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"ESISTE UN RUOLO PER LA RADIOTERAPIA NELLA MALATTIA OLIGOMETASTATICA?"

Filippo Alongi MD

Radiotherapy and Radiosurgery
Istituto Clinico Humanitas
Rozzano(Milan)

filippo.alongi@humanitas.it

Associazione Italiana Radioterapia Oncologica

Clinical "dogma" of metastases

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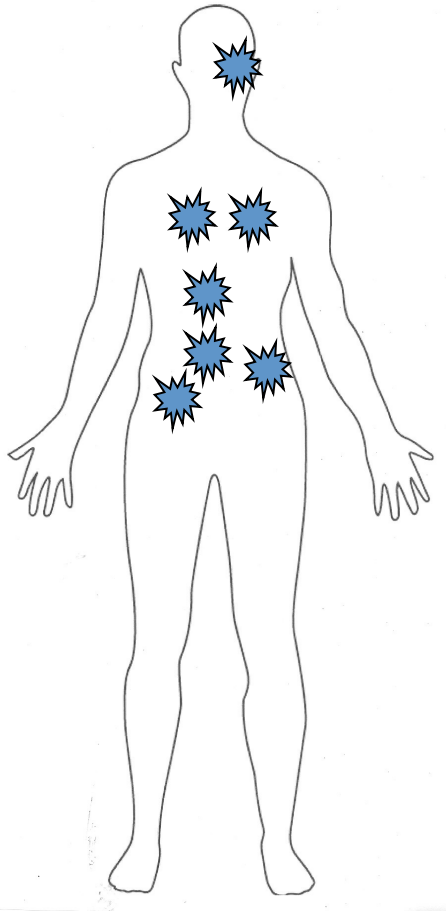
•The clinical dogma proposes that metastases are either absent or are present in uncountable numbers.

• In accordance with this clinical dogma, when patient is metastatic :

-*systemic therapies* are usually proposed to increase survival

- *local therapy* is indicated only for palliative/ sympthomatic intent.



1. Okunieff P.Seminars in Radiation Oncology Vol: 16 Issue: 2, April, 2006

Oligo-metastases: only a definition?

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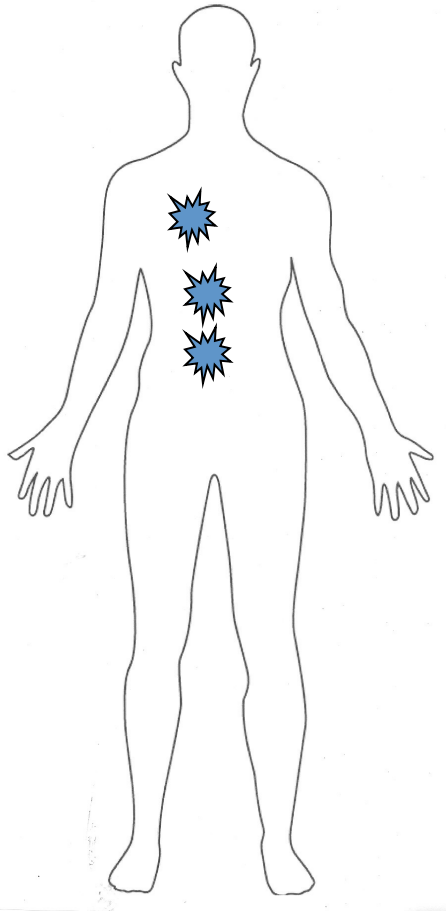
- Improvement in the early detection of metastasis frequently allows the diagnosis of single or limited organ metastases (Oligometastatic stage is defined as 1-5 secondary lesions in 1-2 organs).

- Hellman and Weichselbaum (1995).. *"there is a subgroup of patients with an intermediate phase of metastatic disease, that presents a potential for disease control with the ablation of the few metastases"*

- Are to prescribe only ***palliative local treatments*** for this kind of patients?



1. Rubin P, et al. Semin Radiat Oncol, 16: 120-130, 2006.

To Treat Oligometasatases: a mirage?

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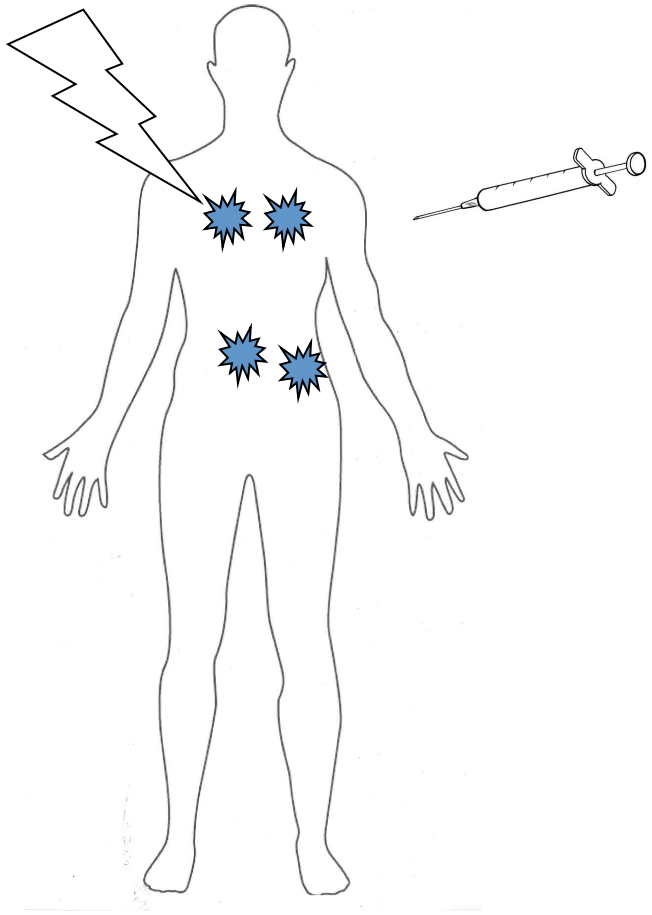
•*Systemic therapy* can potentially treat microscopic metastatic disease in the body but the response rates for gross disease have been suboptimal in most of solid cancers.

•*Local Therapies* for metastases usually fails because of the presence of :
-either undetected micrometastases
-or simply too many lesions.

•But what is the potential of *local therapies* to few lesions (preferable in a single organ), in a patients with good PS?

•Can we>survival in oligomts combining chemotherapy for micrometasteses and aggressive local therapies for the macroscopic ones?



1. JC Yang. Seminars in Radiation Oncology Vol: 16 Issue: 2, April, 2006

Surgery of metastases: the best choice?

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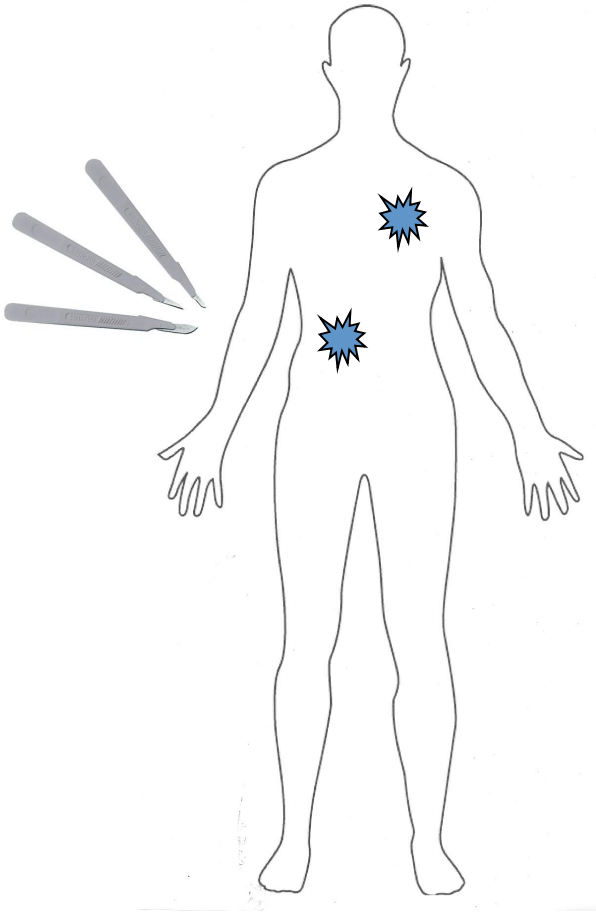
- In several sites, *surgery of metastases prolongs survival* in selected patients.
- For example, *surgical resection* is the standard choice for patients with oligometastatic lung cancer.
- Unfortunately the benefits of resection and appropriate *selection criteria* in patients who develop metastasis are still poorly defined.



1. Miller G, et al. J Am Coll Surg, 205: 231-238, 2007.
2. Rubin P, et al. Semin Radiat Oncol, 16: 120-130, 2006.

SBRT: an option or the new best choice?

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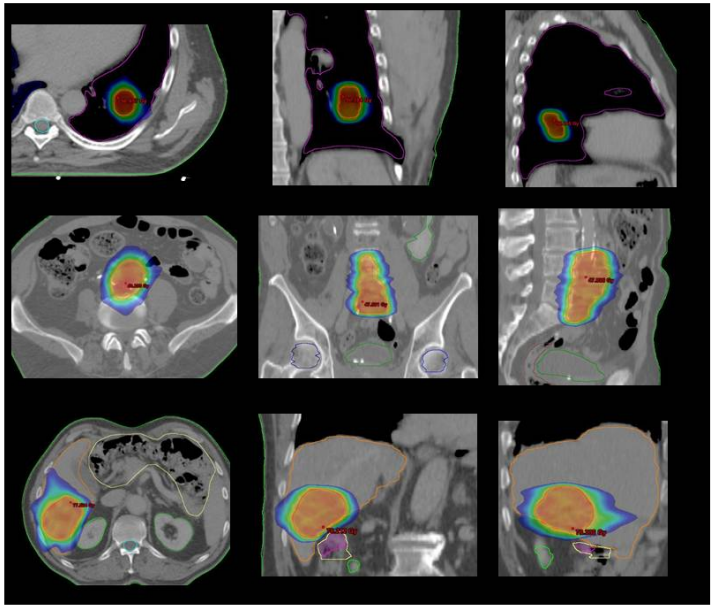
- The primary goal of SBRT is to achieve local control of targeted tumor deposits with *ablative* doses.

- In general SBRT for oligometastases should follow the same treatment philosophy relating to indications for surgical metastasectomy.

- As smaller foci of metastases are found, high conformal radiation, such as SRT or similar techniques, may well prove *less invasive and more/equal effective* than surgery because of decreasing morbidity and the potential of delivering ablative treatment more economically on an outpatient basis.



1. Thariat J et alTrends in radiation therapy for the treatment of metastatic and oligometastatic disease in 2010.Bull Cancer. 2010

2. Timmerman RD, et al: Stereotactic body radiation therapy in multiple organ sites, J Clin Oncol, 25: 947-952, 2007.

SBRT in primary early LUNG

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2010

CLINICAL INVESTIGATION

STEREOTACTIC BODY RADIOTHERAPY (SBRT) FOR OPERABLE STAGE I NON–SMALL-CELL LUNG CANCER: CAN SBRT BE COMPARABLE TO SURGERY?

HIROSHI ONISHI, M.D.,* HIROKI SHIRATO, M.D.,† YASUSHI NAGATA, M.D.,‡ MASAHIRO HIRAOKA, M.D.,§

RESULTS

- **The survival rate for SBRT is potentially comparable to that for surgery.**

SBRT in LUNG: NSCLC and MTS

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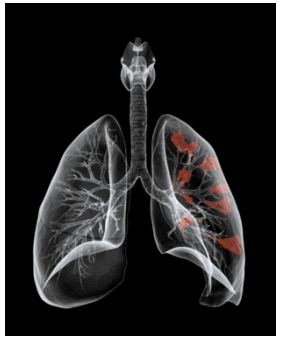

ELSEVIER

2006: Review of data until 2005

Seminars in RADIATION ONCOLOGY

Stereotactic Body Radiation Therapy for Extracranial Oligometastases: Does the Sword Have a Double Edge?

Madeleine Carey Sampson, MD, Alan Katz, MD, MPH, and Louis S. Constine, MD

Author	No. of Patients	% NSCLC (v mets) (%)	Median Lesion Size (mL)	Total dose (Gy)	Crude Local Control (LC) (%)	Median Follow-up Time in months (range)	Acute Toxicity (Grade 1–2) (%)	Acute Toxicity (Grade 3–5) (%)	Chronic Toxicity (Grade 3–5) (%)
Blomgren et al[21]	13	18	48 mL	15–45	94	8.2	NR	NR	6
Uematsu et al[22]	45	35	7.2 mL* (mean)	30–75	97	11	11	0	0
Wulf et al[23]	26	44	57 mL	30	85	8	22	0	7 1 death
Nakagawa et al[24]	15	5	Lung 4.5 mL (CW 40 mL)	15–25	95	10	0	0	0
Fukumoto et al[25]	22	100	10 mL*	48–60	94	24 (2–44)	27	0	0
Nagata et al[26]	40	78	12.6 mL	40–48	94 lung ca) 67 (mets)	18–19	NR	0	0
Hof et al[27]	10	100	12 mL	19–26	80	14.9	0	0	0
Timmerman et al[28]	37	100	22.5 mL	24–60	84 (resp 87)	15.2	49	8	0
Hara et al[29]	23	22	5.8 mL (mean)	20–30	83	13	13	4	0
Lee et al[30]	28	32	41.4 mL (PTV)	30–40	89	18	0	0	0
Onimaru et al[31]	45	57	9.2 mL*	48–60	88	17	4	2 1 death	0
Uematsu et al[32,33]	50	100	17 mL*	50–60	94	60	16	0	0
Whyte et al[34]	23	65	NR (range 0.5–65 mL*)	15	~91 (2/23 PD, NR)	7	0	0	0
Onishi et al[35]	245	100	11.5 mL*	18–75	85.5	24	11	4	1.2
Wulf et al[36]	61	33	22 mL	10–26	95 (lung ca) 90 (mets)	9–11	16	0	0

SBRT in LUNG oligometastases

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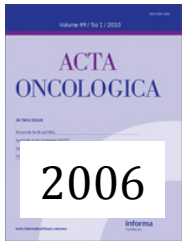
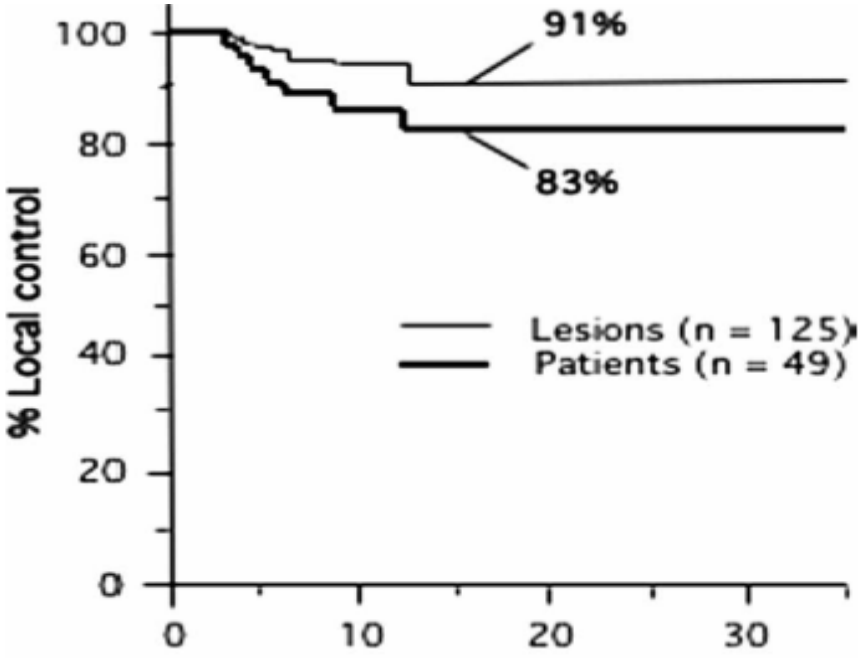
Stereotactic Body Radiation Therapy (SBRT) for lung metastases

PAUL OKUNIEFF[1], ANNCATRINE L. PETERSEN[1], ABRAHAM PHILIP[1], MICHAEL T. MILANO[1], ALAN W. KATZ[1], LASZLO BOROS[2] & MICHAEL C. SCHELL[1]





SBRT in LUNG oligometastases

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2008

STEREOTACTIC BODY RADIOTHERAPY FOR OLIGOMETASTATIC LUNG TUMORS

YOSHIKI NORIHISA, M.D.,* YASUSHI NAGATA, M.D., PH.D.,* KENJI TAKAYAMA, M.D.,* YUKINORI MATSUO, M.D., PH.D.,* TAKASHI SAKAMOTO, M.D.,† MASATO SAKAMOTO, M.D.,‡ TAKASHI MIZOWAKI, M.D., PH.D.,* SHINSUKE YANO, B.S.,* AND MASAHIRO HIRAOKA, M.D., PH.D.*

* Department of Radiation Oncology and Image-Applied Therapy, Kyoto University Graduate School of Medicine, Kyoto, Japan; † Department of Radiation Oncology, Kumamoto University Graduate School of Medical Sciences, Kumamoto, Japan; and ‡ Department of Radiology, Japanese Red Cross Society Wakayama Medical Center, Wakayama, Japan

Purpose: Since 1998, we have treated primary and oligometastatic lung tumors with stereotactic body radiotherapy (SBRT). The term "oligometastasis" is used to indicate a small number of metastases limited to an organ. We evaluated our clinical experience of SBRT for oligometastatic lung tumors.

Methods and Materials: A total of 34 patients with oligometastatic lung tumors were included in this study. The primary involved organs were the lung ($n = 15$), colorectum ($n = 9$), head and neck ($n = 5$), kidney ($n = 3$), breast ($n = 1$), and bone ($n = 1$). Five to seven, noncoplanar, static 6-MV photon beams were used to deliver 48 Gy ($n = 18$) or 60 Gy ($n = 16$) at the isocenter, with 12 Gy/fraction within 4–18 days (median, 12 days).

Results: The overall survival rate, local relapse-free rate, and progression-free rate at 2 years was 84.3%, 90.0%, and 34.8%, respectively. No local progression was observed in tumors irradiated with 60 Gy. SBRT-related pulmonary toxicities were observed in 4 (12%) Grade 2 cases and 1 (3%) Grade 3 case. Patients with a longer disease-free interval had a greater overall survival rate.

Conclusion: The clinical result of SBRT for oligometastatic lung tumors in our institute was comparable to that after surgical metastasectomy; thus, SBRT could be an effective treatment of pulmonary oligometastases.

SBRT in LUNG oligometastases

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Contents lists available at ScienceDirect

Lung Cancer In press

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

Stereotactic body radiation therapy for lung metastases

Umberto Ricardi[a], Andrea Riccardo Filippi[a,*], Alessia Guarneri[a], Riccardo Ragona[b], Cristina Mantovani[a], Francesca Giglioli[b], Angela Botticella[a], Patrizia Ciammella[c], Cristina Iftode[a], Lucio Buffoni[d], Enrico Ruffini[e], Giorgio Vittorio Scagliotti[f]

[a] Radiation Oncology Department, University Hospital S. Giovanni Battista di Torino, Via Genova 3, 10126, Torino, Italy
[b] Medical Physics, University Hospital S. Giovanni Battista di Torino, Via Genova 3, 10126 Torino, Italy
[c] Radiation Oncology Department, Arcispedale S.M. Nuova Hospital, Viale Risorgimento 80, 42123 Reggio Emilia, Italy
[d] Medical Oncology Department, University Hospital S. Giovanni Battista di Torino, Via Genova 3, 10126 Torino, Italy
[e] Thoracic Surgery Department, University Hospital S. Giovanni Battista di Torino, Via Genova 3, 10126 Torino, Italy
[f] Thoracic Oncology Department, University Hospital S. Luigi, Regione Gonzole 10, 10043 Orbassano, Italy

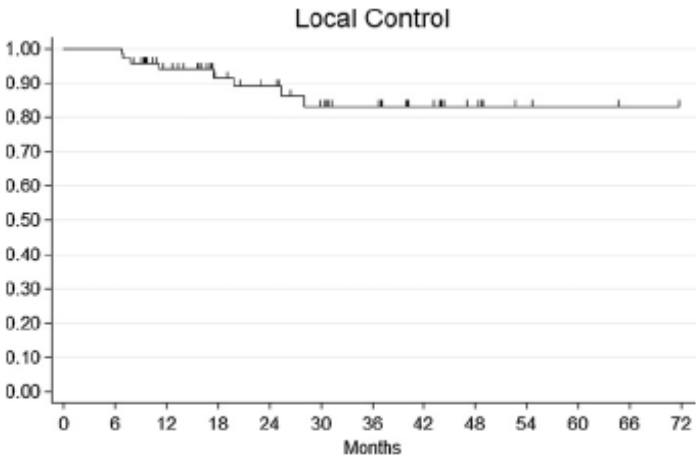

Fig. 1. Actuarial local control.

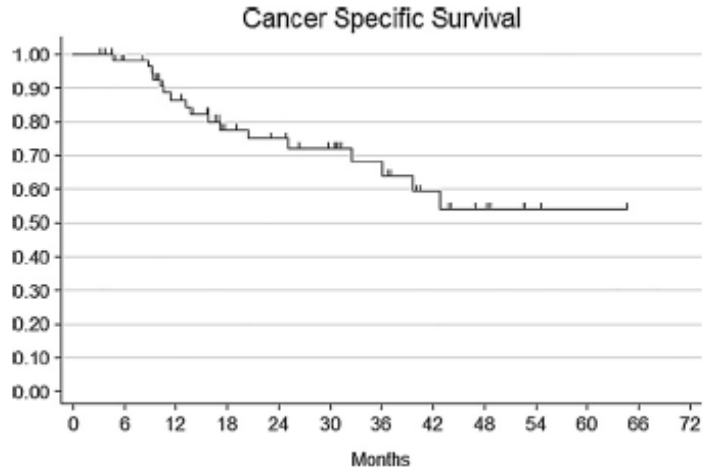

Fig. 3. Cancer-specific survival.

TRUE BEAM in LUNG: preliminary clinical results @ICH

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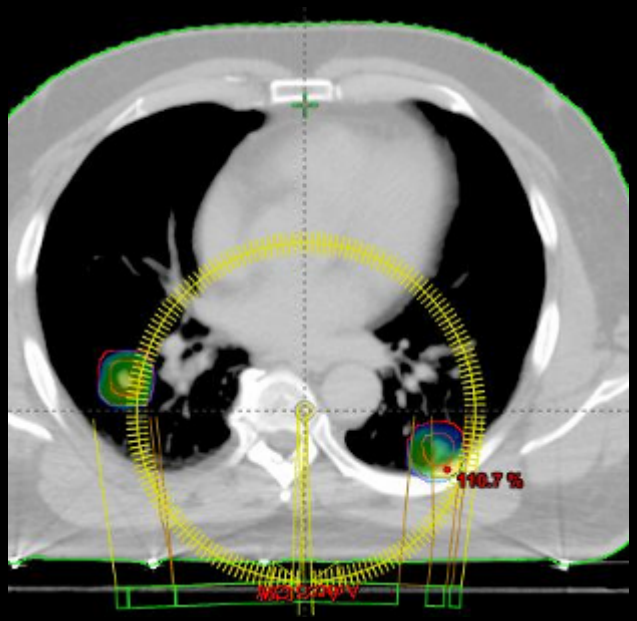
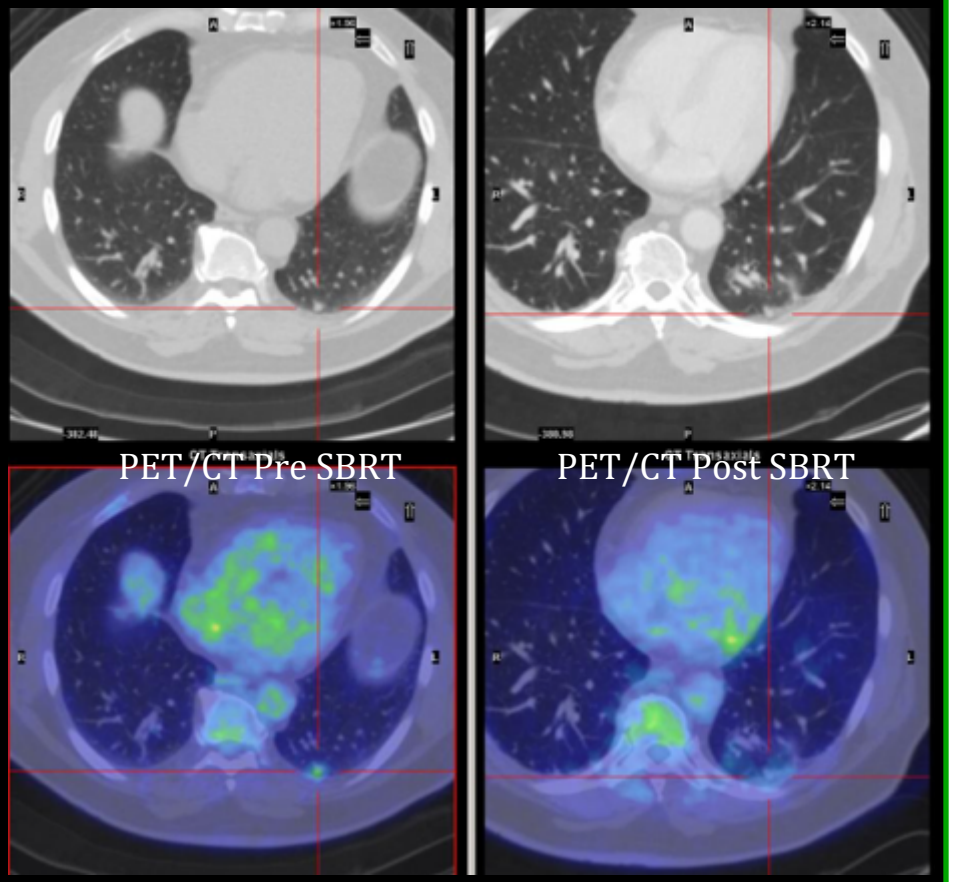
SBRT treatment for rectum bilateral lung metastases





PET/CT Pre SBRT

PET/CT Post SBRT

CR @ PET/TC after 48 Gy in 4 fr. with FFF beams

SBRT in LUNG oligometastases

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CRITICAL ISSUES

- Heterogeneity of fractions and planning method
- Necessary evaluation of the pulmonary function and organ motion
- Absence of phase III trials

CONCLUSIONS

- Percentages of local control (>85% in most trials)
- Low toxicity profile
- Optimal doses and fractions being defined

SBRT liver lesions

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Reference	N° of patients	N° of Targets	Radiation Dose	Median FUP	Outcomes
Hoyer et al [21]	44		45 Gy in 3 fractions of 15 Gy prescribed to 95%		LC: 86% OS: 38% at 24 months.
Kavanagh et al [22,23]	36		60 Gy in 3 fractions of 20 Gy	19 months	LC: 93% at 18 months
Herfarth et al. [24,25]	33	56	14–26 Gy in single fraction prescribed to 80%	18 months	LC: 78% (crude); 75%, 71% and 67% at 6, 12 and 18 months, respectively OS: 72% at 1 year RILD: 0%
Goodman et al [26]	26	19	18–30 Gy in single fraction prescribed to 80%	17.3 months	OS: 61.8% and 49.4% at 1 and 2 year, respectively Late G2 GI toxic effects: 2/26 pts
Lee et al. [27]	70	143	27.7–60.0 Gy in 6 fractions prescribed to isodose line covering PTV (median 41.4 Gy)	10.8 months for 68 assessable patients	LC: 71% at 1 year OS: 47% at 18 months PFS: median 3.7 months Acute grade 3 toxic effects: 10% Late grade 4 and 5 toxic effects: 2.9% and 1.5%, respectively
Mendez Romero et al. [28]	14	34	37.5 Gy in 3 fractions prescribed to 65%	12.9 months	LC: 94% (crude); 100% and 86% at 1 and 2 years, respectively OS: 85% and 62% at 1 and 2 years, respectively Grade 3 toxic effects: acute (n = 3); late (n = 1) Grade 4 or higher toxic effects: 0%
Rusthoven et al. [29]	47	63	12–20 Gy in 3 fractions prescribed to isodose line covering PTV	16 months	LC: 95% and 92% at 1 and 2 years, respectively OS: 30% at 2 years Grade 4 toxic effects: 0%

SBRT liver lesions

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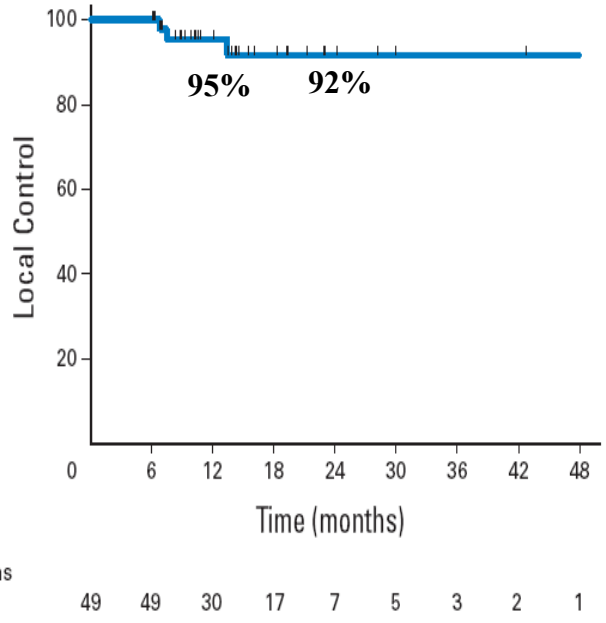
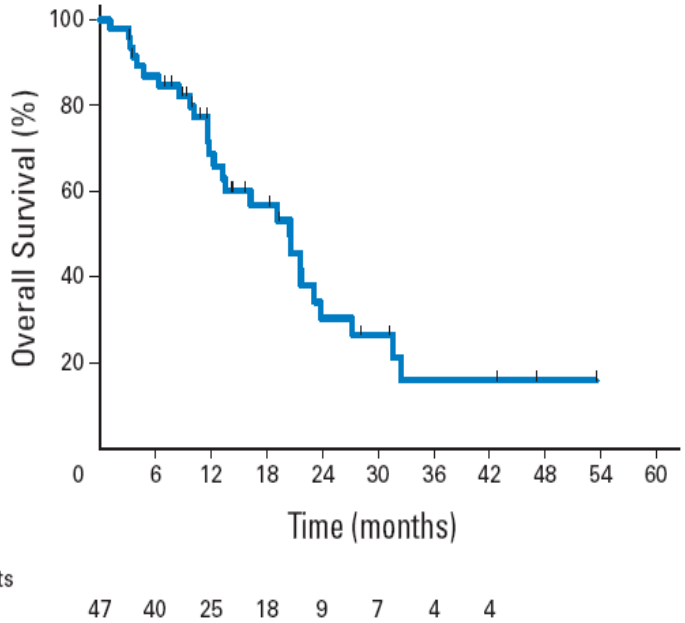
Multi-Institutional Phase I/II Trial of Stereotactic Body Radiation Therapy for Liver Metastases

Kyle E. Rusthoven, Brian D. Kavanagh, Higinia Cardenes, Volker W. Stieber, Stuart H. Burri, Steven J. Feigenberg, Mark A. Chidel, Thomas J. Pugh, Wilbur Franklin, Madeleine Kane, Laurie E. Gaspar, and Tracey E. Schefter





Humanitas protocol in LIVER OLIGOMTS

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- From December 2009 to April 2011
- 43 patients (48 lesions)
- 75Gy: 38 lesions, 67.5Gy: 2 lesions and 56.25Gy 8 lesions
- Only 3 acute toxicity gr2 (vomiting)
- Median FU: 7 months 22 CR - 16 PR - 7 SD - 3 PD

LOCAL CONTROL 93,7%

INCLUSION CRITERIA

- Inoperable or medically unsuitable for resection
- Maximum tumour diameter < 6cm
- ≤ 3 discrete lesions
- Performance status 0-2
- Good compliance to treatment

	Dose/fraction	Number fractions	Median dose
Standard dose	**25Gy**	**3**	**75 Gy**
Dose reduction 10%	**22.5 Gy**	**3**	**67.5 Gy**
Dose reduction 20%	**20. 63 Gy**	**3**	**61.89 Gy**
Dose reduction 30%	**18.75 Gy**	**3**	**56.25 Gy**

SBRT liver: **25Gy x 3; 10FFF; DR 2400.**

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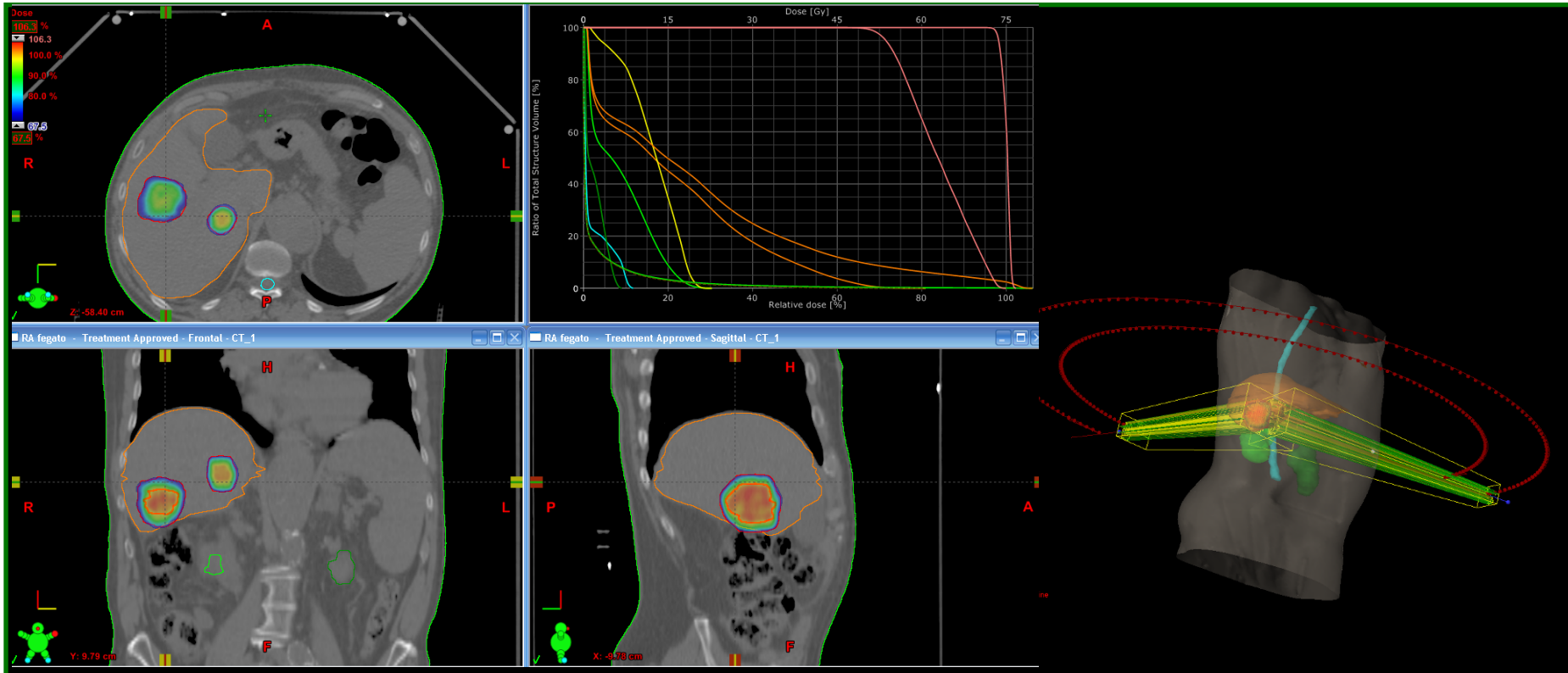

1 isocentre, 2 arcs
Jaw tracking

MU:3174+3004
BOT:170s

SBRT liver Clinical Response after TB FFF

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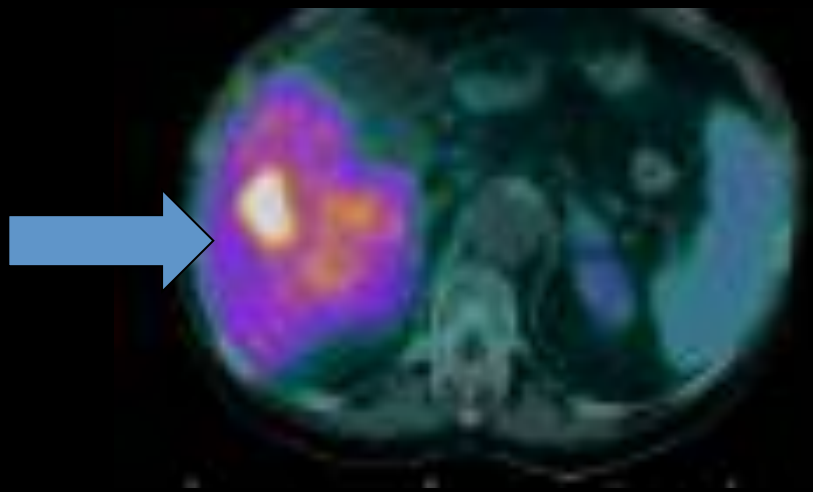
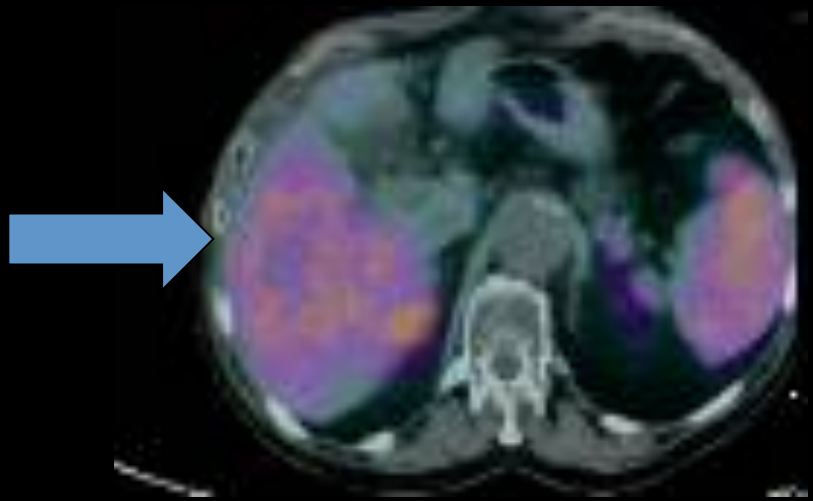


PET pre TB



PET post TB

SBRT:75 Gy in 3 fr. with TB-FFF

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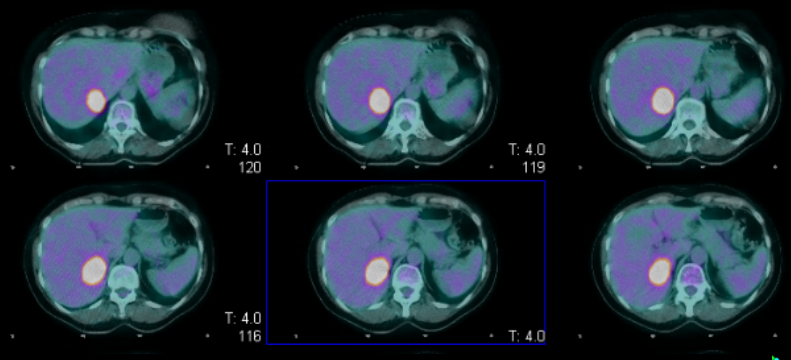
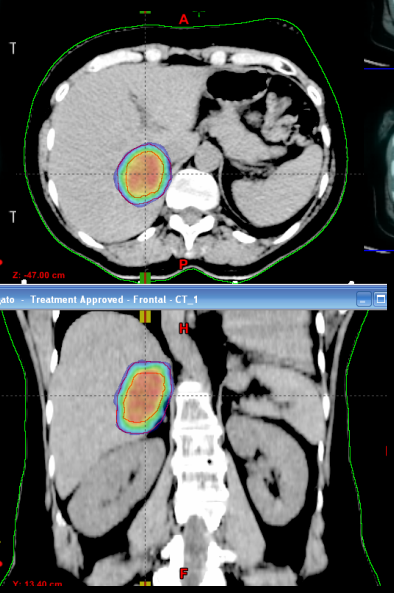
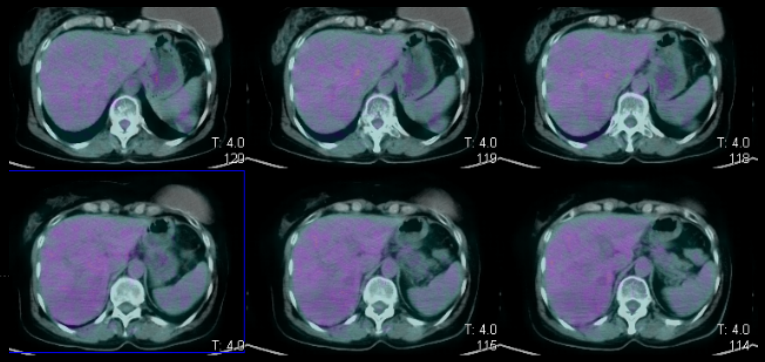
PET pre

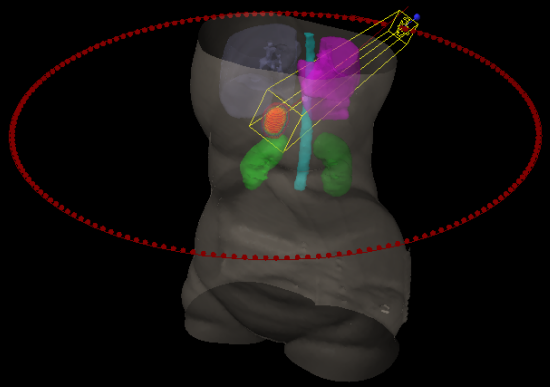
RapidArc
1 isocentre
1 arc
Jaw tracking

PET post

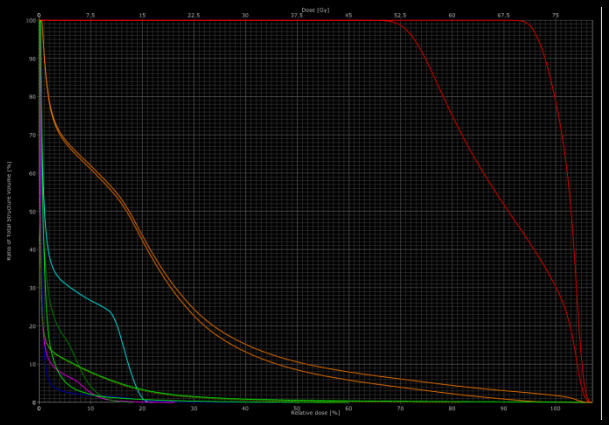








MU:5103
BOT:130s



buschi

SBRT in LIVER oligometastases

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CRITICAL ISSUES

•It is possible to treat a partial liver mass with much higher tumouricidal doses than those generally considered tolerable (RILD), on condition that an adequate amount of healthy parenchyma is spared.

•The follow-up of trials reported in the literature is relatively short-term, typically less than 18 months

CONCLUSIONS

•Local control reported in the literature varies between 57 and 100%; this could be advantageous in terms of survival in diseases where the presence of hepatic metastases is not necessarily a sign of systemic dissemination.

•Tolerance to treatments is usually good.

SBRT in lymph node mts

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Author	Pts	Fractionation	Primary	Planning	Disease control	Survival	Toxicity	Complications
Jereczek-Fossa IEO	14	27Gy/2-3fr 33Gy/3-5fr	Prostatic ca.	Choline Pet	5/14 PD other sites 1/14 Bpd	-	0%	-
Klim	7	48Gy/3fr	Gastric ca.	-	5/7 CR 2/7 PR	43% (3yrs OSS 29%	0%	-
Choi	30	33-45Gy/3fr	Uterus ca.	CAT o PET	55% PD altre sedi	50,1% (4yrs)	20%	6 tox G3
Bignardi ICH	19	45Gy/6fr	Heterogenous	CAT	77,88%	-	0%	-
Di Muzio HSR	27	57.5Gy-72.6Gy/28fr	prostatic ca.	Choline Pet	13/15 CR 2/15 PR	-	-	

CRITICAL ISSUES

- Isolated experiences > necessity for phase II and III trials.
- Necessity for devices ad hoc to reduce respiratory events
- Evaluation of tolerance doses to the vascular walls

DATA: Courtesy of AIRO GRUPPO STRT

SBRT abdominal lymph nodes

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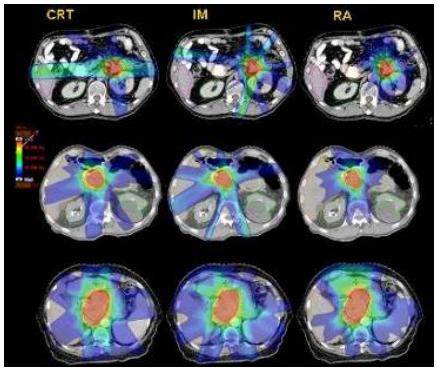
Abdomen:LN mts

CRITICAL APPRAISAL OF VOLUMETRIC MODULATED ARC THERAPY IN STEREOTACTIC BODY RADIATION THERAPY FOR METASTASES TO ABDOMINAL LYMPH NODES

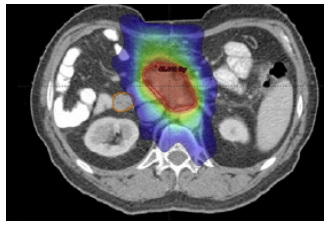
MARIO BIGNARDI, M.D.,* LUCA COZZI, PH.D.,† ANTONELLA FOGLIATA, M.SC.,† PAOLA LATTUADA, M.SC.,* PIETRO MANCOSU, M.SC.,* PIERA NAVARRIA, M.D.,* GAETANO URSO, M.SC.,* SABRINA VIGORITO, M.SC.,* AND MARTA SCORSETTI, M.D.*

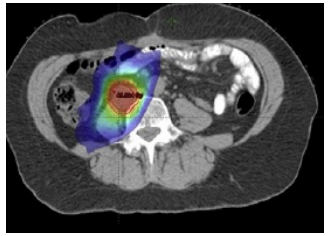


DOSE: 45 Gy/ 6 Fr

CLINICAL OUTCOME OF HYPOFRACTIONATED STEREOTACTIC RADIOTHERAPY FOR ABDOMINAL LYMPH NODE METASTASES

MARIO BIGNARDI, M.D.,* PIERA NAVARRIA, M.D.,* PIETRO MANCOSU, M.SC.,* LUCA COZZI, PH.D.,† ANTONELLA FOGLIATA, M.SC.,† ANGELO TOZZI, M.D.,* SIMONA CASTIGLIONI, M.D.,* CARLO CARNAGHI, M.D.,† MARIA CHIARA TRONCONI, M.D.,† ARMANDO SANTORO, M.D.,† AND MARTA SCORSETTI, M.D.*





SBRT in abdominal TARGETS

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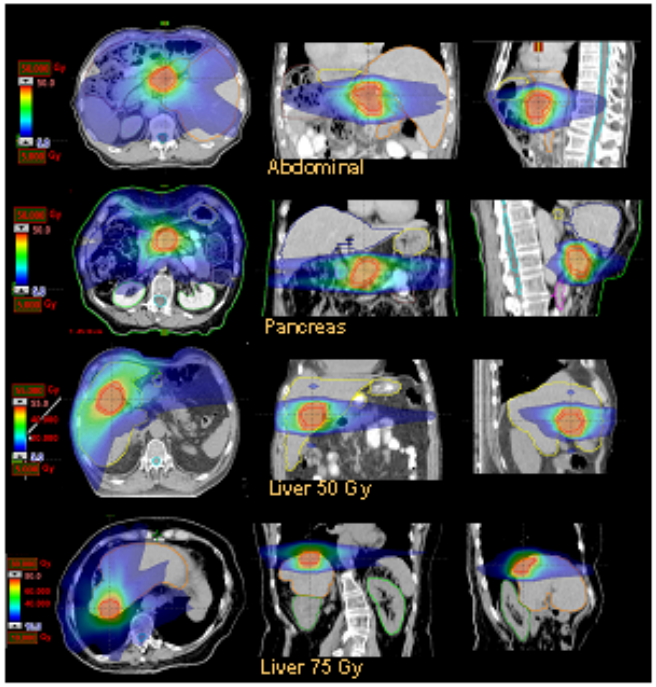

Stereotactic body radiation therapy for abdominal targets using volumetric intensity modulated arc therapy with RapidArc: feasibility and clinical preliminary results

Marta Scorsetti,1 Mario Bignardi M,1 Filippo Alongi,1 Antonella Fogliata c,2 Pietro Mancosu 1 Piera Navarria,1 Simona Castiglioni,1 Sara Pentimalli,1 Angelo Tozzi MD,1 Luca Cozzi,2

1 IRCCS Istituto Clinico Humanitas, Rozzano (Milano), Italy
2 Oncology Institute of Southern Switzerland, Bellinzona, Switzerland

Abdominal lymph nodes

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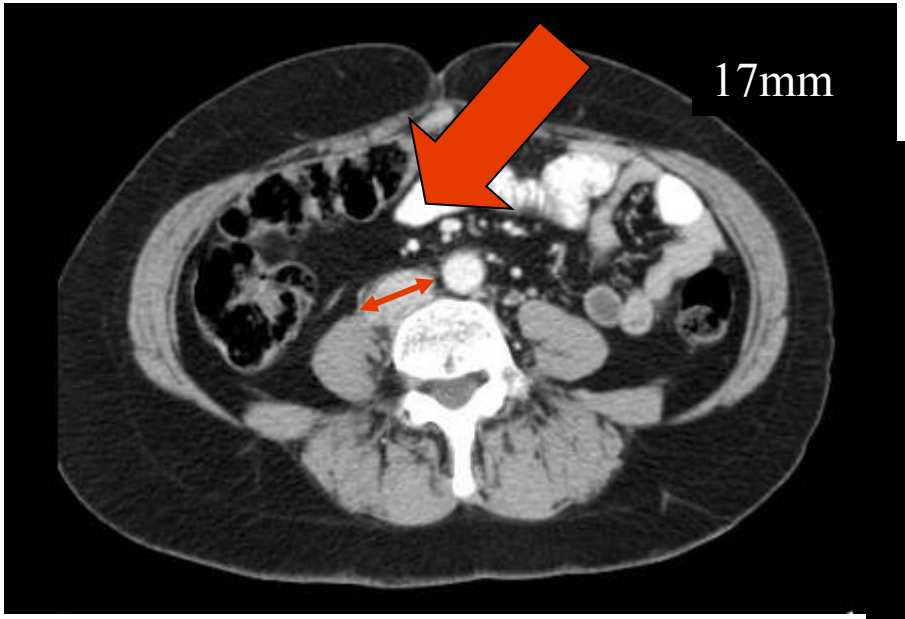
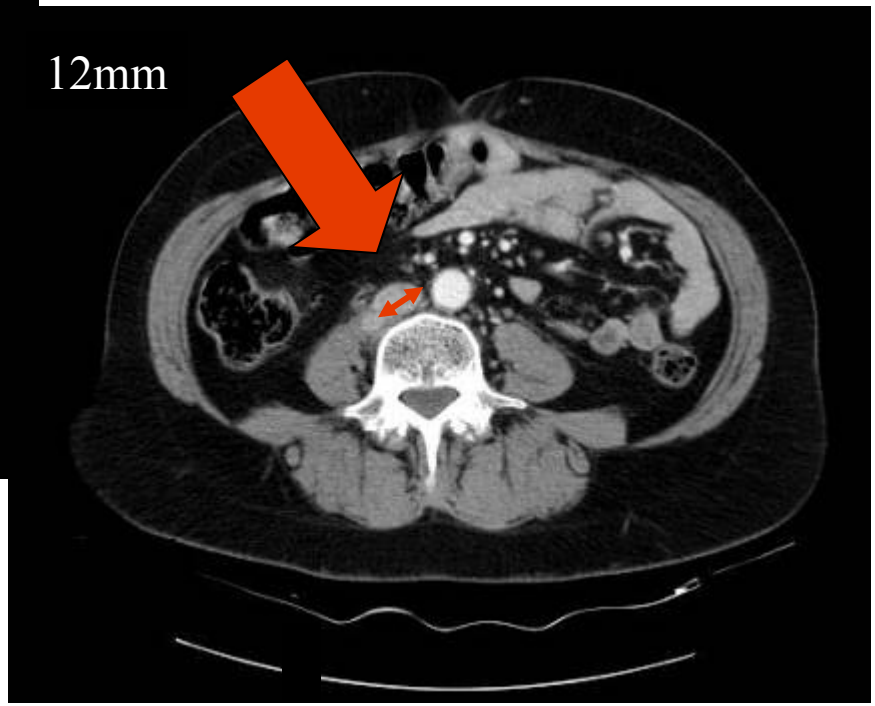
Pz. 66 y, M+ from colon cancer





After 30 days

Abdominal lymph nodes

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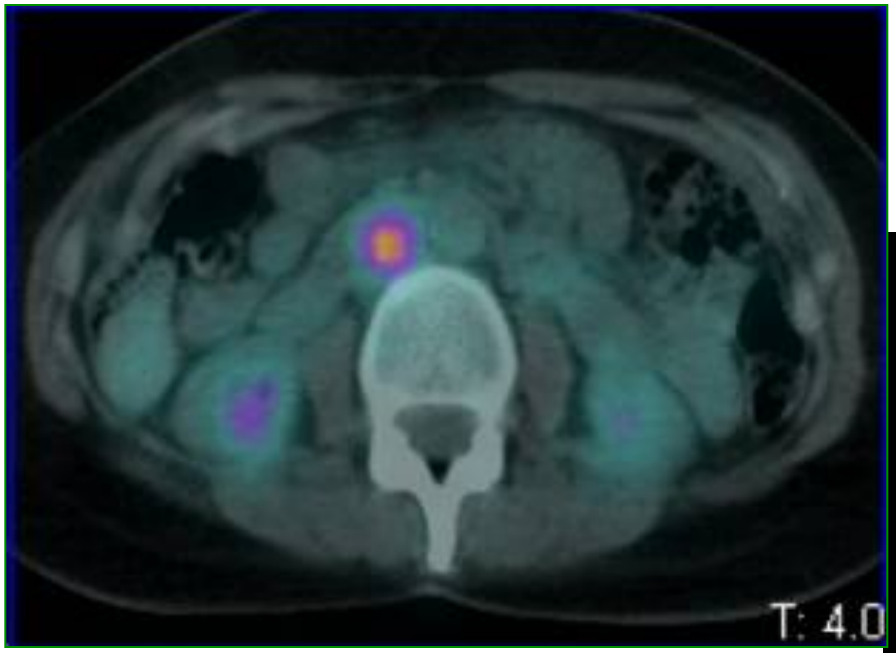
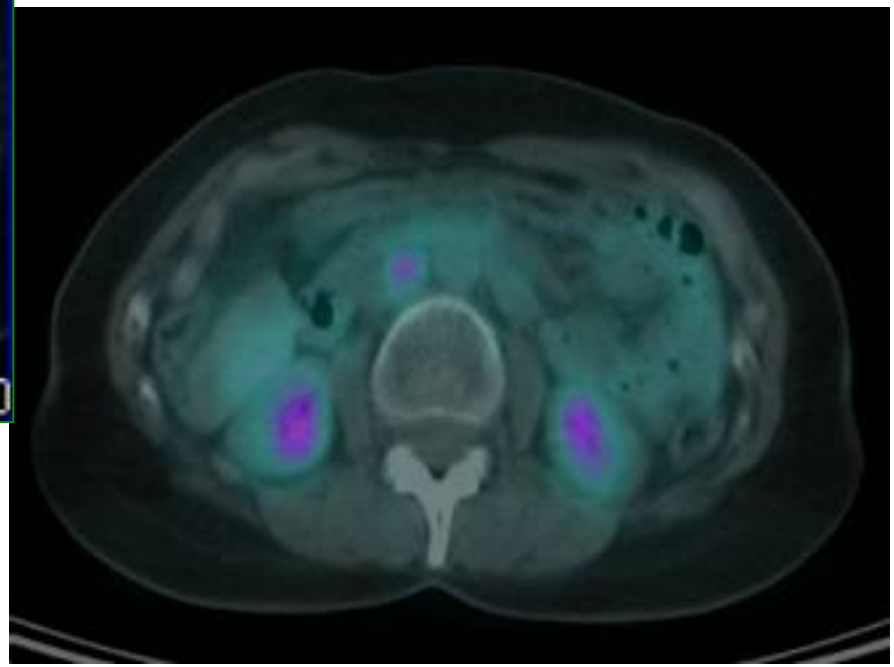


Pz. 59 y, M+ from rectal cancer



Paracaval lymph-node → RC at 6 months with PET

SBRT: 7.5Gyx6;10FFF;DR 2400.

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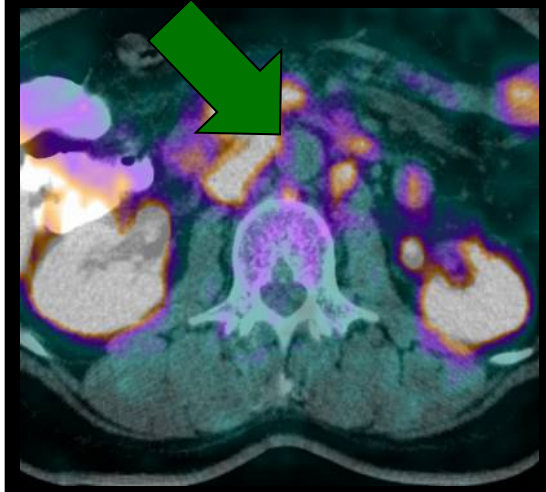
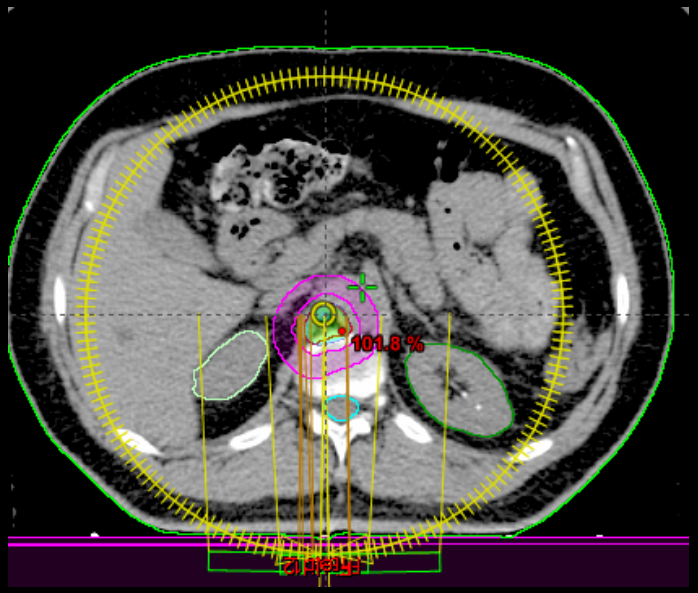
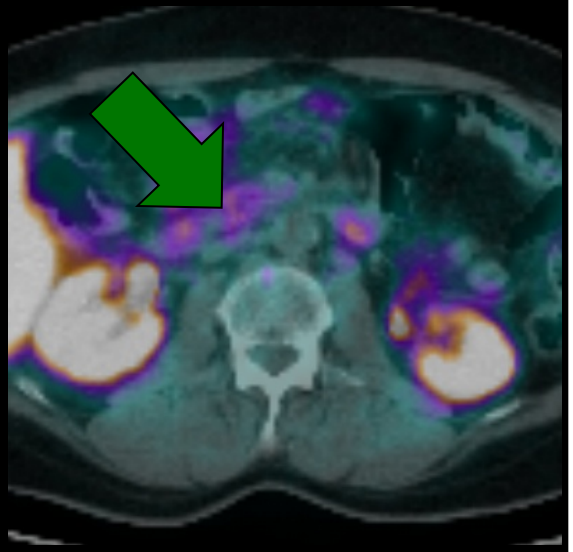
11C-Choline PET for prostate cancer oligomets







PSA pre SBRT: 17,4ng/mL

RapidArc planning

PSA post SBRT: 1,02ng/mL

SBRT in adrenal gland oligometastases

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Study	Number of pts.	Median dose and n of fractions(fr.)	Median Follow-up in months	Local control rate	Overall Survival	Toxicity
Casamassima et al.[21]	48	36Gy/3 fr.	16.2(3-63)	90%(at 1 -2 years)	39.7%(at 1 year) 14.5%(at 2 year)	1 case of grade II adrenal insufficiency
Chawla et al.[17]	30	40Gy/10 fr.	9.8(3.2–28.3)	55%(at 1 year)	44%(at 1 year) 25%(at 2 year)	mild fatigue/ nausea grade 1 were “common”
Oshiro et al.[18]	19	45Gy/10 fr.	11.5 months (5.4–87.8 months).	68%(objective response rate)	56%(at 1 year) 33%(at 2 year) 22%(at 3 year)	1 grade 2 duodenal ulcer
Holy et al.[19]	18	20 Gy/5 fr. or 40 Gy/ 8fr.	21	77%(objective response rate)	23 months(median)	-
Torok et al.[20]	7	16 Gy/1 fr. or 27/3fr.	14(1-60)	63%(at 1 year)	8 months(median)	-

CRITICAL ISSUES

- SBRT for adrenal metastases has been employed and reported in few series
- There is no consensus regarding prescription doses

SBRT in adrenal gland oligometastases

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MATERIALS AND METHODS

•March - July 2010, 34 patients, 36 adrenal metastatic lesions @Istituto Clinico Humanitas and at University of Turin.

•Total RT doses: from 20 Gy in 4 fractions to 45 Gy in 18 fractions (median dose:32 Gy; median number of fraction: 4), prescribed at isodose of 95%.

RESULTS

•TOXITIES: No cases of Grade≥3 ; grade 2 nausea in 2 patients (6%).

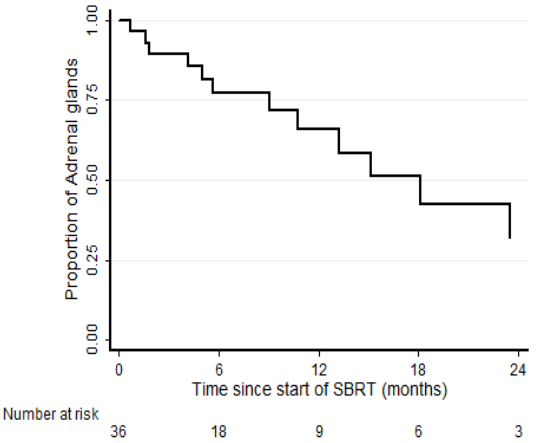
•OS. Median survival was 22,8 months.

•LC: 3/28 lesions (11%) CR, 13/28 (46%) PR, 10/28 (36%) SD and 2/28(7%) progressed in the treated area.

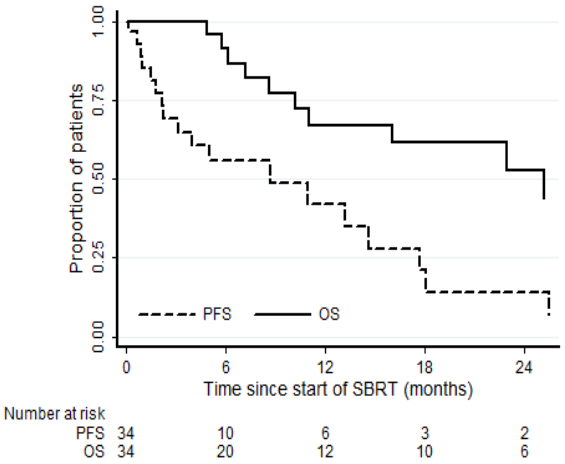
•In 18 cases systemic progression was evident at a median time of occurrence of 10,3 months.

CONCLUSION

•SBRT in adrenal gland metastasis is feasible without significant acute and late side toxicities. **LC was 66 and 32% at 1 and 2 years**, with a median duration of local control greater than 19 months.



Kaplan Meier Curve describing local progression



Kaplan Meier Curve describing PFS and OS

Submitted by Scorsetti M, Alongi F, Filippi AR et al.

SBRT in BONE oligometastases

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Author	Pts/Lesions	Fractionation	Tumour size	Follow-Up	Loca control	OS	Toxicity
Ryu S et Al. 2004	49 / 61 spinal lesionsi	10-16 Gy Single fraction	single vertebral body	6-24 mos	Pain control 85% patientsi	/	/
Yamada Y et Al. 2007	93 / 103 Spinal	18-24 Gy Single fraction	44-316 cm3	15 mos (2-45)	LC 90% Pain control in 100% with dose of 21Gy	OS 15 mos	1 G3 pain 2 vertebral fracture 2 esophagitis G2 1 tracheo-esofageal fistula
Milano MT et Al. 2008	121 / 293 22 bone	50 Gy/5Fr	21.5 ml (0.03-422.4)	41 mos (27-77)	LC 2yrs 67% LC 4yes 60% PFS 2yrs 26% PFS 4yrs 20%	OS 50% OS 28%	1 pleural effusion
Greco C et Al. 2010	103 / 126 94 bone	18-24 Gy Single fraction	104.8 cm3 (8.5-1150)	18 mos (2-45)	LC 2yrs 85% (23/24 Gy) LC 2yrs 38% (21/22 Gy) LC 2yrs 25% (18/20 Gy)	/	ACUTE: 2 Gatrointestinal G3 LATE (G3<4%): 1 Gatrointestinal G3 3 radicolopathy 3 peripheral neuropatihy
Nguyen QN et Al. 2009	48 / 55 spinal	24 Gy single Fr (8) 27 Gy/3Fr (34) 30 Gy/5Fr (13)	24-210 cm3	13.1 mos (3.3-54.5)	LC 1aa 82.1% Pain controllo 64% at 9 mos	OS 1yr 2% Median survival 22 mos	pain G3 2% Anemia G3 2% Fatigue G2 13% Nausea G2 11% Sickness G2 7%

DATA: Courtesy of AIRO GRUPPO STRT

SBRT in BONE oligometastases

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CRITICAL ISSUES

- Heterogeneic fractionations: single or multiple.
- Risk of bone fractures, particular attention to vertebral bodies.
- Tolerance dose to the spinal cord variable from the equivalent of 13Gy/single fraction or 20Gy/three fractions (QUANTEC); for the other OAR there are no unique dose constraints.

CONCLUSIONS

- Tumour size and histotype are not correlated with LC, with the exception of metastases from colon adenocarcinoma which shows greater radioresistence.
- From a prognostic viewpoint patients with lesions confined to just one organ have a better life expectancy.
- Doses > 22Gy are necessary in single fractions.

SBRT in "multiorgan" oligometastases

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2011

CRITICAL REVIEW

STEREOTACTIC RADIOTHERAPY OF PRIMARY LUNG CANCER AND OTHER TARGETS: RESULTS OF CONSULTANT MEETING OF THE INTERNATIONAL ATOMIC ENERGY AGENCY

YASUSHI NAGATA, M.D.,* JOERN WULF, M.D.,† INGMAR LAX, PH.D.,‡ ROBERT TIMMERMAN, M.D.,§ FRANK ZIMMERMANN, M.D.,¶ IGOR STOJKOVSKI, M.D.,‖ AND BRANISLAV JEREMIC, M.D.‖

*Hiroshima University Hospital, Department of Radiation Oncology, Hiroshima, Japan; †Institut of Radiation Oncology, Lindenhospital, Bern, Switzerland; ‡Division of Oncology and Hospital Physics, Radiumhemmet, Karolinska University Hospital, Sweden; §Department of Radiation Oncology, The University of Texas Southwestern Medical Center, Dallas, USA; ¶Department of Radiation Oncology, University Hospital, University Basel, Basel, Switzerland; and ‖International Atomic Energy Agency, Vienna, Austria

To evaluate the current status of stereotactic body radiotherapy (SBRT) and identify both advantages and disadvantages of its use in developing countries, a meeting composed of consultants of the International Atomic Energy Agency was held in Vienna in November 2006. Owing to continuous developments in the field, the meeting was extended by subsequent discussions and correspondence (2007–2010), which led to the summary presented here. The advantages and disadvantages of SBRT expected to be encountered in developing countries were identified. The definitions, typical treatment courses, and clinical results were presented. Thereafter, minimal methodology/technology requirements for SBRT were evaluated. Finally, characteristics of SBRT for developing countries were recommended. Patients for SBRT should be carefully selected, because single high-dose radiotherapy may cause serious complications in some serial organs at risk. Clinical experiences have been reported in some populations of lung cancer, lung oligometastases, liver cancer, pancreas cancer, and kidney cancer. Despite the disadvantages expected to be experienced in developing countries, SBRT using fewer fractions may be useful in selected patients with various extracranial cancers with favorable outcome and low toxicity.

How to really select these kind of patients for SBRT?

SBRT in "multiorgan" oligometastases

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•The perfect candidate for local therapy in the case of **"multiorgan oligometastasis"** is difficult to establish.

•Specific selection criteria to offer SBRT to patients with various oligometastatic tumors included:
✓controlled primary,
✓favourable histology,
✓limited metastatic disease,
✓metachronous appearance of metastasis,
✓young age and high performance status of the patient

✓In some reports, the eligibility criteria for SBRT for oligometastatic cancer were:
✓a limited number of metastasis (one or two),
✓ a limited diameter (<4 cm) of metastases,
✓locally controlled primary tumor, and no other metastatic sites.

•Norihisa Y, : Stereotactic body radiotherapy for oligometastatic lung tumors. Int J Radiat Oncol Biol Phys, 72: 398-403, 2008.
•Rubin P,. Solitary metastases: illusion versus reality. Semin Radiat Oncol, 16: 120-130, 2006.
•Nagata Y,. Stereotactic radiotherapy of primary lung cancer and other targets: results of consultant meeting of the International Atomic Energy Agency. Int J Radiat Oncol Biol Phys. 2011 Mar 1;79(3):660-9.

SBRT in multiorgans oligometastases

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An Initial Report of a Radiation Dose-Escalation Trial in Patients with One to Five Sites of Metastatic Disease

Joseph K. Salama,[1,2,3] Steven J. Chmura,[1,2,3] Neil Mehta,[5] Kamil M. Yenice,[1] Walter M. Stadler,[2,4] Everett E. Vokes,[1,2,4] Daniel J. Haraf,[1,2] Samuel Hellman,[1] and Ralph R. Weichselbaum[1,2,3]

Abstract

Purpose: Previous investigations have suggested that a subset of patients with metastatic cancer in a limited number of organs may benefit from local treatment. We investigated whether cancer patients with limited sites of metastatic disease (oligometastasis) who failed standard therapies could be identified and safely treated at one to five known sites of low-volume disease with radiotherapy.

Experimental Design: Patients with one to five sites of metastatic cancer with a life expectancy of >3 months and good performance status received escalating doses of radiation to all known sites of cancer with hypofractionated radiation therapy. Patients were followed radiographically with computed tomography scans of the chest, abdomen, and pelvis and metabolically with [^{18}F] fluorodeoxyglucose-positron emission tomography 1 month following treatment and then every 3 months. Acute toxicities were scored using the National Cancer Institute Common Terminology Criteria for Adverse Events version 3.0 and late toxicities were scored using the Radiation Therapy Oncology Group late toxicity scoring system.

Results: Twenty-nine patients with 56 metastatic lesions were enrolled from November 2004 to March 2007, with a median follow-up of 14.9 months. Two patients experienced acute (radiation pneumonitis and nausea) and one experienced chronic (gastrointestinal hemorrhage) grade ≥3 toxicity. Fifty-nine percent of patients responded to protocol therapy. Twenty-one percent of patients have not progressed following protocol treatment. Fifty-seven percent of treated lesions have not progressed at last follow-up. Progression was amenable to further local therapy in 48% of patients.

Conclusions: Patients with low-volume metastatic cancer can be identified, safely treated, and may benefit from radiotherapy.

Conclusions

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- Data from primarily retrospective literature series suggest that there is a subgroup of patients with limited metastases in site and number—oligometastases—who may benefit from local aggressive therapy

- Some of those patients may potentially have prolonged survival, although such studies are subject to bias.

- Currently, the best clinical evidence comes from prospective phase II trials or large retrospective series

- The best way to define clinical outcome benefits is to perform phase III randomized trials comparing patients with oligometastases treated with systemic therapy alone to patients with oligometastases treated with systemic therapy and local therapy.

RT in OLIGOMTS: Open questions

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- *Selection criteria: who does deserve the treatment?*
- *What is the real cut off between pure palliative or hypothetical curative intent in oligomets pts?*
- *Timing with chemotherapy: how much after, before (or during chemotherapy)?*
- *What is our target? Only oligomets in a single organ? Or more?*