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Aifm Associazione Italiana di Fisica Medica

IPOFRAZIONAMENTO E TECNICHE INNOVATIVE

29 Aprile 2014

Ipofrazionamento nel trattamento craniale

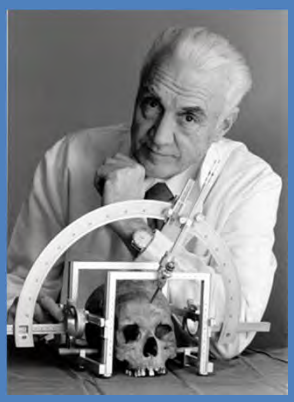
P. Fossati (IEO – Milano; CNAO - Pavia)

Ospedale "S. Giovanni Calibita" Fatebenefratelli

UNIVERSITÀ DEGLI STUDI DI MILANO

IEO Istituto Europeo di Oncologia

L'ipofrazionamento è iniziato col cranio



Leksell → gammaknife
Descritto 1949
Brevettato 1968

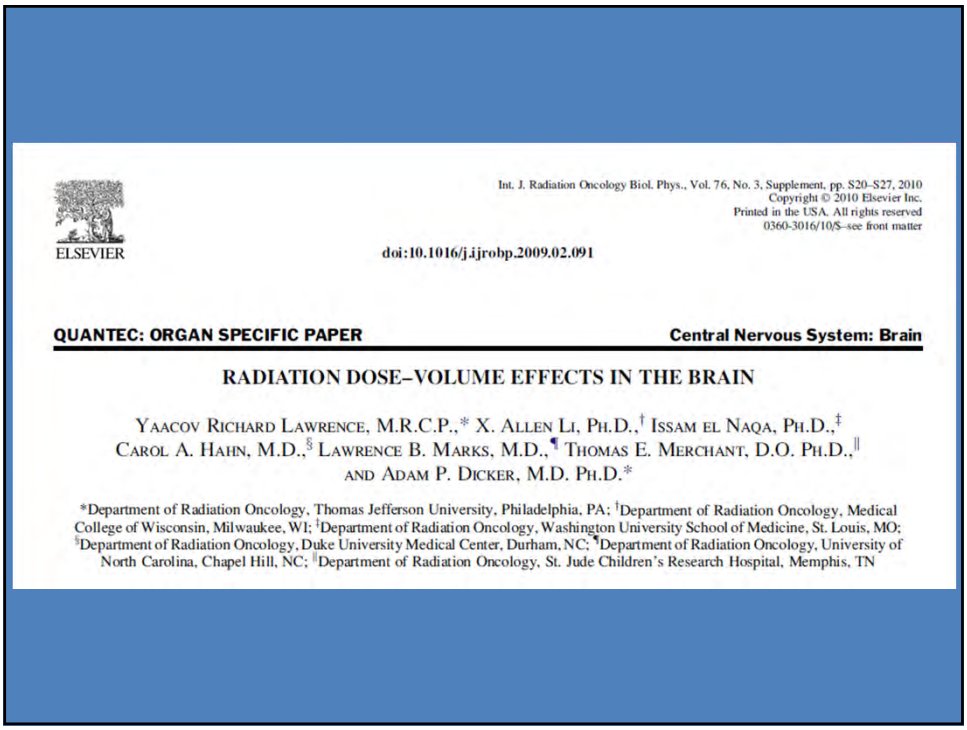
Ipofrazionamento

Si può fare ?

- Si: organ motion trascurabile, reperi ossei attendibili
- Frameless SRT, LINAC, cyberknife, gammaknife,optic tracking, IMRT, 3D.CRT…

E' una buona idea farlo ?

- Tossicità **tardiva**: sanguinamento, edema, deficit neurocognitivo, **radionecrosi**
- Outcome: ma è davvero meglio ?



ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. 76, No. 3, Supplement, pp. S20–S27, 2010

0360-3016/10/$–see front matter
doi:10.1016/j.ijrobp.2009.02.091

QUANTEC: ORGAN SPECIFIC PAPER **Central Nervous System: Brain**

RADIATION DOSE–VOLUME EFFECTS IN THE BRAIN

YAACOV RICHARD LAWRENCE, M.R.C.P.,* X. ALLEN LI, PH.D.,† ISSAM EL NAQA, PH.D.,‡ CAROL A. HAHN, M.D.,§ LAWRENCE B. MARKS, M.D.,¶ THOMAS E. MERCHANT, D.O. PH.D.,‖ AND ADAM P. DICKER, M.D. PH.D.*

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IRRADIAZIONE DELL'ENCEFALO

- METASTASI
- TUMORI PRIMITIVI
- MAV
- TUMORI DELLA BASE DEL CRANIO/ TESTA COLLO

Dati su circa 5000 pazienti

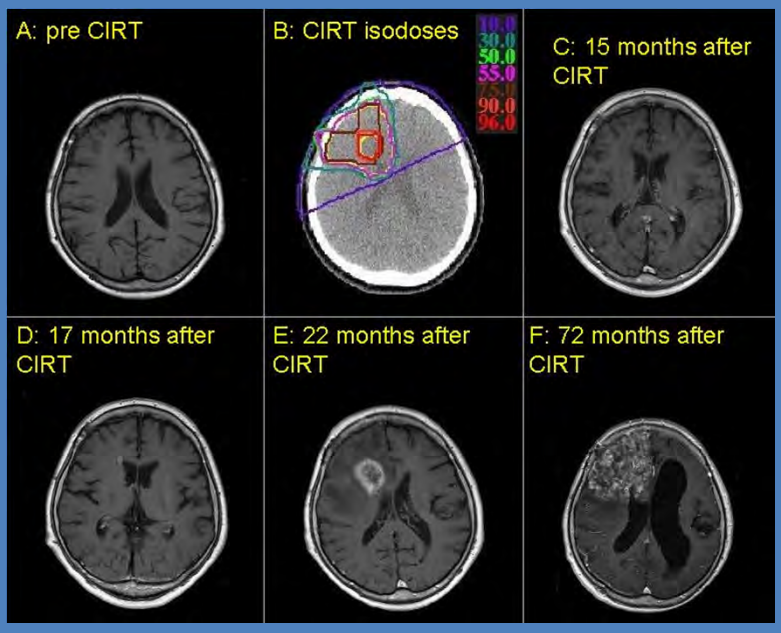
The acute side effects of RT to the brain include nausea, vomiting, and headache; vertigo and seizures are less frequent. These symptoms are transient and generally respond to medication.

STEROIDI

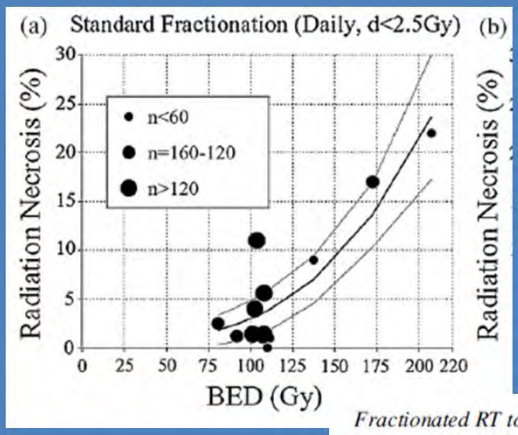
for the principal late side effects of RT to the brain: radiation necrosis and cognitive deterioration. A biopsy is rarely per-

Cerebral radionecrosis is a well known side effect of RT. It usually begins as contrast enhancing lesions that can produce mass effect and or edema. Necrotic lesions tend to grow and can cause high intracranial pressure that can necessitate surgical decompression and eventually can lead the patient to death

Radionecrosis is traditionally considered progressive and unremitting. Although it had already been described as early as 1930 (Fischer A, Holfelder H. Lokales amyloid in Gehirn [Localamyloid in the brain]. *Dtsch Z Chir* 1930;227:475– 483.) there are still many aspects of this phenomenon that are not completely understood. Vascular injury, direct damage to glial cells, changes in the fibrinolytic enzymes system and immune response are all relevant pathophysiological mechanisms, but their relative role is not completely clear



Partial brain RT frazionata (dose < 2.5 Gy)



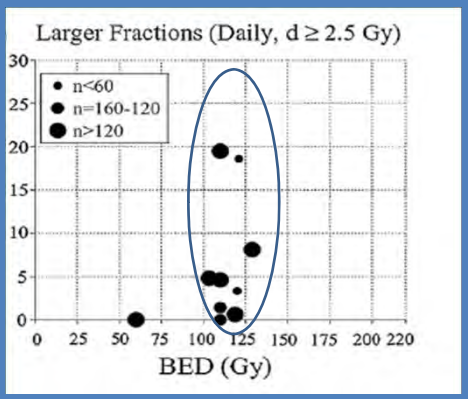
72 Gy → 5% rischio
90 Gy → 10% rischio

α/β = 3 Gy

Fractionated RT to partial brain

For standard fractionation, a 5% and 10% risk of symptomatic radiation necrosis is predicted to occur at a BED of 120 Gy (range, 100–140) and 150 Gy (range, 140–170), respectively (corresponding to 72 Gy [range, 60–84] and 90 Gy [range, 84–102] in 2-Gy fractions). The brain is especially

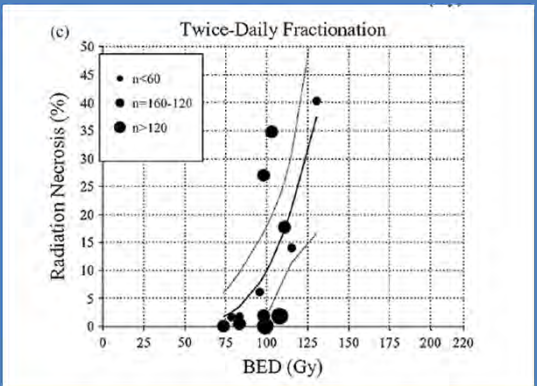
Partial brain RT frazionata (dose > 2.5 Gy)



Per dosi frazione > 2.5 non si riesce ad avere una predizione attentibile

α/β = 3 Gy → non adatto a a descrivere i dati

Partial brain RT frazionata (BID)



A sorpresa la bifrazionata è più tossica per l'encefalo

α/β = 3 Gy

Dose escalation nel glioblastoma

ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. 73, No. 3, pp. 699–708, 2009

0360-3016/09/$–see front matter

doi:10.1016/j.ijrobp.2008.05.034

CLINICAL INVESTIGATION **Brain**

PHASE I THREE-DIMENSIONAL CONFORMAL RADIATION DOSE ESCALATION STUDY IN NEWLY DIAGNOSED GLIOBLASTOMA: RADIATION THERAPY ONCOLOGY GROUP TRIAL 98-03

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209 pazienti

Table 4. Late radiotherapy toxicities

	Group 1 ($PTV_2 < 75$ cm^3)								Group 2 ($PTV_2 \geq 75$ cm^3)							
	66 Gy ($n = 20$)		72 Gy ($n = 20$)		78 Gy ($n = 26$)		84 Gy ($n = 20$)		66 Gy ($n = 29$)		72 Gy ($n = 18$)		78 Gy ($n = 33$)		84 Gy ($n = 14$)	
	Grade		Grade		Grade		Grade		Grade		Grade		Grade		Grade	
Site	3	4	3	4	3	4	3	4	3	4	3	4	3	4	3	4
Brain	1	0	1	1	1	1	0	1	1	0	0	0	1	0	0	0
Skin	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Eye	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Subcutaneous tissue	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Other	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Worst overall	1 (5)	0	1 (5)	1 (5)	1 (4)	1 (4)	0	1 (5)	1 (3)	0	0	0	1 (3)	0	0	0

Poca tossicità anche a 84 Gy

Ma non funziona…

Table 9. Progression-free survival in Group 1 ($PTV_2 < 75$ cm^3)

	66 Gy		72 Gy		78 Gy		84 Gy	
Variable	Survival*	No. at risk	Survival	No. at risk	Survival	No. at risk	Survival	No. at risk
Month								
0	100	21† (22)	100	23	100	27	100	22
3	76 (52–89)	16	70 (47–84)	16	81 (61–92)	22	77 (54–90)	17
6	48 (26–67)	10	52 (31–70)	12	59 (39–75)	16	50 (28–68)	11
9	38 (18–58)	8	30 (14–49)	7	30 (14–47)	8	36 (17–56)	8
12	14 (4–32)	3	26 (11–45)	6	22 (9–39)	6	27 (11–46)	6
18	14 (4–32)	3	13 (3–30)	3	4 (0.3–16)	1	18 (6–36)	4
24	10 (2–26)	2	13 (3–30)	3	4 (0.3–16)	1	18 (6–36)	4
30	5 (0.3–20)	1	13 (3–30)	3	—	0	14 (3–31)	3
36	—	0	9 (1–24)	2	—	0	9 (2–25)	1
Median survival (mo)	5.8		6.5		6.9		6.0	
Fail /total	21/21		21/23		27/27		21/22	

Table 10. Progression-free survival in Group 2 ($PTV_2 \geq 75$ cm^3)

	66 Gy		72 Gy		78 Gy		84 Gy	
Variable	Survival*	No. at risk	Survival	No. at risk	Survival*	No. at risk	Survival	No. at risk
Month								
0	100	33	100	23	100	35	100	18
3	67 (48–80)	22	48 (27–66)	11	77 (59–88)	27	56 (31–75)	10
6	18 (7–33)	6	39 (20–58)	9	23 (11–38)	8	33 (14–55)	6
9	9 (2–22)	3	22 (8–40)	5	11 (4–24)	4	22 (7–43)	4
12	6 (1–18)	2	22 (8–40)	5	9 (2–21)	3	6 (0.4–22)	1
18	3 (0.2–13)	1	—	0	3 (0.2–13)	1	—	0
24	3 (0.2–13)	1	—	0	3 (0.2–13)	1	—	0
30	3 (0.2–13)	1	—	0	3 (0.2–13)	1	—	0
36	3 (0.2–13)	1	—	0	3 (0.2–13)	1	—	0
Median survival (mo)	3.8		3.0		4.4		3.2	
Fail /total	32/33		23/23		34/35		18/18	

Ipofrazionare ?

ELSEVIER

Int. J. Radiation Oncology Biol. Phys., Vol. 81, No. 4, pp. 1066–1074, 2011

0360-3016/$ - see front matter

doi:10.1016/j.ijrobp.2010.07.021

CLINICAL INVESTIGATION **Brain**

PHASE I TRIAL OF HYPOFRACTIONATED INTENSITY-MODULATED RADIOTHERAPY WITH TEMOZOLOMIDE CHEMOTHERAPY FOR PATIENTS WITH NEWLY DIAGNOSED GLIOBLASTOMA MULTIFORME

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Table 2. Hypofractionated intensity-modulated radiotherapy regimens

		PTV1		PTV2	
Level	Fractions (*n*)	Total dose (Gy)	Fraction size (Gy)	Total dose (Gy)	Fraction size (Gy)
1	20	60	3	45	2.25
2	15	60	4	40.5	2.7
3	12	60	5	36	3
4	10	60	6	30	3

Abbreviation: PTV = planning target volume.

Mediana OS
16.2 Mesi

CONCLUSIONS

The present trial was designed with an ultimate goal of intensifying radiation effect (*i.e.,* increasing BED while keeping the total radiation dose at 60 Gy), because using the current standard radiation regimen (60 Gy in 2-Gy fractions), a vast majority of GBM patients develop recurrence in the primary tumor site. Intensification of the radiation effect could increase local tumor control. Level 4 (60 Gy radiation delivered in 6-Gy fractions with concurrent and adjuvant TMZ) appeared tolerated, with acceptable toxicity in selected patients with a T_1-weighted enhancing tumor <6 cm.

Ipofrazionamento nel glioblastoma

Temozolomide versus standard 6-week radiotherapy versus hypofractionated radiotherapy in patients older than 60 years with glioblastoma: the Nordic randomised, phase 3 trial

Annika Malmström, Bjørn Henning Grønberg, Christine Marosi, Roger Stupp, Didier Frappaz, Henrik Schultz, Ufuk Abacioglu, Björn Tavelin, Benoit Lhermitte, Monika E Hegi, Johan Rosell, Roger Henriksson, for the Nordic Clinical Brain Tumour Study Group (NCBTSG)

Lancet Oncol 2012; 13: 916–26
Published Online August 7, 2012
http://dx.doi.org/10.1016/S1470-2045(12)70265-6
See Comment page 857

Division of Cell Biology, Department of Clinical and Experimental Medicine, Faculty of Health Sciences, Linköping University, Unit of Advanced Palliative Home Care

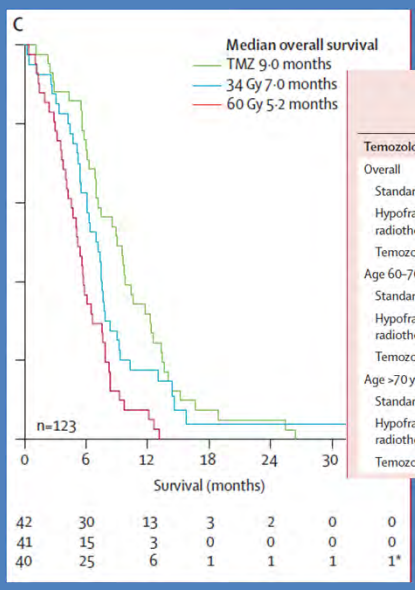
Summary

Background Most patients with glioblastoma are older than 60 years, but treatment guidelines are based on trials in patients aged only up to 70 years. We did a randomised trial to assess the optimum palliative treatment in patients aged 60 years and older with glioblastoma.

Methods Patients with newly diagnosed glioblastoma were recruited from Austria, Denmark, France, Norway, Sweden, Switzerland, and Turkey. They were assigned by a computer-generated randomisation schedule, stratified by centre, to receive temozolomide (200 mg/m² on days 1–5 of every 28 days for up to six cycles), hypofractionated radiotherapy (34·0 Gy administered in 3·4 Gy fractions over 2 weeks), or standard radiotherapy (60·0 Gy administered in 2·0 Gy fractions over 6 weeks). Patients and study staff were aware of treatment assignment. The primary endpoint was overall survival. Analyses were done by intention to treat. This trial is registered, number ISRCTN81470623.

Perché ipofrazionamento

- Minor impatto sulla vita del paziente (2 settimane e non 6) per pazienti > 60 anni
- 34 Gy in 10 frazioni vs 60 Gy in 30 frazioni
- BED_{3Gy} 72.5 Gy vs. 100 Gy
- Miglior outcome !!



	Number of deaths/ patients	Hazard ratio (95% CI)	Log-rank p value	Median (95% CI) survival (months)	1-year (95% CI) survival (%)
Temozolomide or hypofractionated radiotherapy *vs* standard radiotherapy*					
Overall					
Standard radiotherapy	100/100	1·0	..	6·0 (5·1–6·8)	17% (10–24)
Hypofractionated radiotherapy	94/98	0·85 (0·64–1·12)	0·24	7·5 (6·5–8·6)	23% (14–31)
Temozolomide	90/93	0·70 (0·52–0·93)	0·01	8·3 (7·1–9·5)	27% (18–36)
Age 60–70 years					
Standard radiotherapy	59/59	1·0	..	7·6 (5·2–10·1)	24% (13–35)
Hypofractionated radiotherapy	57/58	1·06 (0·73–1·54)	0·77	8·8 (6·9–10·8)	26% (15–38)
Temozolomide	49/51	0·87 (0·59–1·28)	0·48	7·9 (6·5–9·3)	24% (12–35)
Age >70 years					
Standard radiotherapy	41/41	1·0	..	5·2 (4·0–6·3)	7% (0·6–15)
Hypofractionated radiotherapy	37/40	0·59 (0·37–0·93)	0·02	7·0 (5·2–8·8)	18% (6–29)
Temozolomide	41/42	0·35 (0·21–0·56)	<0·0001	9·0 (6·2–11·8)	32% (18–46)

Ma ipofrazionare per dare un miglior outcome si può?

frontiers in ONCOLOGY

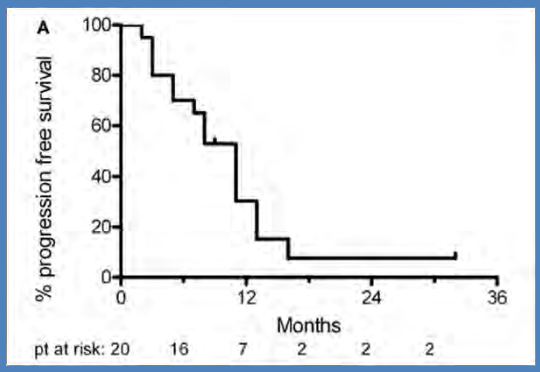
CLINICAL TRIAL ARTICLE
published: 16 October 2012
doi: 10.3389/fonc.2012.00122

Hypofractionated radiotherapy and stereotactic boost with concurrent and adjuvant temozolamide for glioblastoma in good performance status elderly patients – early results of a phase II trial

*Scott R. Floyd[1,2], Ekkehard M. Kasper[1,2], Erik J. Uhlmann[1,2], Ekokobe Fonkem[1,2], Eric T. Wong[1,2] and Anand Mahadevan[1,2]**

[1] *Beth Israel Deaconess Medical Center, Boston, MA, USA*
[2] *Harvard Medical School, Boston, MA, USA*

TMZ concomitante, 40 Gy in 15 frazioni (BED_{3Gy} 75 Gy), boost stereotassico (1 x 15-22Gy o 3 x 8 Gy a seconda delle dimensioni)



Clinical Investigation: Central Nervous System Tumor

Phase 2 Trial of Hypofractionated High-Dose Intensity Modulated Radiation Therapy With Concurrent and Adjuvant Temozolomide for Newly Diagnosed Glioblastoma

Toshihiko Iuchi, MD, PhD,* Kazuo Hatano, MD, PhD,† Takashi Kodama, PhD,‡ Tsukasa Sakaida, MD, PhD,* Sana Yokoi, MD, PhD,† Koichiro Kawasaki, MD,* Yuzo Hasegawa, MD, PhD,* and Ryusuke Hara, MD, PhD†

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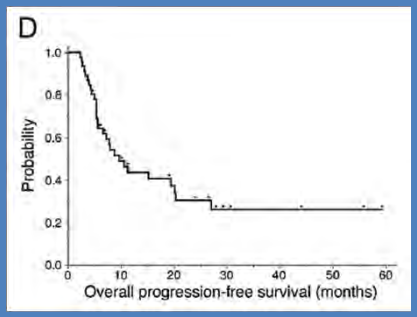

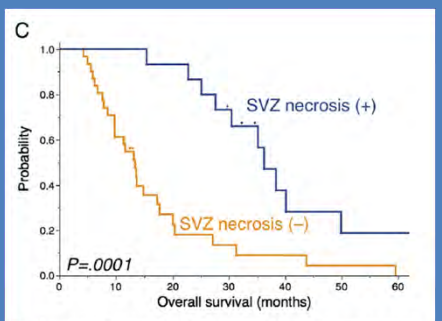

Fig. 3. Overall survival of the 46 patients. The median survival time was 20.0 months (A). Methylation (Met) of the *O-6-methylguanine-DNA methyltransferase* (MGMT) gene promoter (B) and necrosis in the subventricular zone (SVZ) (C) were significantly correlated with better survival (log−rank $P = .034$ and .0001, respectively).

Concomitnat TMZ 8 fractions
CTV1 68 Gy in 8.5 Gy fr
CTV2 40 Gy in 5 Gy fr
CTV3 32 Gy in 4 Gy fr

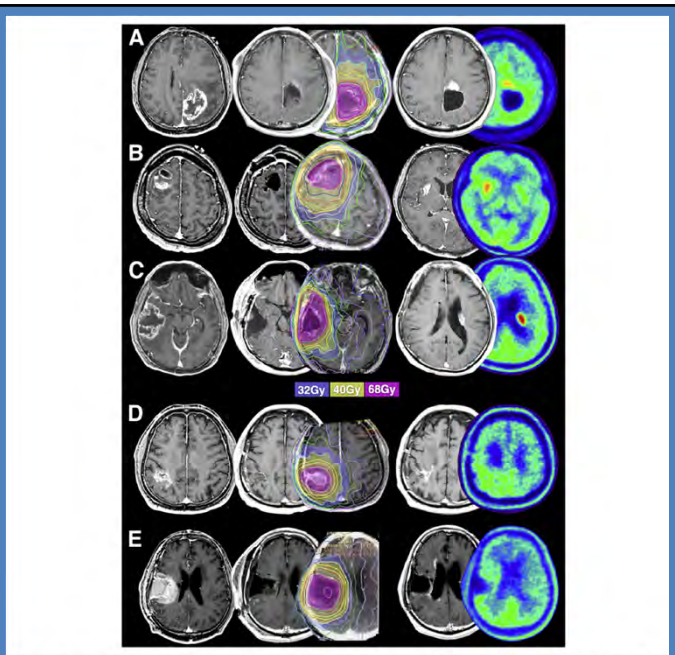

Fig. 1. Failure patterns and radiation necrosis patterns. Three different patterns of failure were evident: local (A), distant (B), an disseminated (C). Two different patterns of radiation necrosis were evident: regional necrosis (D) and necrosis in the subventricular zor (E). Enhanced magnetic resonance imaging (MRI) performed before (left) and after (middle) surgery and at the reappearance of enhance lesions on MRI was demonstrated with isodose maps and methionine-positron emission tomography.

Conclusioni ?

- Cattiva prognosi
- Poca compliance
- Schemi diversi
- Altri fattori prognostici
- Poche conclusioni

The British Journal of Radiology, 85 (2012), e770–e781

REVIEW ARTICLE

Hypofractionated radiotherapy for glioblastoma: strategy for poor-risk patients or hope for the future?

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- A trend toward increased OS (median 20 months) with TMZ and hypofractionated RT
- Better survival in patient developing necrosis
- To be investigated in phase III RCT

Come fare a decidere gli schemi di dose escaltion

Clinics based

- 3 Gy
- 4 Gy
- 5 Gy
- 6 Gy

Model based


NIH Public Access
Author Manuscript

Can Drugs Enhance Hypofractionated Radiotherapy? A Novel Method of Modeling Radiosensitization Using In Vitro Data

Generalized Linear Quadratic Model: $S=e^{-\alpha d-\beta Gd^2}$, where

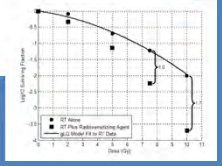
$G = 2\,[\varepsilon T - 1 + e^{-\varepsilon T}]/\varepsilon^2 T^2$,

$\varepsilon = \mu + \beta_2 I_0$,

$\mu = \ln(2)/T_r$,

$\beta_2 = \mathrm{sqrt}(\beta)$, and

$I_0 = d/T$



terapia della radionecrosi

Traditionally, physicians have tried to combat CNS radiation necrosis with corticosteroids, antiplatelet agents, anticoagulants, hyperbaric oxygen, high-dose vitamins, and surgery However, none of these approaches has proven effective in controlled clinical trials.

Published in final edited form as:
Int J Radiat Oncol Biol Phys. 2011 April 1; 79(5): 1487–1495. doi:10.1016/j.ijrobp.2009.12.061.

Randomized double-blind placebo-controlled trial of bevacizumab therapy for radiation necrosis of the CNS

Victor A. Levin, M.D.[*], **Luc Bidaut, Ph.D.**[¶], **Ping Hou, Ph.D.**[¶], **Ashok J. Kumar, M.D.**[†] **Jeffrey S. Wefel, Ph.D.**[*], **B. Nebiyou Bekele, Ph.D.**[‡], **Sujit Prabhu, M.D.**[*], **Monica Log M.D.**[*], **Mark R. Gilbert, M.D.**[*], and **Edward F. Jackson, Ph.D.**[¶]

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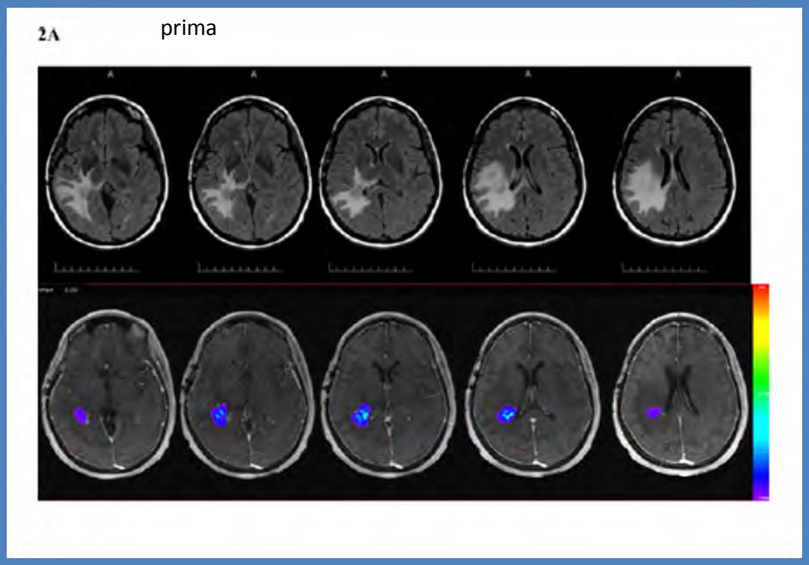
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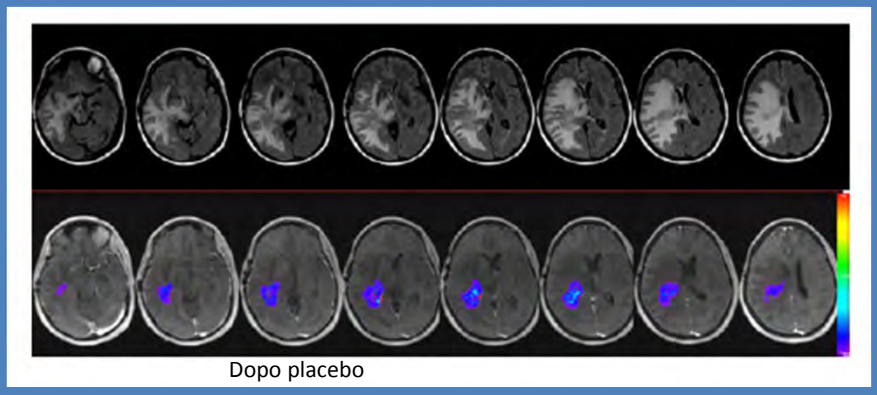
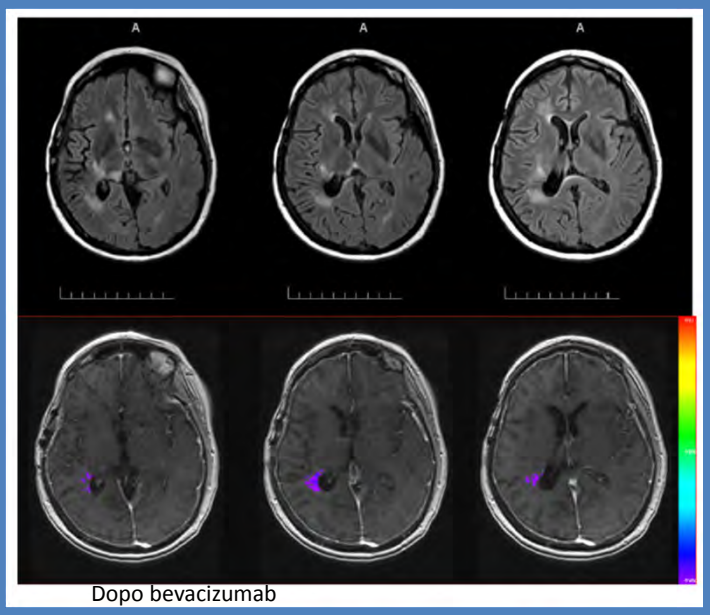

Dopo placebo



Dopo bevacizumab

Radionecrosi confermata con biopsia

Placebo controlled double blind RCT

Crossover

Tumori a buona prognosi

14 pazienti

Bevacizumab per tutte le radionecrosi ?

Results: The volumes of necrosis estimated on T_2-weighted fluid-attenuated inversion recovery and T_1-weighted gadolinium-enhanced magnetic resonance imaging scans demonstrated that although no patient receiving placebo responded (0 of 7), all bevacizumab-treated patients did so (5 of 5 randomized and 7 of 7 crossover) with decreases in T_2-weighted fluid-attenuated inversion recovery and T_1-weighted gadolinium-enhanced volumes and a decrease in endothelial transfer constant. All bevacizumab-treated patients—and none of the placebo-treated patients—showed improvement in neurologic symptoms or signs. At a median of 10 months after the last dose of bevacizumab in patients receiving all four study doses, only 2 patients had experienced a recurrence of magnetic resonance imaging changes consistent with progressive radiation necrosis; one patient received a single additional dose of bevacizumab and the other patient received two doses.
Conclusion: The Class I evidence of bevacizumab efficacy from the present study in the treatment of central nervous system radiation necrosis justifies consideration of this treatment option for people with radiation necrosis secondary to the treatment of head-and-neck cancer and brain cancer.

Radiochirurgia: frazione singola

Radiochirurgia: frazione singola

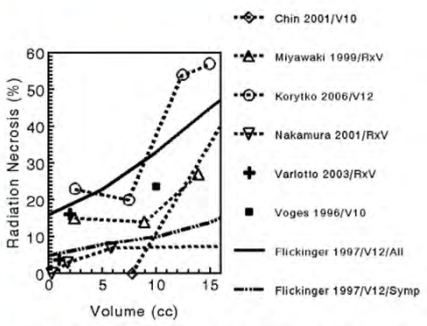


Fig. 1. Relationship between volume receiving high-dose irradiation and incidence of radiation necrosis in single-fraction stereotactic radiosurgery. Studies differed in their completeness of follow-up, definition of volume, and definition of radiation necrosis. Graph based on data presented in Table 1. Volume plotted as a point, representing mid-point of volume range. V_{10} = volume receiving 10 Gy; V_{12} = volume receiving 12 Gy; RxV = treatment volume. Flickinger data is shown for patients with either radiologic or symptomatic evidence of necrosis (marked as "All"), or only those with symptomatic necrosis (Symp). The other authors' data refers to symptomatic necrosis.

Volume ad alta dose è il fattore critico (10 Gy ? 12 Gy ?)

1. Lax I, Karlsson B. Prediction of complications in gamma knife radiosurgery of arteriovenous malformation. *Acta Oncol* 1996; 35:49–55.

defined for the determination of N_0 and D_0. Three obvious hypotheses are:

(A) All of the irradiated volume, including that of the AVM, is of importance for the genesis of complications.

(B) Only the irradiated volume outside the AVM is of relevance in this context (22).

(C) All of the volume outside the AVM plus a fraction of the volume of the AVM (i.e. normal brain tissue within the AVM) is of relevance.

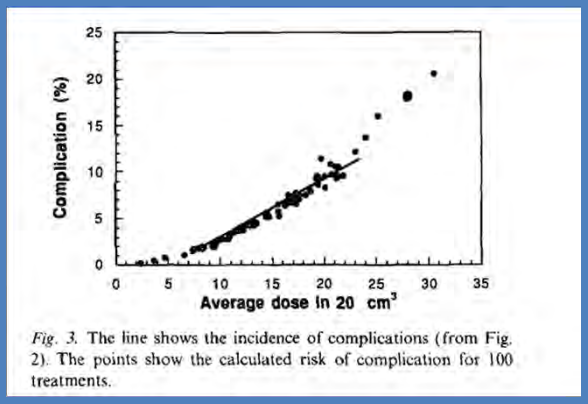


Fig. 3. The line shows the incidence of complications (from Fig. 2). The points show the calculated risk of complication for 100 treatments.

Cubo di 2.7 cm di lato

sfera di 3.3 cm di diametro

Int. J. Radiation Oncology Biol. Phys., Vol. 38, No. 3, pp. 485–490, 1997

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PII S0360-3016(97)00111-9

● *Clinical Investigation*

COMPLICATIONS FROM ARTERIOVENOUS MALFORMATION RADIOSURGERY: MULTIVARIATE ANALYSIS AND RISK MODELING

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Original article

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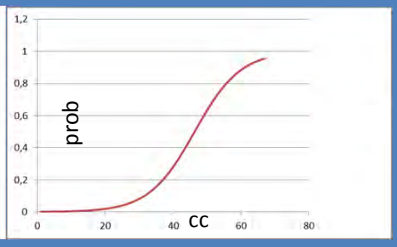
Retrospective analysis of linac-based radiosurgery for arteriovenous malformations and testing of the Flickinger formula in predicting radiation injury

Formula di Flickinger

- SPIE (significant post-radiosurgery injury expression) = 0.1 * vol (cm^3)+ 0.02 età (anni) + 0.3 * sede (frontale/temporale = 0, parietale/ occipitale/corpo calloso/cervelletto/ventricoli = 1, tronco/gangli della base/talamo = 2)

$$P\,(\text{necrosis}) = \frac{e^{B}}{(1+e^{B})},$$

$$B = \text{constant}\,(-7.8713) + 0.7506 * (\text{SPIE}) + 0.0734 * (V12)$$



1. Complications from radiosurgery (T2 imaging changes with or without symptoms) are a function of both dose and volume.

2. The volume receiving greater than a specified dose (such as 8, 10, or 12 Gy) from radiosurgery should reflect the risk of complications.
3. The target (AVM nidus) inside the treatment volume contributes to radiosurgery complications.
4. Complications vary within the different dose rates used in the clinical practice of gamma knife radiosurgery.
5. The difference between asymptomatic and symptomatic post-radiosurgery imaging changes is due primarily to location.

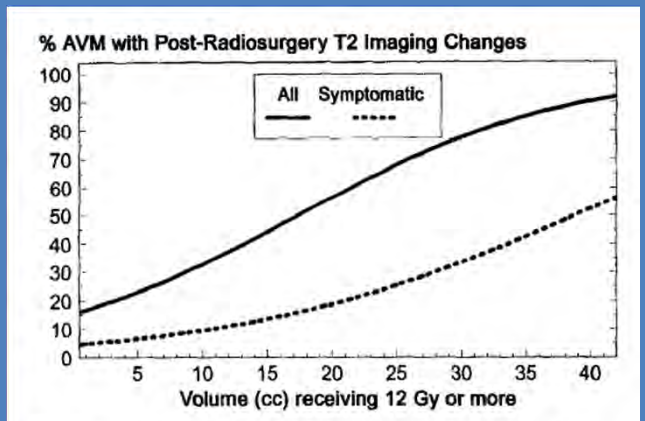


Fig. 3. Risk prediction curves derived from multivariate logistic regression analysis that correlate 12 Gy volume to risks for developing all (symptomatic and asymptomatic) post-radiosurgery imaging changes (upper solid curve) and symptomatic post-radiosurgery imaging changes (lower dashed curve) for AVM patients.

CLINICAL INVESTIGATION **Brain**

12 GY GAMMA KNIFE RADIOSURGICAL VOLUME IS A PREDICTOR FOR RADIATION NECROSIS IN NON-AVM INTRACRANIAL TUMORS

TIMOTHY KORYTKO, M.D.,* TOMAS RADIVOYEVITCH, PH.D.,† VALDIR COLUSSI, PH.D.,* BARRY W. WESSELS, PH.D.,* KUNJAN PILLAI, M.S.,* ROBERT J. MACIUNAS, M.D., M.P.H.,*‡ AND DOUGLAS B. EINSTEIN, M.D., PH.D.*

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Chondrosarcoma	1
Lesion characteristics	
12 Gy volume	Number of lesions
<5 cc	113, 99*
5–9.99 cc	38, 32*
10–14.99 cc	24, 18*
>15 cc	23, 18*

* Nonglioma lesion

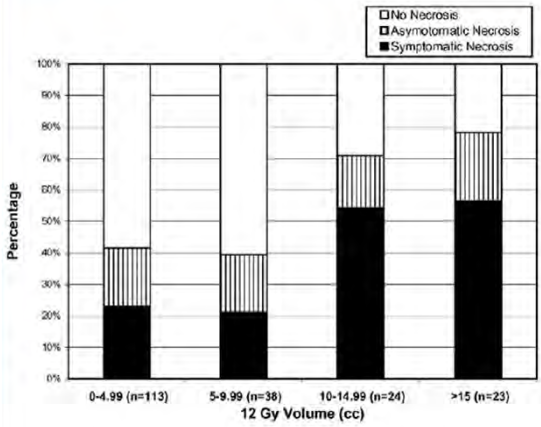
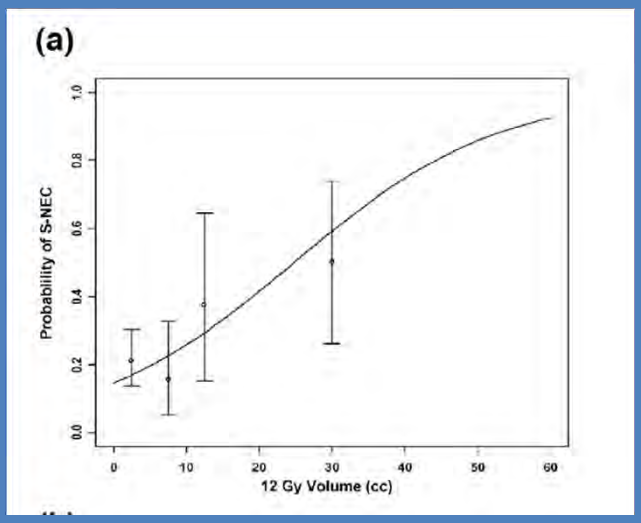


Fig. 1. Percentage of necrosis in all lesions.



Radiosurgery

The risk of complications increases with the size of the target volume. Toxicity increases rapidly once the volume of the brain exposed to >12 Gy is >5–10 cm^3. Eloquent areas of the brain (brain stem, corpus callosum) require more stringent limits. The substantial variation between the reported treatment parameters and outcomes from different centers has prevented us from making precise toxicity risk predictions.

Non solo necrosi

- Complicanze sul tronco
- Sanguinamento
- Nervi cranici

Cancer Treatment Reviews 37 (2011) 567–578

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journal homepage: www.elsevierhealth.com/journals/ctrv

Complications of Treatment

Stereotactic radiosurgery and hypofractionated stereotactic radiotherapy: Normal tissue dose constraints of the central nervous system

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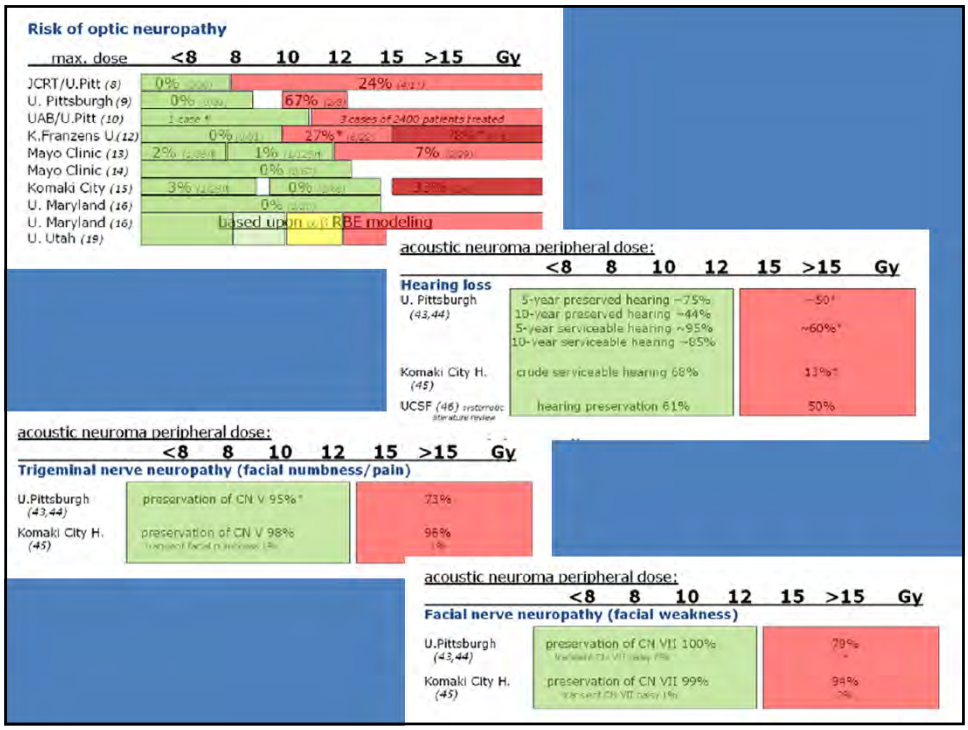

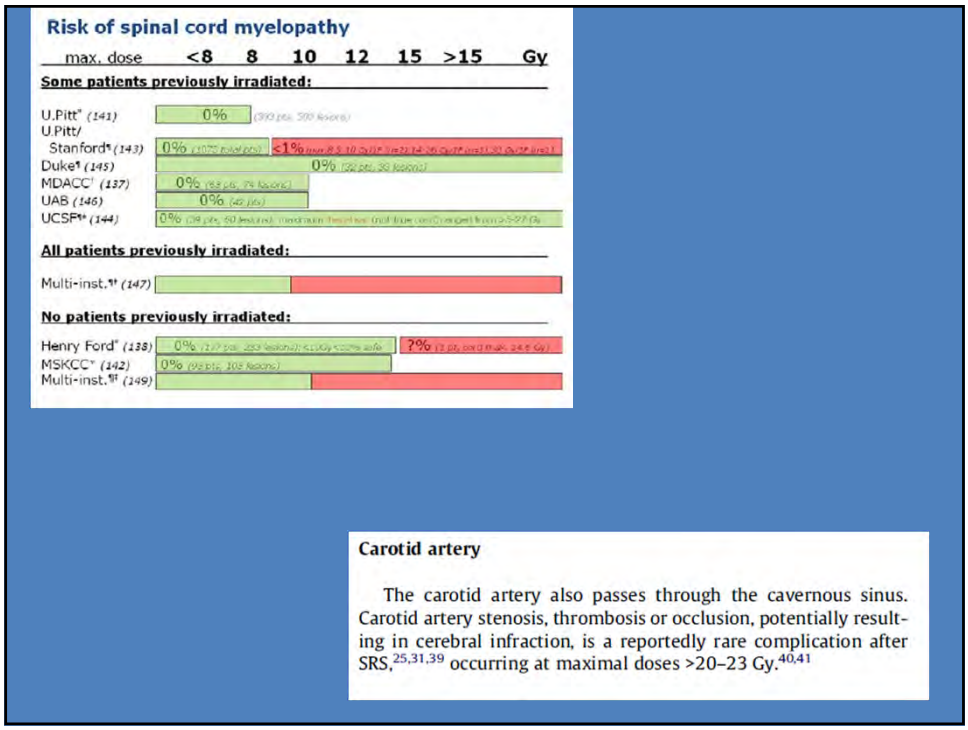

Carotid artery

The carotid artery also passes through the cavernous sinus. Carotid artery stenosis, thrombosis or occlusion, potentially resulting in cerebral infraction, is a reportedly rare complication after SRS,[25,31,39] occurring at maximal doses >20–23 Gy.[40,41]

Tronco

- 10-12 Gy dose massima in single shot → 1-2% rischio di tossicità

  - Quantec:

Dose 1/3 tronco (Gy)	12.5	14.2	16	17.5
Rischio tossicità	1%	13%	61%	94%

Edema senza necrosi

JJCO Japanese Journal of Clinical Oncology
Jpn J Clin Oncol 2011;41(5)609–616
doi:10.1093/jjco/hyr022
Advance Access Publication 16 March 2011

Significance of Tumor Volume Related to Peritumoral Edema in Intracranial Meningioma Treated with Extreme Hypofractionated Stereotactic Radiation Therapy in Three to Five Fractions

Masahiro Morimoto[1,*], Yasuo Yoshioka[1], Hiroya Shiomi[1], Fumiaki Isohashi[1], Koji Konishi[1], Tadayuki Kotsuma[1], Shoichi Fukuda[1], Naoki Kagawa[2], Manabu Kinoshita[2], Naoya Hashimoto[2], Toshiki Yoshimine[2] and Masahiko Koizumi[3]

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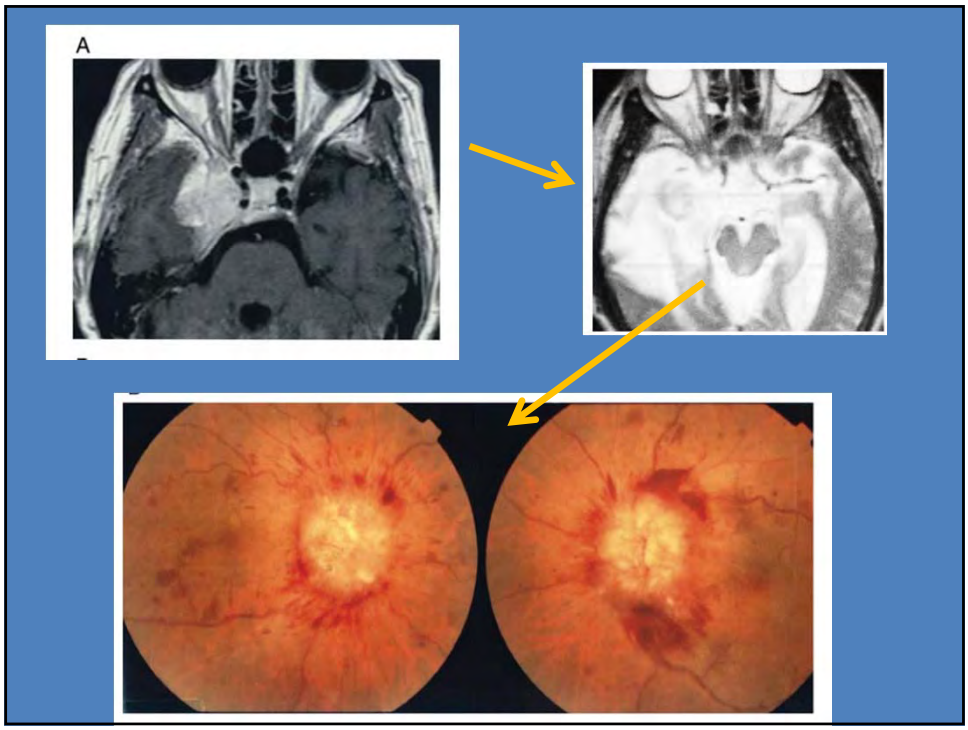
21- 34 Gy in 3-5 frazioni



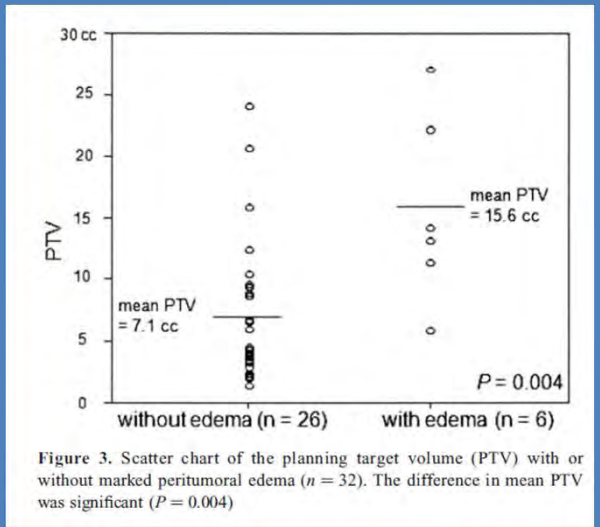


Figure 3. Scatter chart of the planning target volume (PTV) with or without marked peritumoral edema ($n = 32$). The difference in mean PTV was significant ($P = 0.004$)

Sanguinamento

Acta Neurochir (Wien) (2004) 146: 741–742
DOI 10.1007/s00701-004-0226-3

Acta Neurochirurgica
Printed in Austria

Brief Report of Special Case

Delayed bleeding after gamma knife surgery for meningioma

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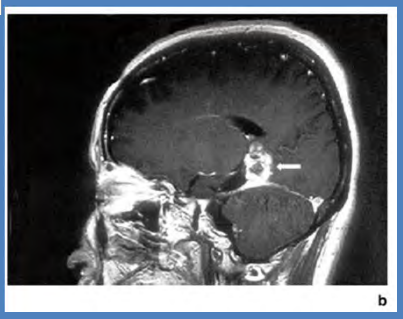
Emorragia 3 anni dopo 15 Gy in singola frazione per meningioma



b

conclusioni

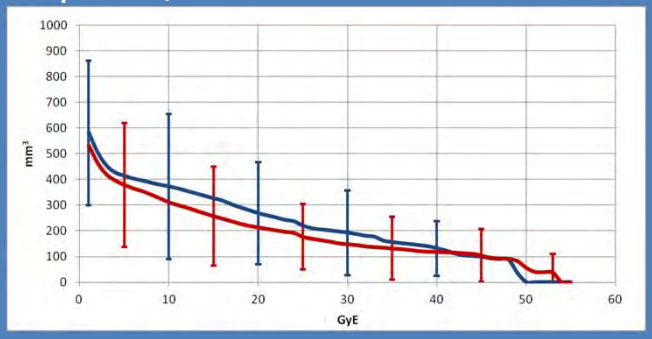
- Tanti pazienti non hanno il tempo di sviluppare la tossicità
- Ipofrazionare potrebbe miglirare il controlo locale del glioblastoma, anche 68 Gy in 8 frazioni sono tollerabili
- In singola seduta il parametro fondamentale resta il volume (inclusa la malattia) che riceve 12 Gy (5 – 10 cc OK, di più rischioso)

Conclusioni (2)

- I constraints dei tratatmenti sterotassici (3-5 frazioni) restano empirici
- La scelta tra ipofrazionamento moderato, spinto o singola seduta si basa spesso su fattori empirici
- Nulla vieterebbe la tecnica stereotassica con frazionamento convenzionale

Proposta

- Considerare necrosi e recidiva come eventi, in prima ipotesi, locali



Astrocitomi di basso grado trattati al NIRS con CIRT, la curva rossa è il DVH medio +- SD dei pazienti che hanno sviluppato necrosi e si sovrapone a quella dei paziwenti che non la hanno sviluppata

- Ricontornamento della necrosi (e della recidiva)
- Fusione della RM di FU con il piano
- DVH della necrosi (e della recidiva)
- Confronto (ratio) dei DVH differenziali