Radioterapia stereotassica ipofrazionata nei pazienti con recidiva da glioma maligno

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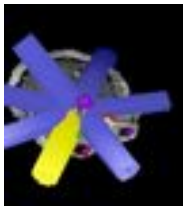


XXIV CONGRESSO NAZIONALE AIRO
Padova 8-11 Novembre 2014

Associazione Italiana Radioterapia Oncologica

Background

- Nei pazienti con glioma maligno il controllo locale e la sopravvivenza sono limitati, in quasi tutti i pazienti entro 1-2 anni dal trattamento si verifica la recidiva locale

- La terapia di salvataggio include

  - Chemioterapia

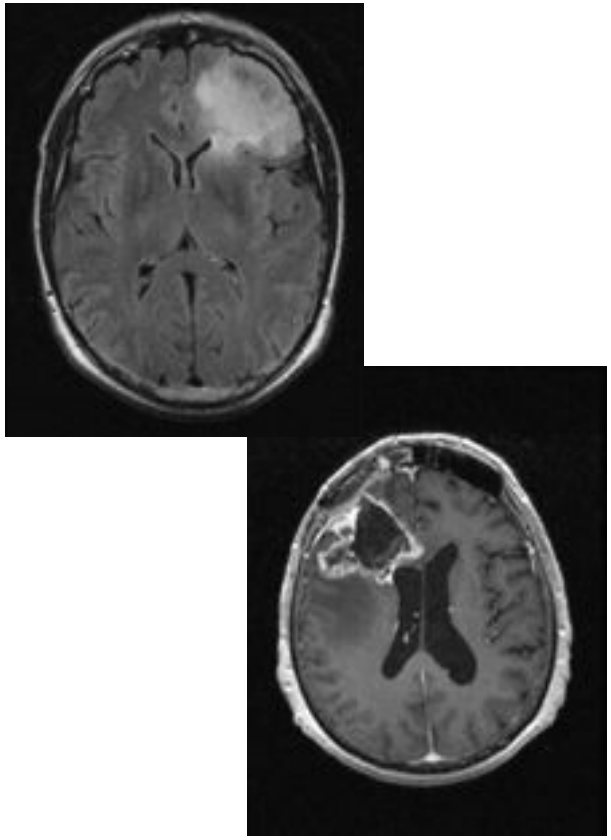
Wick J Clin Onc 2007, Kreisl J Clin Onc 2009, Perry J Clin Onc 2010

  - Chirurgia

Dirks Can J Surg 1993

  - Radioterapia

Combs Cancer 2005, Patel J Neuroncol 2009, Fogh J Clin Onc 2010



Background

- La radioterapia stereotassica, da sola o in combinazione con la chemioterapia, è stata recentemente utilizzata nel trattamento delle recidive dei gliomi maligni.

- Sia dopo radiochirurgia stereotassica (1-5 fr) che dopo radioterapia stereotassica frazionata (6-15 fr) è stata riportata una sopravvivenza di 6-10 mesi con una tossicità accettabile.

Combs Cancer 2005, Patel J Neuroncol 2009, Minniti 2011

Background

➢ FSRT

Author	Pts Number	Interval (months)	Dose (Gy)	Volume (cc)	Cumulative BED	OS months	Toxicity
Combs (2005)	42 Gr.III	34.5	36 Gy	56.2	190.8	16	Not severe
	59 GBM	10		49	186	8	
Grosu (2005)	44 (Grade III/IV)	16	30 Gy	18	219-255	8	13%
Combs (2008)	25 *	36	36 Gy **	50	192	8	Not severe
Cho (1999)	25 (Grade III/IV)	19	37,5 Gy	25	198.4	7,1	4%

*8 GBM, 10 grade III, 7 low grade
**concomitant temozolomide chemotherapy

Background

- HSRT

Author	Pts GBM	Interval months	Dose (Gy)	Volume (cc)	Cumulative BED	OS months	Toxicity
Shepherd (1997)	36 *	29	20-50	24	226.8	11	12 %
Selch (2000)	21 (Grade III/IV)	20	25	12	207.5	6.7	Not severe
Lederman (1998)	14	6.3	24	32.7	210	14.2	8%
Hudes (1999)	20	3	24-35	13	210	10.5	Not severe

*32 grade III/IV

Background

Studi sulla reirradiazione con tecnica stereotassica associata a CHT nei gliomi

Authors	Patients	Treatment	Radiation dose (Gy)	Chemotherapy	Interval	Volume (cm^3)	KPS	Median PFS (months)	Median OS (months)	Radiation necrosis
Lederman et al. [33]	18	HSRT	24/4 fr	Paclitaxel	7.8	32.7	70	NR	7 (17 % at 12 months)	0 %
Arcicasa et al. [34]	31	FSRT	34.5/23 fr	Concomitant/adjuvant CCNU	14	NR	70	NR	13.7 (53 % at 12 months)	0 %
Minniti et al. [27]	36	HSRT	37.5/15 fr	Concomitant TMZ	14	13.1	70	5	9.4 (33 % at 12 months)	8 %
Combs et al. [25]	25*	FSRT	36/18 fr	Concomitant TMZ	36	NR	70	5	8 (25 % at 12 months)	
Grosu et al. [24]	44*	HSRT	30/6 fr	Concomitant TMZ (29 pts)	NR	15	NR	NR	11 (HSRT + TMZ)	7 %
				HSRT alone (15 pts)					6 (HSRT alone)	
Gutin et al. [26]	25*	HSRT	30/5 fr	BVZ	15	34**	80	7.3	12.5 (54 % at 12 months)	0 %
Cuneo et al. [28]	49*	SRS	15	BVZ (33 pts)	21	4.5	80	5.2	11.9 (50 % at 12 months)	10 %
				SRS alone (16 pts)				2.1	3.9 (20 % at 12 months)	
Park et al. [30]	11	SRS	16	BVZ	17.2	13.6	90	14.9	17.9 (73 % at 12 months)	9 %
Niyazi et al. [29]	30*	FSRT	36/18 fr	BVZ (20 pts)	NR	NR	80	8	12[a] (67 % at 12 months)	0 %
				FSRT alone (10 pts)				5	6[a] (0 % at 12 months)	
Current study	54*	HSRT	30/5 fr	Concomitant/adjuvant TMZ	15.5	9.8	80	6	12.4 (54 % at 12 months)	7 %

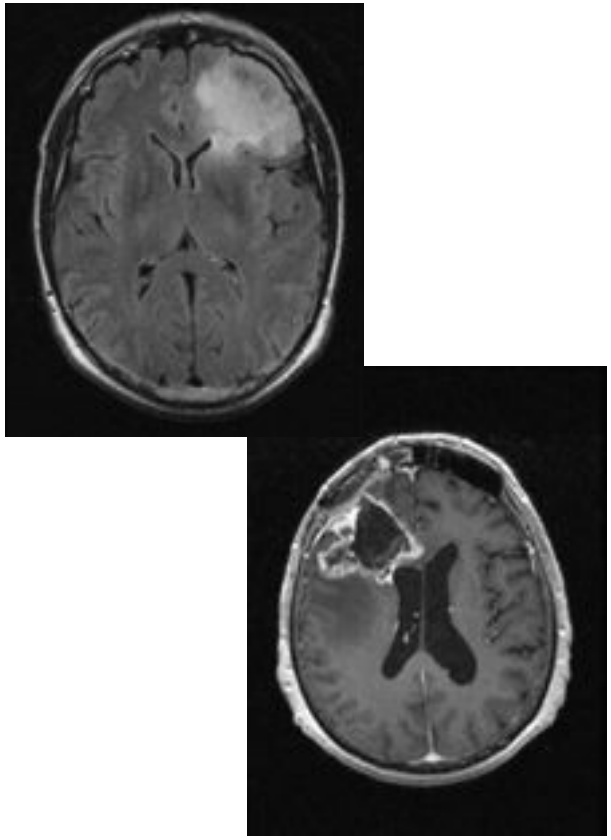
HSRT hypofractionated stereotactic radiotherapy, FSRT fractionated stereotactic radiotherapy, SRS stereotactic radiosurgery, TMZ temozolomide BVZ bevacizumab

Minniti J Neurooncol 2013

Scopo dello studio

Nel nostro istituto abbiamo indagato l'efficacia e la sicurezza della radioterapia stereotassica ipofrazionata, in combinazione con la chemioterapia, come terapia di salvataggio in 58 pazienti con recidiva da glioma maligno.

- Sopravvivenza
- Controllo locale
- Tossicità

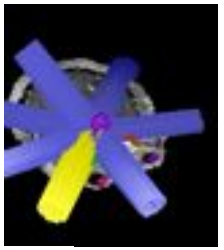


Disegno dello studio

Studio retrospettivo

Da maggio 2006 a Dicembre 2013 sono stati trattati 58 pazienti con recidiva da glioma maligno

- Precedentemente trattati con RT standard (60 Gy) con TMZ concomitante e adiuvante



- KPS $\geq$ 60

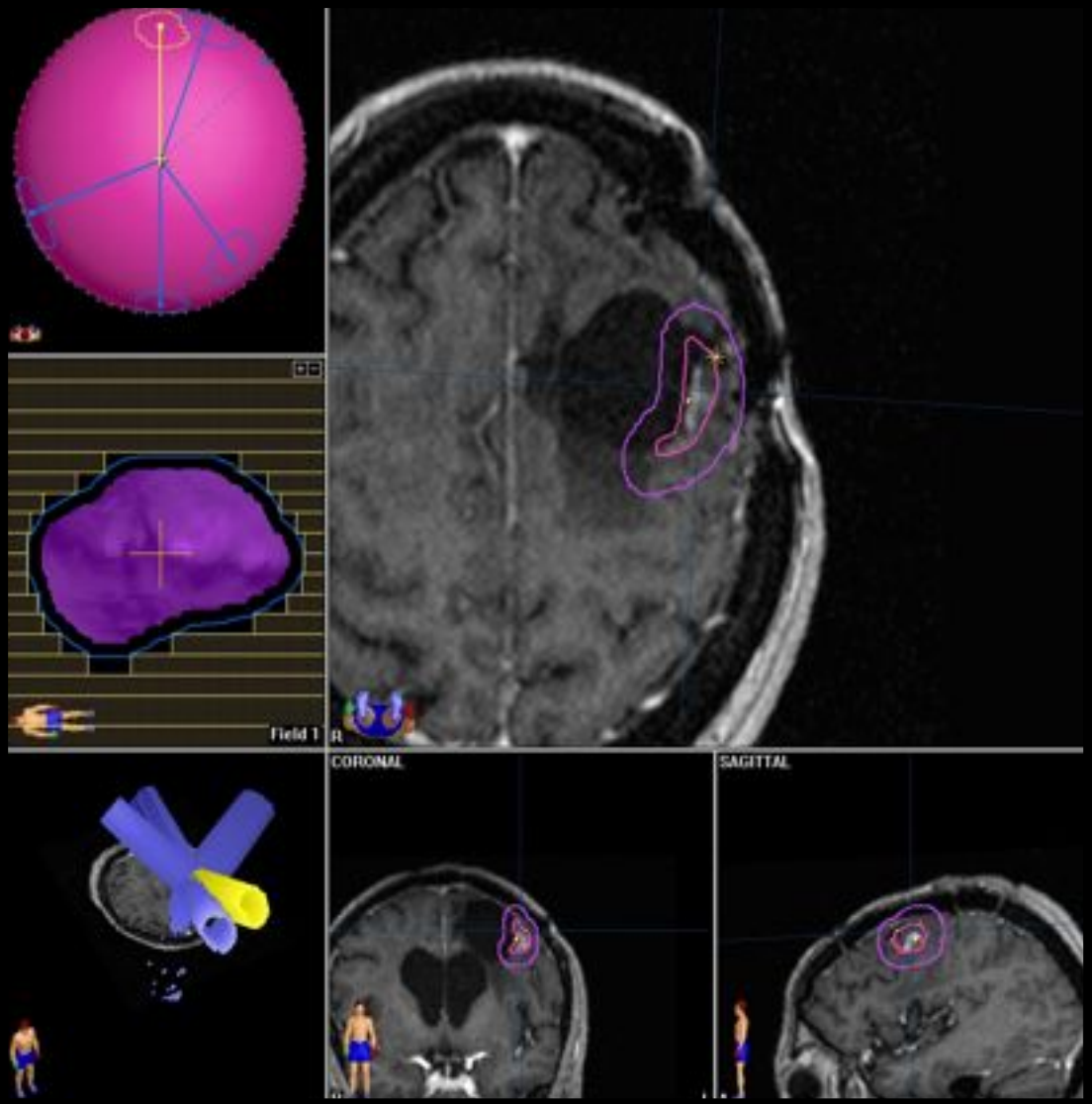
- Intervallo di tempo mediano tra prima RT e reirradiazione di 16 mesi

Pazienti e metodi

HSRT : 5 Gy x 5 se < 4 cm
2,5 Gy x 15 se > 4 cm
+
TMZ 75mg/m2/die
o
BVZ 10mg/Kg/ogni 2 sett

- PTV medio (GTV + 3/5mm) 30,6 cc
- 4-10 campi non coplanari o 3-6 archi dinamici
- PTV nel 90% dell'isodose

Caratteristiche dei pazienti	
Età (anni)	
Mediana (Range)	52 (30–72)
Sesso	
Uomini	33
Donne	25
Grado WHO	
III	17
IV	41
Karnofsky performance status (KPS)	
Median (Range)	80 (60–100)
Reintervento	
Si	9
No	49
Metilazione MGMT	
Metilati	28
Non Metilati	30
Chemioterapia	
Temozolomide	42
Bevacizumab	16
Intervallo tra prima RT e reirradiazione	
Mediana (Range) (mesi)	16 (6–108)
Volume recidiva (cm3)	
Mediana (Range)	9.8 (3.1–32.3)
Tipo HSRT	
5GyX5	21
2,5Gyx15	37
PTV (cm3)	
Mediana (Range)	30.6 (12.3–53.4)

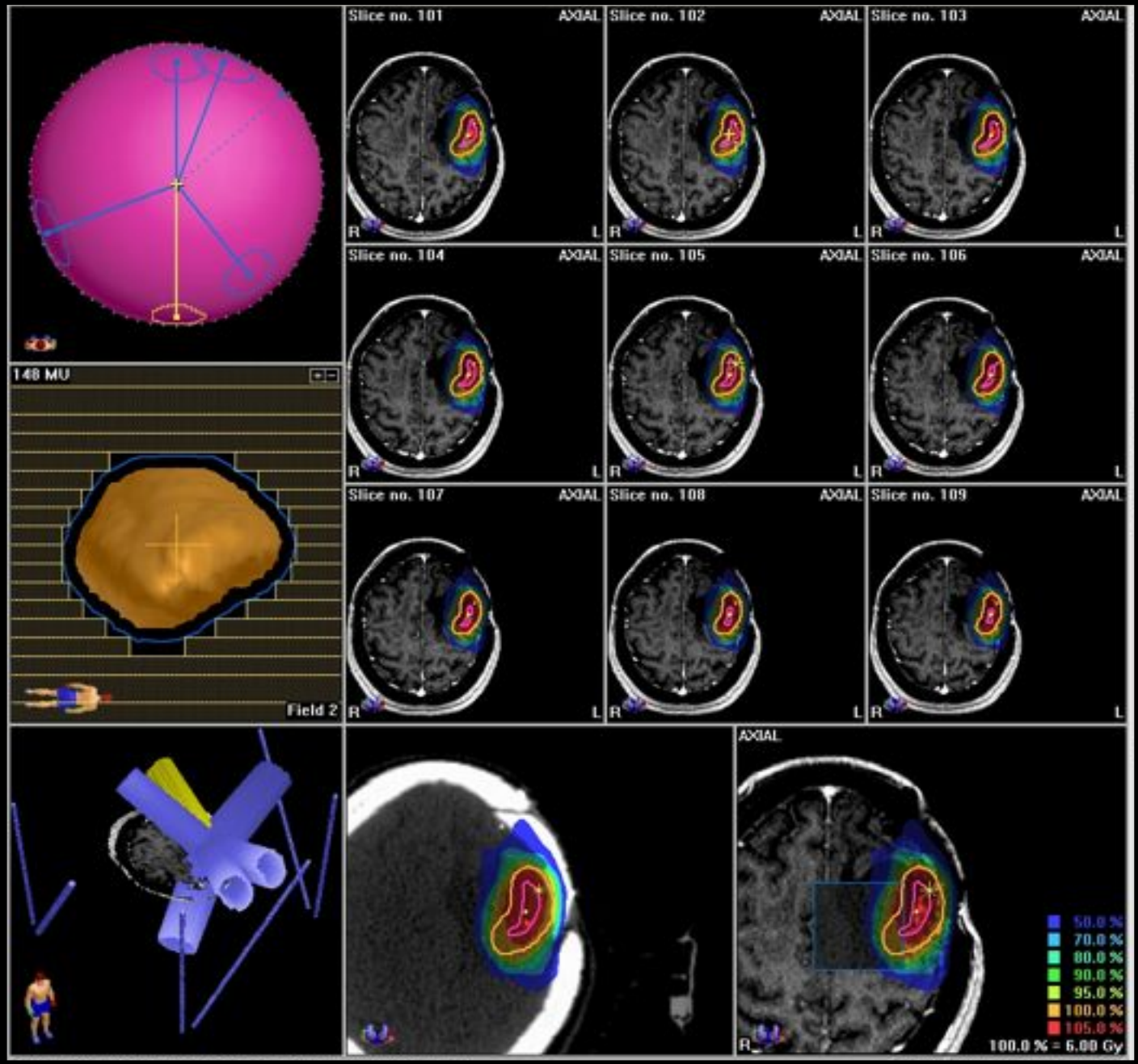


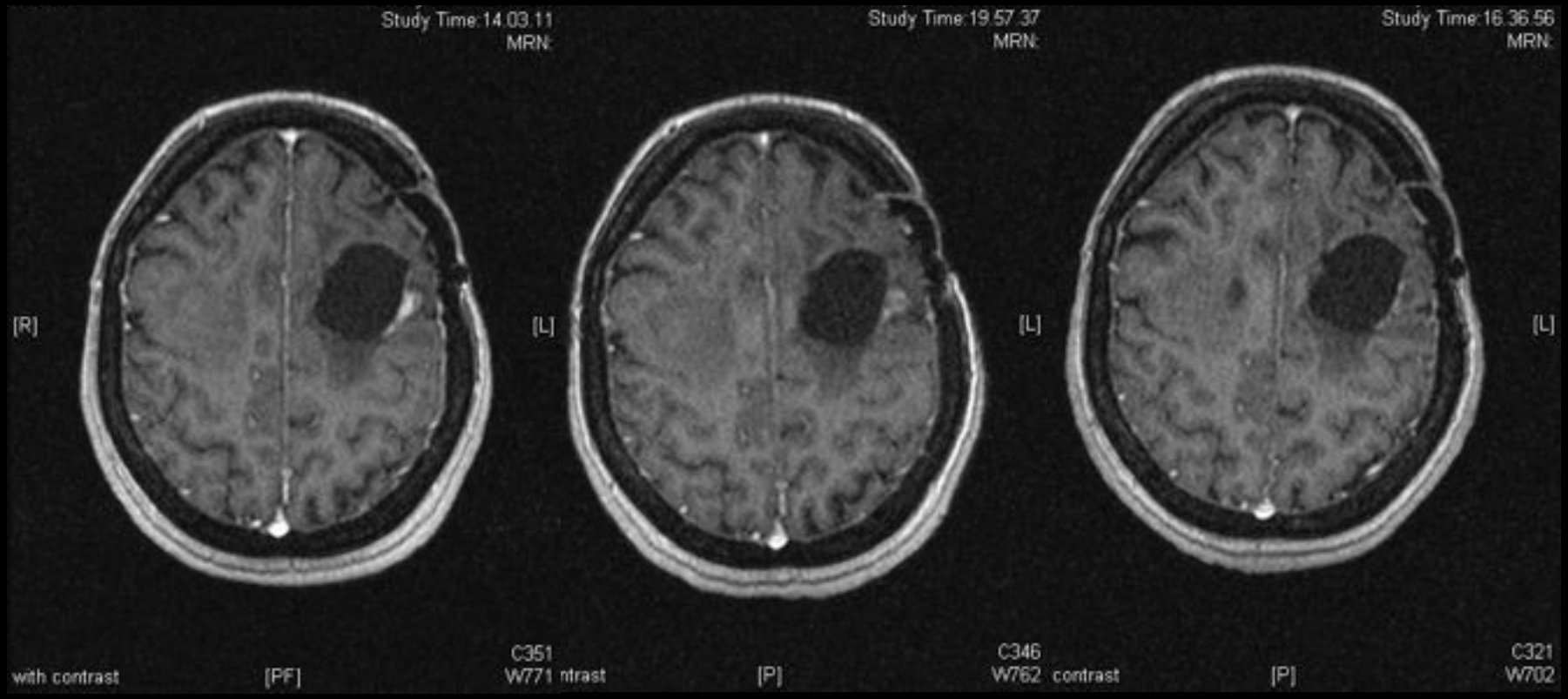
GTV = (T1 dopo mdc)

CTV = GTV + 5 mm
modificato in rapporto alle barriere anatomiche

PTV = CTV + 2 mm

HSRT + TMZ

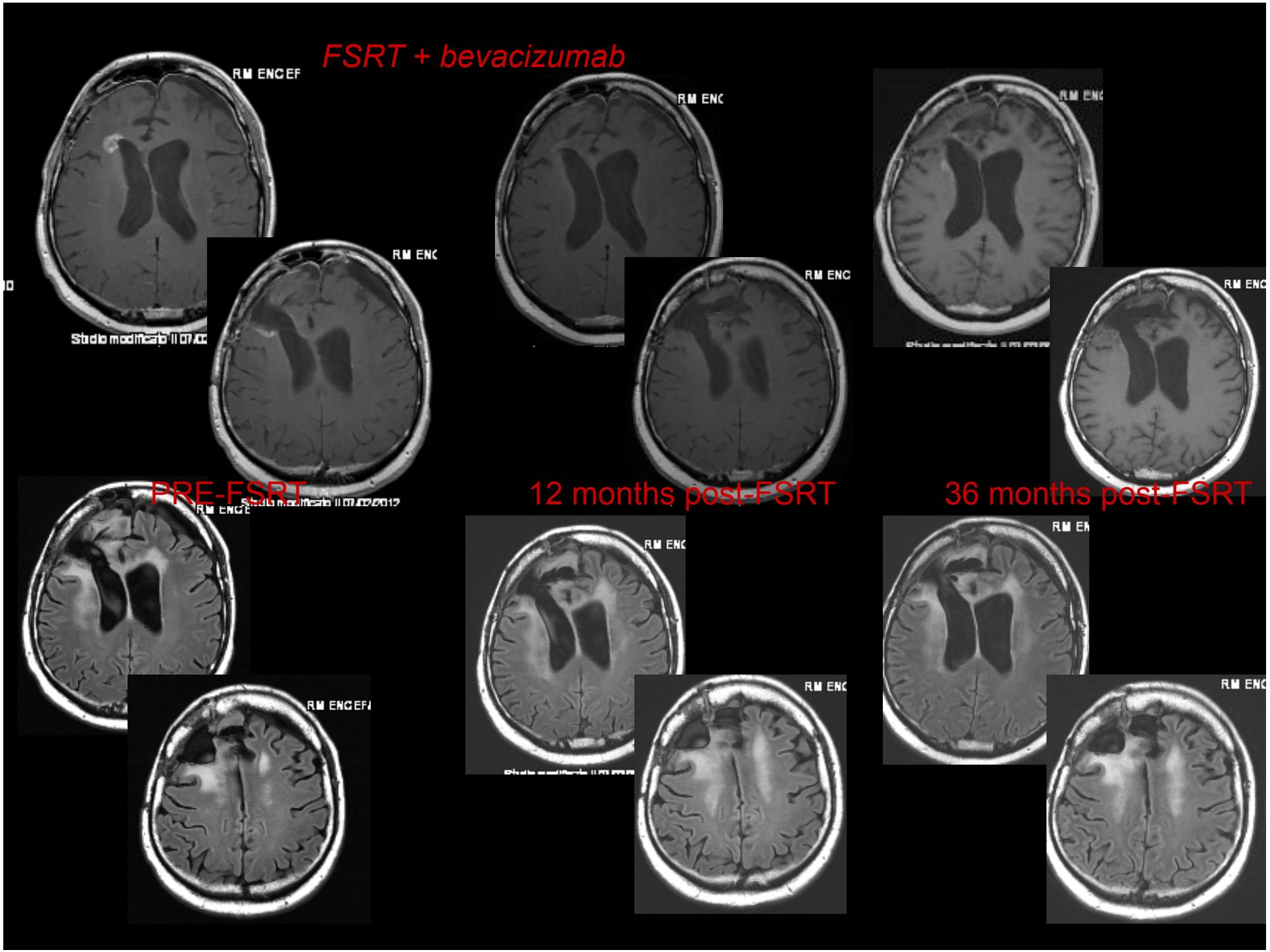

Slice no. 101 AXIAL
Slice no. 102 AXIAL
Slice no. 103 AXIAL
Slice no. 104 AXIAL
Slice no. 105 AXIAL
Slice no. 106 AXIAL
Slice no. 107 AXIAL
Slice no. 108 AXIAL
Slice no. 109 AXIAL
148 MU
Field 2
AXIAL
50.0 %
70.0 %
80.0 %
90.0 %
95.0 %
100.0 %
105.0 %
100.0 % = 6.00 Gy



Pre-FSRT

3 mesi

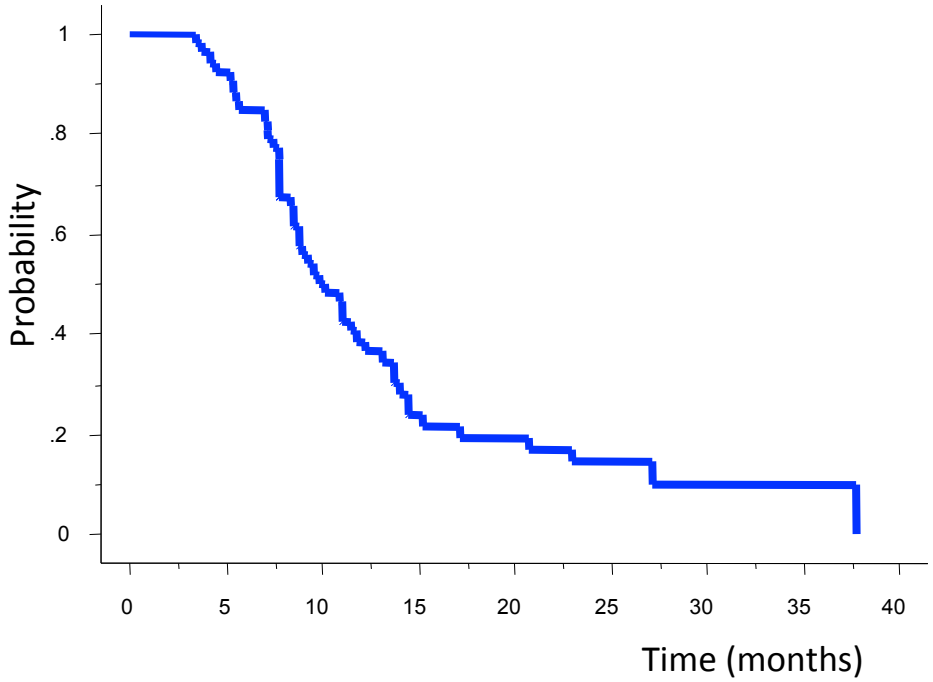
6 mesi


FSRT + bevacizumab
PRE-FSRT
12 months post-FSRT
36 months post-FSRT

Outcome

OS mediana dopo HSRT→9,7 mesi

Tasso di sopravvienza:
a 12 mesi → 39%
a 24 mesi → 16%

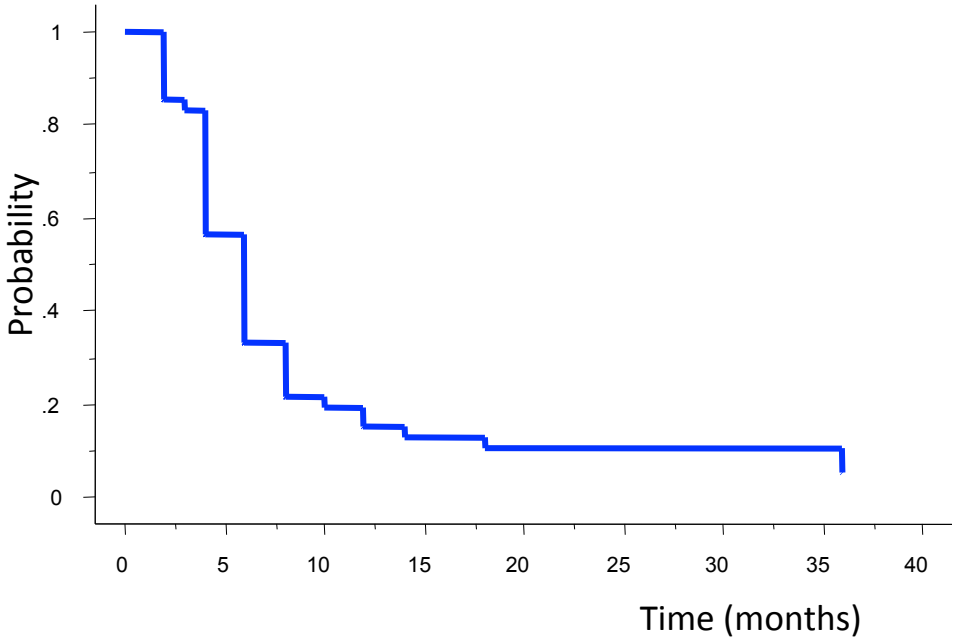


Kaplan-Meier method

Outcome

PFS mediana dopo HSRT→5,2 mesi

Tasso di sopravvivenza libera da malattia
a 12 mesi → 15%



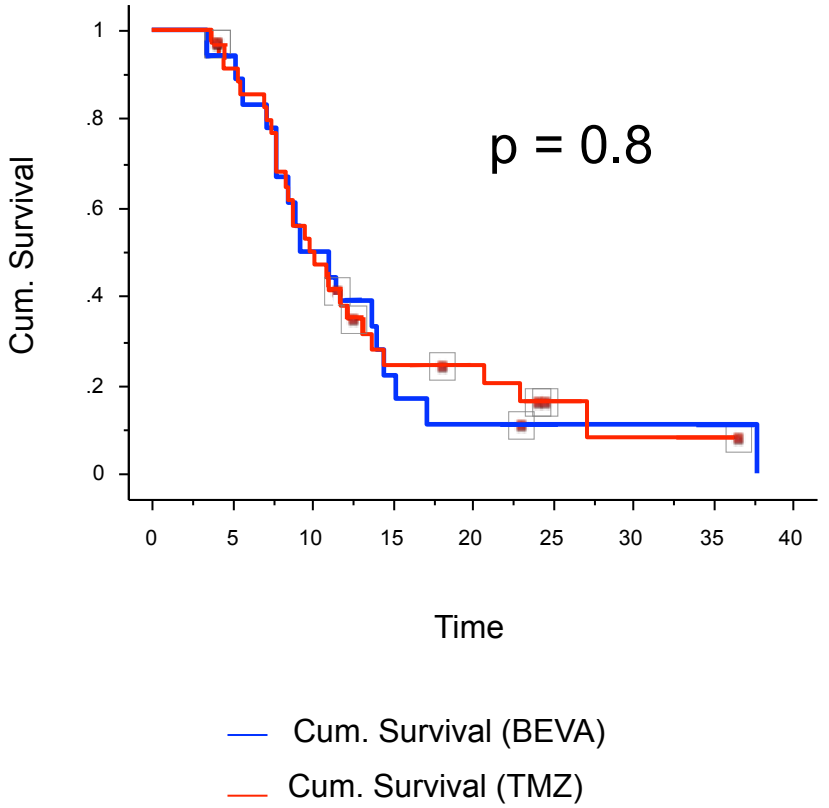
Kaplan-Meier method

Outcome

OS è stata simile in pazienti trattati con TMZ o con Bevacizumab

HSRT + bevacizumab

HSRT + TMZ

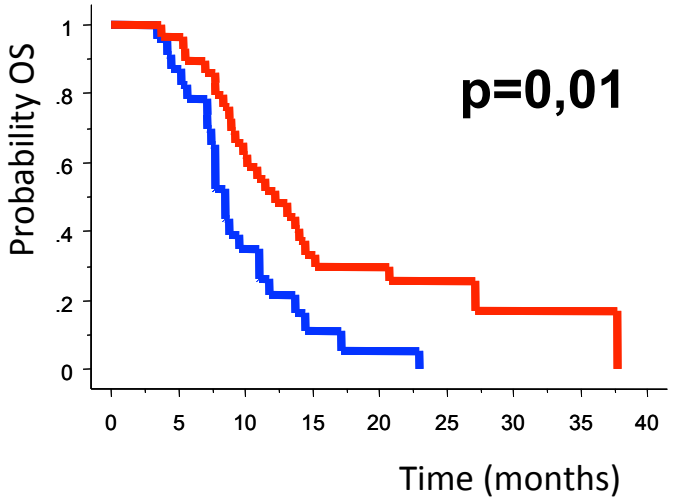


Fattori Prognostici OS

KPS:

KPS >70

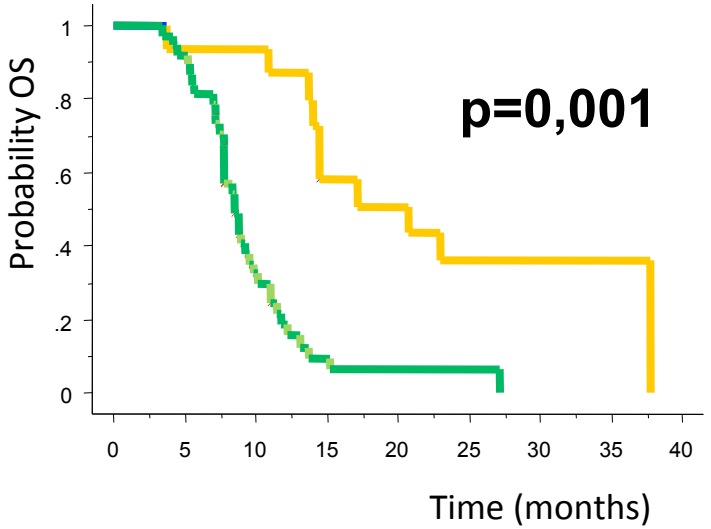
KPS <70



Istologia:

Glioma di III grado

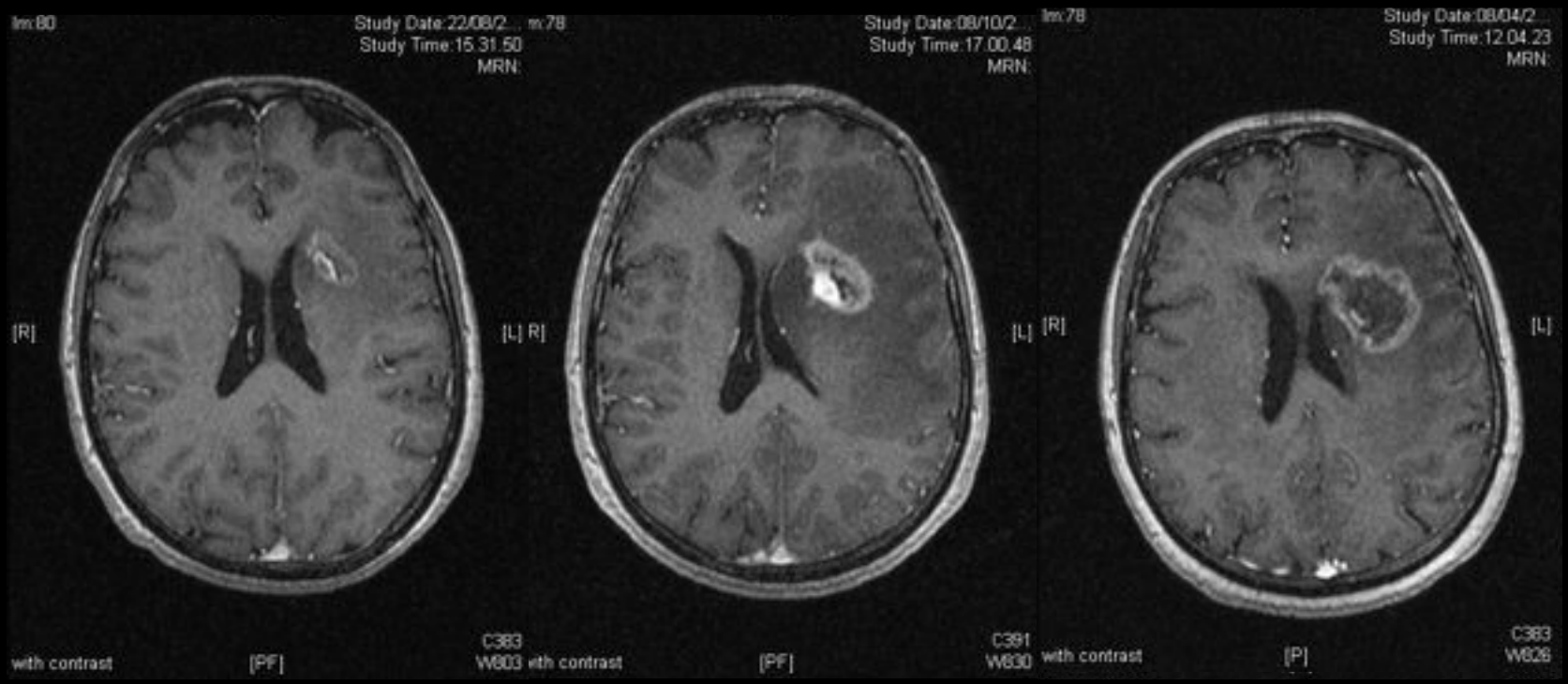
GBM



Tossicità

Tossicità	TMZ			BVZ		
Ematologici	**G2**	**G3**	**G4**	**G2**	**G3**	**G4**
Trombocitopenia	3 (7%)	2 (5%)	0	0	0	0
Anemia	2 (5%)	0	0	1 (6%)	0	0
Neutropenia	3 (7%)	2 (5%)	0	1 (6%)	0	0
Linfocitopenia	9 (21%)	7 (16%)	0	3 (18%)	1 (6%)	0
Non Ematologici	**G2**	**G3**	**G4**	**G2**	**G3**	**G4**
Nausea/Vomito	3 (7%)	1 (2%)	0	0	0	0
Cute	1 (2%)	0	0	1 (6%)	0	0
Neurologici	3 (7%)	3 (7%)	0	1 (6%)	1 (6%)	0
Epatici	2 (5%)	1 (2%)	0	2 (12%)	1 (6%)	0
Ipertensione	0	0	0	2 (12%)	0	0
Fatigue	7 (16%)	4 (9%)	0	3 (18%)	1 (6%)	0

Radionecrosi dopo HSRT



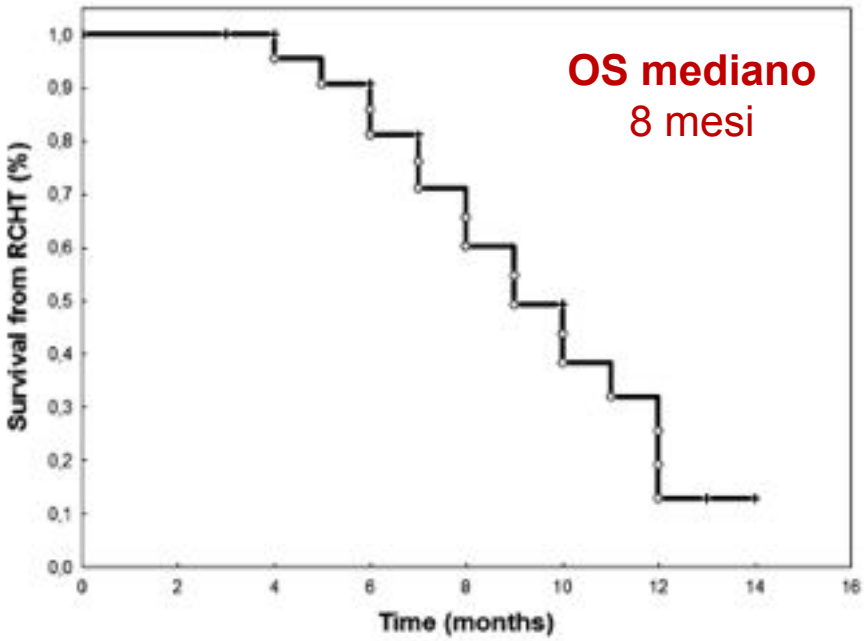
Grade 3 neurological deterioration attributable to radiation-induced necrosis

J Neurooncol (2008) 89:205–210
DOI 10.1007/s11060-008-9607-4

CLINICAL-PATIENT STUDIES

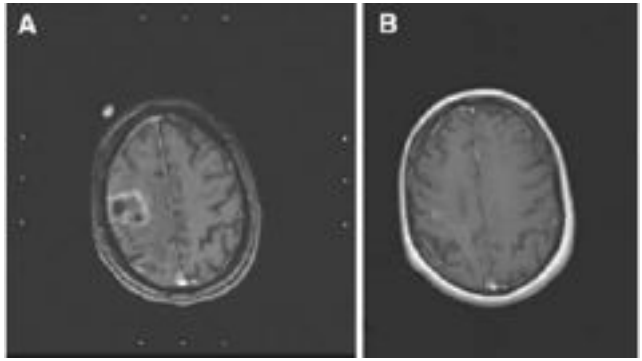
Radiochemotherapy with temozolomide as re-irradiation using high precision fractionated stereotactic radiotherapy (FSRT) in patients with recurrent gliomas

Stephanie E. Combs · Marc Bischof · Thomas Welzel · Holger Hof · Susanne Oertel · Jürgen Debus · Daniela Schulz-Ertner



OS mediano
8 mesi

Fig. 1 Survival calculated from initiation of FSRT in 25 patients treated with RCHT using TMZ for recurrent gliomas



Tossicità

No severe treatment-related side effects could be observed.

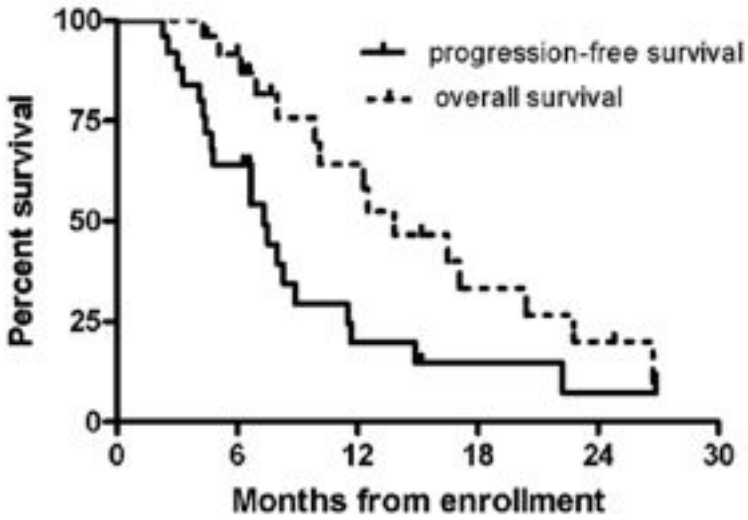
Dose 36 Gy

Combs et al. 2008

Published in final edited form as:
Int J Radiat Oncol Biol Phys. 2009 September 1; 75(1): 156–163. doi:10.1016/j.ijrobp.2008.10.043.

Safety and Efficacy of Bevacizumab with Hypofractionated Stereotactic Irradiation for Recurrent Malignant Gliomas

Philip H. Gutin, MD[1,2,7], Fabio M. Iwamoto, MD[1,3], Kathryn Beal, MD[1,5], Nimish A. Mohile, MD[3], Sasan Karimi, MD[1,4], Bob L. Hou, PhD[1,4,6], Stella Lymberis, MD[5], Yoshiya Yamada, MD, FRCPC[1,5], Jenghwa Chang, PhD[6], and Lauren E. Abrey, MD[1,3]



OS mediana 12,5 mesi

PFS mediana 7,3 mesi

Dose 30 Gy

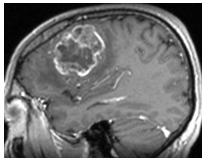
Gutin et al. 2009

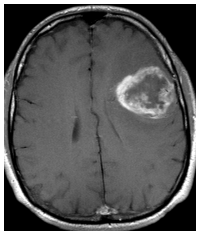
Conclusioni

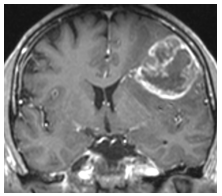
- La radioterapia stereotassica ipofrazionata è un'opzione praticabile e ben tollerata in pazienti con glioma maligno recidivante.

- Per la valutazione di un potenziale vantaggio nell'aggiunta della chemioterapia in questi pazienti sono necessari ulteriori studi.

  (bevacizumab o temozolomide?)







REGIONE LAZIO

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UNIVERSITÀ DI ROMA

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PSICOLOGIA

….grazie dell'attenzione

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