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Grey Matters: The Principles of Brain Tumor Management -Radiotherapy

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I have no disclosures

Epidemiology of primary brain tumors

	new cases	deaths (estimated)
• 2012 (US)	23,130*	14,080

- Incidence 11.47 per 100,000 (annual rate)
- Adjusted 5 yr survival rate (1995-2000)
  - 33% adults
  - 73% children

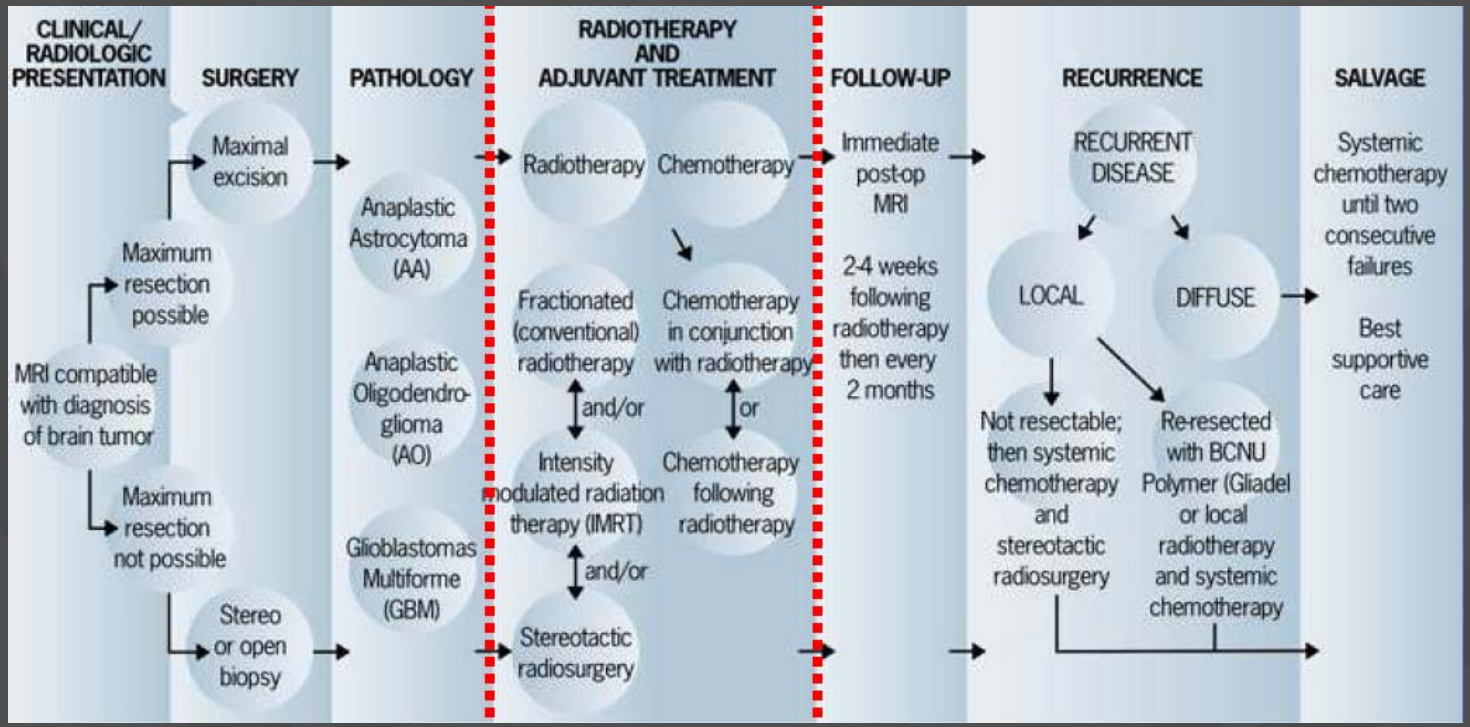
2nd leading cause of cancer deaths in persons ≤ 39 years (in the US in 2002)

* Does not include benign brain tumors or metastatic tumors

Jemal et al CA: a cancer journal for clinicians 63:11-30, 2013.

Overview of Management of High Grade Gliomas

Role for Radiotherapy



Adapted from LJ Cerulo, http://www.cin.org/craticles/CR-gliomas.html

Primary Indications for Radiation Therapy

- Definitive (primary)
  - Medically inoperative
  - Technically (functionally) unresectable
  - Patients decline surgery
- Postoperative (adjuvant)
  - After curative resection
  - After partial resection
- Salvage
- Palliative

The Role of Radiation Therapy in Management of Gliomas

Glioblastoma, WHO grade IV

Radiation is the most commonly used modality in management of glioblastoma !

Why postoperative radiation therapy

- High recurrence rate even with gross total resection due to infiltrative nature of glioma
- Postoperative radiation improves survival
  - MS increased from 14 to 36 weeks (BTSG)
- Highly tolerated with very few contra-indications
- Added benefits when given with chemotherapy

Prognostic:

RPA Stages For GBM WHO Grade IV (No TMZ)

Stage	Characteristics	Median Survival (mo)	1-year OS	2-year OS
III	Age <50, KPS 90-100	18	70%	35%
IV	Age <50, KPS <90 *or* Age >=50, surgical resection, good neurologic function	11	45%	15%
V	Age >=50, KPS >=70, surgical resection, unable to work *or* Age >= 50, KPS >= 70, biopsy only and RT dose > 54.4 *or* Age >=50, KPS <70 and normal MS	9	30%	6%
VI	Age >=50, KPS >=70, biopsy only and RT dose <=54.4 Gy *or* Age >=50, KPS <70, abnormal MS	5	20%	4%

Scott et al., Int J Radiat Oncol Biol Phys. 1998

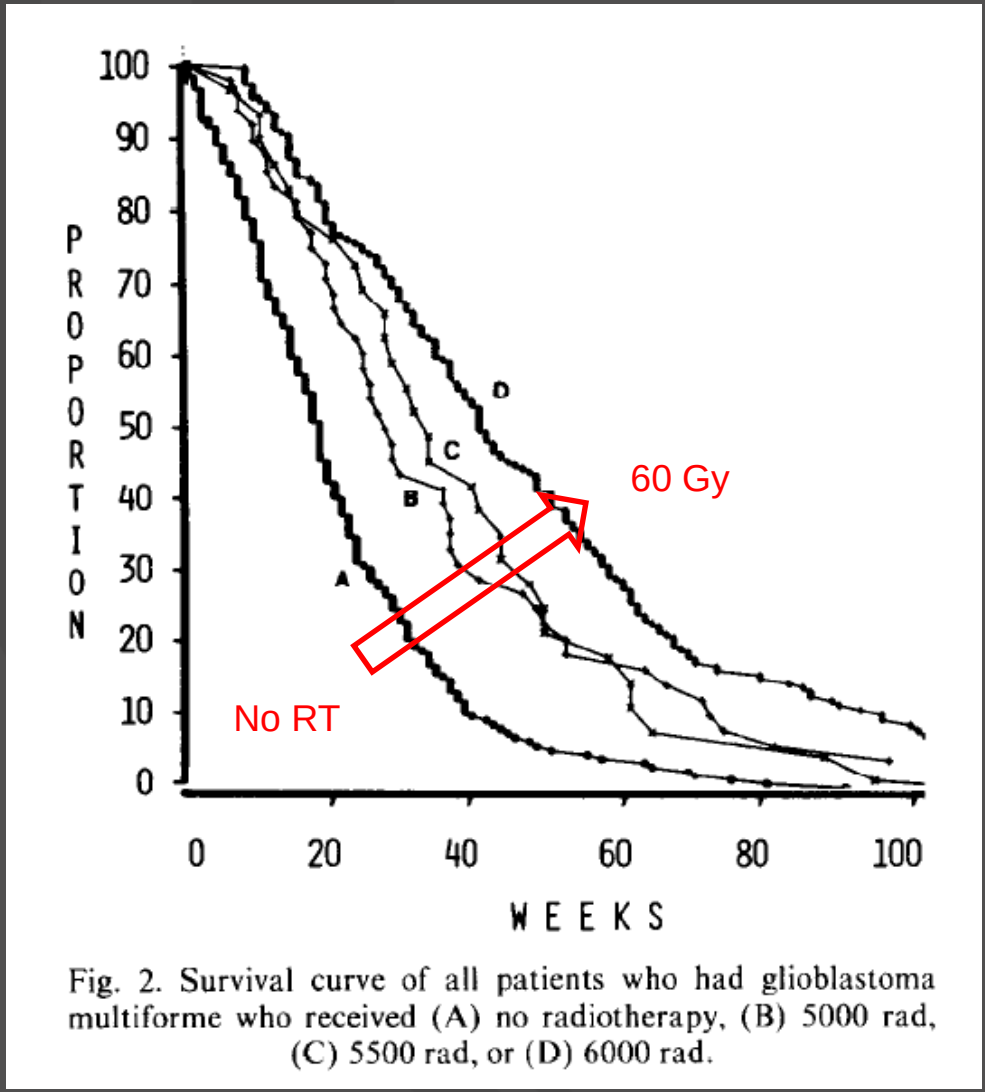


Fig. 2. Survival curve of all patients who had glioblastoma multiforme who received (A) no radiotherapy, (B) 5000 rad, (C) 5500 rad, or (D) 6000 rad.

- There was dose-response up to 60Gy
- Higher dose of radiation, not proven to be more effective, but higher toxicity

Walker et al. Int J Radiat Oncol Biol Phys 1979;5:1725-31.

Radiotherapy for Glioblastoma in the Elderly

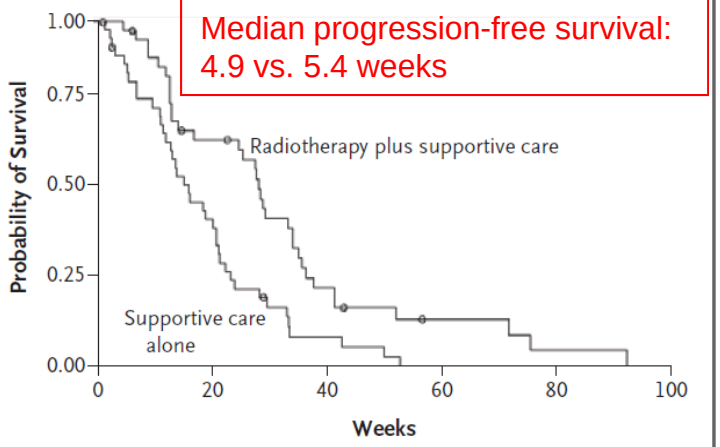


Figure 2. Kaplan–Meier Estimates of Overall Survival According to Treatment Group.

The hazard ratio for death among patients who received radiotherapy plus supportive care as compared with those who received supportive care alone was 0.47 (95% CI, 0.29 to 0.76; P=0.002).

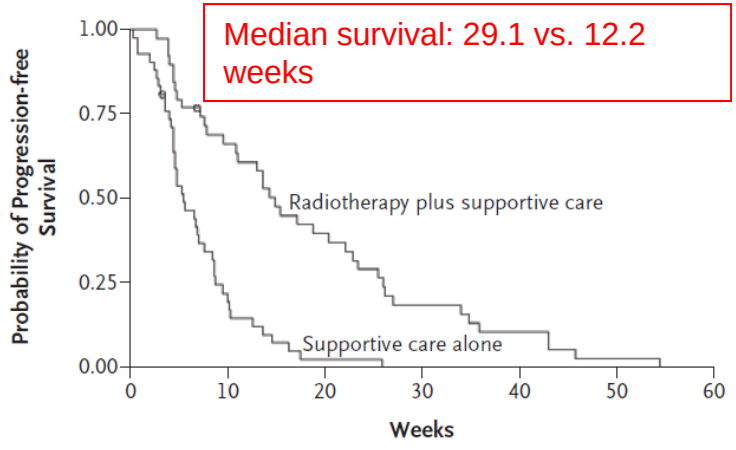


Figure 3. Kaplan–Meier Estimates of Progression-free Survival According to Treatment Group.

The hazard ratio for disease progression among patients who received radiotherapy plus supportive care as compared with those who received supportive care alone was 0.28 (95% CI, 0.17 to 0.47; P<0.001).

The survival benefit of radiotherapy was independent of the extent of surgery.

N Engl J Med 2007;356:1527-35.

Radiotherapy for Glioblastoma in the Elderly

Conclusions:

- RT increases the median survival of elderly patients with a good performance status at the start of treatment.
- RT does not cause further deterioration in the KPS, health-related quality of life, or cognitive functions, but the survival benefit is modest.

Low grade glioma, WHO grade II

Prognostic Factors for Survival in Adult Patients With Cerebral Low-Grade Glioma

By Francesco Pignatti, Martin van den Bent, Desmond Curran, Channa Debruyne, Richard Sylvester, Patrick Therasse, Denes Áfra, Philippe Cornu, Michel Bolla, Charles Vecht, and Abul B.M.F. Karim for the European Organization for Research and Treatment of Cancer Brain Tumor Cooperative Group and Radiotherapy Cooperative Group

Table 4. Prognostic Factors for Survival in Adults Patients with Cerebral LGG: Multivariate Model Construction and Validation

	Construction Set (n = 281)			Validation Set (n = 253)		
Prognostic Factor (reference level)	HR	95% CI	*P*	HR	95% CI	*P*
Age at randomization						
< 40 years	1			1		
≥ 40 years	1.26	1.06-1.48	.0077	1.43	1.17-1.74	.0005
Largest diameter of the tumor						
< 6 cm	1			1		
≥ 6 cm	1.39	1.16-1.66	.0003	1.23	1.02-1.50	.0350
Tumor crossing midline						
No	1			1		
Yes	1.37	1.15-1.63	.0005	1.43	1.11-1.84	.0051
Histology type						
Oligo/mixed	1			1		
Astrocytoma	1.30	1.08-1.56	.0050	1.46	1.18-1.82	.0006
Neurologic deficit						
Absent	1			1		
Present	1.35	1.13-1.62	.0013	1.29	1.02-1.63	.0310

NOTE. Forty-one and 35 observations were excluded from the construction and validation sets, respectively, due to missing data.

J Clin Oncol 20:2076-2084, 2002

Risk factors for low-grade glioma

Risk Factors
Astrocytoma histology
Age >=40
Tumor >=6 cm
Tumor crossing midline
Neurologic deficit

Risk Group	Score	Median OS
Low risk	0 - 2	7.8 years
High risk	3 - 5	3.7 years

Long-term efficacy of early versus delayed radiotherapy for low-grade astrocytoma and oligodendroglioma in adults: the EORTC 22845 randomised trial

M J van den Bent, D Afra, O de Witte, M Ben Hassel, S Schraub, K Hoang-Xuan, P-O Malmström, L Collette, M Piérart, R Mirimanoff, A B M F Karim, for the EORTC Radiotherapy and Brain Tumor Groups and the UK Medical Research Council

Lancet 2005; 366: 985–90

Overall survival

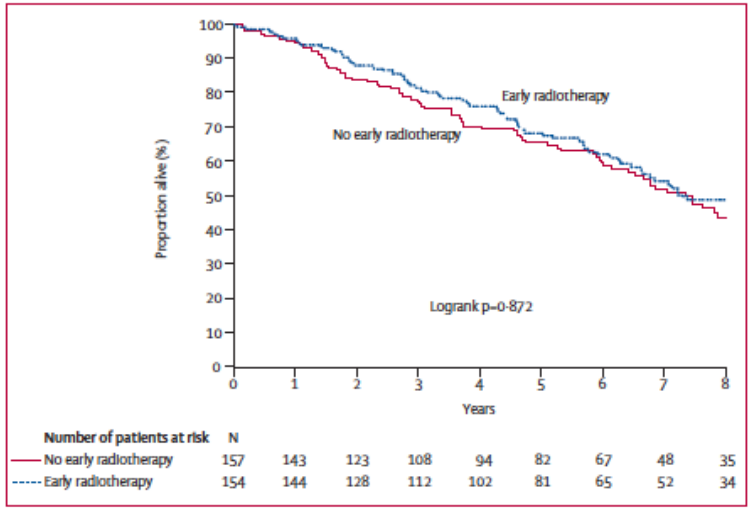


Figure 2: **Overall survival by intention-to-treat analysis**
Number of events: 0=80 for control group; 0=76 for early radiotherapy group.

Progression-free

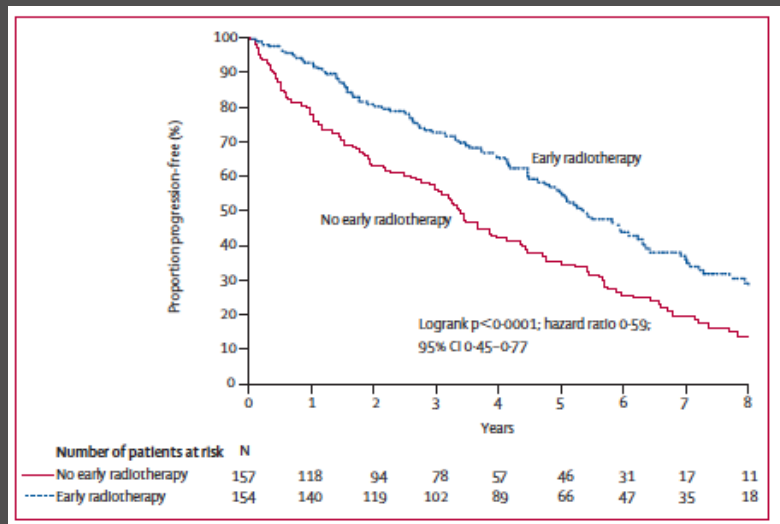


Figure 3: **Progression-free survival by intention-to-treat analysis**
Number of events: 0=121 for control group; 0=96 for early radiotherapy group.

No survival benefit in patients receiving early radiation

	No early radiotheraphy (n=157)	Early radiotherapy (n=154)	Hazard ratio (95% CI)
Overall survival			
Median years (95% CI)	7·4 (6·1–8·9)	7·2 (6·4–8·6)	0·97 (0·71–1·34)
Proportion alive at 5 years	65·7% (57·8–73·5)	68·4% (60·7–76·2)	
Progression-free survival			
Median years (95% CI)	3·4 (2·9–4·4)	5·3 (4·6–6·3)	0·59 (0·45–0·77)
Proportion free from	34·6% (26·7–42·5)	55·0% (46·7–63·3)	

The Role of RT in Management of Glioma

Summary

Malignant gliomas

WHO grade

2 Low grade glioma: early radiation does not confer a survival benefit. Patients with focal or cognitive deficits or seizures should be considered for radiotherapy.

3 Intermediate grade (anaplastic) glioma: the optimal post-operative therapy has not been defined. Chemoradiation for OA with 1p19q co-deletion.

4 Glioblastoma: radiation is the most commonly used modality. Addition of TMZ with radiotherapy confers a survival benefit.

Thank you!

www.nebraskamed.com/brainandspinecancercenter