Stereotactic radiotherapy and target therapy for oligometastatic patients with renal cell carcinoma

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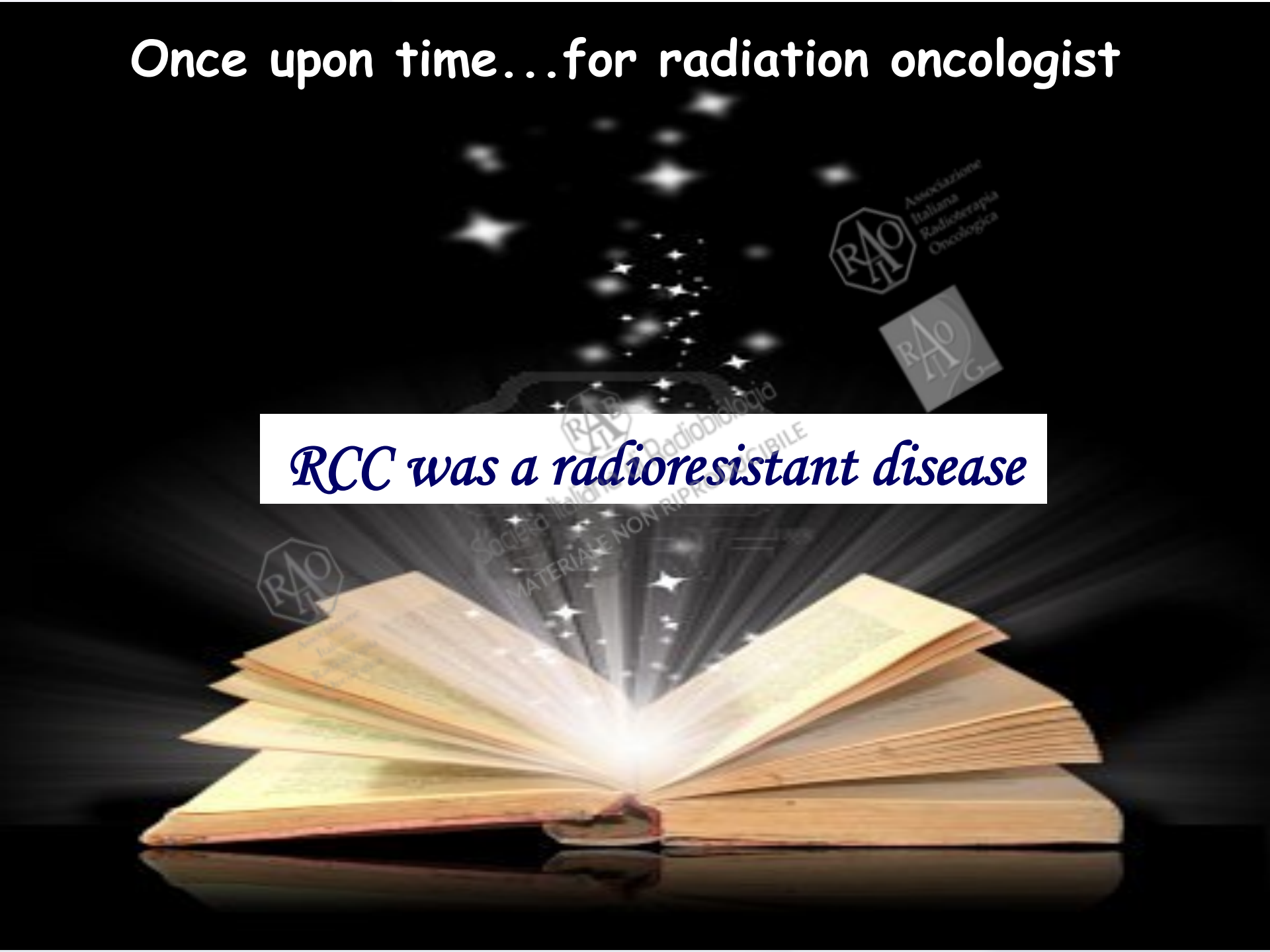
Once upon time...for radiation oncologist



Radiotherapy…????

Supportive Care

Supportive care remains a mainstay of therapy for *all* patients with metastatic RCC (See NCCN Guidelines for Palliative Care). This includes surgery for patients with solitary brain metastasis whose disease is well controlled extracranially. Stereotactic radiotherapy, if available, is an alternative to surgery for limited volume brain metastasis, and whole brain irradiation is recommended for those patients with multiple brain metastases.[191]

Analysis of the SEER database indicates that the 5-year survival rate for kidney cancer has increased over time for localized disease (from 88.4% during 1992–1995 to 91.8% during 2004–2010) and for advanced disease (from 7.3% during 1992–1995 to 12.3% during 2004–2010).[2] The most important prognostic determinants of 5-year survival are the tumor stage, grade, local extent of the tumor, presence of regional nodal metastases, and evidence of metastatic disease at presentation.[7-16] RCC primarily metastasizes to the lung, lymph nodes, bone, liver, adrenal gland, and brain.[6]

"(Oligo)metastatic patients"

The clinical state of oligometastatic disease was proposed in 1995 by Hellman and Weichselbaum.

They hypothesized that, in some patients with a limited number of clinically detectable metastatic tumors, the extent of disease exists in a transitional state between localized and widespread systemic disease.

In this model, oligometastatic disease has the potential of progressing to widespread metastatic disease.

Local control of oligometastases may yield improved systemic control

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The high-dose per fraction employed SBRT may be particularly advantageous due to the radiobiological behaviour of RCC.

The existence of a dose response relationship using stereotactic radiotherapy has been suggested in previous studies, with improved LC rates with delivery of a higher BED, although these are noncomparative studies

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The role of radiotherapy

RCC: Palliative radiotherapy treatment for metastatic disease

To improve pain

To improve LC

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Renal cell carcinoma (RCC)
prognostic factor

- ✓ 50% of pts develop metastatic disease
- ✓ The **median survival time** in metastatic pts is 6-12 months (3 months if brain mts)
- ✓ The principal sites are brain, lung, bones

JAMA1999 ; 281 : 1628 – 31
J Urol 1986 ; 136 : 376 – 9
J Clin Oncol 1984 ; 2 : 169 – 73 .

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

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…103 pts (94 bone) were stratified into 3 groups:

-High dose (23-24 Gy)
-intermediate (21-22 Gy)
-Low (18-20 Gy)

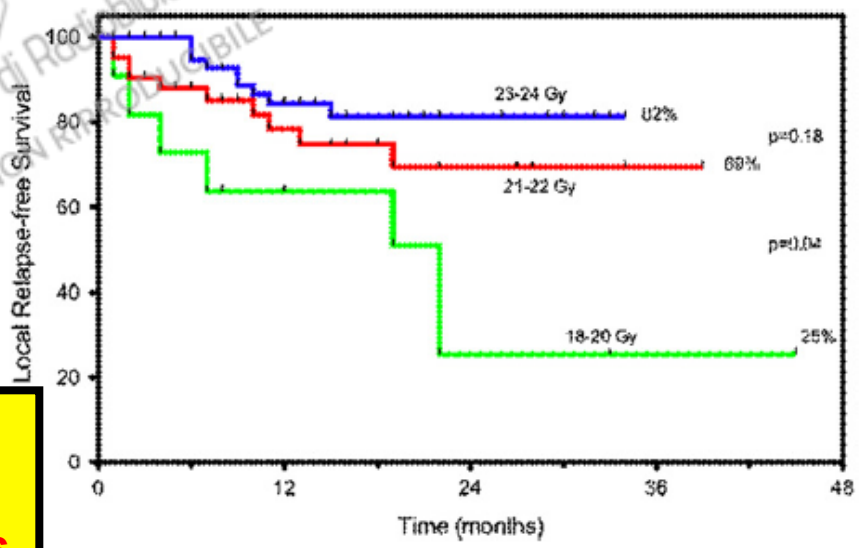

Fig. 1. Actuarial local control (Kaplan-Meir method) by dose level. Y axis represents local relapse-free survival (%).

…Local Control rate after 2 years : 64 %

…the median time of failure : 9,6 months

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TUMOR CONTROL OUTCOMES AFTER HYPOFRACTIONATED AND SINGLE-DOSE STEREOTACTIC IMAGE-GUIDED INTENSITY-MODULATED RADIOTHERAPY FOR EXTRACRANIAL METASTASES FROM RENAL CELL CARCINOMA

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LOCAL CONTROL AND PAIN RELIEF

…We can consideret the importance of radiosensitization of SBRT for metastatic RCC using targeted therapies (sunitinib, sorafenib, bevacizumab)

…Using RT + targeted therapies could produce synergistic effect and result in more durable responses

…clinical data for the use of anti-angiogenic agents as a first line monotherapy treatment have been reported from Dana Faber Cancer Center with response rate of 37-9 and 13% respectively

Int J Radiat Oncol Biol Phys 2012;82:1744–8.

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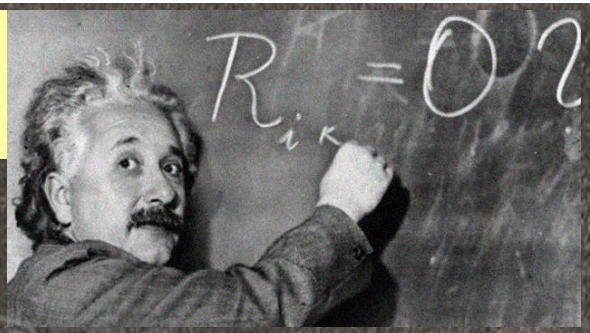
OUR EXPERIENCE



From 2012 to 09/2015
23 pts and 30 lesions treated with SBRT
- Cyberknife or VERO-

***23** patients affected by RCC (19 men and 4 women)*

The median age was 62.9 years (range 47-85)

Staging and re-staging with CT scan and/or [^{18}F]FDG-PET/CT

Open or robot-assisted laparoscopic radical nephrectomy was performed in all patients (stage pT1- pT3) +/- lymph node dissection (LND)

The histotype was clear cell carcinoma in all patients

Patients and methods

Table 1. Dose delivered (group 1-2-3) and site of treatment, per lesion (n=30)

*EQD	Group 1 EQD2 (12-36 Gy) BED (15-43)	Group 2 EQD2 (42-50 Gy) BED (50-60)	Group 3 EQD2(66-126 Gy) BED (79-151)	Total
SRT alone	4	4	5	13
Systemic + SRT	9	5	3	17
Treatment site				
Non-spine bone	2	1	1	4
Spine	6	4	1	11
Lymph node	2	1	1	4
Lung	-	-	4	4
Brain	1	1	-	2
Other	2	2	1	5
Tot. lesions	13	9	8	30

* 2Gy-per-fraction equivalent dose (EQD2) and biological equivalent dose (BED) using the α/β=10 for tumors.

***13** patients received SRT during systemic therapy: 10 patients received Sunitinib and 3 patients Pazopanib as first-line treatment.*

***10** patients underwent SRT alone*

17 patients were treated for 1 lesion

5 patients for 2lesi

1 for 3 lesions.

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* 2Gy-per-fraction equivalent dose (EQD2) and biological equivalent dose (BED) using the $\alpha/\beta=10$ for tumors.

The total radiotherapy doses ranged from 10 to 54 Gy (1 to 3 fr)

The median equivalent of the dose (EQD2) was 50.6 Gy

Median of 2.7 fractions (range 1-5)

Median biological equivalent dose (BED) was 51 Gy

Results

The median follow up was **9.4** months (range 1-36)

The progression of the disease was registered in 6 patients at the median of 5.1 months (range 2-8) from the end of SRT

27% (3 pts per group) > 12 months : 5 SRT only
4 SRT + STH

2 PD: 1 start STH, 1 SRT (lung lesion)

No in-field progression was registered

LC was 100 % for all 30 lesio

Table 3. % of response of target lesion in group 1-2-3: CR, SD, PD in the others site (out-field of SRT)

	Group 1 (13 pts)	Group 2 (9 pts)	Group 3 (8 pts)	Total
CR	7/13 (53.8 %)	6/9 (66.6 %)	6/8 (75 %)	19
SD	6/13 (46.1 %)	3/9 (33.3 %)	2/8 (25 %)	11
PD in the others site (out-field of SRT)	4/13 (30.7 %)	1/9 (11.1 %)	1/8 (12.5 %)	6

CONCLUSIONS RCC radiotherapy

Using RT + targeted therapies could produce synergistic effect and result in more durable responses

Change the view that RCC is a radioresistant disease

The high dose/fraction may be advantageous due to radiobiological behaviour

The treatment related toxicity and mortality was very low and favourable compared to rates reported for patients undergoing neurosurgery

Median follow-up was generally limited, ranging from 5.2 to 16 months in the intracranial setting, and 5 to 52 months in the extracranial setting, this length of follow-up, however, may be sufficient in the metastatic setting

Thanks to IEO multidisciplinary team

Grazie per la vostra attenzione

Federico Fellini La dolce vita 1960

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