

# XXIV CONGRESSO NAZIONALE AIRO 2014

Padova, 8-11 novembre

## RISULTATI DI UNO STUDIO DI FASE II SULLA RADIOTERAPIA IPOFRAZIONATA ACCELERATA (PROTOCOLLO SHARON) NEL TRATTAMENTO DELLE METASTASI OSSEE COMPLICATE

L. Caravatta 1-2, G. Torre 3, A. A. Woldemariam 4, T. Wondemagegnhu 4,  
F. Deodato 1, C. Digesù 1, D.A. Dawotola 5, J. Kigula-Mugambe 6, G. Macchia 1, G.  
Mantini 7, S. Mignogna 3, V. Picardi 1, T. Salah 8, V. Valentini 7, A.G. Morganti 1-3-7



Fondazione Giovanni Paolo II  
Università Cattolica  
Campobasso

UO Radioterapia Oncologica (1), UO Oncologia Generale (3), Fondazione di Ricerca e Cura "Giovanni Paolo II", Università Cattolica del S. Cuore, Campobasso, Italia;

U.O. Radioterapia sperimentale (2), Centro di Radioterapia e Medicina Nucleare, P.O. Businco, Cagliari, Italia;

Dipartimento di Oncologia (4), Black Lion Hospital, Addis Ababa, Etiopia;

Dipartimento di Radioterapia (5), Centro di Radioterapia e Oncologia, Abuth, Zaria, Nigeria;

Dipartimento di Radioterapia (6), Mulago Hospital, Kampala, Uganda;  
Cattedra di Radioterapia (7), Università Cattolica del S. Cuore, Roma, Italia;

Facoltà di Medicina (8), Università di Assiut, Assiut, Egitto.



**ASL Cagliari**   
SISTEMA SANITARIO DELLA SARDEGNA

**RISULTATI DI UNO STUDIO DI FASE II SULLA RADIOTERAPIA  
IPOFRAZIONATA ACCELERATA (PROTOCOLLO SHARON)  
NEL TRATTAMENTO DELLE METASTASI OSSEE COMPLICATE**

**Up to 70% of cancer patients with bone metastases have symptoms.**

**Bone metastases are the most common cause of cancer pain requiring treatment.**

**Much clinical data has confirmed the effectiveness of RT in local symptomatic control.**

## RISULTATI DI UNO STUDIO DI FASE II SULLA RADIOTERAPIA IPOFRAZIONATA ACCELERATA (PROTOCOLLO SHARON) NEL TRATTAMENTO DELLE METASTASI OSSEE COMPLICATE

**Table 3.** Palliative Radiotherapy for Metastatic Cancer as Delineated in American Society for Therapeutic Radiology and Oncology Treatment Guidelines<sup>13,14</sup>

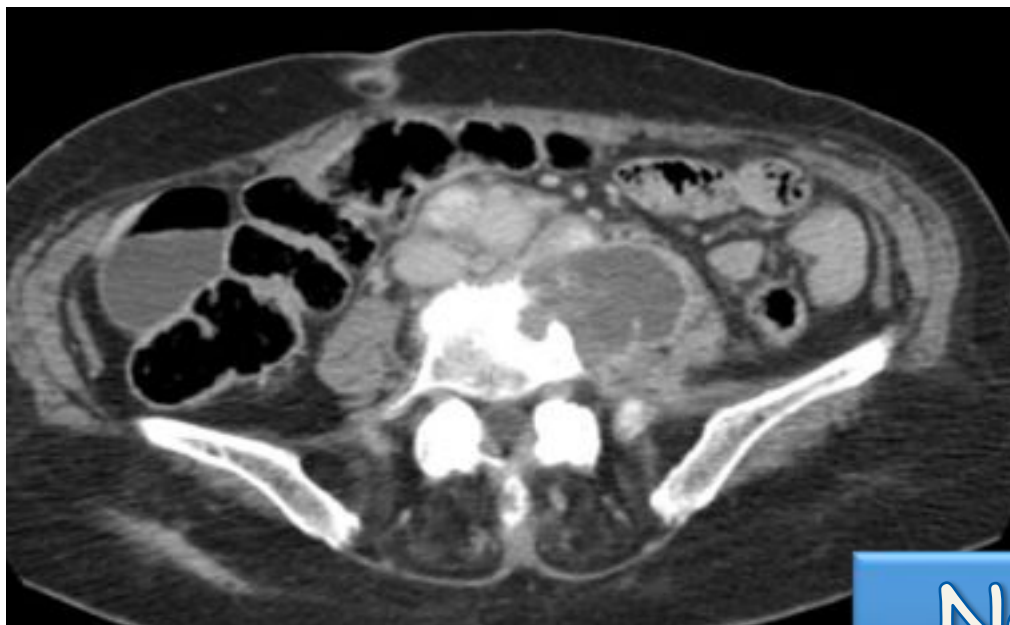
Primary Site and Clinical Circumstances	Recommendations
<b>Bone metastases</b>	
Uncomplicated, painful bone metastases	<ul style="list-style-type: none"> <li>● Acceptable fractionation schemes: 30 Gy in 10 fractions, 24 Gy in six fractions, 20 Gy in five fractions, 8 Gy in one fraction</li> </ul>
Recurrent pain at same skeletal site	<ul style="list-style-type: none"> <li>● Re-treatment may be attempted, taking into account normal tissue tolerance</li> </ul>
Multiple painful osteoblastic metastases	<ul style="list-style-type: none"> <li>● Consider radiopharmaceutical injection</li> </ul>
Spinal cord compression	<ul style="list-style-type: none"> <li>● Surgical decompression plus postoperative radiotherapy</li> <li>● Radiotherapy alone in those who do not qualify for or desire surgery</li> </ul>
Metastases in bones of the spine	<ul style="list-style-type: none"> <li>● Standard external beam radiotherapy</li> <li>● Stereotactic body radiation therapy may be used, although preferably on a trial</li> </ul>

Lutz S. 2014 J Clin Oncol 32:2913-2919

Lutz S. Palliative radiotherapy for bone metastases:an ASTRO evidence-based guideline. 2014

RISULTATI DI UNO STUDIO DI FASE II SULLA RADIOTERAPIA  
IPOFRAZIONATA ACCELERATA (PROTOCOLLO SHARON)  
NEL TRATTAMENTO DELLE METASTASI OSSEE COMPLICATE

## Complicated bone metastases



No evidence-based  
recommendations!

ASTRO Accessed January 10, 2013.

(<http://www.choosingwisely.org/astro-releases-list-of-five-radiation-oncology-treatments-to-question-as-part-of-national-choosing-wisely-campaign/>)

## RISULTATI DI UNO STUDIO DI FASE II SULLA RADIOTERAPIA IPOFRAZIONATA ACCELERATA (PROTOCOLLO SHARON) NEL TRATTAMENTO DELLE METASTASI OSSEE COMPLICATE

- Ideally palliative treatment should be as short as possible to decrease the discomfort for patients.
- For example, treatment duration of 2 days, instead of the traditional treatments of 1 or 2 weeks, could reduce the economic and logistical problems for both patients and health systems.
- Very short treatments could also promote integration with chemotherapy, avoiding the interruption of systemic treatment.
- Finally, for patients referred to hospice, or admitted to hospice, a short course treatment would prevent a long delay or interruption of this kind of assistance.

***SH*ort course *AC*celerated *R*adiation therapy = ***SHARON*****

reduction of total treatment time

improving the physical and psychological comfort

faster resolution of clinical symptoms

2 daily  
fractions  
over 2 days

# RISULTATI DI UNO STUDIO DI FASE II SULLA RADIOTERAPIA IPOFRAZIONATA ACCELERATA (PROTOCOLLO SHARON) NEL TRATTAMENTO DELLE METASTASI OSSEE COMPLICATE

## DOSE ESCALATION STUDY RESULTS

26 enrolled patients

M/F: 14/12;  
median age: 61 yrs (range: 39-83)

20 Gy/ 5 Gy

18 Gy/ 4.5 Gy

16 Gy/ 4 Gy

Table 1. Acute toxicity

Dose level	16 Gy; 4 Gy/fx	18 Gy; 4.5 Gy/fx	20 Gy; 5.0 Gy/fx
Skin G1	0/12	1/8	0/6
Skin G2	0/12	0/8	0/6
Gastro-intestinal G1	0/12	0/8	0/6
Gastro-intestinal G2	0/12	0/8	0/6
Urinary G1	1/12	0/8	0/6
Urinary G2	0/12	0/8	0/6
DLT	0	0	0

# RISULTATI DI UNO STUDIO DI FASE II SULLA RADIOTERAPIA IPOFRAZIONATA ACCELERATA (PROTOCOLLO SHARON) NEL TRATTAMENTO DELLE METASTASI OSSEE COMPLICATE

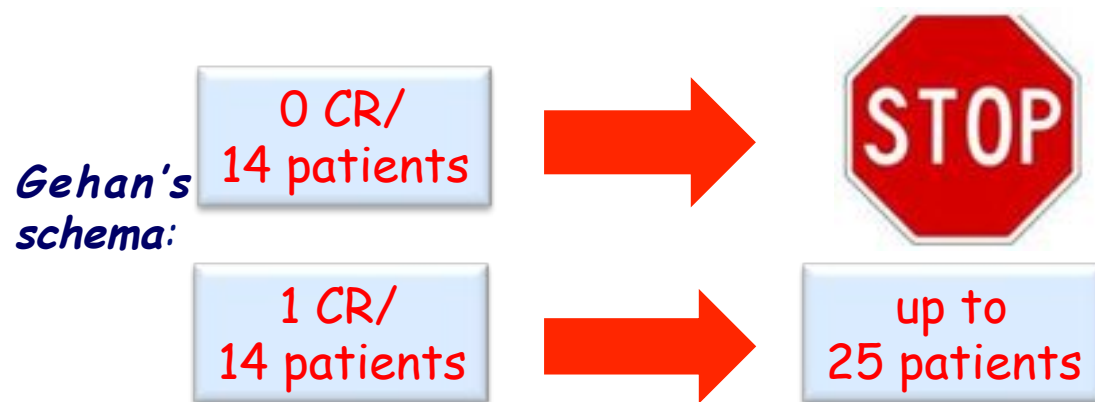
## STUDY DESIGN

### Inclusion criteria:

Pathologically proven cancer  
ECOG performance status  $\leq 3$   
Ineligible for curative treatment

**Primary end point:** symptoms response

**Secondary endpoints:** acute and late toxicity & QoL



Gehan EA: J Chron Dis 13:346-353, 1961

**RISULTATI DI UNO STUDIO DI FASE II SULLA RADIOTERAPIA  
IPOFRAZIONATA ACCELERATA (PROTOCOLLO SHARON)  
NEL TRATTAMENTO DELLE METASTASI OSSEE COMPLICATE**

## Tools for toxicity & QoL evaluation

RTOG-EORTC toxicity criteria	<i>Cox JD, IJROBP 1995</i>
ECOG performance status	<i>Schag CC, J Clin Oncol 1984</i>
Visual Analog Scale (VAS): symptoms intensity	<i>Priestman TJ, Lancet 1976.</i>
Pain Score = Pain Severity X Pain Frequency Drug score = Drug severity x Drug frequency	<i>Salazar OM, IJROBP 2001</i>
Well-being (CLAS1), Fatigue (CLAS2), Daily activity(CLAS3)	<i>Sutherland HJ, Cancer Nurs 1988</i>
Pain relief	<i>Chow E, IJROBP, 2012</i>

Symptoms severity and Quality of Life were evaluated  
**before and after (3 weeks) treatment**



# RISULTATI DI UNO STUDIO DI FASE II SULLA RADIOTERAPIA IPOFRAZIONATA ACCELERATA (PROTOCOLLO SHARON) NEL TRATTAMENTO DELLE METASTASI OSSEE COMPLICATE

**Table 1: Patient characteristics**

	n	%
Patients	25	100
Age (years)		
Median	65	
Range	46-85	
Gender		
Male	14	56
Female	11	44
ECOG		
0	10	40
1	7	28
2	5	20
3	3	12
Treated site		
Spine	13	52
Pelvis	4	16
Extremities	4	16
Chest wall	4	16

## RESULTS

**Table 2. Site of primary tumor and histopathology**

	n	%
Patients	25	100
NSCLC	9	36
Breast	8	32
Prostate	3	12
Others	5	20

**RISULTATI DI UNO STUDIO DI FASE II SULLA RADIOTERAPIA  
IPOFRAZIONATA ACCELERATA (PROTOCOLLO SHARON)  
NEL TRATTAMENTO DELLE METASTASI OSSEE COMPLICATE**

## **RESULTS**

### *Pain relief*



**Overall response rate =  
92.5% (23/25) (CI 0.95: 68.7%-99.1)**

complete pain relief = 8 pts (32%)  
partial pain relief = 16 pts (69%)  
indeterminate = 2 pts (8%)

**Pret-treatment vs. post-treatment mean VAS =  
5.9 ± 2.6 vs. 2.7 ± 2.5;  $p = 0.039$  ( $\chi^2$  test)**

***Only 1 patient required retreatment at 12 months***

RISULTATI DI UNO STUDIO DI FASE II SULLA RADIOTERAPIA  
IPOFRAZIONATA ACCELERATA (PROTOCOLLO SHARON)  
NEL TRATTAMENTO DELLE METASTASI OSSEE COMPLICATE

## RESULTS

QoL



improved ECOG = 7 pts (27%)  
stable ECOG = 9 (35%)

18 pts (69%) were able to rank the different aspects of QoL as Well-being (CLAS1), Fatigue (CLAS2) and Daily activity (CLAS3).

No significant differences were recorded between baseline and post-treatment evaluation, even if an improvement in all indices was noted.

# RISULTATI DI UNO STUDIO DI FASE II SULLA RADIOTERAPIA IPOFRAZIONATA ACCELERATA (PROTOCOLLO SHARON) NEL TRATTAMENTO DELLE METASTASI OSSEE COMPLICATE

Table 1. Acute toxicity

	n	%
<b><i>Patients</i></b>	<b>25</b>	<b>100</b>
Skin G1	5	20
Haematological G1 (Anemia)	1	4
Haematological G2 (Anemia)	2	8
Gastro-intestinal G1	2	8
Gastro-intestinal G2	3	12

## RESULTS

Median follow-up =  
6 months (range 1-36 m)

no late toxicities are  
recorded

RISULTATI DI UNO STUDIO DI FASE II SULLA RADIOTERAPIA  
IPOFRAZIONATA ACCELERATA (PROTOCOLLO SHARON)  
NEL TRATTAMENTO DELLE METASTASI OSSEE COMPLICATE

## CONCLUSION

Short-course accelerated RT to 20Gy in twice daily fractions for 2 consecutive days is effective in terms of symptom relief and well tolerate and in terms of acute and late toxicity.

This treatment could be particularly useful in daily practice for patients with difficulties in transfers to the RT center and for departments with waiting list problems.

A phase III trial should be planned to compare this scheme with 20 Gy in 5 fractions or 30Gy in 10 fractions.

**RISULTATI DI UNO STUDIO DI FASE II SULLA RADIOTERAPIA  
IPOFRAZIONATA ACCELERATA (PROTOCOLLO SHARON)  
NEL TRATTAMENTO DELLE METASTASI OSSEE COMPLICATE**

LUCIANA CARAVATTA  
lcaravatta@hotmail.com



Centro di Radioterapia e Medicina Nucleare  
U.O. Radioterapia sperimentale  
Presidio Ospedaliero Oncologico "A. Businco",  
Cagliari



**Grazie per  
l'attenzione**