FATTIBILITA' E RUOLO DELLA REIRRADIAZIONE IN PAZIENTI CON RECIDIVA DI GLIOMA AD ALTO GRADO DI MALIGNITA'

A.M. Ascolese, P. Navarria, A. Tozzi, E. Clerici, F. De Rose, E. Villa, C. Iftode, S. Pentimalli, T. Comito, G. D'Agostino, C. Franzese, M. Scorsetti

Radiotherapy and Radiosurgery department, Humanitas Cancer Center, Istituto Clinico Humanitas, Rozzano Milano.

Reirradiation in Recurrent Gliomas

Maximal surgical resection, followed by radiotherapy with concomitant and adjuvant temozolomide (TMZ) improved survival

Recurrence is still a significant problem affecting more than 90% of patients

Median OS	15–18 months
2 years OS	27%
5 years OS	< 10%

HUMANITAS
CANCER CENTER

Reirradiation in Recurrent Gliomas

A lot of non phase III trials
Heterogeneous patients cohorts → Available
Different end-point

Location, size and patient clinical status

Surgical re-resection	mOS 6 mos
Second line Chemotherapy	mOS 8 mos
Re-irradiation	mOS 8 mos
RT+CT	mOS 10-12 mos

Not be compared directly with each other OS is more or less similar
No standard of care

HUMANITAS
CANCER CENTER

Reirradiation in Recurrent Gliomas

Radiation is EFFECTIVE TREATMENT in high grade glioma

UNWILLINGNESS to retreat local recurrence:

- CNS tissue are not capable of repairing injury
- High risk of side effect

Animal experiments: recovery of critical CNS structures Ang KK et al IJROBP 1993

Improvement of imaging modalities

Development of high-precision RT techniques

SAFE ADMINISTRATION of a second course of irradiation

HUMANITAS
CANCER CENTER

Aim and Patients

The aim of this study was to evaluate the effect of HSRT in recurrent high grade glioma in terms of toxicity, rate of local control and patients survival

The present retrospective study includes patients with MRI evidence of recurrent or progressive high grade glioma (HGG), occurring at least 6 months after RT completion, in order to exclude pseudo-progression

Progression was defined using the Response Assessment in Neuro-Oncology (RANO) criteria

HUMANITAS
CANCER CENTER

Aim and Patients

At diagnosis all patients underwent surgery followed by adjuvant RT with concomitant and adjuvant TMZ as for Stupp scheme

At recurrence they were evaluated for salvage treatment

- re-resection
- hypofractionated stereotactic radiation therapy (HSRT)
- chemotherapy
- combined approaches

in *relation to patient clinical conditions, tumor site and size , and hematologic rescue*

HUMANITAS
CANCER CENTER

Aim and Patients

From January 2006 to December 2013: 25 patients underwent HSRT

15 were male and 10 female with a median age of 41 years (range 26-75 years)

GBM	13 patients
Grade III glioma	12 patients

Inclusion criteria

Karnosky performance status (KPS) ≥70

Interval time from first RT > 1 year

No multifocality

HUMANITAS
CANCER CENTER

Treatments at Recurrence

Time to Relapse from initial diagnosis	
≤12 months	10 patients
12-24 months	6 patients
> 24 months	9 patients
Treatment at Recurrence	
Surgery + Chemotherapy and/or Radiotherapy	19 patients
Radiotherapy only	6 patients
Median Volume of recurrent disease (cc)	
<35cc	13 patients
≥35 cc	12 patients
Dose Prescription	
25 Gy/5 fr	24 patients
50 Gy/10 fr	1 patient

HUMANITAS
CANCER CENTER

Radiation Technique and Dose Prescription

PROCEDURE and PLANNING

The frameless stereotactic system was used

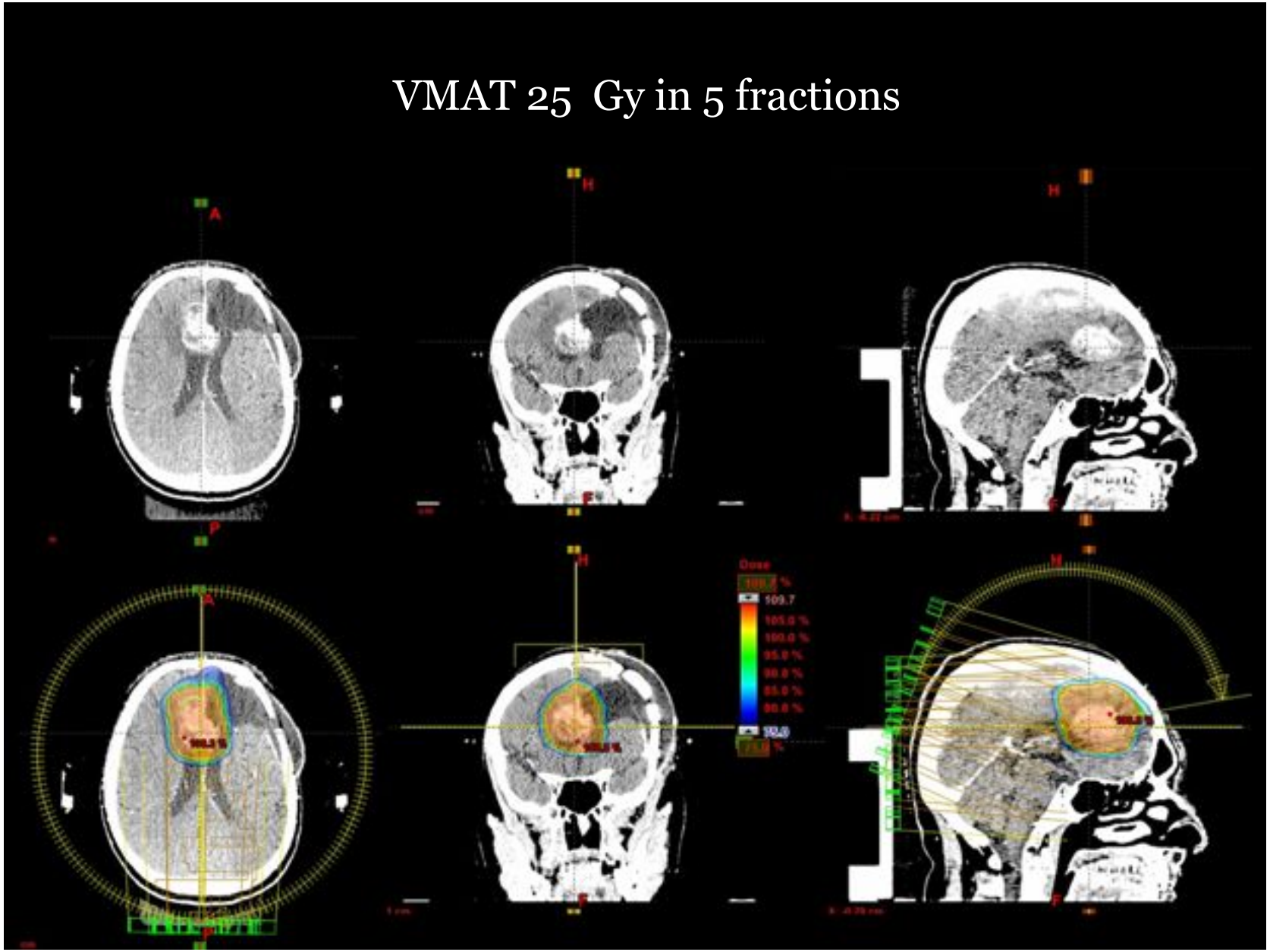
GTV was delineated on ec T1MRI
CTV was generated adding an isotropic margin of 5 mm to GTV
PTV was generated by the expansion of CTV of 3 mm.

ExacTrac X-Ray 6D system and 3Dcone-beam CT (CBCT) images were used for daily patient set-up and isocenter positioning.

Plans were processed using the RapidArc volumetric modulated arc therapy to ensure maximal dose conformity and rapid dose falloff towards critical structures

HUMANITAS
CANCER CENTER

Treatment Planning



HUMANITAS
CANCER CENTER

Results

The median Follow up time from recurrence was 18 months (range 4-36months)

No severe toxicity was observed

PFS at 1 year	72%
PFS at 2 years	34%

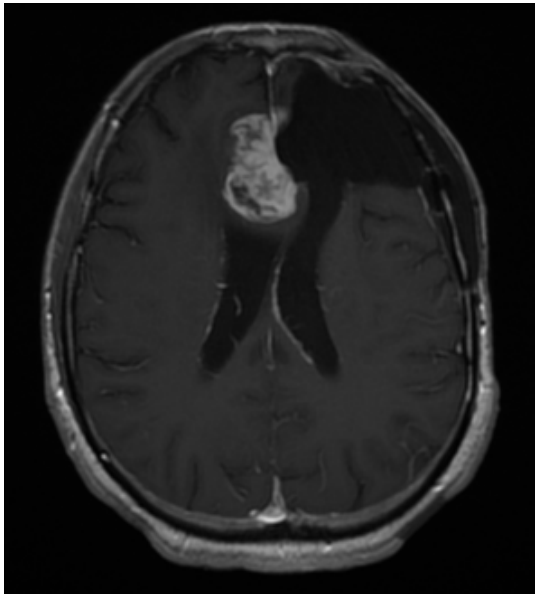
Median PFS 16 months (range 3-36)

OS at 1 year	76%
OS at 2 years	50%

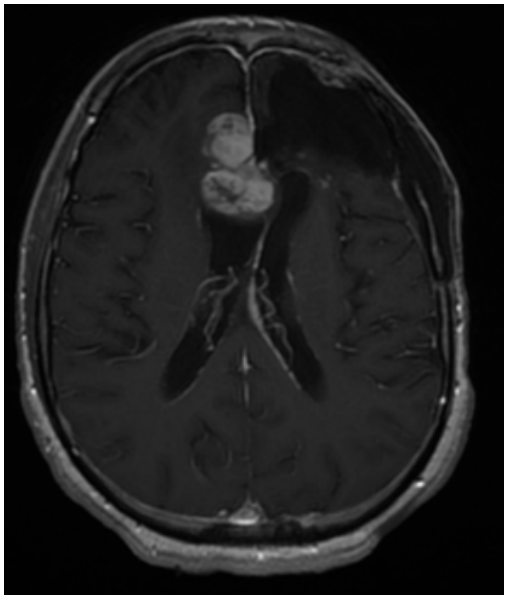
Median OS 18 months (range 4-36)

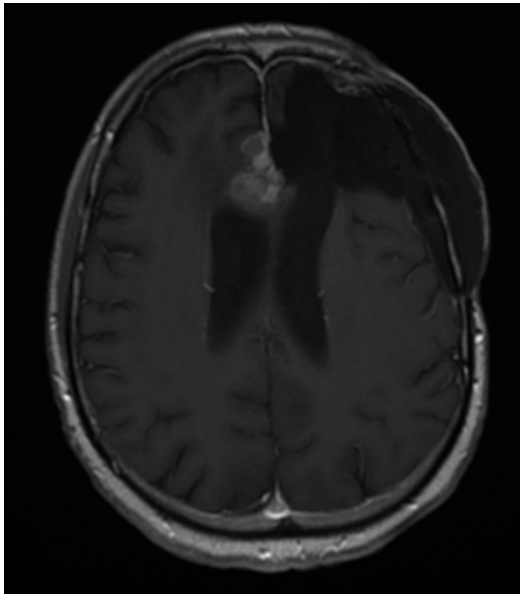
At the last FU 8 patients (32%) were alive and 17 (68%) were dead

HUMANITAS
CANCER CENTER

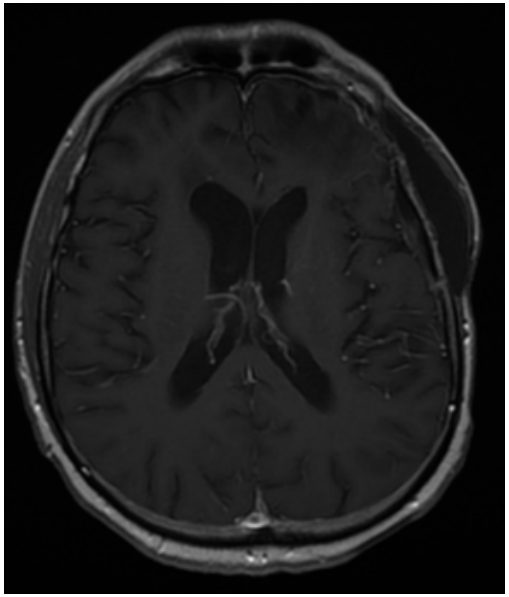


RM PRE RT





RM POST RT



HUMANITAS
CANCER CENTER

Prognostic factors

On univariate and multivariate analysis no significant factors affected survival were recorded

Histology	OS 1- 2 years	61% and 35% vs 89% and 66%
EOR	CR vs SR/PR/B	p<0.01
MGMT	OS 1- 2 years	100% and 83 % vs 67%
Tumor volume	PFS 2 years	42% vs 11%
	OS 2 years	56% vs 33%
Combined treatment/RT	PFS 1-2 years	74% and 32% vs 67% and 0%
	OS 1-2 years	83% and 51% vs 73% and 0%

HUMANITAS
CANCER CENTER

Conclusion

Reirradiation is feasible, safe and effective local treatment option for patients with recurrent malignant brain tumor

VMAT RA technique improves target coverage while minimizing higher dose to normal tissue

Good radiological response

Minimal toxicity

HUMANITAS
CANCER CENTER

“PATIENT TARGETED” APPROACH

SURGERY
Dott. Federico Pessina
Prof. Lorenzo Bello
Dott. Marco Riva

RADIOTHERAPY
Dott.ssa Marta Scorsetti
Dott. ssa Piera Navarria
Dott. ssa Anna Maria Ascolese

NEURO-RADIOLOGY
Dott. Alberto Bizzi
Dott. Marco Grimaldi

ONCOLOGY
Dott.Paolo Zucali
Dott. Matteo Simonelli

NEURO-ONCOLOGY
Prof. Riccardo Soffietti
Dott. ssa Roberta Rudà

HUMANITAS
CANCER CENTER