

Incontri di aggiornamento del Dipartimento Oncologico

Terapia del dolore nell'anziano oncologico

RUOLO DELLA RADIOTERAPIA

ALBA FIORENTINO

Radioterapia Oncologica



Terapia del dolore nell'anziano oncologico

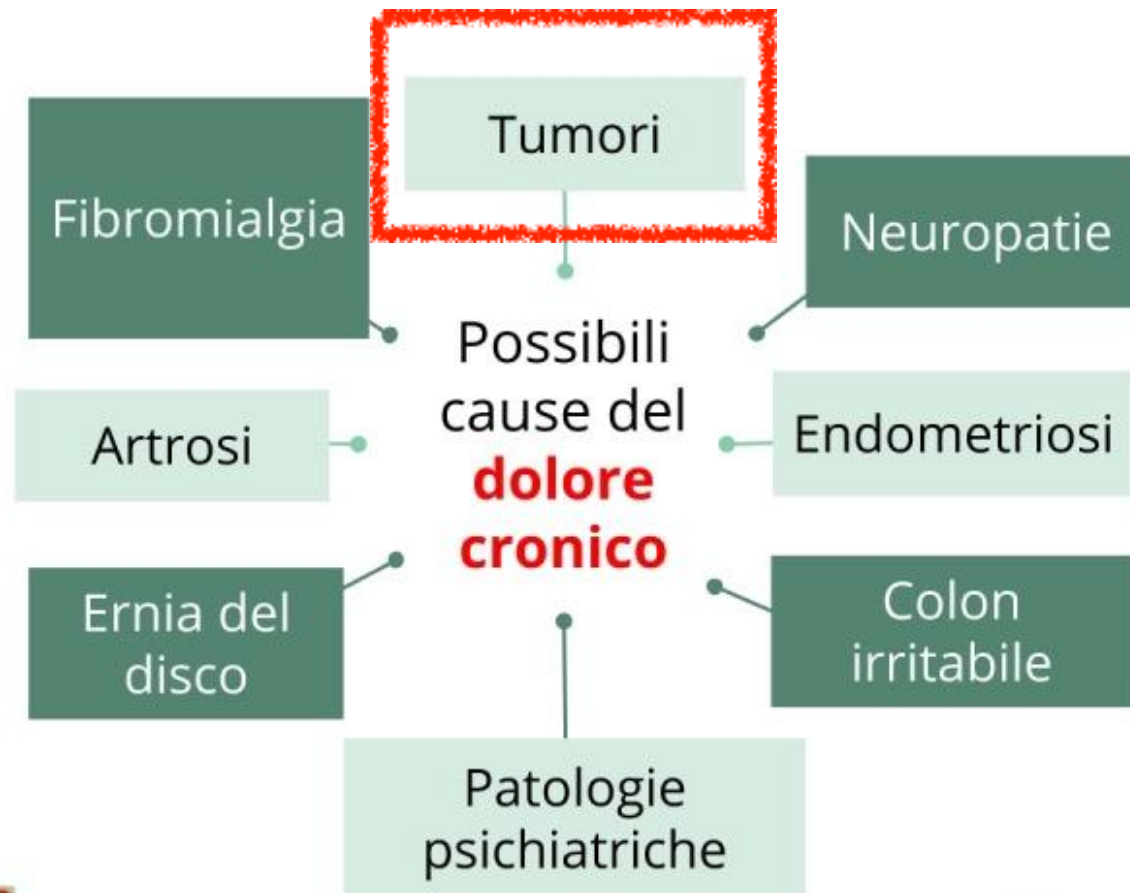
RUOLO DELLA RADIOTERAPIA



- [dolore nocicettivo](#) basato primordialmente sull'irritazione dei sensori di dolore ([nocicettori](#)) e trasmissione
- [dolore neuropatico](#) in seguito a lesioni del [sistema nervoso periferico](#) o del [sistema nervoso centrale](#)

Terapia del dolore nell'anziano oncologico

RUOLO DELLA RADIOTERAPIA



Terapia del dolore nell'anziano oncologico

RUOLO DELLA RADIOTERAPIA

Il paziente anziano:
cronicità e fragilità



Il dolore è uno dei fattori che maggiormente condiziona la qualità di vita per i pazienti di tutte le età, ma in particolare modo per quelle più fragili.

Terapia del dolore nell'anziano oncologico

RUOLO DELLA RADIOTERAPIA

- Il dolore da **metastasi ossee** è responsabile di circa il 50% dei casi di dolore neoplastico.
- I meccanismi che mediano l'effetto antalgico della radioterapia non sono del tutto noti.
- **Probabile effetto citocida** → < compressione/infiltrazione → < citochine sui recettori del dolore
- **Verosimile effetto bersaglio su metabolismo osteoclasti aggiuntivo:** nel 25% risposta in 24-48h dopo l'inizio della RT, anche senza riduzione della massa (effetto delle radiazioni su *osteoclasti*)

Terapia del dolore nell'anziano oncologico

RUOLO DELLA RADIOTERAPIA

Med Oncol (2012) 29:3467–3471
DOI 10.1007/s12032-012-0246-4

ORIGINAL PAPER

Il paziente anziano:
cronicità e fragilità



Comorbidity assessment and adjuvant radiochemotherapy in elderly affected by glioblastoma

Alba Fiorentino · Rocchina Caivano · Costanza Chiumento ·

The cancer development and the normal tissue radiation-sensitivity or response could be affected by the aging process [20, 21]. Due to the organ alterations and the decreasing of functional reserve, the oldest could tolerate a lower dose of radiotherapy, experiencing higher toxicity than the younger. Moreover, the organ alterations could be caused by comorbidities, which are closely related with age [20–22].

Terapia del dolore nell'anziano oncologico

RUOLO DELLA RADIOTERAPIA

Il paziente anziano:
cronicità e fragilità



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JOURNAL OF CLINICAL ONCOLOGY

A Plethora of Therapeutic Opportunities for Elderly Patients With Cancer: A Nontrivial Choice

Alba Fiorentino, Rosario Mazzola, Niccolò Giaj Levra, Francesco Ricchetti, Sergio Fersino, and Filippo Alongi
Sacro Cuore Don Calabria Hospital, Negrar-Verona, Italy

In conclusion, the nihilism in the treatment of the elderly might be anachronistic

METASTASI OSSEE & RT

Palliative Radiotherapy—New Approaches

Birgitt van Oorschot,^a Dirk Rades,^b Wolfgang Schulze,^c Gabriele Beckmann,^d and Petra Feyer^e

- “.. In **up to 70% to 80%** of patients, significant pain relief can be achieved. This pain relief results in both an improved quality of life and a significant reduction of pain medication..”
- Complete Response in 30-50% of cases (opioids interruption)

METASTASI OSSEE: EFFETTO ANTALGICO

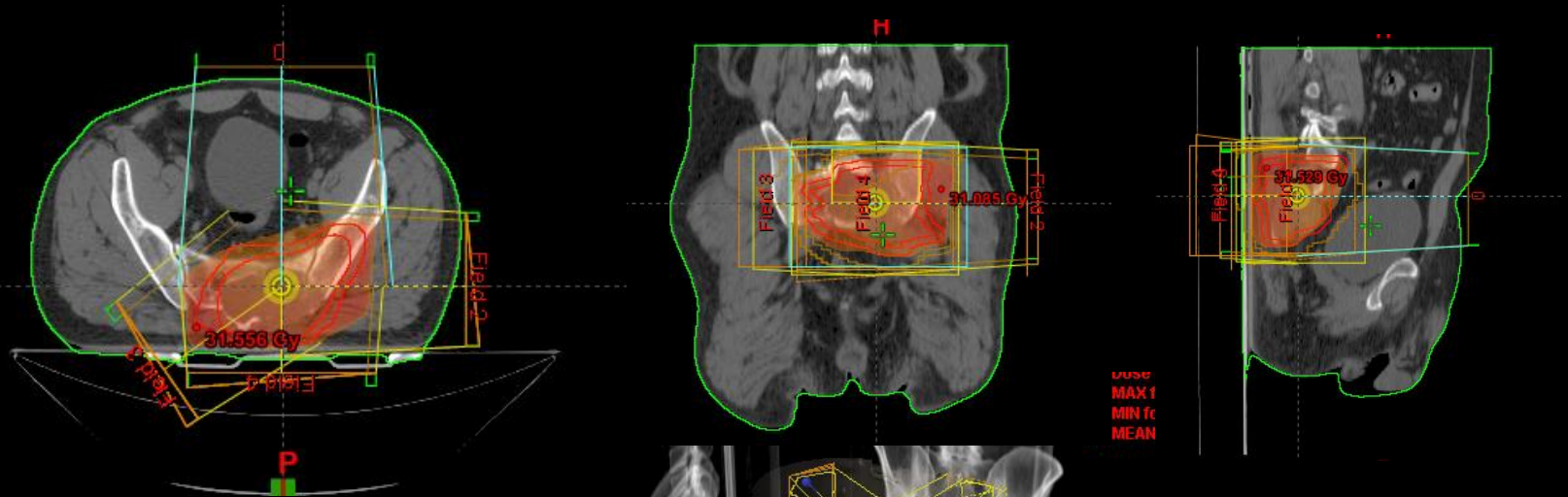
- Riposta antalgica fino all'85%, completa nel 30%.
- Talora “Pain Flair” durante RT da edema radioindotto, di solito remissione del fenomeno in quasi tutti casi.
- Effetto Antalgico garantito storicamente con dosi relativamente basse di RX *empiricamente/utilitaristicamente* scelte tra:
 - 30 Gy in 10 sedute
 - 20 Gy in 5
 - 8Gy seduta unica.

METASTASI OSSEE: QUALE SCHEMA?

Tab.1 Randomized Trials comparing multiple fraction treatments for palliation of bone metastases

Study	N° of Pz (N° Eval.)	Dose (Gy/fractions)	Complete Response (%)	Overall Response	Path Fractures(%)
Tong et al,1982, USA (solitary treatment site)	266 (146)	20/5	53	82	4
		40/15	61	85	18
(multiple site)	750 (613)	15/5	49	87	5
		20/5	56	85	7
		25/5	49	83	9
		30/10	57	78	8
Hirokawa et al., 1988, Japan	128	25/5	NA	75	NA
		30/10		75	
Rasmusson et al., 1995, Danmark	217 (127)	15/3	NA	69	NA
		30/10		66	
Niewald et al., 1996, Germany	100	20/5	33	77	8
		30/10	31	86	13

PALLIATIVE/SYMPHTOMATIC BONE RADIOTHERAPY



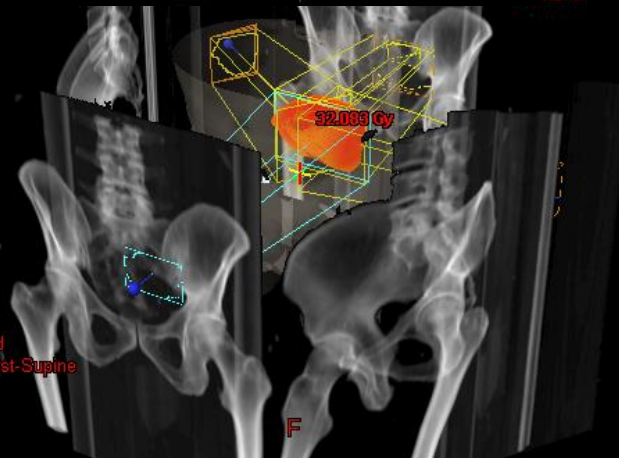
Sacral bone metastasis

**Dose prescription:
30 Gy in 10 fractions**

**Technique:
3DCRT**



Standard
Head First-Supine



METASTASI OSSEE: QUALE SCHEMA?

TABLE 1
Prospective Randomized Trials That Included Single-fraction Radiation for Painful Bony Metastasis

Reference	no. of patients	Primary tumor site	Dose, Gy	Fractions	Response, %	Significance	Retreatment rate, %
Price et al, 1986 ⁷	288	Any	8 30	1 10	45 28	NS	11 3
Cole, 1989 ⁸	29	Any	8 24	1 6	90 86	NS	25 0
Hoskin et al, 1992 ⁹	270	Any	4 8	1 1	44 69	$P < .001$	20 9
Gaze et al, 1997 ¹⁰	265	Any	10 22.5	1 5	81 89	NS	
Nielsen et al, 1998 ¹¹	241	Any	8 20	1 4	62 71	NS	21 12
Jeremic et al, 1998 ¹²	327	Any	4 6 8	1 1 1	59 73 78	$P = .025$ $P = .0019$	
Steenland et al, 1999 ¹³	1171	Any	8 24	1 6	72 69	NS	25 7
Yarnold, 1999 ¹⁴	765	Any	8 20	1 5	72 68	NS	23 10
Kirkbride et al, 2000 ¹⁵	398	Any	8 20	1 5	51 48	NS	
Hartsell et al, 2005 ¹⁶	949	Breast or prostate	8 30	1 10	65 66	NS	18 9
Roos et al, 2005 ¹⁷	272	Any (neuropathic)	8 20	1 5	53 61	NS	24 29

Gy indicates grays; NS, not significant.

METASTASI OSSEE: SINGOLA FRAZIONE?

Tabella.2 Randomized Trials of Single versus Multiple Fractions: Results

Study	N° of Pz (N° Eval.)	Dose (Gy/fractions)	Median Survival (mo)	Complete Response	Overall Response	Retreat Rate (%)	Path Fractures(%)	Toxicity
Gaze et al., 1997 UK (9)	265	10/1 vs 22.5/5	NA	37 47	81 76	NA	NA	21% p=NS 26% emesis
Nielsen et al., 1998, Denmark (10)	241 (239)	8/1 vs 20/5	NA	15 15	73 76	21 12	NA	No difference
Steenland et al., 1999, Netherlands (11)	1171 (1073)	8/1 vs 20/5	7	37 33	72 69	25 7	4 2	No difference
Bone Pain Working Party, 1999, UK/New Zeland (12)	765(681)	8/1 vs 20/5	NA	57 58	78 78	23 10	2 <1	No difference
Koswing & Budach, 1999, Germany (18)	107	8/1 vs 30/10	NA	33 31	81 78	NA	NA	NA
Kirkbride et al, 2000, Canada (19)	398 (287)	8/1 vs 20/5	NA	22 29	51 48	NA	NA	NA
Hartsell et al., 2005 USA/Canada (13)	949 (898)	8/1 vs 30/10	9.1 9.3	15 18	65 66	18 9	5 4	10% G 2-4 17% p=.002
Kaasa et al., 2006 Norway/Sweden (14)	376	8/1 vs 30/10	9.6 7.9	NA	No difference	16 4	4 11	NA
Arnallot et al., 2008 Spain (68)	160	8/1 vs 30/10	NA	13 11	75 86	28 2	NA	No difference
Kaasa et al., 2009 Norway/Sweden (69)	(198)180	8/1 vs 30/10	NA	NA	NA	27 9	4 5	NA

NA, not available

NS, not statistically significant.

METASTASI OSSEE: SINGOLA FRAZIONE?

Da una recente metanalisi che ha valutato ulteriori 5 studi randomizzati rispetto a quelli precedenti citati si evince che non c'è differenza statisticamente significativa nella risposta antalgica tra le due modalità di frazionamento. (*Livello di Evidenza SIGN 1++*).

E. Chow, L. Zeng, N. Salvo Update on the Systematic Review of Palliative Radiotherapy Trials for Bone Metastases
Clinical Oncology 24 (2012) 112e124

Comunque...

nella pratica clinica molti Radioterapisti Oncologi Italiani, Europei e Americani continuano ad adottare l'ipofrazionamento (3-30 Gy, 4 – 20 Gy) piuttosto che la dose unica di 8 Gy.

Questo atteggiamento può trovare una spiegazione nel fatto che in genere gli studi randomizzati di fase III a favore del frazionamento unico non sono considerati definitivi perché non “doppio-cieco” e perché privi di una valutazione della qualità di vita.

Incremento dei Re-treatment

METASASI OSSEE:

DECISIONE IN BASE A PROGNOSI E INTENTO

Dosage	Prognosis and Indications	Duration of Therapy	Response Rate
1 x 8 Gy	Prognosis: life expectancy <3 mo —painful uncomplicated bone metastases	1 d	60%–90%
2 x 7.5 Gy	Prognosis: life expectancy only a few weeks —bronchogenic carcinoma with bronchial occlusion/compression	1 wk	30%–90%
4–6 x 0.5–1 Gy	Inhibition of inflammation	1 wk	70%–90%
5 x 3–4 Gy	Prognosis: life expectancy <3–6 mo —bone metastases affecting soft tissue —metastatic bronchogenic carcinoma with imminent bronchial occlusion / bleeding, —ulcerated or painful metastases in soft tissue —multiple brain metastases, poor general condition and uncontrolled extracranial tumor manifestations	1 wk	60%–90%
10 x 3 Gy	Prognosis: life expectancy <1 year —bone metastases with the aim of recalcification —advanced bronchogenic carcinoma —multiple brain metastases, Karnofsky index >70 %	2 wks	60%–90%
13–15 x 3 Gy	Prognosis: life expectancy not very much longer than 1 year —bone metastases without any further tumor manifestations —advanced bronchogenic carcinoma, reasonable general condition, comorbidities	3 wks	60%–90%
20–30 x 2 Gy	Prognosis: life expectancy >1 year —advanced bronchogenic carcinoma stage III and good general condition (possibly also in the form of palliative radiochemotherapy)	4–6 wks	60%–90%
20–30 x 2–3 Gy IMRT	Patients in sufficient general condition with advanced tumors, re-irradiation, Patients in good general condition with, eg, isolated paraspinal metastases, isolated vertebral metastases affecting intraspinal areas	5–6 wks	65%–90%
1–3 x 12–26 Gy stereotaxy	Patients in good general condition with individual/ few solitary or singular brain metastases Individual/few solitary lung or liver metastases	max. 1 wk	70%–90%

METASTASI OSSEE: IN PALLIAZIONE PURA?

*“...**Shorter courses** exemplify common sense end-of-life care, especially because most patients who are treated for symptom palliation will not survive to face the increased risk of long-term side effects associated with hypofractionated regimens.”*

*“...for patients with a limited lifespan or poor performance status, the **single fraction** treatment should provide palliation as effectively as a longer course, higher dose, less convenient, multiple-fraction regimen.”*

METASTASI OSSEE: QUALE FRAZIONAMENTO?

LINEE GUIDA TRATTAMENTO DELLE METASTASI OSSEE



- Se invece:
Istologia favorevole,
primitivo controllato,
prognosi > 6 mesi,
rimane preferibile il trattamento frazionato più protratto in 5/10 sedute

Velleità non solo sintomatiche palliative ma anche di controllo locale?..Dosi ablative e tecniche focali

OLIGOMETASTASES:

THE NEW PARADIGMA FOR ABLATIVE DOSES WITH RT

**The
Oncologist[®]**

Radiation Oncology

Review and Uses of Stereotactic Body Radiation Therapy for Oligometastases

FILIPPO ALONGI,^a STEFANO ARCANGELI,^a ANDREA RICCARDO FILIPPI,^b UMBERTO RICARDI,^b
MARTA SCORSETTI^a

VOLUME 32 • NUMBER 26 • SEPTEMBER 10 2014

JOURNAL OF CLINICAL ONCOLOGY

REVIEW ARTICLE

Radical Irradiation of Extracranial Oligometastases

Joseph K. Salama and Michael T. Milano

METASTASI OSSEE: SOLO PALLIAZIONE?

**OLIGOMETASTASI
(Metastasi precoce)**

CONTROLLO LOCALE

*Dosi elevate ablative
ALTA conformazione DOSE*

PLURIMETASTATICO

CONTROLLO SINTOMO (Qualità di vita)

IPOFRAZIONATO

OLIGOMETASTASES:

THE NEW PARADIGMA FOR ABLATIVE DOSES WITH RT

Critical Reviews in Oncology/Hematology xxx (2015) xxx–xxx



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Review

Spinal metastases: Is stereotactic body radiation therapy supported by evidences?

Berardino De Bari^{a,*}, Filippo Alongi^b, Gianluca Mortellaro^c, Rosario Mazzola^{b,c},
Schiappacasse Luis^a, Guckenberger Matthias^d

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A B S T R A C T

Stereotactic body radiotherapy (SBRT) is becoming widely adopted in the treatment of primary and secondary tumors. Spinal bone metastases are frequently discovered in cancer patients, and in the past have been usually treated with a palliative goal. Nevertheless, in some particular clinical settings, such as oligometastatic patients and/or those with a long life expectancy, spinal SBRT could be considered a valid therapeutic option to obtain long-lasting palliation and, when possible, with a curative goal.

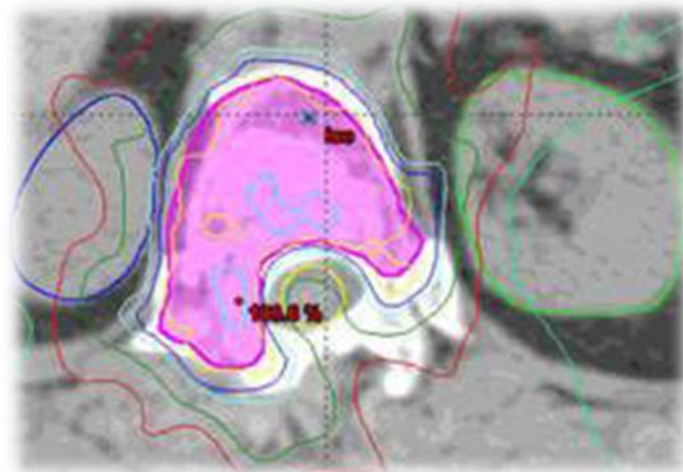
This review aims to summarize available clinical and dosimetric data of published studies about spinal SBRT.

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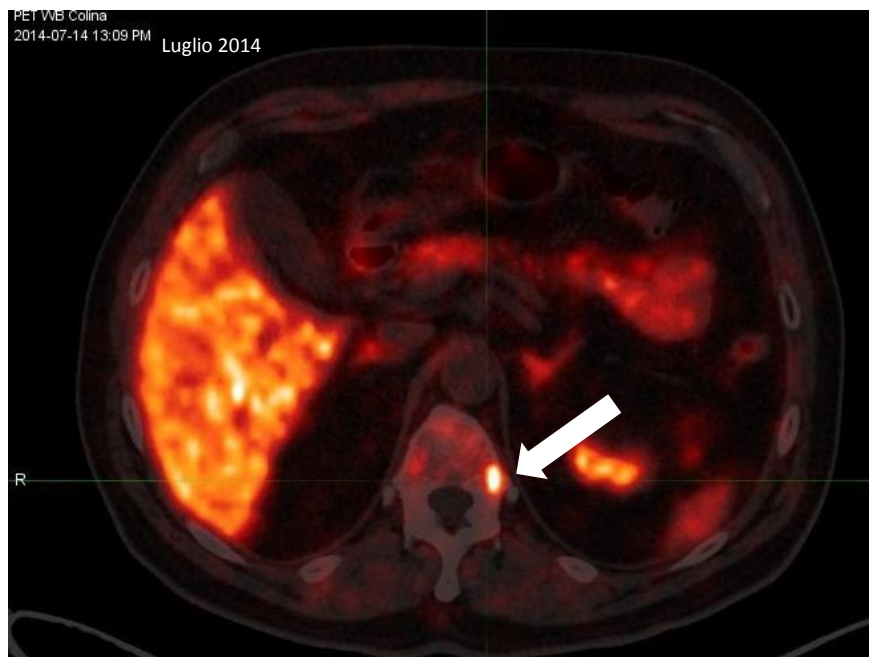
STEREOTACTIC BODY RT(SBRT): SPINAL OLIGOMTS

- **Spinal radiosurgery** has been proven to be an option in the treatment of spinal metastases in properly selected patients, even though only retrospective and phase I–II studies are available.
- Local control based on imaging and/or pain control is achieved in 80% of presentations.
- SBRT can also be safely applied in the postoperative setting, with the intent of reducing the extent of surgery (which can be limited to epidural decompression and fixation).

Sahgal et al J of Neursurg Spine, 2011.

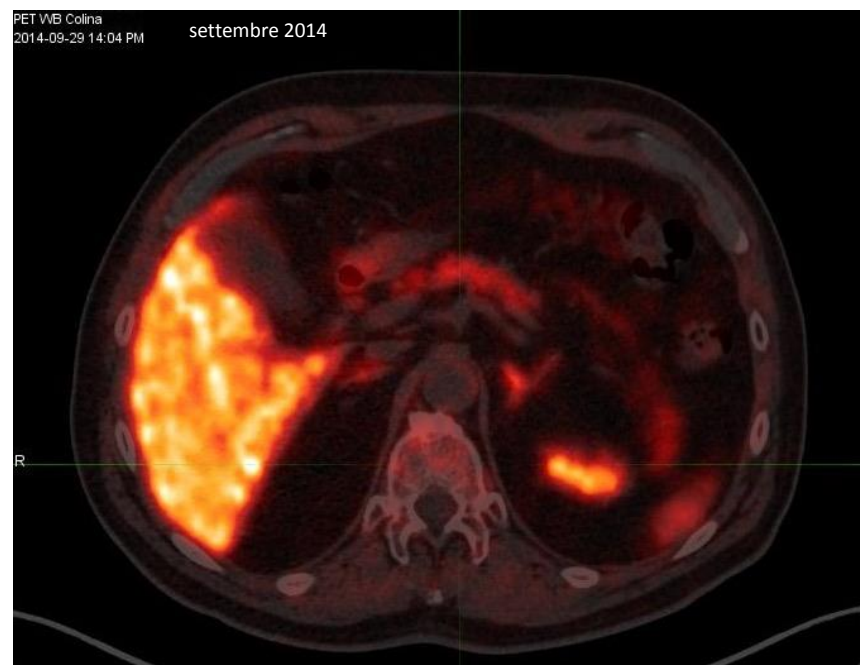


PET-colina pre-RT



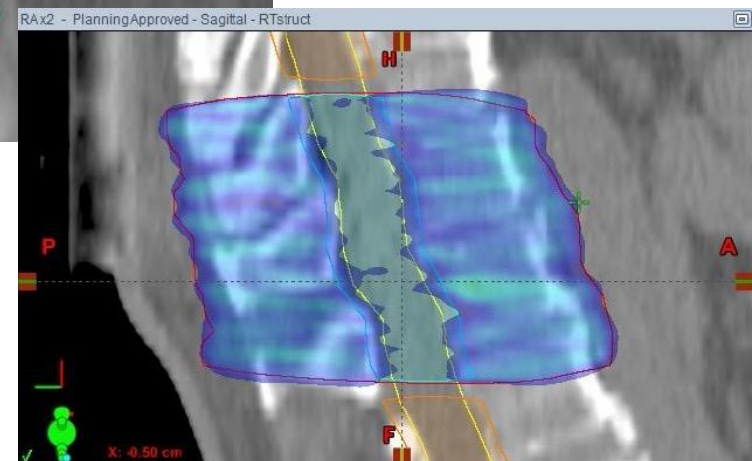
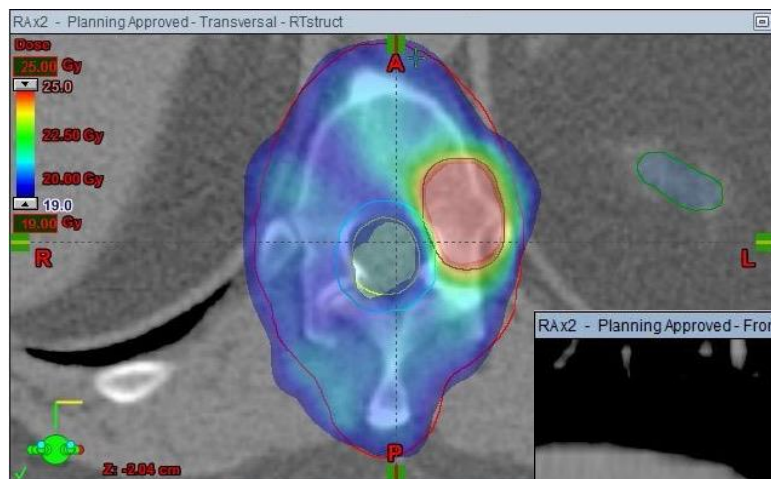
PSA: 2.52 ng/ml
Dolore VAS 5

PET-colina post-RT



PSA: 1.49 ng/ml
Dolore VAS 1

RT su D11-D12



- Dosi: 25 Gy su D11-D12 in 5 frazioni
30 Gy sulla lesione con Boost Simultaneo

COMPRESSIONE MIDOLLARE

Palliative Radiotherapy—New Approaches

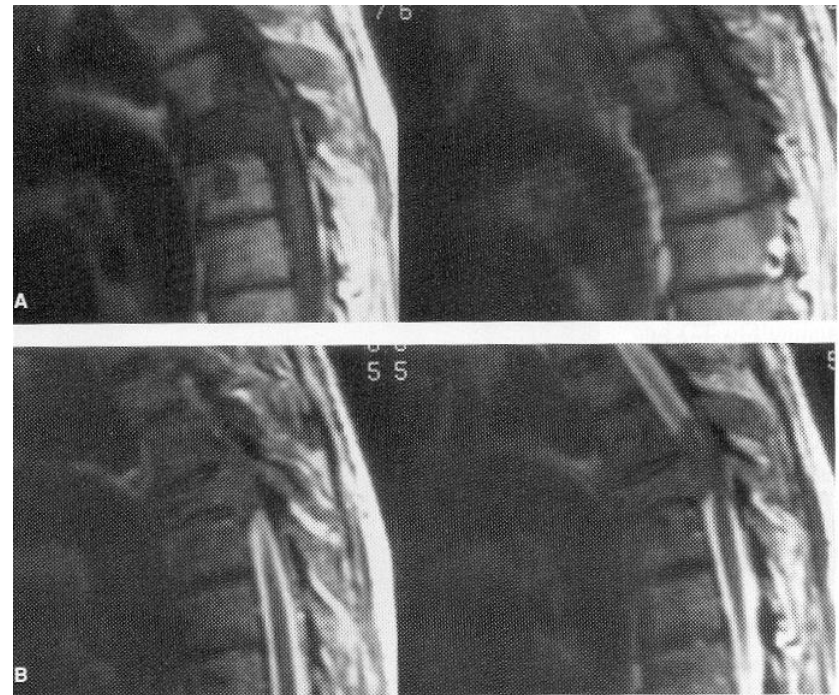
Birgitt van Oorschot,^a Dirk Rades,^b Wolfgang Schulze,^c Gabriele Beckmann,^d and Petra Feyer^e

PRINCIPALI :

- Metastasi ossee
- **Compressione midollare**

COMPRESSIONE MIDOLLARE

- Incidenza in aumento per il prolungamento della sopravvivenza dovuto all' utilizzo di terapie sistemiche.
- **EMERGENZA ONCOLOGICA:** possono provocare radicolopatie sensoriali o gravi alterazioni sensitivo-motorie fino alla paraplegia.



COMPRESSIONE MIDOLLARE

SINTOMATOLOGIA:

- Dolore che può precedere gli altri sintomi (*back pain*)
- Ipostenia
- Deficit Sensoriale

TERAPIA: terapia Cortisonica, Radioterapia, chirurgia decompressiva

RADIOTERAPIA

- Trattamenti RT più brevi (“short-course”) con la somministrazione di dosi singole più elevate sono fortemente consigliati
- Le analisi dei dati della letteratura hanno mostrato la pari efficacia terapeutica nel controllo del dolore degli ipofrazionamenti rispetto a quelli convenzionali.

.Rades D, Kukas JA, Veniga T, et al: Evaluation of five schedules and prognostic factors for metastatic spinal cord compression. J Clin Oncol 2005; 23: 3366-3375.

.Maranzano E, Bellavita R, Rossi R, et al: Short-course versus split-course radiotherapy in metastatic spinal cord compression. Results of a phase III, randomized, multicenter trial. J Clin Oncol 2005; 23: 3358-3365.

.Maranzano E., Trippa F., Casale M., et al: Single-dose (8 Gy) versus short-course (8 Gy x 2) radiotherapy in metastatic spinal cord compression: results of a phase III, randomized, multicentre trial. Radiother Oncol 2009; 93:174-179.

.Maranzano E, Latini P, Perrucci E, et al. Short-course radiotherapy (8 Gy x 2) in metastatic spinal cord compression: an effective and feasible treatment. Int J Radiat Oncol Biol Phys 1997; 38: 1037-1044.

FUTURO ALL'ORIZZONTE

- Team **Multidisciplinare e Multiprofessionale**
- “Percorso Palliativo” **Individuale** (che includa la Radioterapia!)
- Medicina Palliativa come parte integrante del **Core Curriculum** specialistico

Seminars in Oncology, Vol 38, No 3, pp 443-449, June 2011

Kaasa et al. Lancet Oncol Vol 12: 925-927, 2011



GRAZIE!