Clinical Case Conference

Palliative radiation therapy for bone metastasis

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7/20/2015

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Overview

- Epidemiology
- Pathophysiology
- Common presentations and symptoms
- Imaging
- Surgery
- Radiation therapy
  - Conventional (RTOG 97-14, TROG 96-05, Norway/Sweden, Spanish)
  - SBRT (Pittsburgh, Henry Ford, RTOG 0613)

Clinical Case

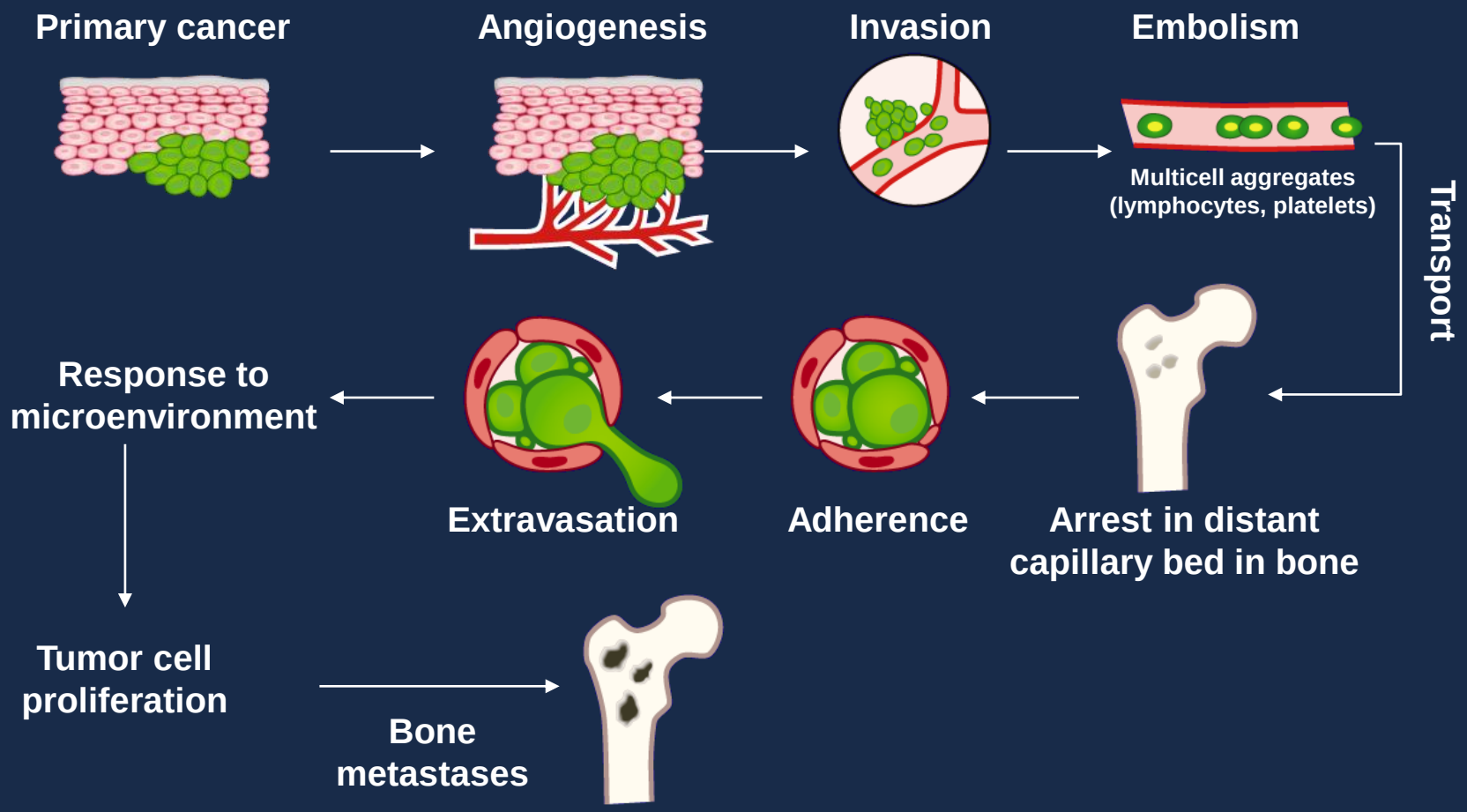
- 66 year old male with metastatic prostate cancer, originally diagnosed in 2006
- S/p radical prostatectomy in 2006 with Gleason 3+4=7 prostate adenocarcinoma, confined to prostate with negative margins
- XRT to prostate fossa 70Gy in 35 fractions, completed 2008
- Progressed through Lupron, abiraterone, and enzalutamide treatment, with osseous metastases discovered on bone scan in 2012 (C3/4, bilateral ribs)
- Started docetaxel in 2015
- 2015, began experiencing right sided leg pain, mostly at night
- Found to have large right intertrochanteric femur and L3 bony mets on bone scan

Case – Epi – Pathophys – Sxs – Imaging – Surgery – XRT

Epidemiology

- Common manifestation of distant relapse for many solid cancers (breast, lung, prostate most common)
- Up to 80% of patients with solid tumors will develop painful bone metastases to spine, pelvis, and extremities
- Breast, prostate, lung, thyroid, and kidney cancer account for 80% of all skeletal metastases
- Bone metastases develop in 50, 44, and 37% of patients with thyroid, lung, and renal cancer
- 70% of patients who die of cancer have spinal metastases at autopsy
  - <14% are symptomatic

Pathophysiology



Case – Epi – **Pathophys** – Sxs – Imaging – Surgery – XRT

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Osteolytic and osteoblastic metastases

- Osteolytic
  - Lung
  - Kidney
  - Thyroid
  - Multiple myeloma
- Osteoblastic
  - Prostate
- Mixed
  - Breast
  - Testicular
  - Ovarian

Case – Epi – **Pathophys** – Sxs – Imaging – Surgery – XRT

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Common presentations and symptoms

- Many metastatic lesions cause little to no symptoms
- Pain is most common (~90%) presenting symptom
  - Typically constant, present at night
  - Can be poorly characterized, such as referred pain to the ribs
- Neurologic signs frequently preceded by pain
  - Radiculopathy, myelopathy, cauda equina syndrome

Imaging

- Bone scan is more sensitive than plain films for sclerotic lesions
  - CT scans are more specific, better for differentiating between
- Plain films and CT are helpful for detecting pathologic fracture
- MRI spine series is indicated in setting of suspected neurologic compromise
- PET/CT similar sensitivity to bone scan, but higher specificity
  - Not effective for more differentiated tumors, i.e. prostate cancer

DG Imaging

Case – Epi – Pathophys – Sxs – **Imaging** – Surgery – XRT

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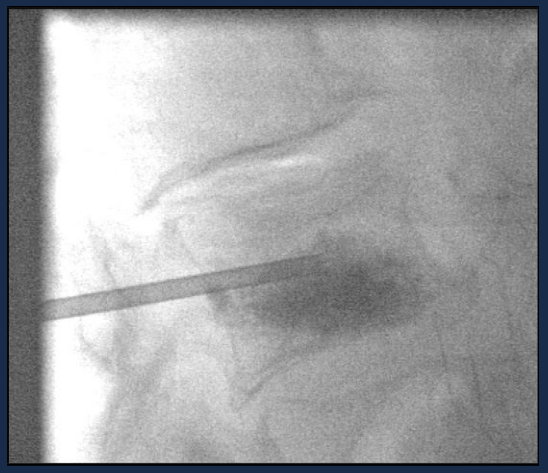
Goals of care

- Goals of palliative treatment of painful bone metastases
  - Pain relief
  - Function preservation
  - Maintenance of skeletal integrity
- Local XRT to painful sites can provide relief in ~ 60-85% of cases
- Early intervention may be useful in maintaining quality of life and minimizing side effects of analgesic medications

Surgery

- Vertebroplasty:
  - Injection of bone cement to support weakened bones
  - Provides immediate and substantial pain relief



- Kyphoplasty:
  - Balloon inflation of compressed spine bone is performed before cement injection
  - Used for compression fractures

Radiation therapy

- Conventional
  - RTOG 97-14
  - TROG 96-05
  - Norway/Sweden
  - Spanish study
- SBRT
  - Pittsburgh
  - Henry Ford
  - RTOG 0613

Single versus multiple fraction treatment

- **RT0G 94-17**
- Phase III prospective randomized trial
- 898 patients with painful bone metastases (prostate or breast cancer)
- Excluded spinal cord compression, prior RT to area
- Life expectancy >3 months, KPS ≥40
- Randomized to 2 arms: 8Gy x 1 fraction versus 3Gy x 10 fractions
- Primary endpoint: pain relief at 3 months
- Secondary endpoints
  - Narcotic dose
  - Subsequent pathologic dose
  - Re-treatment dose

XRT – **94-17** – 96-05 – Norway/Sweden – Spanish – SBRT

RTOG 94-17

Table 2. Toxicity of treatment*

	Acute toxicity, No. of patients								Late toxicity, No. of patients							
	8-Gy arm (n = 433)				30-Gy arm (n = 414)				8-Gy arm (n = 354)				30-Gy arm (n = 342)			
Type of toxicity	G1	G2	G3	G4	G1	G2	G3	G4	G1	G2	G3	G4	G1	G2	G3	G4
Skin	15	1	0	0	32	15	1	0	7	1	0	0	3	2	0	0
Lung	0	0	2	0	3	4	0	0	3	0	0	0	2	1	0	0
CNS	3	1	0	0	3	1	1	0	2	1	1	0	1	1	0	0
GI	29	21	3	0	47	27	6	0	5	1	0	0	4	2	0	0
Hematologic	10	7	2	0	11	10	5	1	5	3	1	0	5	3	0	0
Other	11	6	6	0	15	13	4	1	4	5	0	0	4	6	2	0
Maximum toxicity per patient	43	31	11	0	65	55	13	2	10	11	2	0	11	13	2	0

XRT – **94-17** – 96-05 – Norway/Sweden – Spanish – SBRT

RTOG 94-17

Table 3. Brief Pain Inventory (BPI) worst pain score and overall response to treatment at 3 months after treatment

Parameter	No. of patients (%)		*P**
	8-Gy arm (n = 288)	30-Gy arm (n = 285)	
BPI worst pain score			
0	44 (15)	51 (18)	.854
1–4	99 (34)	98 (34)	
5–6	56 (19)	53 (19)	
7–10	89 (31)	83 (29)	
No answers/2 answers	2	5	
Overall response type			
Complete	44 (15)	51 (18)	.6
Partial	143 (50)	137 (48)	
Stable	74 (26)	69 (24)	
Progressive	27 (9)	28 (10)	

XRT – **94-17** – 96-05 – Norway/Sweden – Spanish – SBRT

RTOG 94-17

Table 4. Overall rates of analgesic and narcotic use at 3 months

Drug	No. of patients (%)		*P**
	8-Gy arm (n = 318)	30-Gy arm (n = 310)	
None	65 (20)	69 (22)	.483
Nonnarcotic analgesic	40 (13)	30 (10)	
Narcotic	213 (67)	211 (68)	

XRT – **94-17** – 96-05 – Norway/Sweden – Spanish – SBRT

RTOG 94-17

Outcomes	8 Gy x 1	3 Gy x 10	Significance
Complete Pain Relief	15%	18%	NS
Partial Pain Relief	50%	48%	NS
Stable Pain	26%	24%	NS
Progressive Pain	9%	10%	NS
Acute toxicity	10%	17%	SS
Retreatment	18%	9%	SS

- Both regimens equivalent for pain control and narcotic relief at 3 months
- 8 Gy x 1 regimen: less acute toxicity; higher retreatment rate

XRT – **94-17** – 96-05 – Norway/Sweden – Spanish – SBRT

Single versus multiple fraction treatment

- **TROG 96-05**
- Phase III prospective randomized trial
- 272 patients with neuropathic pain from bone metastasis
- No spinal cord compression, cauda equina syndrome, prior RT
- Life expectancy >3 months, KPS ≥40
- Randomized to 2 arms: 8Gy x 1 fraction versus 4Gy x 5 fractions
- Primary endpoint:
  - Whether 8Gy x 1 is as effective as 20Gy in 5 fractions in relieving neuropathic bone pain with respect to pain response within 2 months of start of RT and time to treatment failure (TTF)
- Secondary endpoints
  - Acute side effects
  - Rates of serious complications (pathological fracture and spinal cord/cauda equina compression) at index site

XRT – 94-17 – **96-05** – Norway/Sweden – Spanish – SBRT

TROG 96-05

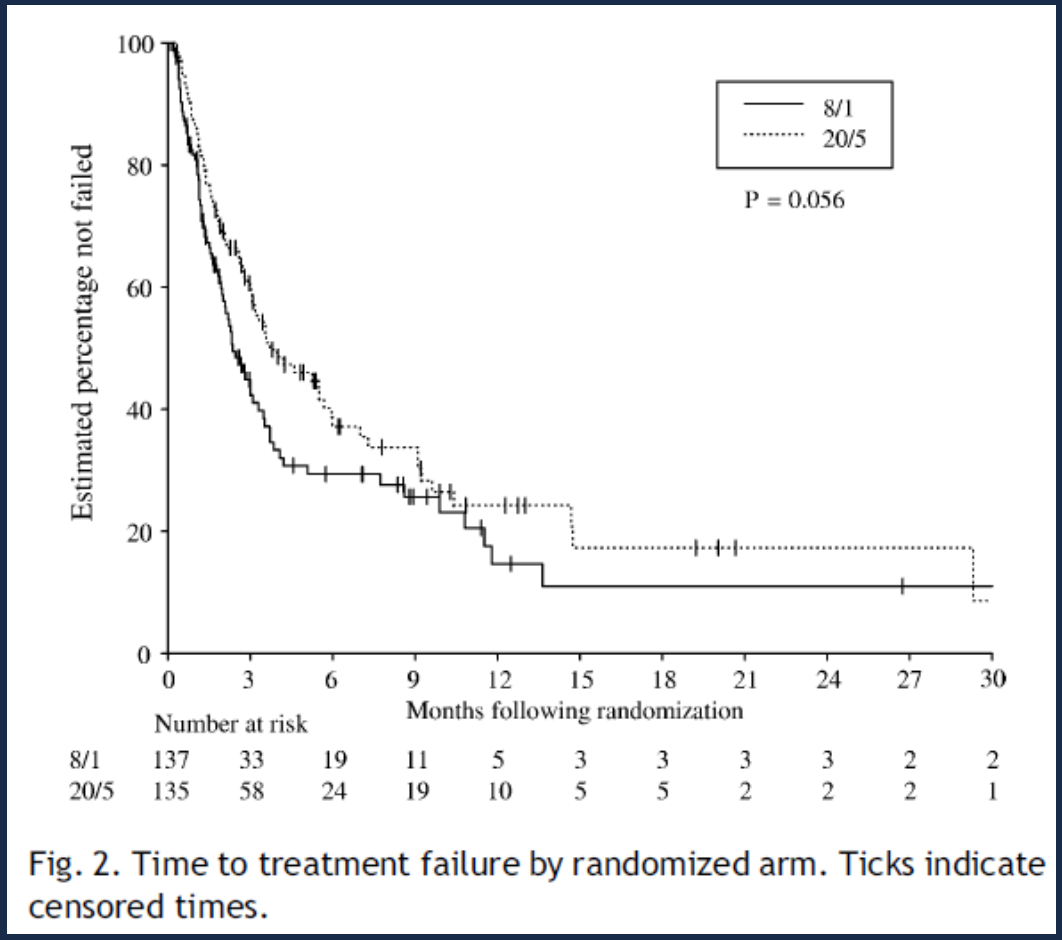


Fig. 2. Time to treatment failure by randomized arm. Ticks indicate censored times.

XRT – 94-17 – **96-05** – Norway/Sweden – Spanish – SBRT

TROG 96-05

Table 3
Radiotherapy details

	8/1 (n=137), No. (%)	20/5 (n=135), No. (%)
RT given		
Per-protocol fractionation	133 (97)	129 (96)
Non-protocol fractionation	1 (1)	4 (3)
No protocol RT	3 (2)	2 (1)
Modality		
Linac photons (4-10 MV)	129 (94)	129 (96)
Linac electrons (9-21 MeV)	4 (3)	4 (3)
Deep X-rays (250 kV)	1 (1)	0 (0)
Days from randomization to commencing RT		
0	40 (29)	26 (19)
1-14	83 (61)	88 (65)
>14	11 (8)	19 (14)
Protocol dose violations		
Minimal (within ±5%)	13 (9)	12 (9)
Minor/acceptable (>5%-10%)	7 (5)	8 (6)
Major/unacceptable (>10%)	7 (5)	10 (7)
Concurrent RT to other sites	30 (22)	18 (13)

RT, radiotherapy; MV, megavolts; MeV, mega-electron volts; kV, kilovolts.

XRT – 94-17 – **96-05** – Norway/Sweden – Spanish – SBRT

TROG 96-05

Table 4
Response to radiotherapy

	8/1 (n=137)	20/5 (n=135)
Best response, n (%)		
Complete response	35 (26)	36 (27)
Partial response	38 (28)	47 (35)
No change	22 (16)	16 (12)
Worsening of pain	24 (18)	16 (12)
Not assessable	18 (13)	20 (15)
Reasons not assessable, n		
No radiotherapy given	3	2
Early death (within 32 days)	7	6
No follow-up/non-compliance	2	4
No pre-treatment assessment	0	1
Masked by other pain or changes in analgesia/ systemic therapy	6	7
Overall response rate, % (95% CI)	53 (45-62)	61 (53-70)
Complete response rate, % (95% CI)	26 (18-34)	27 (19-35)

XRT – 94-17 – **96-05** – Norway/Sweden – Spanish – SBRT

TROG 96-05

Outcome	8 Gy x 1	4 Gy x 5	Significance
Overall response rate (2 mo)	53%	61%	NS
Complete response rate (2 mos)	26%	27%	NS
Time to treatment failure	2.4 mo	3.7 mo	NS

- Median OS: 4.8 months
- 8Gy x 1 was not shown to be as effective as 20Gy in 5 fractions, nor was it statistically significantly worse
- No significant differences in the rates of re-treatment, cord compression, or pathological fracture by treatment arm

XRT – 94-17 – **96-05** – Norway/Sweden – Spanish – SBRT

Single versus multiple fraction treatment

- **Norway/Sweden**
- Phase III prospective randomized trial
- 376/1000 patients (trial closed early due to interim analysis findings)
- Included biopsy- or cytology-proven disease, bone metastasis (any site), KPS >40
- Excluded spinal cord compression, previous RT to symptom site, life expectancy <6 weeks, bone surgery needed
- Randomized to 2 arms: 8Gy x 1 fraction versus 30Gy x 10 fractions
- Primary endpoint:
  - Degree and duration of pain relief over the first 28 weeks
- Secondary endpoints
  - Fatigue
  - Quality of life

XRT – 94-17 – 96-05 – **Norway/Sweden** – Spanish – SBRT

Norway/Sweden

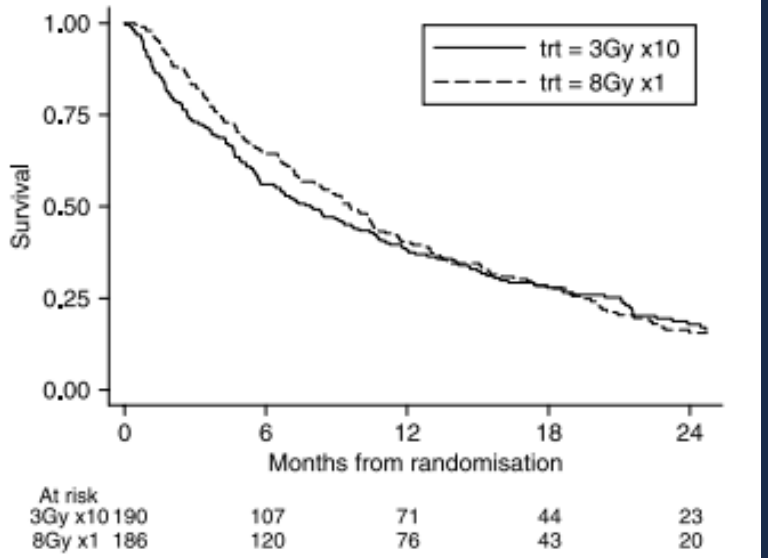


Fig. 1. Overall survival in 376 patients treated with single or multiple fraction radiotherapy for painful bone metastases.

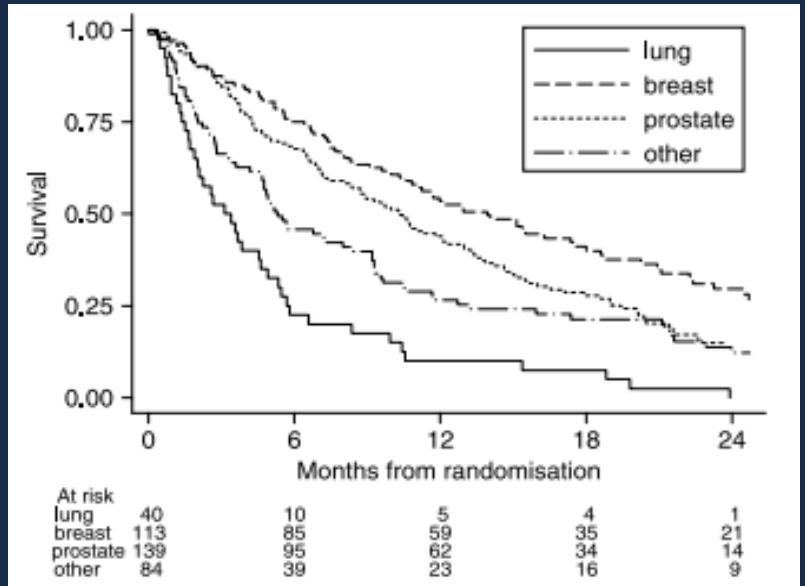


Fig. 2. Survival by diagnosis in 376 patients treated with single or multiple fraction radiotherapy for painful bone metastases.

XRT – 94-17 – 96-05 – **Norway/Sweden** – Spanish – SBRT

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Norway/Sweden

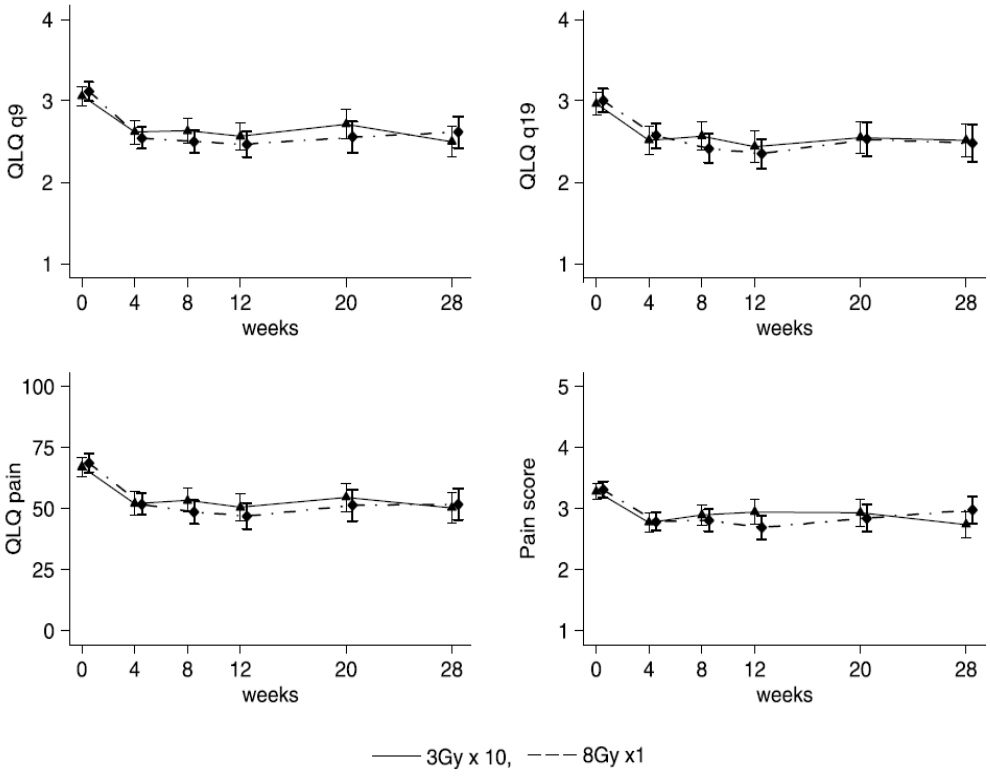

Fig. 3. Pain in patients randomised to single or multiple fractions radiotherapy for painful bone metastases. QLQ q9 = 'Have you had pain?' QLQ q19 = 'Did pain interfere with your daily activities?'.

XRT – 94-17 – 96-05 – **Norway/Sweden** – Spanish – SBRT

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Norway/Sweden

Table 4
Additional treatment in patients having received radiotherapy for painful bone metastases

Type of treatment	3 Gy×10 (M) 8 Gy×1 (*n*)	8 Gy×1 (*n*)
Radiotherapy to new painful sites	61	78
Re-treatment of previous volume	7	29
Treatment for pathological fractures[a]	21	8
Treatment for spinal cord compression[a]	5	10
Chemotherapy	32	22
Surgery	15	9

[a] Not referable to treatment site only.

XRT – 94-17 – 96-05 – **Norway/Sweden** – Spanish – SBRT

Norway/Sweden

- Study terminated early at interim analysis
- Conclusions
  - 8Gy x1 versus 30Gy in 10 fractions provides same degree of pain relief and impact on fatigue and overall quality of life is equivalent
  - Recommend 8Gy x1 as standard treatment due to its much lower cost, greater convenience to patients, and being as effective for relief of pain due to bone metastasis as multiple fraction regimens

Norway/Sweden long-term follow-up

- 180 pts were included in the analysis
- Follow-up time until death
- 32 pts (18%) needed re-irradiation
- Conclusions:
  - Similar efficacy between 8 Gy x 1 and 3 Gy x 10 for treatment of painful bony mets
  - Higher re-irradiation rate for 8 Gy x 1 group
  - Single fraction treatment is considered more convenient as well as more cost-effective

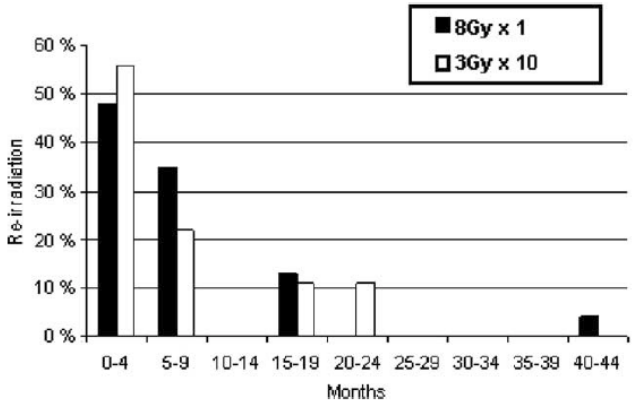


Fig. 2. Time to re-irradiation by initial randomisation for 32 patients with painful bone metastases randomised to single- or multiple-fraction radiotherapy.

Table 2
Re-irradiations, pathological fractures and spinal cord compressions according to primary treatment regimen, ($n = 180$).

	8 Gy × 1	3 Gy × 10	*p*-Value	Total
Re-irradiation	23 (27% [a])	9 (9%)	0.002	32 (18% [b])
Pathological fracture	4 (5%)	5 (5%)	1.00	9 (5%)
Spinal cord compression	1 (1%)	4 (4%)	0.37	5 (3%)
Skeletal-related events (SRE)[c]	28 (33%)	18 (19%)	0.011	46 (26%)
Total	85 (100%)	95 (100%)		180 (100%)

[a] Percent within treatment arms.
[b] Percent within the total of patients.
[c] Includes at least one event of re-irradiation, pathological fracture or spinal cord compression following irradiation for bone metastases.

XRT – 94-17 – 96-05 – **Norway/Sweden** – Spanish – SBRT

Single versus multiple fraction treatment

- **Spanish study**
- Phase III prospective randomized trial
- 160 patients with painful bone metastases
- Included presence of multiple bone metastases but only one site of pain, life expectancy ≥ 4 weeks
- Excluded pain due to pathological fracture, spinal cord compression, pain at > 1 site, received prior RT at same site
- Randomized to 2 arms: 8Gy x 1 fraction versus 30Gy x 10 fractions
- Primary endpoint:
  - Overall, complete, and partial responses
- Secondary endpoints
  - Acute toxicity
  - Re-treatment

XRT – 94-17 – 96-05 – Norway/Sweden – **Spanish** – SBRT

Spanish study

Table 2
Overall response rates

Weeks	30 Gy		8 Gy		*p*
	n	Rates%	*n*	Rates%	
3	71	86	59	75	ns
12	51	62	51	65	ns

XRT – 94-17 – 96-05 – Norway/Sweden – **Spanish** – SBRT

Spanish study

Table 3
Complete response rates

Weeks	30 Gy		8 Gy		*p*
	n	Rates %	*n*	Rates %	
3	11	13	12	15	ns
12	9	11	10	13	ns

Table 4
Partial response rates

Weeks	30 Gy		8 Gy		*p*
	n	Rates %	*n*	Rates %	
3	60	73	47	60	ns
12	42	51	41	52	ns

XRT – 94-17 – 96-05 – Norway/Sweden – **Spanish** – SBRT

Spanish study

Table 5
Gain and percentage of pain progression, net pain relief, toxicity, and re-treatment

	30 Gy	8 Gy	*p*
Gain	4	3.5	ns
Pain progression %	43	28	ns
Net pain relief %	71	68	ns
Toxicity %	18	12	ns
Re-treatment %	2	28	0.001

XRT – 94-17 – 96-05 – Norway/Sweden – **Spanish** – SBRT

Spanish study

	3 Gy x 10	8 Gy x 1	Significance
Overall Response	86%	75%	NS
Complete Response	13%	15%	NS
Partial response	73%	60%	NS
Acute toxicity	18%	12%	NS
Retreatment	2%	28%	SS

- 8 Gy x 1 is as effective as 3 Gy x 10 in terms of complete, partial and overall response rate
- 8 Gy x 1 group had higher rate of re-irradiation

XRT – 94-17 – 96-05 – Norway/Sweden – **Spanish** – SBRT

Single versus multiple fraction treatment summary

Study	Patient number, tumor histology	Fractionation	Overall response (%)	Complete response (%)	Acute toxicity (%)	Late toxicity (%)	Re-treatment rate (%)
Radiation Therapy and Oncology Group 97-14[a]	*n* = 898, breast or prostate cancer	8 Gy per 1 fraction	66%	15%	10%	4%	18%
		30 Gy per 10 fractions	66%	18%	17%	4%	9%
Trans-Tasman Radiation Oncology Group 96-05 (neuropathic pain)[b]	*n* = 272, various histologies	8 Gy per 1 fraction	53%	26%	5%	5%	29%
		20 Gy per 5 fractions	61%	27%	11%	4%	24%
Prospective randomized multicenter trial on single-fraction radiotherapy versus multiple fractions[c]	*n* = 376, various histologies	8 Gy per 1 fraction	Equivalent	NR	NR	4%	15%
		30 Gy per 10 fractions	Equivalent	NR	NR	11%	4%
Randomized clinical trial with two palliative radiotherapy regimens in Spain[d]	*n* = 160, various histologies	8 Gy per 1 fraction	75%	15%	12%	NR	28%
		30 Gy per 10 fractions	86%	13%	18%	NR	2%

XRT – 94-17 – 96-05 – Norway/Sweden – Spanish – SBRT

Conventional Radiation

- Symptomatic relief with conventional RT (ie. 30/10, 8/1) provides unsatisfactory results
- RTOG 97-14
  - Arm 1) RT 8/1 vs. Arm 2) 30/10. Primary outcome pain relief at 3 months
  - Outcome: 3-month complete pain relief 8/1 15% vs. 30/10 18% (NS); partial 50% vs. 48% (NS); stable 26% vs 24%; progressive 9% vs 10%
- TROG 96.05
  - Randomized trial of 8 Gy in 1 versus 20 Gy in 5 fractions
  - Response rate: 53% vs. 61% (p=NS)
  - TTF 2.4 mo vs. 3.7 mo

XRT – 94-17 – 96-05 – Norway/Sweden – Spanish – SBRT

SBRT

- **UPMC**
- Single institution prospective cohort study
- 500 cases of spinal metastases (cervical 15%, thoracic 42%, lumbar 22%, sacral 20%), treated with radiosurgery
- Maximum dose 12.5-25 Gy (mean 20 Gy). Prior EBRT 69% (typically 30/10 or 35/14)
- PTV = GTV
- Long-term pain control 86%; at least some improvement in neurologic function in 85%

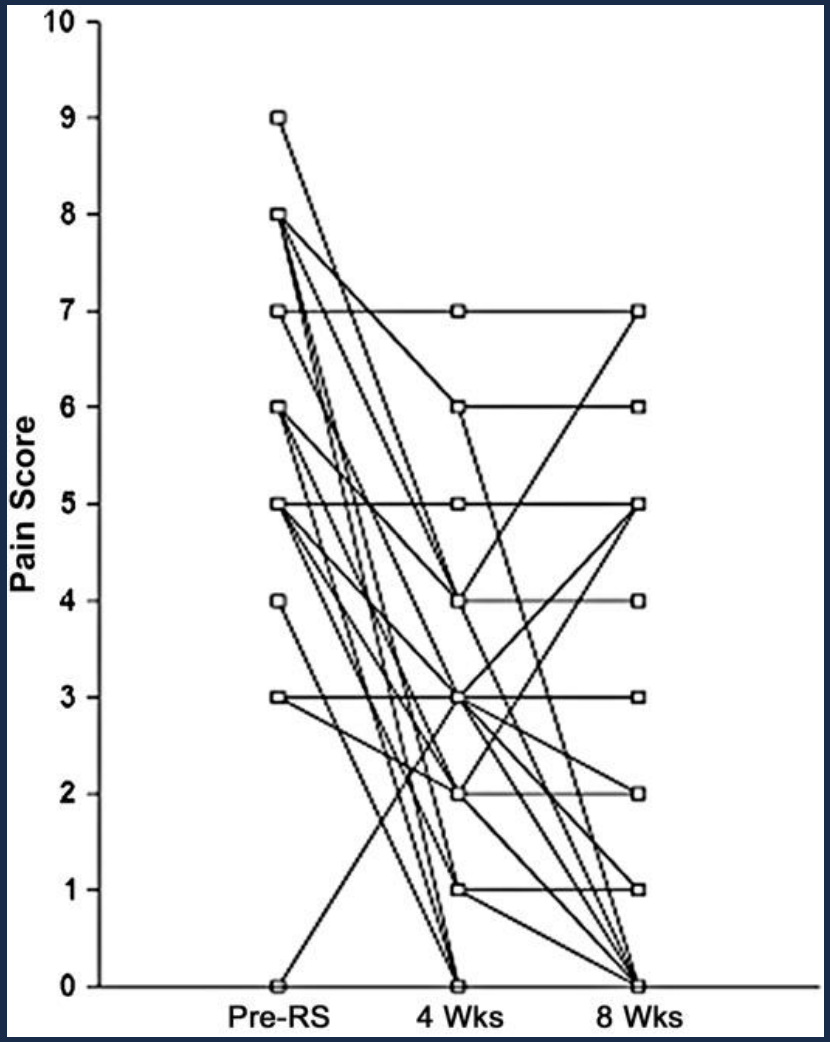
Table 3. Summary of Pain and Radiographic Outcome for the 4 Most Common Histopathologies (n = 294)

Long-term pain improvement	
All patients	86%
Renal cell	94%
Breast	96%
Lung	93%
Melanoma	96%
Long-term radiographic control	
All patients	88%
Renal cell	87%
Breast	100%
Lung	100%
Melanoma	75%

XRT – 94-17 – 96-05 – Norway/Sweden – Spanish – **SBRT**

SBRT

- **Henry Ford**
- Single institution prospective cohort study
- 49 patients with 61 separate spinal metastases were treated with radiosurgery
- Dose ranged from 10-16 Gy, single fraction
- PTV = involved spinal segment
- Median time to pain relief 14 days, fastest 24 hrs
- 1 yr overall pain control rate 84%
- Strong trend of increasing pain control with dose ≥ 14 Gy



XRT – 94-17 – 96-05 – Norway/Sweden – Spanish – **SBRT**

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SBRT

- **RTOG 0613**
- Phase III randomized control trial
- 352 patients to be recruited
- Included are localized spine metastasis with up to 3 separate sites
- Excluded are cord compression/cauda equina, prior RT to site, non-ambulatory
- Randomized to 2 arms (2:1): SBRT 16/18Gy x1 versus 8Gy x1
- Primary endpoint: pain control at 3 months
- Secondary endpoints
  - Rapidity of pain control
  - Duration of pain response
  - Quality of life
  - Adverse events

XRT – 94-17 – 96-05 – Norway/Sweden – Spanish – **SBRT**

SBRT Summary

- Dose escalation provides potential to improve local control and symptom relief over conventional treatment, especially in the setting of oligometastases and prolonged survival
- SBRT makes dose escalation possible while limiting dose to the spinal cord
- Rapid pain control
- Spares bone marrow especially in patients with multiple segments involved
- Shorter overall treatment time more convenient and less likely to interfere with systemic therapy

XRT – 94-17 – 96-05 – Norway/Sweden – Spanish – **SBRT**

ASTRO SBRT consensus guidelines

Characteristic	Inclusion	Exclusion
Radiographic	1) Spinal or paraspinal metastasis by MRI (50, 51) 2) No more than 2 consecutive or 3 noncontiguous spine segments involved (50–53)	1) Spinal MRI cannot be completed for any reason (50, 51) 2) Epidural compression of spinal cord or cauda equina 3) Spinal canal compromise >25% (58) 4) Unstable spine requiring surgical stabilization (50, 51, 54, 57) 5) Tumor location within 5 mm of spinal cord or cauda equina (50, 51) (relative*)
Patient	1) Age ≥18 y (50, 54) 2) KPS of ≥40–50 (50, 51, 54, 55) 3) Medically inoperable (or patient refused surgery) (50, 51)	1) Active connective tissue disease (50) 2) Worsening or progressive neurologic deficit (50–52, 57) 3) Inability to lie flat on table for SBRT (50–52) 4) Patient in hospice or with <3-month life expectancy
Tumor	1) Histologic proof of malignancy (50, 51, 56) 2) Biopsy of spine lesion if first suspected metastasis 3) Oligometastatic or bone only metastatic disease (50)	1) Radiosensitive histology such as MM[50-52] 2) Extraspinal disease not eligible for further treatment[51]
Previous treatment	Any of the following: 1) Previous EBRT <45-Gy total dose 2) Failure of previous surgery to that spinal level (50–52) 3) Presence of gross residual disease after surgery	1) Previous SBRT to same level 2) Systemic radionuclide delivery within 30 days before SBRT (50–52) 3) EBRT within 90 days before SBRT (50–52) 4) Chemotherapy within 30 days of SBRT (50–53)

XRT – 94-17 – 96-05 – Norway/Sweden – Spanish – **SBRT**

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RTOG 94-17

- Evaluated outcome differences by gender and partner status
- Gender, marital status, KPS and treatments were variables tested when evaluating the time to re-treatment
- Results:
  - Longer time to retreatment in married men, married women, and single woman receiving 30Gy in 10 fractions
  - No difference in retreatment rate over time in single men receiving either 8 Gy x 1 or 30Gy in 10 fractions
  - Univariate analysis of the entire group with 30Gy in 10 fractions → less likely to receive retreatment
- Conclusions:
  - 8Gy x 1 group had higher retreatment rates
  - Non-disease related variables, such as social support, might influence the results such as retreatment rate

RT0G-94-17

- No difference in retreatment rates in men without partners receiving either 8Gy x 1 or 30Gy in 10 fractions
- Patients receiving 8Gy x 1 had significantly higher retreatment rates compared with patients receiving 30Gy in 10 fractions
- Retreatment rates not influenced by initial pain score

Table 2. 36-month retreatment by radiation dose within gender and partner status subgroups*

	30 Gy	8 Gy	*p* value*
Female			
Partner	7%	16%	0.0052
No partner	1%	15%	0.0009
Male			
Partner	8%	18%	0.0067
No partner	9%	6%	0.5551

* The cumulative incidence method was used to estimate the retreatment rates, and Gray's test was used to test for difference between the radiation dose treatment groups.

Table 4. 36-month retreatment rates by partner grouping with baseline pain severity subgroups*

	Males with no partner		Males with partner/females		
Pain severity	*n*	36-month rate	*n*	36-month rate	*p* value
None/Mild	18	0%	98	15%	0.1317
Moderate/Severe	94	9%	589	11%	0.6522

* The cumulative incidence method was used to estimate the retreatment rates, and Gray's test was used to test for differences between the partner status groups.

RTOG 94-17: Economic Analysis

- RTOG 97-14: Is multiple fraction treatment cost-effective in treating patients with bone metastasis by preventing further re-treatment
- Markov Model to evaluate the cost-effectiveness
- Results:
  - Incremental cost-effectiveness ration (ICER): $6973/quality-adjusted life year.
- Conclusions:
  - Single fraction treatment was less expensive treatment in the treatment of patients with bone metastasis treated on RTOG 97-14

	3 Gy x 10	**8 Gy x 1**
Mean cost	$ 2316	$ 998
Quality-adjusted survival	9.53 mos	7.26 mos

International patterns of practice in palliative radiotherapy for painful bone metastases: Evidence-base practice?

- Surveys showed single fraction schedules remain underused despite multiple randomized control trials demonstrating the equivalence of single fraction radiotherapy compared to multi-fraction radiotherapy
- Current patterns of practice internationally and factors influencing this practice
- Internet-based survey of members of ASTRO, CARO, Royal Australian and New Zealand College of Radiologists
- 5 hypothetical cases describing pts with single or multiple painful bone metastases from breast, lung, prostate cancer
  - XRT dose fractionation recommended?
  - Rating the importance of patient, tumor, institution, and treatment factors.

International patterns of practice in palliative radiotherapy for painful bone metastases: Evidence-base practice?

- Results
  - 962 respondents (75% ASTRO members)
  - 101 different dose schedules (3 Gy/1 to 60 Gy/20); overall median dose: 30 Gy/10
  - Single fractionation used least often by ASTRO members practicing in the US and most often by CARO members
  - Case, membership affiliation, country of training, location of practice and practice type = Independent predictive factors of use of the single fraction radiotherapy
  - Prognosis, risk of spinal cord compression, and performance status: principal factors considered when prescribing

International patterns of practice in palliative radiotherapy for painful bone metastases: Evidence-base practice?

Table 2. Dose fractionation by primary affiliation

Case	Membership affiliation	*n*	Dose fractionation used: Median dose (range)	Dose fractionation used: SF used (*n*)	*p**
Case 1, breast cancer with thoracic spine metastases					
	ASTRO (US)	428	30 Gy/10 (8 Gy/1–50 Gy/25)	16 (3.7)	< .0001†
	ASTRO (non-US)	206	30 Gy/10 (8 Gy/1–50 Gy/25)	35 (17.0)	.003†
	CARO	115	20 Gy/5 (8 Gy/1–30 Gy/10)	36 (31.3)	—
	RANZCR	97	20 Gy/5 (8 Gy/1–40 Gy/20)	19 (19.6)	.05
Case 2A, prostate cancer with shoulder metastasis					
	ASTRO (US)	447	30 Gy/10 (7 Gy/1–50 Gy/25)	70 (15.6)	< .0001†
	ASTRO (non-US)	198	8 Gy/1 (6 Gy/1–40 Gy/20)	77 (38.9)	< .0001†
	CARO	118	8 Gy/1 (8 Gy/1–30 Gy/10)	81 (68.6)	—
	RANZCR	97	8 Gy/1 (8 Gy/1–30 Gy/10)	63 (64.9)	.56
Case 2B, prostate cancer with femur metastasis					
	ASTRO (US)	276	30 Gy/10 (7 Gy/1–60 Gy/20)	31 (11.2)	< .0001†
	ASTRO (non-US)	122	30 Gy/10 (8 Gy/1–50 Gy/20)	29 (23.8)	< .0001†
	CARO	55	8 Gy/1 (8 Gy/1–30 Gy/10)	31 (56.4)	—
	RANZCR	37	20 Gy/5 (8 Gy/1–30 Gy/10)	13 (35.1)	.045
Case 3, NSCLC with spine metastasis					
	ASTRO (US)	441	30 Gy/10 (3 Gy/1–55 Gy/22)	25 (5.7)	< .0001†
	ASTRO (non-US)	208	30 Gy/10 (6 Gy/1–50 Gy/25)	55 (26.4)	.03
	CARO	113	20 Gy/5 (8 Gy/1–30 Gy/10)	43 (38.4)	—
	RANZCR	98	20 Gy/5 (8 Gy/1–30 Gy/10)	40 (40.8)	.68
Case 4, NSCLC with neuropathic pain, spine BM					
	ASTRO (US)	423	30 Gy/10 (3 Gy/1–45 Gy/18)	11 (2.6)	< .0001†
	ASTRO (non-US)	202	30 Gy/10 (6 Gy/1–44 Gy/20)	22 (10.9)	.142
	CARO	114	20 Gy/5 (8 Gy/1–30 Gy/10)	19 (16.7)	—
	RANZCR	98	20Gy/5 (6Gy/1–33Gy/10)	9 (9.2)	.109
Case 5A, prostate cancer with spine retreatment					
	ASTRO (US)	178	20 Gy/10 (4 Gy/1–50 Gy/20)	27 (15.2)	< .0001†
	ASTRO (non-US)	190	8 Gy/1 (4 Gy/1–40 Gy/20)	47 (24.7)	< .0001†
	CARO	69	8 Gy/1 (6 Gy/1–25 Gy/10)	36 (52.2)	—
	RANZCR	74	8 Gy/1 (6 Gy/1–25 Gy/10)	29 (39.2)	.119
Case 5B, prostate cancer with hip retreatment					
	ASTRO (US)	259	20 Gy/10 (6 Gy/1–50 Gy/20)	50 (19.3)	< .0001†
	ASTRO (non-US)	101	8 Gy/1 (4 Gy/1–30 Gy/12)	49 (48.5)	.001†
	CARO	77	8 Gy/1 (6 Gy/1–25 Gy/10)	52 (67.5)	—
	RANZCR	74	8 Gy/1 (6 Gy/1–30 Gy/10)	38 (51.4)	.043

Abbreviations: SF = single fraction; NSCLC = non–small-cell lung cancer; BM = bone metastasis; other abbreviations as in Table 1.
Data in parentheses are percentages, unless otherwise noted; percentages might not sum to 100% because of rounding.
* Reference category: CARO.
† Statistically significant; significance level, $p < .007$.

International patterns of practice in palliative radiotherapy for painful bone metastases: Evidence-base practice?

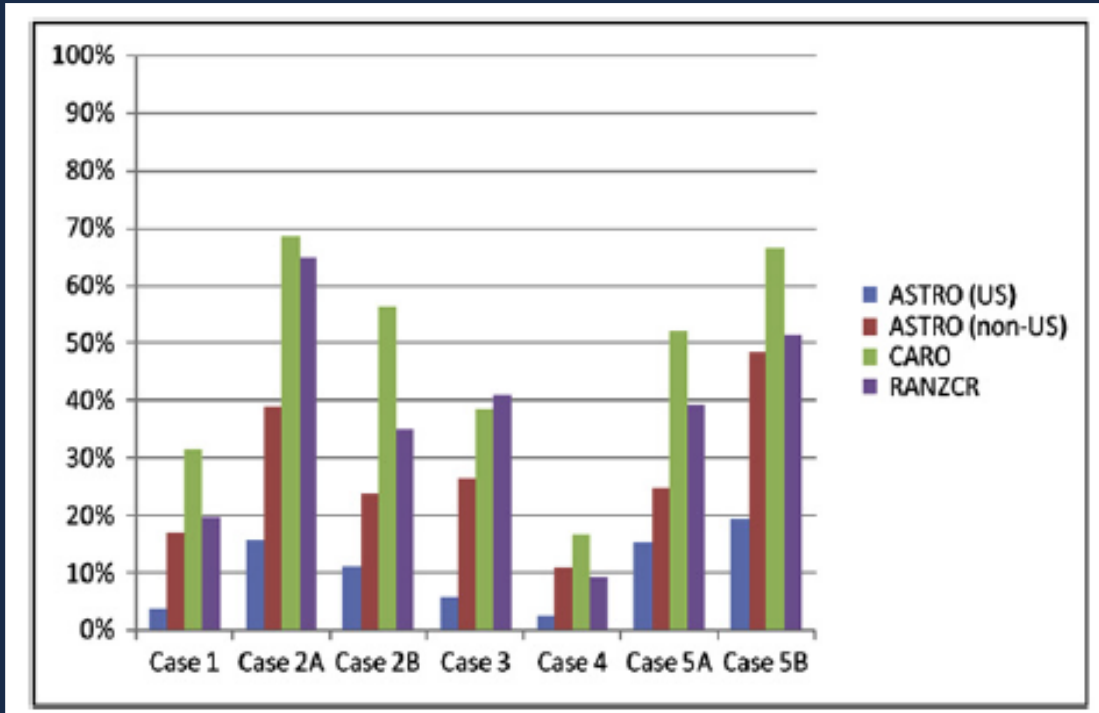

Fig. 1. Use of single-fraction radiotherapy.

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International patterns of practice in palliative radiotherapy for painful bone metastases: Evidence-base practice?

- Conclusions:
  - Most radiation oncologists continue to prescribe multi-fractionation schedules, despite abundant evidence
  - Delay in the incorporation of evidence into practice for palliative radiotherapy for painful bone metastases

Re-irradiation

- 2004-2014: Multicenter, non-blinded, randomized, controlled trial
  - 850 patients with painful bony metastases with prior radiation therapy
  - Arm 1: 8 Gy/1 (425 pts)
  - Arm 2: 20 Gy/8 (425 pts)

	8 Gy x 1	2.5 Gy x 8	Significance
Overall response (intention-to-treat)	28%	32%	NS
Overal response in per-protocol population	45%	51%	NS
Lack of appetite	56%	66%	SS
Diarrhea	23%	31%	SS

- No statistical difference in pathological fractures or cord/cauda equina compression
- Conclusions
  - 8 Gy x 1 seems to be non-inferior and less toxic than 20 Gy in multiple fractions

Consortium SBRT contouring guidelines

- GTV
  - Contour gross tumor using all available imaging
  - Include epidural and paraspinal components of tumor
- CTV
  - Include abnormal marrow suspicious for microscopic invasion
  - Include bony CTV expansion to account for subclinical spread
  - Should contain GTV
  - Circumferential CTVs encircling the cord should be avoided
- PTV
  - Uniform expansion around CTV
  - CTV to PTV margin ≤ 3mm
  - Never overlaps with cord
  - Should contain entire CTV and GTV

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Cox et al. IJROBP 2012