XXXIII CONGRESSO NAZIONALE AIRO

AIRO2023

BOLOGNA,
27-29 OTTOBRE 2023
PALAZZO DEI CONGRESSI

Radioterapia Oncologica: l'evoluzione al servizio dei pazienti

Radioterapia stereotassica nelle metastasi vertebrali: sempre e comunque?

Perché NO

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Radioterapia e Oncologia clinica

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ART
Advanced Radiation Therapy

OUTLINE

- Introduction & general consideration
- OligoMts Spine
- Non-OligoMts Spine (Trials ; Systematic Reviews)
- Final Considerations
- Conclusions

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Introduction

SBRT in Metastasi vertebrali: Domande alternative a ″Perché no″

- ″Perché si **?**″
- ″Perché no **!!!**″
- ″Per-chi ?″
- ″Per-come ?″

General Considerations

- ″Perché si ?″

″A questo paziente vorrei dargli un po' di più″

″Si può dare di più….
….perché è dentro di noi…
….come fare non so….non lo sai neanche tu…
…ma di certo si può dare di più…″

G. Morandi, U.Tozzi, E. Ruggeri; Sanremo 1987

General Considerations

- ″Perché si ?″

″A questo paziente vorrei dargli un po' di più″

Standard RT not enough?!

Overall Pain Response: 62%
Complete Pain Response: 24%

1 yy Local Control: 81%

Rich et al; Radiother Oncol - 2018

Singh et al; Radiother Oncol - 2020

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General Considerations

A critical appraisal of the four systematic reviews and meta-analysis on stereotactic body radiation therapy versus external beam radiotherapy for painful bone metastases and where we go from here

Henry C. Y. Wong[1#^], Adrian Wai Chan[2#], Peter Johnstone[3], Charles B. Simone II[4], Inmaculada Navarro-Domenech[5], Peter Hoskin[6,7], Candice Johnstone[8], Abram Recht[9], Johan Menten[10], Yvette M. van der Linden[11,12], Joanne M. van der Velden[13], Quynh-Nhu Nguyen[14], Stephen Lutz[15], Nicolaus Andratschke[16], Jonas Wilmann[16], Joanna Kazmierska[17,18], Mateusz Spalek[19,20], Fiona Lim[1], H. Michael Yu[3], Brad Perez[3], Gustavo Nader Marta[21,22], Vassilios Vassiliou[23], Shing Fung Lee[2,24], Pierluigi Bonomo[25], Agata Rembielak[26,27], Edward Chow[28], Eva Oldenburger[10*], Srinivas Raman[5*]

- "Perché si ?"

➢ Claiming a new standard implies to make it affordable and available to all patients

➢ Cost-effictiveness:

✓ The estimated cost of spine SBRT based on the US national Medicare reimbursement rate for 2020 are more than double the cost of a five-fraction cEBRT treatment;

✓ more than triple that of a single-fraction treatment

Wong et al; Ann Pall Med - 2023

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General Considerations

Contents lists available at ScienceDirect
Radiotherapy and Oncology
journal homepage: www.thegreenjournal.com
ELSEVIER

Guidelines

ESTRO ACROP guidelines for external beam radiotherapy of patients with uncomplicated bone metastases

Joanne van der Velden [a,1], Jonas Willmann [b,1], Mateusz Spałek [c], Eva Oldenburger [d], Stephanie Brown [e], Joanna Kazmierska [g,h], Nicolaus Andratschke [b], Johan Menten [d,i], Yvette van der Linden [a,2], Peter Hoskin [e,f,2,*]

- "Perché no !!!"

Indications and treatment aims of radiotherapy for uncomplicated painful bone metastases

What is the role of radiotherapy in the treatment of painful uncomplicated bone metastases?

Recommendations:

- Conventional radiotherapy should be used to treat uncomplicated painful bone metastases, especially if pain is not sufficiently controlled by pain medication or when a reduction of pain medication is desired. [Grade A, Level 1]
- For diffuse pain caused by multiple bone metastases single fraction hemibody or wide field irradiation should be considered. [Grade A, Level 1b]
- Radionuclide therapy can be considered as a palliative treatment in patients with painful osteoblastic or mixed pattern bone metastases of prostate cancer. [Grade A, Level 1a]

Is there a role for treating oligometastatic bone disease with SBRT irrespective of pain?

Recommendation:

- Patients with oligometastatic bone lesions may be offered local ablative SBRT but should be carefully informed about the potential risks and benefits, while evidence for an overall survival benefit from phase 3 trials is still lacking. [Grade B, Level 2b]

What is the evidence for using high-dose radiotherapy to treat pain from oligometastatic bone disease?

Recommendation:

- There is no advantage to higher dose conventional radiotherapy or SBRT over single dose conventional radiotherapy for pain response in oligometastatic bone disease. [Grade B, Level 1b]

Recommendations:

- Oligometastatic bone lesions may be offered local ablative SBRT but should be carefully informed about the potential risks and benefits, while evidence for an overall survival benefit from phase 3 trials is still lacking. [Grade B, Level 2b]

- There is no advantage to higher dose conventional radiotherapy or SBRT over single dose conventional radiotherapy for pain response in oligometastatic bone disease. [Grade B, Level 1b]

Van der Velde et al; Radiother Oncol - 2022

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General Considerations

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Guidelines

ESTRO ACROP guidelines for external beam radiotherapy of patients with complicated bone metastases

Eva Oldenburger [a,1], Stephanie Brown [b,1], Jonas Willmann [c], Joanne M. van der Velden [d,e], Mateusz Spałek [f], Yvette M. van der Linden [d,e], Joanna Kazmierska [g,h], Johan Menten [a,i], Nicolaus Andratschke [c,2], Peter Hoskin [b,j,*,2]

- ″Perché no !!!″

What is the optimal technique and dose fractionation for primary radiotherapy for treatment of MSCC?

Stereotactic body radiotherapy (SBRT) in the context of MSCC

Recommendation:

- SBRT should not be used routinely outside clinical trials for MSCC. [Grade D, Level 5]

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- SBRT should not be used routinely outside clinical trials for MSCC. [Grade D, Level 5]

Oldenburger et al; Radiother Oncol - 2022

General Considerations

- "Perché no !!!"

METASTASI OSSEE E SALUTE DELL'OSSO — LINEE GUIDA 2021 — AIOM

6.8. Il paziente con metastasi ossee può beneficiare anche delle tecniche di Radiochirurgia e Radioterapia Stereotassica?

Qualità dell'evidenza SIGN	Raccomandazione clinica	Forza della raccomandazione clinica
BASSA	Per pazienti, sintomatici, a buona prognosi con coinvolgimento del rachide, l'impiego di moderne tecnologie radioterapiche dovrebbe essere preso in considerazione preferibilmente all'interno di studi clinici, oppure per casi selezionati, applicando l'approccio riportato da Shagal et al., preferibilmente in Centri ad alto volume per SBRT IGRT.	**Positiva Debole**

AIOM; Linee Guida Metastasi Ossee e Salute Osso – 2021, 2022, 2023

General Considerations

- ″ Per-chi ? ″

Clinical Presentations:

- Oligometastatic Asymptomatic
- Oligometastatic Symptomatic
- Multiple Metastatic (Bone ± Visceral) Symptomatic
- (Multiple Metastatic Asymptomatic)

Metastasis Presentations
(type, stability, compression, "extra-bone", etc…):

- Spinal (cervical, C1-C2)
- Non-Spinal (Sacral, Pelvic, Long bone)

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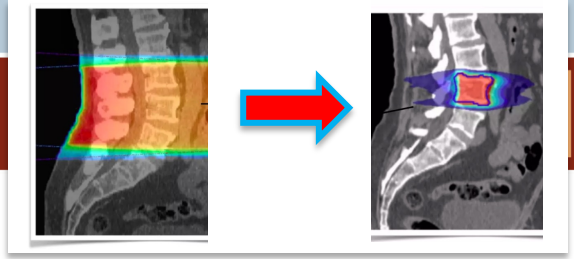
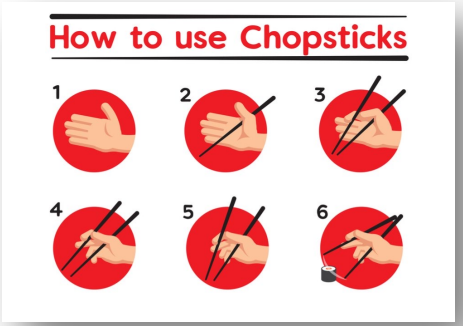
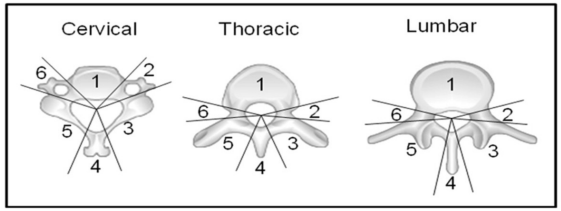
General Considerations



- ″ Per-come ? ″

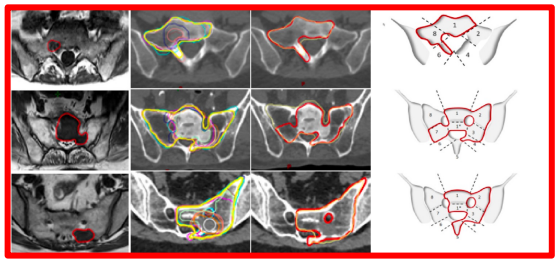


Spinal Non-Sacral



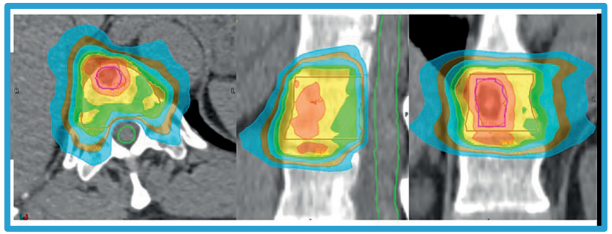
Cox et al; IJROBP - 2012

Spinal Sacral



Dunne et al; Radiother Oncol - 2022

SIB



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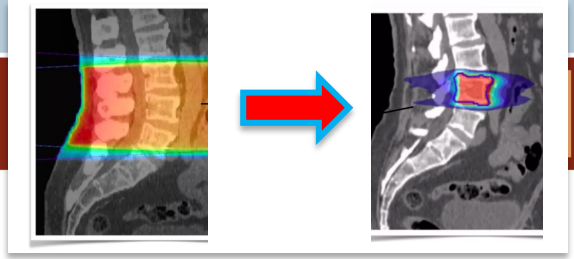
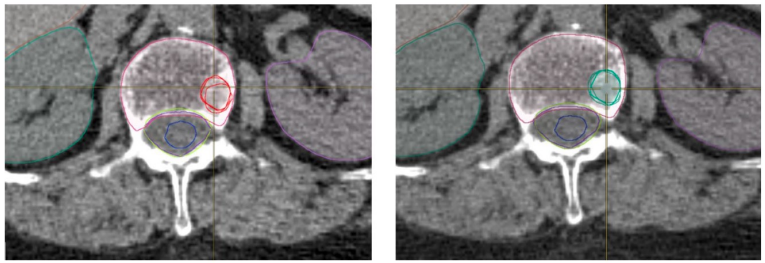
General Considerations

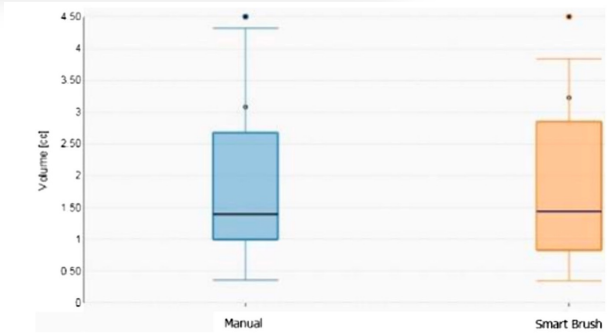


- ″ Per-come ? ″

Reduction of inter-observer differences in the delineation of the target in spinal metastases SBRT using an automatic contouring dedicated system

Niccolò Giaj-Levra[1*], Vanessa Figlia[1], Francesco Cuccia[1], Rosario Mazzola[1], Luca Nicosia[1], Francesco Ricchetti[1], Michele Rigo[1], Giorgio Attinà[1], Claudio Vitale[1], Gianluisa Sicignano[1], Antonio De Simone[1], Stefania Naccarato[1], Ruggero Ruggieri[1] and Filippo Alongi[1,2]





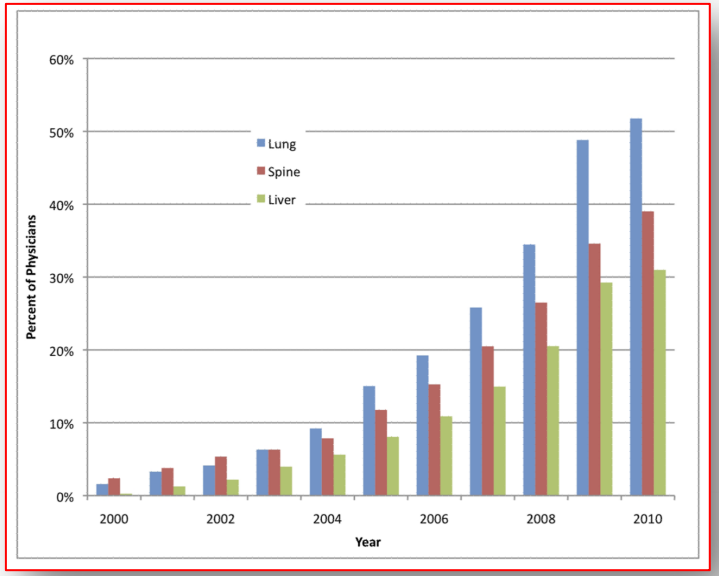
Giaj-Levra et al; Radiat Oncol - 2021

General Consideration

Survey on SBRT Application in USA

- 1373 contactable physicians → 551 responses (40.1%) were received;

The most common disease sites treated were lung (89.3%), spine (67.5%), and liver (54.5%).



Pan et al; Cancer - 2011

General Consideration

Survey on SBRT Application Worldwide

- 1007 completed surveys from RTs in 43 countries

- USA (42%), Canada (11%), Japan (10%), Western Europe (7%), Australia/New Zealand (6%)
- Treated organs : lung (90%), liver (75%), and spine (70%)

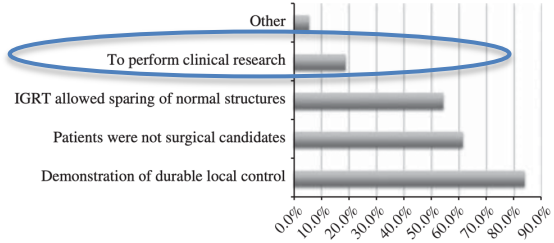


FIGURE 2. Reasons for adopting stereotactic body radiotherapy (SBRT) to treat oligometastases. IGRT indicates image-guided radiation therapy.

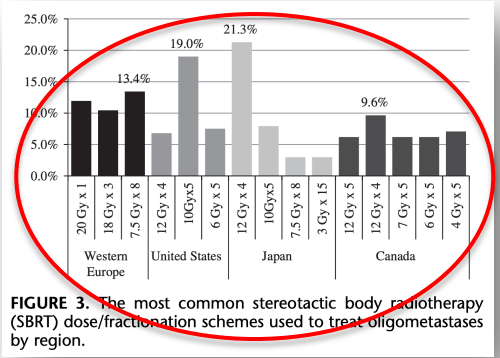


FIGURE 3. The most common stereotactic body radiotherapy (SBRT) dose/fractionation schemes used to treat oligometastases by region.

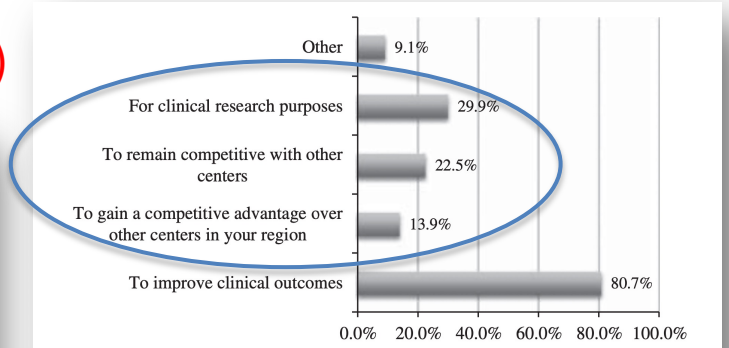


FIGURE 4. Reasons cited by respondents not currently using stereotactic body radiotherapy (SBRT) for oligometastases to start offering this procedure in the near future.

Lewis et al; Am J Clin Oncol - 2015

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Radiotherapy and Oncology
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Original Article

Recommendations for radiation therapy in oligometastatic prostate cancer: An ESTRO-ACROP Delphi consensus

OligoMts Spine

✓ Heterogeneity

Minimal Agreement: 60%

23. For patients with oligoprogressive PCa (with no visceral metastases), which treatment do you recommend?	**MDRT of all lesions without switch of systemic therapy**	**Consensus Round 1: 56%; round 2: 76%; round 3: 84%**
Target volume and dosimetric considerations		
25. For bone lesions, when do you consider MDRT?	There is an uptake on PET but must be associated with the presence of a radiologically visible lesion	Agreement Round 1: 72%; round 2: 72%; round 3: 68%
26. For vertebral bone lesions, when you consider a MDRT, do you treat:	**The lesion (GTV) and the vertebral body (CTV)**	**Consensus Round 1: 60%; round 2: 76%; round 3: 84%**
28. For extraspinal bone lesions, when you consider a MDRT, do you treat:	The lesion (GTV) and a 4–5 mm isotropic CTV	Agreement Round 1: 32%; round 2: 44%; round 3: 68%

omy for 68%, 16% and 12% of the panelists, respectively). Practices differed with regards to dose prescription, as 60% of the panelists voted for an homogeneous dose prescription on the planning target volume (PTV), and 40% voted for a dose prescription to an isodose line (80% isodose line recommended by the 87% of the 15 voting experts). The most recommended fractionation for spinal lesions SBRT was 35 Gy in 5 fractions (42%, n = 10), followed by 30 Gy in 3 fractions (37.5%, n = 9), and use of simultaneous integrated boost (SIB) in 3 or 5 fractions recommended by 33% of the experts (n = 8) (Fig. 3). For the treatment of extra-spinal bone metastases, a 3-fraction SBRT schedule (i.e., 30 Gy in 3 fractions) was recommended by 72% of the experts (n = 18).

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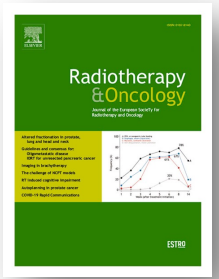
Zilli et al; Radiother Oncol - 2022

OligoMts Spine

✓ Heterogeneity



- Retrospective (2007-2016)
- Oligometastatic (<5 cumulative extracranial metastases)
- 356 patients (Bone lesions: Spine; NON Spine; Both)
- 288 spine and 233 NON Spine

- Local Recurrence: @6 mth=6,3%; @1 yr = 12,6% ; @2 yrs=19,3%

- Notes: Univariable analysis suggested inferior LC and OS in spine patients; this did not hold true in multivariable analysis

Cao et al.; Radiother Oncol; 2021 Nov;164:98-103

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Radioterapia Oncologica:

OligoMts

- ✓ Heterogeneity

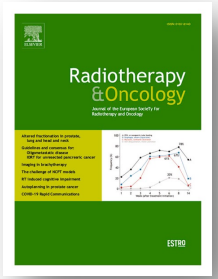

Table 2: Summary of lesion and treatment characteristics

Lesion-level characteristics	Non-spine bone lesions n = 233	Spine lesions n = 288	pValue
Non-Spine Bone Location			
Hip/Lower Limb	38 (16.3%)		
Pelvis	82 (35.2%)		
Rib	68 (29.2%)	N/A	
Shoulder/Upper Limb	27 (11.6%)		
Skull	3 (1.3%)		
Sternum	10 (4.3%)		
Other	5 (2.1%)		
Spinal Level Location			
C-Spine		15 (5.2%)	
T-Spine	N/A	147 (51.0%)	
L-Spine		80 (27.8%)	
Sacrum		30 (10.4%)	
Overlapping		16 (5.6%)	
Soft Tissue/Paraspinal Extension	37 (15.9%)	78 (27.1%)	0.002
Epidural Disease	N/A	51 (17.7%)	
Dose/Fractionation (Gy/fx)			
15-18/1	6 (2.6%)	12 (4.2%)	
20-28/1	10 (4.3%)	27 (9.4%)	
24-31/2	27 (11.6%)	28 (9.7%)	
24-28/3-5	10 (4.3%)	116 (40.3%)	
30-35/3-5	87 (37.3%)	76 (26.4%)	
40-45/4-5	10 (4.3%)	--	
50/5	47 (20.2%)	15 (15.2%)	
50/10	36 (15.5%)	14 (4.9%)	
Mean BED10, Gy (SD)	66.5 (18.3)	57.6 (14.8)	<0.001
Mean PTV, cc (SD)	71.7 (123.3)	82.7 (72.3)	0.204
Mean PTV Dmax (BED10), Gy (SD)	81.9 (26.5)	86.1 (22.6)	0.051
Mean PTV Dmin (BED10), Gy (SD)	43.9 (17.3)	22.8 (12.7)	<0.001
Mean PTV Dmean (BED10), Gy (SD)	70.6 (20.9)	63.8 (15.8)	<0.001
Re-irradiation	10 (4.3%)	9 (3.1%)	0.637

Cao et al.; Radiother Oncol; 2021 Nov;164:98-103

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Non OligoMts Spine - Trials

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

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,*]

Stereotactic ablative radiotherapy (SBRT) trials and type of study in bone metastases patients.

Author, year [Ref.]	SABR use	Study Type	Pain Response (%)	Local Control	Number of Patients	Total Dose (Gy)	Number of Fractions	Device	RT Prescription Parameters
Gerszten, 2005 [56]	POS	Prospective Single arm	92	-	26	mean 18 (16 to 20)	1	CyberKnife	80% isodose line
Gagnon, 2007 [57]	RIR, CCRT	Retrospective Matched-pair analysis of historical controls	-	-	35	21–28	3–5	CyberKnife and Linac	Not mentioned
Choi, 2010 [58]	RIR	Retrospective	65 (considering patients presenting with pain)	73 (1y)	42	median 20 (10–30)	median 2 (1–5)	CyberKnife	77% isodose line (median) (range, 68–88%)
Staehler, 2010 [59]	RRT	Retrospective	-	94.1(1y)	55	20 median (19–20)	1	CyberKnife	70% isodose line (median) (range 50–85%).
Garg, 2011 [60]	RIR	Prospective	-	76 (1y)	59	27–30	3–5	Linac	80% to 90% of the target volume received the prescription dose
Mahadevan, 2011 [61]	RIR	Retrospective	65 (1 month after SBRT)	93 (last visit)	60	24–30	3–5	CyberKnife	Mean prescription isodose 79% range(68–90%)
Nikolajef, 2011 [62]	RIR	Retrospective	significant reduction in VAS score of patients with pain (2 months)	88 (1y)	54	median 18 (10–28)	1	CyberKnife	Median prescription isodose line 70% (range 50–80%)
Chang, 2012 [63]	RIR, PRI	Retrospective	81–89 (1y)	Retreatment: 81 (1y) Initial RT 89 (1y)	185	Retreatment: 14.7–26.5 Initial RT: 16.6–23.2	1	CyberKnife	Retreatment: 78.3 % isodose line Initial RT 79.3 % isodose line
Heron, 2012 [64]	PRI	Retrospective	88 MF vs 100 SF	96 MF vs 70 SF (2y)	228	MF: 20.6 (9–26.3) SF: 16.3 (6–20) 1	MF: 3–5 SF: 1	CyberKnife	MF: 80% isodose line (range 70%–95%) SF: 72% isodose line (range 50%–85%)
Hunter, 2012 [65]	CCRT, RRT	Retrospective	CRT: 68 - SBRT:62 (overall)	-	110	8–30	1–10	Linac	CRT: prescribed to a depth, or the isocentre SBRT: not mentioned
Jahanshahi, 2012 [66]	RRT, OLI	Retrospective	-	72–100 (1y)	50	mean 24.1 (7.7–54)	1–5	CyberKnife	Mean prescription isodose 78.7%
Massicote, 2012 [67]	POS, RRT	Retrospective	Median improvement on VAS was 6 points (5 months)	70	10	median 24 (18–35)	1–5	Linac	80–90% of CTV coverage
Wang, 2012 [68]	PRI, RIR, POS	Prospective	Increase in patients without 26.2 vs 53.9 (6 months)	80.5	149	27–30	3	Linac	Not mentioned
Al-Omair, 2013 [69]	POS, RRT	Retrospective	-	84 (1y)	80	median 24 (18–40)	median 2 (1–5)	Linac	Median CTV V80 in 90% of the patients
Laufer, 2013 [70]	POS, RRT	Retrospective	-	83,6 (1y)	186	18–36	1–6	-	Not mentioned
Muacevic, 2013 [71]	OLI, RRT	Prospective	-	95 (1y)	40	median 20 (16.5–22)	1	CyberKnife	Median peripheral isodose 70% (60–80)
Folker, 2014 [72]	RRT, OLI	Retrospective	-	87.9 (1y)	88	18–36	1–6	Linac	Median prescription D95% coverage 95% of PTV
Amini, 2015 [73]	RRT, CCRT	Retrospective	74.9 SBRT, 39,9 Conv (1y)	74.1 S – 45,1C (1y)	46	8–40	1–12	Linac	Not mentioned
Colaco, 2015 [74]	OLI	Retrospective	-	89 (1y)	78	10–17	1–3	Linac and Gamma Knife	Not mentioned
Thibault, 2015 [75]	RIR	Retrospective	-	81 (1y)	40	20–35	1–5	Linac	Aimed to cover > 80% of the PTV minus the CNT with 95–100% dose.
Ghia, 2016 [76]	RRT, POS	CRT	-	82 (1y)	43	24–30	1–5	Linac	isodose was normalized to the isocenter and the dose prescribed to the volume included by the 90% isodose line

, Radiother Oncol - 2021

Non OligoMts Spine - Trials

I Magnifici 7-1960

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Trials

Radioterapia Oncologica:
l'evoluzione al servizio dei pazienti

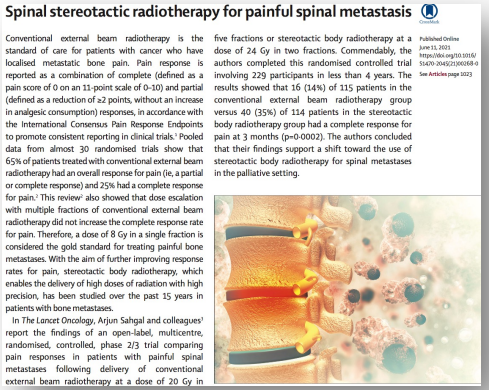
Author/ Year	N° Pts	Setting	Shedule (Gy/n° fx)	Spine Quote	MRI pre-RT Use	Delineation	1° Endpoint	Result for SBRT
Ryu 2023	339	Ph 2/3 R (planned)	8/1fx VS 16 or 18/1fx	Spine OLIGO	Mandatory	Partial Vertebra	Over Resp	
Shagal 2021	229	Ph 2/3 R (unplanned)	20/5fx VS 24/2fx	Spine	Mandatory	Cox et al	Complete Resp	
Pielkenrood 2021	89	Ph 2 R	8/1fx or 20/5fx or 30/10fx VS 8-18/1fx or 15-30/3fx or 20-35/5	Spine 50%	Mandatory	SIB	Over Resp	
Sakr 2020	22	Ph 2 R	20/5fx VS 27/3fx	Not specified	Optional	Whole Vertebra	Over Resp	
Nguyen 2019	160	Ph 2 R (Non-Inferiority)	30/10fx VS 12 or 16/1fx	Mostly not Spine	Not specified	GTV+5mm (both arms)	Over Resp	
Sprave 2018	55	Ph 2 R (Explorative)	30/10fx VS 24/1fx	Spine (not Cervical)	Mandatory	GTV+5mm+ (CTV in 3 sections)	Over Resp	
Berwouts 2015	45	Ph 2 R 3 arms (on DPBN)	8/1fx VS 8/1fxDPBN VS 16/1fx DPBN	Mostly not Spine	Mandatory	Dose Paint By Number	Over Resp	

Non Oligo - Systematic Reviews

Author/ Year	N° Trials RcT/other	Missing ″7 Magnificents″	Global Outcome for SBRT
Wong 2023 (Radiother Oncol)	3/0	Pielkenrood 2021, Nguyen 2019, Sakr 2020, Berwouts 2015	
Song 2023 (IJROBP)	6/4 (1 prospective +3 retrospective)	Ryu 2023	
Ito 2022 (Radiat Oncol)	7/0	-	
Lee 2022 (Crit Rev Oncol Haemat)	6/0 (refers to ″old″ Ryu 2019)	Berwouts 2015	
Wang 2022 (Frontiers Oncol)	4/0	Ryu 2023, Sakr 2020, Berwouts 2015	

OUTLINE

- Introduction & general consideration
- OligoMts Spine
- Non-OligoMts Spine (Trials ; Systematic Reviews)
- Final Considerations
- Conclusions



Spinal stereotactic radiotherapy for painful spinal metastasis

Conventional external beam radiotherapy is the standard of care for patients with cancer who have localised metastatic bone pain. Pain response is reported as a combination of complete (defined as a pain score of 0 on an 11-point scale of 0-10) and partial (defined as a reduction of ≥2 points, without an increase in analgesic consumption) responses, in accordance with the International Consensus Pain Response Endpoints to promote consistent reporting in clinical trials.[1] Pooled data from almost 30 randomised trials show that 65% of patients treated with conventional external beam radiotherapy had an overall response for pain (ie, a partial or complete response) and 25% had a complete response for pain.[1] This review[2] also showed that dose escalation with multiple fractions of conventional external beam radiotherapy did not increase the complete response rate for pain. Therefore, a dose of 8 Gy in a single fraction is considered the gold standard for treating painful bone metastases. With the aim of further improving response rates for pain, stereotactic body radiotherapy, which enables the delivery of high doses of radiation with high precision, has been studied over the past 15 years in patients with bone metastases.

In *The Lancet Oncology*, Arjun Sahgal and colleagues[3] report the findings of an open-label, multicentre, randomised, controlled, phase 2/3 trial comparing pain responses in patients with painful spinal metastases following delivery of conventional external beam radiotherapy at a dose of 20 Gy in five fractions or stereotactic body radiotherapy at a dose of 24 Gy in two fractions. Commendably, the authors completed this randomised controlled trial involving 229 participants in less than 4 years. The results showed that 16 (14%) of 115 patients in the conventional external beam radiotherapy group versus 40 (35%) of 114 patients in the stereotactic body radiotherapy group had a complete response for pain at 3 months (p=0·0002). The authors concluded that their findings support a shift toward the use of stereotactic body radiotherapy for spinal metastases in the palliative setting.

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See Articles page 1023

- Pooled data from almost 30 randomised trials show conventional EBRT response for pain
- Multiple fractions of conventional EBRT did not increase complete response rate for pain
- In other available Random Trials overall response rates for pain in the ITT at 3 months did not find a significant difference between conventional EBRT and SBRT
- Shagal et al. did not compare significance for Overall and specifically Partial Response
- Other Random Trials differ in size of study population and location of bone mets.
- Relevant difference among other Random Trials in applied SBRT Schedule

van der Velden, van der Linden Lancet Oncol 2021; 22
Shagal et al.; Lancet Oncol 2021; 22: 1023–33

Stereotactic body radiotherapy for painful spinal metastases

We would like to congratulate Arjun Sahgal and colleagues[1] on the excellent trial they have presented. The relevant results and innovative approach make their work a cornerstone in current radiotherapy. However, we would like to direct the

Discussion, other randomised trials did not show significant results in term of pain relief.[2–4] The associated biological equivalent dose (appendix) might hold a key role for the interpretation of this discrepancy, but the issue remains open. In other words, why is a schedule of 12 Gy in two daily fractions (biological equivalent dose: 52·8 Gy) effective, whereas a schedule of a single 18 Gy dose (biological equivalent dose: 50·4 Gy)[3,4] or of a single 24 Gy dose

the inclusion criteria and treatment conditions of the presented trial are followed. However, we believe that it is still too early to replace conventional palliative schedules with stereotactic body radiotherapy for the investigated clinical presentation.

We declare no competing interests.

Francesco Cellini, Stefania Manfrida, Maria Antonietta Gambacorta, Vincenzo Valentini

Author/Protocol	N° of Fractions	Total Dose	Dose per Fraction	BED10	Symptom Relief Statistical Significance
Sprave et al[2]	1	24	24	81,6	Not significant
Ryu et al /RTOG 0631[4]	1	18	18	50,4	Not significant
Pielkenrood et al/VERTICAL[3]	1	18	18	50,4	Not significant
Pielkenrood et al/VERTICAL[3]	3	30	10	60	Not significant
Pielkenrood et al/VERTICAL[3]	5	35	7	59.5	Not significant
Shagal et al[1]	**2**	**24**	**12**	**52,8**	**Significant**
Cellini et al/PREST[5]	3	30/21 (SIB GTV/vertebra)	10/7 (SIB GTV/vertebra)	60 /35,7 (SIB GTV/vertebra)	Ongoing study

(Abbreviations: N°= number; BED_{10}= Biological Equivalent Dose; SIB= Simultaneous Integrated boost

- ✓ The workflow to select the best treatment for each presentation needs to be further refined
- ✓ The biological equivalent dose (BED) associated to different schedules applied might hold a key role for the interpretation of this discrepancy
- ✓ Delineation is not yet unanimously agreed on by clinicians and could affect realword practice
- ✓ We believe that it is still too early to replace conventional palliative schedules with SBRT

Cellini, Manfrida, Gambacorta, Valentini; Lancet Oncol 2021; 22
van der Velden, van der Linden; Lancet Oncol 2021; 22
Shagal et al.; Lancet Oncol 2021; 22: 1023–33

- It might be argued that a 25% improvement was already an ambitious expectation (unfortunate loss of participants in the SBRT arm, a clinically significant difference of say 10% or more would be easily missed)
- Higher response rates in the SBRT arm; however wide confidence intervals highlights the statistical uncertainty
- Pielkenrood et al suggests that SBRT logistics remain less efficient
- Cost effectiveness is also not addressed in the current literature
- Dose response for metastatic bone pain at greater than a single dose of 8 Gy, not demonstrated: tumor cell kill is not the entire answer to pain relief
- Central issue in this discussion: we must not be transfixed by the lure of new technology but acknowledge that a small subgroup, possibly those with spinal oligometastases

Hoskin et al.; IJROBP 2021; Vol. 110, No. 2, pp. 368-370, 2021
Pielkenrood et al.; IJROBP 2021; Volume 110 Number 2 2021

- Efficient Pain Control ?
- Easy to set and deliver?
- Repeatable?
- Good Local Control?
- Tested and tested?
- Homogeneous?

Standard Palliative RT

(By now…unless Clinical Trial)

Conclusions

- La SBRT rappresenta il futuro per il trattamento delle Metastasi Spinali: resta solo da capire il ″perché″, ″per-chi″ e ″per-come″.

- Al momento meglio riservarla a casi selezionati, Centri di ampio volume e preferibilmente Studi Clinici