Malattia oligometastatica: quando trattamento sistemico e quando loco-regionale?

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BONE METASTASES:
ROLE OF RT

- Approximately *one third* of all cancer patients will develop bone metastases and approximately 70% will present metastases involving the vertebral column.
- *Conventional fractionated radiotherapy (RT) has an historical role* in the management of spine metastases and the most commonly used regimen of RT is 30 Gy in 10 fractions
- *Single-dose treatments are usually preferred in patients with a limited lifespan* and/or poor performance status or in case of long waiting lists of the treating centers
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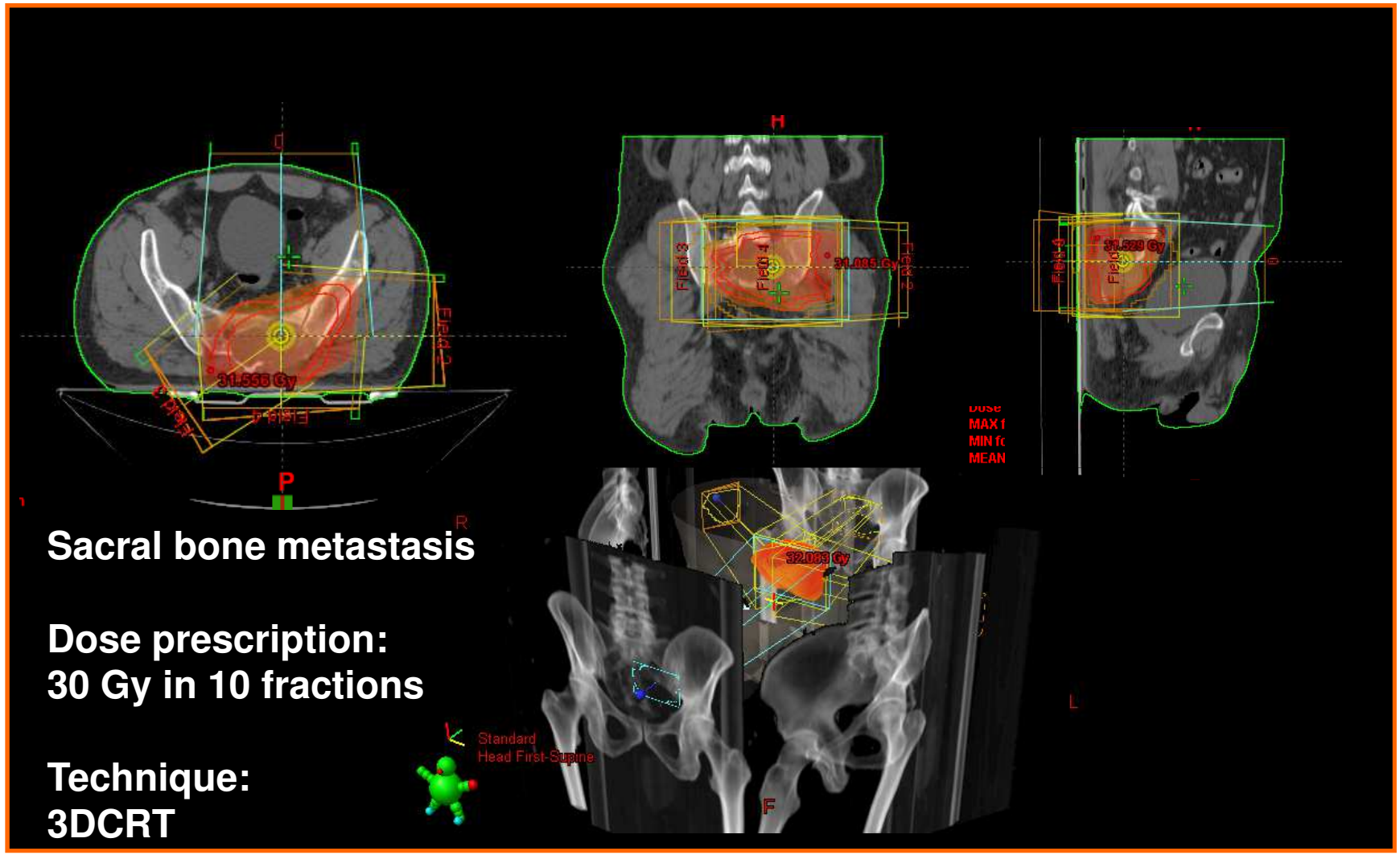
De Bari, Alongi et al, Critical review Oncology and Hematology 2016

PALLIATIVE/SYMPHTOMATIC BONE RADIOTHERAPY



Sacral bone metastasis

Dose prescription:
30 Gy in 10 fractions

Technique:
3DCRT

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Combined treatment opportunities

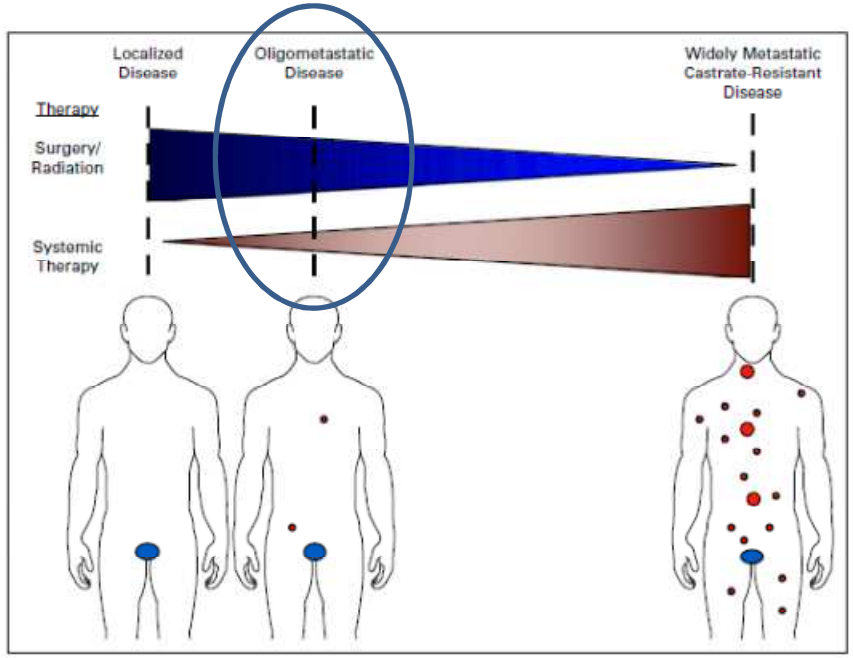


FIG 1. The oligometastatic disease state. The spectrum of malignant disease is represented by blue ovals for primary prostate cancer and red circles for macroscopic metastases. Patients are considered in relation to the putative benefits of local versus systemic therapies. Men in the oligometastatic disease state may benefit from both systemic therapy and local therapies.

Tran and Antonarakis Clinical Reviews ascopubs.2017

- Recent advances in RT treatment planning and dose delivery allow radiation oncologists to deliver treatments with along-lasting palliation potential (and sometimes also potentially curative) also to patients that would be traditionally candidates only to palliative systemic therapies, possibly at a reasonable price in terms of toxicity.

- Ideal candidates for these treatments are oligometastatic

OLIGOMETASTASES:

HOW TO DEFINE THE IDEAL CANDIDATE FOR LOCAL THERAPIES?

The term "oligometastases" was first described by Hellman and Weichselbaum in 1995 as "…a less advanced state of metastatic disease amenable to and potentially curable with local therapy"

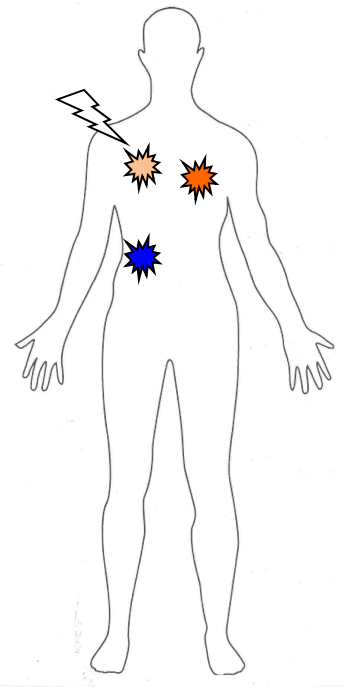
Hellman S, Weichselbaum RR: JCO, 1995

The term "oligometastases" is usually used for five or fewer metastatic lesions

Milano MT, et al. JROBP, 2012

Often, this clinical situation has a slow rate of progression, justifying focal treatments

Alongi F, et al. The Oncologist, 2011



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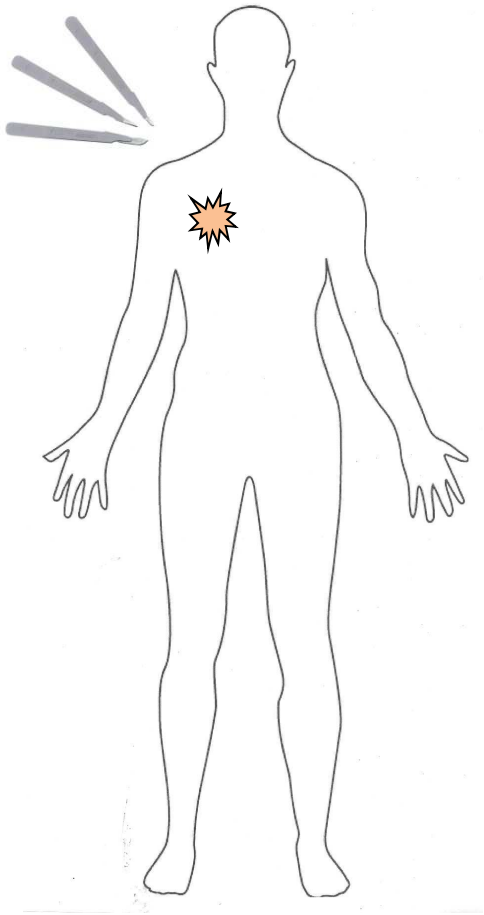
OLIGOMETASTASES: IMPACT OF SURGERY

For several anatomical sites, ***surgical resection*** of metastases prolongs survival in selected patients.
Rubin P, et al. Semin Radiat Oncol,2006

For example, *surgical resection* is the standard choice for patients with oligometastatic lung cancer.

Unfortunately the benefits of resection and appropriate *selection criteria* in patients who develop metastasis are still poorly defined.
Miller G, et al. J Am Coll Surg, 2007.



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OLIGOMETASTASES:
THE NEW PARADIGMA FOR ABLATIVE DOSES WITH RT

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Oligometastases: the new paradigm and options for radiotherapy

A critical review

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]

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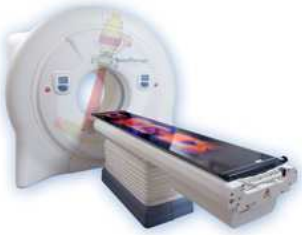
Extracranial Oligometastases: A Subset of Metastases Curable With Stereotactic Radiotherapy

Kimberly S. Corbin, Samuel Hellman, and Ralph R. Weichselbaum, *University of Chicago Medical Center, Chicago, IL*

TECHNOLOGY & PROSTATE CANCER




PRECISION DEVISES TO DELIVERY EBRT

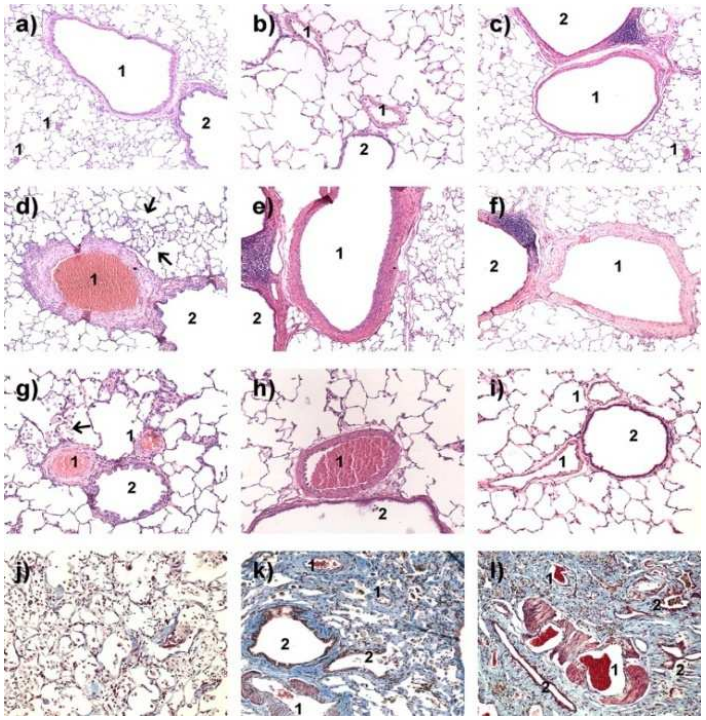
- SBRT may be realized with different technical solutions…..
- A Potential technology gain derives from the use of upgraded IGRT, IMRT or integration of both.
- Modern **SBRT** adopts static, dynamic or volumetric IMRT techniques to provide sharper dose fall-offs and better dose conformity

ABLATIVE (SB)RT:
A NEW BIOLOGY FOR NEW INDICATIONS?

•In terms of ***Radiobiology, Radiosurgery and SBRT*** may add a novel mechanism of radiation-induced damage.

•At higher doses per fraction (***ablative doses***), emerging data suggest that a different mechanism involving microvascular damage begins to have a substantial effect on the tumor cell kill.***Garcia - Barros M., et al. Science, 2003***

Targeting the tumor vasculature for obliteration with high-dose radiation may be beneficial for tumor control.
Fuks and Kolesnick, Cancer Cell 2005 .



OLIGOMETASTASES:
THE NEW PARADIGMA FOR ABLATIVE DOSES WITH RT

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Review

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

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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.

Author and publication year [reference]	Years of enrollment	Type of study	No. of patients (No. of lesions)	De-novo irradiations/reirrad. (pts)	SBRT Schedule [Gy]	Primary endpoints
(Benzil et al., 2004)	2001–2004	Case series	31 (35)	31/0	10–25 Gy/2–10 fx	Efficacy; Toxicity
(Chang et al., 2007)	NR	Phase I/II study	63 (74)	53/10	27–30/3–5 fx	Safety; effectiveness; patterns of failure
(Gerszten et al., 2007)	NR	Prospective data collection	393 (500)	156/344 (by lesions)	12.5–25Gy/1 fx	Efficacy; Toxicity
(Hamada et al., 2008)	2003–2006	Prospective study	93 (103)	93/0	18–24 Gy/1 fx	Efficacy; Toxicity
(Chang et al., 2009)	2002–2007	Retrospective study	129 (167)	76/53	16–39/1–5 fx	Efficacy; Safety
(Gagnon et al., 2009)	2002–2006	Prospective study	200 (274)	82/118	21–37.5/3–5 fx	Pain; quality-of-life
(Sheehan et al., 2009)	2004–2007	Retrospective study	40 (110)	40/0	10–24/1 fx	Efficacy; Safety
(Sahgal et al., 2009)	2003–2006	Retrospective study	39 (60)	14/25	24/3 fx	actuarial outcomes; dosimetric analysis
(Choi et al., 2010)	2002–2008	Retrospective study	42 (51)	0/42	10–30/1–5 fx	Efficacy; safety
(Nguyen et al., 2010)	2002–2007	Retrospective study (only CCRC metastases)	48 (55)	22/26	24 Gy/1 fx 27 Gy/3 fx 30 Gy/5 fx	Efficacy; Safety
(Greco et al., 2011)	2004–2007	Retrospective study	103 (126)	103/0	18–24/1 fx	LC
(Klish et al., 2011a)	2002–2007	Phase I/II study	58 (65)	58/0	18 Gy/1Fx 27 Gy/3 Fx 30 Gy/5 fx	To evaluate the rates of failure in adjacent and distant spine
(Chang et al., 2012)	2002–2008	Retrospective study	185 (185)	131/54	Mean radiation doses (EQD2, alpha/beta ratio 10 Gy) *De novo* irradiations: 50.7 Gy Re-irradiations: 51.1 Gy	LC
(Wang et al., 2012)		phase 1–2 study	149 (166)	70/79	27–30/3 fx	Efficacy; safety
(Zelefsky et al., 2012)	2004–2010	Retrospective study (only RCC metastases)	105 (105)	105/0	18–24/1 fx 20–30/3–5 fx	Local control; toxicity
(Garg et al., 2012)	2005–2010	phase 1–2 study	61* (63)	61/0	non-renal spinal metastases : 18 Gy/1 fx renal spinal metastases : 24 Gy/1 fx	Efficacy; Safety
(Balagamwala et al., 2012)	NR	Retrospective study	57(88)	39/18	8–16 Gy/1 fx	Efficacy; safety
(Schipani et al., 2012)	2005–2008	Retrospective study	124(165)	165/0	8 Gy/1 fx	Dosimetric analysis
(Heron et al., 2012)	2000–2008	Retrospective study	228(348)	246/102	Mean doses: 16.3 Gy/1fx 20.6 Gy/3 fx 23.8 Gy/4 fx 24.5 Gy/5 fx	Efficacy; safety
(Laufer et al., 2013a)	2002–2011	Retrospective study(post-surgery spinal metastases)	186(186)	186/0	24 Gy/1fx 18–36 Gy/5–6 fx 24–30 Gy/3 fx	clinical outcome
(Folkert et al., 2014)	2005–2012	Retrospective study(only sarcoma metastases)**	88(120)	108/12(lesions)	18–24/1 fx 24–36/3–6 fx	Efficacy; safety
(Mantel et al., 2014)	2004–2010	Retrospective study	32(36)	32/0	48.5–65/17–33 fx	Efficacy; safety
(Guckenberger et al., 2014)	2004–2013	Multicentric retrospective study	301(387)	301/0	10–60 Gy/ 1–20 fx	Safety and clinical outcome
(Sellin et al., 2015)	2005–2013	Retrospective study(only RCC metastases)	37(40)	37/0	24/1 fx 27/3 fx 30/5 fx	Overall survival;toxicity

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OLIGOMETASTASES:
THE NEW PARADIGMA FOR ABLATIVE DOSES WITH RT

- Compared to surgery, SBRT potential benefits are:

- the *short treatment time* (which is also interesting as it reduces the delay for the beginning of systemic treatments),
-*good local control* rates
-*acceptable toxicity*.

- Although, compared to surgery and to other local approaches, including, radiofrequency ablation, cryosurgery etc, the non-invasiveness of SBRT is really attracting in the panorama of local treatment options,

-*prospective studies* with standardized outcome measures to make accurate conclusions, and ultimately,
-*randomized studies* to prove superiority of SBRT to other local options are required.

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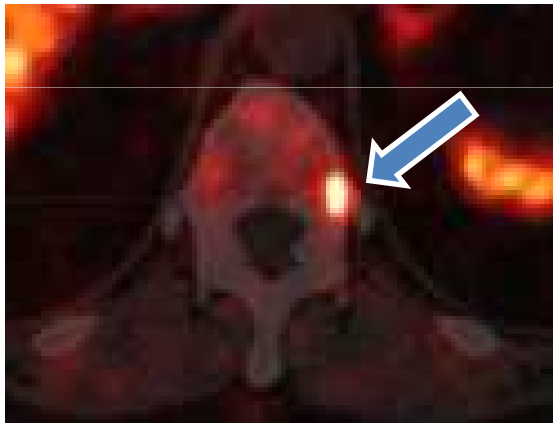
- One of the most challenging issues in this clinical setting, is the *correct selection* of patients candidates to potentially curative SBRT.
- Indeed, it could be easily argued that it *is crucial to identify those who would really benefit of more intensive treatments and those who would be candidate only to palliative* treatments.

OLIGOMETASTASIS FOR PROSTATE CANCER:

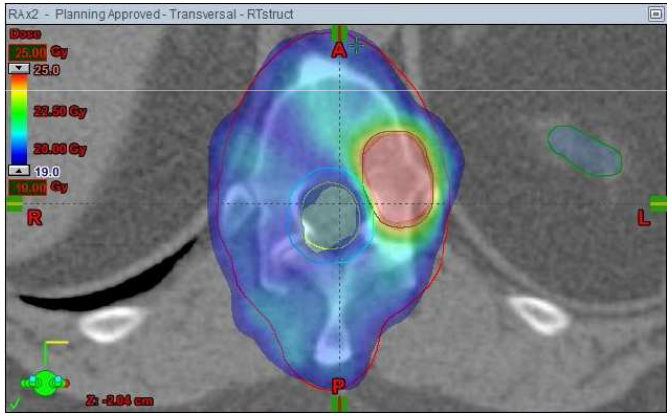
SBRT AS A NEW POSSIBILITY

Isolated Lymph bone spine metastasis from prostate cancer during ADT

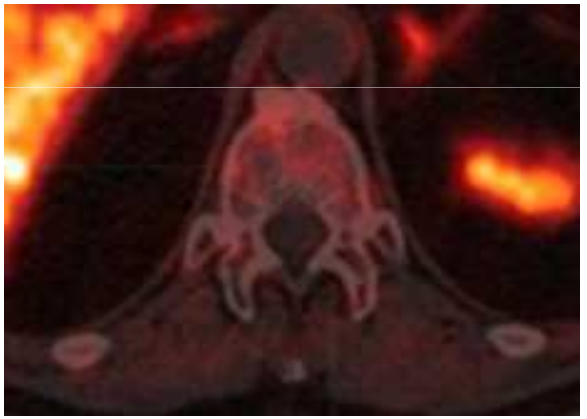


Choline PET/CT before RT

PSA: 2.52 ng/ml
PAIN VAS 5



SBRT treatment
6 Gy X 5 times



Choline PET/CT after RT

PSA: 1.49 ng/ml
PAIN VAS 1

STEREOTACTIC BODY RT(SBRT):

OLIGOPROGRESSION AND CONSOLIDATIVE SBRT: A NEW APPROACH?

«iceberg» disease

Evidence of Systemic disease in macroscopic sites

➢ **How to approach an iceberg disease?**

managed. More than 70 years later, a second model became popular in oncological practice: using the breast cancer model (also used by Halsted), this model proposed that cancer is a systemic disease that always metastasizes and thus will already have done so early in the disease course, meaning that local therapies are less important than the tumor microenvironment or systemic therapies [2-4]. Later a third theory was proposed based

«in Selected Patients»

…traditional new targeted drugs may promote greater control on systemic disease and ablative radiactions acts on NON RESPONSIVE macroscopic sites

CONCLUSIONS

- In summary, although only retrospective and some phase I-II studies are available, SBRT seems to be a promising technique for isolated or few spinal metastases.
- In particular, SBRT should be probably considered as a standard approach in some clinical situations, such as re-treatments, or when a more “curative” dose would be delivered, such as in patients with a long life expectancy and/or in oligometastatic/oligoprogressive settings.

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Thanks for your attention