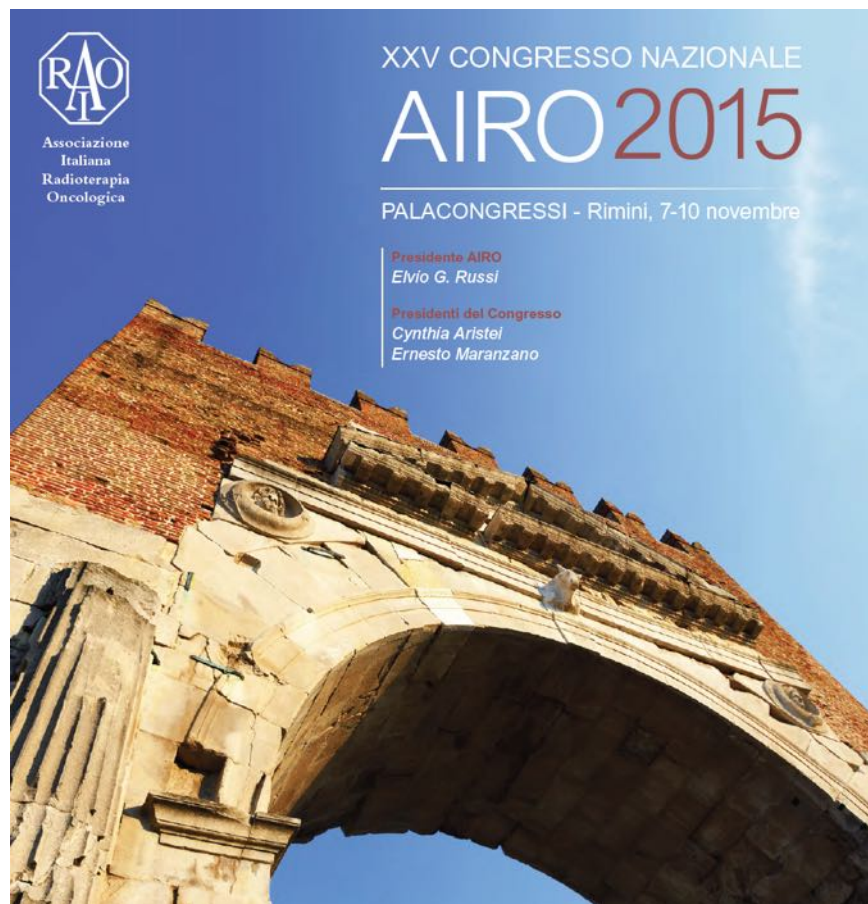


Rete Oncologica Veneta

Ricerca, innovazione, assistenza



RADIOCHIRURGIA CON GAMMA-KNIFE: INDICAZIONI ED ESPERIENZA DI VERONA

M Longhi¹,

*R Foroni², E Zivelonghi², A. Gasparini³, PM Polloniato², L Rosta³,
S Dall'Oglio⁴, N Tommasi⁵, A Grazioli³, C. Parisi, A. D'Ottavio¹,
R Mazzarotto⁴, G Pinna¹, C Cavedon²,
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DAI Neuroscienze:

¹Istituto di Neurochirurgia

DAI Patologia e Diagnostica:

²Fisica Sanitaria dO

³Neuroradiologia dO

DAI Chirurgia e Oncologia:

⁴Radioterapia dO

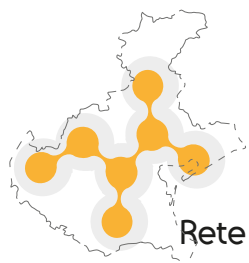
**²Centro Interdipartimentale di Documentazione Economica
(C.I.D.E)**

Università di Verona



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VERONA





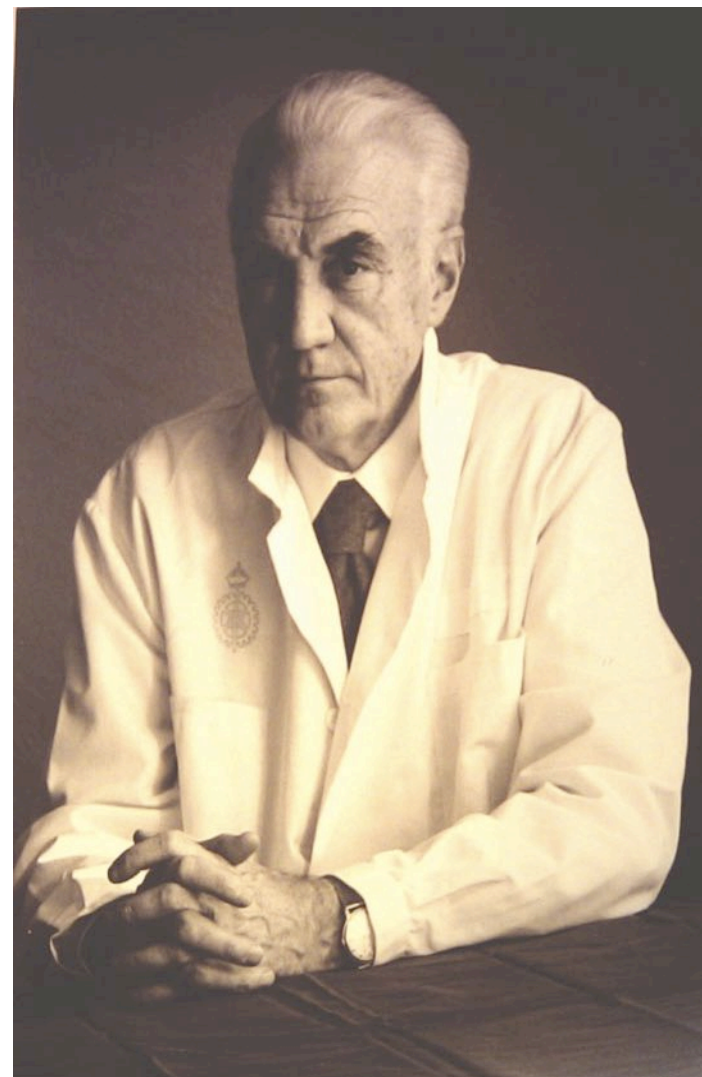
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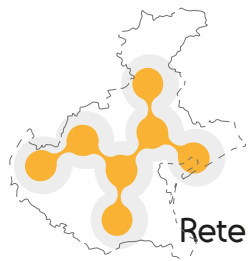
Ricerca, innovazione, assistenza

GAMMA KNIFE IN LOW- GRADE GLIOMAS

DEFINITION (Leksell 1949)

**TECHNIQUE OF CLOSED-SKULL
DESTRUCTION OF A
PREDETERMINED INTRACRANIAL
TARGET BY SINGLE FRACTION,
HIGH-DOSE OF IONIZING
RADIATION USING A PRECISION
STEREOTACTIC APPARATUS**



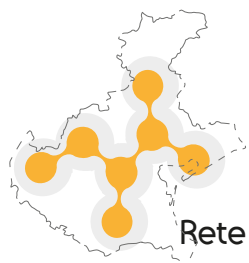


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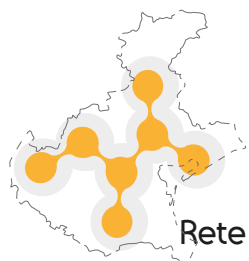
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GAMMA KNIFE IN LOW- GRADE GLIOMAS

ANCHE IN ANESTESIA GENERALE





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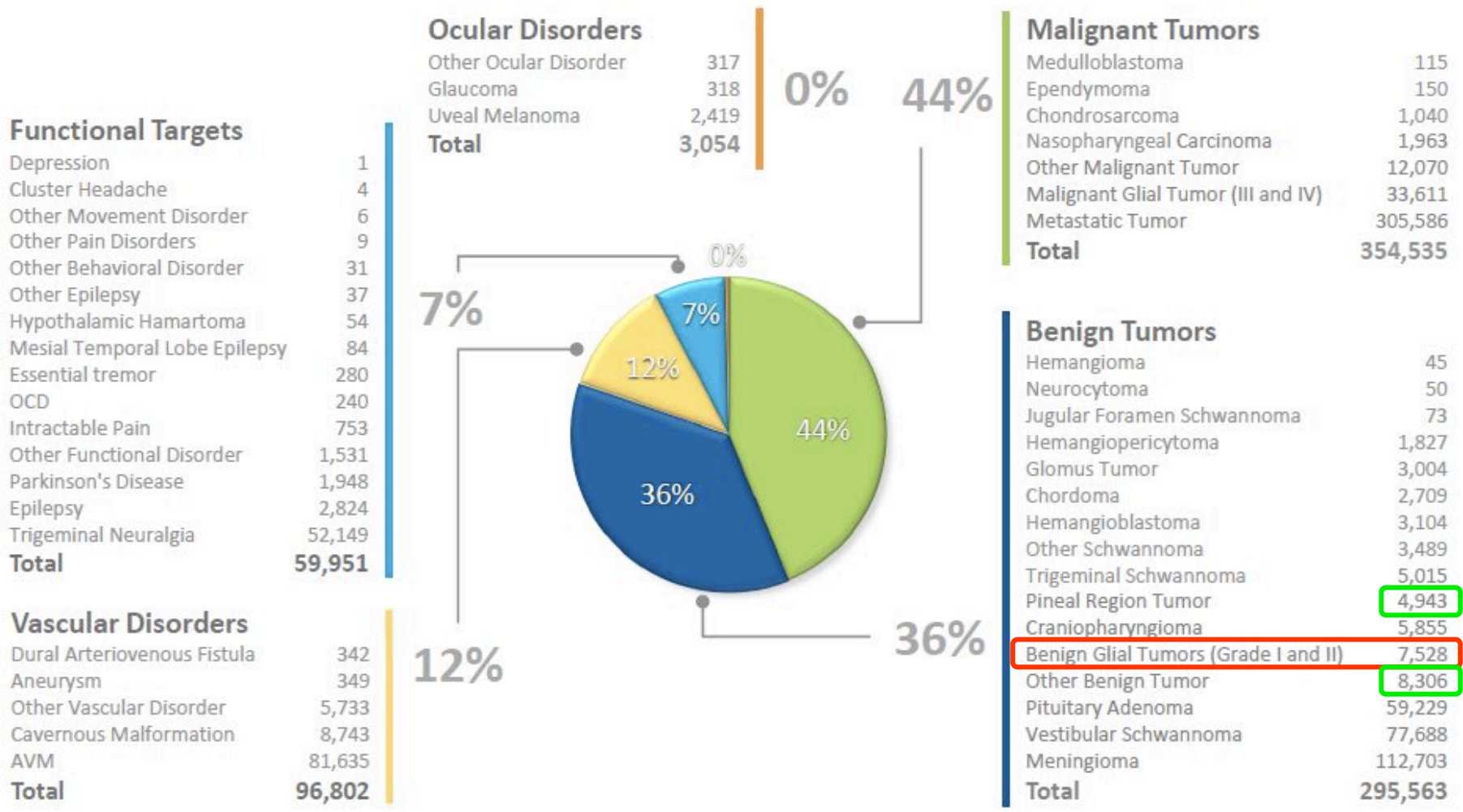
Ricerca, innovazione, assistenza

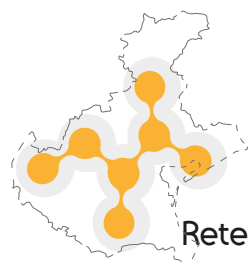


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Cumulative indications worldwide 1991 – 2013





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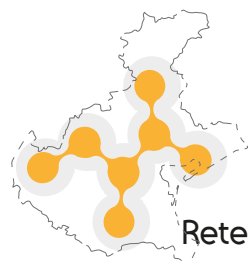
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LITERATURE

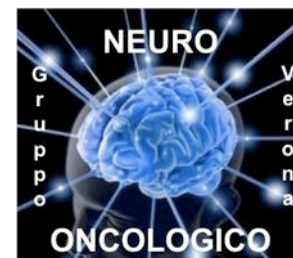
AUTHOR	PTS.
Ganz, Acta N. 1994	7
Kihlström, ActaN. 1994	7
Barcia, Acta N. 1994	16
Baumann, Ped. N. 1996	7
Somaza, Ped. N. 1996	9
Grabb, Neurosurg.1996	13
Larson, IJROBP 1996	49
Kida, J Ns.2000	51
Raco, Child'sNS 2000	19
Eder, Child'sNS 2000	12
Hadjipanayis, J Ns 2002	37
Gerosa, CurrO Onl. 2003	43

AUTHOR	PTS.
Hadjipanayis, N. F. 2003	49
Simonová, J Ns. 2005	68
Heppner, Ns. 2005	49
Lo, JNOncol 2006	8
Wang, JNS 2006	21
Szeifert, ProgNSur. 2007	74
Lekobic, NeurFocus 2007	17
Kano J Noncol 2009	50
Kano J Noncol 2009	14
Kano, JNSur.P. 2012	12
Weintraub, JNSur.P. 2012	24
El-Shehaby ActaN, 2015	15
Tanaka CLinNAM 2015	rev.
Eksi Child Nerv System 2015	rev



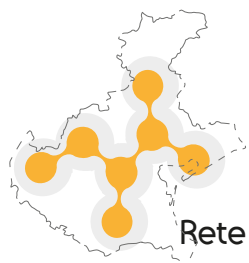
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Ricerca, innovazione, assistenza



GAMMA KNIFE IN LOW-GRADE GLIOMAS

**RADIOSURGERY IN
"LOW-GRADE"
GLIOMAS**



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Ricerca, innovazione, assistenza

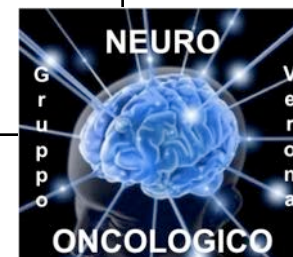


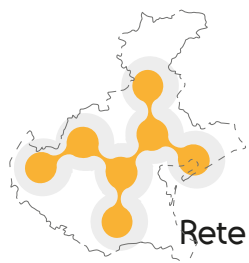
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RATIONALE

- **VERY LOW RISK OF RADIATION INJURY:**
 - highly conformal radiation treatment
- **NO TOXIC SYSTEMIC SIDE EFFECTS**
- **TO PRESERVE NEUROLOGIC FUNCTION****
- **TO PREVENT FURTHER TUMOR GROWTH**
- **TO PREVENT FURTHER INTERVENTIONS:**
 - in residual/recurrence LGNTs
- **TO PREVENT RT-RELATED SEQUELAE**
 - usually, young-adult patients





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Ricerca, innovazione, assistenza



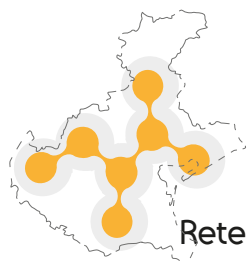
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INDICATIONS

- DEEP-SEATED AREAS OR ELOQUENT BRAIN REGIONS
- REFUSAL OF OPEN SURGERY
- TUMOR VOLUME < 10-15 cc.
- WELL DEFINED BORDERS
- CLINICALLY SYMPTOMATIC OR RADIOLOGICALLY PROGRESSING NEOPLASMS
- SMALL RESIDUAL/RECURRENCE LGNTs





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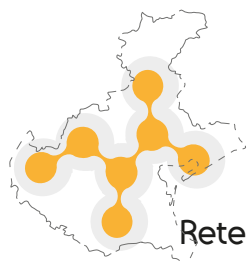


OUR EXPERIENCE

February 1993 – November 2014
144 TREATED PATIENTS / 154 TREATED LESIONS

M/F	82/62
MEAN AGE (Range)	32.3 yrs. (2–72)
PRIMARY/RESIDUAL*	114/144 pts. (79%)
MEAN VOLUME (RANGE)	4.2 mL (0.16–22.8)
GENERAL ANESTHESIA	24/144 pts. (17%)
Mean PI/ PD/ MD /#ISOCENTERS	50.1% / 16.4Gy / 32.9Gy / 8.8

** All histologically confirmed*



Rete Oncologica Veneta

Ricerca, innovazione, assistenza

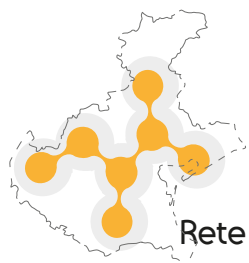


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OUR EXPERIENCE

HISTOLOGY	N°	%
Pilocytic astrocytoma	58	38.0
Astrocytoma GII	32	21.0
Pineocytoma	14	9.0
Choroid plexus papilloma	13	8.5
Ependimoma	11	7.0
Central neurocytoma	10	6.5
Oligodendroglioma	5	3.0
Pleomorphic xanthoastrocytoma	5	3.0
Ganglioglioma	3	2.0
Other	3	2.0



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PATIENTS WITH AT LEAST 1-year FU: 137

MEDIAN SURVIVAL TIME

48.5 Mos

CLINICAL IMPACT

85% Impr./Stable

TGC

90%

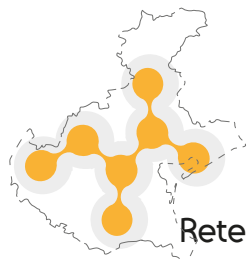
ALIVE/DEATH

124/13 Pts

ACTUARIAL PFS RATE

87.5% at 5 Ys





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Ricerca, innovazione, assistenza



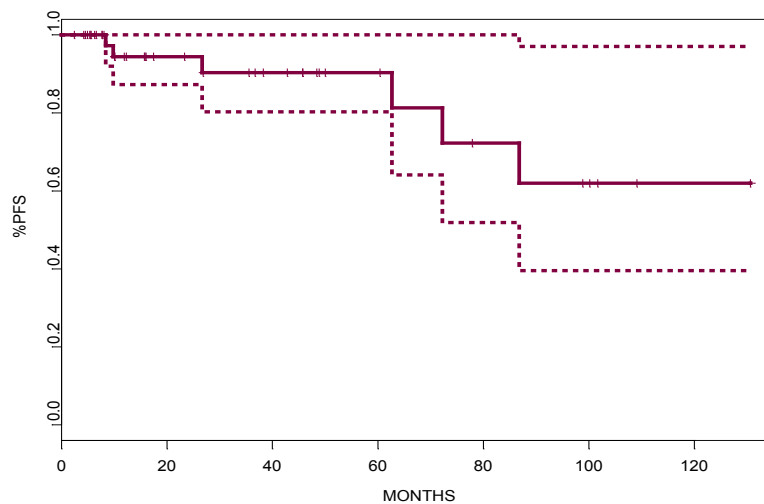
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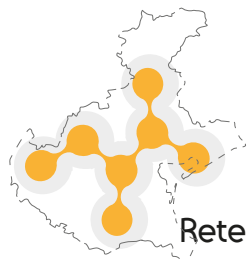


RESULTS

SOPRAVV. A 10 aa	PFS A 5 aa	COMPLICAZ. PERMANENTI
87,0%	87,5%	5,0% (di solito, deficit minori)

LOW GRADE GLIOMAS





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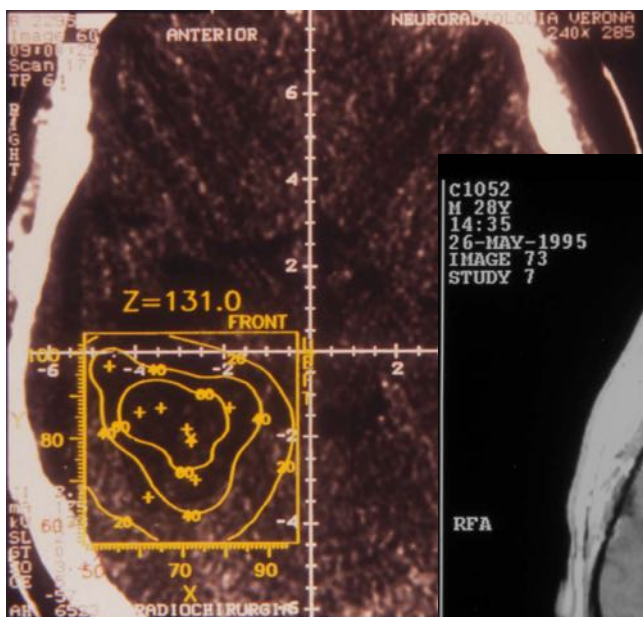
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GK DOSE PLANNING

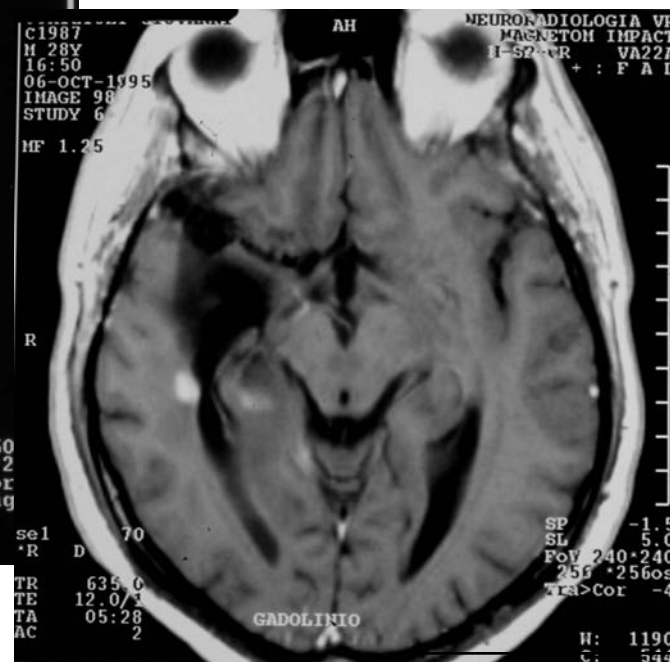


ASTROCITOMA GII

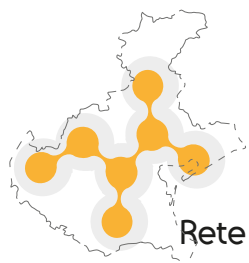
MRI AT 11 Mos.



MRI AT 15 Mos.



Trento, 29 Nov., 2014



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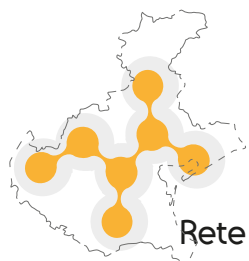


OUR EXPERIENCE

SIDE EFFECTS

- NO GK-INDUCED TUMORS
- NO STROKE OBSERVED
- NO GK-RELATED MORTALITY
- PERMANENT COMPLICATIONS: 5% ONLY (3/5 minor) BUT
- 23.5% ASYMPTOMATIC ADVERSE RADIATION-EFFECT (ARE)





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Ricerca, innovazione, assistenza



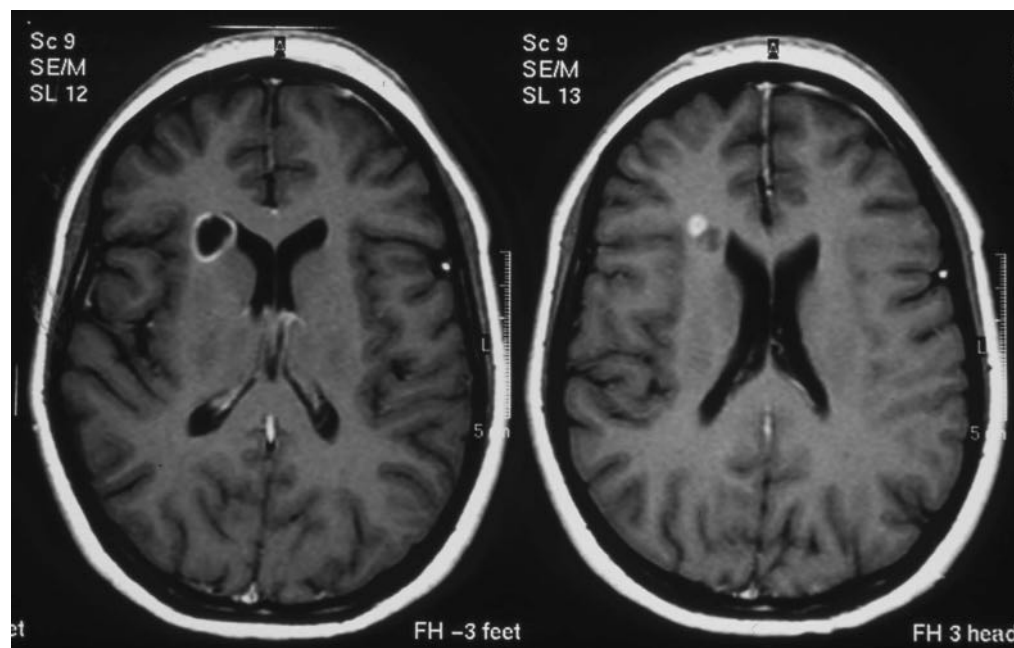
AZIENDA OSPEDALIERA UNIVERSITARIA INTEGRATA
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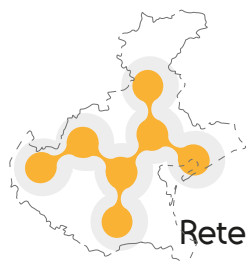


SIDE EFFECTS

- D.C., F, 20-year-old.
- July 20th, 1998: POST-TRAUMATIC BRAIN INJURY. COMA
- TAC/RM: SMALL, DEEP-SEATED RIGHT FRONTAL LESION, PARAVENTRICULAR. NO C.E.
- MRI on March 14th, 1999: INCREASED VOLUME; C.E.

MRI on March
14th, 1999





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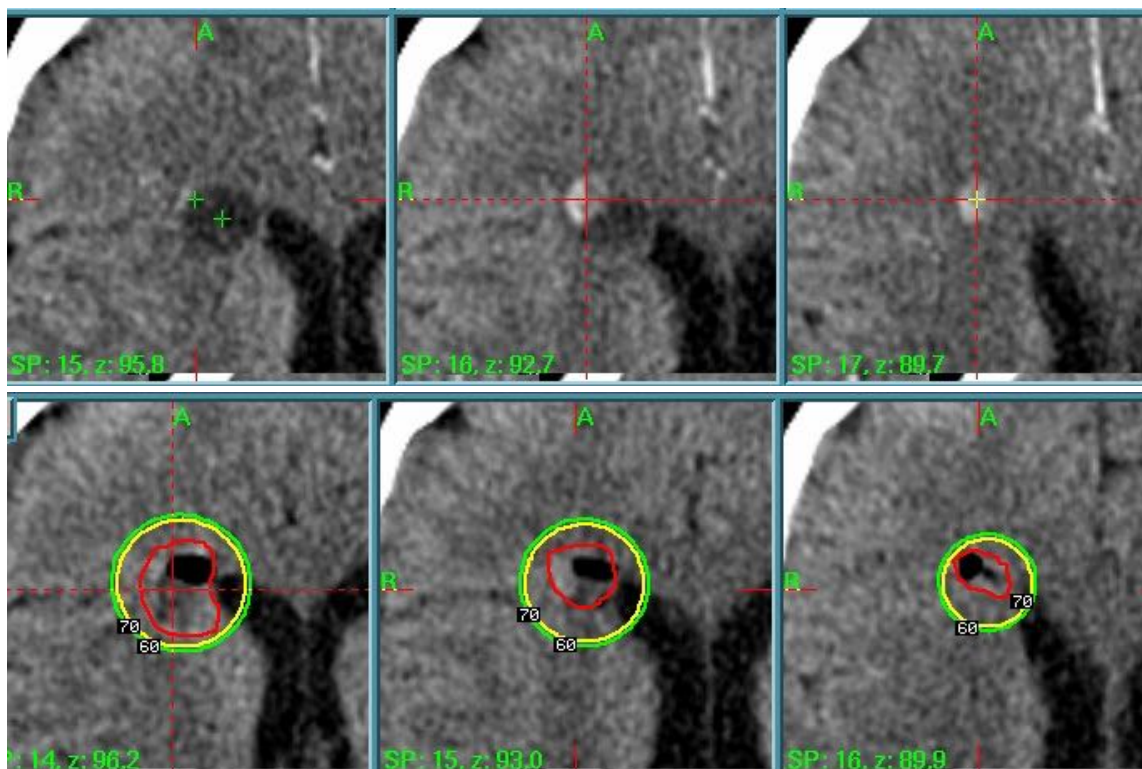


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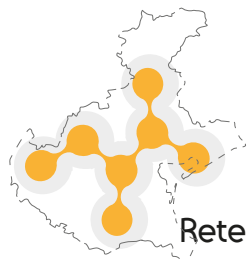
SIDE EFFECTS

- STEREOTACTIC BRAIN BIOPSY: April 6th, 1999
- HISTOLOGY: PAPILLAR GANGLIONEURONAL TUMOR
- GK: April 6th, 1999: VOL.0,9 ML; PI 70%; PD 22,4 Gy; MD 32,0 Gy; # SHOT: 1



CT-GUIDED
BIOPSY

TREATMENT
PLANNING



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Ricerca, innovazione, assistenza

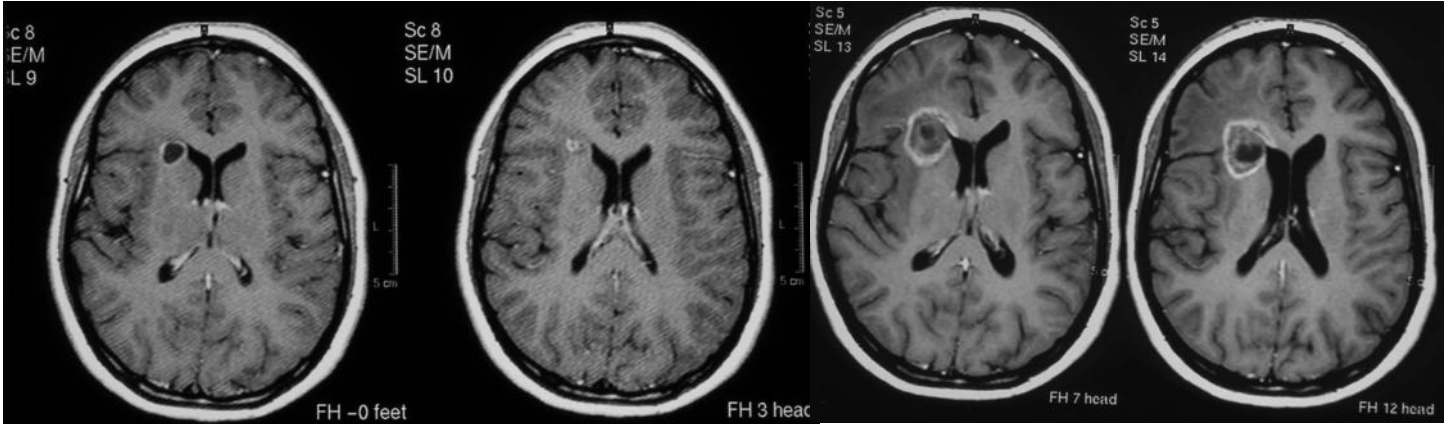


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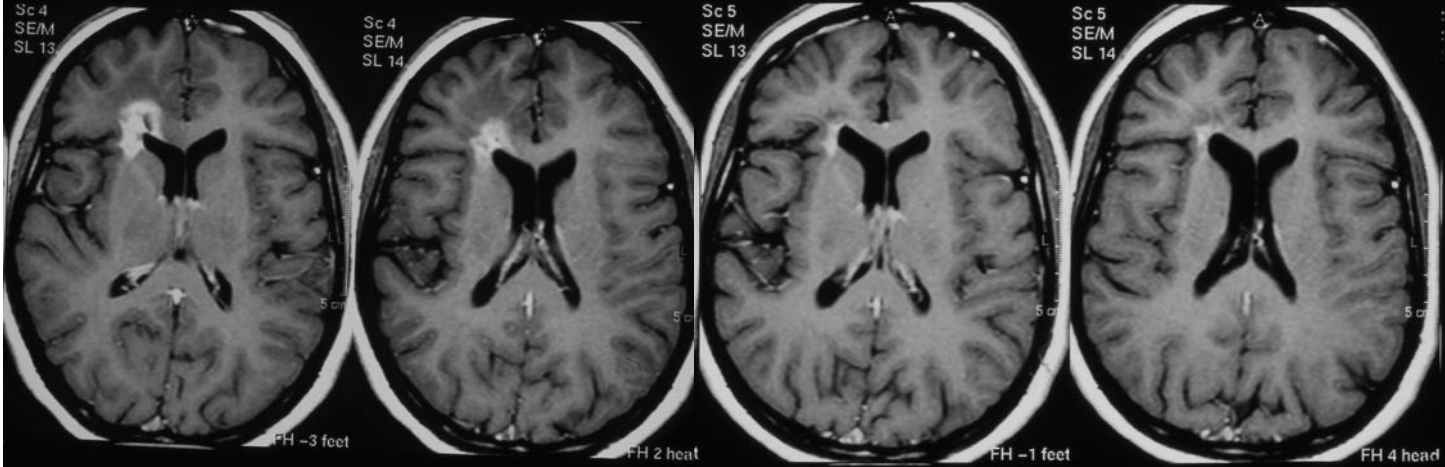
SIDE EFFECTS

MRI FU at
3 mos.

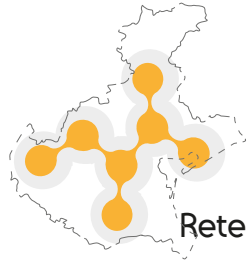


MRI FU at
6 mos.

MRI FU at
9 mos.



MRI FU at
14 mos.



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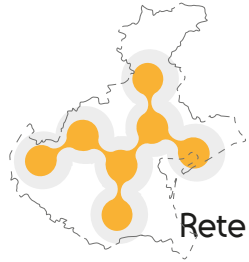


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SIDE EFFECTS

- January, 2007: spontaneous labor
- September, 2011 LAST MR: stable “scar”
- LAST FU.: November, 2011 (Surv.: 153 m.):
 - KPS: 100%
 - ORDER GRADING: I



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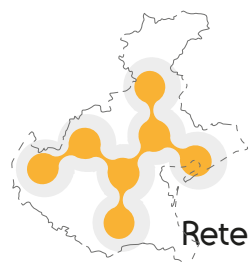
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“UNUSUAL LOW-GRADE” GLIOMAS



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Ricerca, innovazione, assistenza



5

GAMMA KNIFE RADIOSURGERY

Edited by David Mathieu



INTECH

Gamma Knife Radiosurgery in the Management of Unusual Grade I/II Primitive Neuroepithelial Tumours of the Brain

A. Nicolato¹, M. Longhi¹, R. Foroni², F. Alessandrini², A. De Simone¹,
C. Ghimenton², A. De Carlo¹, P. Mirtuono³ and M. Gerosa¹

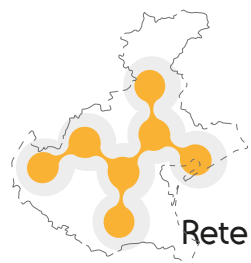
Multidisciplinary Neurooncologic Group of Verona,

¹Department of Neurological Sciences

²Department of Pathology and Diagnosis

*³Department of Neurological, Neuropsychological,
Morphological and Movement Sciences*

*Section Anatomy, University Hospital (AOUI) of Verona,
Italy*

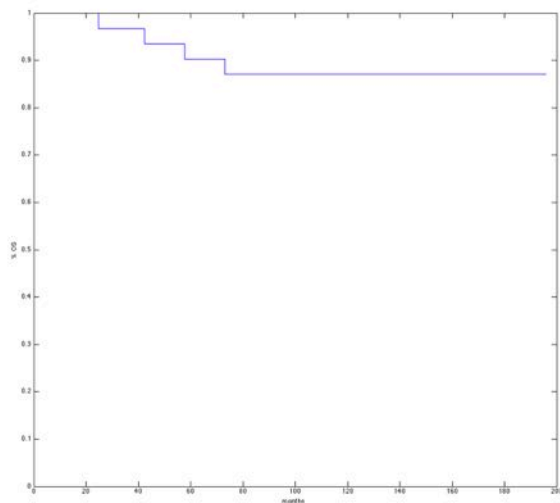


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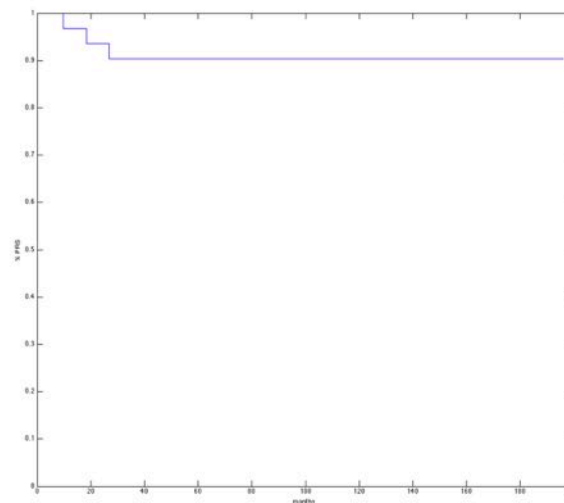
Ricerca, innovazione, assistenza



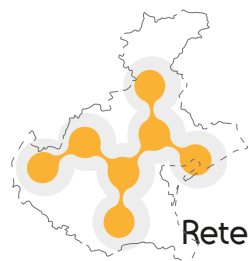
“UNUSUAL LOW-GRADE” GLIOMAS



Kaplan-Meier estimate of overall survival curve in 30 LGPNTs.



Kaplan-Meier local PFS curves in 30 LGPNTs.



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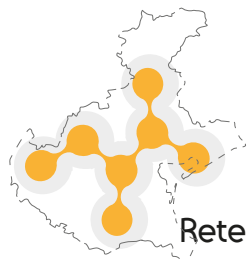
Ricerca, innovazione, assistenza



“UNUSUAL LOW-GRADE” GLIOMAS

Histology	N° Pt	Me/Med FU mos.	No def. / Impr	Clinical Results		Alive/ Dead (OS%)
				Stable	Wors.	
Overall series	30	85.7/66.8	16/30	8/30	6‡/30	26/4¶ (86.7)
Pineocytoma	10	66.7/54.6	6/10	3/10	1/10	9/1 (90.0)
CPP	8	92.6/71.8	2/8	2/8	4/8	6/2 (75.0)
CN	4	172.0/180.6	4/4	-	-	4/4 (100.0)
PXA	3	45.6/43.7	1/3	1/3	1/3	2/3 (66.6)
Miscellaneous	5	68.0/68.3	3/5	2/5	-	5/5 (100.0)

Histology	Act. Surv. %		Ov. TGC%	Act. Local PFS%		GK-related sequelae		Post-GK treats.
	At 5y	At 10y		At 5y	At 10y	Mort.	Perm Compl	
Overall series	90.0	87.0	90.0	91.0	91.0	0.0	0.0	3 surg.int. 1 VPS 3 RT
Pineocytoma	92.0	92.0	100.0	100.0	100.0	0.0	0.0	1 RT
CPP	90.0	80.0	87.5	90.0	90.0	0.0	0.0	1 surg.int. 1 RT
CN	100.0	100.0	75.0	83.0	83.0	0.0	0.0	1 surg.int. 1 RT
PXA	80.0	80.0	66.7	80.0	80.0	0.0	0.0	1 VPS
Miscellaneous	100.0	100.0	100.0	100.0	100.0	0.0	0.0	1 surg.int.

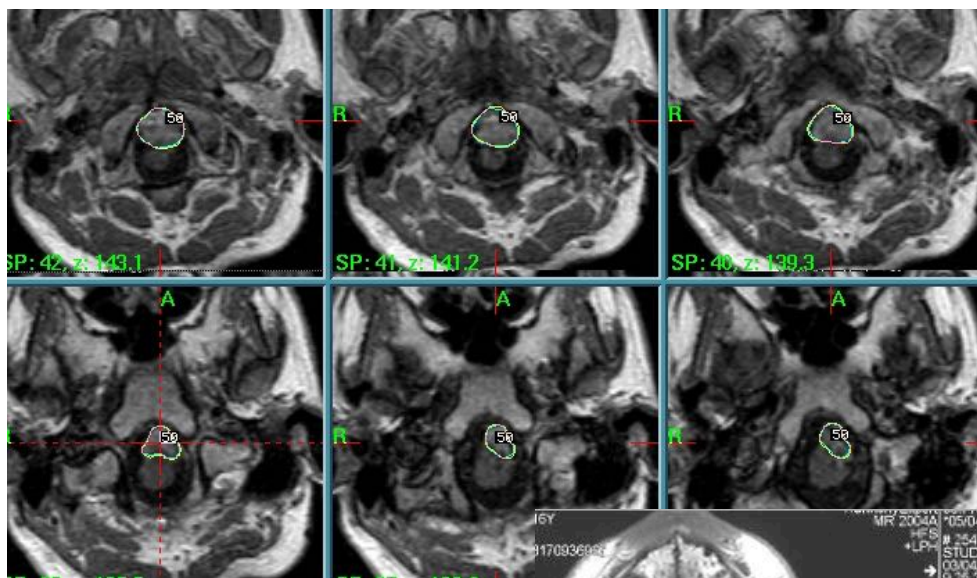


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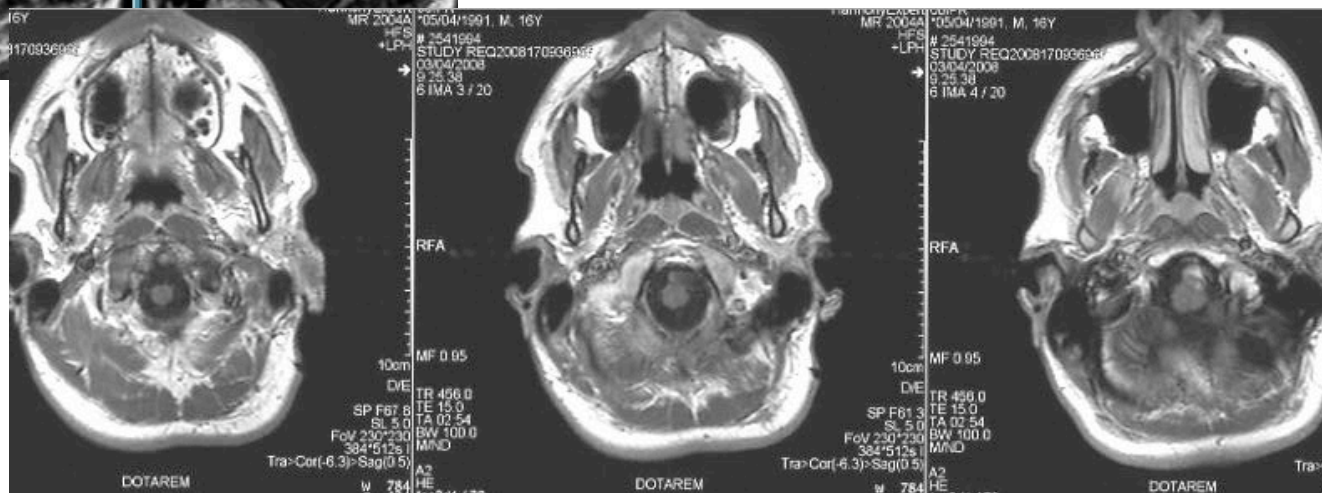


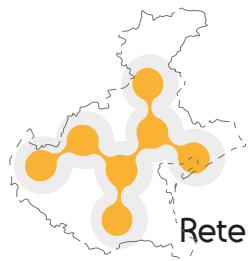
CHOROID PLEXUS PAPILLOMAS



MRI ON GK DAY
Dose Planning

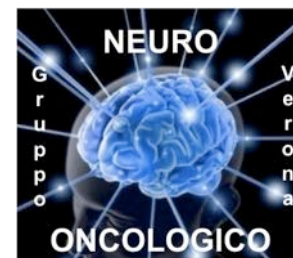
MRI AT 38 Mos.





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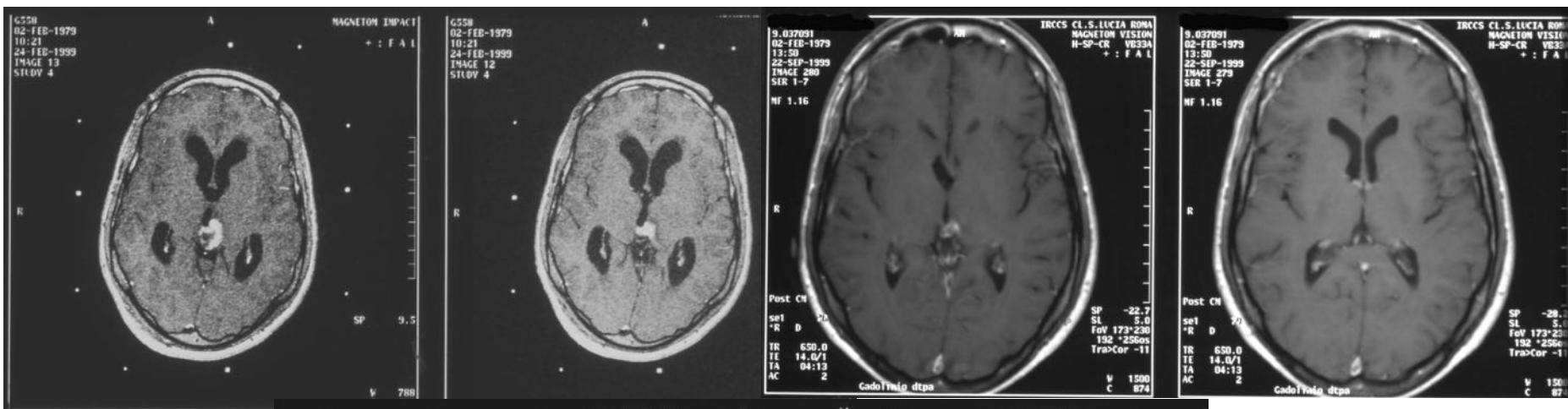
Ricerca, innovazione, assistenza



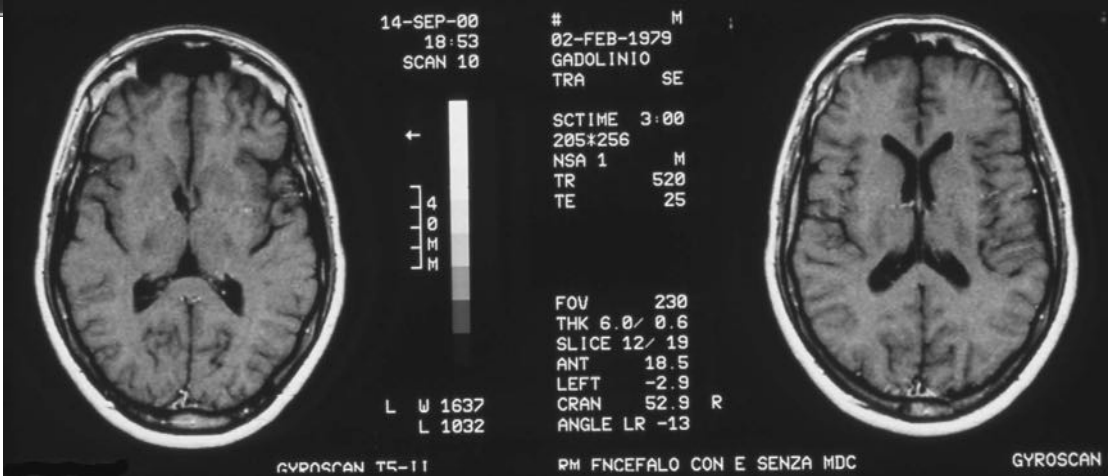
PINEOCYTOMA

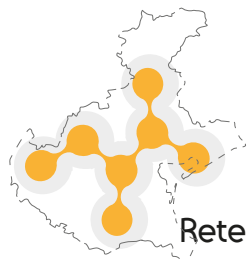
PRE-GK MRI

MRI AT 3 Mos.



MRI at 18 Mos.



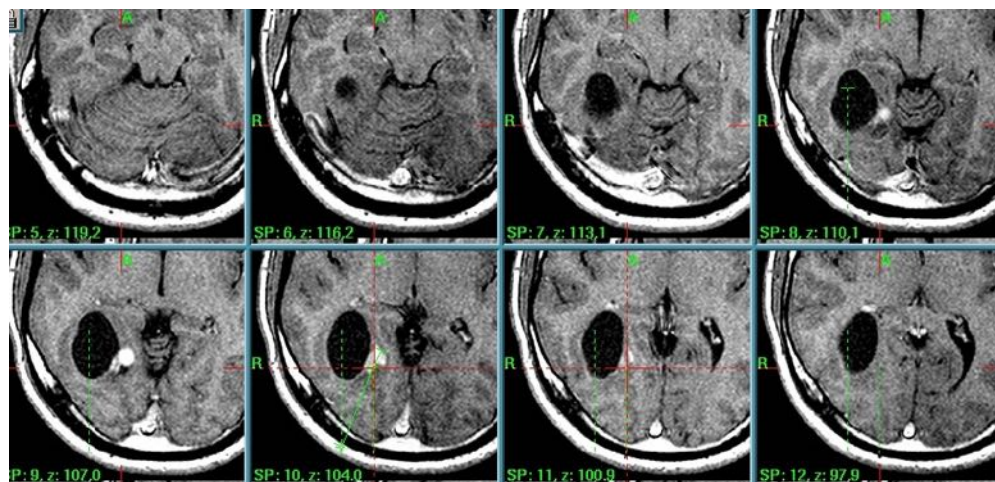


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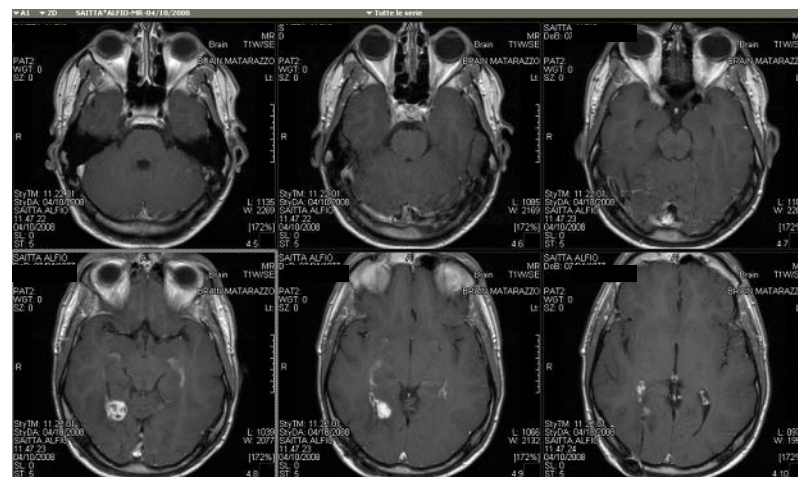
Pleomorphic Xanthoastrocytoma



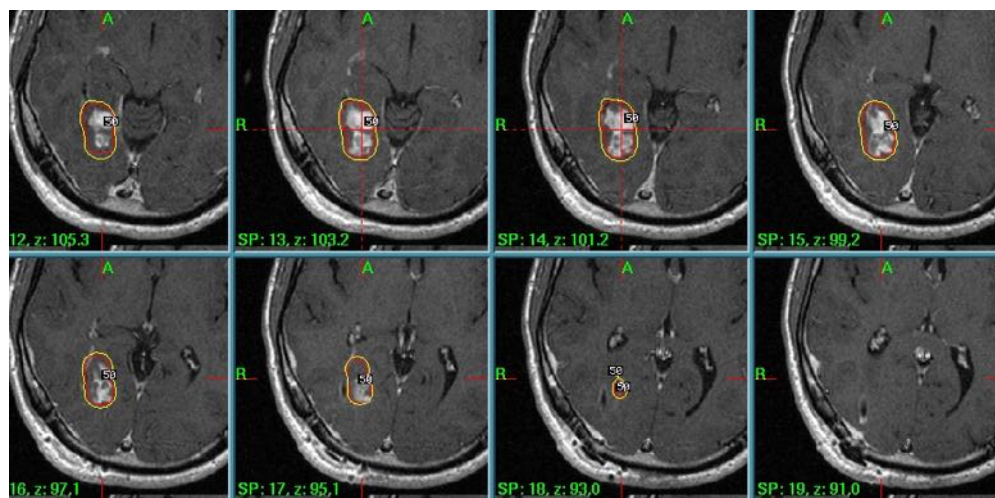
MR PRE-OMMAYA



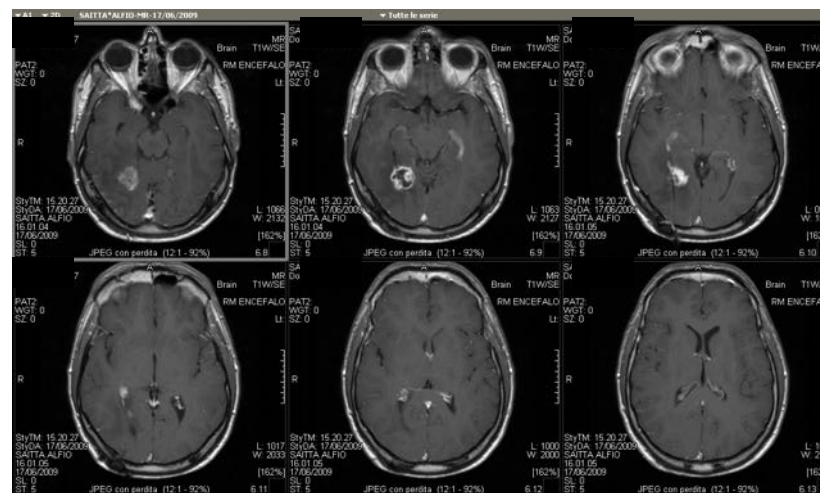
MR FU AT 32 Mos.

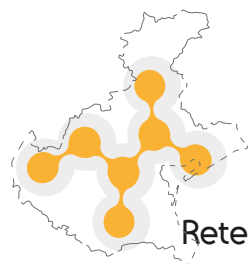


TREATMENT PLANNING



MR FU AT 40 Mos.



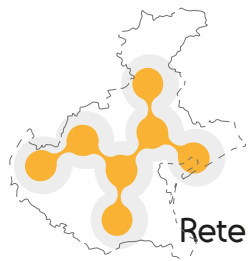


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TRATTAMENTI COMBINATI



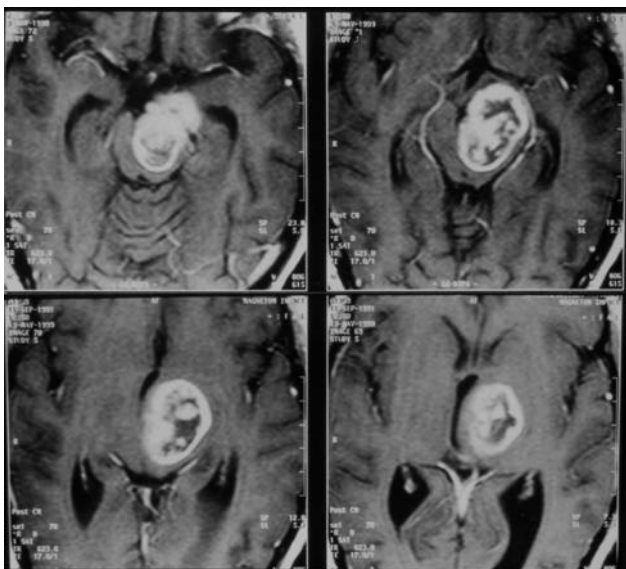
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Ricerca, innovazione, assistenza

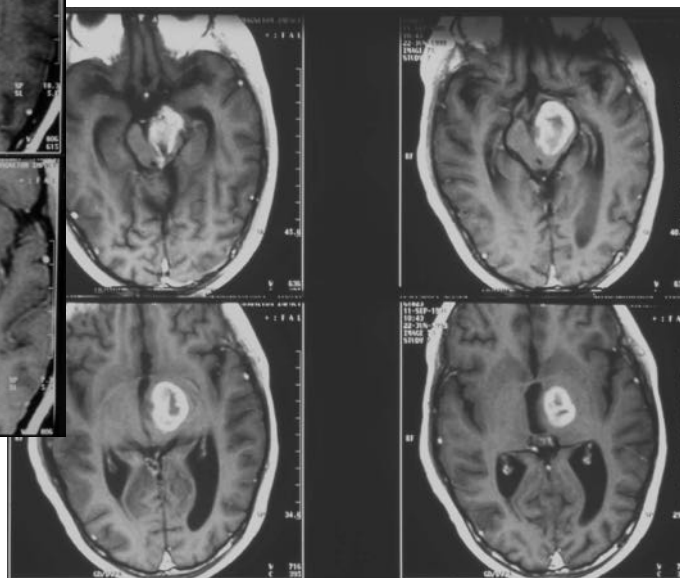


PILOCYTIC ASTROCYTOMA

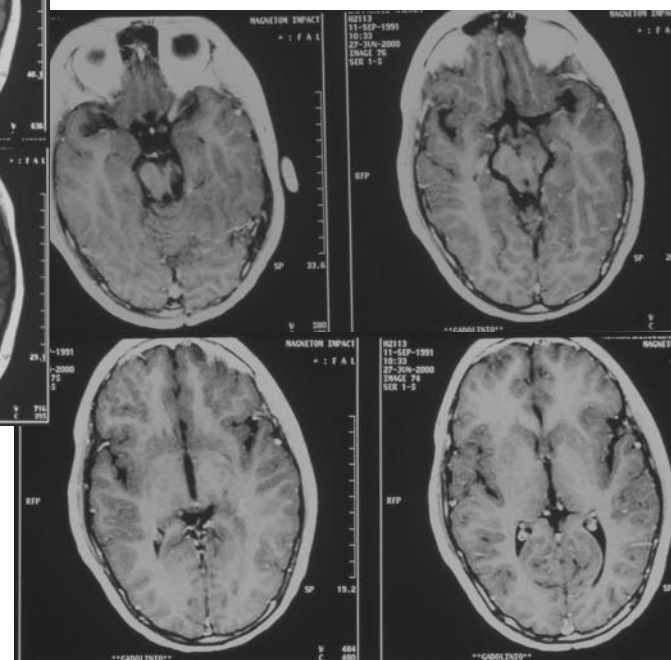
Pre-Surgery and GK

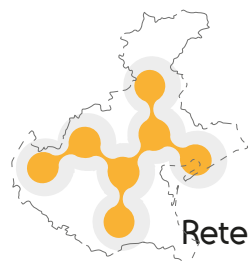


Post-Surgery/Pre-GK



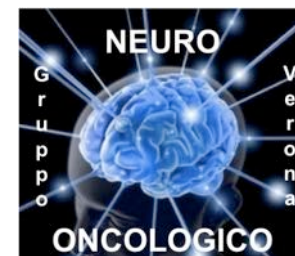
FU at 11 mos.post-GK





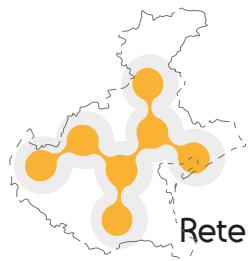
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EVOLUZIONE DELLA METODICA

- TRATTAMENTI IPOFRAZIONATI:
 - MULTISESSION/EXTEND SYSTEM
 - "VOLUME STAGING" TREATMENTS
- COREGISTRAZIONE STEREO-RM E RM DTI

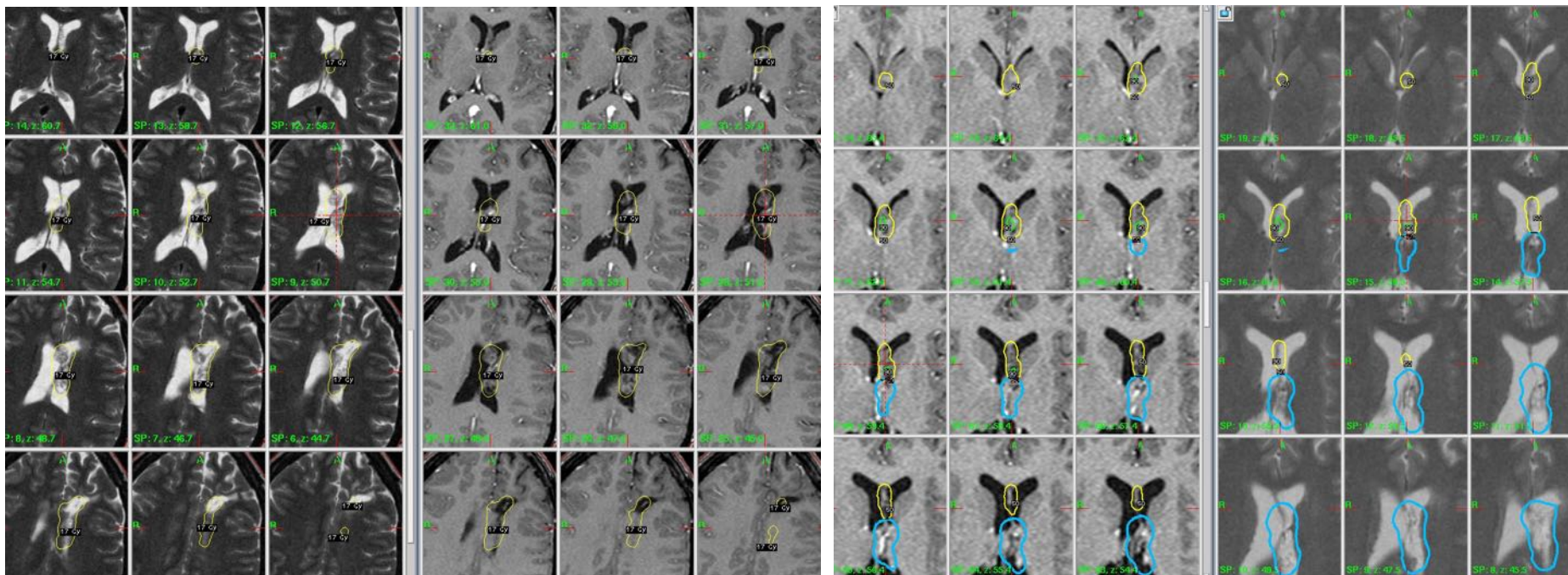


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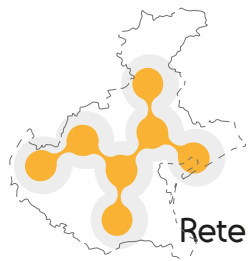


"VOLUME STAGING" TREATMENTS



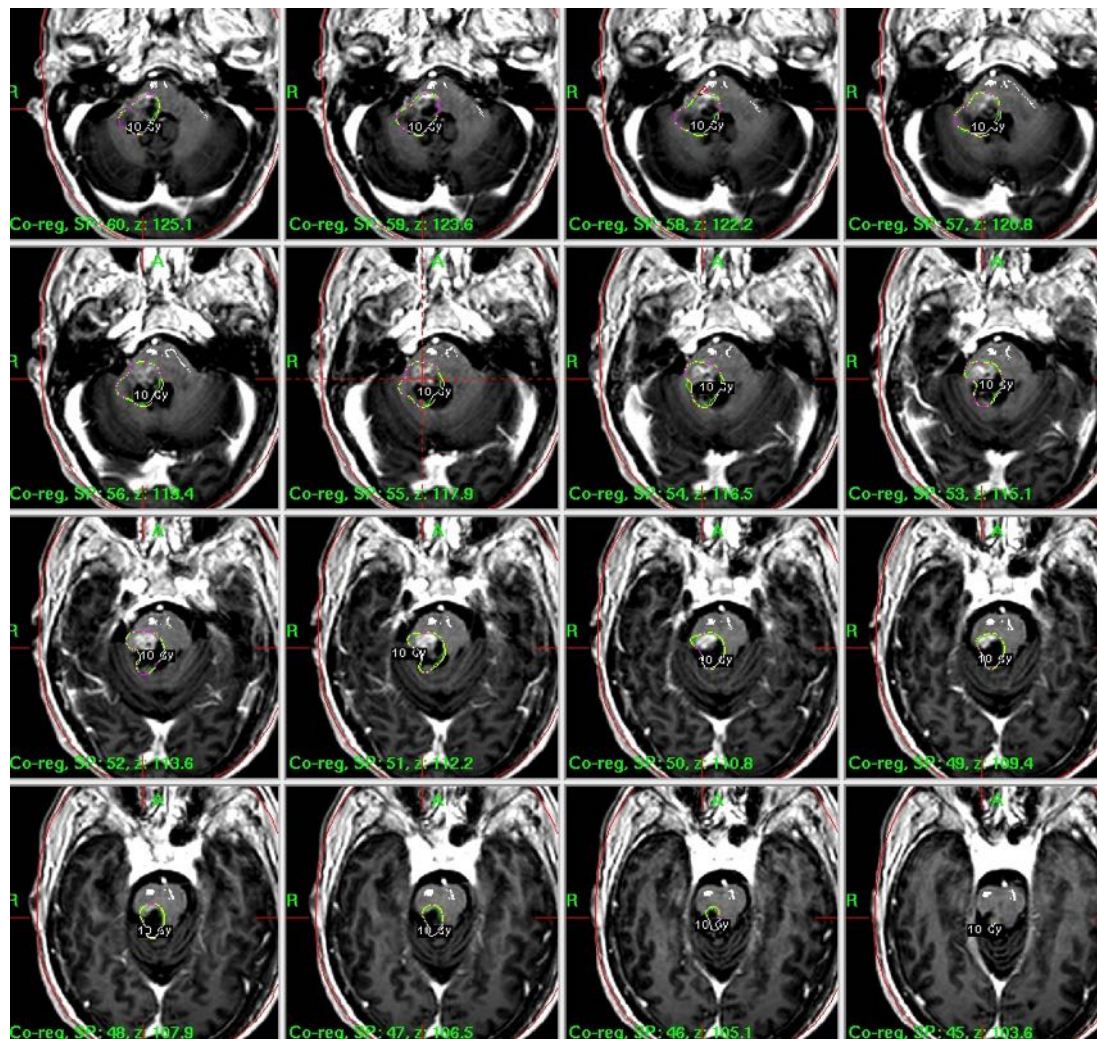
1st GK treatment on
March 28th, 2014

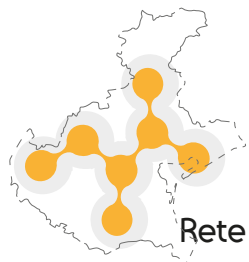
2nd GK treatment on
June 6th, 2014



Rete Oncologica Veneta

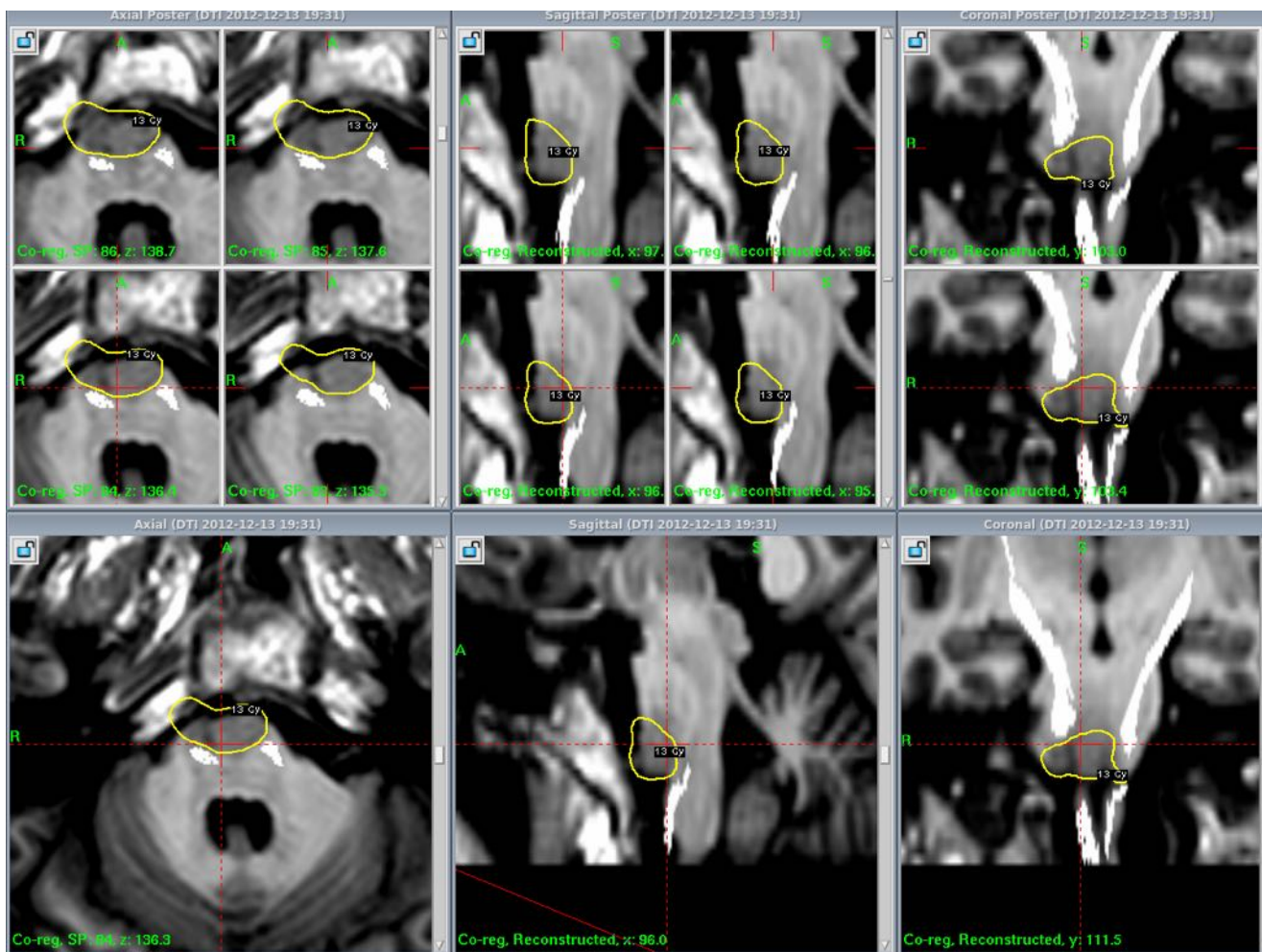
Ricerca, innovazione, assistenza

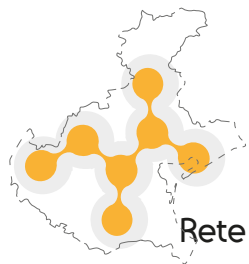




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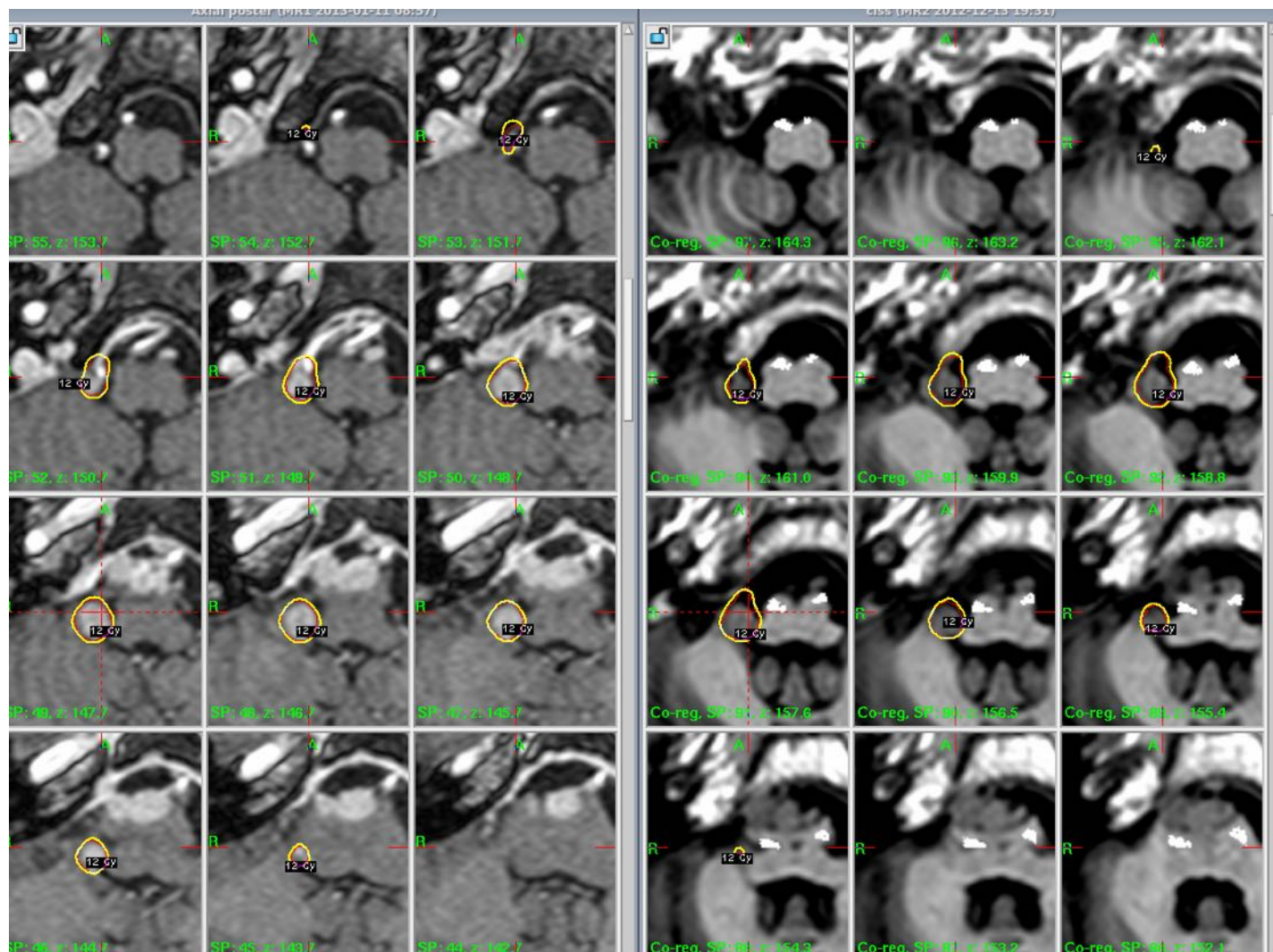
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CONCLUSIONS

GK ALONE OR COMBINED WITH SURGERY, MAY BE CONSIDERED A VALID TREATMENT FOR LGNTs (GOOD NEUROLOGICAL RESULTS AND HIGH TGC RATES) IN SELECTED PATIENTS

SAFE TREATMENT TOOL (NO MORTALITY; VERY LOW PERMANENT MORBIDITY RATES)

GK SEEMS TO PRESERVE THESE RELATIVELY YOUNG ADULT PATIENTS FROM DELAYED SEVERE SIDE EFFECTS

CONCLUSIONS

CONSIDERING THESE EXTREMELY FAVOURABLE RESULTS ON LARGE SERIES OF PATIENTS WITH LONG FOLLOW-UP PERIODS, RADIOSURGERY SHOULD BE INCLUDED IN LOW-GRADE GLIOMA TREATMENT'S GUIDE-LINES IN SELECTED PATIENTS:

- DEEP-SEATED OR ELOQUENT BRAIN REGIONS
- VOLUME <10-15 mL