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ARTE

L'arte (altra possibile declinazione del termine "ART") è il metodo di approccio al paziente, in quanto è il veicolo più immediato ed empatico per parlare al cuore della persona malata. La bellezza dell'arte come linguaggio universale consente di far sentire il paziente accolto, rassicurato e partecipe di un percorso non facile della sua vita. Il sentimento di eternità ed infinito trasmesso dalla bellezza artistica permette al paziente di immergersi in un contesto che rompe gli schemi dell'ambiente ospedaliero e predispone all'accettazione del percorso di cura attraverso un complessivo miglioramento del benessere psicofisico.

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ARTE

Le due sale di terapia rappresentano il cuore di tutto il progetto, ognuna delle quali ospita un paesaggio ispirato al familiare territorio pugliese, colto in ore e stagioni diverse: uno in pieno sole d'estate, l'altro in primavera all'alba. In ogni paesaggio si raccontano piccole storie: una fanciulla il cui abito mosso dal vento disperde fiori

che vanno a posarsi sui prati e una funambola che, guidata da un palloncino a forma di luna, percorre una fune che unisce due paesi immaginari. Sono storie semplicissime, ma che danno movimento all'immagine e possono costruire un legame positivo con quel luogo, mostrando giorno dopo giorno un dettaglio o un particolare da scoprire, come piccole ancore di salvezza.

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La Radioterapia nella malattia oligometastatica
Alba Fiorentino

Background

Results

Conclusions

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MIULLI art
Advanced Radiation Therapy

La Radioterapia nella malattia oligometastatica
Alba Fiorentino

Background

Results

Conclusions

Background

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Oligometastatic Disease
WHERE ARE WE?

EDITORIAL

Oligometastases

CANCER TREATMENT is based on an often unstated paradigm of disease pathogenesis. Since 1894, when W.S. Halsted[1,2] 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 orderly, extending in a contiguous fashion from the primary tumor through the lymphatics to the lymph nodes and then to distant sites. Radical en-
as radical neck dissection is continu-
the primary tumor, radical hysterectom
regional irradiation for a variety of
based on this notion of cancer spre
another hypothesis has gained promin
greatest with regard to breast cancer.
pothesis proposes that clinically appa
temic disease. Small tumors a
manifestation of such systemic dise
to metastasize, has already metastas
involvement is not orderly contiguous extension, but
rather a marker of distant disease. Systemic metastases
are multiple and widespread, and when subclinical are
referred to as micrometastases. Under these circum-
stances, treatment of local or regional disease should not
affect survival.

more about the multistep nature of the development of malignancy.[3-5] Once tumors become invasive, they may gradually acquire the properties necessary for efficient and widespread metastatic spread.[6] Therefore the likelihood, number, and even sites of metastases may reflect the state of tumor development. This suggests that there are tumor states intermediate between purely localized lesions and those widely metastatic. Such clinical circumstances are not accounted for by either the contiguous
or concomitant these metastases to a single or a limited number of organs. The likelihood of the oligometastatic state *should* correlate with the biology of tumor progression, rough clinical surrogates of which, for many tumors, might be primary tumor size and grade. Metastasizing cells may seed specific organs as a function of the seeding

An oligometastatic state is an "**intermediate state between purely localized lesions and those widely metastatic**". The state was expounded to be "**amenable to a curative therapeutic strategy**" and "**amenable to localized therapy**".

Hellman S, Weichselbaum RR. JCO 1995

Solitary or few detectable metastatic lesions that are usually confined to a single organ and may be more than one organ

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Oligometastatic Disease
WHERE ARE WE?

Journal of Clinical Oncology
An American Society of Clinical Oncology Journal

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1995

Oligometastases.

S Hellman , R R Weichselbaum
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https://doi.org/10.1200/JCO.1995.13.1.8

Hellman created heaven for patients and doctors

EDITORIAL

Oligometastases

CANCER TREATMENT is based on an often unstated paradigm of disease pathogenesis. Since 1894, when W.S. Halsted[1,2] clearly elucidated a mechanism of breast cancer spread and used it to design and support the radical mastectomy, surgical and radiothera-

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Background

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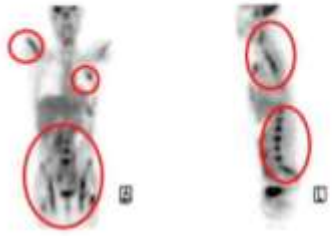
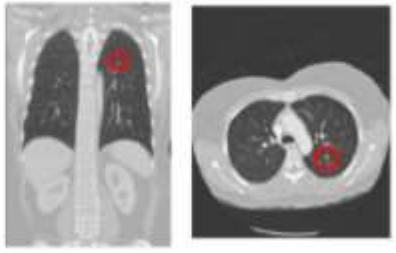
Oligometastatic Disease
WHERE ARE WE?

1. Improved imaging (role of **PET-CT/FDG**)
2. Increased availability of **locoregional treatments** (radiofrequency, stereotactic radiotherapy,vertebroplasty,minimally invasive surgery)
3. Availability of more efficacious systemic treatments (targeted therapies for oncogene addicted NSCLC, immunotherapy)
4. Multidisciplinary approach

Widely Metastatic Disease



Limited Metastatic Disease



- Distinct clinical state
- Metastases limited in number and site (3 to 5 in 1-3 sites)
- More indolent biology
- Amenable to local ablative approaches

Background

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Definition of oligometastatic state

Oligometastatic state includes different clinical situations

- Oligometastasis
  - –Synchronous oligometastasis
  - –Metachronus oligometastasis
- Oligopersistance
- Oligorecurrence
- Oligoprogressive

Background

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I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica
Alba Fiorentino

Prevalence of OMBC

Table 1. Frequency of Patients Enrolled on First-Line Metastatic Breast Cancer Trials With a Limited Number of Metastatic Sites Who Appear Potentially Eligible for Ablative Therapy

First Author	Phase	n	ER/PR + (%)	HER2+	≤ 2 Met sites (%)	≤ 4 Met Sites (%)	Arms	PFS (mo)
Albain 2008[54]	II	599	32	—	57	91	1. Gem + Paclitaxel	9.89
							2. Paclitaxel	8.4
Bergh 2012[55]	III	593	72	Pos	52	—	1 Sunitinib+ Docetaxel	8.6
							2. Docetaxel	8.3
Tawfik 2013[56]	II	30	77	Neg	50	—	1. Vinorelbine, capecitabine	8.6*
Hurvitz 2013[57]	IIR	137	54	Pos	49.3	—	1. Trastuz + Docetaxel	9.2
							2. T-DM1	14.2
Gianni 2013[58]	III AVEREL	424	51	Pos	50	—	1. Docetaxel+ Trastuz	13.7
							2. Docet + Tras + BEV	16.5
Sledge 2003[59]	III E1193	739	45	—	49	—	1. Doxorubicin	6*
							2. Paclitaxel	6.3*
							3. Doxorubicin + Paclitaxel	8.2*

* Time to failure.
Abbreviations: ER/PR, estrogen receptor/progesterone receptor; met sites, metastatic sites; PFS, progression-free survival; Pos, positive; Neg, negative; Gem, gemcitabine; T-DM1, trastuzumab emtansine; Docet, docetaxel; Tras, trastuzumab; BEV, bevacizumab.

«**49 – 57 %** of metastatic breast cancer patients enrolled on major phase II and phase III clinical trials of systemic therapy have **2 or fewer** clinically detected **metastases**»

Salama JK, Chmura SJ. The role of Surgery and ablative radiotherapy in oligometastatic breast cancer. Seminars in Oncology 2014; 41 (6): 790-797

Background

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I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

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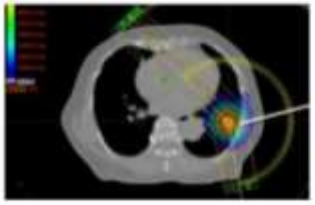
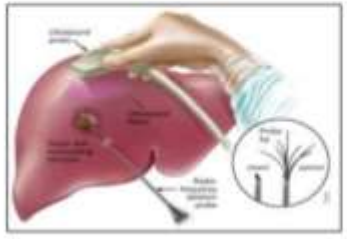
Local ablative therapies

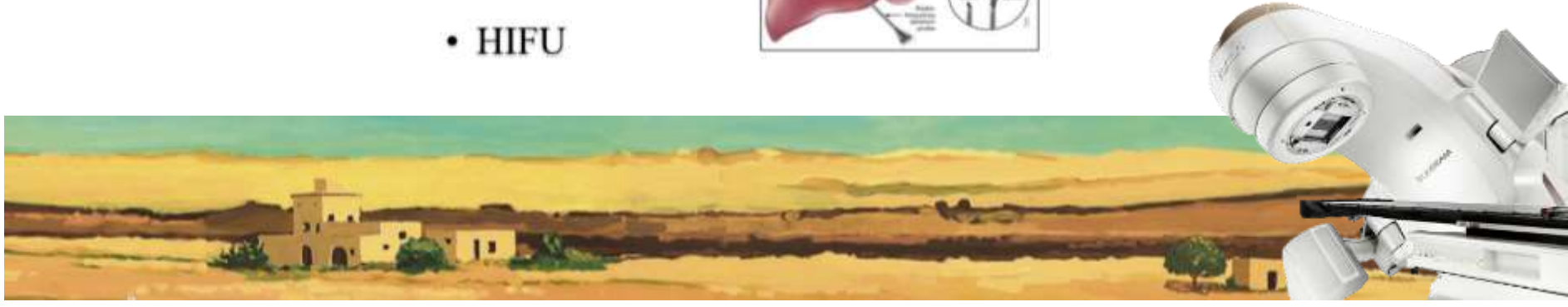
- Surgery

- SBRT



- MWA
- RFA
- HIFU





Background

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I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica
Alba Fiorentino

Surgery

Bartlett EK Cancer 2015

Of the 5 most common cancer types, **colorectal cancer** has been the subject of the largest number of studies of metastasectomy with demonstrated **5-year survival rates of >50%, and 10-year survival ranging from 17% to 36%.**

The role of metastasectomy in **other cancer types remains more controversial**. Multiple metastasectomy series have now been published for **breast cancer, lung cancer, and melanoma**, all of which with relatively favorable survival in carefully selected patients, but the series are smaller and less frequently report long-term follow-up.

TABLE 1. National Estimates of Admissions for Metastasectomy by Cancer Type, 2000 Through 2011

	Colorectal Cancer		Lung Cancer		Breast Cancer		Melanoma	
	No.	95% CI	No.	95% CI	No.	95% CI	No.	95% CI
All admissions	87,407	(86,307-88,507)	58,245	(57,453-59,036)	26,271	(25,672-26,870)	20,298	(19,897-20,699)
Mean age (SE), y	62.2	0.10	61.4	0.10	56.8	0.17	58.1	0.22
Female sex	46.0%	(45.3%-46.8%)	45.8%	(44.9%-46.7%)	99.4%	(99.2%-99.6%)	33.6%	(32.2%-35.1%)
Liver metastasectomy	41,312	(40,500-42,125)	503	(405-601)	1663	(1486-1839)	550	(448-652)
Lung metastasectomy	19,590	(18,994-20,185)	NA[a]	NA[a]	6609	(6266-6951)	5839	(5534-6144)
Brain metastasectomy	5588	(5263-5912)	52,944	(52,167-53,720)	16,091	(15,591-16,590)	11,094	(10,718-11,471)
Small bowel metastasectomy	20,916	(20,303-21,529)	2762	(2535-2988)	1724	(1544-1905)	2440	(2233-2646)
Adrenal metastasectomy	599	(493-705)	2067	(1870-2264)	230	(165-295)	471	(377-566)
Mean no. of Elixhauser comorbidities	1.98	(1.96-2.00)	2.72	(2.69-2.75)	1.87	(1.83-1.91)	1.84	(1.80-1.88)
Inpatient mortality rate	2.13%	(1.91%-2.34%)	3.18%	(2.86%-3.51%)	1.91%	(1.54%-2.28%)	1.65%	(1.26%-2.04%)

Background

WHY SBRT FOR OLIGO?

- Ablative dose
- Better technology
- No delay in Systemic therapy
- Good number of studies
- High dose per fraction SBRT appears to be mediated through pathways beyond DNA damage and may enhance immune surveillance of tumors

Metastasectomy increases local control with significant improvement of survival in selected patients

Most patients are inoperable for comorbidities or sites of metastases

Background

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I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

Alba Fiorentino

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- High dose per fraction SBRT appears to be mediated through pathways beyond DNA damage and may enhance immune surveillance of tumors

SBRT INDUCES IMMUNOGENIC REACTION
THAT IS NOT SEEN IN CONVENTIONAL FRACTIONATION.

VERY HIGH DOSE CAUSES MASSIVE DAMAGE OF CANCER CELLS
THAT LEADS TO MASSIVE RELEASE OF ANTIGENS BY CANCER CELLS.

RELEASED MASSIVE ANTIGENS LEADS TO 'T' CELL SENSITIZATION
EFFECTOR T CELLS KILL TUMOR CELLS AFTER RECOGNITION.

INCREASE IN T-CELL PRIMING IN DRAINING LYMPH NODES
LEADING TO ERADICATION OF THE PRIMARY & METASTATIC TUMORS.

WAYS TO ENHANCE IMMUNO-STIMULATORY EFFECTS OF RADIATION
COMBINATION WITH IMMUNODRUGS ARE UNDER INVESTIGATION.

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La Radioterapia nella malattia oligometastatica
Alba Fiorentino

Background

Results

Conclusions

Results

2019 CARCINOMA MAMMARIO

I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

Alba Fiorentino

Local ablative therapies

- Selection of patients
- SBRT in OMBC: clinical results

Results

2019 CARCINOMA MAMMARIO

I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

Alba Fiorentino

Local ablative therapies

- Selection of patients

Imaging

Genetic

Clinic

Results

2019 CARCINOMA MAMMARIO

I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

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Local ablative therapies

- Selection of patients

EJC 2017

Strategies and technical challenges for imaging oligometastatic disease: Recommendations from the European Organisation for Research and Treatment of Cancer imaging group

deSouza NM et al

	disease	surveillance imaging at follow-up		abdomen CT	without contrast FDG-PET/CT can be used to	PET/MRI if available
Breast	New primary	Node positive at presentation, high-risk	Lymph, nodes, liver, bone,	Chest and abdomen CT Bone scan	Chest, abdomen±: pelvic CT with contrast	Conventional staging imaging per routine practice

^{18}F-FDG PET/CT is favoured in breast cancer (with WB-MRI as an alternative) but needs supplementing with liver-specific MRI

Brain imaging (MRI) is only warranted in the presence of extra-cranial disease or in patients with neurological symptoms

biopsy if possible

Results

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I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

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Local ablative therapies

- Selection of patients

OPEN ACCESS Freely available online 2011 PLoS one

MicroRNA Expression Characterizes Oligometastasis(es)

Yves A. Lussier[1,2,3,4*], H. Rosie Xing[1,2,5,6], Joseph K. Salama[8], Nikolai N. Khodarev[1,5], Yong Huang[1,3], Qingbei Zhang[3,6], Sajid A. Khan[7], Xinan Yang[3], Michael D. Hasselle[5], Thomas E. Darga[5], Renuka Malik[5], Hanli Fan[6], Samantha Perakis[5], Matthew Filippo[5], Kimberly Corbin[5], Younghee Lee[3], Mitchell C. Posner[7], Steven J. Chmura[5], Samuel Hellman[2,5], Ralph R. Weichselbaum[1,2,5*]

1 Comprehensive Cancer Center, University of Chicago, Chicago, Illinois, United States of America, 2 Ludwig Center for Metastasis Research, University of Chicago, Chicago, Illinois, United States of America, 3 Department of Medicine Center for Biomedical Informatics, University of Chicago, Chicago, Illinois, United States of America, 4 Institute for Genomics and Systems Biology, University of Chicago, Chicago, Illinois, United States of America, 5 Department of Radiation and Cellular Oncology, University of Chicago, Chicago, Illinois, United States of America, 6 Department of Pathology Committee on Cancer Biology, University of Chicago, Chicago, Illinois, United States of America, 7 Department of Surgery, University of Chicago, Chicago, Illinois, United States of America, 8 Department of Radiation Oncology Duke University Medical Center, Durham, North Carolina, United States of America

… we have identified **microRNA expression** features of a potential classifier that predict the distinct outcomes of metastatic patients who maintained stable oligometastatic disease from those who progressed to polymetastases.
We also provide biological confirmation for molecular differences, in this case the **microRNA regulation**, that underlie oligometastic to polymetastatic progression.

Results

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I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

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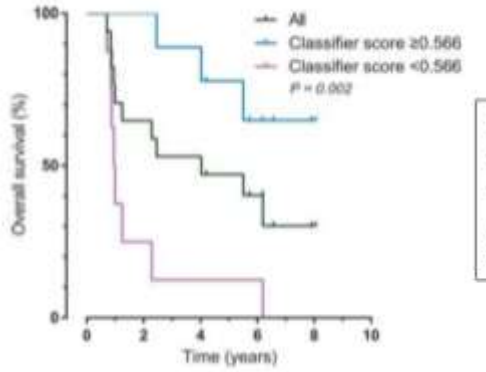
Local ablative therapies

- Selection of patients

Cancer 2016

Clinical and Molecular Markers of Long-Term Survival After Oligometastasis-Directed Stereotactic Body Radiotherapy (SBRT)

Wong AC, et al.



A candidate classifier using expression levels of 3 microRNAs (miR-23b, miR-449a, and miR-449b) predicted survival among 17 patients who had primary tumor microRNA expression data available

Results

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La Radioterapia nella malattia oligometastatica

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Local ablative therapies

- Selection of patients

Stereotactic body radiotherapy for oligometastases

Alison C Tree, Vincent S Khoo, Rosalind A Eeles, Marina Ahmed, David P Dearnaley, Maria A Hawkins, Robert A Huddart, Christopher M Nutting, Peter J Ostler, Nicholas J van As

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)

Results

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I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

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Local ablative therapies

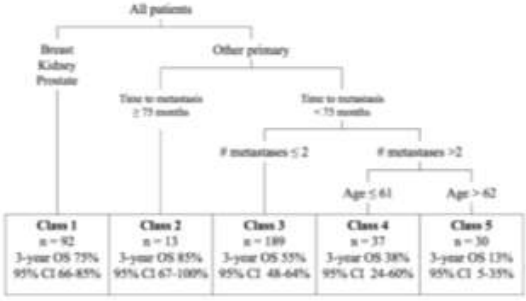
- Selection of patients

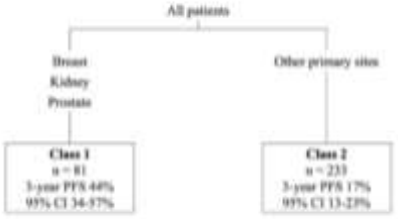
RESEARCH ARTICLE

Classification for long-term survival in oligometastatic patients treated with ablative radiotherapy: A multi-institutional pooled analysis

Julian C. Hong[1], Diandra N. Ayala-Peacock[2], Jason Lee[3], A. William Blackstock[4], Paul Okunieff[5], Max W. Sung[6], Ralph R. Weichselbaum[7], Johnny Kao[8], James J. Urbanic[9], Michael T. Milano[10], Steven J. Chmura[7]*, Joseph K. Salama[1]*

1 Department of Radiation Oncology, Duke University, Durham, NC, United States of America, **2** Department of Radiation Oncology, Vanderbilt University, Nashville, TN, United States of America, **3** Memorial & St. Elizabeth's Cancer Treatment Center, Swansea, IL, United States of America, **4** Department of Radiation Oncology, Wake Forest University, Winston-Salem, NC, United States of America, **5** Department of Radiation Oncology, University of Florida, Gainesville, FL, United States of America, **6** Division of Hematology and Medical Oncology, Mount Sinai School of Medicine, New York, NY, United States of America, **7** Department of Radiation and Cellular Oncology, University of Chicago, Chicago, IL, United States of America, **8** Department of Radiation Oncology, Good Samaritan Hospital Medical Center, West Islip, NY, United States of America, **9** Department of Radiation Medicine and Applied Sciences, University of California, San Diego, La Jolla, CA, United States of America, **10** Department of Radiation Oncology, University of Rochester Medical Center, Rochester, NY, United States of America





Results

2019 CARCINOMA MAMMARIO

I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

Alba Fiorentino

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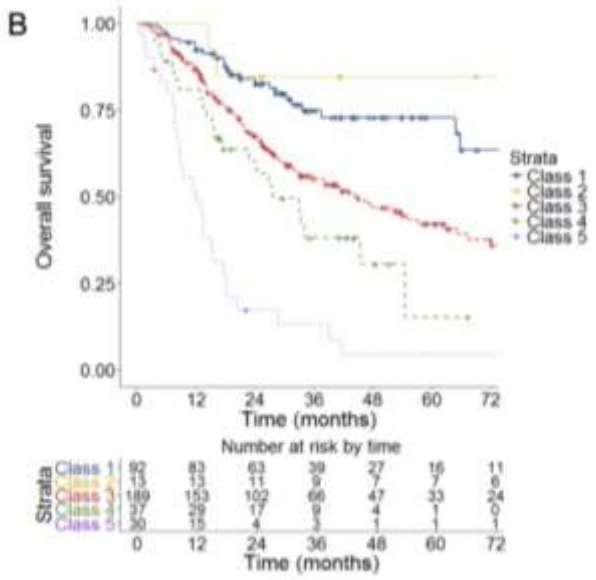

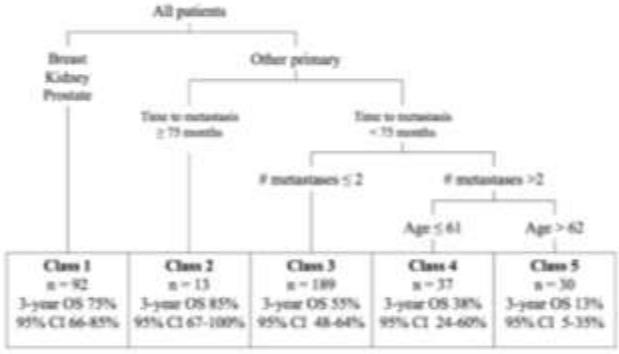

Results

2019 CARCINOMA MAMMARIO

I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

Alba Fiorentino

Local ablative therapies

- Selection of patients

RESEARCH ARTICLE

Classification for long-term survival in oligometastatic patients treated with ablative radiotherapy: A multi-institutional pooled analysis

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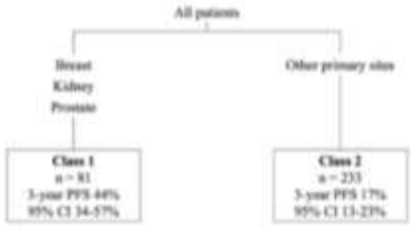

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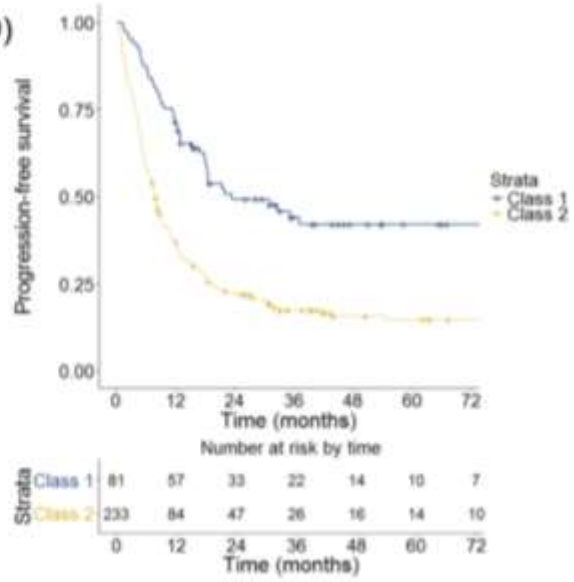


Results

2019 CARCINOMA MAMMARIO

I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

Alba Fiorentino

Local ablative therapies

- Selection of patients
- SBRT in OMBC: clinical results

Results

2019 CARCINOMA MAMMARIO

I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

Alba Fiorentino

Local ablative therapies

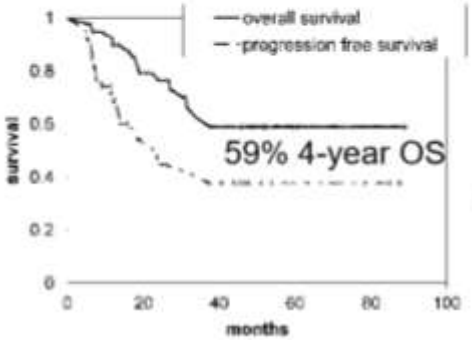
- SBRT in OMBC: clinical results

Breast Cancer Res Treat (2009) 115:601–608
DOI 10.1007/s10549-008-0157-4

CLINICAL TRIAL

Oligometastatic breast cancer treated with curative-intent stereotactic body radiation therapy

Michael T. Milano · Hong Zhang · Su K. Metcalfe · Ann G. Muhs · Paul Okunieff



MBC patients

25.9% 5-year OS

(*SEER database Cancer Statistic Review, 2015*)

Results

2019 CARCINOMA MAMMARIO

I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

Alba Fiorentino

Local ablative therapies

- SBRT in OMBC: clinical results

Contents lists available at ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

Review

Stereotactic radiotherapy in metastatic breast cancer

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[c] Radiotherapy Department, Business Oncological Hospital, Cagliari, Italy

«This review provides preliminary evidence that **ablative radiotherapy** may play an **important role in management of oligometastatic breast cancer** and its use is rapidly gaining consensus due to its **non-invasive nature, excellent safety profile, established efficacy** in achieving durable local control in a cost-effective manner»

Stereotactic body radiotherapy in metastatic breast cancer patients.

Study	Site	Patients/lesions (n)	Therapy (dose)	LC (%)	PFS (%)	OS (%)	Pain relief	Toxicity (grade)
Gerszten et al. [80], 2005	Spinal	50/68 (48 recurrent)	sSBRT (15–22.5 Gy, median 19 Gy)	100	NR	NR	96%	NA
Gagnon et al. [116], 2007	Recurrent spinal after CRT	18/NA (17 recurrent)	fSBRT (21–28 Gy/3–4fr.)	NR	NR	median 21	Near complete	≤2
Milano et al. [43], 2009	Liver, lung, bone, Lymph nodes	40/85	fSBRT (NA)		44 (2-year)	76 (2-year)		NA
				89 (4-year)	38 (4-year)	59 (4-year)		
Scorsetti et al. [119], 2016	Lung, liver	22/33 liver, 10/14 lung	fSBRT (liver 56.25–75 Gy/3 fr., median 75 Gy)	98 (1-year)	48 (1-year)	93 (1-year)		≤2
			fSBRT (lung 48–60 Gy/3–4 fr., median 48 Gy/4fr.)	90 (1-year)	27 (2-year)	66 (2-year)		
Scorsetti et al. [82], 2017	Liver	22/33	fSBRT (56.25–75 Gy/3 fr., median 75 Gy)	96 (1-year)	35 (1-year)	92 (1-year)		G1 39%
				87 (2-year)	18 (2-year)	66 (2-year)		
Trovo et al. [85], 2018	Bone, lymph nodes, lung, liver	54/92 (10 fractionated fMRT)	fSBRT (30–45 Gy/3fr.) or fMRT (60 Gy/25 fr.)	97 (2-year)	75 (1-year)	95 (2-year)		≤2
					53 (2-year)			

Note: VMAT = Volumetric Modulated Arc Therapy; fSBRT = fractionated Stereotactic Body Radiation Therapy; sSBRT = single dose Stereotactic Body Radiation Therapy; NA = Not Available.

OS 2-year: 66-95%

PFS 2-year: 18-53%

Results

2019 CARCINOMA MAMMARIO

I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

Alba Fiorentino

Local ablative therapies

Table 2 Prospective and retrospectives trials reporting clinical results of SABR in oligometastatic breast cancer

Author	Study type	n	MTs, n	Elderly patient, n	Primary neoplasm	MT location(s), n	RT dose	Local control rate	Median OS (months)	PFS (months)	Toxicity ≥ G3
Yang *et al.* (41)	Retrospective	136	186	NR	Breast	Brain	21 Gy/1–3 fx	1-y: 90%; 2-y: 73%	17,6	14.8	No
Xu *et al.* (42)	Retrospective	103	283	NR	Breast	Brain	20 Gy/1 fx	NR	TN:10; Others: 18	NR	No
Dyer *et al.* (43)	Retrospective	51	51	11	Breast	Brain	NR	NR	16.2	NR	NR
Gagnon *et al.* (44)	Retrospective	18	NR	4	Breast	Spinal cord	21–28 Gy/3–4 fx	NR	21	NR	No
Muacevic *et al.* (45)	Retrospective	151	620	114	Breast	Brain: 620	15–41 Gy/1–5 fr	1-y 94%	10	NR	No
Onal *et al.* (46)	Retrospective	22	29	5	Breast	Liver: 29	18 Gy ×3 fr	1-y: 100%; 2-y: 88%	Not reached	7.4	4.54%
Vern-Gross *et al.* (47)	Retrospective	154	NR	4	Breast	Brain	9–24 Gy single fr	HER2–: 1-y 76.5%; 3-y 59.5%; HER2+ 1-y 79.4%; 3-y 55.9%	8.4	NR	NR
Sharma *et al.* (48)	Retrospective	206	327	76	CCR, Lung, Melanoma, Sarcoma, Breast (7), Other	Lung	51–60×3 fr; 30×1 fr; 50–60×5 fr; 48 ×6 fr; 56 ×7 fr; 49×7 fr	2-y: 85%; 3-y: 83%; 5-y: 81%	33	13	2.40%
Kased *et al.* (49)	Retrospective	176	348	NR	Breast	Brain	19 Gy ×1 fr	1-y: 90%; 2-y: 83%	16	8.6	NR
Cho *et al.* (50)	Retrospective	131	NR	NR	Breast	Brain	14–24 Gy single fx	NR	15.7	NR	
Scorsetti *et al.* (51)	Prospective	33	47	NR	Breast	Liver: 33; Lung 14	18,75 Gy ×3 fr; –25 Gy ×3 fr	1-y: 98%; 2-y: 90%	48	11	
Trovo *et al.* (52)	Prospective	54	92	NR	Breast	Bones:60; Nodes:23; Lung: 4; Liver: 5	30–45 Gy/3 fx; 60 Gy/25 fx	2-y: 97%	NR. Actuarial 2-y survival: 95%	1-y: 75% 2-y: 53%	
Gerszten *et al.* (53)	Prospective	50	68	NR	Breast	Spinal cord	15–22, 5 Gy/1 fx	100%	NR	NR	No

Results

2019 CARCINOMA MAMMARIO

I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

Alba Fiorentino

Local ablative therapies

- SBRT in OMBC: clinical results

Table 1
Patient and tumor characteristics (n = 54).

Characteristics	No. of patients	%
Age, years		
Median	55	
Range	36-83	
Status at diagnosis		
Early-stage disease (stage I-II)	14	26
Locally-advanced disease (stage III)	27	50
Metastatic disease (stage IV)	13	24
Oligometastatic status		
At diagnosis	40	74
Induced	14	26
Histology		
Ductal	48	89
Lobular	6	11
Grade		
Well differentiated (G1)	3	6
Moderately differentiated (G2)	19	35
Poorly differentiated (G3)	28	52
Not described	4	7
Estrogen receptor		
Positive	43	80
Negative	11	20
Her2-neu		
Negative	41	76
Positive	11	20
Not described	2	4
Tumor phenotype		
Luminal A/B	43	80
Her-2 Rich	4	7
"Triple-negative"	7	13
Systemic treatment concomitant with radiation		
Hormonal therapy	9	17
Chemotherapy	33	61
Chemotherapy + Trastuzumab	2	4
Trastuzumab	4	7
None	6	11

Radiotherapy and Oncology 126 (2018) 177–180

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Radiotherapy and Oncology

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Phase II trial

Radical radiation therapy for oligometastatic breast cancer: Results of a prospective phase II trial

Marco Trovo [a,*], Carlo Furlan [a], Jerry Polesel [b], Francesco Fiorica [c], Stefano Arcangeli [d], Niccolò Giaj-Levra [e], Filippo Alongi [e], Alessandro Del Conte [f], Loredana Militello [f], Elena Muraro [g], Debora Martorelli [g], Simon Spazzapan [e,f], Massimiliano Berretta [f]

[a] Department of Radiation Oncology, Udine General Hospital, Udine; [b] Department of Epidemiology and Biostatistics, Centro di Riferimento Oncologico of Aviano; [c] Department of Radiation Oncology, University Hospital Ferrara; [d] Department of Radiation Oncology, San Camillo and Forlanini Hospitals, Rome; [e] Department of Radiation Oncology, Sacro Cuore Cancer Care Center Hospital; [f] Department of Medical Oncology, Centro di Riferimento Oncologico of Aviano; and [g] Department of Translational Research, Centro di Riferimento Oncologico of Aviano, Italy

Results

2019 CARCINOMA MAMMARIO

I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

Alba Fiorentino

Local ablative therapies

- SBRT in OMBC: clinical results

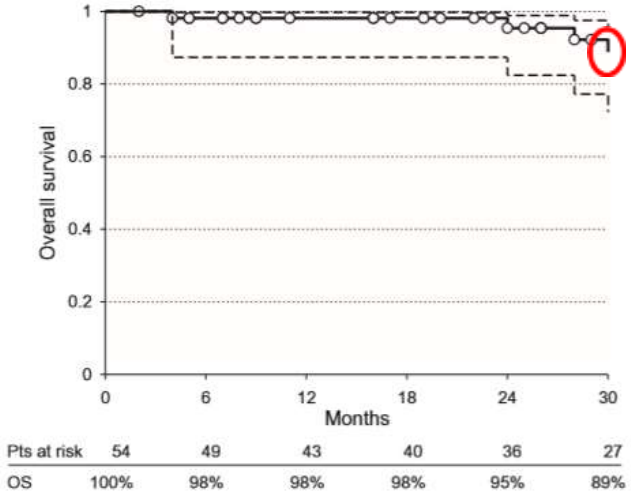


Fig. 2. Kaplan–Meier estimates of overall survival.

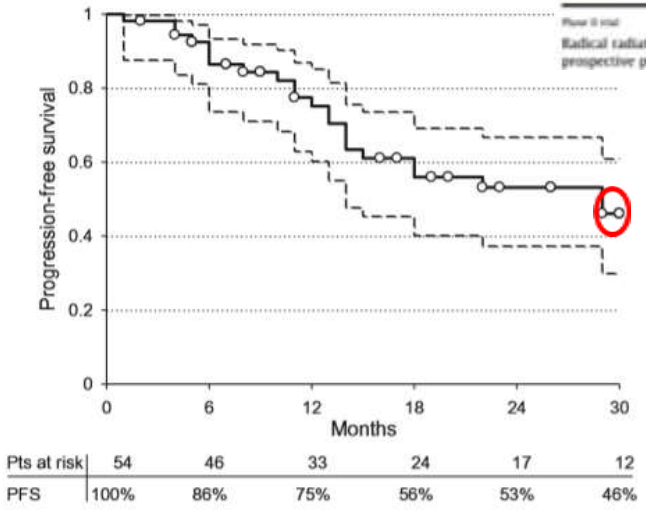


Fig. 1. Kaplan–Meier estimates of progression-free survival.

Results

2019 CARCINOMA MAMMARIO

I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

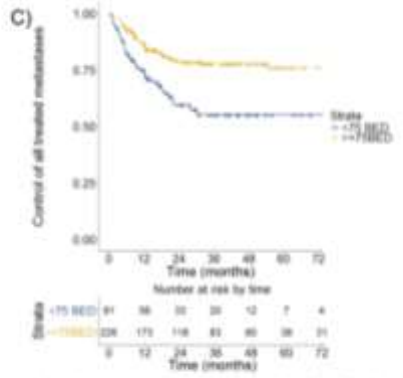
Alba Fiorentino

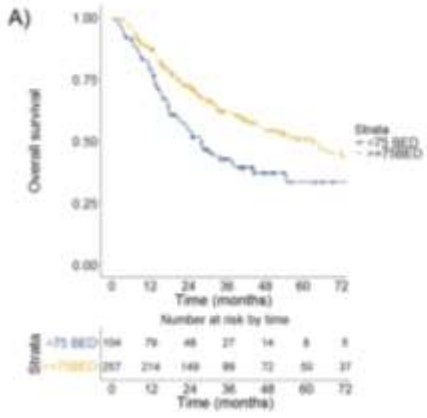
Local ablative therapies

- SBRT in OMBC: clinical results

RESEARCH ARTICLE

Classification for long-term survival in oligometastatic patients treated with ablative radiotherapy: A multi-institutional pooled analysis





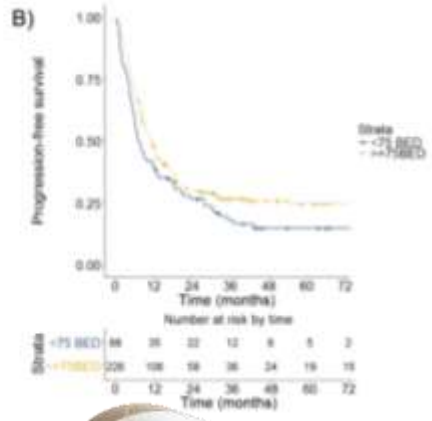


Fig 3. Overall and progression free survival, treated metastasis control by minimum biologically effective dose (BED). BED ≥75 Gy was associated with greater overall survival ($p < 0.01$) (A) and treated metastasis control ($p < 0.01$) (C), with trend for progression free survival ($p = 0.06$) (B).

Results

2019 CARCINOMA MAMMARIO

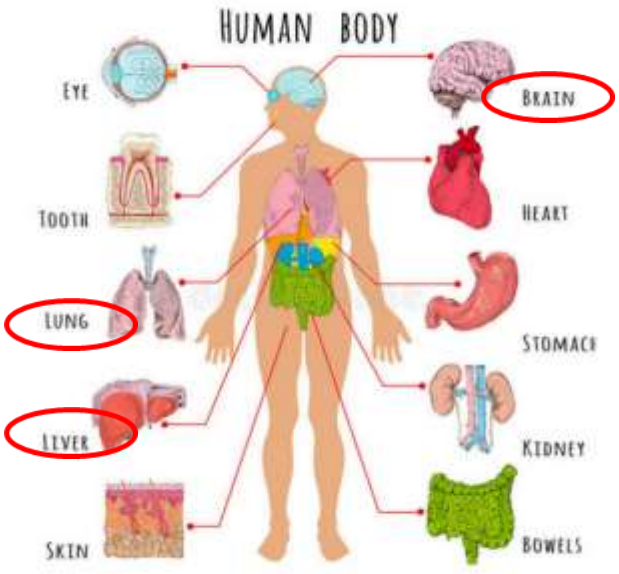
I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

Alba Fiorentino

Local ablative therapies

- SBRT in OMBC: clinical results



Results

2019 CARCINOMA MAMMARIO

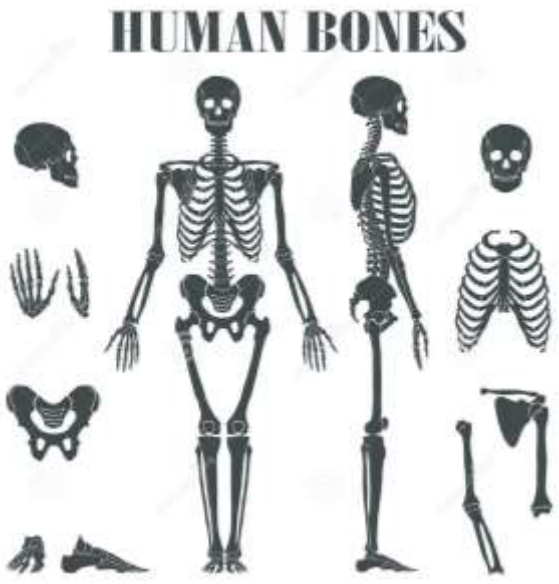
I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

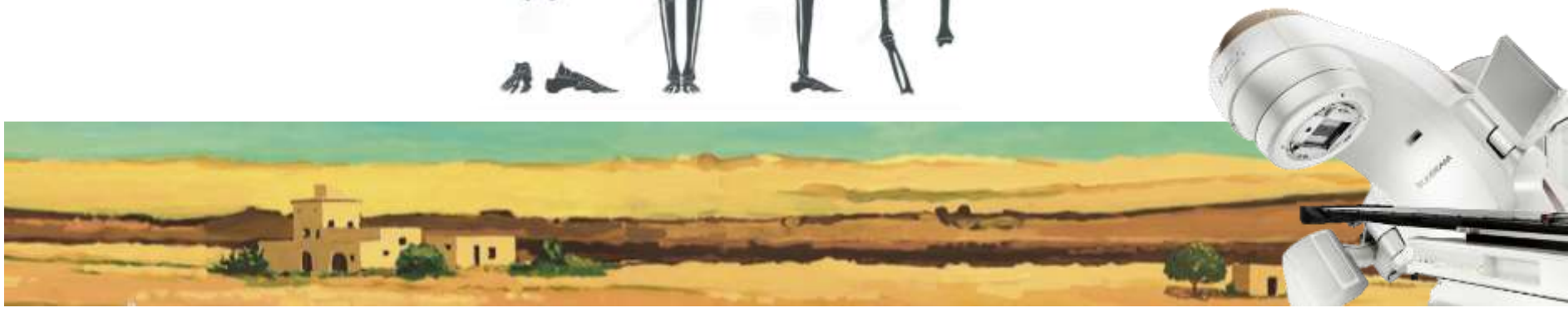
La Radioterapia nella malattia oligometastatica

Alba Fiorentino

Local ablative therapies

- SBRT in OMBC: clinical results





Results

2019 CARCINOMA MAMMARIO

I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

Alba Fiorentino

Local ablative therapies

- SBRT in OMBC: clinical results

Radiotherapy and Oncology 131 (2019) 45–51

Contents lists available at ScienceDirect

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Original Article

Oligometastatic breast cancer treated with hypofractionated stereotactic radiotherapy: Some patients survive longer than a decade

Michael T. Milano [a,*], Alan W. Katz [a], Hong Zhang [a], Christine F. Huggins [a], Khush S. Aujla [a], Paul Okunieff [b]

[*] Department of Radiation Oncology, University of Rochester; and [b] Department of Radiation Oncology, University of Florida, Gainesville, United States

Results

2019 CARCINOMA MAMMARIO

I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

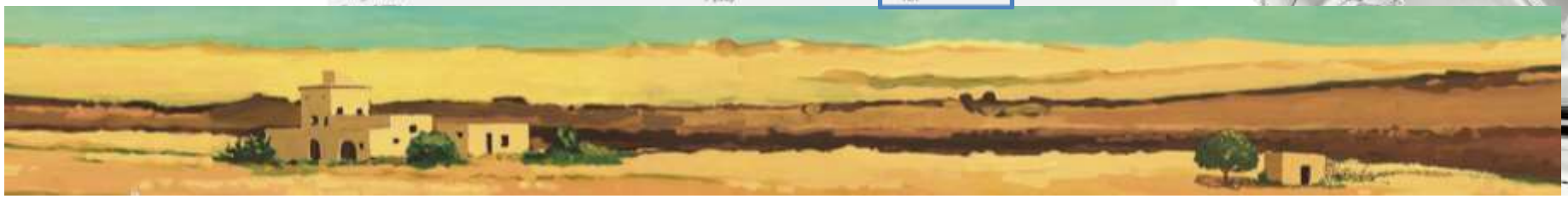
Alba Fiorentino

Local ablative therapies

- SBRT in OMBC: clinical results

Table 1
Patient and treatment characteristics.

	Excluding bone-only oligometastases	Bone-only oligometastases	p value
Number of patients	36	12	
Age (years)			
Median [range]	60.0 [42.8–64.9]	43.9 [36.3–84.6]	**0.020**
Time interval (months)			
– Primary diagnosis to metastases[1]			
Synchronous (<2 months)	3 (8%)	5 (42%)	**0.007**
Metachronous	33 (92%)	7 (58%)	
– Median [range] (months)	54 [11–228]	36 [8–82]	0.13
– Metastases[1] to oligometastases[*]			
Synchronous (<2 months)	31 (86%)	12 (100%)	
Metachronous	5 (14%)	0	
– Median [range] (months)	24 [12–55]		
– Oligometastases[*] to protocol enrollment			
– Median [range] (months)	7 [1–77]	10 [1–96]	
Estrogen and/or progesterone receptor positivity	20 (56%)	11 (92%)	**0.024**
Sites involved with oligometastatic disease			Not analyzed
– Lung	15 (42%)	NA	
– Thoracic lymph nodes	11 (31%)	NA	
– Liver	14 (39%)	NA	
– Pelvic or abdominal lymph nodes	3 (8%)	NA	
– Adrenal	2 (6%)	NA	
– Bone	2 (6%)	12 (100%)	
Number of oligometastases treated			0.41
– 1	12 (33%)	7 (58%)	0.13 (1 vs.2–5)
– 2	12 (33%)	3 (25%)	
– 3	5 (14%)	2 (16%)	
– 4	3 (8%)	0	
– 5	4 (11%)	0	
Number of involved organs			
– 1	26 (72%)	12 (100%)	Not analyzed
– 2	9 (25%)	NA	
– 3	1 (3%)	NA	



Results

2019 CARCINOMA MAMMARIO

I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

Alba Fiorentino

Local ablative therapies

- SBRT in OMBC: clinical results

Sum of GTVs			
Median [range]	29.0 [1.3–402] cc	20.9 [4.8–79.4] cc	0.10
<25 cc	17 (47%)	6 (50%)	0.87
Dose in EQD2			
Median [range] (Gy)	62.5 [39.3–83.3]	57.3 [38.3–70]	0.54
Systemic therapy for oligometastases prior to HSRT			
– Any	32 (89%)	12 (100%)	0.23
– Chemotherapy and/or antibody therapy	23 (64%)	7 (58%)	
– Hormonal therapy	16 (44%)	11 (92%)	
Treated lesion response to systemic therapy			
– stable	4 (11%)	4 (33%)	
– partial response	7 (19%)	1 (8%)	
– progression	14 (39%)	1 (8%)	**0.037**
– not applicable (no systemic therapy used)	4 (11%)	0	
– unable to assess**	7 (19%)	6 (50%)	
Systemic therapy after HSRT (before potentially developing widespread disease)			
– Any	26 (72%)	11 (92%)	0.17
– Chemotherapy and/or antibody therapy †	19 (53%)	4 (33%)	
– Hormonal therapy	17 (47%)	10 (83%)	
Systemic therapy for widespread disease			Not analyzed
– Any	16 (44%)	6 (50%)	
– Chemotherapy and/or antibody therapy	15 (42%)	6 (50%)	
– Hormonal therapy	8 (22%)	6 (50%)	
– None	3 (8%)	0	
– NA (i.e. no widespread disease)	7 (19%)	6 (50%)	
– Unknown	10 (28%)	0	

Results

2019 CARCINOMA MAMMARIO

I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

Alba Fiorentino

Local ablative therapies

- SBRT in OMBC: clinical results

Table 2
Patient survival and tumor control outcomes.

	Excluding bone-only oligometastases	Bone-only oligometastases	Univariate p value	Multivariate p value*
Overall survival			**0.002**	**0.026**
– Median [range] (years)	3.2 [0.5–17.9]	not reached [2.9–16.8]		
– 5-year	31%	83%		
– 10-year	17%	75%		
Freedom from LR of treated lesion(s)			0.076	0.052
– 2-year, 5-year and 10-year[†]	73%	100%		
Freedom from widespread metastases			**0.018**	**0.037**
– 2-year	42%	75%		
– 5-year	30%	67%		
– 10-year	15%	67%		
Repeat hypofractionated metastasis-directed radiotherapy				
– For local recurrence	2 (6%)[‡]	1 (8%)	Not analyzed	Not analyzed
– Median [range] (years)	1.0 (0.8–1.2)	13.8		
– 2nd course for new oligometastases	11 (31%)	4 (33%)		
– Median [range] (years)	0.8 [0.6–11.6]	6.3 [5.0–9.8]		
– ≥3 courses for new oligometastases	5 (14%)	2 (17%)		

Results

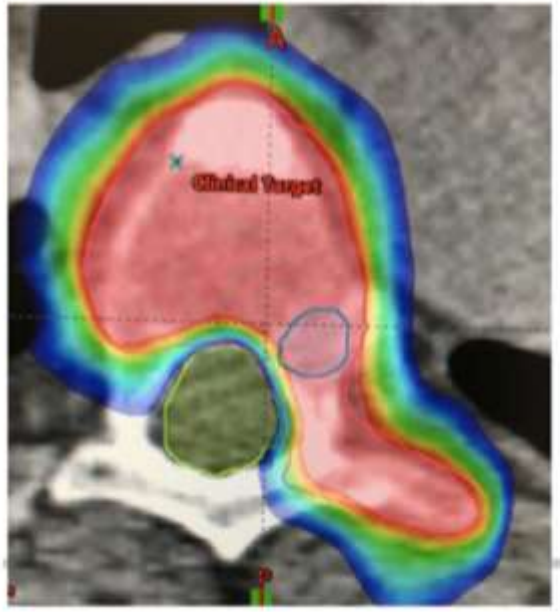
2019 CARCINOMA MAMMARIO

I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

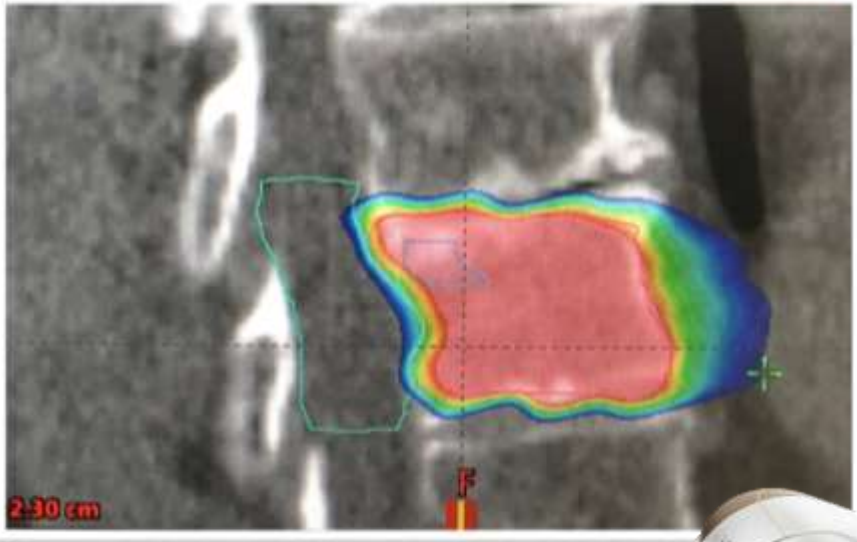
La Radioterapia nella malattia oligometastatica

Alba Fiorentino

Local ablative therapies



Colonna



Results

2019 CARCINOMA MAMMARIO

I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

Alba Fiorentino

Table 3. Selected Spine SBRT Series for Spinal Metastases With No Prior History of Radiation.

Study Authors (Year)	Study Design	No. of Tumors/ No. of Patients	No. of Postoperative Tumors	Histology	Total Dose (Range)/ No. of Fractions (Range)	Follow-up in Months (Range)	Local Control	Overall Survival	Pain Response
Gerszten et al[52] (2007)	Prospective	156/na[a]	9	Mixed	Mean: 20 Gy (12.5-25 Gy)/1	Median: 21 (3-53)	90% (crude)	na	86% reported long-term improvement
Yamada et al[127] (2008)	Retrospective	103/93	0	Mixed	Median: 24 Gy (18-24 Gy)/1	Median: 15 (2-45)	90% (15 months)	Median: 15 months	na
Salgal et al[59] (2009)	Retrospective	23/14	0	Mixed	Median: 24 Gy (7-40 Gy)/3 (1-5)	Median: 9 (1-26)	85% (1 year)/ 69% (2 years)	45% (2 years)	na
Nguyen et al[49] (2010)	Prospective	na/22[a]	0[b]	Renal cell carcinoma	Median: 27 Gy (24-30 Gy)/3 (1-5)	Median: 13.1 (3.3-54.5)	82% (1 year)[c]	72% (1 year)[c]	BPI: no pain 23% (baseline) to 52% (12 months)
Wang et al[76] (2012)	Prospective	166/149	0[d]	Mixed	27-30 Gy/3	Median: 15.9 (1.0-91.6)	80.5% (1 year)/ 72.4% (2 years)	68.5% (1 year)/ 46.4% (2 years)	BPI: no pain 26% (baseline) to 54% (6 months)
Ahmed et al[75] (2012)	Retrospective	63/46[a]	0	Mixed	Median: 24 Gy (10-40 Gy)/3 (1-5)	Mean: 8.2	91.2% (1 year)	59% (1 year)	na
Thibault et al[128] (2014)	Retrospective	60/37[a]	10	Renal cell carcinoma	Median: 24 Gy (18-30 Gy)/2 (1-5)	Median: 12.3 (1.2-55.4)	83.4% (1 year)/ 66.2% (2 years)	64.1% (1 year)/ 45.6% (2 years)	na
Guckenberger et al[74] (2014)	Retrospective	387/301	0	Mixed	Median: 24 Gy (10-60 Gy)/3 (1-20)	Median: 11.8 (0-105)	89.9% (1 year)/ 83.9% (2 years)	64.9% (1 year)/ 43.7% (2 years)	na
Sohn et al[129] (2014)	Retrospective	13/13	0	Renal cell carcinoma	Mean: 38.0 Gy/median: 4	na	85.7% (1 year)	Median: 15 months	23.1% complete; 53.8% partial
Folkert et al[73] (2014)	Retrospective	108/88[a]	33	Sarcoma	Median: 24 Gy (18-24 Gy)/1 or median: 28.5 Gy (24-36 Gy)/3 (3-6)	Median: 12.3 (1-80.7)	87.9% (1 year)	60.6% (1 year)	na
Park et al[130] (2014)	Retrospective	45/28[a]	1	Mixed	Median: 27 Gy (18-35 Gy)/3 (1-5)	Median: 7.4 (1.1-42.5)	93.2% (1 year)/ 93.2% (2 years)	47.4% (1 year)/ 27.9% (2 years)	VAS: median 4 (pre-SBRT) to 1 (1-3 months post-SBRT)
Anand et al[50] (2015)	Retrospective	76/52[a]	8	Mixed	Median: 24 Gy (24-27 Gy)/3 (1-3)	Median: 8.5 (3.0-40.0)	94% (1 year)/ 82.6% (2 years)	68% (1 year)/ 45.4% (2 years)	92.3% complete; 5.8% partial
Sellin et al[131] (2015)	Retrospective	40/37	0	Renal cell carcinoma	Median: 24 Gy (24-30 Gy)/1 (1-5)	Median: 49.0 (38.2-75.8)	57%	Median: 16.3 months	VAS: 41.4% improved pain
Bishop et al[132] (2015)	Retrospective	332/285[f]	0	Mixed	Median (tumor dose): 43 Gy (biologically equivalent dose, alpha/ beta = 10)	Median: 19 (0-111)	88% (1 year)/ 82% (3 years)	64% (1 year)/ 33% (3 years)	na
Bate et al[71] (2015)	Retrospective	48/36[a]	0	Mixed	16-23 Gy/1 or 20-30 Gy/2-5	Median: 9.8	95.8% (1 year)	44% (crude)	na
Azad et al[72] (2015)	Retrospective	25/25	0	Mixed	Median: 20 Gy (15-25.5)/2 (1-5)	Median: 18 (1-81)	84.2% (crude)	Median: 28 months	na

Results

2019 CARCINOMA MAMMARIO

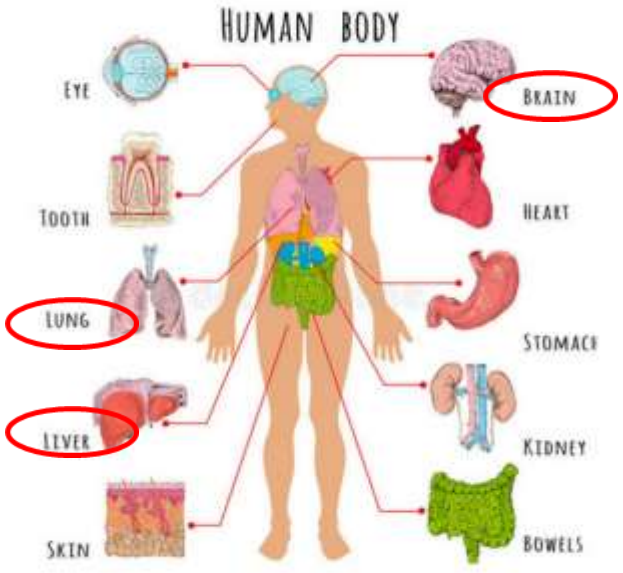
I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

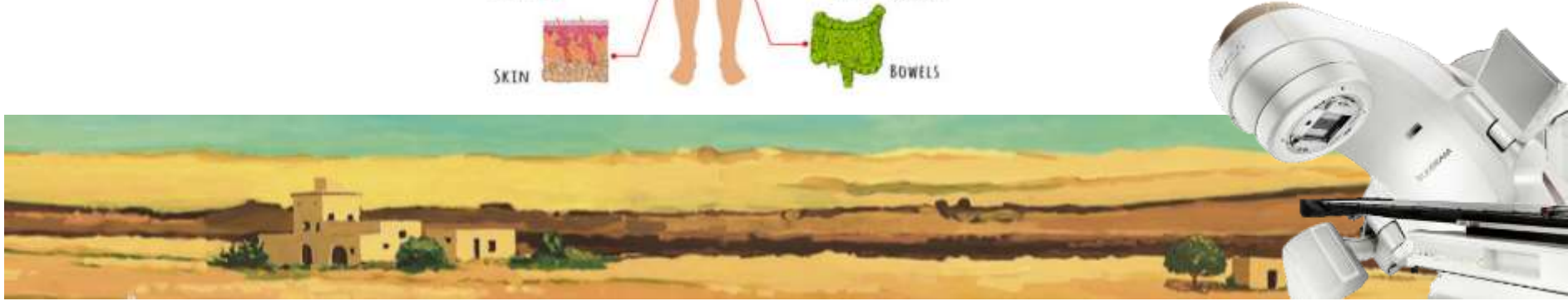
La Radioterapia nella malattia oligometastatica

Alba Fiorentino

Local ablative therapies

- SBRT in OMBC: clinical results





Results

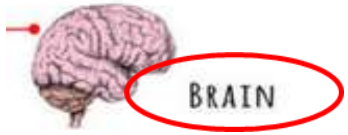
2019 CARCINOMA MAMMARIO

I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

Alba Fiorentino

Local ablative therapies



The Breast 41 (2018) 57–66

Contents lists available at ScienceDirect

The Breast

journal homepage: www.elsevier.com/brst

Review

Stereotactic radiotherapy in metastatic breast cancer

Marco Possanzini [a, b, c, *], Carlo Greco [a]

[a] Radiotherapy Department, Fundação Champalimaud, Lisbon, Portugal
[b] Breast Unit Fundação Champalimaud, Lisbon, Portugal
[c] Radiotherapy Department, Businco Oncological Hospital, Cagliari, Italy

Results

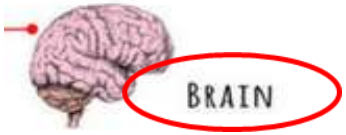
2019 CARCINOMA MAMMARIO

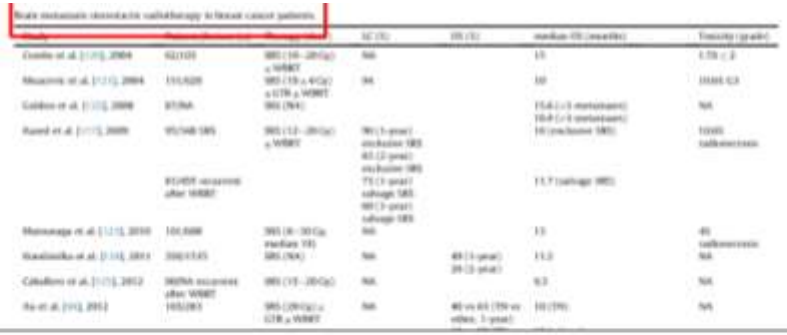
I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

Alba Fiorentino

Local ablative therapies





BMBC incidence between 3% and 6% in early-stage, and up to 30% in stage IV disease

Triple negative MBC patients have 25-46% estimated probability of brain recurrence (vs 10% in Hormone receptor positive HER2 negative MBC)

High heterogeneity in dose/fractionation and modalities (WBRT/SRS/Surgical resection)

2-year LC ranged from 73% to 83% and 2-year OS from 41% to 21%

Radionecrosis ranged from 4% to 10,6% (excluding Geraud et al study)

Results

2019 CARCINOMA MAMMARIO
I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica
Alba Fiorentino

Local ablative therapies

eness analysis of SRS/SRT alone compared to SRS/SRT with upfront WBRT for BMs, it seems that SRS alone was found to be more cost-effective for patients with 1–3 BMs compared to upfront WBRT plus SRS/SRT (46). The emerging interest to treat patients affected by more than four BMs allowed to introduce a new technology of linac-based SRS/SRT for multiple BMs in daily clinical practice. The main intent of this new technology is to reduce the overall treatment time and the costs for the health systems due to the ability of delivering SRS/SRT for multiple BMs within a single session (47).

In conclusion, the role of SRS/SRT for brain metastases seems to be definitively assessed as a crucial part on the management of BMs patients. SRS/SRT has shown to be a safe and effective treatment procedure, able to pursuit a high level of local control.

Role of Radiosurgery/Stereotactic Radiotherapy in Oligometastatic Disease: Brain Oligometastases

*Rosario Mazzola[1], Stefanie Corradini[2], Fabiana Gregucci[3], Vanessa Figlia[1], Alba Fiorentino[3] and Filippo Alongi[1,4]**

[1] Radiation Oncology Department, IRCCS Sacro Cuore Don Calabria Hospital, Negrar, Italy, [2] Radiation Oncology Department, LMU Munich University Hospital, Munich, Germany, [3] Radiation Oncology Department, General Regional Hospital "F. Miulli", Acquaviva delle Fonti, Italy, [4] Radiation Oncology Department, University of Brescia, Brescia, Italy

April 2019 | Volume 9 | Article 206

Results

2019 CARCINOMA MAMMARIO

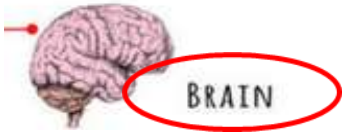
I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

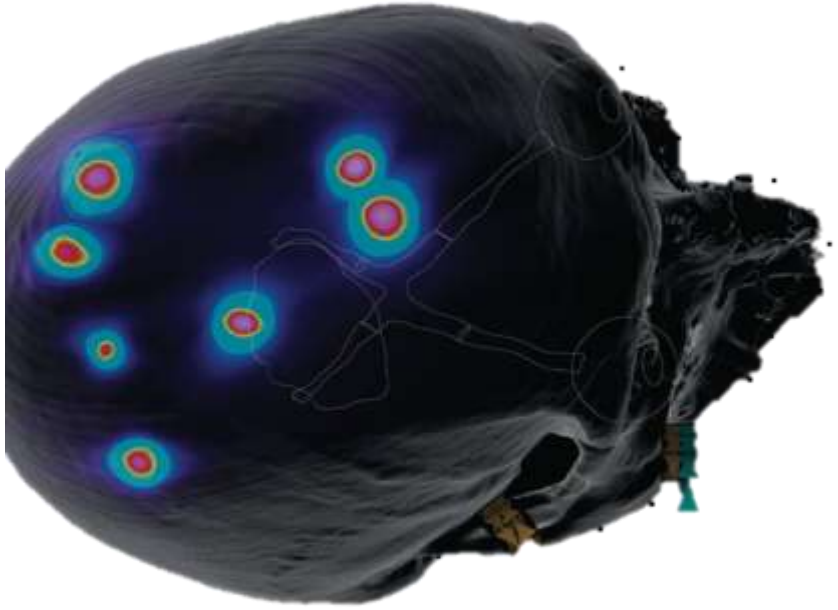
La Radioterapia nella malattia oligometastatica

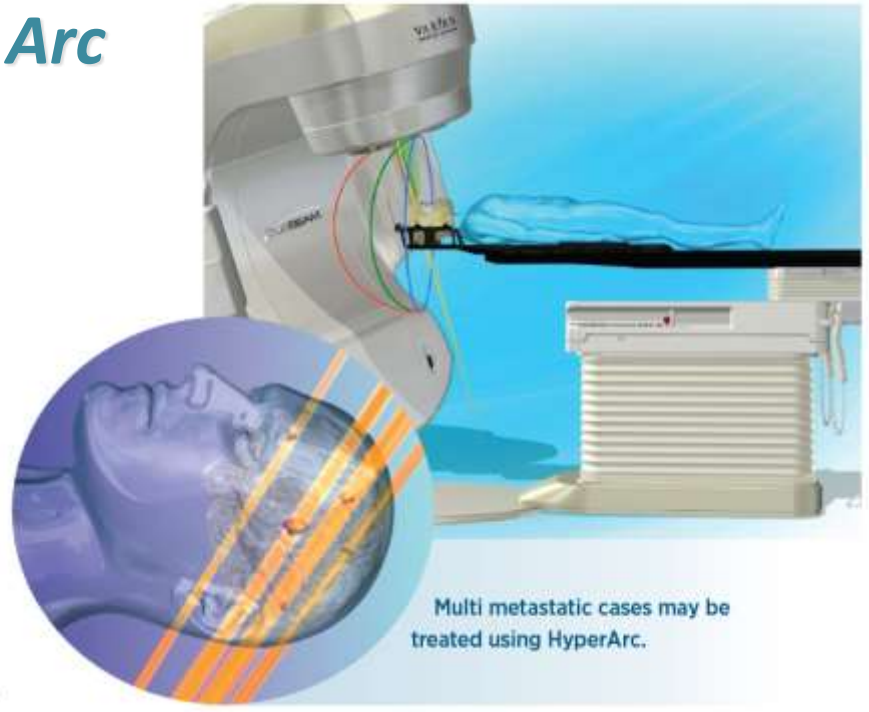
Alba Fiorentino

RADIOTERAPIA STEREOTASSICA

Hyper Arc







Results

2019 CARCINOMA MAMMARIO

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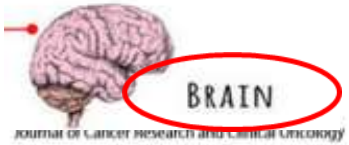
La Radioterapia nella malattia oligometastatica

Alba Fiorentino

Local ablative therapies

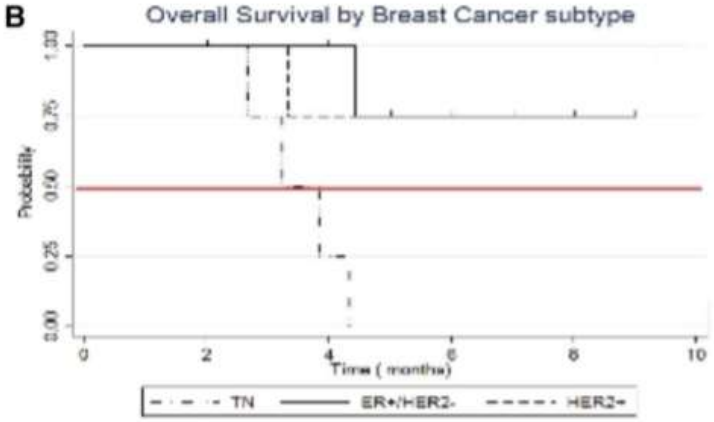


Journal of Cancer Research and Clinical Oncology
https://doi.org/10.1007/s00432-018-2781-7

ORIGINAL ARTICLE – CANCER RESEARCH

First experience and clinical results using a new non-coplanar mono-isocenter technique (HyperArc™) for Linac-based VMAT radiosurgery in brain metastases

Filippo Alongi[1,2] · Alba Fiorentino[1] · Fabiana Gregucci[1] · Stefanie Corradini[3] · Niccolo Giaj-Levra[1] · Luigi Romano[4] · Michele Rigo[1] · Francesco Ricchetti[1] · Alberto Beltramello[4] · Gianluigi Lunardi[5] · Rosario Mazzola[1] · Ruggero Ruggieri[1]



Results

2019 CARCINOMA MAMMARIO

I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

Alba Fiorentino

Local ablative therapies

cancers

MDPI

Review

Local Treatment of Breast Cancer Liver Metastasis

Reto Bale *, Daniel Putzer and Peter Schullian *

Department of Radiology, Section of Interventional Oncology-Microinvasive Therapy, Medical University of Innsbruck, 6020 Innsbruck, Austria; daniel.putzer@tirol-kliniken.at

* Correspondence: reto.bale@i-med.ac.at (R.B.); peter.schullian@i-med.ac.at (P.S.); Tel.: +43-512-504-22761 (R.B. & P.S.)

Received: 12 August 2019; Accepted: 9 September 2019; Published: 11 September 2019

Results

2019 CARCINOMA MAMMARIO
I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica
Alba Fiorentino

Local ablative therapies

3.3.1. Stereotactic Body Radiation Therapy (SBRT)

The liver parenchyma has low radiation tolerance doses. However, by delivering higher doses to small volumes, organ function can be maintained without causing functional compromise [67]. Due to the delivery of conformal doses and steep dose gradients SBRT allows normal liver tissues to be spared. Retrospective and prospective studies have demonstrated the feasibility of SBRT for LM from different tumor entities with local control (LC) rates ranging from 60–90% at 2 years after treatment [70,71]. In a recent paper, Onal et al. [43] combined liver SBRT and systemic treatment in a total of 22 patients with 29 BCLM, with a mean size of 2.1 ± 1.2 cm. After a median follow-up time of 16.0 months (range 4.4–59.4 months), 18 patients (82%) had disease recurrence. The 1- and 2-year OS rates were 85% and 57%, and the 1- and 2- year PFS rates were 38% and 8%, respectively. The 1- and 2-year LC rates were 100% and 88%, respectively. The authors concluded that SBRT may be an effective and safe treatment option in selected patients with BCLM. Mahadevan et al. [44] reported the results after SBRT of a total of 427 patients with liver metastases from different origin including 42 patients with BCLM. At a median follow-up of 14 months (1–91 months) the median OS for patients with BCLM was 21 months. In the whole cohort, smaller tumor volumes (<40 cm^3) and BED10 ≥ 100 Gy correlated with improved OS ((25 months vs. 15 months, $p = 0.0014$) and (27 months vs. 15 months $p < 0.0001$)), respectively. In BCLM the LC rate after 2 years was 24%.

Hypoxia particularly within large lesions may cause local failure [72] and the distance between treated lesions and the surrounding visceral organs at risk should be more than 8 mm [71]. Liver SBRT is technically challenging, requiring daily imaging guidance and insertion of fiducial markers and/or image fusion to localize the target and assess respiration-related organ motion [44]. The patient selection criteria, and optimal dose and fractionation for liver SBRT are still under investigation.

cancers

MDPI

Review

Local Treatment of Breast Cancer Liver Metastasis

Reto Bale *, Daniel Putzer and Peter Schullian *

Department of Radiology, Section of Interventional Oncology-Microinvasive Therapy, Medical University of Innsbruck, 6020 Innsbruck, Austria; daniel.putzer@tirol-kliniken.at

* Correspondence: reto.bale@i-med.ac.at (R.B.); peter.schullian@i-med.ac.at (P.S.); Tel.: +43-512-504-22761 (R.B. & P.S.)

Received: 12 August 2019; Accepted: 9 September 2019; Published: 11 September 2019

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Results

2019 CARCINOMA MAMMARIO

I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

Alba Fiorentino

Local ablative therapies

Stereotactic Body Radiotherapy (SBRT) for Oligometastatic Lung Nodules: A Single Institution Series

Rodney E. Wegner[1], Stephen Abel[1], Shaakir Hasan[1], Lana Y. Schumacher[2] and Athanasios Colonias[1]*

[1] Division of Radiation Oncology, Allegheny Health Network Cancer Institute, Pittsburgh, PA, United States, [2] Department of Cardiothoracic Surgery, Allegheny Health Network, Pittsburgh, PA, United States

ORIGINAL RESEARCH
published: 07 May 2019
doi: 10.3389/fonc.2019.00334

Results

2019 CARCINOMA MAMMARIO

I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

Alba Fiorentino

Local ablative therapies

Stereotactic Body Radiotherapy (SBRT) for Oligometastatic Lung Nodules: A Single Institution Series

Rodney E. Wegner[1], Stephen Abel[1], Shaakir Hasan[1], Lana Y. Schumacher[2] and Athanasios Colonias[1]*

[1] Division of Radiation Oncology, Allegheny Health Network Cancer Institute, Pittsburgh, PA, United States, [2] Department of Cardiothoracic Surgery, Allegheny Health Network, Pittsburgh, PA, United States

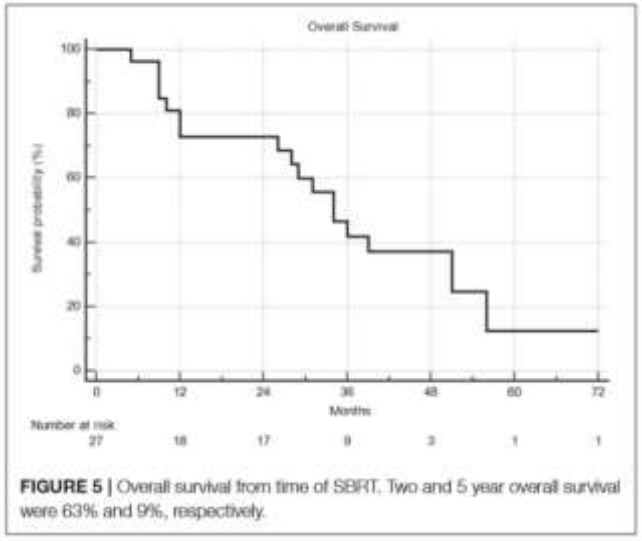


FIGURE 5 | Overall survival from time of SBRT. Two and 5 year overall survival were 63% and 9%, respectively.

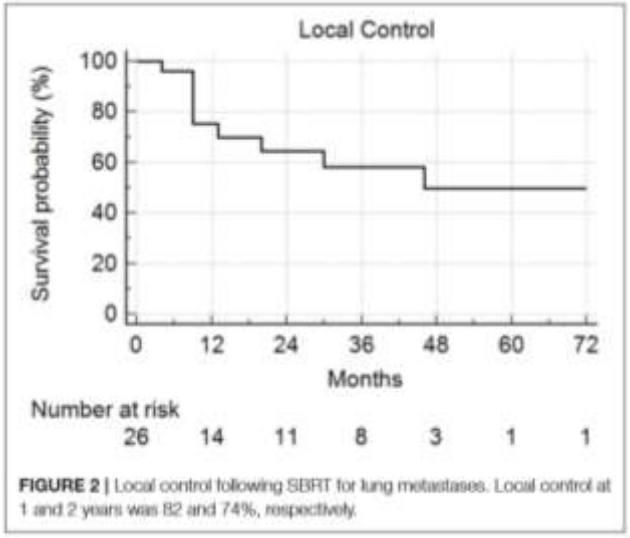


FIGURE 2 | Local control following SBRT for lung metastases. Local control at 1 and 2 years was 82 and 74%, respectively.

Local control by BED using a cutoff of 72Gy. One year local control was 90% compared to 57%, in favor of higher biologic dose

Local control based on pretreatment SUV. Local control at one year was 92% compared to 67%, in favor of lesions with less avidity.

Results

2019 CARCINOMA MAMMARIO

I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

Alba Fiorentino

Local ablative therapies

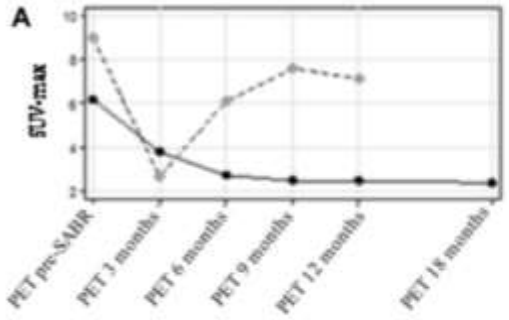
ORIGINAL ARTICLE

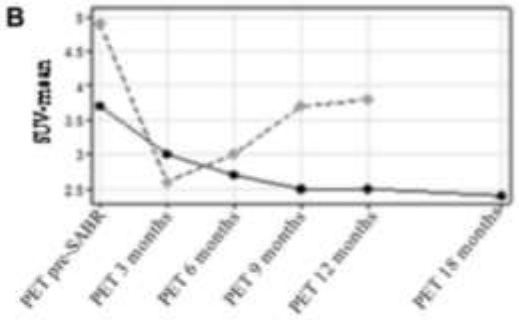
Stereotactic Ablative Radiation Therapy for Lung Oligometastases: Predictive Parameters of Early Response by ^{18}FDG-PET/CT

Rosario Mazzola, MD,[a,*] Alba Fiorentino, MD,[a] Gioacchino Di Paola, MSc,[b] Niccolò Giaj Levra, MD,[a] Francesco Ricchetti, MD,[a] Sergio Fersino, MD,[a] Umberto Tebano, MD,[c] Stefano Pasetto, MS,[d] Ruggero Ruggieri, MS,[a] Matteo Salgarello, MD,[d] Filippo Alongi, MD[a]

[a]*Radiation Oncology, Sacro Cuore Don Calabria Cancer Care Center, Negrar-Verona, Italy*
[b]*Statistic Sciences Faculty, University of Palermo, Palermo, Italy*
[c]*Radiation Oncology School, University of Padua, Padua, Italy*
[d]*Nuclear Medicine, Sacro Cuore Don Calabria Cancer Care Center, Negrar-Verona, Italy*

Received 28 June 2016; revised 28 October 2016; accepted 15 November 2016





Results

2019 CARCINOMA MAMMARIO

I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

Alba Fiorentino

Local ablative therapies

Metastasectomy increases local control with significant improvement of survival in selected patients

Most patients are inoperable for comorbidities or sites of metastases

Results

2019 CARCINOMA MAMMARIO

I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica

Alba Fiorentino

Local ablative therapies

Review Article

Stereotactic ablative radiotherapy for oligometastatic breast cancer in elderly patients

Ignacio Morales-Orue[1,2,3], Juan Zafra-Martin[3], Laura Garcia[3], Rodolfo Chicas-Sett[3], Juan Castilla-Martinez[3], Maria Auxiliadora Cabezon[3], Javier Burgos[4], Marta Lloret[3], Pedro C. Lara[4,5]

Submitted Jul 05, 2019. Accepted for publication Aug 23, 2019.
doi: 10.21037/tcr.2019.08.29

Results

2019 CARCINOMA MAMMARIO
I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

La Radioterapia nella malattia oligometastatica
Alba Fiorentino

Local ablative therapies

Could SABR improve OS in elderly patients?

Most of the patient groups encompassed in the articles in this review have not specifically included elderly patients. When a general analysis is performed on these series, only 13 out of the 17 total studies have reported survival outcomes. As such, the data provided is quite heterogeneous, ranging from 8 to 48 months, with one study (28) even reaching an actuarial survival up to 120 months. Thus, it is not possible to extrapolate these results to an old population. Even then, it stands out that, in Muacevic's *et al.* study (46), 114 elderly patients were included and achieved a median OS of 10 months. A similar case can be seen on the studies published by Sharma *et al.* and Dyer *et al.*, which also specified to have involved the inclusion of aging individuals, reaching a median OS of 33 and 16.2 months, respectively. These seem as very promising results in a group of subjects that, in addition to their advanced age, usually present a myriad of other comorbidities (even though this topic was not reported in any of these references) and where their life expectancy is not generally defined by the presence of an oncologic disease.

In the recent SABR-COMET study, oligometastatic patients presented similar rates of grade ≥3 toxicity in both the standard RT and the SABR arms (15). In contrast, patients treated with SABR presented higher rates of grade 2 adverse effects (29% *vs.* 9%), and three treatment-related deaths occurred in this arm (*vs.* none in the control arm). These results, however, were not stratified by age.

In the particular case of brain metastases, it must be taken into account that traditional palliative whole brain radiotherapy (WBRT) has largely been associated with a decline in cognitive status and quality of life (60). This can be critical in the elder population. In this scenario, SRS represents an opportunity to avoid these toxicities. SRS seems to be a safe treatment with minimal acute side effects. And, even though radionecrosis can be present as a finding in control MRI in up to 34% of cases, only 10–17% are actually symptomatic (61,62). Again, none of the evidence that we analyzed specified any differences regarding the subgroup of older patients.

Results

2019 CARCINOMA MAMMARIO

I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

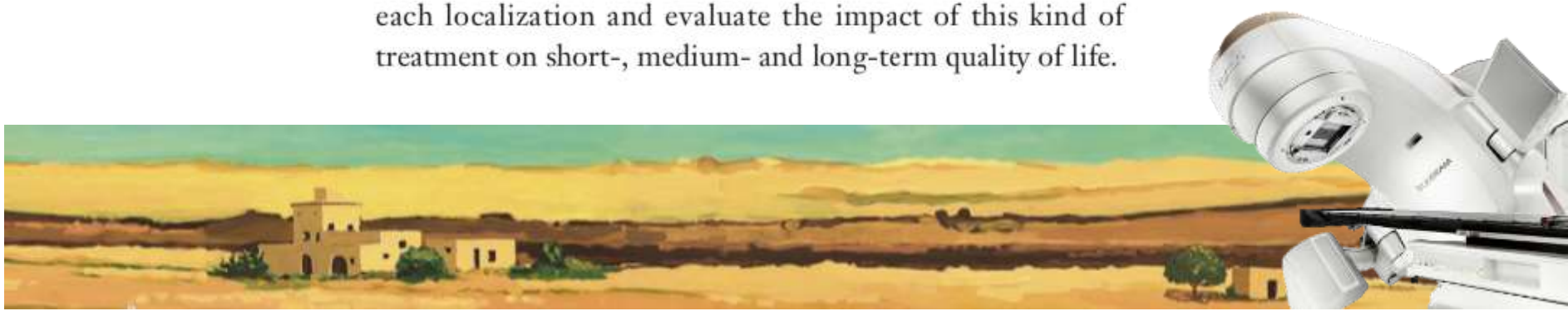
La Radioterapia nella malattia oligometastatica

Alba Fiorentino

Local ablative therapies

Conclusions

A SABR approach in oligometastatic BC poses a promising therapeutic option, with excellent clinical results, such as long-term LC, low toxicity and an increase in OS in particular cases. Even though there is limited evidence available, SABR in elderly patients represents an auspicious option that avoids more invasive therapeutic strategies that involve hospitalization (and their intrinsic risks) and allows for a short-course, tolerable, safe and effective treatment. Further studies are required to improve patient selection, establish the most effective fractionation schemes for each localization and evaluate the impact of this kind of treatment on short-, medium- and long-term quality of life.



Results

2019 CARCINOMA MAMMARIO

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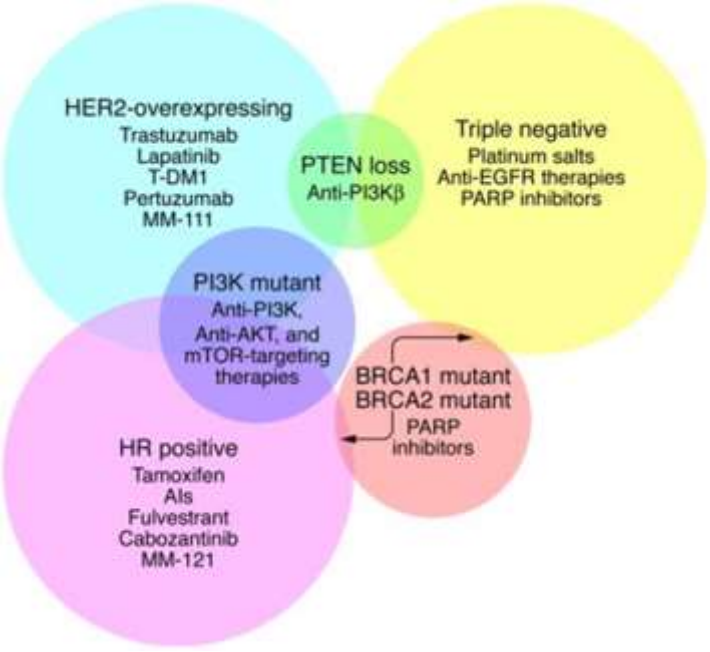
La Radioterapia nella malattia oligometastatica

Alba Fiorentino

Metastatic breast cancer



Small molecule inhibitors

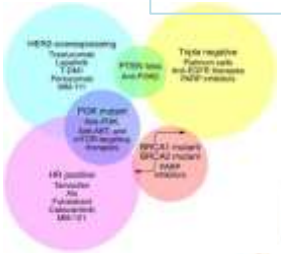
Results

2019 CARCINOMA MAMMARIO

I TRAGUARDI RAGGIUNTI E LE NUOVE SFIDE.

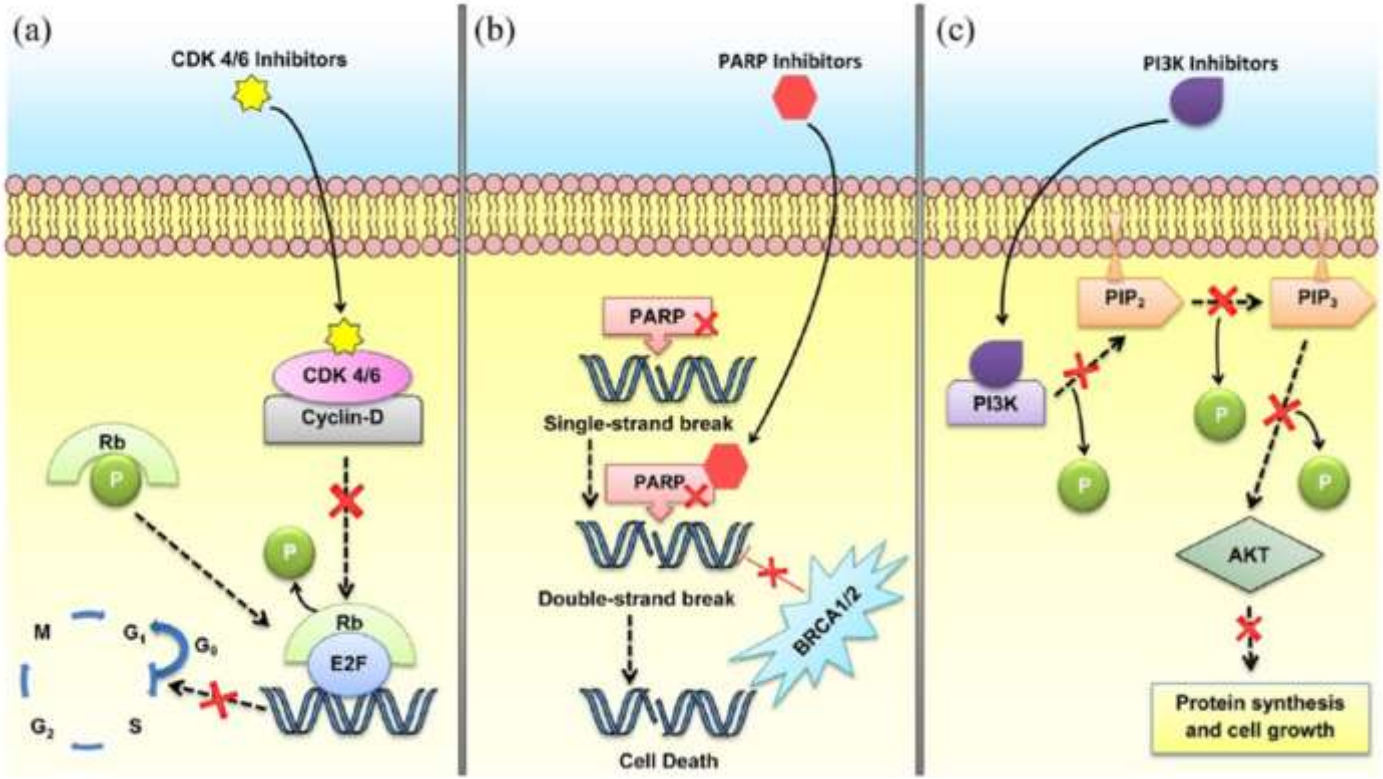
La Radioterapia nella malattia oligometastatica

Alba Fiorentino



Metastatic breast cancer

Therapeutic Advances in Medical Oncology *Review*



Ther Adv Med Oncol
2018, Vol. 10: 1–21
DOI: 10.1177/1758835918808509

Results

2019 CARCINOMA MAMMARIO

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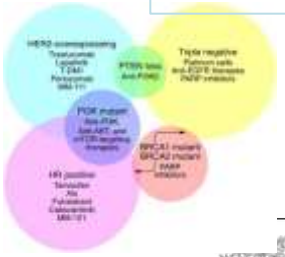
La Radioterapia nella malattia oligometastatica

Alba Fiorentino



Small molecule inhibitors : CDK 4/6

Radiotherapy and Oncology 126 (2018) 181

Contents lists available at ScienceDirect

Radiotherapy and Oncology

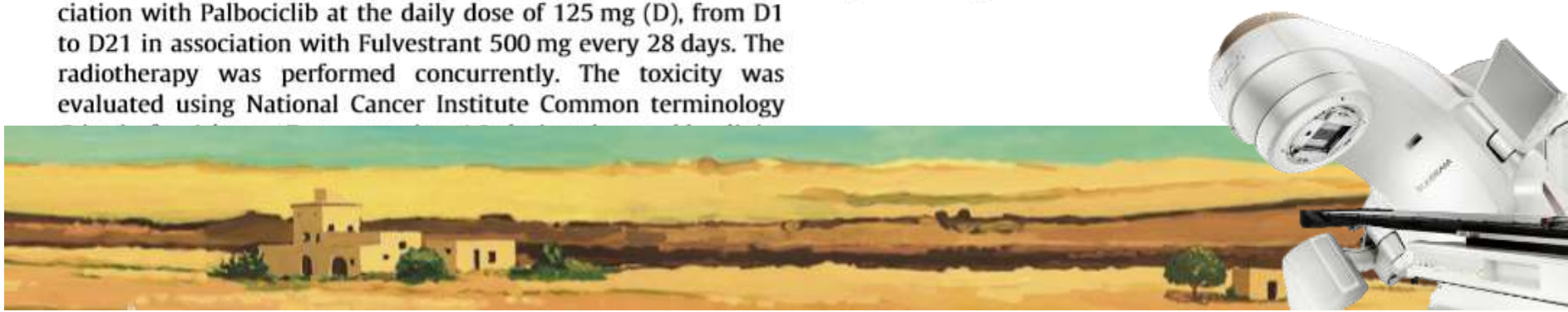
journal homepage: www.thegreenjournal.com

Letter to the Editor

Preliminary results of the association of Palbociclib and radiotherapy in metastatic breast cancer patients

After the official authorization of use of Palbociclib, we treate 5 metastatic breast cancer patients with symptomatic RT in asso ciation with Palbociclib at the daily dose of 125 mg (D), from D1 to D21 in association with Fulvestrant 500 mg every 28 days. The radiotherapy was performed concurrently. The toxicity was evaluated using National Cancer Institute Common terminology

In conclusion, in this very first report of Palbo-RT association, there was no increased toxicity and this treatment can be used in symptomatic patients. Further larger prospective studies with longer follow-up are needed to confirm these results.



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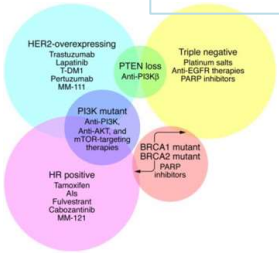


Small molecule inhibitors : CDK 4/6

Article in Press

Severe acute radiation-induced enterocolitis after combined palbociclib and palliative radiotherapy treatment

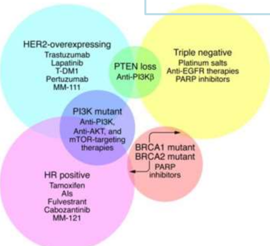
Terufumi Kawamoto, Naoto Shikama, Keisuke Sasai

Graduate School of Medicine Department of Radiation Oncology, Juntendo University, Japan

We administered conformal radiotherapy of 30 Gy in 10 fractions, over 2 weeks. She experienced grade 1 diarrhoea during treatment with Palbo-RT. Three days after radiotherapy completion, she experienced left abdominal pain, bloating and bloody diarrhoea and was diagnosed with grade 3 colitis (CTCTE v4.0). Colonoscopy revealed erosion and angiectasis of the descending colon (Fig. 1D); therefore, acute radiation-induced enterocolitis was diagnosed.

Treatment with palbociclib before and during 5 daily fractions of irradiation exacerbates GI-ARS in mice [7]. *Lee C.L.,Int J Radiat Oncol Biol Phys 2018.*

Results



Small molecule inhibitors : PARP

Gynecol Oncol. 2018 Sep;150(3):534-544. doi: 10.1016/j.ygyno.2018.07.002. Epub 2018 Jul 17

Radiosensitization by the PARP inhibitor olaparib in BRCA1-proficient and deficient high-grade serous ovarian carcinomas.

Bi Y, Verginadis II, Dey S, Lin L, Guo L, Zheng Y, Koumenis C.

Author information

Abstract

OBJECTIVE: Approximately 15-25% of high-grade serous ovarian carcinomas (HGSOC) harbor BRCA1/2 mutations. Inhibition of Poly (ADP-ribose) polymerase (PARP) is synthetically lethal to cells and tumors with BRCA1/2 mutation. Our goal was to investigate the radiosensitizing effects of PARP inhibitor olaparib in HGSOC with different BRCA1 status.

METHODS: The radiosensitizing effects of olaparib were tested on BRCA1-proficient and deficient HGSOC by clonogenic survival and tumor growth assays. The effects of olaparib and radiation on DNA damage, PARP activity, and apoptosis were determined.

RESULTS: BRCA1-deficient HGSOC cells were more sensitive to RT alone and exhibited significantly higher levels of olaparib-mediated radiosensitization compared to BRCA1-proficient cells. Furthermore, when combined with RT, olaparib inhibited DNA damage repair and PARP1 activity, increased apoptosis, decreased growth of HGSOC xenografts and increased overall host survival. The growth-inhibitory effects of the combined olaparib and RT treatment were more pronounced in mice bearing BRCA1-deficient tumors compared to BRCA1-proficient tumors.

CONCLUSIONS: These results provide a preclinical rationale for improved treatment modalities using olaparib as an effective radiosensitizer in HGSOC, particularly in tumors with BRCA1-deficiencies.

Jang et al. BMC Cancer (2015) 15:89
DOI 10.1186/s12885-015-1090-7

BMC Cancer

RESEARCH ARTICLE Open Access

Radiosensitization with combined use of olaparib and PI-103 in triple-negative breast cancer

Na Young Jang[1,6†], Dan Hyo Kim[2†], Bong Jun Cho[2†], Eun Jung Choi[2], Jong-Soo Lee[3], Hong-Gyun Wu[4], Eui Kyu Chie[4] and In Ah Kim[2,4,5*]

Clin Cancer Res. 2018 Oct 15;24(20):4949-4959. doi: 10.1158/1078-0432.CCR-18-0467. Epub 2018 Jul 5.

Final Report of a Phase I Trial of Olaparib with Cetuximab and Radiation for Heavy Smoker Patients with Locally Advanced Head and Neck Cancer.

Karam SD, Reddy K, Blatchford PJ, Waxweiler T, DeLouize AM, Oweida A, Somerset H, Marshall C, Young C, Davies KD, Kane M, Tan AC, Wang XJ, Jimeno A, Aisner DL, Bowles DW, Raben D.

Author information

Abstract

Purpose: Our goal was to evaluate the safety and toxicity of combining a PARP inhibitor, olaparib, with cetuximab and fractionated intensity-modulated radiotherapy for patients with locally advanced head and neck cancer and heavy smoking histories. **Patients and Methods:** Patients with ≥10 packs/year history of smoking were treated with olaparib at doses ranging from 25-200 mg orally twice daily beginning approximately 10 days prior to initiation of and with concurrent radiation (69.3 Gy in 33 fractions) using a time-to-event continual reassessment method model. Cetuximab was administered starting approximately 5 days prior to radiation per standard of care. **Results:** A total of 16 patients were entered onto the study, with 15 evaluable for acute toxicity. The most common treatment-related grade 3-4 side effects were radiation dermatitis and mucositis (38% and 69%, respectively). The MTD was determined to be 50 mg orally twice daily, but the recommended phase II dose was deemed to be 25 mg orally twice daily. At a median follow-up of 26 months, the actuarial median overall survival was 37 months, but was not reached for other endpoints. Two-year overall survival, progression-free survival, local control, and distant control rates were 72%, 63%, 72%, and 79%, respectively. Patients who continued to smoke during therapy experienced higher recurrence rates. MYC and KMT2A were identified as potential correlatives of response on gene amplification and mutational analysis. **Conclusions:** Olaparib at 25 mg orally twice daily with concurrent cetuximab and radiation was well tolerated with reduced dermatitis within the radiation field. Response rates were promising for this high-risk population. Clin Cancer Res; 24(20); 4949-59. ©2018 AACR.

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La Radioterapia nella malattia oligometastatica

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Background

Results

Conclusions

Conclusions

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«This review provides preliminary evidence that **ablative radiotherapy** may play an **important role in management of oligometastatic breast cancer** and its use is rapidly gaining consensus due to its **non-invasive nature, excellent safety profile, established efficacy** in achieving durable local control in a cost-effective manner»

- Oligometatatic BC is a distinct state characterized by an indolent biology and associated with a favorauble prognosis
- SBRT should improve clinical outcome
- Selection of the true oligometastatic patient is the challenge
- Level 1 evidence lacking
- Need to enroll oligometastatic patients into randomized trials

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Thank you