IL RUOLO DELLA RADIOTERAPIA NEL TRATTAMENTO DEL DOLORE ONCOLOGICO CRONICO

XII EDIZIONE

MALATTIA DOLORE
E RETE TERRITORIALE

IL DIRITTO DEL PAZIENTE AD ESSERE CREDUTO

MILANO 23 › 24 MARZO 2017
AULA MAGNA · OSPEDALE NIGUARDA

RED
RETE TERAPIA DEL DOLORE - MILANO

Mauro Palazzi – SC Radioterapia
Niguarda Cancer Center / Dipartimento Ematologico Oncologico
ASST Ospedale Niguarda, Milano

Sistema Sanitario Regione Lombardia

Azienda Ospedaliera
Ospedale Niguarda Ca' Granda

ARTe Amici della RadioTerapia di Niguarda

ARGOMENTI TRATTATI

1. Ruolo del radioterapista nelle cure oncologiche “palliative”
2. Radioterapia e metastasi osse sintomatiche
3. Linea guida ASTRO
4. Dose e frazionamento
5. Ri-trattamento
6. Il “flare”
7. Radioterapia stereotassica

MODALITA' TERAPEUTICHE IN ONCOLOGIA

	guarigione	palliazione
• CHIRURGIA	+++	+
• RADIOTERAPIA	++	++
• TERAPIE MEDICHE	+	+++

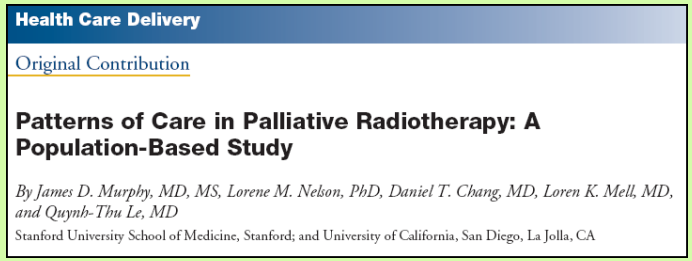
LA RADIOTERAPIA PROVIENE DA UN AMBITO PALLIATIVO MA ATTUALMENTE E' FORTEMENTE PROIETTATA IN UN AMBITO CURATIVO

alcuni esempi di patologie nelle quali la RT (+/- CHT) si propone come un'alternativa equivalente alla chirurgia:

- **tumori del canale anale / del rinofaringe**
- **tumori della prostata**
- **tumori di laringe e faringe**
- **tumori cerebrali selezionati**
- **tumori polmonari**
- **tumori del retto ?**

LA RADIOTERAPIA

CURATIVA		PALLIATIVA
alte	dosi somministrate	basse
alta	tecnologia	bassa
alti	costi	bassi



Health Care Delivery

Original Contribution

Patterns of Care in Palliative Radiotherapy: A Population-Based Study

By James D. Murphy, MD, MS, Lorene M. Nelson, PhD, Daniel T. Chang, MD, Loren K. Mell, MD, and Quynh-Thu Le, MD

Stanford University School of Medicine, Stanford; and University of California, San Diego, La Jolla, CA

Journal of Oncology Practice, 2013

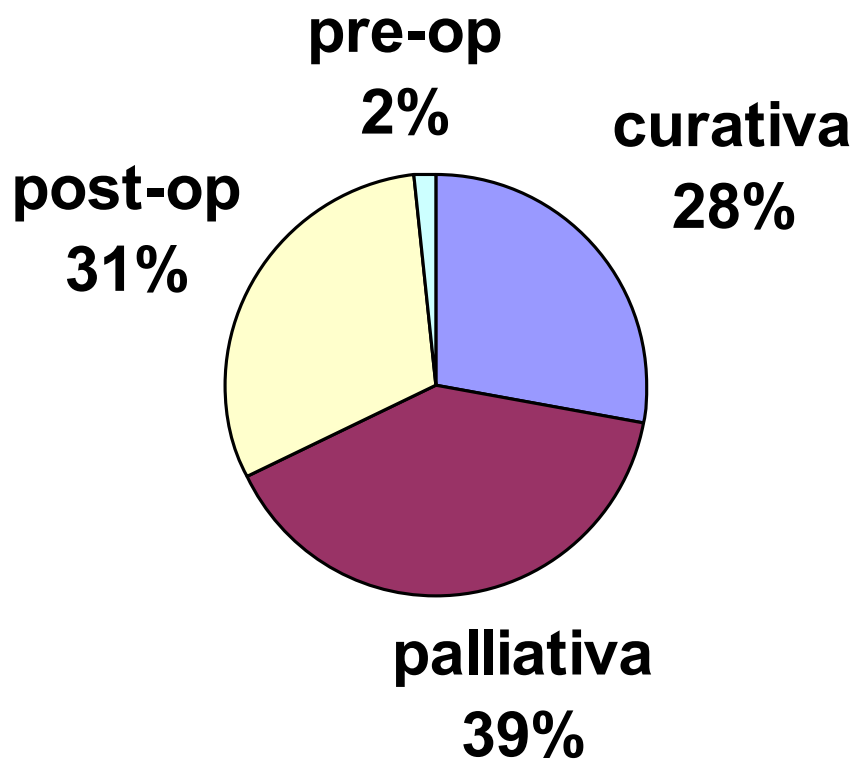
background: circa 50% dei trattamenti RT in USA hanno intento palliativo

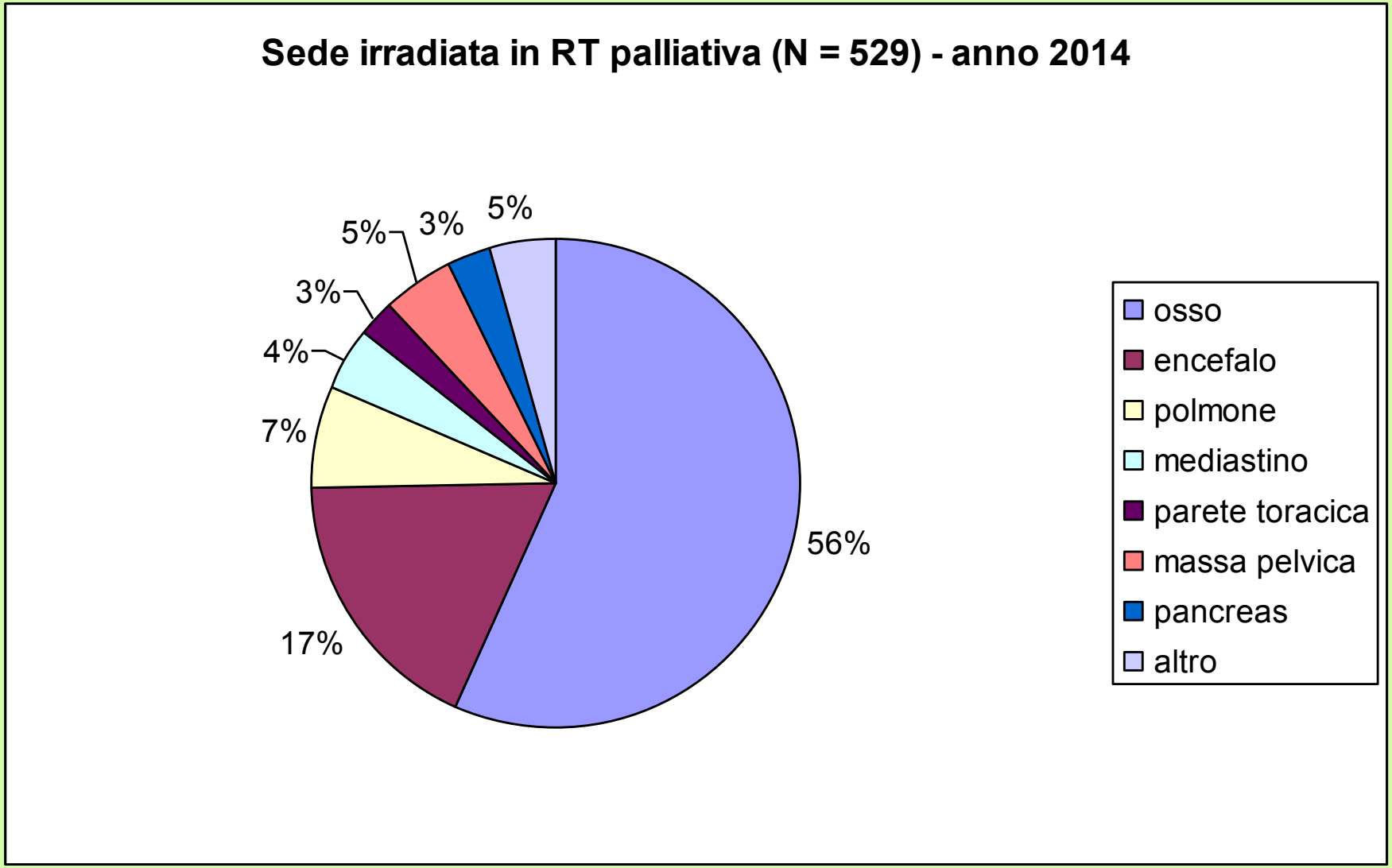
metodi: § studio di popolazione (USA – SEER)
§ 50.000 pazienti con tumore solido diagnosticati in stadio IV (M+) nel periodo 2000-2007

risultati: § 41% dei casi sottoposti a RT (polmone 53%, mammella 42%, prostata 40%, colon-retto 12%)
§ disomogeneità nell'accesso alla RT (neri, anziani ..)
§ 8-23% pazienti morti entro 2 settimane dalla RT

conclusioni: ulteriori studi necessari per migliorare l'accesso e la qualità di RT palliativa

RT Niguarda - 2014 (N = 1323)
finalità della RT




Sede irradiata in RT palliativa (N = 529) - anno 2014
5%
3%
5%
3%
4%
7%
56%
17%
osso
encefalo
polmone
mediastino
parete toracica
massa pelvica
pancreas
altro

Review Article

Palliative radiotherapy for advanced malignancies in a changing oncologic landscape: guiding principles and practice implementation

Joshua A. Jones, Charles B. Simone II

Department of Radiation Oncology, Hospital of the University of Pennsylvania, Philadelphia, PA, USA

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Annals of Palliative Medicine, Vol 3, No 3 July 2014

VOLUME 32 · NUMBER 26 · SEPTEMBER 10 2014

JOURNAL OF CLINICAL ONCOLOGY

REVIEW ARTICLE

Role of Radiation Therapy in Palliative Care of the Patient With Cancer

Stephen T. Lutz, Joshua Jones, and Edward Chow

COMMENTARY

Palliative Radiation Oncology: Moving Beyond the Single Fraction

Lauren M. Hertan, MD, MS,*,† Joshua A. Jones, MD, MA,‡ and Tracy A. Balboni, MD, MPH*,†

**Department of Radiation Oncology, Dana-Farber/Brigham and Women's Cancer Center, Boston, Massachusetts; †Department of Psychosocial Oncology and Palliative Care, Dana-Farber Cancer Institute, Boston, Massachusetts; and ‡Department of Radiation Oncology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania*

International Journal of Radiation Oncology biology • physics

Palliative Radiotherapy at the End of Life: A Critical Review

Joshua A. Jones, MD, MA[1]*; Stephen T. Lutz, MD[2]; Edward Chow, MBBS[3]; Peter A. Johnstone, MD, FACR[4]

When delivered with palliative intent, radiotherapy can help to alleviate a multitude of symptoms related to advanced cancer. In general, time to symptom relief is measured in weeks to months after the completion of radiotherapy. Over the past several years, an increasing number of studies have explored rates of radiotherapy use in the final months of life and have found variable rates of radiotherapy use. The optimal rate is unclear, but would incorporate anticipated efficacy in patients whose survival allows it and minimize overuse among patients with expected short survival. Clinician prediction has been shown to overestimate the length of survival in repeated studies. Prognostic indices can provide assistance with estimations of survival length and may help to guide treatment decisions regarding palliative radiotherapy in patients with potentially short survival times. This review explores the recent studies of radiotherapy near the end of life, examines general prognostic models for patients with advanced cancer, describes specific clinical circumstances when radiotherapy may and may not be beneficial, and addresses open questions for future research to help clarify when palliative radiotherapy may be effective near the end of life.
CA Cancer J Clin 2014;64:295-310.

Keywords: palliative care, radiation oncology, radiotherapy, survival.

TABLE 1. Symptoms of Cancer That May Be Successfully Addressed by Palliative Radiotherapy

Primary sites of disease
• Brain: headaches, seizures, neurologic dysfunction
• Head and neck: pain, bleeding, dysphagia, shortness of breath
• Lung: pain, cough, hemoptysis, postobstructive pneumonia, superior vena cava syndrome
• Esophagus: dysphagia, odynophagia, bleeding, obstruction
• Gynecologic: pain, bleeding, urinary outlet obstruction, hydronephrosis
• Genitourinary: pain, hematuria, urinary outlet obstruction
• Rectum: pain, bleeding, tenesmus, rectal obstruction
Secondary sites of disease (metastases)
• Brain: headaches, seizures, neurologic dysfunction
• Bone: pain, spinal cord compression, postsurgical fixation status
• Skin and subcutaneous tissues
• Orbit: pain, double vision, blindness
• Spleen: pain, early satiety, portal hypertension

- la Radioterapia “palliativa” può essere un trattamento:
  - efficace
  - ben tollerato
  - time-efficient
  - cost-effective
  - CRUCIALE per una appropriata “cura palliativa”
- approcci innovativi (“in academic centers”?):
  - “rapid response RT palliative care clinics”
  - “palliative RT sub-specialty services”
  - specific guidelines
  - integration of education and training between RT and palliative care specialties

METASTASI OSSEE E RADIOTERAPIA (in sintesi)

- M+ ossee nel 50-75% dei pazienti in stadio IV
- circa 70% delle M+ ossee sono sintomatiche (dolore, calo QoL)
- la Radioterapia può ottenere un riduzione del dolore in circa il 70% dei casi (circa 20-30% risposta completa)
- durata effetto antalgico: media 5-6 mesi
- Problemi:
  - ❖ dose, frazionamento e tecnica della RT
  - ❖ quando ri-trattare?
  - ❖ il fenomeno del “flare”
  - ❖ ruolo della “HiTech” RT

AZIONE RT SUL DOLORE

CAUSE FISICHE DEL DOLORE

- **Invasione ossea e distruzione della matrice**
- **Compressione delle radici nervose**
- **Infiltrazione del periostio**
- **Infiltrazione dei tessuti molli**
- **Spasmo muscolare**
- **Alterazione della postura (posizione di difesa)**

cortesia dr.ssa L. Lozza (INT)

RT E RISPOSTA ANTALGICA

- Il controllo del dolore ottenuto già dai primi giorni di trattamento è legato ad una **rapida riduzione di mediatori chimici del dolore**.

  (Poulsen HS Cancer Treatment Rev 1989; Mercadante S Pain 1997; Saarto T Eur J Pain 2002)

- Il controllo del dolore che si ottiene da 2 a 8 settimane dalla fine del trattamento radioterapico coincide con l'inizio del **processo di ricalcificazione delle lesioni osteolitiche**.

  (Poulsen HS Cancer Treatment Rev 1989; Saarto T Eur J Pain 2002)

cortesia dr.ssa L. Lozza (INT)

Practical Radiation Oncology (2017) 7, 4-12

practical radiation oncology
pro
www.practicalradonc.org

Special Article

Palliative radiation therapy for bone metastases: Update of an ASTRO Evidence-Based Guideline

Stephen Lutz MD [a,*], Tracy Balboni MD MPH [b], Joshua Jones MD [c], Simon Lo MB ChB [d], Joshua Petit MD [e], Shayna E. Rich MD PhD [f], Rebecca Wong MB ChB [g], Carol Hahn MD [h]

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[b]*Department of Radiation Oncology, and Department of Psychosocial Oncology and Palliative Care Brigham and Women's Hospital and Dana-Farber Cancer Institute, Boston, Massachusetts*
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[d]*Department of Radiation Oncology, University of Washington School of Medicine, Seattle, Washington*
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[h]*Department of Radiation Oncology, Duke University Medical Center, Durham, North Carolina*

RACCOMANDAZIONI COLLEGATE A 8 "KEY QUESTIONS"

1. quale frazionamento nelle M+ periferiche "non complicate"?

R: frazione singola 8 Gy equivalente a schemi multi-frazione (20-24 Gy in 5-6 F; 30 Gy in 10 F)

2. quale frazionamento nelle M+ spinali "non complicate"?

R: frazione singola accettabile anche in questo contesto

3. la frazione singola può causare danni tardivi limitanti?

R: NO

RACCOMANDAZIONI COLLEGATE A 8 "KEY QUESTIONS"

4. quando indicato il ri-trattamento nelle M+ periferiche?

R: dolore persistente o ricorrente a >1 mese da RT

5. quando indicato il ri-trattamento nelle M+ spinali?

R: idem, ma ATTENZIONE a vincoli di dose per il midollo spinale

6. quale potenziale per RT "HiTech" (stereotassica) nel primo trattamento delle M+ ossee?

R: solo nelle M+ spinali, e in trial o "registri controllati"

RACCOMANDAZIONI COLLEGATE A 8 "KEY QUESTIONS"

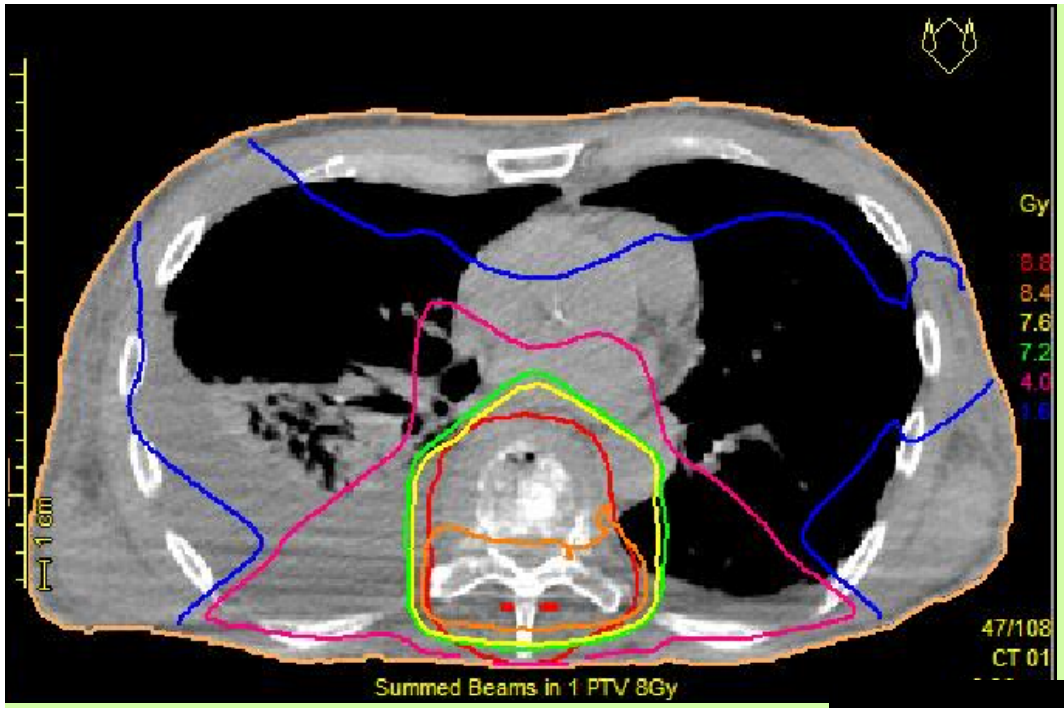
7. quale potenziale per RT "HiTech" (stereotassica) nel ri-trattamento delle M+ spinali?

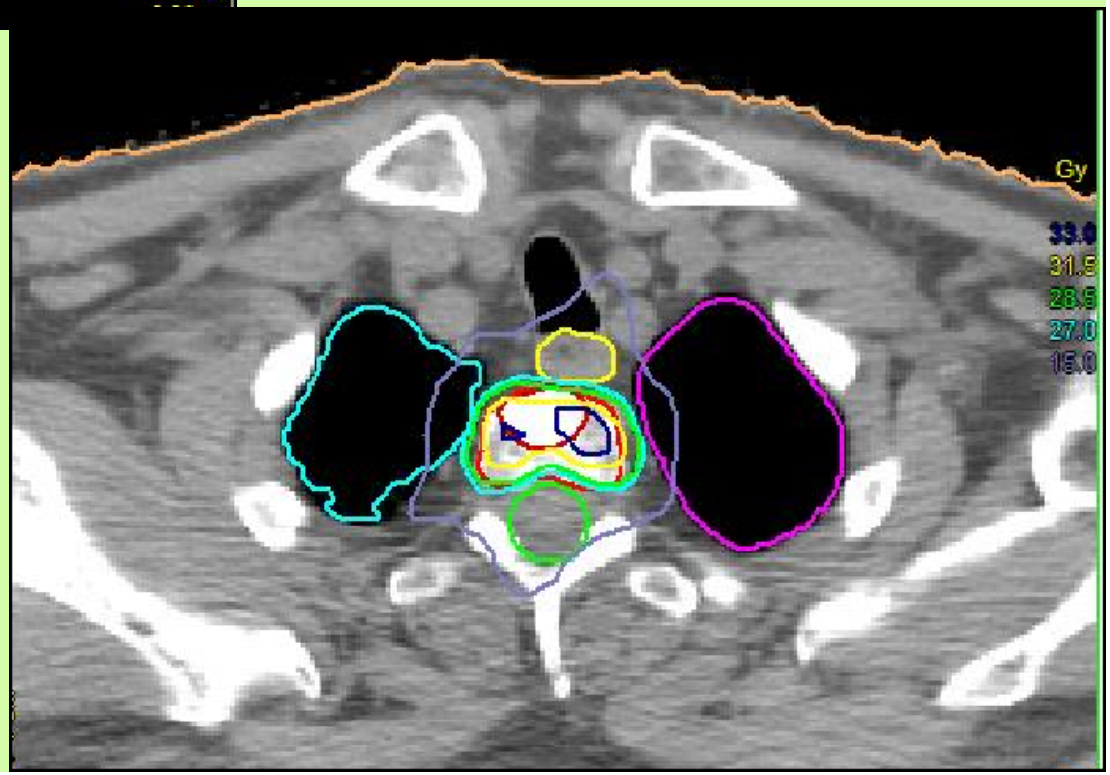
R: RT "HiTech" può essere un trattamento fattibile, efficace e sicuro, ma indicazione limitata a trial o "registri"

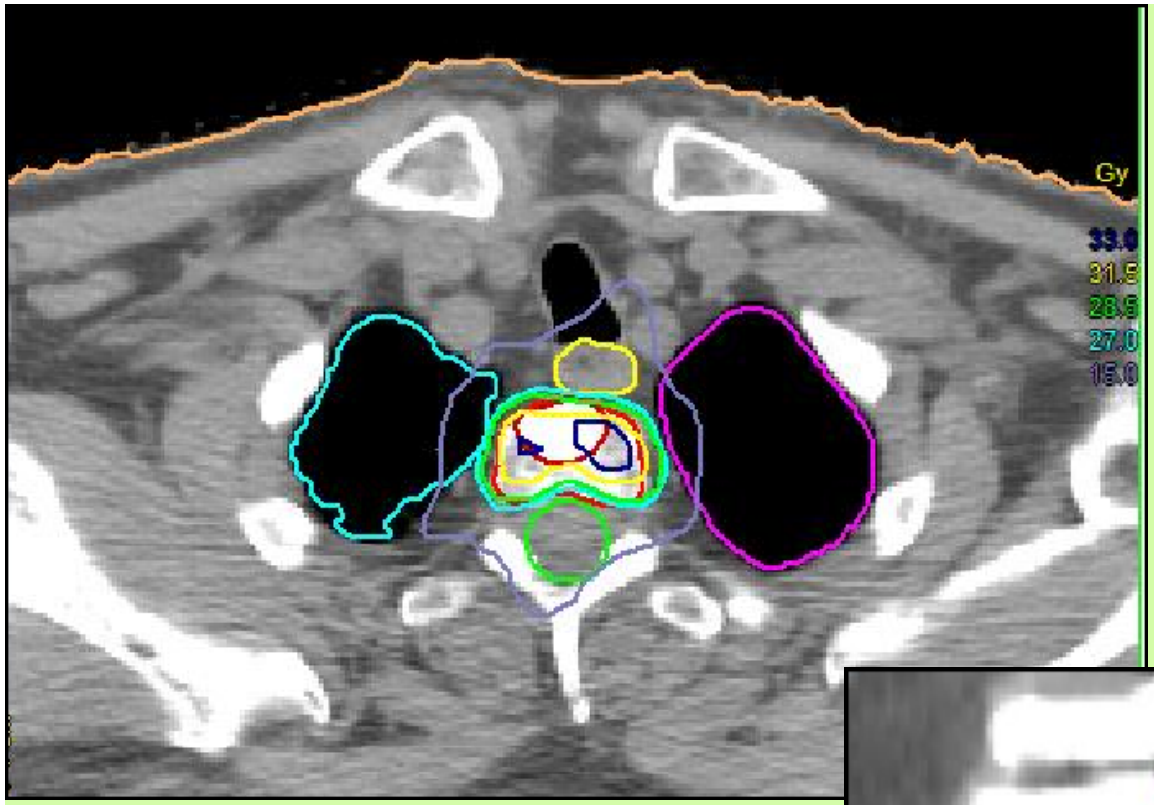
8. l'impiego di chirurgia, vertebroplastica, difosfonati o RT metabolica consente di soprassedere alla RT esterna?

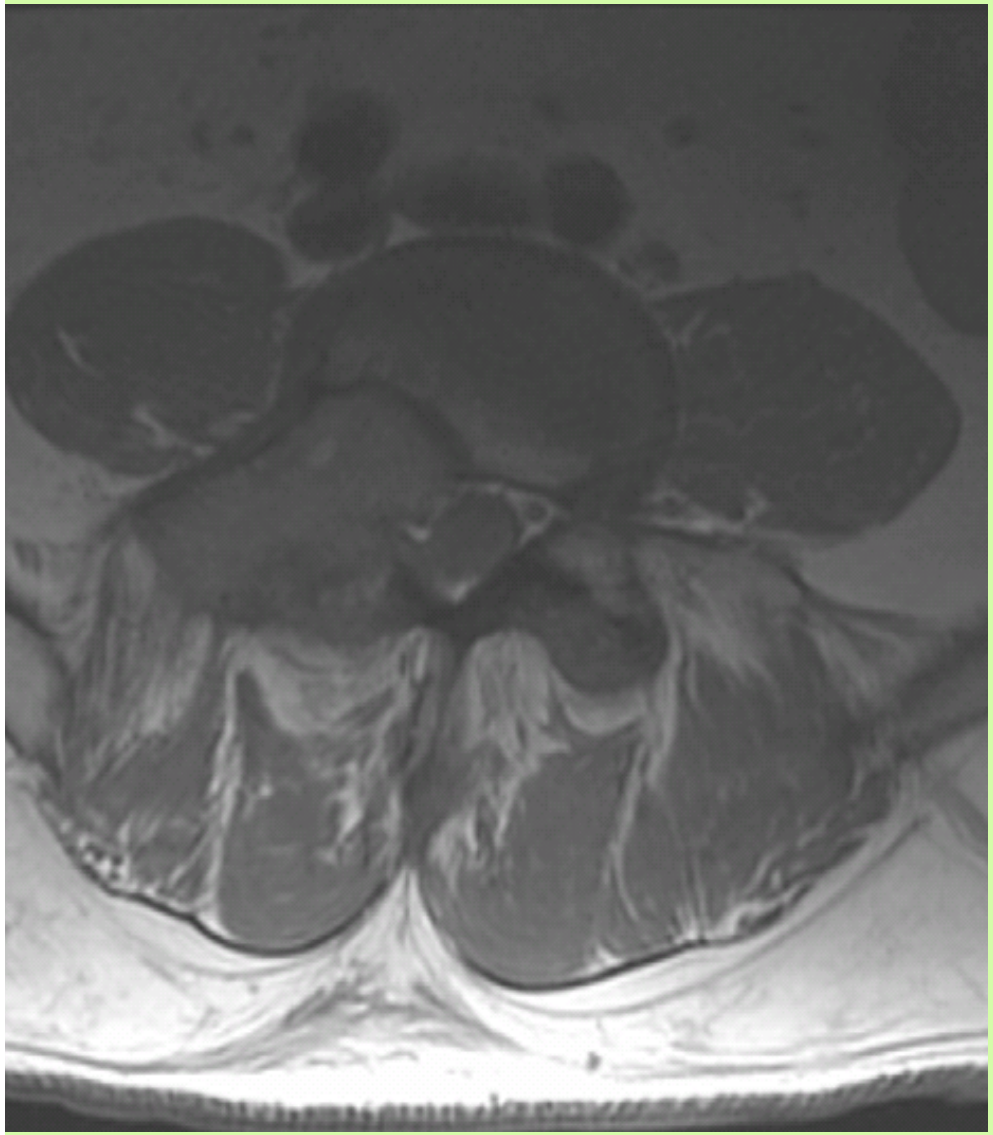
R: NO

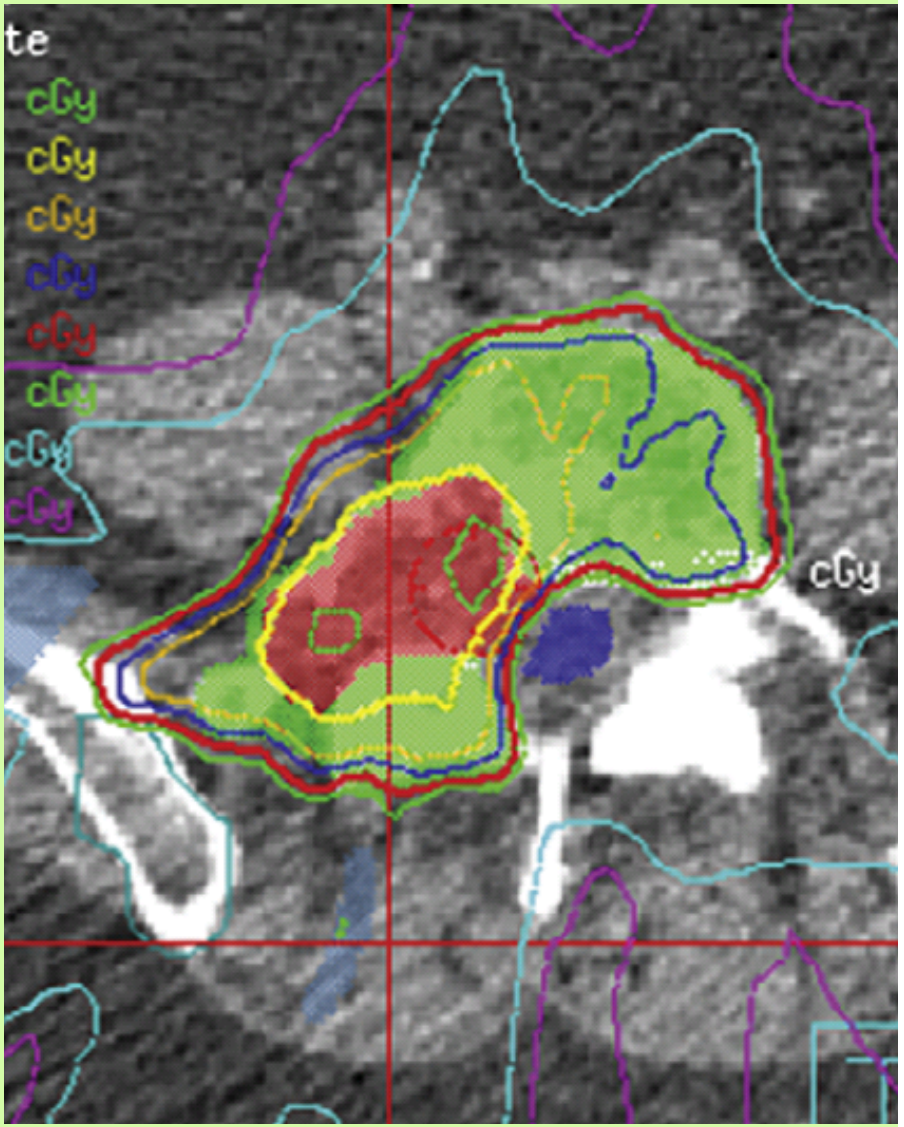
qualche immagine …

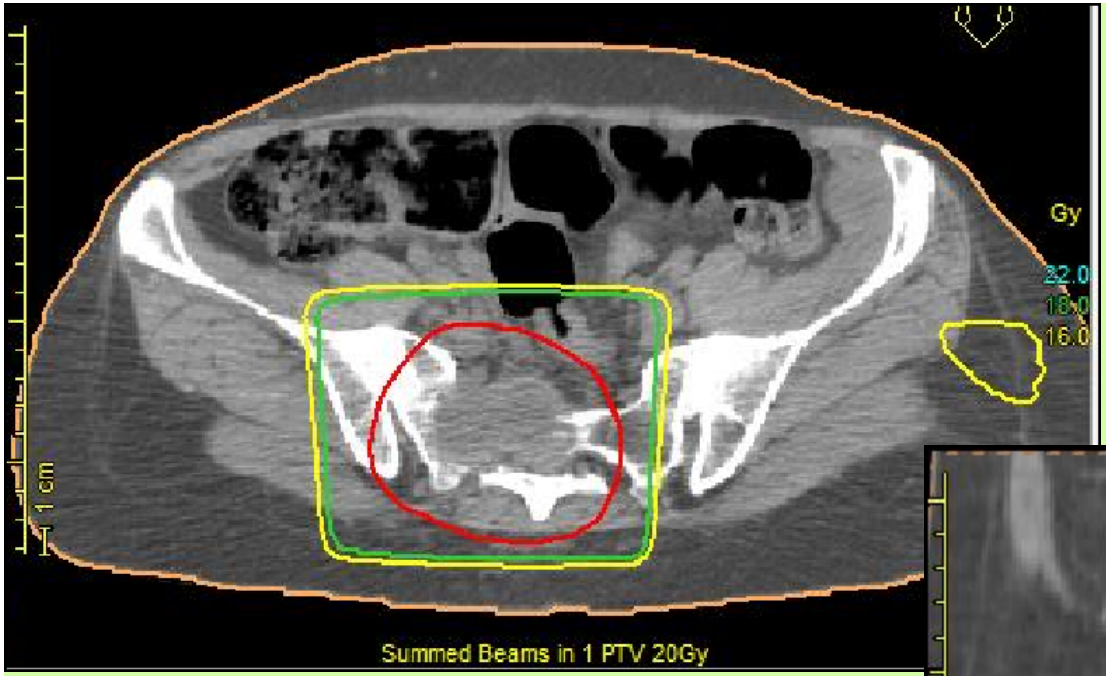

Gy
8.4
7.6
7.2
47/108
CT 01
Summed Beams in 1 PTV 8Gy

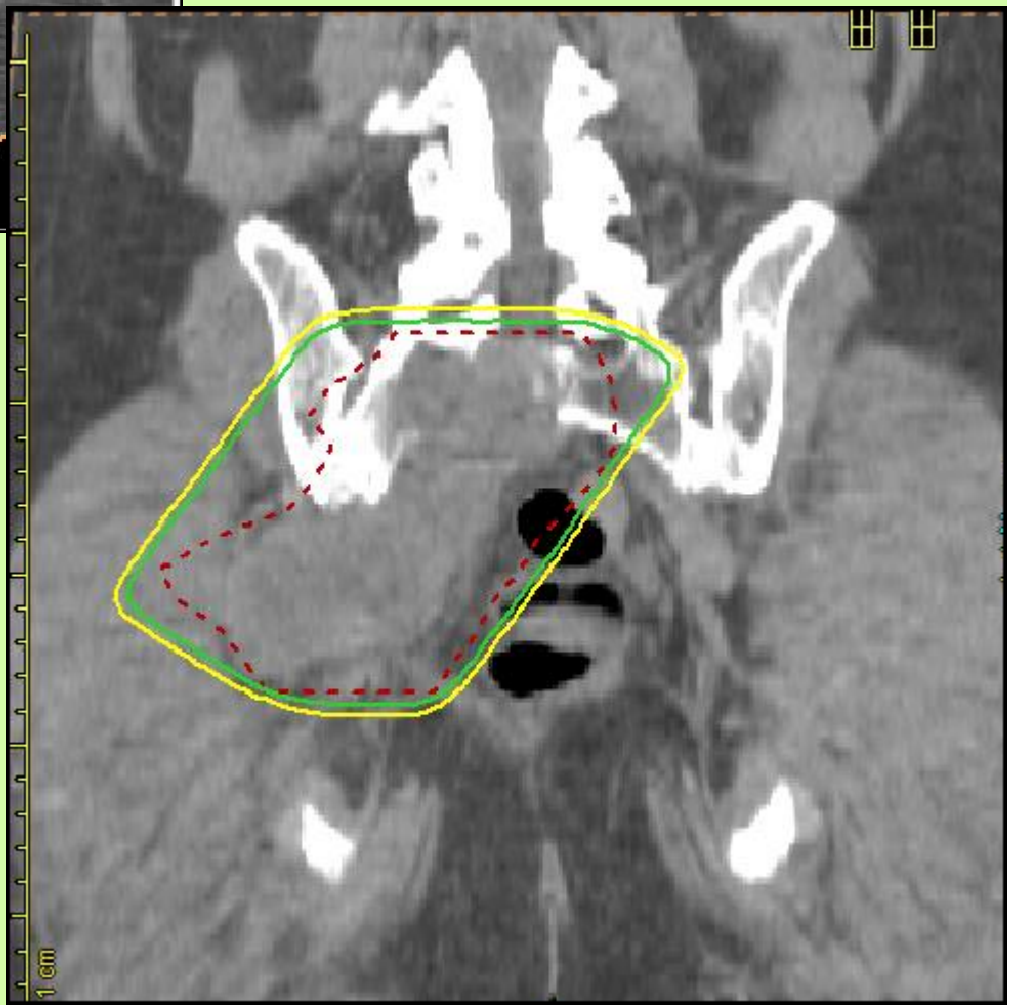

Gy
31.9
28.9
27.0


Gy
33.0
31.5
28.5
27.0
16.0




te
cGy
cGy
cGy
cGy
cGy
cGy
cGy
cGy


Gy
22.0
18.0
16.0
1 cm
Summed Beams in 1 PTV 20Gy


1 cm

Clinical Oncology 24 (2012) 112–124

Contents lists available at SciVerse ScienceDirect

Clinical Oncology

journal homepage: www.clinicaloncologyonline.net

Original Article

Update on the Systematic Review of Palliative Radiotherapy Trials for Bone Metastases

E. Chow *, L. Zeng *, N. Salvo *, K. Dennis *, M. Tsao *, S. Lutz †

* *Department of Radiation Oncology, Odette Cancer Centre, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada*
† *Department of Radiation Oncology, Blanchard Valley Regional Cancer Center, Ohio, USA*

25 trials frazione singola (8 Gy) vs multiple (5-10 F)

(circa 5600 pazienti)

- **risposta antalgica analoga (60% vs 61%) (>> 72% vs 74%)**
- **risposta completa analoga (23% vs 24%) (>> 28% vs 30%)**
- **ri-trattamento > nella frazione singola (20% vs 8%)**
- **rischio di frattura patologica analogo (3.3 % vs 3%)**
- **rischio di compressione midollare > nella FS (2.8% vs 1.9%)**

… a proposito della re-irradiazione …

Single versus multiple fractions of repeat radiation for painful bone metastases: a randomised, controlled, non-inferiority trial

Edward Chow, Yvette M van der Linden, Daniel Roos, William F Hartsell, Peter Hoskin, Jackson S Y Wu, Michael D Brundage, Abdenour Nabid, Caroline J A Tissing-Tan, Bing Oei, Scott Babington, William F Demas, Carolyn F Wilson, Ralph M Meyer, Bingshu E Chen, Rebecca K S Wong

Lancet Oncol 2014; 15: 164–71

Summary

Background Although repeat radiation treatment has been shown to palliate pain in patients with bone metastases

425 pazienti randomizzati a 8 Gy SF vs 20 Gy in 5F

tutti ri-trattamenti per dolore persistente (non-responders) o ricorrente (responders)

risposta 28% vs 32% (>> 45% vs 51%)

Conclusioni: SF non inferiore come efficacia e meno tossica rispetto a 20 Gy/5F

Radiotherapy and Oncology 112 (2014) 125–127

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Bone metastases

Overall response rates to radiation therapy for patients with painful uncomplicated bone metastases undergoing initial treatment and retreatment

Gillian Bedard [a], Peter Hoskin [b], Edward Chow [a,*]

[a] Sunnybrook Health Sciences Centre, Odette Cancer Centre, University of Toronto, ON, Canada; [b] Mount Vernon Hospital Cancer Centre, Middlesex, United Kingdom

Table 2
Overall response rate to both treatments with evaluable patients.

Initial treatment	Retreatment	Overall response rate (%)
Single fraction	Single fraction	85
Single fraction	Multiple fractions	86
Multiple fractions	Single fraction	86
Multiple fractions	Multiple fractions	87

… a proposito del “flare” …

- ✓ **il “flare” è il peggioramento transitorio del dolore locale che si manifesta subito dopo l’inizio di una RT su M+ ossea**
- ✓ **è il più significativo effetto collaterale (acuto o tardivo) della RT per M+ ossee**

Journal of Bone Oncology 3 (2014) 84–89

Contents lists available at ScienceDirect

Journal of Bone Oncology

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

Review Article

Incidence of pain flare in radiation treatment of bone metastases: A literature review

Rachel McDonald, Edward Chow, Leigha Rowbottom, Carlo DeAngelis, Hany Soliman *

Odette Cancer Centre, Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Ontario, Canada

incidenza: 2-44% >> 10-68% (stereotassi)

Dexamethasone in the prophylaxis of radiation-induced pain flare after palliative radiotherapy for bone metastases: a double-blind, randomised placebo-controlled, phase 3 trial

Edward Chow, Ralph M Meyer, Keyue Ding, Abdenour Nabid, Pierre Chabot, Philip Wong, Shahida Ahmed, Joda Kuk, A Rashid Dar, Aamer Mahmud, Alysa Fairchild, Carolyn F Wilson, Jackson S Y Wu, Kristopher Dennis, Michael Brundage, Carlo DeAngelis, Rebecca K S Wong

Summary

Background Pain flare occurs after palliative radiotherapy, and dexamethasone has shown potential for prevention of

Lancet Oncol 2015; 16: 1463–72

cortisone diminuisce "flare" (35% > 26%)

quando la RT stereotassica per M+ ossea?

ultime 2 diapo!

MINI-REVIEW

Stereotactic Body Radiation Therapy for Treatment of Spinal Bone Metastasis

Yasemin Benderli Cihan

Abstract

Stereotactic body radiation therapy (SBRT) appears an effective and safe treatment modality for spinal bone metastasis, which can enhance local control and improve quality of life. Life expectation, predicted fracture risk, localization, quality, size and number of metastasis and presence or absence of nerve compression seem to be important factors in decision-making for treatment. Further studies are needed to identify subsets of patient which will most benefit from treatment.

Keywords: Stereotactic body radiation therapy - spinal bone metastasis

Asian Pac J Cancer Prev, **17 (3)**, 937-938

Critical Reviews in Oncology/Hematology 98 (2016) 147–158

Contents lists available at ScienceDirect

Critical Reviews in Oncology/Hematology

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

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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[b] Radiation Oncology Department, Sacro Cuore-Don Calabria Hospital, Negrar-Verona, Italy
[c] Radiation Oncology Department, University of Palermo, Palermo,Italy
[d] Department for Radiation Oncology, University Hospital Zurich, University of Zurich, Zurich, Switzerland

RADIOTERAPIA STEREOTASSICA PER M+ OSSEE

in sintesi:

- ❖ è ormai uno standard (tecnica fattibile, affidabile, efficace, sicura)
- ❖ necessita di HiTech (Centro) ed expertise (staff)
- ❖ da utilizzare solo in casi SELEZIONATI
  - ✓ es. ri-trattamento M+ spinali
  - ✓ es. trattamento pazienti a ottima prognosi (oligometastatici, ca. mammella/prostata ecc) >> dose più alta (maggiore efficacia/durata ?)
- ❖ attenzione al “flare” (profilassi con cortisone)

... grazie per l'attenzione !

Mercatino di Pasqua

Blocco sud dal 6 al 12 aprile 2017
dalle 10 alle 16

Festeggiate la Pasqua e sostenete gli Amici della RadioTerapia!

Grazie alle vostre donazioni dal 2015 abbiamo garantito:

- Oltre 1.000 trasporti per 70 pazienti accompagnati in Ospedale durante la terapia
- 10 corsi di aggiornamento al personale del reparto di Radioterapia
- La decorazione artistica della sala d'attesa dell'accettazione

Venite a trovarci: al banchetto troverete prodotti dolciari e piccoli oggetti.

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