Trattamenti sistemici e radioterapia nel Carcinoma Prostatico:

Ruolo della Radioterapia nel paziente oligometastatico

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UOC di Radioterapia Oncologica - AOU Policlinico of Modena

(Padova 9/ 11/ 2014)

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliero - Universitaria di Modena
Policlinico

Perchè parlare di RT nelle Oligometastasi

In base a revisioni recenti della letteratura vi è un aumentato utilizzo della RTT in presenza di “oligometastasi”, pur in assenza di dati robusti di “evidence based medicine”

controllo locale (“in field”) ottimale

profili di tossicità assai bassi.

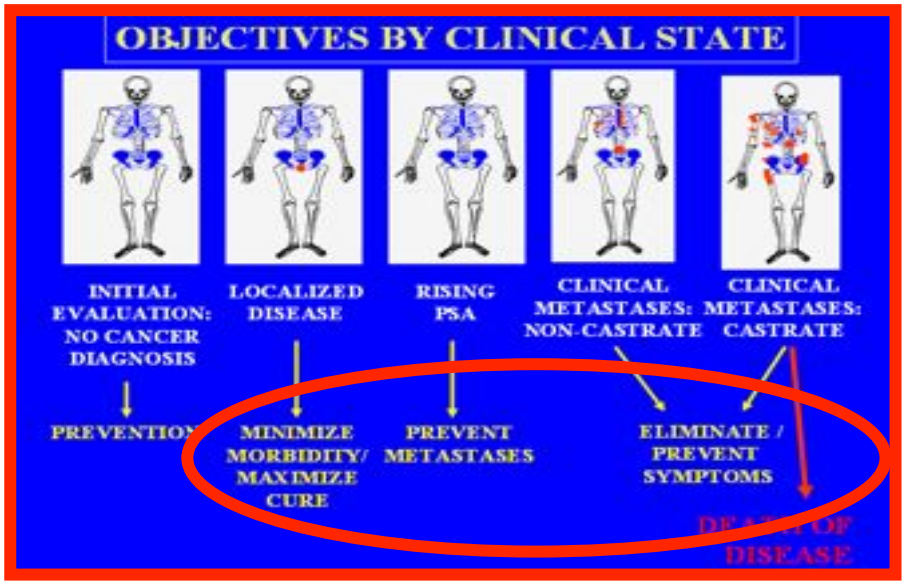
Le terapie dei tumori solidi metastatici
prevedono di norma l'utilizzo di trattamenti sistemici, somministrati per lo più con intenti palliativi

….Nelle neoplasie prostatiche , in presenza di…..

- **Diffusione sistemica di malattia (**in organi diversi dal sito primitivo)
- **Diffusione locoregionale** , ivi incluse le **recidive linfonodali**, in pazienti precedentemente trattati con intento radicale

Deprivazione androgenica → chemioterapia
Supportive care

.... un ruolo sempre più importante per la RT ...



con diverse finalità in funzione della fase evolutiva della malattia

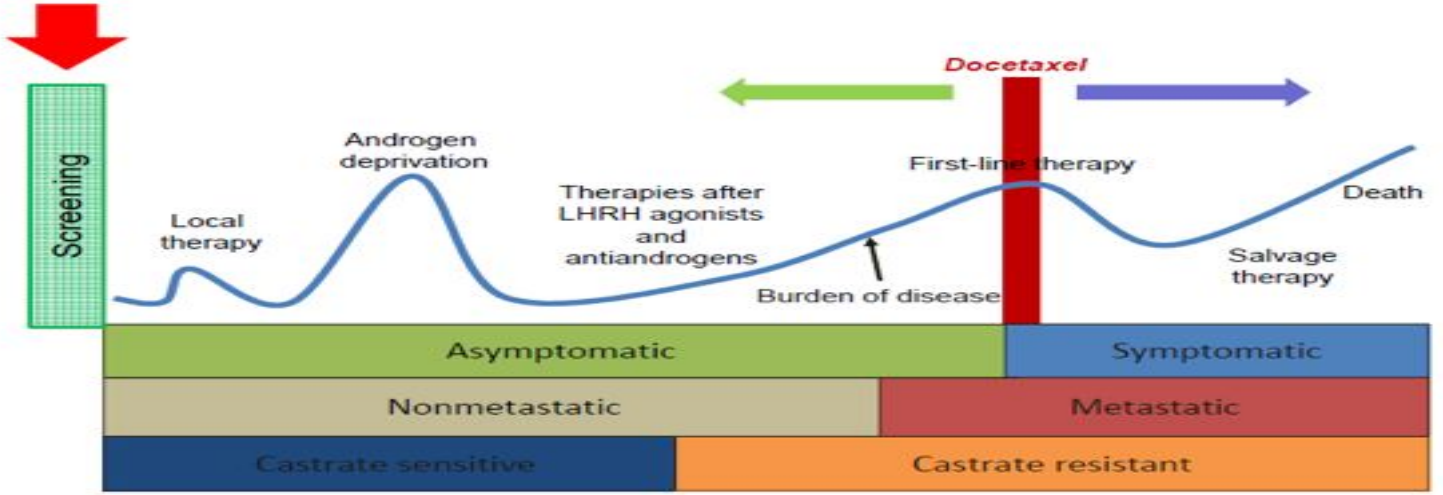
dalla fase locale/locoregionale alla fase <u>oligometastatica</u> e metastatica

frequentemente è presente una malattia "*castration resistent*"

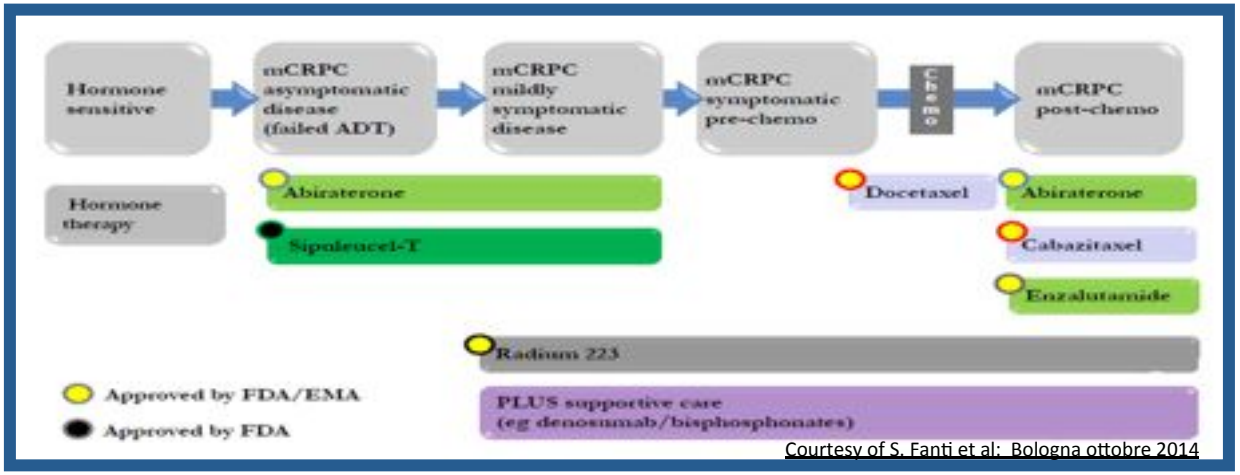
per la quale la terapia standard è costituita da rimodulazione ormonale e chemioterapia (Taxani) alla quale si aggiungono oggi antiandrogeni promettenti di ultima generazione e anche la <u>radioterapia metabolica con 223Ra</u>.

Evolving treatment paradigm in CRPC

Ca prostatico: una o più malattie?



RT curativa → **RT curativa/pall** → **RT sintomatica**



Courtesy of S. Fanti et al: Bologna ottobre 2014

THE UNIVERSITY OF CHICAGO
BIOLOGICAL SCIENCES

1995: the term "oligometastases" is coined

Hellman S, Weichselbaum RR. J Clin Oncol. 1995;13(1):8-10

EDITORIAL

Oligometastases

CANCER TREATMENT is based on an often unstated paradigm of disease pathogenesis. Since 1894, when W.S. Halsted[1] clearly elucidated a mechanism of breast cancer spread and used it to design and support the radical mastectomy, surgical and radiotherapeutic approaches to most cancers have been based on this theory. The Halsted theory proposed that cancer spread is

more about the multistep nature of the development of malignancy.[2,3] Once tumors become invasive, they may gradually acquire the properties necessary for efficient and widespread metastatic spread.[3] Therefore the likelihood, number, and even sites of metastases may reflect the state of tumor development. This suggests that there are tumors more intermediate between poorly localized

- "Oligometastasi": termine coniato nel 1995 come corollario alla **"Spectrum theory "** descritta per le neoplasie mammarie nel 1994"
- Una neoplasia, alla sua comparsa, può presentare uno **spettro di aggressività biologica** cui corrispondono potenzialità metastatiche variabili e aggressività intermedie una delle quali è rappresentato dalla malattia "oligometastatica"

(malattia che rimane locale ←→malattia con diffusa metastatizzazione all'esordio)

2011

OPINION

Oligometastases revisited

Weichselbaum, R. R. & Hellman, S. Nat. Rev. Clin. Oncol. 8, 378–382 (2011)

Nat Rev Clin Oncol. 2014 Sep;11(9):549-57. doi: 10.1038/nrclinonc.2014.96. Epub 2014 Jun 24.

The oligometastatic state - separating truth from wishful thinking.

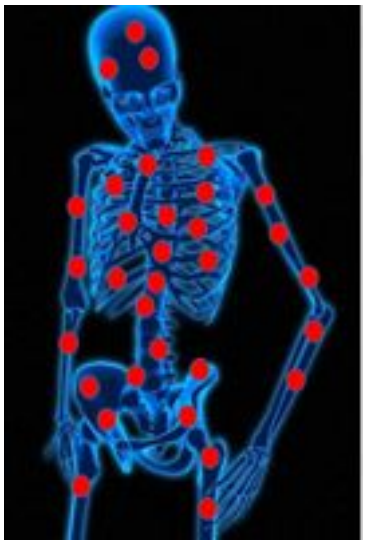
Palma DA[1], Salama JK[2], Lo SS[3], Senan S[4], Treasure T[5], Govindan R[6], Weichselbaum R[7].

OLIGOMETASTASI

....diverse definizioni / diversi scenari clinici....

" Condizione nella quale il paziente presenta **riprese di malattia** a distanza **in un numero limitato di sedi e lesioni** "

≤ 5 localizzazioni



> 5 localizzazioni

"..did not eliminate the uncontrolled primary site with several distant metastases.."

Y.Niibe, K Hayakawa: JJCO 2010

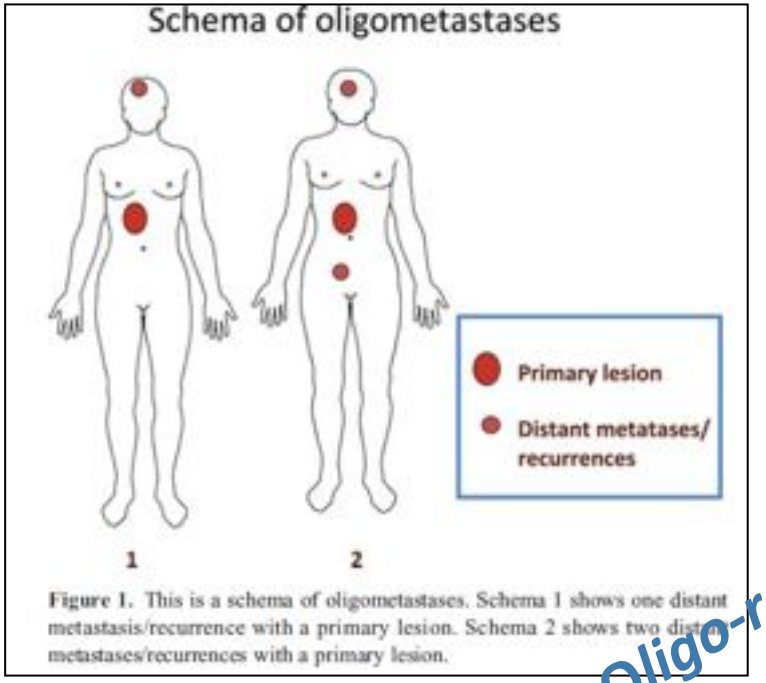


Figure 1. This is a schema of oligometastases. Schema 1 shows one distant metastasis/recurrence with a primary lesion. Schema 2 shows two distant metastases/recurrences with a primary lesion.

JJCO Japanese Journal of Clinical Oncology

Jpn J Clin Oncol 2010;40(2)107–111
doi:10.1093/jjco/hyp167
Advance Access Publication 4 January 2010

Review Article

Oligometastases and Oligo-recurrence: The New Era of Cancer Therapy

An Oligo-recurrent disease is more easily amenable to local therapies applied with curative intent than an oligometastasic one.

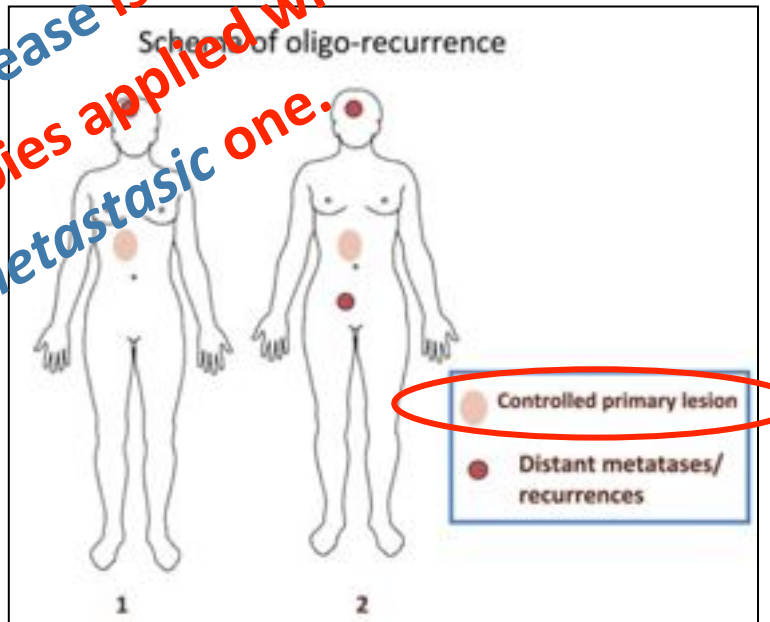


Figure 2. This is a schema of oligo-recurrence. Schema 1 shows one distant metastasis/recurrence with a controlled primary lesion. Schema 2 shows two distant metastases/recurrences with a controlled primary lesion. The biggest difference between oligometastases and oligo-recurrences lies in the uncontrolled or controlled primary lesion. Oligo-recurrence requires a controlled primary lesion.

Oligometastases and oligo-recurrence

	Oligometastasis	Oligo-recurrence
Reference	Hellman and Weichselbaum (1)	Niibe et al. (2,3,4)
Primary lesion	Uncontrolled/controlled	Controlled
No. of distant/metastases/ recurrences	One to several	One to several (one is better)

Semin Radiat Oncol 16:120-130 © 2006

Solitary Metastases: Illusion Versus Reality

Philip Rubin, MD, Ralph Brasacchio, MD, and Alan Katz MD, MPH

… le possibilità diagnostiche e di "cura" per M in fase iniziale potrebbero richiedere modifiche della classificazione TNM

- Mic: circulating cancer cells persisting after surgery or radiation treatment of the primary tumor and regional nodes, 0.1 mm or 100 μ
- M1mic: micrometastases, 0.2 mm to 2.0 mm in size (200 μ to 2000 μ)
- M1: a solitary metastasis in a single organ
- M2: oligometastases, designate number and limited to 1 organ (5 nodules, 5 cm in total)
- M3: multiple metastases, limited to 1 organ site (5 nodules, 5 cm in aggregate, more than 1 lung)
- M4: multiple metastases, multiple organs

Addition of serum molecular markers as follows:

- S0: not detectable
- S1: detectable, low level
- S2: intermediate level
- S3: high level

Once metastases are staged a the modified Karnofsky scale as follows should be used.

- H0: normal activity; asymptomatic
- H1: symptomatic; fully ambulatory
- H2: symptomatic; in bed 50% of time
- H3: symptomatic, in bed 50% of time, not bedridden
- H4: 100% bedridden

Stage IV needs to be modified (similar to Hodgkin's disease).

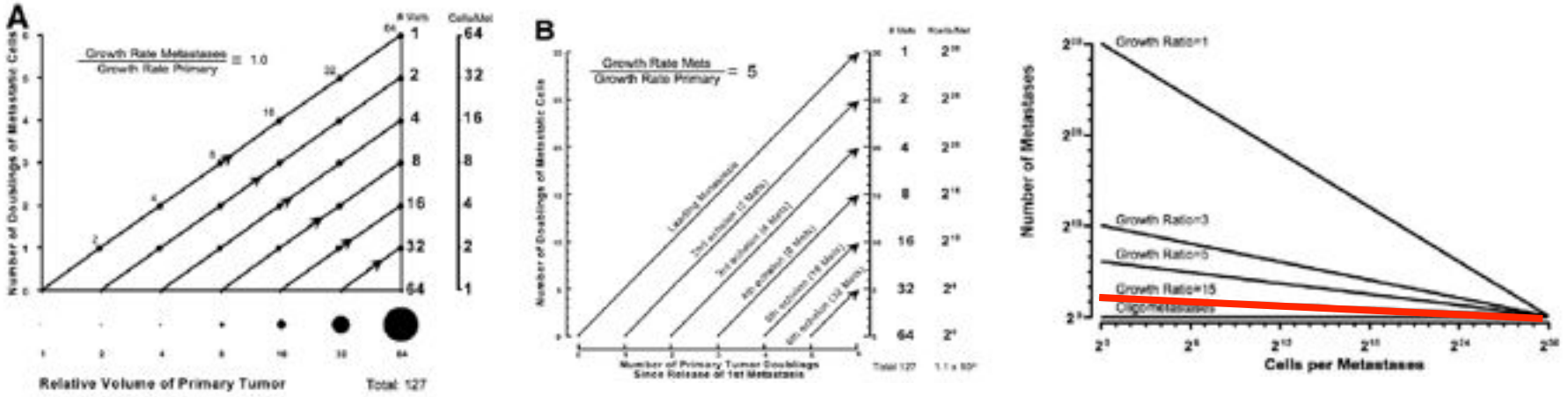
A. no systemic signs: minimal 5% weight loss, minimal lab abnormalities.

B. systemic signs: 100% weight loss, cachexia, fevers nexplained, lab abnormalities, i.e. altered lung function, abnormal liver enzymes, etc.

Modeling Growth Kinetics and Statistical Distribution of Oligometastases

H. Rodney Withers MD, DSc, and Steve P. Lee MD, PhD

Seminars in RADIATION ONCOLOGY
Semin Radiat Oncol 16:111-119 © 2006



(A) For an equal growth rate of primary and metastases for a period of time allowing 6 doublings.
(B) The same as for A, except for a growth rate of micrometastases which is 5 times faster than the growth rate of the primary.

High ratios predispose to an oligometastatic distribution: for example, for a growth ratio of 15, there would be 1 metastasis of large volume (230 cells), 2 with 215 cells, and 4 would be starting as single cells.

A model relating the numbers and volumes of metastases to the exponential growth of a primary tumor assuming that the release of metastatic clonogens is proportional to the volume of the primary and that metastases grow exponentially

... Il numero e il volume delle metastasi è correlabile al volume e alle modalità di crescita del T primitivo ...

....condizioni che favoriscono quadri di Oligometastasi....

Modeling Growth Kinetics and Statistical Distribution of Oligometastases

H. Rodney Withers MD, DSc, and Steve P. Lee MD, PhD

Seminars in ONCOLOGY
Semin Radiat Oncol 16:111-119 © 2006

Selection of Patients for Attempted Cure of oligometastases

Clinical history favoring development of an oligometastatic includes :

- prior concomitant chemoradiation or chemosurgery
- slowly growing large primary tumor followed by a **long metastasis-free interval** after which a solitary metastasis emerges.
- high ratio of growth rate of metastases to that of the primary, as evidenced by a large difference between volumes of sequential metastases, signals the possibility of oligometastases (for shorter intervals between resection of the primary and emergence of a small number of metastases)

T primitivo voluminoso

Growth Rate Metastasi / Growth Rate T primitivo

Lungo intervallo tra rimozione T e comparsa di singole Metastatasi

Chemioterapia

...l'anticipazione diagnostica è determinante ...

Semin Radiat Oncol 16:120-130 © 2006

Solitary Metastases: Illusion Versus Reality

Philip Rubin, MD, Ralph Brasacchio, MD, and Alan Katz MD, MPH

- **Solitary Pulmonary Metastases**
- **Solitary Liver Metastasis**
- **Solitary Brain Metastases**
- **Solitary Bone Metastases**
- **Other Solitary Site Metastases**
  - Head and Neck
  - Eye and Orbit
  - Ovary-Uterus
  - Heart
  - Intestines

Survival of Solitary and Oligometastases Treated by Stereotactic Body Radiation Therapy (SBRT)

	In Liver
Number of patients	83
Number of liver Mets	117
Primary sites: colorectal	62
other	65
Mean tumor volume	44cc
Radial margins	5mm
Cardiocranial margins	10mm
PTV dose	14–26, Gy single dose (Gy = Gray) 30, Gy 3 fractions 20–45, Gy 2 fractions 7–45, Gy 4 fractions
Time for treatment	1–7 days
Follow-up	9–24 months
Median survival	72% actuarial at 1 year
Toxicity	Hemorrhagic gastritis Duodenal ulcer

Reprinted with permission from Stereotactic body radiation therapy for liver tumors: Kavanagh BD, Timmerman RD (eds). Stereotactic Body Radiation Therapy. Philadelphia, PA, Lippincott Williams & Wilkins, 2005, pp 115–127.

The key strategy to eradicate metastatic cancer is to **meticulously search the "target organ" for solitary or oligometastatic foci** before they manifest themselves overtly and metastasize to additional distant organs

Molecular markers and PET-CT screening ?

Semin Radiat Oncol 16:120-130 © 2006

Solitary Metastases: Illusion Versus Reality

Philip Rubin, MD, Ralph Brasacchio, MD, and Alan Katz MD, MPH

Table 1 Imaging Technology Status: Minimal Threshold Size

		1 = High/4 = Low		1 = Good/4 = Poor		
Technique	Resolution (mm)	Functional Potential	Size/ Threshold Reached	Sensitivity/ Specificity	Metabolic Imaging Potential	Comments
MRI/MRS/MRF	5	1	Probably	2/2	2	Potential for improved functional data
CT	5	3	Yes	2/3	3	Virtual endoscopy potential
Radiographs	5–10	4	Yes	2/3	4	Size threshold reached; digital imaging potential
SPECT	10–15	3	Probably	3/2	2–3	Improvement with better radionuclides
PET	10–15	1	Probably	2/1	1	Tumor staging/response; potential high
Ultrasonography	5–10	3	Probably	3/3	4	
Mammography	5	4	Yes	2/2	4	Digital mammography should improve specificity
Angiography	5–10	3	Yes	2/2	4	Interventional potential
Conventional Nuclear Medicine	10–15	3	Yes	3/2	3	Improvement with better radionuclides

Reprinted with permission from Imaging strategies for oncologic diagnosis and multidisciplinary treatment, in Bragg DG, Rubin P, Hricak H (eds): Oncologic Imaging (ed 2). Philadelphia, PA, Saunders, 2002, pp 3–20.

Table 2 Cancer-Site Imaging Status: Accuracy, Specificity, Sensitivity

	1 = High/4 = Low		1 = Good/4 = Poor			
Cancer Site	T Detection/ Accuracy	Diagnostic Specificity/ Sensitivity	N Staging	M Staging	Tumor Response	Comments
Brain	1	1/1	NA	NA	2	Tumor biology major issue; functional yield will increase
Lung	1/2	2/1–2	2	2–3	1–2	PET-improved specificity; need better detection
Liver	1–2	1–2/1–2	NA	1–2	1–2	Anatomic endpoint reached; functional/interventional yield
Bone	1	1–2/1	NA	1–2	2	Imaging endpoints reached

Abbreviation: NA, not applicable.

Reprinted with permission from Imaging Strategies for oncologic diagnosis and multidisciplinary treatment, in Bragg DG, Hricak H (eds): Oncologic Imaging (ed 2). Philadelphia, PA, Saunders, 2002, pp 3–20.

Oligometastasi e neoplasie prostatiche

La presenza di oligometastasi **non è condizione comune** nei pazienti con neoplasia prostatica

...ma....

- in una **serie autoptica** è riportata la presenza di una o due lesioni ossee nel 60-70% dei casi e **solo in un 10% un numero di 4 o più lesioni.**
- Alcuni autori hanno segnalato **sopravvivenze a 5 anni nettamente superiori in pazienti che presentano fino a 5 metastasi** con percentuali simili a quelle dei pazienti non metastatici (indicativo di presenza di una neoplasia meno aggressiva caratterizzata da un basso indice di crescita).
- **In questi casi potrebbero essere proposti trattamenti locali più aggressivi** tra i quali la radioterapia può avere un ruolo significativo in associazione o meno a trattamenti farmacologici.

Le sedi più frequentemente coinvolte sono le stazioni linfonodali

(in prima istanza quelle pelviche e successivamente quelle lomboaortiche)

Assai raramente le localizzazioni ossee si presentano come singole.

R.Miralbell:Eur J Nucl Med Mol Imaging (2014); 41: 1267 – 1269
M. Harada et Al : Adv Exp Med Biol 1992; 324: 173-182
D. Singh et Al: Int J Radiat Oncol Biol Phys 2004; 58: 3-10

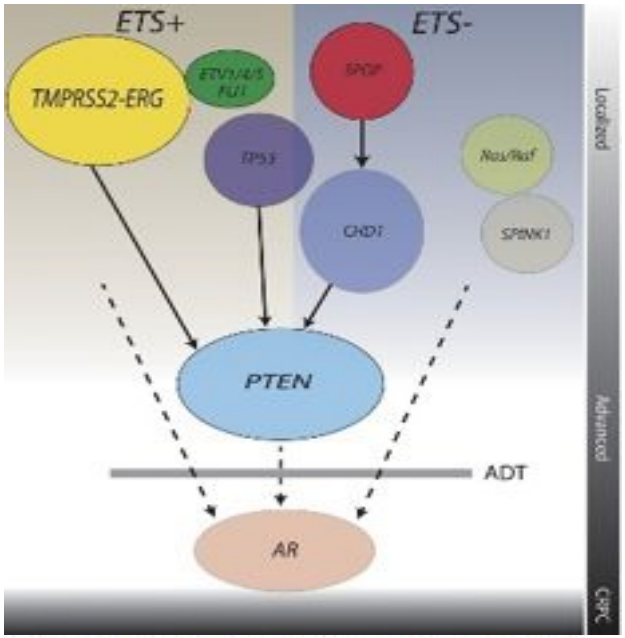
...è possibile una caratterizzazione biologica di aggressività ?....

Review article Urologic Oncology: Seminars and Original Investigations 32 (2014) 53.e15–53.e22

The prostate cancer genome: Perspectives and potential

Christopher E. Barbieri[a,b,*], Scott A. Tomlins[c,d]

- Review of the relevant literature, with a focus on recent studies on somatic alterations in prostate cancer ....
  - ETS gene fusions
  - SPOP mutations and CHD1 deletions
  - Androgen signaling
  - PI3K pathway
  - SPINK1
  - Ras/Raf/MAPK pathway



Genomic lesions in the timeline of prostate cancer.

These findings raise the possibility that prostate cancer could transition from a poorly understood, heterogeneous disease with avariable clinical course to a collection of homogenous subtypes, identifiable by molecular criteria, associated with distinct risk profiles, and perhaps amenable to specific managements trategies or targeted therapies

...per ora solo informazioni generali su parametri già in uso....

METASTATIC CARCINOMA OF THE PROSTATE: IDENTIFYING PROGNOSTIC GROUPS USING RECURSIVE PARTITIONING

TRACY R. GLASS, CATHERINE M. TANGEN, E. DAVID CRAWFORD AND IAN THOMPSON*

From the Fred Hutchinson Cancer Research Center, Seattle, Washington, University of Colorado Health Science Center, Denver, Colorado, and University of Texas Health Science Center at San Antonio, San Antonio, Texas

THE JOURNAL OF UROLOGY Vol. 169, 164–169, January 2003

SWOG 8894: 1076 pts/1286 trattati con Orchiec.+ Flutamide vs orchictomia+Placebo

Good prognosis:

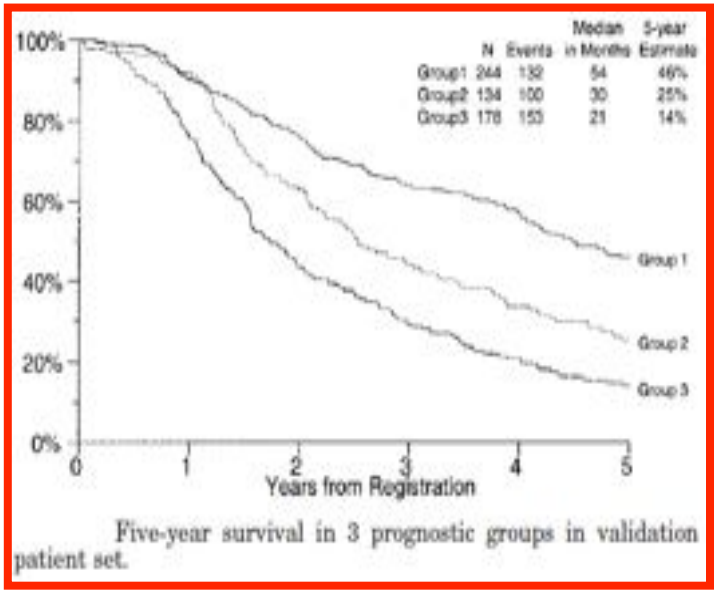
- no appendicular disease (HR 1) or
- with appendicular disease, a performance status of 0 and a Gleason sum of less than 8 (HR ratio 1.28),

Intermediate prognosis

- appendicular disease, a performance status of 0 and a Gleason sum of 8 or greater (hazards ratio 2.01) or
- appendicular disease, a performance status of 1 or greater and PSA less than 65 ng./ml. (HR ratio 1.75)

Poor prognosis

- appendicular disease, a performance status of 1 or greater and PSA 65 ng./ml. or greater (HR ratio 3).



Five-year survival in 3 prognostic groups in validation patient set.

M1 → **OS a 3 anni :** 45 % – 25 % – 14%

Ca prostatico:

Quale imaging diagnostico per le Oligometastasi ?

EDITORIAL COMMENTARY

Eur J Nucl Med Mol Imaging (2014) 41:1267–1269

PET/CT imaging and the oligometastatic prostate cancer patient: an opportunity for a curative approach with high-dose radiotherapy?

Raymond Miralbell · Franz Buchegger

- Several groups have expressed doubts about the detection of positive lymph node and bone metastases with **choline tracers** probably because of **potential uptake artefacts caused by inflammatory reactions and degenerative bone disease**, respectively
- While the widely used **choline tracers** for prostate cancer show **good detection rates notably for local recurrences**, they **appear less specific for lymph node and bone metastases.**

In summary

Despite limited sensitivity and specificity for acetate and choline tracers, patients with oligometastatic prostate cancer **may benefit from targeted high-dose irradiation** of the suspected lesions associated with a short course of AD.

This hypothesis **needs to be confirmed in a phase III trial** comparing intermittent AD with or without a complement of targeted irradiation.

Imaging and nodal metastases

Performances of the magnetic resonance imaging (MRI) in detecting nodal metastases.

Authors (year of publication)	References	Number of patients	Inferior threshold (mm)	LNM %	Sensitivity %	Specificity %	Accuracy %
Heesakkers et al. (2008)	12	375	8–10	16	34	97	NA
Lecouvet et al. (2012)	17	100	10	NA	77 (R3) 82 (R4)	95 (R3) 96 (R4)	NA
Bezzi et al. (1988)	18	51	10	25	69	95	88
Rifkin et al. (1990)	19	185	10	12.5	[illegible]	95	NA
Jager et al. (1996)	20	63	8	[illegible]	60	98	89
Perrotti et al. (1996)	21	56	10	9	0	90	86
Harisinghani et al. (2003)	22	80	10	NA	45 (standard MRI) 100 (USPIO-MRI)	79 (standard MRI) 96 (USPIO-MRI)	NA
Wang et al. (2006)	23	411	8	5.5	27	98	NA
Eiber et al. (2010)	24	29	6	NA	86[a]	85	86
Budiharto et al. (2011)	25	36	4	47	18.8	97.6	NA

Note: Inferior threshold: Figure above which a lymph node is considered pathological; % LNM: Percentage of patients with positive lymph nodes histopathologically controlled; USPIO contrast agent: UltraSmall Particles of Iron Oxide (no longer commercially available).

[a] Correlation with histopathology in only 10 patients; NA: Not available; R1 and R2: Two different readers.

RMN

Sensibilità 0 – 86%; Specificità 79 -98%

Performances of the conventional CT scan in detecting nodal metastases.

Authors (year of publication)	References	Number of patients	Inferior threshold (mm)	LNM %	Sensitivity %	Specificity %	Accuracy %
Heesakkers et al. (2008)	12	375	8–10	16	34	97	NA
Golimbu et al. (1981)	13	46	10	37	30	93	70
Flanigan et al. (1985)	14	53	15	26.5	50	[illegible]	91
Van Poppel et al. (1994)	15	285	6	16	78	[illegible]	96.5
Rorvik et al. (1998)	16	64	10	15	[illegible]	98	NA
Lecouvet et al. (2012)	17	100	10	[illegible]	[illegible] (R3) 82 (R4)	95 (R3) 96 (R4)	NA
Perrotti et al. (1996)	21	56	10	9	0	90	86
Harisinghani et al. (2003)	22	80	10	NA	45 (standard MRI) 100 (USPIO-MRI)	79 (standard MRI) 96 (USPIO-MRI)	NA
Wang et al. (2006)	23	[illegible]	8	5.5	27	98	NA
Eiber et al. (2010)	24	29	6	NA	86[a]	85	86
Budiharto T et al. (2011)	25	36	4	47	18.8	97.6	NA

Note: Inferior threshold: Figure above which a lymph node is considered pathological; % LNM.: Percentage of patients with positive lymph nodes histopathologically controlled; USPIO contrast agent: UltraSmall Particles of Iron Oxide (no longer commercially available.

[a] Correlation with histopathology in only 10 patients; NA: Not available; R3 and R4: Two different readers.

TC

Sensibilità 0 – 100%; Specificità 79 -100%

EAU Guidelines clearly discourage the routinely use of [11C]-choline PET/CT
for the early diagnosis of nodal relapses from prostate cancer.

B. De Bari et al. / Critical Reviews in Oncology/Hematology 90 (2014) 24–35

Critical Reviews in Oncology/Hematology 90 (2014) 24–35

Salvage therapy of small volume prostate cancer nodal failures: A review of the literature

SUMMARY

- Conventional **contrast enhanced CT and MRI still remain** the standard for lymph node relapse detection;
- In this setting, DWI–MRI is interesting, but data about its usefulness are not conclusive yet;
- Despite its diffusion in the clinical practice**, [11C]CholinePET/CT,** remains object of investigation due to the uncertainness regarding PSA value related to its accuracy.

B. De Bari et Al.: Critical Reviews in Oncology/Hematology 90 (2014) 24–35

Oligometastasi
esperienze e risultati con RT

.....in generale e nel Ca. prostatico ….

REVIEW Journal of Surgical Oncology 2008;98:202–206

A Rationale for the Targeted Treatment of Oligometastases With Radiotherapy

DHARA M. MacDERMED, MD,[1] RALPH R. WEICHSELBAUM, MD,[1,2,3] AND JOSEPH K. SALAMA, MD[1,2,3]*

Local treatment of oligometastases is an important area of investigation to improve survival in a clinically significant subset of cancer patients.

- **Biology of the metastatic and oligometastatic state**
- **Clinical evidence for the oligometastatic state**
- **Role of radiotherapy as non-invasive local therapy for lung and liver metastases**

"..... we are entering a new era in cancer therapy which will result in long term survival for many adult patients who were historically considered to be incurable...."

Trials should be designed to optimize targeted therapies and to demonstrate the benefit of targeted treatment of oligometastases.

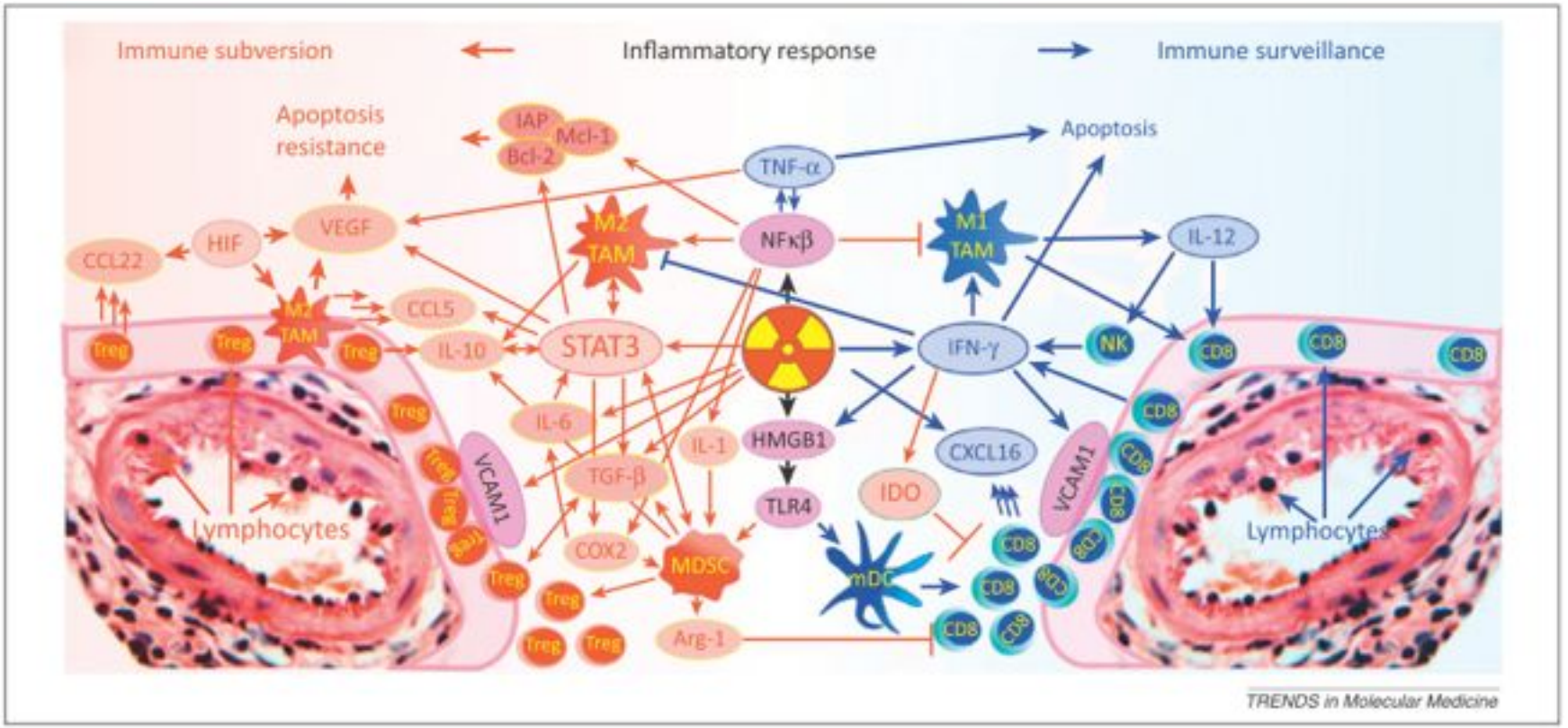
Display Settings: Abstract

2013

Trends Mol Med. 2013 Sep;19(9):565-82. doi: 10.1016/j.molmed.2013.05.007. Epub 2013 Jul 4.

Immunologically augmented cancer treatment using modern radiotherapy.

Durante M[1], Reppingen N, Held KD.



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2013

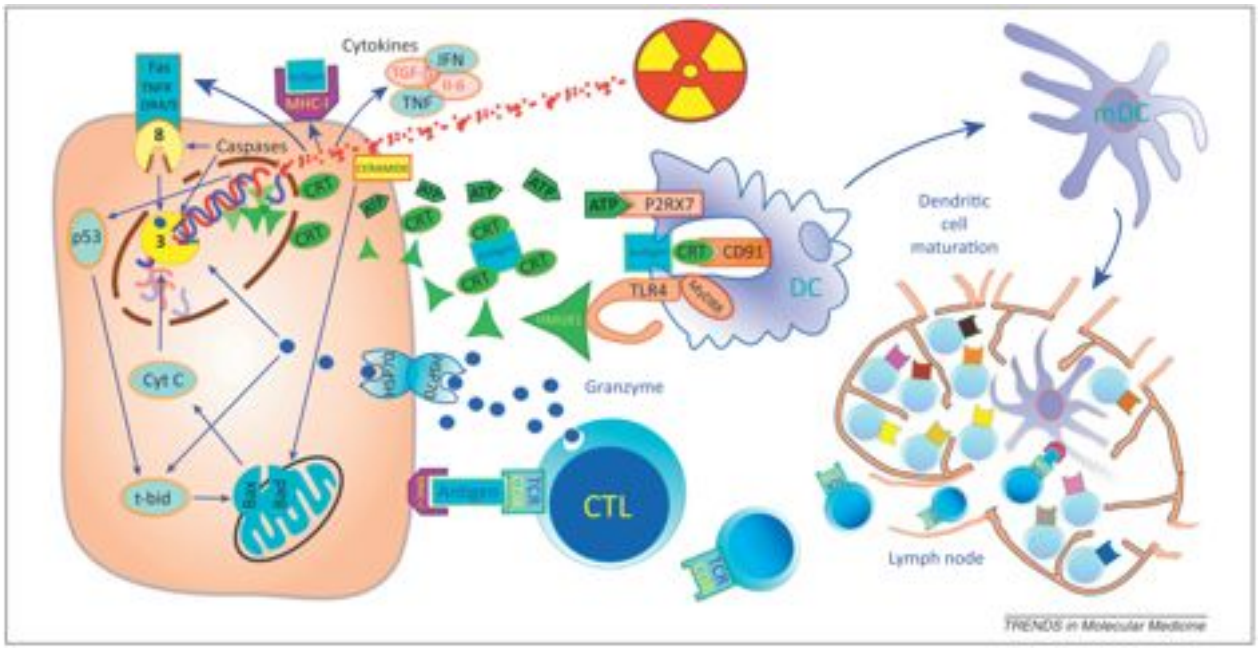
Trends Mol Med. 2013 Sep;19(9):565-82. doi: 10.1016/j.molmed.2013.05.007. Epub 2013 Jul 4.

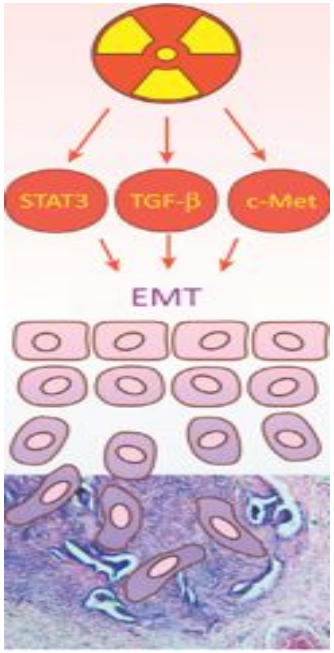
Immunologically augmented cancer treatment using modern radiotherapy.

Durante M[1], Reppingen N, Held KD.

Abscopal Effect

A rare phenomenon in the treatment of metastatic cancer where localized irradiation of a tumor shrinks both the irradiated tumor as well as a metastasis far from the irradiated area. ***The abscopal effect is considered to be immune-mediated***.





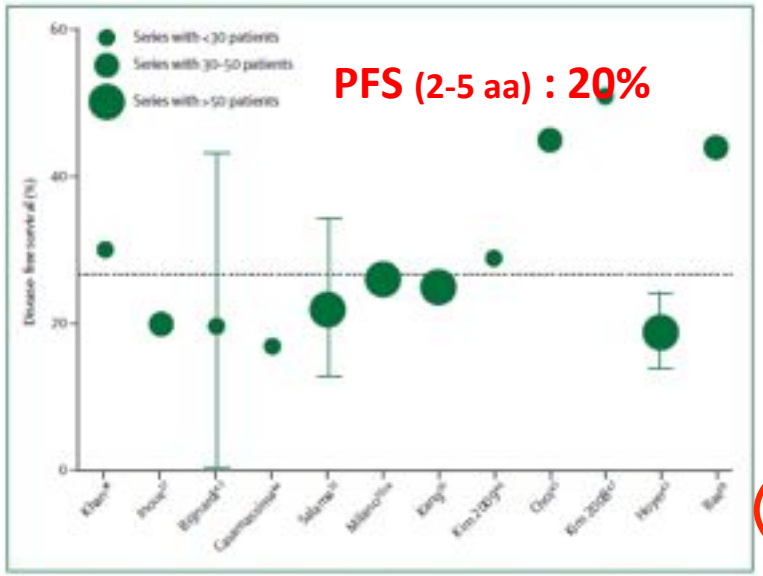
THE LANCET Oncology

Volume 14, Issue 1, January 2013, Pages e28–e37

Review

Stereotactic body radiotherapy for oligometastases

Dr Alison C Tree, FRCR[a], Vincent S Khoo, MD[a,b], Prof Rosalind A Eeles, FRCR[c], Merina Ahmed,



PFS (2-5 aa) : 20%

Figure 2: Disease-free survival in patients with oligometastatic disease at 17–48 months' follow-up
Dotted line represents mean proportion of patients who were disease free at the reported timepoint, weighted for number of patients in each cohort. Error bars represent 95% confidence intervals.

Panel: Evidence-based practice for extracranial oligometastases

- Stereotactic body radiotherapy results in a high control rate of treated metastases (~80%)
- About 20% of patients are progression free at 2–3 years after stereotactic body radiotherapy
- Toxicity is low
- Stereotactic body radiotherapy should be considered in patients with isolated metastases, especially if the disease-free interval is longer than 6 months
- Randomised trials are needed to establish whether stereotactic body radiotherapy improves progression free and/or overall survival
- Patients most likely to benefit from stereotactic body radiotherapy have:
  - Long disease-free interval
  - Breast histology
  - One to three metastases
  - Small metastases
  - Higher radiation dose delivered (biologic effective dose >100 Gy)

Many non-randomised studies have shown that SBRT for oligometastases is safe and effective, with local control rates of about 80%. Importantly, these studies also suggest that the natural history of the disease is changing, with 2–5 year progression-free survival of about 20%. Although complete cure might be possible in a few patients with oligometastases, the aim of SBRT in this setting is to achieve local control and delay progression, and thereby also postpone the need for further treatment. We review published work showing that SBRT offers durable local control and the potential for progression-free survival in non-liver, non-lung oligometastatic disease at a range of sites. However, to test whether SBRT really does improve progression-free survival, randomised trials will be essential.

THE LANCET Oncology
Volume 14, Issue 1, January 2013, Pages e28–e37

Review

Stereotactic body radiotherapy for oligometastases

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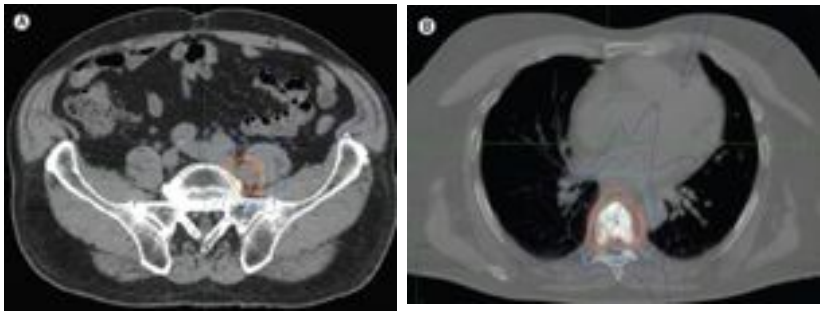
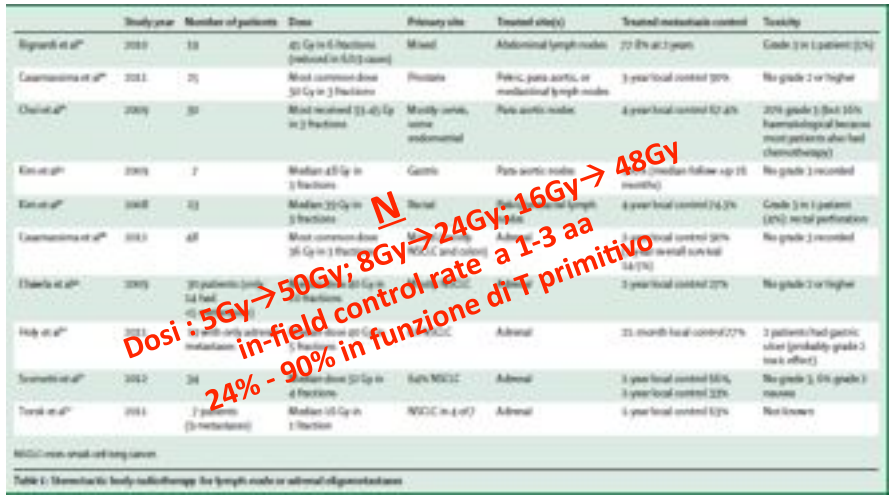
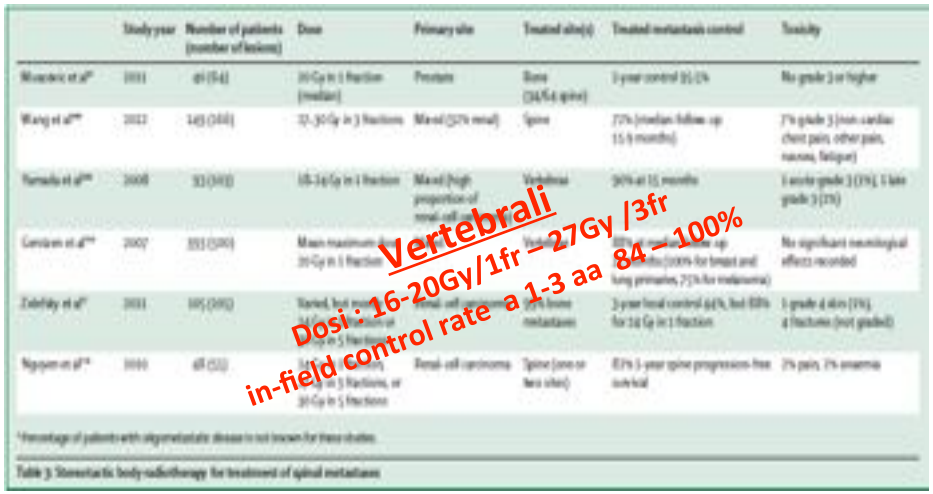


- Pazienti oligometastatici
- Studi fase II e III o retrospettivi
- F.U. mediano di 12 mesi

Miste
Dosi : 5Gy→50Gy; 8Gy→24Gy; 40-50-60Gy/in 3-5 fr
in-field control rate a 1-3 aa
25% - 90% in funzione di T primitivo



N
Dosi : 5Gy→50Gy; 8Gy→24Gy; 16Gy→ 48Gy
in-field control rate a 1-3 aa
24% - 90% in funzione di T primitivo



Vertebrali
Dosi : 16-20Gy/1fr → 27Gy /3fr
in-field control rate a 1-3 aa 84 – 100%

A.C. Tree et al : The Lancet Oncology 2013

…per le neoplasie prostatiche: diverse revisioni recenti…

REVIEW ARTICLE *Asia-Pacific Journal of Clinical Oncology* 2014

Advances in local and ablative treatment of oligometastasis in prostate cancer

Henry HI YAO,[1] Matthew KH HONG,[1] Niall M CORCORAN,[1,2] Shankar SIVA[3] and Farshad FOROUDI[3]

Platform	Search criteria	Results	Excluded articles	Included articles
PubMed	(oligometastatic[All Fields] AND ("prostatic neoplasms"[MeSH Terms] OR ("prostatic"[All Fields] AND "neoplasms"[All Fields]) OR "prostatic neoplasms"[All Fields] OR ("prostate"[All Fields] AND "cancer"[All Fields]) OR "prostate cancer"[All Fields]))	7 articles	2	5
PubMed	(oligometastases[All Fields])	104 articles	100	4[1]
PubMed	(metastasectomy[MeSH Terms] AND ("prostatic neoplasms"[MeSH Terms] OR ("prostatic"[All Fields] AND "neoplasms"[All Fields]) OR "prostatic neoplasms"[All Fields] OR ("prostate"[All Fields] AND "cancer"[All Fields]) OR "prostate cancer"[All Fields]))	3 articles	3	0
PubMed	("solitary"[All Fields] AND ("neoplasm metastasis"[MeSH Terms] OR ("neoplasm"[All Fields] AND "metastasis"[All Fields]) OR "neoplasm metastasis"[All Fields] OR "metastasis"[All Fields]) AND ("prostatic neoplasms"[MeSH Terms] OR ("prostatic"[All Fields] AND "neoplasms"[All Fields]) OR "prostatic neoplasms"[All Fields] OR ("prostate"[All Fields] AND "cancer"[All Fields]) OR "prostate cancer"[All Fields]))	55 articles (in the last 10 years)	42	13[1]
EMBASE	prostate carcinoma/or prostate cancer/AND metastasis/or oligometastases AND stereotactic body radiation therapy or robotic stereotactic radiotherapy	156 Articles	144	12[5]

[1]One article had already been identified. [1]One article had already been identified. [5]Two articles previously identified, four articles are abstracts that are subsequently published and already identified, one article has been updated with longer follow-up in subsequent publication.

Chirurgia e RT (normo o ipofrazionata)

….dal 2004 al 2013…

Chirurgia : 13 studi

RT : 12 studi (F.U. mediano da 6 – 48 mesi)

Asia-Pacific Journal of Clinical Oncology 2014

REVIEW ARTICLE *Asia-Pacific Journal of Clinical Oncology* 2014

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Table 3 Summary of studies using radiotherapy in the management of oligometastatic lesion in prostate cancer: Part I – sample size, demographics and treatment regimens

Article	Modality	Metastasis criteria	No. of CaP Patients (No. of lesions)	Median age	Sites of metastasis	Radiation dose/fractions	Treatment of primary prostate cancer	Note
Schick *et al.* (2013)[64]	EBRT	1–4 metastatic lesions	50 (79)	63.2	• Regional LN (n = 32) • Distant LN (n = 18) • Bone (n = 25) • Lung (n	Median 64 Gy	• None (n = 7) • RT ± ADT (n = 10) • Surgery ± salvage RT ± ADT	• Patients also received neo-adjuvant and concomitant ADT for median of 12 months • ADT was subsequently restarted on progression of disease
Tabuta *et al.* (2012)[63]	EBRT	1–5 vertebral metastases (each site < 50% of size of vertebral body)	35 (median 2 per patient)	71.5	• Bone	Median 40 Gy/ 10–[illegible]	RP (n = 10) • RT (n = 8) • None (n = 17)	• Patients received concomitant ADT
Rades *et al.* (2007)[66]	EBRT	≤3 vertebral metastases –with no other bony and visceral metastasis	[illegible]	64[†]	• Bone and [illegible] vertebra)	[illegible] Gy/[illegible]	N/A	
Berkovic *et al.* (2013)[67]	SABR	≤3 synchronous bone or lymph node metastases	24 (29)	[illegible]	• LN (n = 13) – pelvic and extra-pelvic • Bone (n = 16)	Median 30 Gy/10	• RT (n = 3) • RP (n = 4) • RP then RT (n = 16) • RT then RP (n = 1)	• Patient had neo-adjuvant ADT (total duration of 1 month)
Ahmed *et al.* (2013)[68]	SABR	[illegible] synchronous metastases	17 (21)	65	• LN (n = 1) • Bone (n = 19) • Liver (n = 1)	Median 20 Gy/1 (bone) 50 Gy/3 (LN) 60 Gy/5 (liver)	• RP (n = 15) • EBRT (n = 2)	• Only 16 of 21 lesions were evaluable for local control • 11 of 17 patients had hormone refractory disease at time of SABR • Androgen deprivation therapy was not routinely discontinued or changed for this study • 15 of 17 patients went on to receive additional hormone therapy after SABR
Kao *et al.* (2013)[69]	SABR	≤3 metastatic lesions	5	64[†]	N/A	40–60 Gy/10[†]	N/A	• Treatment was combined with sunitinib, confounding the side effect profile • No specific data for prostate cancer patients reported apart from overall survival

12 studi su RT

Sedi trattate: prevalentemente ossee e linfonodali (N regionali o a distanza / Osso /Polmone / fegato)

Dosi: 20 -54 – 60 Gy / in 1-3-5-10-25 Fr.

Spesso **ADT associata**

REVIEW ARTICLE *Asia-Pacific Journal of Clinical Oncology* 2014

Advances in local and ablative treatment of oligometastasis in prostate cancer

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Table 3 Continued

Article	Modality	Metastasis criteria	No. of CaP Patients (No. of lesions)	Median age	Sites of metastasis			Note
Muacevic *et al.* (2013)[30]	SABR	1–2 metastatic lesions	40 (64)	66	• P			• Surgical metastasectomy, chemotherapy, ADT and conventional EBRT were performed before SABR in 3, 8, 19 and 8 patients, respectively.
Jereczek-Fossa *et al.* (2012)[31]	SABR	Single abdominal lymph node	16			24 Gy/3†	N/A	• Concomitant ADT was used in 22 of 24 prostate cancer lesions
Jereczek-Fossa *et al.* (2012)[32]	SABR	Single recurrent canc lesion			-anastomosis ($n = 4$) • LN ($n = 18$) • Bone ($n = 1$)	Median 30 Gy/ 4.5	• RT ± ADT ($n = 20$) • RRP ± LND ± ADT ± RT ($n = 14$)	• Concomitant ADT was used in 21 lesions (18 patients) for a median of 16.6 months • Concurrent chemotherapy in 1 patient • 68% did not have any toxicity at all
Greco *et al.* (2011)[33]			64)	64†	N/A	18–24 Gy†	N/A	
Casamassima *et al.* (2011)[34]			25	63–68†	• Pelvic ± Para-aortic LN ($n = 22$) • Mediastinal LN ($n = 3$)	• SABR: 30 Gy/3 • EBRT + SABR: 50 Gy/25 to whole pelvis +24 Gy/3 to positive lymph nodes	• RP ($n = 28$) • RT ($n = 15$) • RP and RT ($n = 28$)	
Petrongari *et al.* (2011)[35]	SABR	Nodal recurrence	12	70	• LN ($n = 12$)	30 Gy/3 ($n = 10$) 35 Gy/5 ($n = 1$) 27 Gy/3 ($n = 1$)	• RP ($n = 7$) • RP and RT ($n = 2$) • RT ± ADT with salvage surgery ($n = 3$)	

Controllo locale 66-90% a 3 anni
Progression free survival 17-54.5% a 3 anni
Overall survival 54-92% a 3 anni

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SELEZIONE DEI PAZIENTI PER TERAPIE LOCALI AGGRESSIVE

- fewer comorbidities,
- longer life expectancy
- lower ECOG Group performance status.
- target lesion in a suitable location with a reasonable size
- Oligometastasis in parallel organ are more suitable (e.g. bone, lymph node, lung, liver)
- longer disease-free interval and single metastasis

Difficile definire sottogruppi di paz. oligometastatici con maggior indicazione a trattamenti locali aggressivi:

"…Radiotherapy remains the preferred treatment option in deep seated sites not amenable to surgery..."

REVIEW ARTICLE *Asia-Pacific Journal of Clinical Oncology* 2014

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"Oligo-recurrence" versus synchronous oligometastasis

In other cancer types, a long disease-free interval from the primary to evidence of metastatic disease has been reported to be a significant prognostic factor

Tabata *et al.* did not find a significant difference in the overall survival following targeted radiotherapy to metastatic lesions for oligo-recurrence versus oligometastasis group.

However, the study was small with only 18 patients in the oligo-recurrence arm and 17 in the oligometastasis arm

Androgen deprivation therapy

- Concomitant ADT was used in many of the studies
- Although ADTs have therapeutic benefits, they are also associated with side effects such as vasomotor flushing, fatigue, decrease in libido, erectile dysfunction, symptomatic anaemia, osteoporosis, fractures, insulin resistance, diabetes mellitus and dyslipidemia

Delay in the onset of ADT or prolongation of off-ADT duration, may provide a qualityof-life benefit for patients involved

Clin Genitourin Cancer. 2013 Mar;11(1):27-32. doi: 10.1016/j.clgc.2012.08.003. Epub 2012 Sep 24.

2013

Clinical Genitourinary Cancer

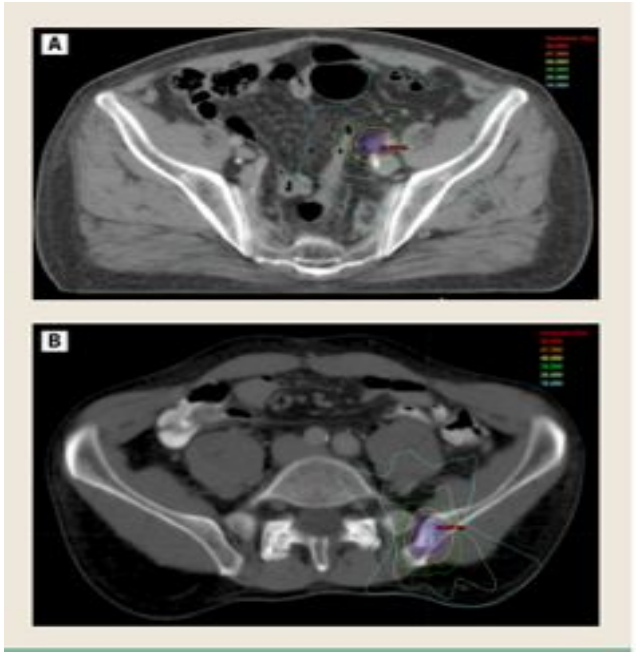
Salvage stereotactic body radiotherapy for patients with limited prostate cancer metastases: deferring androgen deprivation therapy.

Berkovic P[1], De Meerleer G, Delrue L, Lambert B, Fonteyne V, Lumen N, Decaestecker K, Villeirs G, Vuye P, Ost P

This is the first study reporting on the interesting end point of deferring systemic treatment (ADT)

At SBRT	
PSA (ng/mL)	
Median	6.59
Range	0.34-72.9
Age (years)	
Median	67
Range	54-78
Location of lesions, n (%)	
Bones	
Axial	18 (37)
Nonaxial	9 (18)
Lymph nodes	
Pelvic	15 (31)
Extrapelvic	7 (14)

29 lesions (node/bone mts) were treated in 24 patients



Limitations : small number of patients
lack of a control group undergoing active clinical surveillance
Concomitant single injection of 1-month LHRH-analogue shortly before SBRT

2013

Clin Genitourin Cancer. 2013 Mar;11(1):27-32. doi: 10.1016/j.clgc.2012.08.003. Epub 2012 Sep 24.

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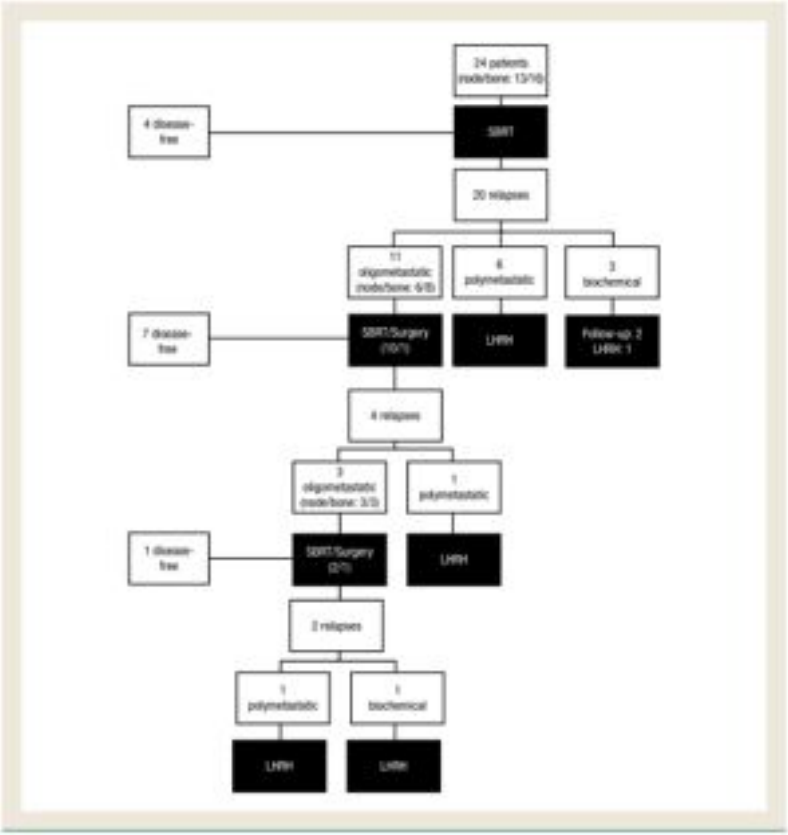
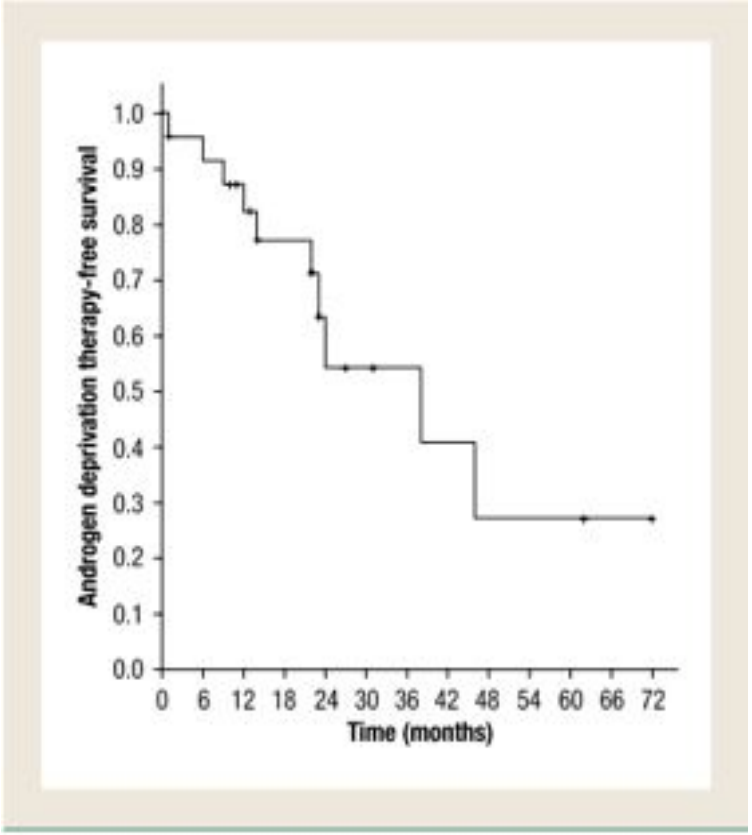




There were **no in-field recurrences**, resulting in a local control of 100%.

Median deferrement of palliative ADT = 38 months

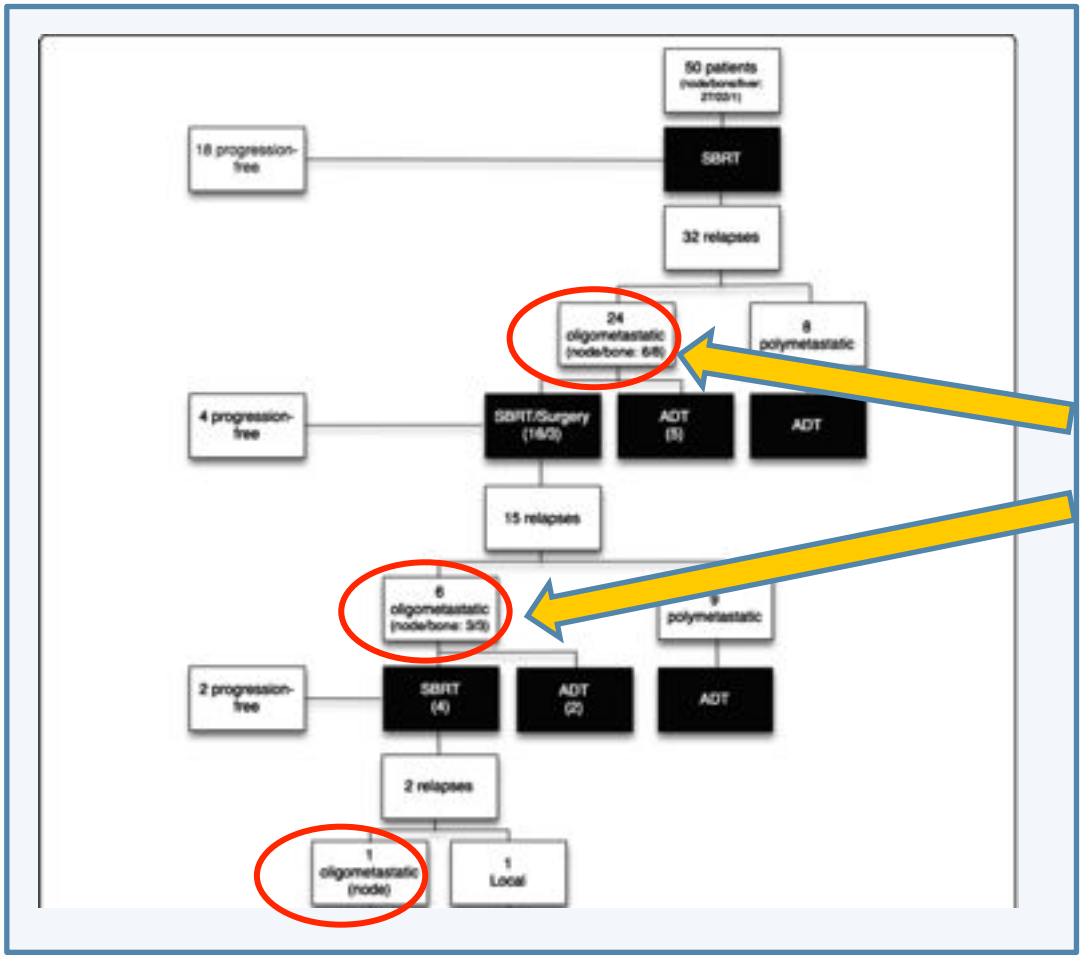
Radiat Oncol. 2014 Jun 12;9:135. doi: 10.1186/1748-717X-9-135.

2014

RADIATION ONCOLOGY

Repeated stereotactic body radiotherapy for oligometastatic prostate cancer recurrence.

Decaestecker K, De Meerleer G, Lambert B, Delrue L, Fonteyne V, Claeys T, De Vos F, Huysse W, Hautekiet A, Maes G, Ost P[1].



…. after SBRT most of **patients relapsed again as «oligometastatic»** with low volume prostatic cancer…..

Radiat Oncol. 2014 Jun 12;9:135. doi: 10.1186/1748-717X-9-135.

2014

RADIATION ONCOLOGY

Repeated stereotactic body radiotherapy for oligometastatic prostate cancer recurrence.

Decaestecker K, De Meerleer G, Lambert B, Delrue L, Fonteyne V, Claeys T, De Vos F, Huysse W, Hautekiet A, Maes G, Ost P[1].

Univariate Cox proportional hazards model predicting androgen deprivation therapy-free survival and progression-free survival

Covariate	ADT-FS		PFS	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Prognostic group at diagnosis				
Low-Intermediate	1	0.72	1	0.41
High	0.99 (0.36 – 2.74)		0.78 (0.33 – 1.88)	0.58
Very high	1.45 (0.48 – 4.4)		1.40 (0.56 – 3.53)	0.47
Interval from diagnosis to metastases (yr)	1 (0.99 – 1.01)	0.51	1 (0.99 – 1.01)	0.55
PSA level at time of metastases (ng/ml)	1 (0.97 – 1.03)	0.96	1 (0.98 – 1.03)	0.67
PSA DT at time of metastases (mo)	0.83 (0.71 – 0.97)	**0.02**	0.90 (0.82 – 0.99)	**0.04**
Number of lesions at diagnosis of metastases	1.11 (0.56 – 2.22)	0.75	1.02 (0.53 – 1.94)	0.96
Pattern of metastatic spread				
Minimal	1	0.37	1	0.27
Extensive	1.48 (0.63 – 3.49)		1.53 (0.72 – 3.2)	
Location of metastasis*				
Node	1	0.10	1	0.25
Bone	2.02 (0.87 – 4.72)		1.54 (0.74 – 3.27)	

Abbreviation: HR hazard ratio, CI confidence interval, yr year, mo month, ADT-FS androgen deprivation therapy-free survival, PFS progression-free survival.
The patient with liver metastasis was excluded from the analysis of this variable. P-values in bold represent significant values <0.05.

- SBRT for oligometastatic disease is accompanied with low toxicity and excellent local control (20% of patients remain progression free at 2–3 years after SBRT).
- **100% local control with out grade III toxicity**.

.... Con trend per risultati migliori su N e con malattia minima .....

Radiat Oncol. 2014 Jun 12;9:135. doi: 10.1186/1748-717X-9-135.

2014

RADIATION ONCOLOGY

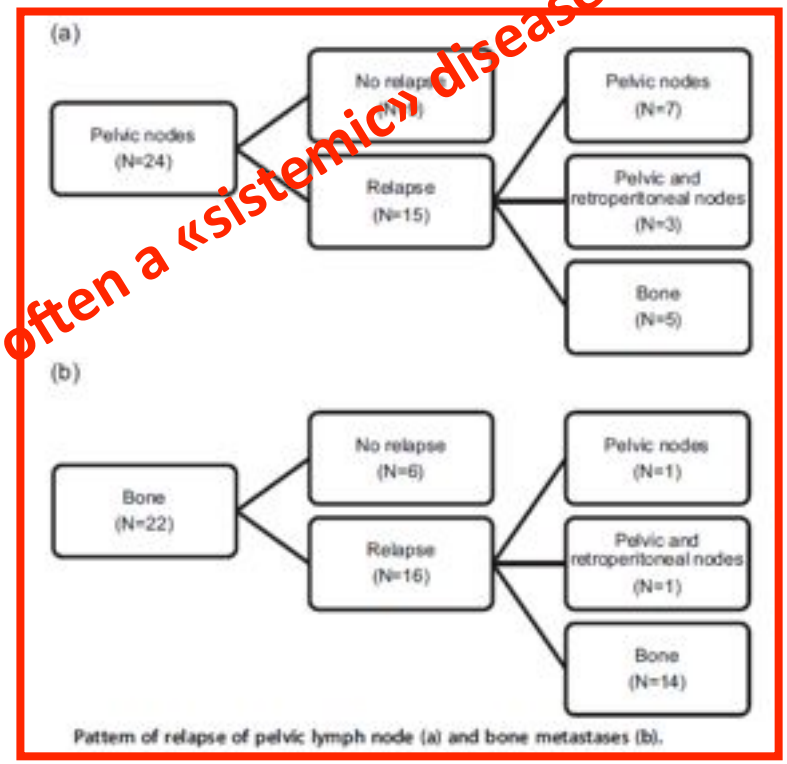
Repeated stereotactic body radiotherapy for oligometastatic prostate cancer recurrence.

Decaestecker K, De Meerleer G, Lambert B, Delrue L, Fonteyne V, Claeys T, De Vos F, Huysse W, Hautekiet A, Maes G, Ost P[1].

Number of lesions at diagnosis of metastases	
1 metastasis	37 (74%)
2 metastases	8 (16%)
3 metastases	6 (12%)
Primary site of metastases	
Lymph nodes	
Pelvic	24 (50%)
Obturator	1 (2%)
Internal iliac	6 (12%)
External iliac	10 (20%)
Presacral	2 (4%)
Common iliac	3 (6%)
Combination of nodal sites	2 (4%)
Extrapelvic	1 (2%)
Both	2 (4%)
Bones	
Axial	(16%)
Appendicular	11 (22%)
Both	3 (6%)
Viscera	
Liver	1 (2%)
Treatment at time of metastases (%)	
SBRT 10 × 5 Gy + 1 mo ADT	35 (70%)
SBRT 3 × 10 Gy	15 (30%)

Abbreviations: yr year, mo months, IQR interquartile range.

Bone meastasis are more often a «sistemic» disease



Pattern of relapse of pelvic lymph node (a) and bone metastases (b).

RT su localizzazioni ossee con RCST

CLINICAL INVESTIGATION **Metastasis**

PREDICTORS OF LOCAL CONTROL AFTER SINGLE-DOSE STEREOTACTIC IMAGE-GUIDED INTENSITY-MODULATED RADIOTHERAPY FOR EXTRACRANIAL METASTASES

CARLO GRECO, M.D.,* MICHAEL J. ZELEFSKY, M.D.,* MICHAEL LOVELOCK, PH.D.,† ZVI FUKS, M.D.,* MARGIE HUNT, M.S.,† KENNETH ROSENZWEIG, M.D.,* JOAN ZATCKY, B.S., N.P.,* BALEM KIM, B.A.,* AND YOSHIYA YAMADA, M.D.*

Departments of *Radiation Oncology and †Medical Physics, Memorial Sloan-Kettering Cancer Center, New York, NY

Int. J. Radiation Oncology Biol. Phys., Vol. 79, No. 4, pp. 1151–1157, 2011

Patient characteristics

All lesions (n = 124)	n
Gender	
Male	71
Female	32
Age (y), median (range)	4 (33–91)
Treatment site	
Bone	94
Lymph node	14
Lung	8
Liver	6
Other soft tissues	2
Histologic type	
Prostate	42
Renal cell	35
Colorect	15
Sarc	5
N cer	4
Cho	4
Breast	3
Melanom	3
Bladder	2
Leydig cell	2
Small-cell lung cancer	2
Thyroid cancer	2
Esophageal	1
Germ cell	1
Chordoma	1
Ovarian	1
Pancreatic	1

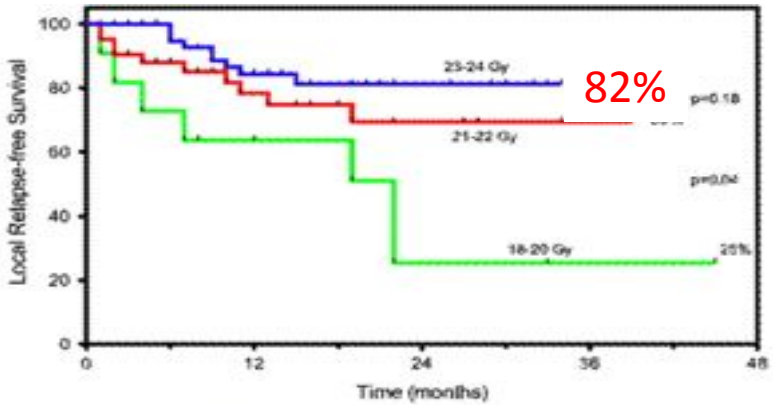
34 % localizzazioni da K prostata

Distribution by prescription dose (all lesions, n = 124)

Planning target volume dose (Gy)	n
18	10
20	2
21	3
22	38
23	1
24	70

Dose constraints :

- <12 Gy maximum to the spinal cord contour
- <=16 Gy to the bowel



Actuarial local control (Kaplan-Meir method) by dose level.
Y axis represents local relapse-free survival (%).

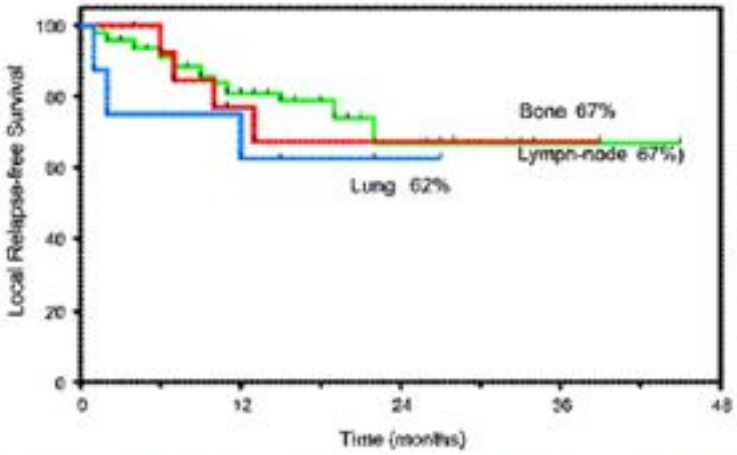
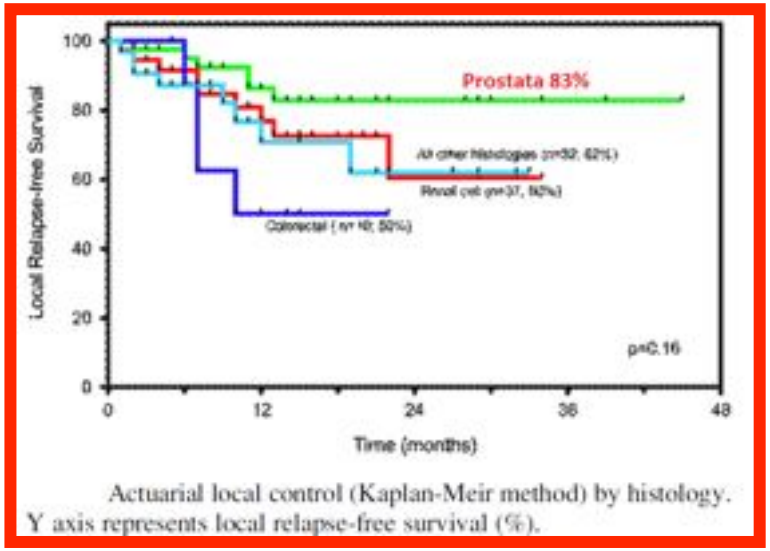


Fig. 5. Actuarial local control (Kaplan-Meir method) as a function of lesion location. Y axis represents local relapse-free survival (%; $p = 0.50$).



Actuarial local control (Kaplan-Meir method) by histology.
Y axis represents local relapse-free survival (%).

Multivariate analysis: prescription dose retained significance as a predictor of longterm LRFS (p = 0.003)

The overall incidence of Grade 3 late toxicity was <4%.

Migliori risultati :

per lesioni ossee da neoplasia prostatica e lesioni trattate a dosi elevate

Oligometastasi:
RT su N

RTT precauzionale su N pelvici per RT con intento radicale o RT post-prostatectomia

RTT di salvataggio dopo ripresa biochimica con RT precauzionale su linfonodi pelvici

RTT di salvataggio su N clinici

RTT di salvataggio dopo ripresa biochimica con RT precauzionale su linfonodi pelvici

Clinical Trials > Protocol Table > Study Details

RTOG 0534 Protocol Information

A Phase III Trial of Short Term Androgen Deprivation With Pelvic Lymph Node or Prostate Bed Only Radiotherapy (SPPORT) in Prostate Cancer Patients With a Rising PSA After Radical Prostatectomy

Protocol Documents

Protocol **Current Version Date:** 11/23/2011

SCHEMA (1/8/09) (3/24/10)

	SV Involvement		
	1. No		
S	2. Yes	**R**	**Arm 1: PBRT Alone**
T		**A**	PBRT 64.8-70.2 Gy
R	**Prostatectomy Gleason Score**	**N**	
A	1. Gleason ≤ 7	**D**	
T	2. Gleason 8-9	**O**	**Arm 2: PBRT + NC-STAD**
I		**M**	PBRT 64.8-70.2 Gy + NC-STAD for 4-6 months,
F	**Pre-Radiotherapy PSA**	**I**	beginning 2 months before RT
Y	1. PSA ≥ 0.1 and ≤ 1.0 ng/mL	**Z**	
	2. PSA > 1.0 and < 2.0ng/mL	**E**	
			Arm 3: PLNRT + PBRT + NC-STAD
	Pathology Stage		PLNRT to 45 Gy and PBRT to 64.8-70.2 Gy,
	1. pT2 and margin negative		NC-STAD for 4-6 months,
	2. All others		beginning 2 months before RT

SV = seminal vesicle; RT = radiotherapy; PBRT = prostate bed RT; PLNRT = pelvic lymph node RT; NC-STAD = neoadjuvant and concurrent short term androgen deprivation

NOTE: It is mandatory the treating physician determine the radiation therapy technique (3D-CRT vs. IMRT) to be used prior to the site registering the patient. See pre-registration requirements in Section 5.1. See details of radiation therapy and hormone therapy in Sections 6.0 and 7.0.

Accrual: 1694 pts /1764 (24/9/2014)

Dati previsti 2023?

Critical Reviews in Oncology/Hematology 90 (2014) 24–35

Salvage therapy of small volume prostate cancer nodal failures: A review of the literature

Published series of salvage external beam irradiation (EBRT) for lymph node metastases from prostate cancer.

Authors (year of publication) [reference]	Number of pts treated for LN relapse (the whole series)	Concomitant systemic therapy	EBRT technique	Re-irradiation	Treated volume	Median total dose/nr fraction (dose/fraction)	Median follow-up (months)	Local control rate ± pattern of failure	Overall survival	Toxicity
Engels et al. (2009) [75]	8 pts (28 pts)	ADT in all pts	Helical Tomotherapy	No	PTV1: prostate PTV2: positive LN regions PTV3: pelvic LN	SIB: PTV1:70.5 Gy/30fr PTV2: 60 Gy/30fr PTV3: 54 Gy/30fr (2.35–1.8-2 Gy/fr)	?	?	?	*Acute GI: G2 7%, G3 0% *Acute GU: G2 14% G3 4%
Alongi et al. (2010) [76]	1 (1)	Estramustine + ADT	Helical Tomotherapy	Yes	PTV 1: positive LN PTV 2: bilateral iliac LN	SIB: PTV1: 67.2 Gy/28fr PTV2: 50.4 Gy/28 fr (2.4–1.8 Gy/fr)	24	No local progression at 24 mos	Alive at 24 months	0
Ricchetti et al. (2011) [74]	1 (4)	ADT	Helical Tomotherapy	Yes	PTV 1: positive LN PTV 2: pelvic LN	SIB: PTV1: 60 Gy/30fr PTV2:46 Gy/30fr (2–1.53 Gy/fr)	12	No local progression at 12 mos but DM at 16 mos	Alive at 16 months	0
Jereczek-Fossa et al. (2009) [85]	14	ADT in 7 pts, CHT + ADT in 1 pt	SBRT: Linac 7pts – CBK 7 pts	Yes	PTV1: positive LN	30 Gy/3fr (10 Gy/fr)	18	No local progression, 2 pts with DM and 3 pts with LN relapse	1 pt died of cardiovascular reason	Acute: 0 Late GI G2 1 pt
Jereczek-Fossa et al. (2012) [84]	[b]16 (34)	ADT in 75% of pts	SBRT (CBK)	Yes	PTV1: positive LN	33 Gy/3 fr (11 Gy/fr)	22	No local progression, 5 pts with DM	All pts alive at 22 months	Acute GU: G3 1 pt Late GU: G1: 2pts, G2 1 pt, G3 1 pt Late GI G1 1 pt
Scorsetti et al. (2011) [79]	1 (12 LN and whole series: 95 pts)	No	SBRT (VMAT-RA)	No	PTV1: positive LN	45 Gy/6 fr (7.5 Gy/fr)	*12	Local control: 10/11 LN pts	NA	*Acute GI G1 3 pts/95pts *Late GI G1 1 pts/12 LN pts

Legend: pts – patients, ADT – androgen deprivation therapy, SBRT – stereotactic body radiotherapy, CBK – CyberKnife Robotic Radiosurgery System (Accuray Inc., Sunnyvale, CA), LN – lymph nodes, SIB – simultaneous integrated boost, fr – fraction,

* Data from the whole cohort of pts.

[b] Including updated information of 7 pts from previous series [84], PTV – planning target volume, CHT – chemotherapy, RA-VMAT – volumetric intensity modulated arc therapy delivered with RapidArc (Varian Medical Systems, Palo Alto, CA), NA – not available, GU – genitourinary, GI – gastrointestinal.

B. De Bari et Al.: Critical Reviews in Oncology/Hematology 90 (2014) 24–35

Critical Reviews in Oncology/Hematology 90 (2014) 24–35

Salvage therapy of small volume prostate cancer nodal failures: A review of the literature

Conclusions

- EBRT and SBRT represent promising non-invasive anatomically-targeted treatment for oligorecurrent prostate cancer;
- these therapies seem to offer excellent in-field tumor control with very good toxicity profile;
- data regarding large series and/or prospective studies still remain lacking also for EBRT and SBRT;

The optimal combination of high precision radiation therapy with systemic treatment remains to be investigated.

B. De Bari et Al.: Critical Reviews in Oncology/Hematology 90 (2014) 24–35

Quale RT ?

3D-CRT, IMRT/IGRT, SBRT

....quale RT ?

RapidArc

DAO

RT MODERNA

IMRT - IGRT - SBRT - ART

CyberKnife

Tomotherapy

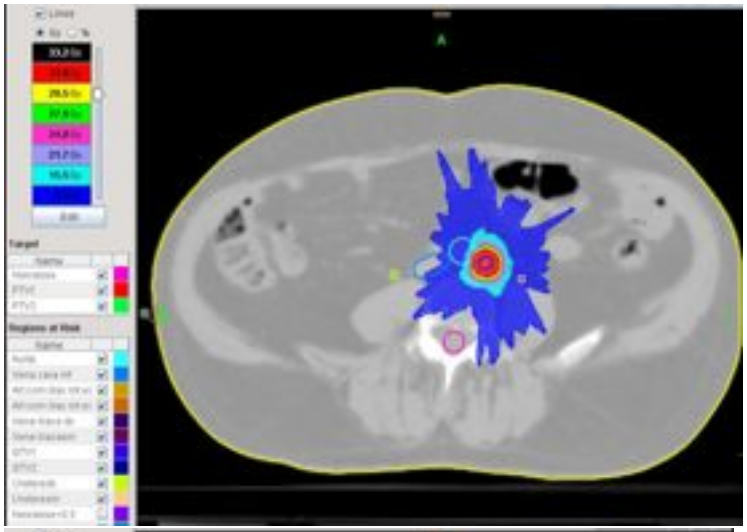
Vmat

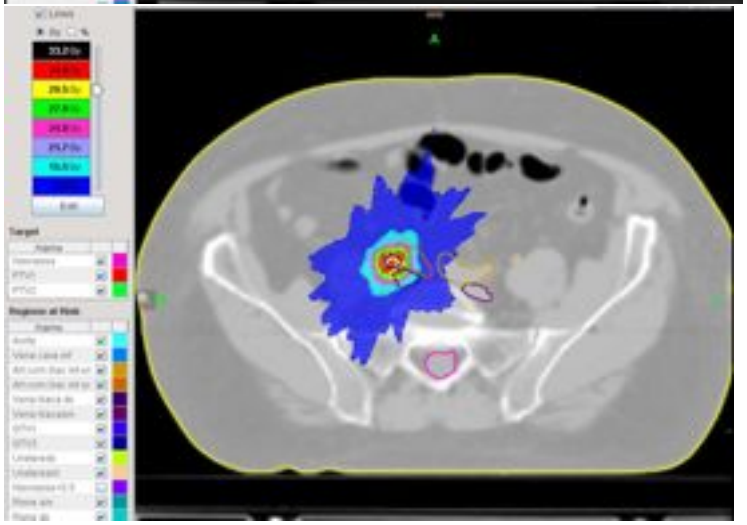
Tomotherapy

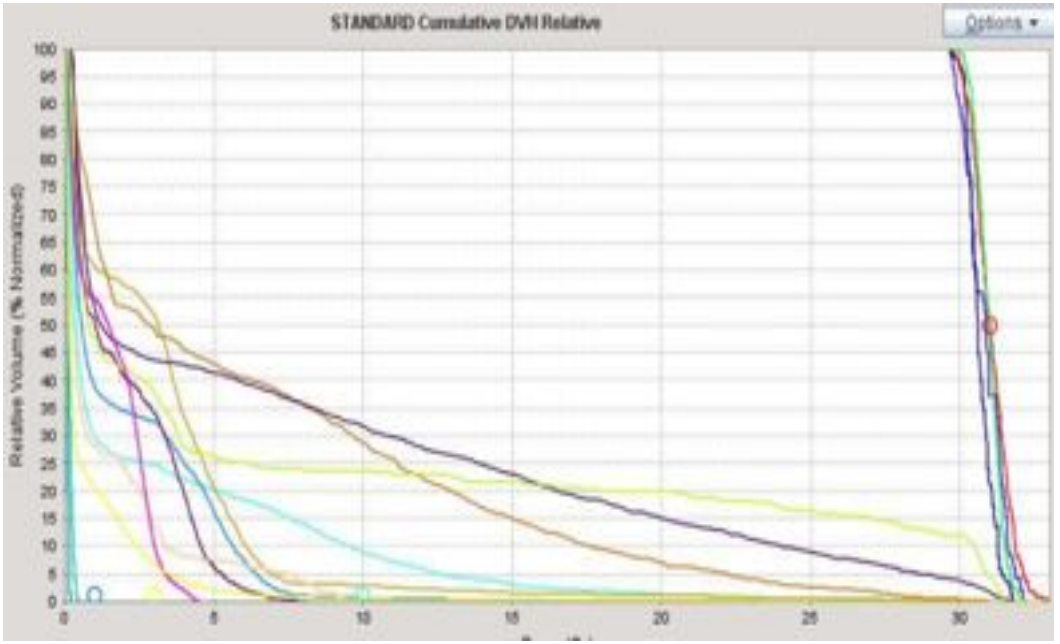
Oligometastasi Linfonodali da Adenoca prostatico (1 pelvica dx e 1 LA sin)

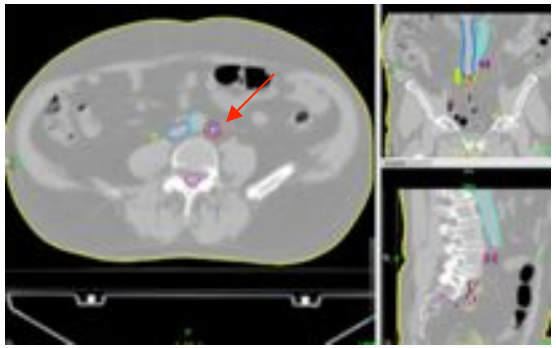
DT 30 Gy - 6Gy/die x 5 frazioni

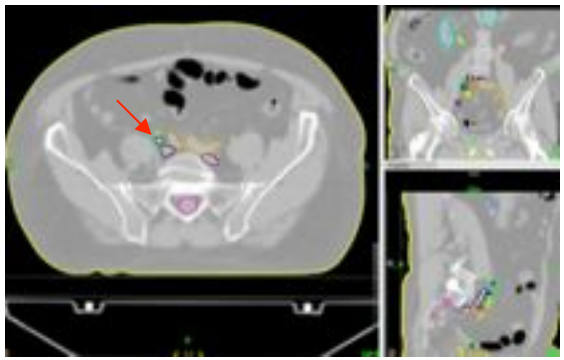
(equivalenti a circa 64 Gy con frazionamento standard di 2 Gy)











- La **radioterapia convenzionale** può essere utilizzata nel paziente oligometastatico ....ma la **radioterapia stereotassica ipofrazionata**, può offrire notevoli opportunità nelle le neoplasie prostatiche, caratterizzate da un basso α/β ratio (circa 1,5 Gy)

Arcangeli S et al : CritRevOncolHematol, 84: 101-108, 2012
Mirabell R, et al : Int J radiat oncol biol phys, 2012, 82: e17-e24, 2012

...dati già confermati da esperienze con RT di prima istanza in neoplasie intracapsulari organoconfinate.....

Costo su tariffe RER:

7500,00 → **3700,00 Euro** (All inclused)

....la più recente revisione sistematica...

Platinum Priority – Review – Prostate Cancer

Editorial by XXX on pp. x–y of this issue

Metastasis-directed Therapy of Regional and Distant Recurrences After Curative Treatment of Prostate Cancer: A Systematic Review of the Literature

Piet Ost [a,], Alberto Bossi [b], Karel Decaestecker [c], Gert De Meerleer [a], Gianluca Giannarini [d], R. Jeffrey Karnes [e], Mack Roach III [f], Alberto Briganti [g]*

....assunto da confermare....

"The oligometastatic state is considered an intermediate state of tumour spread with limited metastatic capacity"

Metastasis directed therapy such as surgery or stereotactic body radiotherapy **may be effective** in these patients

To obtain better clinical outcomes

To spare or to delay the toxicity of systemic therapies

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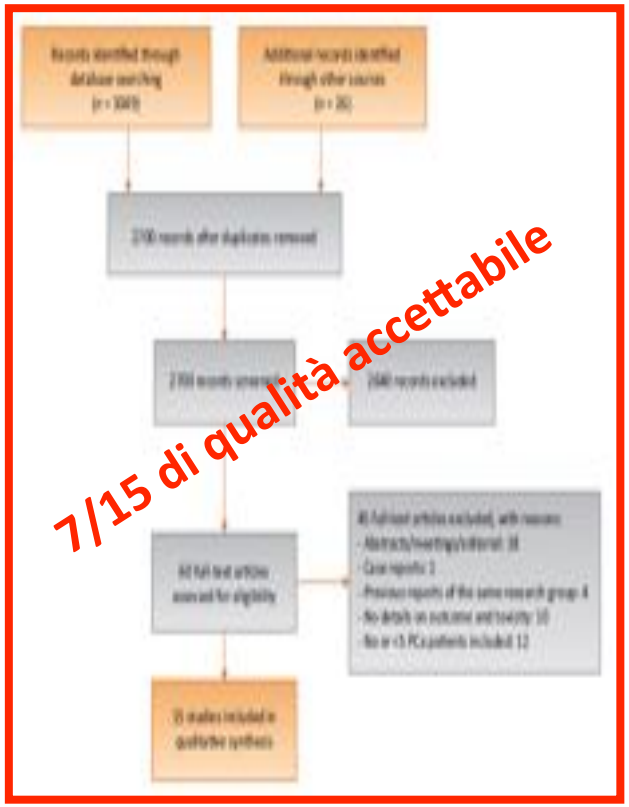
Evidence synthesis: Fifteen single-arm case series reporting on a total of 450 patients met the inclusion criteria. Seven studies were considered of acceptable quality. Oligometastatic PCa recurrence was diagnosed with positron emission tomography with coregistered computed tomography in most of the patients (98%). Nodal, bone, and visceral metastases were treated in 78%, 21%, and 1%, respectively. Patients were treated with either RT (66%) or lymph node dissection (LND) (34%). Adjuvant androgen deprivation was given in 61% of patients ($n = 275$). In the case of nodal metastases, prophylactic nodal irradiation was administered in 49% of patients ($n = 172$). Overall, 51% of patients were progression free 1–3 yr after salvage MDT, with most of them receiving adjuvant treatment. For RT, grade 2 toxicity was observed in 8.5% of patients, with one case of grade 3 toxicity. In the case of LND, 11% and 12% of grade 2 and grade 3 complications, respectively, were reported.

Conclusions: MDT is a promising approach for oligometastatic PCa recurrence, but the low level of evidence generated by small case series does not allow extrapolation to a standard of care.
Patient summary: We performed a systematic review to assess complications and outcomes of treating oligometastatic prostate cancer recurrence with surgery or radiotherapy. We concluded that although this approach is promising, it requires validation in randomised controlled trials.



Eur Urol (2014), http://dx.doi.org/10.1016/j.eururo.2014. 09.004

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15 Studi analizzati: 12 con => 15 pazienti (chirurgia o RT)

Diagnostica con PET/CT nel 98% dei casi (91% Colina; 7% FDG)

Table 1 – Full-text publications of metastasis-directed therapy for oligometastatic prostate cancer recurrence included in the systematic review

Study	No. of patients	Site of metastasis: node/bone/visceral	Median time to metastatic recurrence, mo	Median PSA at time of metastasis	Staging method	Type of MDT	Median follow-up, mo	Median PFS	Adjuvant ADT (%)	Median duration ADT	Prophylactic nodal radiotherapy (%)
Casamassima et al. [23]	25	25/0/0	11.8–36.7	5.65	Choline PET/CT	SBRT	29	24 mo	None	NA	7 (28)
Muacevic et al. [24]	40	0/40/0	NR	5.4	Choline PET/CT	SBRT	14*	NR	27 (68)	NR	NA
Würschmidt et al. [25]	15	15/0/0	NR	1.79	Choline PET/CT	NRT	28	Median not reached; 3-yr PFS: 75%	NR	NR	15 (100)
Ahmed et al. [26]	17	1/15/1	50.4	2.1	Choline PET/CT (n = 9), MRI (n = 5), CT (n = 3), bone biopsy (n = 1)	SBRT	6	12 mo	15 (88)	NR	NA
Jereczek-Fossa et al. [27]	19	18/1/0	66	1.77 (pelvic nodes) 10.7 (MET)	Choline PET/CT	SBRT	17	Median not reached; 30-mo PFS: 63.5%	19 (100)	12–17 mo	None
Schick et al. [28]	50	33/15/2	15.6	6.7	Choline PET/CT (n = 9), bone scintigraphy (n = 41)	SBRT (n = 14), NRT (n = 36)	31	Median not reached; 3-yr PFS: 58.6%	49 (98)	12 mo	25 (50)
Decaestecker et al. [29]	50	27/22/1	57.6	3.8	Choline (n = 18) or FACBC (n = 32) PET/CT	SBRT	25	19 mo	35 (70)	1 mo	None
Picchio et al. [30]	83	83/0/0	NR	2.6	Choline PET/CT	HRT	22	NR	58 (70)	NR	77 (93)
Rinnab et al. [31]	15	15/0/0	NR	1.98	Choline PET/CT	LND	13.7*	NR	11 (73)	NR	1 (7)
Schilling et al. [32]	10	10/0/0	NR	8.75	Choline PET/CT	LND	11*	NR	6 (60)	NR	None
Winter et al. [33]	6	6/0/0	NR	3.4	Choline PET/CT	LND	24 mo	NR	None	NA	None
Busch et al. [37]	6	6/0/0	Mean: 37.6*	37.6*	Choline (n = 3), MRI (n = 1), CT (n = 2)	LND	NR	15.5 mo	6 (100)	Lifelong ADT	None
Jilg et al. [34]	47	47/0/0	22	11.1*	Choline PET/CT	LND	35.5	27 mo**	34 (65)	NR	27 (52)
Martini et al. [35]	8	8/0/0	NR	1.62	Choline PET/CT	LND	NR	NR	None	NA	None
Suardi et al. [36]	59	59/0/0	NR	2.0	Choline PET/CT	LND	76.6	60 mo**	24 (41)	24 mo	21 (36)

ADT = androgen-deprivation therapy; CT = computed tomography; FDG = fluorodeoxyglucose; HRT = hypofractionated radiotherapy; LND = lymph node dissection; MDT = metastasis-directed therapy; MRI = magnetic resonance imaging; NA = not applicable; NR = not reported; NRT = normofractionated radiotherapy; PET/CT = positron emission tomography with coregistered computed tomography; PFS = progression-free survival; PSA = prostate-specific antigen; SBRT = stereotactic body radiotherapy.
* Mean numbers reported instead of median.
** Median estimated from curves.

Sede trattata :
Linfonodi 78% ; M1 ossee 21% ; viscerali 1% (2 polmone , 2 fegato)
Trattamento eseguito:
Chirurgia 151 paz. (34%) ; Alte dosi RT 299 paz. (66%)

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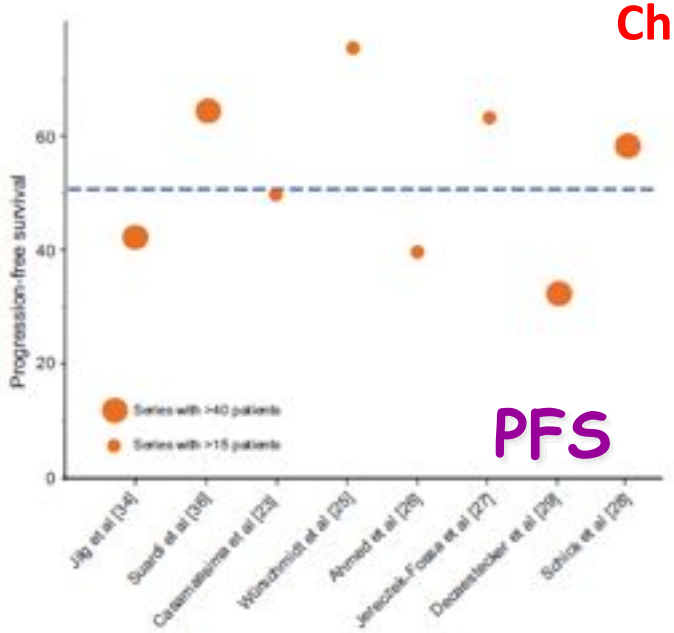
Chirurgia o RT



Altough treatment schedules varied and no comparative studies were available, the findings indicate *that approximately half of the patients were progression free 1–3 yr after MDT*

Controllo locale riportato in 11/12 studi su RT

Solo 4 ricadute locali / 114 paz. trattati

4%

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Radiotherapy

No G3 Toxicities neither GU nor GI

a.

Complication type	Muacevic et al. [24] (*n* = 40), no. (%)	Wurschmidt et al.* [25] (*n* = 15), no. (%)	Ahmed et al. [26] (*n* = 17), no. (%)	Jereczek-Fossa et al. [27] (*n* = 19), no. (%)	Decaestecker et al. [29] (*n* = 50), no. (%)	Total (*n* = 141), no. (%)
Grade 1						
Bone pain	0 (0)	0 (0)	0 (0)	0 (0)	3 (6)	3 (2)
Asymptomatic fracture	1 (2.5)	0 (0)	0 (0)	0 (0)	1 (2)	2 (1.4)
Fatigue	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	1 (0.7)
Rectal toxicity						2 (1.4)
Urinary toxicity						2 (1.4)
Grade 2						
Nausea requiring antiemetics						5 (3.5)
Rectal toxicity	0 (0)	2 (13.3)	0 (0)	1 (5)	2 (4)	5 (3.5)
Urinary toxicity	0 (0)	0 (0)	0 (0)	1 (5)	1 (2)	2 (1.4)
Grade 3						
Urinary toxicity	0 (0)	0 (0)	0 (0)	1 (5)	0 (0)	1 (0.7)

b.

Complication type	Rinnab et al. [31] (*n* = 15), no. (%)	Busch et al. [37] (*n* = 6), no. (%)	Jilg et al. [34] (*n* = 47), no. (%)	Suardi et al. [36] (*n* = 59), no. (%)	Total (*n* = 127), no. (%)
Grade 1					
Lymphorrhea	0 (0)	0 (0)	4 (7.7)	12 (20.3)	16 (12.5)
Fever	0 (0)	0 (0)	3 (5.8)	18 (30.5)	21 (16.5)
Temporary weakness of the hip flexor	0 (0)	0 (0)	1 (1.9)	0 (0)	1 (0.8)
Wound dehiscence	0 (0)	0 (0)	3 (5.8)	0 (0)	3 (2.3)
Grade 2					
Deep vein thrombosis	0 (0)	0 (0)	0 (0)	1 (1.7)	1 (0.8)
Ileus	1 (7)	0 (0)	0 (0)	12 (20.3)	13 (10.2)
Grade 3a					
Lymphocele requiring drainage	1 (7)	0 (0)	2 (3.9)	7 (11.2)	10 (7.8)
Wound dehiscence	0 (0)	0 (0)	0 (0)	3 (5.1)	3 (2.3)
Hydronephrosis requiring stenting	1 (7)	0 (0)	0 (0)	0 (0)	1 (0.8)
Grade 3b					
Lymphocele requiring surgical drainage	0 (0)	0 (0)	0 (0)	1 (1.7)	1 (0.8)

Surgery

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However, the rather random use of a multimodality approach with adjuvant ADT and prophylactic nodal irradiation in 61% and 49% of patients, respectively, makes it difficult to compare PFS between series

MDT is a promising approach for oligometastatic Pca recurrence.
However, due to the absence of comparative or randomised clinical trials, the overall low number of patients treated, the limited follow-up, the eterogeneity of patients treated, and the non standardised use of sequential treatments,
MDT should not be considered the standard of care.

ON GOING CLINICAL TRIALS

www.clinicaltrials.gov Mayo Clinic

Started in *2013*……

Monitoring Anti-Prostate Cancer Immunity Following SBRT

Observational Prospective

20 patients needed

Inclusion Criteria

Histologically proven diagnosis Oligometastatic Prostate Cancer
Prostate cancer pts with <4 metastatic lesions

AIMS

Induction of anti-prostate cancer immunity

ON GOING CLINICAL TRIALS

www.clinicaltrials.gov University of Florida

Started in *2013*……

Radiotherapy for Oligometastatic Prostate Cancer

Phase II non-RCT

48 patients needed

Inclusion Criteria

Metastatic cancer of the prostate
Pts may have received prior surgery, RT, ADT, immunotherapy, bone MTS directed Tx or CHT for PCa.

R

Stereotactic Body Radiation therapy

Hypofractionated Radiation therapy

AIMS

Median progression-free survival

(over historic control rates in hormone receptive and castration resistant subgroups)

ON GOING CLINICAL TRIALS

www.clinicaltrials.gov

Ghent University Hosp.

STOMP Study

Non-systemic Treatment for Patients With Low-Volume Metastatic Prostate Cancer

Phase II RCT

54 patients needed

.....Still On Going!!!!

Inclusion Criteria

Histologically proven diagnosis

- Biochemical relapse a following radical local prostate tx
- N1 and M1a/b disease on imaging, with a combined maximum of 3 synchronous lesions **(any organs, on choline PET-CT)** .
- Performance state 0-1
- Exclusion of local relapse

R

Conventional arm:
Active Surveillance

Experimental Arm
Salvage treatment of metastases
Surgical or RT treatment of metastases

AIMS

Androgen deprivation therapy free survival

STUDY PROTOCOL Open Access

Surveillance or metastasis-directed Therapy for OligoMetastatic Prostate cancer recurrence (STOMP): study protocol for a randomized phase II trial

Karel Decaestecker[1], Gert De Meerleer[2], Filip Ameye[3], Valerie Fonteyne[2], Bieke Lambert[4], Steven Joniau[5], Louke Delrue[6], Ignace Billiet[7], Wim Duthoy[8], Sarah Junius[9], Wouter Huysse[6], Nicolaas Lumen[1] and Piet Ost[2*]

BMC Cancer 2014, 14:671

-Primary endpoint:

- Androgen deprivation Free Surv

- Secondary endpoints:

- Quality of life
- Acute and late toxicity
- Time to castration-resistant disease
- Progression-free survival
  - ✓ PSA or biochemical progression
  - ✓ Local progression
  - ✓ Distant progression
- Prostate cancer specific survival
- Overall survival
- Time to first symptomatic event

Interventions

- **Arm A**: **Active clinical surveillance**, defined as 3-monthly clinical examination and serum PSA measurement. Restaging will be performed in case of symptomatic progression or PSA progression, ADT will be started at time of polymetastatic disease, local progression (defined above) or symptoms.
- **Arm B**: **SBRT or surgery** will depend on localization and size of the metastases, the nearby organs-at-risk and previous treatments in the vicinity of the metastases.

RT volumes

- **GTV**: all visible tumor by combining iconographic and metabolic information. No additional margin will be added for microscopic spread of disease
- The GTV will be expanded with 2-5 mm to the Planning Target Volume (**PTV**) to account for organ motion and setup error.

- Radiotherapy treatment planning and dose prescription:
  - IMRT (static or rotational)
  - Cone-beam CT (CBCT) at each fraction
  - A total dose of 30 Gy (80% of the maximal dose) will be delivered in 3 fractions and fractions will be separated >48 h and <96 h. Treatment will be prescribed to the periphery of the target (80% of the dose (=30 Gy), should cover 90% of the PTV).

CONCLUSION

The overall survival from targeted radiotherapy appears favorable at 3 years of follow-up.

- The present literature suggests removal or ablation of oligometastatic prostate cancer lesions in patients may provide good local control and delay commencement of ADT in selected pts.

  (No direct comparison between aggressive local therapy vs ADT is available)

At present, there remains **more evidence to support the use of radiotherapy** in the management of oligometastatic prostate cancer than surgery.

H HI Yao et al: *Asia-Pacific Journal of Clinical Oncology* 2014

CONCLUSION

- **There is inadequate evidence in the current literature to promote a widespread use of local and ablative treatment** for oligometastasis in prostate cancer outside the context of clinical trials (only a few small studies and case reports).
- The **genetic and biological basis of oligometastatic states** as different from poly-metastatic states also remains uncertain.

There is a clear need for more well-conducted prospective trials to determine the **role of aggressive-targeted local therapy** in oligometastatic prostate cancer, as well as research to **elucidate the genetic and biological rationale for treatment**.

H HI Yao et al: *Asia-Pacific Journal of Clinical Oncology* 2014

GRAZIE

Radiat Oncol. 2014 Jun 12;9:135. doi: 10.1186/1748-717X-9-135.

2014

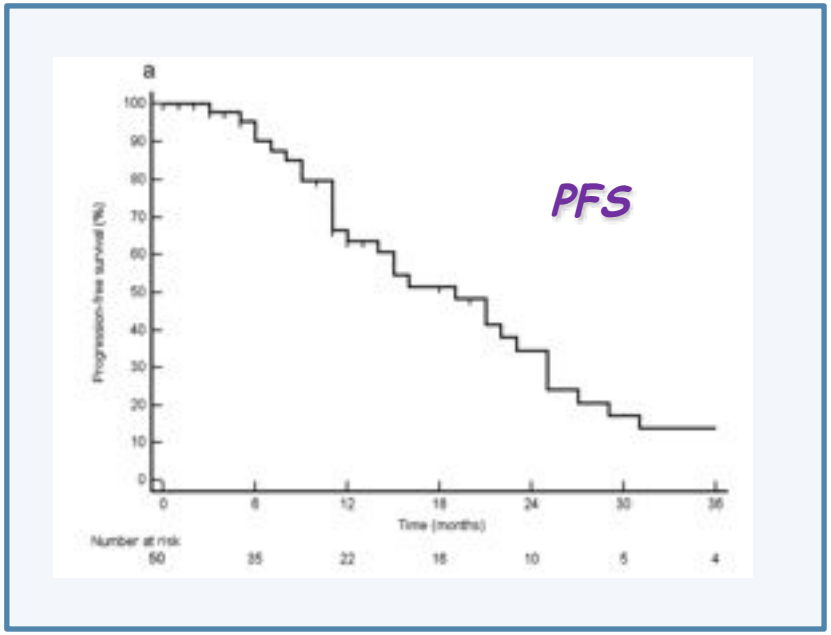
RADIATION ONCOLOGY

Repeated stereotactic body radiotherapy for oligometastatic prostate cancer recurrence.

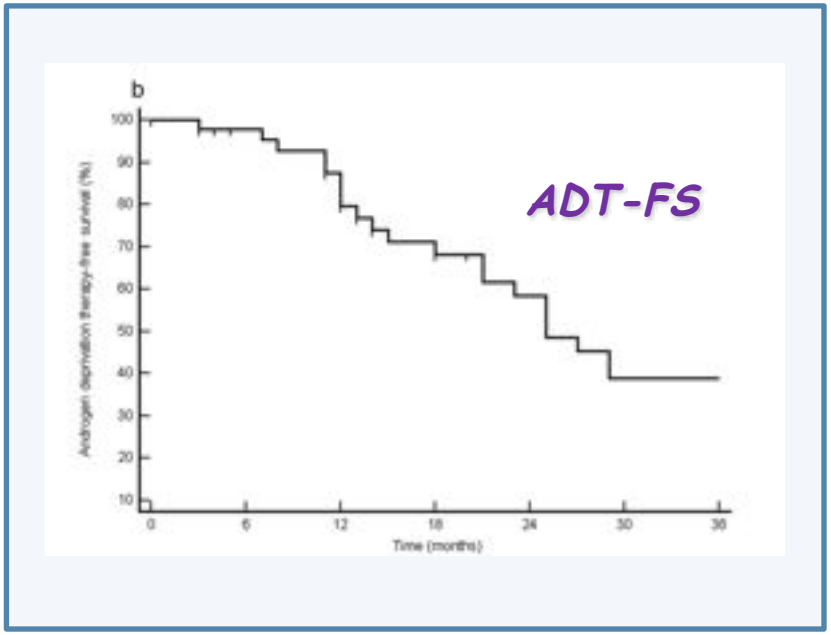
Decaestecker K, De Meerleer G, Lambert B, Delrue L, Fonteyne V, Claeys T, De Vos F, Huysse W, Hautekiet A, Maes G, Ost P[1].

50 pts diagnosed with **≤ 3 metachronous asymptomatic** metastases treated with SBRT

50 Gy in 10 fx to the PTV combined with a single injection of a short acting LHRH analogue or ***30 Gy in 3 fx*** without concomitant LHRH



Median PFS 19 months



Median ADT FS 25 months

Display Settings: Abstract

Int J Radiat Oncol Biol Phys. 2012 Feb 1;82(2):889-97. doi: 10.1016/j.ijrobp.2010.11.031. Epub 2011 Jan 27.

Robotic image-guided stereotactic radiotherapy, for isolated recurrent primary, lymph node or metastatic prostate cancer.

Jereczek-Fossa BA[1], Beltramo G, Fariselli L, Fodor C, Santoro L, Vavassori A, Zerini D, Gherardi F, Ascione C, Bossi-Zanetti I, Mauro R, Bregantin A, Bianchi LC, De Cobelli O, Orecchia R.

Table 2. Patient and CBK-SRT treatment characteristics (n = 34 patients/38 lesions)

Characteristics	P (n = 15)	A (n = 4)	LN (n = 16)	M (n = 3)	All lesions (n = 38)
Pre-CBK-SRT PSA	3.51 (1.69 – 22.9)	6.60 (0.47 – 10.11)	1.77 (0.22 – 15.50)	10.7 (0.30 – 38.3)	3.20 (0.22 – 38.3)
[11C]choline PET/CT before CBK-SRT					
Yes	13 (87%)	2 (50%)	16 (100%)	3 (100%)	34 (89%)
No	2 (13%)	2 (50%)	0	0	4 (11%)
Biopsy of target lesion					
Yes	15 (100%)	3 (75%)	1 (6%)	0	19 (50%)
No	0	1 (25%)	15 (94%)	3 (100%)	19 (50%)
Fiducial marker in target lesion					
Yes	14 (93%)	3 (75%)	9 (56%)	0	26 (68%)
No	1 (7%)	1 (75%)	7 (44%)	3 (100%)	12 (32%)
Localization in previous RT volume					
Yes	15 (100%)	4 (100%)	8 (50%)	0	27 (71%)
No	0	0	8 (50%)	3 (100%)	11 (29%)
Lymph node site (only LN group)					
External iliac			5 (31%)		
Internal iliac			0		
Common iliac			3 (19%)		
Pararectal			1 (6%)		
Obturator			7 (44%)		
Metastasis site (only M group)					
Retroperitoneal lymph node				2 (67%)	
Bone				1 (33%)	
ADT added to CBK-SRT					
Yes	5 (33%)	2 (50%)	12 (75%)	2 (67%)	21 (55%)
Type of ADT added to RT					
CAB	2	0	4	1	7
LHRH alone	2	2	2	1	7
Anti-androgen alone*	1	0	5	0	6
Other (dutasteride)	0	0	1	0	1
Median duration of ADT (range) (mo)	14.2 (3.1–117.3)	22.7 (11–34.4)	17.5 (7–155.3)	12.3 (6.8–17.9)	16.6 (3.1–155.8)
CBK-SRT data					
Median total dose (Gy)	30	30	33	36	30
Dose/fraction	6	6	11	12	7.5
No. of fractions	5	5	3	3	4.5

All patients completed the **CyberKnife SRT** as planned

38 lesions were treated
15 recurrent primary Pca
4 recurrent anastomosis
16 isolated pelvic lymph nodes
3 isolated metastatic lesions

Median dose was 30 Gy in 4.5 fractions

Display Settings: Abstract

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Int J Radiat Oncol Biol Phys. 2012 Feb 1;82(2):889-97. doi: 10.1016/j.ijrobp.2010.11.031. Epub 2011 Jan 27.

Robotic image-guided stereotactic radiotherapy, for isolated recurrent primary, lymph node or metastatic prostate cancer.

Jereczek-Fossa BA[1], Beltramo G, Fariselli L, Fodor C, Santoro L, Vavassori A, Zerini D, Gherardi F, Ascione C, Bossi-Zanetti I, Mauro R, Bregantin A, Bianchi LC, De Cobelli O, Orecchia R.

Acute toxicity of CBK-SRT (for all lesions)					
All urinary toxicity*	5 (33%)	1 (25%)	1 (6%)	0	7 (18%)
Grade 1	2 (13%)	1 (25%)	0	0	3 (8%)
Grade 2	2 (13%)	0	0	0	2 (5%)
Grade 3	1 (7%)	0	1 (6%)	0	2 (5%)
All rectal toxicity					
Grade 1	0	1 (25%)	0	0	1 (3%)
Late toxicity of CBK-SRT (for all patients)					
All urinary toxicity*	3 (20%)	0	4 (30%)†	0	7 (21%)†
Grade 1	1 (7%)	0	2 (15%)	0	3 (9%)
Grade 2	1 (7%)	0	1 (8%)	0	2 (6%)
Grade 3	1 (7%)	0	1 (8%)	0	2 (6%)
All rectal toxicity	0	1 (25%)	1 (8%)†	0	2 (6%)†
Grade 1	0	0	1 (8%)	0	1 (3%)
Grade 2	0	1 (25%)	0	0	1 (3%)
Follow-up duration [median (range)] (mo)	9.5 (3 – 28.9)	23 (3.9 – 30.6)	21.9 (4.3 – 35.4)	13.7 (3.9 – 20.2)	16.9 (3 – 35.4)
Response to CBK-SRT (all lesions)					
Radiologic and/or [11C] choline PET/CT					
Evaluable	2 (13%)	1 (25%)	11 (69%)	1 (33%)	15 (39%)
Complete response	1 (7%)	1 (25%)	10 (62.5%)	0	12 (32%)
Partial response	0	0	0	1 (33%)	1 (3%)
Stable disease	1 (7%)	0	1 (6%)	0	2 (5%)
Progression	0	0	0	0	0
Biochemical response to CBK-SRT in lesions treated with CBK-SRT only, with no neoadjuvant and/or concomitant systemic therapy					
n	9 (60%)	2 (50%)	4 (25%)	1 (33%)	16 (42%)
Complete response (substantial PSA reduction)‡	6 (67%)	1 (50%)	2 (50%)	–	9 (56.25%)
Partial response (partial PSA reduction)‡	2 (22%)	–	1 (25%)	1 (100%)	4 (25%)
Stable PSA	1 (11%)	–	1 (25%)	–	2 (12.5%)
Progression‡	–	1 (50%)	–	–	1 (6.25%)
Disease progression	5/15 (33%)	2/4 (50%)	5/16 (31%)	2/3 (67%)	14/38 (37%)
Site of progression					
In CBK-SRT field	1 (7%)	2 (50%)†	0	0	3 (8%)
Out of CBK-SRT field	4 (27%)	1 (25%)	5 (31%)	1 (33%)	11 (29%)
Biochemical only	0	0	0	1 (33%)	1 (3%)
PFS					
30-mo PFS (%) (95% CI)	22.2 (0–58.2)	33.0 (0–68.7)	63.5 (36.6–90.3)	0 (—)	42.6 (21.6–63.7)
Median PFS (95% CI) (mo)	13 (10, >30)	14 (10, >30)	>30 (—)	11 (6–16)	17 (13, >30)

All treatments for metastatic lesions (100%) were free of late toxicity, as were 13 of 16 lymph node treatments (81%), 10 of 15 treatments for prostate recurrence (67%), and 2 of 4 anastomosis treatments (50%).

A biochemical response was observed in 32 of 38 evaluable lesions (84%).

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Stereotactic radiotherapy for isolated nodal recurrence of prostate cancer.

2014

Detti B[1], Bonomo P, Masi L, Doro R, Cipressi S, Iermano C, Bonucci I, Franceschini D, Di Brina L, Bakhi M, Simontacchi G, Meattini I, Livi L

Abstract

PURPOSE: To report a clinical experience in stereotactic body radiation therapy (SBRT) for isolated nodal metastases from prostate cancer.

MATERIALS AND METHODS: Between November 2011 and December 2013, 30 patients (39 lesions) were treated with SBRT, delivered using Cyberknife, for recurrent prostate cancer with isolated nodal metastases. Prescribed doses and schedules of fractionation varied, ranging from 24 Gy in 1 fraction to 36 Gy in 3 fractions. Most commonly used schedules were 30 Gy in 3 fractions and 27 Gy in 3 fractions on alternating days. Biochemical response, acute and late toxicity were analyzed.

RESULTS: At a median follow-up of 12 months (range 2-24.9) [illegible] 4 cases, while PSA was stable in 1 case and raised in 9 cases. At the time of analysis [illegible] disease; 12 patients experienced a relapse of disease in other sites. Sixteen [illegible] evaluation 3 months after treatment was available. No in-field recurrence was detected [illegible] G2 acute genitourinary toxicity. Late toxicity was evaluated in patients with more than 6 months [illegible] proctitis. We did not observe any acute or late severe toxicity (≥G3).

CONCLUSIONS: Our experience suggests that SBRT for isolated nodal relapse from prostate cancer is a safe treatment, with promising results in terms of efficacy.

30 – 36Gy in 3 frazioni
FU mediano 12 mesi
Riduzione del PSA in 24/34 pazienti