got SRS alone
Results	No significant difference in OS (8.0 mo. vs 7.5 mo. w/ WBRT) WBRT increased LC at 1y (89% vs 73%) and distant control (42% vs 64%)) Salvage therapy more frequent after SRS alone (29 v 10)	WBRT more likely to show decline in NCF at 4 mo. (52% vs 24%) WBRT increased LC (100% vs 67%) and distant control (73% vs 45%) at 1y Increased survival in SRS alone (15 mo. vs 6 mo)	No significant difference in OS (6.8 mo vs. 6.9 mo. for group B) Hazard for local recurrence (0.425) and repeat SRS for new lesions (0.732) were significantly lower in group B No difference in incidence of NCF decline (0.994 HR) or neurological death rates (10% vs 9.4% for group B)
Significance	SRS alone is equivalent in survival but overall increased recurrence requires more frequent salvage therapy	WBRT + SRS provides better control but leads to poorer NCF and survival outcomes	Post-SRS outcomes (OS, intracranial relapse, and NCF) were not inferior for patients with ≥10 BM compared to patients with 2-9 BM

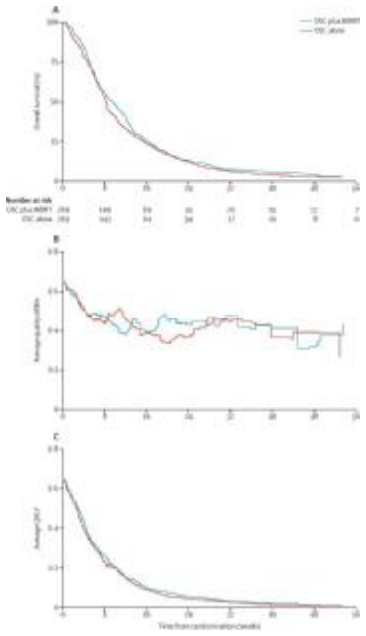
Take-home point

- SRS alone vs SRS + WBRT for multiple BM:
  - Has equivalent if not better OS rates
  - Associated with better neurocognitive outcomes
  - Decreased local and distant control requires more frequent salvage therapy
  - Despite an increased need for salvage treatment, SRS is still cost-effective (Hall et al, 2014)

Equivalent survival with better NCF outcomes has made SRS alone a viable therapeutic option despite higher intracranial relapse rates

- Rades et al (2007) performed a retrospective study of 206 patients with 1-2 BM and concluded no difference in OS or LC

Take home point: no randomized trials comparing SRS to surgery alone but appear to have equivalent survival and LC outcomes with the potential for less toxicity with SRS alone



A non-inferiority trial

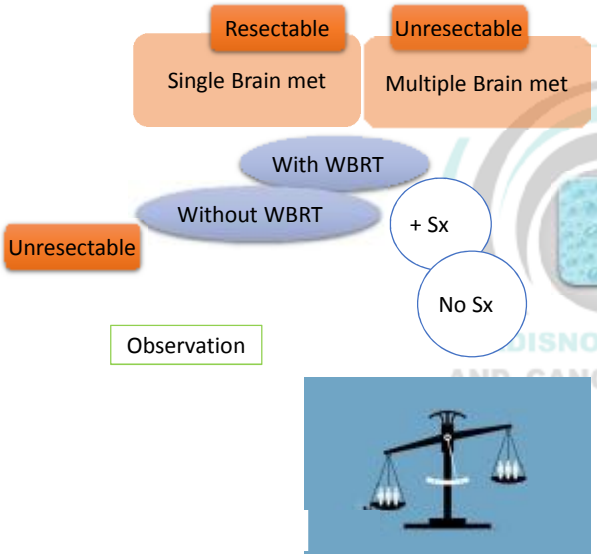
Quartz trial

- 538 patients with BM from NSCLC (not suitable for resection or SRS) randomized to WBRT (20/5) + optimal supportive care (OSC), including dexamethasone, vs. OSC alone
  - No significant difference in OS (65 vs. 57 days for OSC), overall QoL, or steroid use
  - Difference for mean quality adjusted life years (QALYs) was only -1.9 days (OSC+WBRT 43.3 vs. OSC 41.4 days)

Significance: first randomized trial to evaluate utility of WBRT to improve either QoL or survival. Further studies needed but results suggests WBRT may not provide a clinically significant benefit in patients who are not candidates for resection or radiosurgery.

The quality-adjusted life year or quality-adjusted life year (QALY) is **a generic measure of disease burden, including both the quality and the quantity of life lived**.

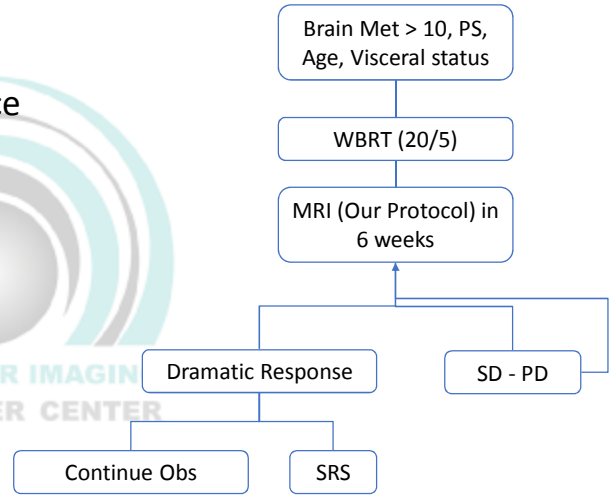
Topics on SRS



- Surgery
  - Rised and uncontrolles ICP
- SRS
  - Safe
  - Minimal side effect if done correctly
  - Very effective

Sara's protocol

- Try to keep WBRT as a later resource
- If really mets > 10-11 and the distribution doesn't make you comfortable for SRS

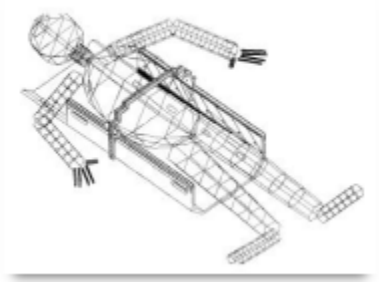


Lars, Dan and Laurent Leksell

- Matthias Greuter (1564-1638)

SBRT

- OligoMetastasis
  - Number of mets
  - Primary histology
  - Progression on systemic disease
  - Systemic disease available or not



1- SBRT Spine

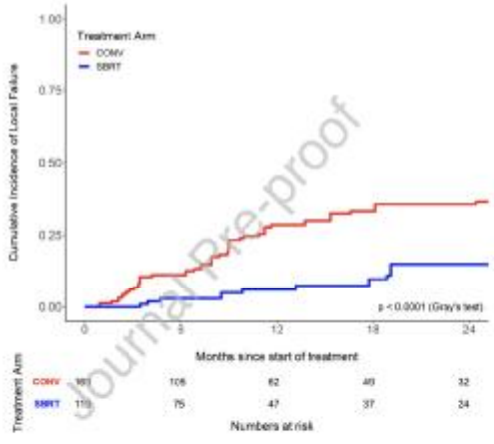


Figure 1. Cumulative incidence of local failure in the SBRT and cEBRT cohort demonstrating statistically significant increase in risk of local failure in the latter

INTERNATIONAL JOURNAL OF RADIATION ONCOLOGY • BIOLOGY • PHYSICS ASTRO

CLINICAL INVESTIGATION | ARTICLES IN PRESS

Mature Local Control and Reirradiation Rates Comparing Spine Stereotactic Body Radiotherapy to Conventional Palliative External Beam Radiotherapy

K. Liang Zeng, MD • Sten Myrehaug, MD • Hany Soliman, MD • Zain A. Husain, MD • Chia-Lin Tseng, MDCM • Jay Detsky, MD • Mark Ruschin, PhD • Esheiu G. Atenafu, PStat • Christopher D. Witiw, MD • Jeremie Larouche, MD • Leodante da Costa, MD • Pejman Jabehdar Maralani, MD • Wendy R. Parulekar, MD • Arjun Sahgal, MD

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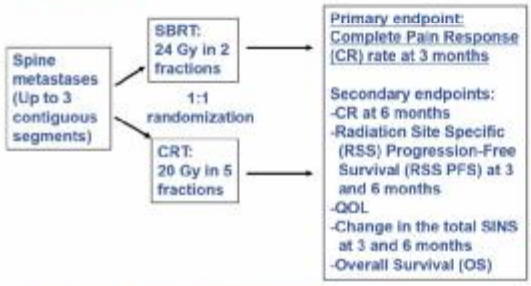
✅ local control (2-yr 14.8% v 35.6%)
✅ re-RT (1-yr 2.2% v 15.8%)
✅ time to re-RT (median 22.9 v 9.5 mo)

New SOC?

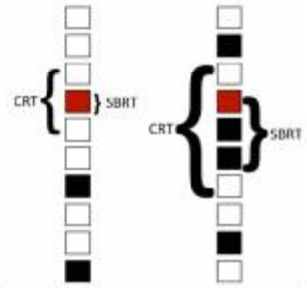
CCTG SC.24/TROG 17.06:
A Randomized Phase II/III Study Comparing 24Gy in 2 Stereotactic Body Radiotherapy (SBRT) Fractions Versus 20Gy in 5 Conventional Palliative Radiotherapy (CRT) Fractions for Patients with Painful Spinal Metastases (NCT02512965)

Arjun Sahgal (PI), Sten Myrehaug, Shankar Siva, Giuseppina L. Masucci, Mathew Foote, Michael Brundage, Jim Butler, Edward Chow, Michael G. Fehlings, Zsolt Gabos, Jeffrey Greenspoon, Marc Kerba, Young Lee, Mitchell Liu, Pejman J. Maralani, Isabelle Thibault, Rebecca K. Wong, Maaike Hum, Keyue Ding, Wendy R. Parulekar

Schema



- Stratification factors: radioresistant (GI, RCC, melanoma, sarcoma) vs. radiosensitive, and presence vs. absence of extra-osseous extension (Mass type)



Red: Target spinal segment volume
Red +/- Black: Treatment Volume
{: Included segments in a SBRT treatment volume and segments encompassed in a CRT treatment field adjusting for margins

Adverse Events per CTCAEv4.0

Adverse Event and Worst Reported Grade (2 to 5 only)	CRT (N=115)	SBRT (N=110)
Dysphagia		
2	0/115	1/110 (1%)
3	0/115	1/110 (1%)
Esophagitis[3]		
2	0/115	4/110 (4%)
3	2/115 (2%)	0/110
Nausea		
2	2/115 (2%)	1/110 (1%)
3	1/115 (1%)	0/110
Pain[1]		
2	4/115 (3%)	2/110 (2%)
3	5/115 (4%)	5/110 (5%)
Fatigue		
3	1/115 (1%)	0/115
Vertebral Compression Fracture		
3	0/115	1/110 (1%)
4	1/115 (1%)	0/110

- Any grade Vertebral Compression Fracture (VCF):
  - 17% CRT p=0.16
  - 11% SBRT
- No radiation myelopathy events
- No concerns on central MR image review
- Central RT plan QA review:
  - CRT: 2 major deviations
  - SBRT: 1 major deviation

P2/3 RCT of painful spine mets (≤3 levels, SINS ≤12) ➡️
-#SBRT (24 Gy/2 fx)
-RT (20 Gy/5 fx)

⬆️ pain CR with SBRT at 3 (35% v 14%) & 6 (32% v 16%) mos.

✅ No diff in toxicity

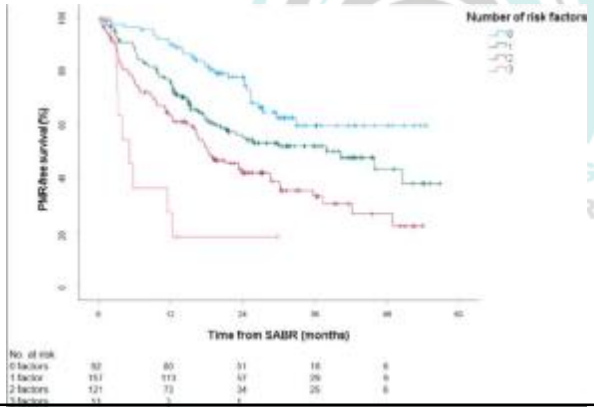
Patient and Treatment Factors Associated with Improved Local Control and Survival in Oligometastatic Bone Disease: Results from a Large Single-Institution Experience Using Stereotactic Body Radiation Therapy

Maria C. Thomas, MD • Yu-Hui Chen, PhD • Elliot Fite, BA • Andrew Pangilinan, BA • Katerina Bubeks, BA • Alexander Spektor, MD, PhD • Tracy A. Balboni, MD, MPH • Mai Anh Huynh, MD, PhD

Published: July 12, 2022 • DOI: https://doi.org/10.1016/j.ijrobp.2022.06.096

- BED10 > 50
- PTV < 150cc for non-spine bone lesions
- Prostate histology
- PS 0-1
- Metachronous

- 2016-2020
- <= 5 mets
- > 18 yrs
- ECOG >0
- Not prostate/breast
- Progression on systemic tx

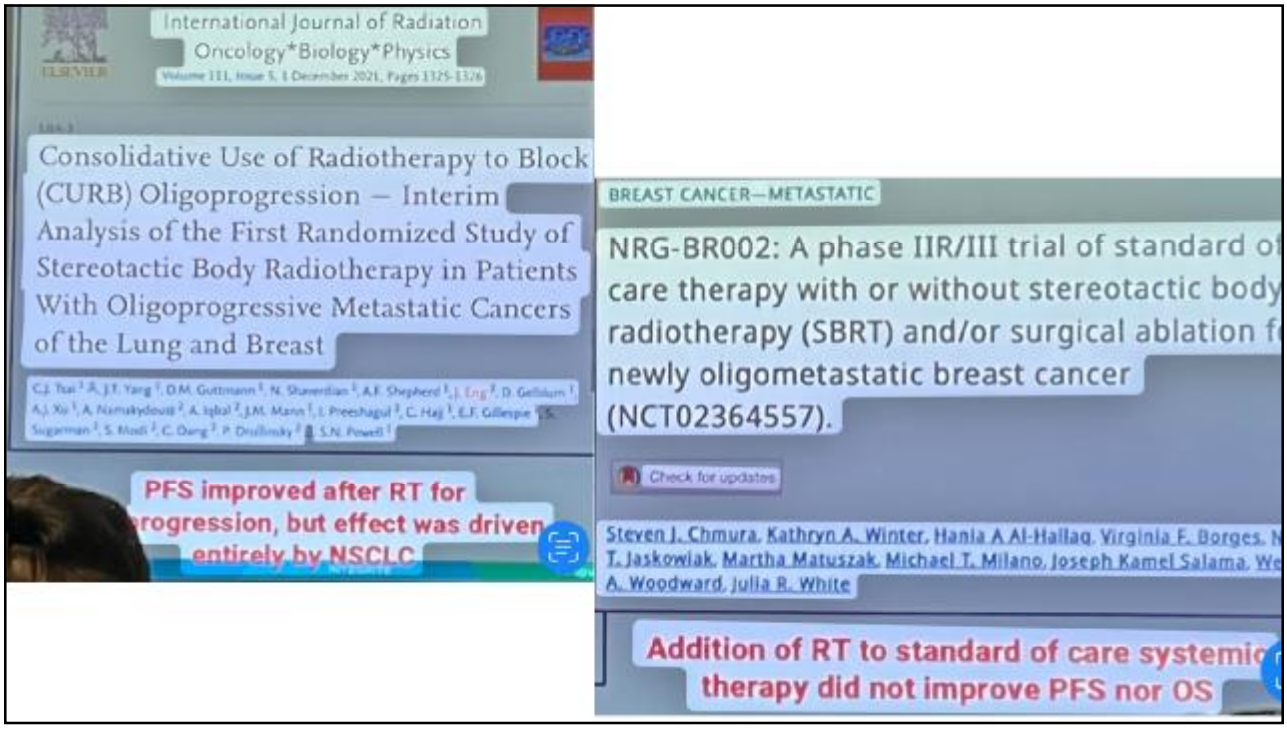


CLINICAL INVESTIGATION | ARTICLES IN PRESS

Predictors of early polymetastatic relapse following stereotactic ablative radiotherapy for up to 5 oligometastases: a secondary analysis of the phase II SABR-5 trial

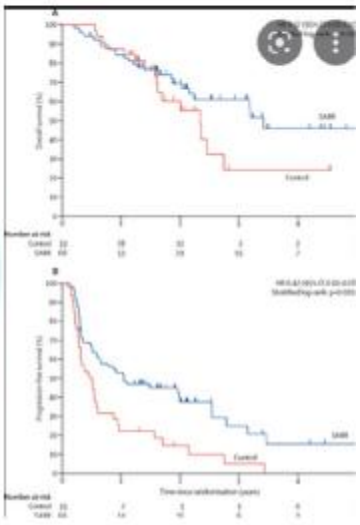
S Baker, MD PhD • B Mou, MD • W Jiang, MD • ... O Matthews, PhD • S Tyldesley, MD • RA Olson, MD MSc • Show all authors • Show footnotes

Published: July 12, 2022 • DOI: https://doi.org/10.1016/j.ijrobp.2022.06.094



My thought process to choose patients for SBRT

- Stable for more than a year on systemic tx
- Young and fit and motivated (me and patient)
- Good performance status
- Real oligomets
  - < 5
    - But I have treated 5-10!!!
      - ACC, RCC, Sarcoma, when you are stuck in a dead-end



<5 met
99 patients

Relax- It's a long way to go!