

#### WHICH ROLE FOR 11C-METHIONINE PET IN RADIOTHERAPY PLANNING IN NEWLY DIAGNOSED GLIOBLASTOMA PATIENTS?

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## DICHIARAZIONE

#### Relatore: Elena Clerici

Come da nuova regolamentazione della Commissione Nazionale per la Formazione Continua del Ministero della Salute, è richiesta la trasparenza delle fonti di finanziamento e dei rapporti con soggetti portatori di interessi commerciali in campo sanitario.

- Posizione di dipendente in aziende con interessi commerciali in campo sanitario (NIENTE DA DICHIARARE)
- Consulenza ad aziende con interessi commerciali in campo sanitario (NIENTE DA DICHIARARE)
- Fondi per la ricerca da aziende con interessi commerciali in campo sanitario (NIENTE DA DICHIARARE)
- Partecipazione ad Advisory Board (NIENTE DA DICHIARARE)
- Titolarità di brevetti in compartecipazione ad aziende con interessi commerciali in campo sanitario (NIENTE DA DICHIARARE)
- Partecipazioni azionarie in aziende con interessi commerciali in campo sanitario (NIENTE DA DICHIARARE)







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Standard of care for newly diagnosed GBM:

maximal safe resection - adjuvant RT with concurrent and adjuvant TMZ



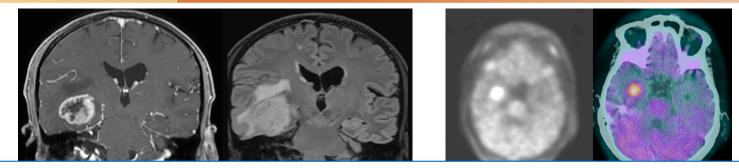
Almost all cases **relapse** in the site of **primary** treatment

A way forward in improving the outcome might be **more precise** identification of the **volume** at the most significant risk of recurrence.



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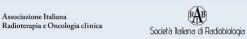


Evidence regarding the predictive and prognostic value is still lacking

Its use in planning local treatments, such as surgery and radiation therapy, is debated

Aims were to evaluate the employment of metabolic imaging, [11C]MET PET, along with morphological ones, MRI, could provide **additional** information to

- maximize the EOR
- improve the target volume delineation for RT planning





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- Materials and Methods:
- Newly diagnosed GBM patients
- ➤ Ages 18–70 years
- ► KPS  $\geq$  70

 $\geq$ 

- ▶ Residual tumor or surgical cavity with a maximum diameter of 10 cm
- Normal liver, kidney and bone marrow functions
- Available MRI and MET PET
- Enrolled in NCT00006353 trial



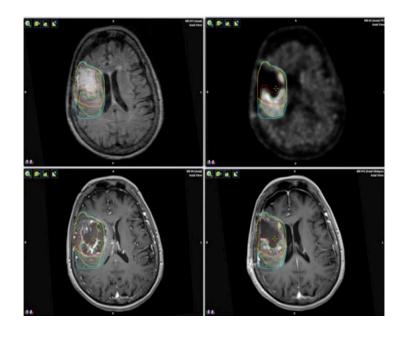


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#### **Target delineation**

CTV1:	entire surgical cavity
	residual tumor after surgery
	abnormality on the T1-weighted post-contrast MPRAGE
	uptake on 11CMETPET
CTV2:	abnormality on FLAIR MRI images after surgery CTV1
PTV1/PTV2:	adding an isotropic margin of <b>5 mm</b> from CTV1 and CTV2



The dose prescribed was 60 Gy on PTV1, and 42 Gy on PTV2 for 15 days, using a simultaneous integrated boost.



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All patients received concurrently/adjuvant TMZ

Corticosteroids

Neurological examination and **MRI**: at 1 month after concurrent CHT–HFRT and every 4 months after that

**MET PET**: at 4 and 12 months during maintenance CHT or to rule out pseudoprogression

Neuropsychological assessment: "Milano Bicocca Battery"



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AIR

	From August 2013 to April 2016	N. (tot 93 pts)	%
Results:	Median age (range)	61 years (range 23–77 years)	
	KPS		
	70	6	6.4
	80	20	21.6
	90-100	67	72
	Gender		
	Female	33	35.5
	Male	60	64.5
	Histology		
	Glioblastoma IDH WT	93	100
	MGMT Methylated	53	57
	MGMT Unmethylated	40	43
	EOR		
	GTR	45	48.3
	STR	18	19.4
	PR	16	17.2
	В	14	15.1

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## Results:

From August 2013 to April 2016	N. (tot 93 pts)	%
<b>CERTV</b> on postoperative MRI		
Yes	63	67.7
No	30	32.3
Median CERTV	4.23 (0.17-35.33)	
BTV on [11C]METPET		
Yes	78	83.9
No	15	16.1
Median BTV on [11C]MET PET Median SUVmax [11C]MET PET	8.47 (0.11–62.20) 4.03 (2.30–13.90)	
Median TBRmax	4.34 (2.36–12.00)	
Location of BTV	78	100
CE + FLAIR abnormalities	63	80.8
Only FLAIR abnormalities	15	19.2
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## Results:

	GTR		STR	PR
No patients	45		18	16
<b>Residual Tumor NO</b> (CERTV/BTV)	15		0	0
<b>Residual Tumor YES</b> CERTV + BTV BTV only	15 15		18 0	16 0
Median SUVmax (range)	3.70 (2.	.20–9.54)	3.25 (2.3–7.5)	4.7 (2.96–9.30)
Median PFS months (range)	10 (6–2	.2)	11 (2–28)	10 (2–35)



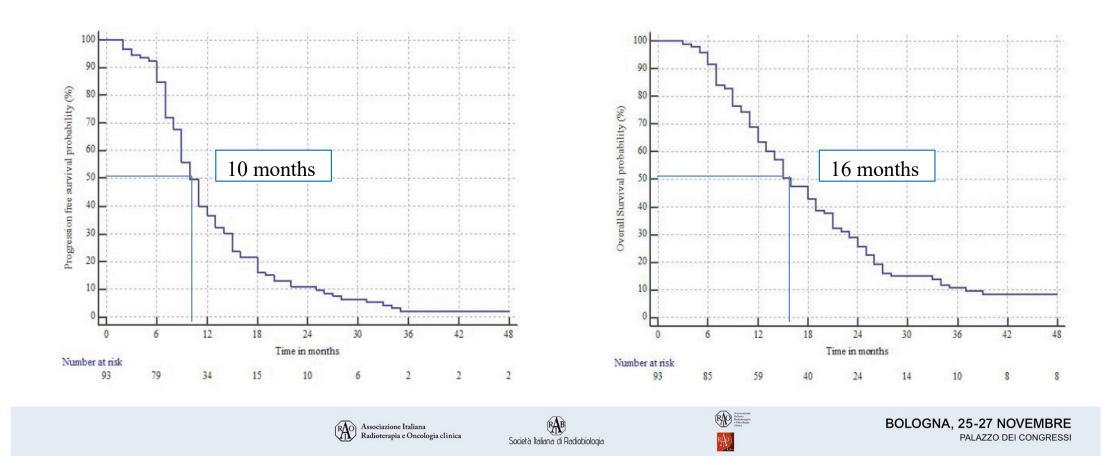
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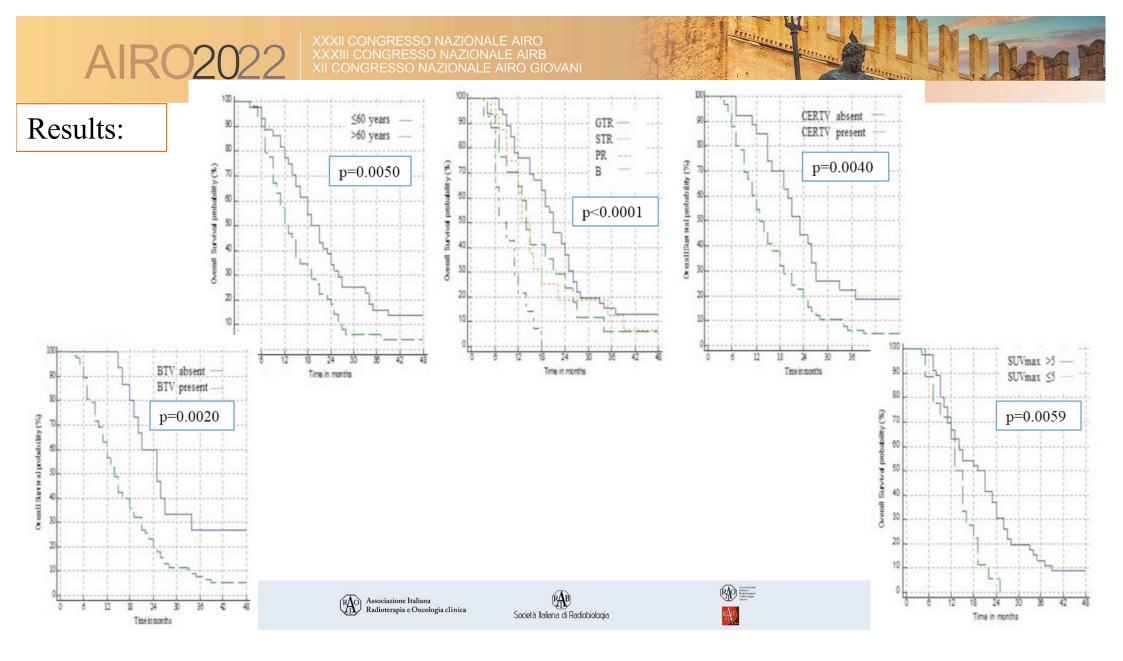


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### **Results:**

### The median follow-up time was 72 months (range 58–90 months)





AIR		Pts	Median OS Months (Months 95% CI)	1 Year OS % (SE)	2 Year OS % (SE)	3 Year OS % (SE)	<i>p</i> Value Univariate	HR Multivariate (95% CI)	<i>p</i> Value Multivariate
	Overall survival	93	16 (14–19)	63.4 (±4.9)	25.8 (±4.5)	10.8 (±3.2)			
Results:	Age ≤60 >60	44 49	19 (16–24) 13 (10–16)	77.3 (±6.3) 51.0 (±7.1)	34.1 (±6.4) 18.4 (±5.5)	15.9 (±5.5) 6.1 (±3.4)	0.0050	2.6038 (1.5578– 4.3524)	0.0003
	EOR GTR STR PR B	46 17 16 14	21 (18–25) 14 (9–24) 13 (12–18) 7 (6–12)	76.1 ( $\pm$ 6.2) 64.7 ( $\pm$ 11.6) 62.5 ( $\pm$ 12.1) 21.4 ( $\pm$ 11.0)	$37.0 (\pm 7.1) 23.5 (\pm 10.3) 18.8 (\pm 9.7) 0$	$\begin{array}{c} 15.2 \ (\pm 5.3) \\ 5.8 \ (\pm 5.7) \\ 6.2 \ (\pm 6.0) \\ 0 \end{array}$	<0.0001	160.2776 (20.3294– 1263.6345)	<0.0001
	MGMT Methylated Unmethylated	53 40	18 (14–23) 15 (12–18)	66.0 (±6.5) 60.0 (±7.7)	34.0 (±6.5) 15.0 (±5.6)	15.1 (±4.9) 5.0 (±3.4)	0.14	0.4626 (0.2776– 0.7711)	0.0031
	CERTV absent present	30 63	23 (19–27) 13 (11-16)	85.2 (±6.5) 54.5 (±6.1)	44.4 (±9.5) 18.2 (±4.7)	22.2 (±8.0) 6.0 (±2.9)	0.0040	4.1696 (2.3985– 7.2485)	<0.0001
	BTV absent present	15 78	25 (20–34) 14 (12–18)	100 56.4 (±5.6)	60.0 (±12.6) 19.2 (±4.4)	26.7 (±11.4) 7.6 (±3.0)	0.0020	0.4800 (0.3772– 0.6109)	<0.0001
	CERTV/BTV CERTV absent BTV absent CERTV absent BTV present CERTV present BTV present	15 15 63	25 (20–34) 21 (15–26) 13 (11–16)	100 73.3 (±11.4) 52.4 (±6.2)	60.0 (±12.6) 33.3 (±12.2) 15.9 (±4.6)	26.7 ( $\pm$ 11.4) 13.3 ( $\pm$ 8.7) 6.3 ( $\pm$ 3.0)	0.0029	1.0728 (0.6131– 1.8770)	0.856
	SUVmax * >5 2.2–5	18 46	13 (12–16) 19 (12–24)	66.7 (±11.1) 63.0 (±7.1)	5.5 (±5.4) 30.4 (±6.7)	0 13.0 (±4.9)	0.0059	2.1071 (1.135–3.909)	0.0181
	TBRmax * ≤4.5 >4.5	36 28	21 (13–24) 13 (10–16)	70.6(±7.8) 57.1(±9.3)	32.4(±8.0) 10.7(±5.8)	14.7(±4.0) 3.5 (±3.5)	0.0077	2.0273 (1.1419– 3.5991)	0.0158



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## Conclusions:

The use of [11C]MET PET and contrast-enhanced T1 and FLAIR MRI proved to be effective in **tumor volume definition** for RT planning

This metabolic imaging allowed to detect **areas at higher risk** of **recurrence** located in the FLAIR abnormalities, confirming the need to perform surgical resection beyond the enhanced boundaries where uptake is visible.





#### **Challenging issues**:

- Extent of the surgical resection to perform
- Margins reduction



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