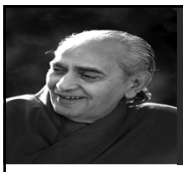

Promoted By HIHT (Estd. 1989)

SRHU

. Interweave . Integrate . Innovate

SWAMI RAMA HIMALAYAN UNIVERSITY

(A University Established Under Section 2(f) of UGC ACT & Enacted by Uttarakhand ACT No. 12 of 2013)

Metaanalysis of Radiotherapy in Brain Tumors

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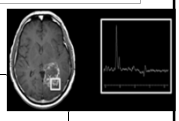
Accademic Inchage Cancer Research Institute, Swami Rama Himalayan University, Dehradun, India

Diagnostic Imaging

Imaging	Remarks	PROS	CONS
CECT BRAIN	FIRST LINE	1. Fast 2. Can be used with metallic object	1. Limited Reconstruction ability 2. Poor Resolution
MRI Brain	Gold Standard	1. True Multiplanar 2. Unparalleled Resolution	1. Motion Artefacts, Metallic objects. 2. Noisy
MR Spectroscopy Brain	Tumor metabolites can be assessed	Can differentiate radiation necrosis and tumor	1. Limited utility near bone, vessels and air space 2. Variability in interpretation
MR Profusion	Blood flow and volume is assessed	Can differentiate from radiation necrosis and tumor Progression	Limited utility near bone, vessels

Meta-Analysis of MR Spectroscopy in diagnosis of Brain Tumors

- 24 studies
- Total of 1013 participants



Sensitivity	Specificity
80.05% **(95% CI=75.97%–83.59%)**	**78.46%** **(95% CI: 73.40%–82.78%)**

- Stratified meta analysis showed higher sensitivity and specificity in child than adult. CSI [Chemical shift imaging] had higher sensitivity and single voxel [SV] had higher specificity.
- Current evidence suggests that MRS may be a valuable adjunct to magnetic resonance imaging for diagnosing brain tumors, but requires selection of suitable technique and TE value. [Echo Times]

Reference : Wenzhi Wang, Yumin Hu. Evaluation of the Diagnostic Performance of Magnetic Resonance Spectroscopy in Brain Tumors: A Systematic Review and Meta-Analysis

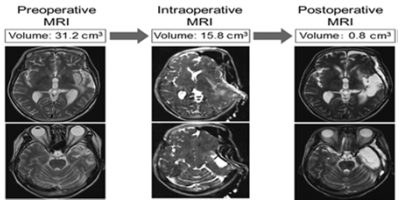
A. Abubakar et al Magnetic resonance imaging in radiotherapy treatment target volumes definition for brain tumours: a systematic review and meta-analysis
December 2017 . Journal of Radiotherapy in Practice

- Studies included were only those that quantitatively compared computed tomography (CT) and MRI in **target volume definition** for radiotherapy of brain tumours.
- Five studies with a total number of 72 patients were included in this review

Conclusion :Brain tumour volumes measured using MRI-based method for radiotherapy treatment planning were larger compared with CT defined volumes but the difference lacks statistical significance.

Intraoperative Magnetic Resonance Imaging (iMRI)

Defines the tumor's location, edema, and involvement of eloquent areas which are crucial tools to determine the appropriate surgical intervention in every patient



Kazuya Motomura et al Surgical benefits of combined awake craniotomy and intraoperative magnetic resonance imaging for gliomas associated with eloquent areas. Jan 2017.Journal of Neurosurgery 127(4):1-8

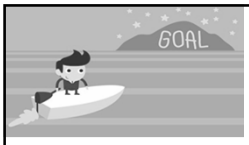
Surgery

- Retrospective systematic meta-analysis study
- 41,000 newly diagnosed GBM patients

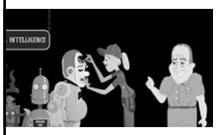
Gross total resection (GTR) of high grade gliomas (HGG) and low grade gliomas (LGG) increases the median survival rate by 200% and 160% respectively, when compared to survival rates for patients subjected to a subtotal resection (STR)

✓GTR proved superior over STR
✓61% increase in likelihood of a one-year survival
✓51% likelihood of a 12-month progression free survival

Montserrat Lara-Velazquez et al .Advances in Brain Tumor Surgery for Glioblastoma in Adults.



90% threshold of resection without compromising functional pathways



When maximal resection is not feasible, supramarginal resection (SMR) of the tumor is an option

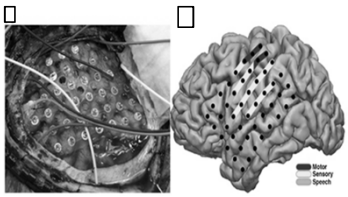
SMR is doing resection beyond tumor mass enhancement displayed by the imaging techniques

Innovation in Neurosurgery

- Obtaining a maximal cytoreduction while preserving functional pathways
- Radiographic analysis such as Intraoperative Magnetic Resonance Imaging (Imri)

Awake Craniotomy

- Permits the surgeon to monitor and rely on the functionality of patient while the patient is awake, and thereby increase the extent of resection.
- Cortical mapping of these areas (through a set of direct electrodes that stimulate or inhibit cortical functions) remains the optimal option to delineate the relationship of tumor to eloquent cortex in order to avoid damage of tissue that can compromise language or movement skills in patients



Montserrat Lara-Velazquez et al .Advances in Brain Tumor Surgery for Glioblastoma in Adults. Brain Sci. 2017

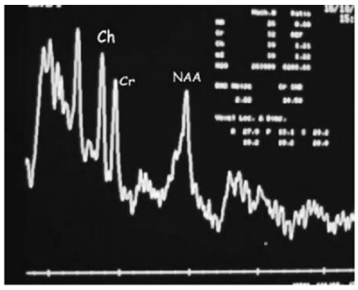
WBRT versus Partial Brain RT

Multiple studies, including the Brain Tumor Cooperative Group 80-01 randomized trial, compared WBRT with partial-brain irradiation

concluded that there was no advantage of WBRT

Standard: Partial-brain RT treatment

LOW GRADE GLIOMAS

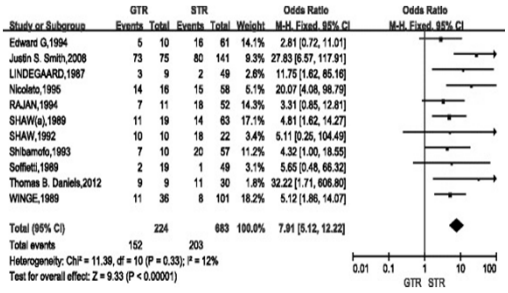


Liang Xia ,Chenyan Fang et al. Relationship between the extent of resection and the survival of patients with low-grade gliomas: a systematic review and meta-analysis .

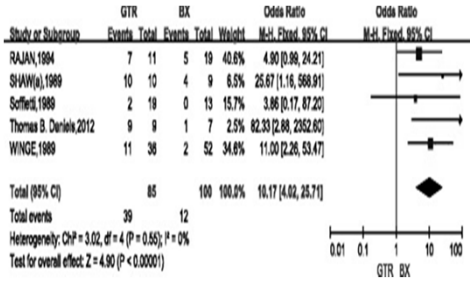
- Relationship between the extent of resection and the prognosis of low-grade gliomas updated until March 2017 were systematically searched in two databases (Pubmed and EMBASE).

Twenty articles (Pubmed and EMBASE). Total of 2128 patients were identified

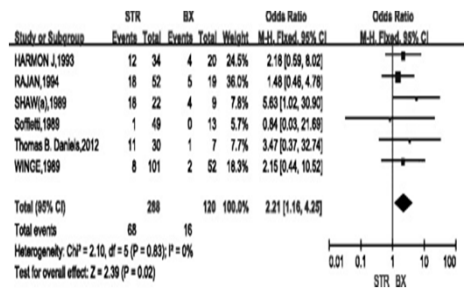
Forest Plot of 10-Year Overall Survival for Gross Total Resection (GTR) vs Subtotal Resection (STR)



Forest Plot of 10-Year Overall Survival for Gross Total Resection (GTR) vs Biopsy (BX)



Forest Plot of 10-Year Overall Survival for Subtotal Resection (STR) vs Biopsy (BX)

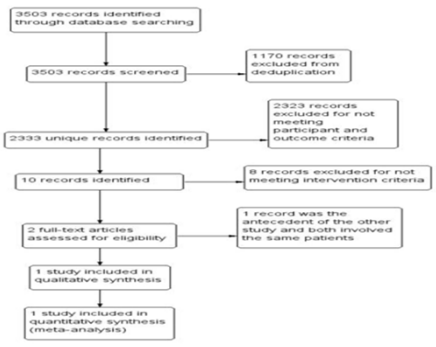


The meta-analysis showed that the 5-year and 10-year associated with gross total resection (GTR) were higher than those associated with subtotal resection (STR). Similarly, as compared with biopsy(BX), the 5-year and 10-year OS were higher after either GTR.

Conclusions
A greater extent of resection could significantly increase the OS of patients with low-grade gliomas.

Optimal timing of radiotherapy

J Manuel Sarmiento, Andrew S Venteicher et al.Early Versus Delayed Postoperative Radiotherapy For Treatment Of Low-grade Gliomas



Karim 2002: van den Bent 2005. Results from the multi-institutional, prospective RCT

Dose of radiotherapy 54 Gy/30 #,1.8 Gy per #, 5# per week

	EARLY RT	DELAYED RT	
OS	**7.2 YEARS**	**7.4 YEARS**	**Log-rank P value = 0.873; HR 0.97, 95% CI 0.71 to 1.33**
PFS	**5.3 YEARS**	**3.4 YEARS**	**log-rank P value < 0.0001; HR 0.59, 95% CI 0.45 to 0.77**

Seizures

EARLY RT	DELAYED RT	P value
25%	**41%,**	**0.0329**

Hikaru Sasaki , Kazunari Yoshida et al. **Treatment Recommendations for Adult Patients with Diffuse Gliomas of Grades II According to the New WHO Classification in 2016 . Landmark Clinical Trials**

Clinical trial	Eligibility	Treatment	Phase	Main results
RTOG9802	**WHO grade II glioma < 40 & neurosurgeon-determined GTR *n*= 111**	**Post-operative observation**	**II**	**PFS at 5 y: 48%, OS at 5 y: 93%**
	WHO grade II glioma ≥ 40 or STR / PR / Biopsy *n* = 254	**RT vs RT + PCV 6**	**III**	**Median PFS (whole): 4.0 y vs. 10.4 y, HR 0.50, *P* < 0.001**
EORTC22033–26033	**WHO grade II glioma *n* = 477**	**RT vs Dose-intense TMZ (21/28)**	**III**	**Median PFS (whole): RT 46 m vs TMZ 39 m, HR (of TMZ vs RT) 1.16, *P* = 0.22**

Treatment Recommendations for Adult Patients with Diffuse Gliomas of Grades III According to the New WHO Classification in 2016

Clinical trial	Eligibility	Treatment	Phase	Main results
NOA-04	**WHO grade III glioma** ***n*** **= 318**	**RT vs Chemotherapy (PCV or TMZ)**	**III**	**Median PFS (whole): RT 30.6 m vs chemo 31.9 m, HR 1.0,** ***P*** **= 0.87**
RTOG9402	**Anaplstic oligodendroglioma / oligoastrocytoma** ***n*** **= 289**	**RT vs PCV 4 + RT**	**III**	**Median PFS (whole): RT 1.7 y vs PCV + RT 2.6 y, HR 0.69,** ***P*** **= 0.004**
EORTC26951	**Anaplstic oligodendroglioma / oligoastrocytoma** ***n*** **= 368**	**RT vs RT + PCV 6**	**III**	**Median PFS (whole): RT 13.2 m vs RT + PCV 24.3 m, HR 0.66,** ***P*** **= 0.0003**
CATNON	**Anaplastic glioma without 1p/19q codeletion** ***n*** **= 745**	**RT vs RT/TMZ vs RT + TMZ 12 vs RT/TMZ + TMZ 12**	**III**	**Adjusted OS (adjuvant TMZ): HR 0.645,** ***P*** **= 0.0014**

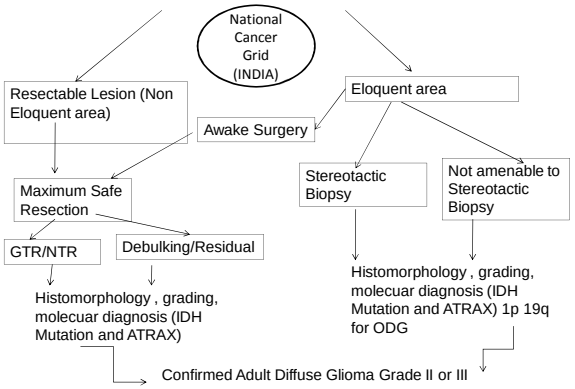
Hikaru Sasaki , Kazunari Yoshida et al .Evidence-based standard of care and treatment recommendation for adult diffuse gliomas

	WHO 2016	Evidence-based standard of care	Treatment recommendation
Grade II	**Oligodendroglioma, IDH-mutant and 1p/19q-codeleted**	**RT[#1] → PCV 6 courses**	**RT[#1] → PAV 4–6[*] courses or PAV 4 courses → RT[#1] or PAV 3–6 courses**
	Diffuse astrocytoma, IDH-mutant	**unknown (may be) RT[#1] → PCV 6 courses**	**RT[#1] → TMZ 6–12[*] courses or RT[#1]/TMZ → TMZ 6–12[*] courses**
RT[#1]: radiotherapy 50–54 Gy in 1.8–2.0 Gy fraction, RT[#2]: radiotherapy 59.4–60 Gy in 1.8–2.0 Gy fraction, PAV 3–6 courses[#3]: for elderly patients or patients with minimal residual disease, [*]The number of treatment courses may be personalized dependent on efficacy, toxicity, and MGMT status.			

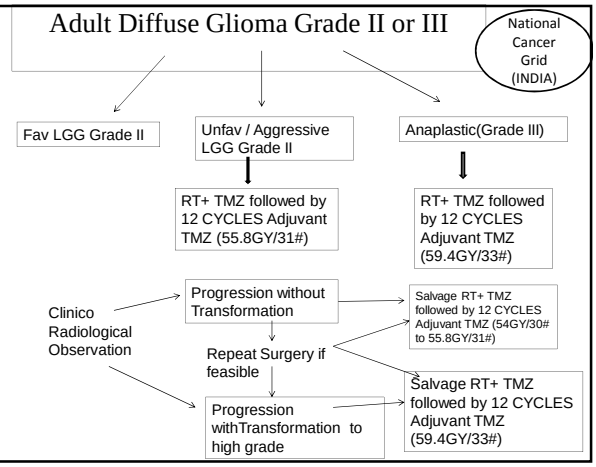
Evidence-based standard of care and treatment recommendation for adult diffuse gliomas

	WHO 2016	Evidence-based standard of care	Treatment recommendation
Grade III	Anaplastic oligodendroglioma, IDH-mutant and 1p/19q-codeleted	PCV 4 courses → RT[#2] or RT[#2] →PCV 6 courses	PAV 4 courses → RT[#2] or RT[#2] → PAV 4–6[*]courses
	Anaplastic astrocytoma, IDH-mutant	unknown (may be) RT[#2] → TMZ 12 courses or RT[#2]/TMZ → TMZ 12 courses	RT[#2] → TMZ 6–12[*] courses or RT[#2]/TMZ → TMZ 6–12[*] courses
RT[#1]: radiotherapy 50–54 Gy in 1.8–2.0 Gy fraction, RT[#2]: radiotherapy 59.4–60 Gy in 1.8–2.0 Gy fraction, PAV 3–6 courses[#3]: for elderly patients or patients with minimal residual disease, [*]The number of treatment courses may be personalized dependent on efficacy, toxicity, and MGMT status.			

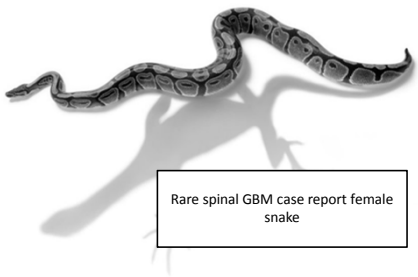
Adult Diffuse Glioma Grade II or III



Adult Diffuse Glioma Grade II or III



Glioblastoma Multiformae

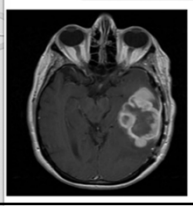


Rare spinal GBM case report female snake

RT treatment volume for GBM

Co-registration of pre- and postoperative MRI with planning CT images

Glioblastoma



Certain brain tumors .e.g. glioma have a distinct appearance on MRI scan . With irregular borders and necrotic center

EORTC treatment volumes (EORTC 22981/22961, 26071/22072 (Centric), 26981–22981, and AVAglio trials)

Phase 1 (to 60 Gy in 30 fractions)
GTV = Surgical resection cavity plus any residual enhancing tumour (postcontrast T1 weighted MRI scans).
CTV = GTV plus a margin of 2 cm
PTV = CTV plus a margin of 3–5 mm

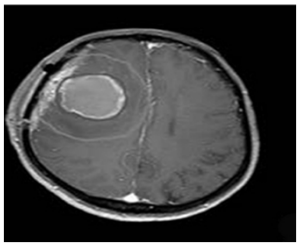
80%–90% of treatment failures occur within this margin

RTOG treatment volumes (RTOG 0525, 0825, 0913, and AVAglio trials)

Phase 1 (to 46 Gy in 23 fractions)
GTV1 = surgical resection cavity plus any residual enhancing tumour (postcontrast T1 weighted MRI scans) plus surrounding oedema (hyperintensity on T2 or FLAIR MRI scans)
CTV1 = GTV1 plus a margin of 2 cm (if no surrounding oedema is present, the CTV is the contrast enhancing tumour plus 2.5 cm.
PTV1 = CTV1 plus a margin of 3–5 mm
Phase 2 (14 Gy boost in 7 fractions)
GTV2 = surgical resection cavity plus any residual enhancing tumour (postcontrast T1 weighted MRI scan
CTV2 = GTV2 plus a margin of 2 cm
PTV2 = CTV2 plus a margin of 3–5 mm

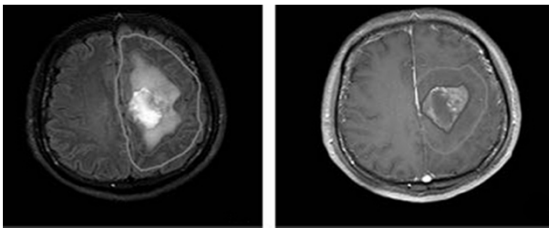
Margins up to 3 cm were allowed in 22981/22961 trial, and 1.5 cm in 26981–22981 trial

One phase Target Delineation for GBM



MRI image , gross total resection. The GTV includes surgical cavity and residual enhancement based on the axial T1 sequence with gadolinium (red line) and CTV is a 2 cm expansion in all directions (green line)

Two phase Target Delineation for GBM



The initial GTV includes postoperative peritumoral edema based on the axial T2 fluid-attenuated inversion recovery sequence (red line); the initial CTV (green line) includes postoperative peritumoral edema plus a 2 cm expansion in all directions. The boost GTV includes the surgical cavity and residual enhancement based on the axial T1 sequence with gadolinium (red line) and the boost CTV is a 2 cm expansion in all directions (green line).

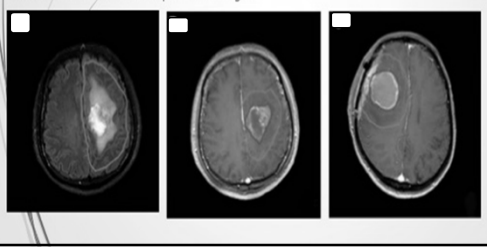
Contouring guidelines

peritumoral oedema as these areas are believed to contain high concentrations of tumour cells

- RTOG

Phase I-CTV- postoperative peritumoral edema plus a 2 cm margin(low grade 1 cm)

Phase II- CTV- residual tumor plus 2 cm margin



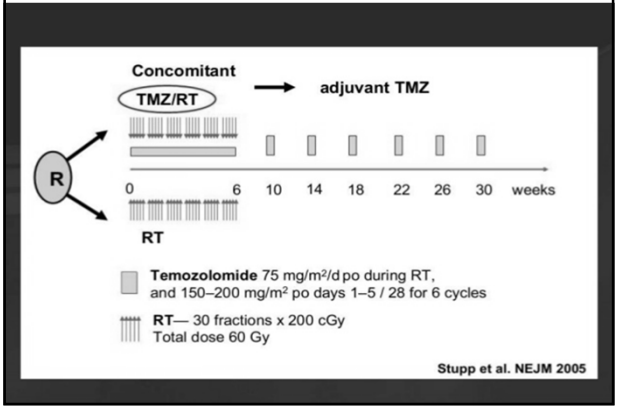
EORTC- 2–3 cm dosimetric margins around the tumor (as evaluated by MRI)

The University of Texas MD Anderson Cancer Center uses a 2 cm margin around the gross tumor volume (GTV), which consists of the resection cavity and any residual contrast enhancing tumor, but ignoring any edema

Conclusion of Studies (Post operative GBM)

Burger et al; Halperin et al	**The distribution of cells of a GBM cannot be inferred from CT images, since the peritumoral area of low density can over- or underestimate the extent of the lesion**
Chang et al; Minniti et al; McDonald et al; Dobelbower et al	**There were no significant differences in relapse patterns between the two target delineation techniques** **The use of this limited-margin RT can significantly decrease the volume of normal brain tissue that is irradiated**

TEMORADIATION



Zhuouozi Yang et al .A comparison between oral chemotherapy combined with radiotherapy and radiotherapy for newly diagnosed glioblastoma A systematic review and meta-analysis

Five RCTs (1655 patients) were eligible in this study

Statistical information and characteristics of included studies.

Study	Period of diagnosis	Therapy	No. of patients	Male	Median PFS (mo)	Median survival (mo)	Age range (y) (n)	PS Good[b], n	PS Poor[b], n	OS, HR (95% CI)	PFS, HR (95% CI)	Follow-up	Time from randomization to radiotherapy
Stupp (2005)	2000–2002	RT+TMZ	287	185	6.9	14.6	≥50 (192)	249	38	0.63 (0.53–0.75)	0.56 (0.47–0.66)	61 mo	<1 wk
		RT	286	175	5.0	12.1	≥50 (198)	251	35				
Kocher (2008)	2002–2004	RT+TMZ	29	15	6.3	14.6	59 (34–67)	29	0	0.98 (0.48–2.01)	0.89 (0.52–1.52)	NA	28 (19–49)
		RT	33	26	7.6	17.1	58 (37–69)	31	2				28 (17–52)
Athanassiou (2005)	2000–2002	RT+TMZ	57	36	10.8[a]	13.41	>50 (42)	17	36	0.44 (0.28–0.69)	0.50 (0.32–0.78)[a]	0.11	11.2 (3.4–27.0)
		RT	53	34	5.2[a]	7.7	>50 (48)	27	30				
Szczepanek (2013)	2003–2005	RT+TMZ	28	18	7.5	16	55 (18–65)	26	2	—	—	33 mo	43 (32–62)
		RT	30	16	5	12.5	56 (20–68)	26	2				48 (38–65)
Levin (2006)	1996–1999	RT+MT	83	51	4.3	11	57 (21–77)	67	16	0.86 (0.625–1.205)	0.83 (0.585–1.163)	<18 mo	NA
		RT+MT	79	57	4.2	9.5	58 (25–79)	63	16				
Michael (2001)	NA	RT+DFMO	59	40	4.8	11	57 (28–82)	NR		0.83 (0.58–1.19)	0.91 (0.64–1.2939)	2 y	NA
		RT	58	35	4	9.2	57 (26–78)	NR					
		HPF+DFMO	57	35	5.5	10.5	58 (29–77)	NR					
		HPF	57	26	4.8	9.8	57 (34–78)	NR					

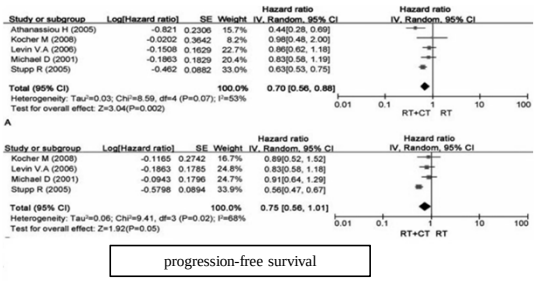
CI = confidential interval, NR = not reported, OS = overall survival, PFS = progression-free survival, PS = performance status, RT = radiotherapy, TMZ = temozolomide, TTP = time to progression.
[a] Time to progression but not progression-free survival.
[b] Good: WHO = 0–1 or KPS > 80; poor: WHO = 2 or KPS ≤ 80.

Adjuvant therapy.

	RT details	CT details	Eligible histology
Athanassiou (2005)	Tumor and margin 60 Gy/30 f (3-D technique)	Concomitant: TMZ dosage was 75 mg/m²/d, 7 d/wk until the last day of radiotherapy. Adjuvant: 150 mg/m² of TMZ on days 1–5 and 15–19 every 28 d	GBM
Kocher (2008)	Tumor and margin 60 Gy/30 f	Concomitant: TMZ dosage was 75 mg/m²/d, /wk Adjuvant was not given.	GBM
Szczepanek (2013)	Tumor and margin 60 Gy/30 f (X-ray ≥4 MV)	Concomitant: TMZ dosage was 75 mg/m²/d orally from the first day of radiotherapy until the last day of radiotherapy. Adjuvant: The dose was 150 mg/m²/d orally for the first cycle; 200 mg/m²/d orally beginning with the second cycle for 5 cycles.	GBM
Stupp (2005)	Tumor and margin 60 Gy/30 f/2 Gy	Concomitant: TMZ dosage was 75 mg/m²/d orally from the first day of radiotherapy until the last day of radiotherapy Adjuvant: the standard 5-d schedule every 28 d. The dose was 150 mg/m²/d orally for the first cycle: 200 mg/m²/d orally beginning with the second cycle for 6 cycles.	GBM
Levin (2006)	60 Gy/30–33 f	Marimastat (MT) dosage was 10 mg orally twice daily, until tumor progression.	GBM/GS
Michael (2001)	Tumor and margin (X-ray: 4–20MV) Accelerated hyperfractionated irradiation: 70.4 Gy/44 f/1.6 Gy Standard fractionated irradiation: 59.4 Gy/33 f/1.8 Gy	Difluromethylornithine (DFMO) dosage was 1.8 gm/m²/8 h orally throughout the whole period of radiation.Modification of the dose of DFMO was made according to the toxity grade.	GBM

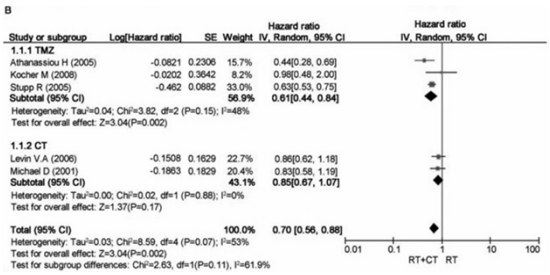
CI = confidential interval, OS = overall survival, PFS = progression free survival, RT = radiotherapy, TMZ = temozolomide.

Meta-analyses result of survival rate



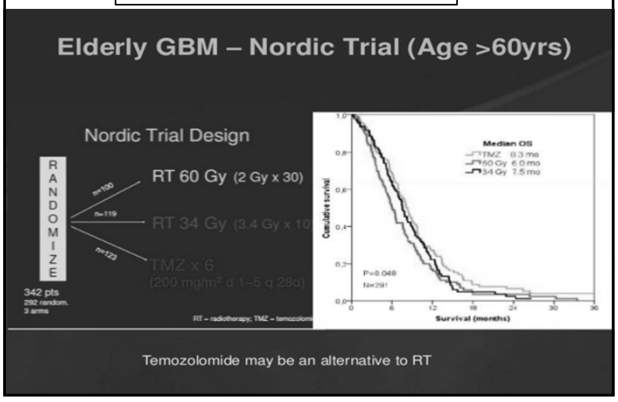
progression-free survival

Subgroup Analysis Of OS

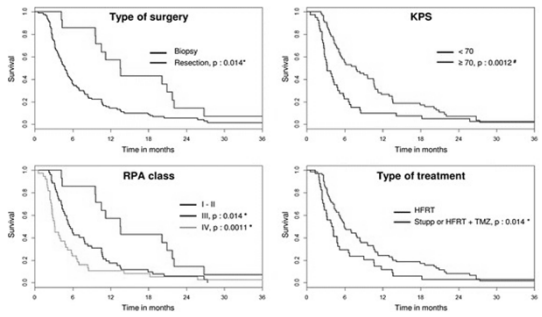


CTRT were associated with a significant improvement in OS compared with that of RT. Besides, the risk of death was reduced by 30% in those received combination of chemotherapy and radiotherapy

STUPP Trial for Elderly GBM



J.Biau,E.Chautard et al Radiotherapy plus temozolomide in elderly patients with glioblastoma: a "real-life" report. J.Rad.Onc 2017



Oral chemotherapy combined with radiotherapy contributes to the survival in patients with newly diagnosed GBM.

Adjuvant chemotherapy confers a survival benefit in patients newly diagnosed with GBM

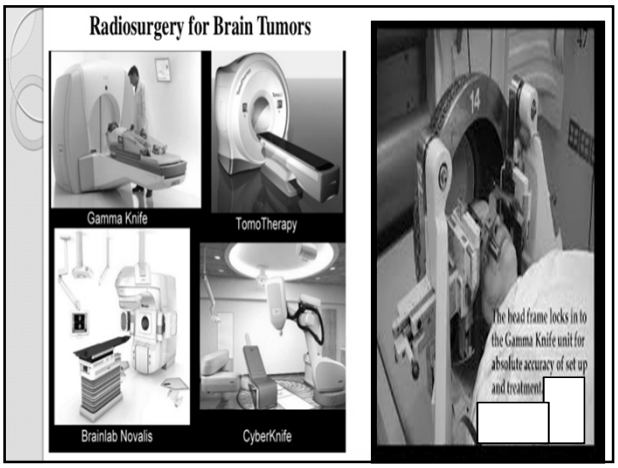
Doaa M. Al Zayat, Ehab M. Attalla et al. Dosimetric Comparison of Intensity-Modulated Radiotherapy versus Three-Dimensional Conformal Radiotherapy for Patients with Brain Tumors . Open Journal of Radiology, 2014, 4, 85-96

Target dose coverage with IMRT planning was better than 3DCRT planning. If PTV is distant to optical nerves, chiasm and brainstem 3D conformal technique can be applied, and if the PTV is nearby OAR intensity-modulated treatment technique should be used.

M. Ding et al Dosimetric Comparison Between 3DCRT and IMRT Using Different Multileaf Collimators in the Treatment of Brain Tumors. Spring 2009

Tumors adjacent to (or partially overlapping with) critical structures, IMRT dramatically spared the volume of the critical structures to be irradiated.

For large and spherical brain tumors, the smaller collimator leaf widths give no significant benefit.

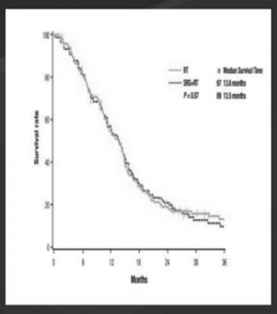


RTOG 9305: Newly Diagnosed GBM Stereotactic Radiosurgery Phase III Trial

Arm 1
RT – 60Gy / 30 #
BCNU 80mg/m2 D1-3 of RT then
Q8weeks for 6 cycles

Arm 2
SRS followed by
RT – 60Gy / 30 #
BCNU 80mg/m2 D1-3 of RT then
Q8weeks for 6 cycles

SRS Dose
24Gy – Lesion < 2cm
18 Gy- Lesion 2.1 -3 cm
15 Gy – Lesion 3.1-4 cm



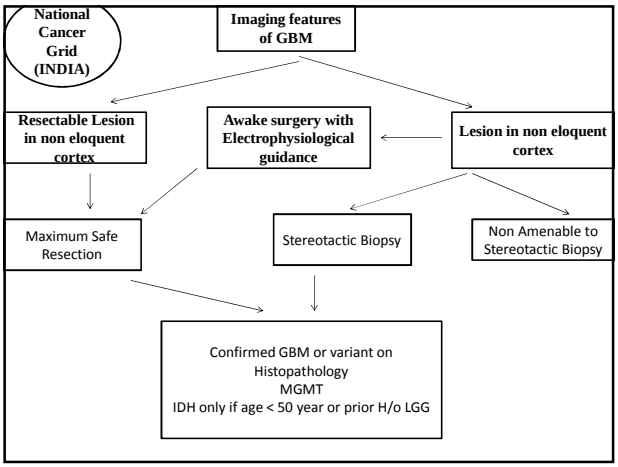
ELSEVIER
doi:10.1016/j.ijrobp.2005.05.024

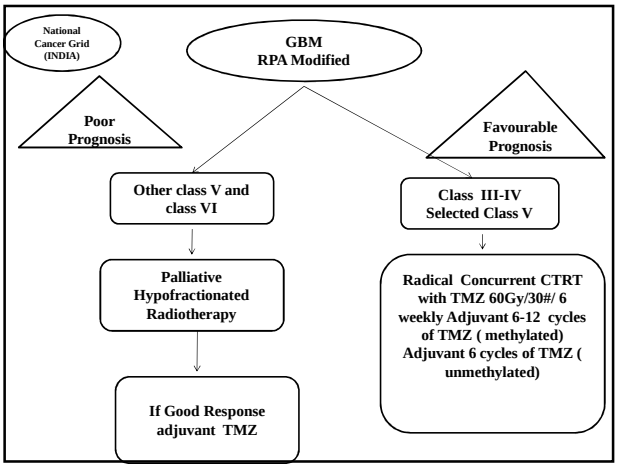
ASTRO REPORT

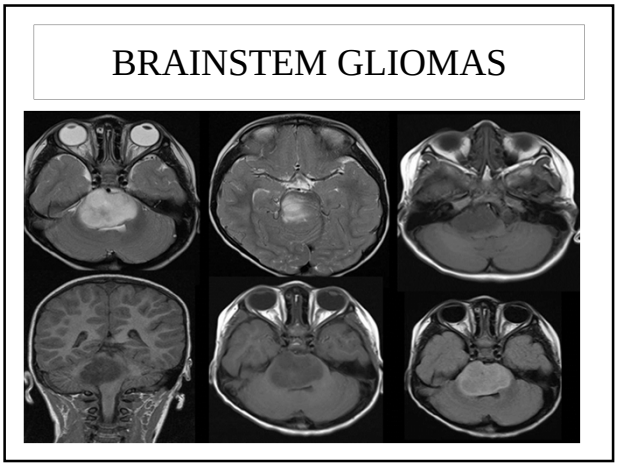
THE AMERICAN SOCIETY FOR THERAPEUTIC RADIOLOGY AND ONCOLOGY (ASTRO) EVIDENCE-BASED REVIEW OF THE ROLE OF RADIOSURGERY FOR MALIGNANT GLIOMA

MAY N. TSAO, M.D., MINESH P. MEHTA, M.D., TIMOTHY J. WHELAN, M.D., DAVID E. MORRIS, M.D., JAMES A. HAYMAN, M.D., JOHN C. FLICKINGER, M.D., MICHAEL MILLS, PH.D., C. LELAND ROGERS, M.D., AND LUIS SOUHAMI, M.D.

- **For patients with malignant glioma, there is Level I-III evidence that the use of radiosurgery boost followed by external beam radiotherapy and BCNU does not confer benefit in terms of overall survival, local brain control, or quality of life as compared with external beam radiotherapy and BCNU.**
- **The use of radiosurgery boost is associated with increased toxicity.**
- **For patients with malignant glioma, there is insufficient evidence regarding benefits / harm of using**
  - radiosurgery at the time progression or recurrence.
  - stereotactic fractionated radiation therapy in patients with newly diagnosed or progressive/recurrent malignant glioma

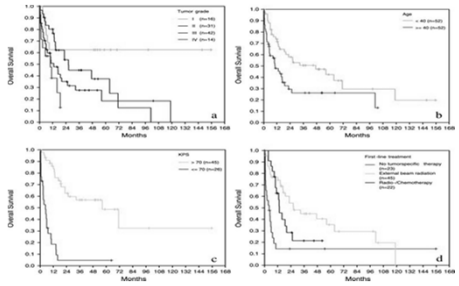

National Cancer Grid (INDIA)
Imaging features of GBM
Resectable Lesion in non eloquent cortex
Awake surgery with Electrophysiological guidance
Lesion in non eloquent cortex
Maximum Safe Resection
Stereotactic Biopsy
Non Amenable to Stereotactic Biopsy
Confirmed GBM or variant on Histopathology
MGMT
IDH only if age < 50 year or prior H/o LGG

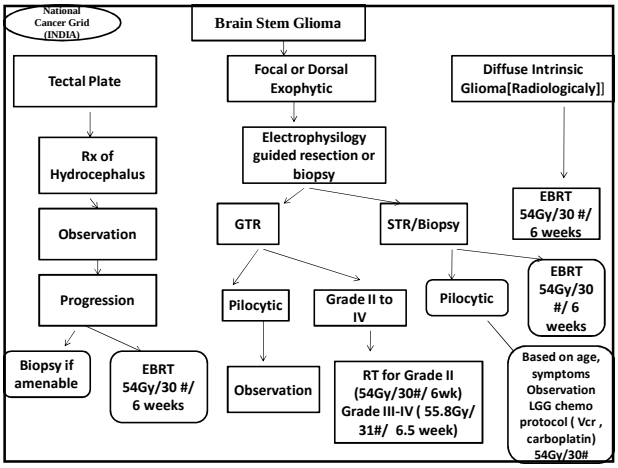

National Cancer Grid (INDIA)
GBM RPA Modified
Poor Prognosis
Favourable Prognosis
Other class V and class VI
Class III-IV Selected Class V
Palliative Hypofractionated Radiotherapy
Radical Concurrent CTRT with TMZ 60Gy/30#/ 6 weekly Adjuvant 6-12 cycles of TMZ (methylated) Adjuvant 6 cycles of TMZ (unmethylated)
If Good Response adjuvant TMZ


BRAINSTEM GLIOMAS

Thomas Reithmeier, Aanyo Kuzeawu et al. Retrospective analysis of 104 histologically proven adult brainstem gliomas: clinical symptoms, therapeutic approaches and prognostic factors. BMC Cancer2014

Between 1997 and 2007, 104 patients (age > 18 years) with histologically proven gliomas of the brainstem were included in this study from five German centres

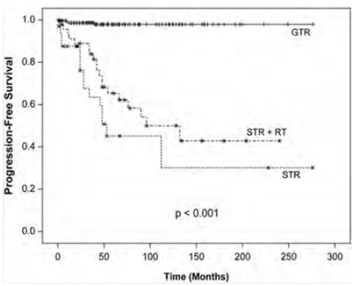




Michael C. Oh, Michael E. Ivan et al Adjuvant radiotherapy delays recurrence following subtotal resection of spinal cord Ependymomas . Neuro-Oncology 15(2):208–215, 2013.

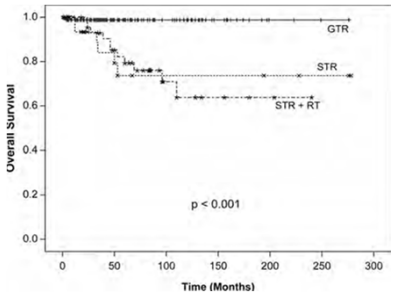
GTR provides the best PFS, which was significantly longer, compared with STR and STR + RT groups (log rank, P =001).

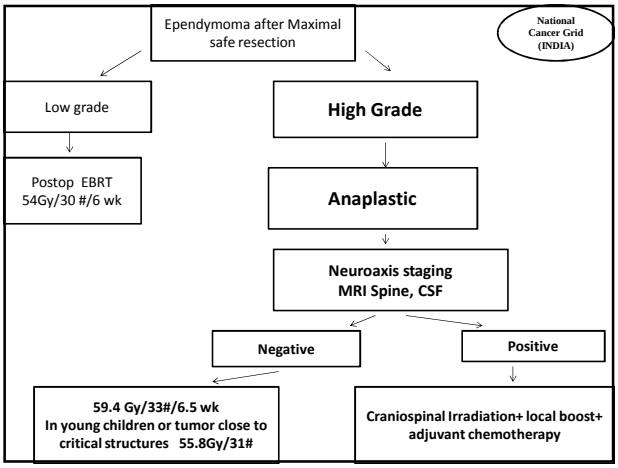
The median survival time (50% PFS) for the STR + RT group was twice as long (96 months), compared with the STR group(48 months).

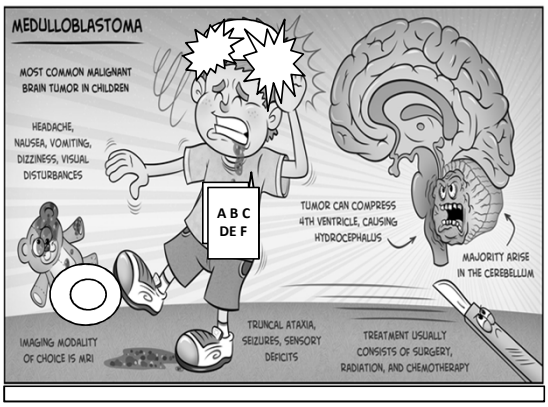


Michael C. Oh, Michael E. Ivan et al Adjuvant radiotherapy delays recurrence following subtotal resection of spinal cord Ependymomas. Neuro-Oncology 15(2):208–215, 2013.

No difference in OS between the STR and STR + RT groups.

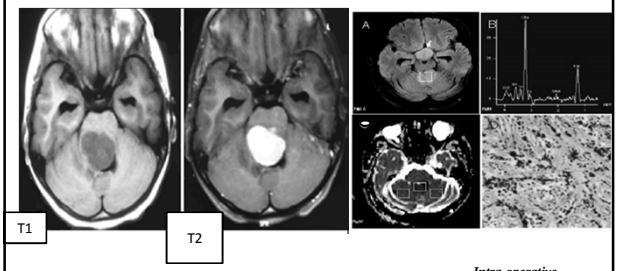






Recommended MRI protocol for suspected medulloblastoma

Minimum desirable (mandatory) acquisitions
Axial T1, T2 and FLAIR images of the brain
Axial, coronal and sagittal T2-sequences of the brain using thin sections (3mm with 0.5-1mm gap) with small field of view and high matrix
Fat-suppressed T1 spin-echo imaging of the brain in at least one plane followed by 3D-FSPGR with contrast. Reconstruction of the 3D images should be done using 3 mm sections with 0.5-1mm gap to match the pre-contrast thin sections
Axial diffusion-weighted imaging of the brain
Post-contrast T1 sagittal screening of the entire spine
Preferable (though optional) aquisitions
Fat-suppressed T1 spin-echo imaging of the brain in all three planes
Multi-voxel MR spectroscopy of the primary tumor in the posterior fossa
ADC map reconstruction through the region of interest in posterior fossa
Axial gradient-echo MRI perfusion imaging of brain during contrast injection
Axial 3D susceptibility-weighted imaging of the brain
Pseudo-continuous 3D-ASL imaging of the brain with correct post-delay labelling
Fat-suppressed sagittal T1 spin-echo imaging of the entire spine in 3 acquisitions, with detailed T2-weighted and axial imaging of any contrast enhancement for further characterization in suspected spinal leptomeningeal metastases
FLAIR = Fluid-attenuated inversion recovery; 3D = Three-dimensional; FSPGR = Fast-spoiled gradient; ADC = Apparent diffusion co-efficient; ASL = Arterial spin labeling

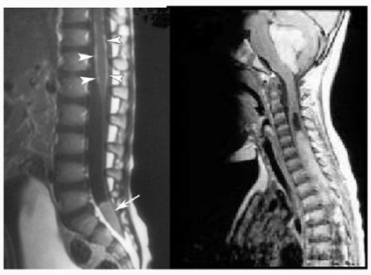


Intra-operative Photomicrograph

Space occupying lesion in midline posterior fossa nearly filling the fourth ventricle.

Spinal MRI

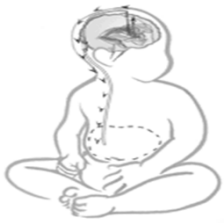
- Most sensitive for spinal cord mets
- Frequency of spinal seeding at diagnosis is 30-35%.
- M.C.seen in the lumbosacral and thoracic areas and are best seen on **post-contrast T1-weighted images.**
- MRI spine should be obtained whenever possible pre-operatively or else at least 2-3 weeks post-operatively.



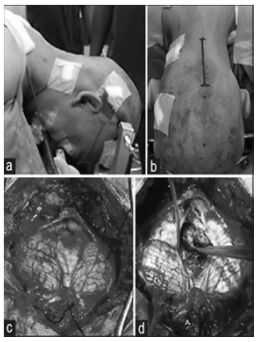
Sagittal and axial MRI, T1 weighted Gadolinium contrast enhancement – Medulloblastoma with metastatic spread to the meninges within the posterior fossa and with a large intramedullary deposit.

Neurosurgery

Routine pre-operative ventriculo-peritoneal (VP) shunt should generally be avoided as definitive surgical resection readily relieves the obstruction by opening the cerebrospinal fluid (CSF) pathways.



Surgical exposure



- Complete surgical resection is ideal, but this may not always be safe or feasible.
- In such cases, it is recommended to attempt maximal safe resection leaving residual tumor behind rather than aggressive surgical resection that can precipitate significant morbidity.

Post-operative Neuro-imaging

- Post-operative MRI of the brain be acquired immediately (**within 24-48 hours of surgical resection**) to accurately identify the extent of resection and quantify the status of the residual disease.
- Whenever immediate post-operative neuro-imaging has not been obtained, it is recommended to **wait for 2-3 weeks** (but no later than 4-weeks) to allow resolution of post-operative changes.

CSF cytology

Mandatory

- **Staging**
- **Risk Stratification**

50% of patients with positive spine MRI studies are asymptomatic and have negative cytologic results.

Recommended testing by diagnostic pathology laboratories for medulloblastoma (Minimum desirable mandatory tests)

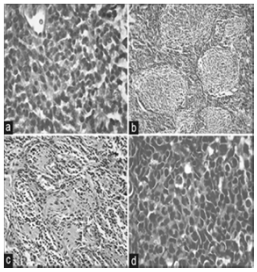
Hematoxylin and eosin(H&E) staining
Reticulin staining

MIB -1 Labelling index (using Ki-67)

Medulloblastoma, Grade IV tumors (WHO Classification)

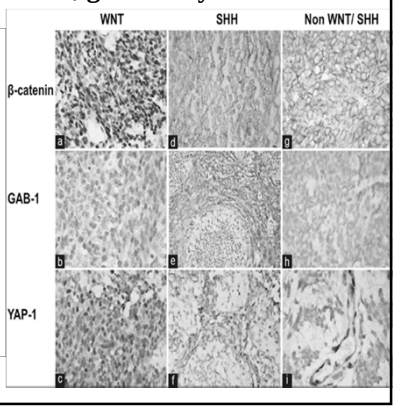
a. **Medulloblastoma, classic**
b. **Desmoplastic/nodular medulloblastoma**
c. **Medulloblastoma with extensive nodularity**
d. **Large-cell/anaplastic medulloblastoma**

Medulloblastoma, not otherwise specified (NOS).



Medulloblastoma, genetically defined

- **Medulloblastoma, WNT-activated**
- **Medulloblastoma, SHH-activated and TP53-mutant**
- **Medulloblastoma, SHH-activated and TP53-wildtype**
- **Medulloblastoma, non-WNT/non-SHH**
  - **Medulloblastoma, group 3**
  - **Medulloblastoma, group 4.**



JAMA Oncology | Original Investigation 2016
Benjamin H. Kann, MD; Henry S. Park et al Postoperative Radiotherapy Patterns of Care and Survival .Implications for Medulloblastoma in Young Children

How are postoperative radiotherapy care patterns changing in young children with medulloblastoma, and what are the survival implications?

In this national database analysis of 816 children with medulloblastoma, ages 3 to 8 years, who received postoperative chemotherapy, there was a 15.1% rate of postoperative radiotherapy deferral overall, and deferral rate increased from 2004 to 2012.
Postoperative radiotherapy deferral was associated with decreased overall survival in this population.

The analysis suggests that postoperative radiotherapy deferral is associated with worse survival in this age group, even in the modern era of chemotherapy

Treatment of the entire neuraxis, i.e. craniospinal irradiation (CSI) followed by boost irradiation of the tumor bed/posterior fossa is recommended

CSF Dissemination 14-16%

Being Radiosensitive, Radiotherapy is curative upto 70% of standard risk patients

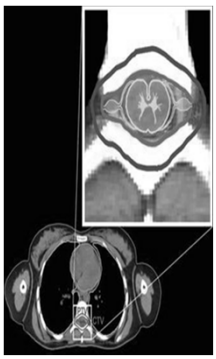
Unavailability of linear accelerators locally, children should ideally be referred in time to an appropriate higher centre with adequate RT facility and infrastructure to prevent unnecessary delays.

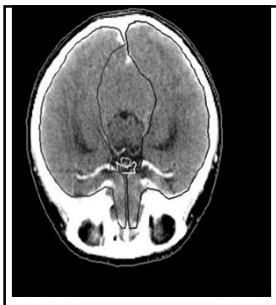
Indian Society of Neuro-Oncology consensus guidelines for the contemporary management of medulloblastoma

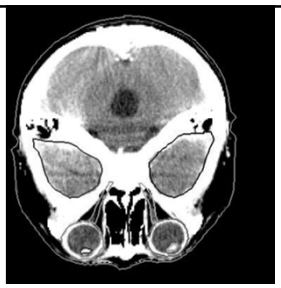
CT-based three-dimensional (3D) simulation

- Supine position is now being increasingly used.
- Target volume coverage is more easily assured and delivery more reproducible with CT-planned supine CSI.
- Axial planning CT images should be acquired from the vertex till the upper thigh region using 5mm slice thickness.

CTV brain	**Brain and its covering meninges till the C2**
PTV brain	**5mm isotropic margin around CTV-brain.**
CTV spine	**Spinal thecal sac and exiting nerve roots from the C2 cervical spine till the lower end of the thecal sac**
PTV spine	**8-10mm isotropic margin is recommended around the CTV-spine**





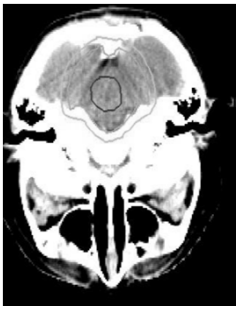


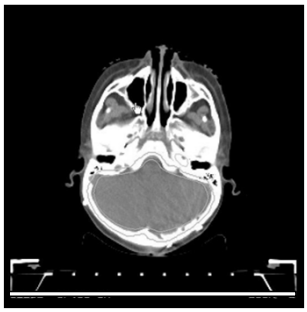
Organs-at-risk (OARs) for CSI should include but may not be limited to eyes, lens, cochlea, mandible, parotids, thyroid, esophagus, lungs, heart, liver, kidneys, bowel bag, rectum, bladder, gonads (ovary/testes), and vertebral bodies plus pelvis (surrogate for red bone marrow)

Boost irradiation planning

Low Risk And Standard Risk	**Pre-operative Tumor-bed With Appropriate Margins (Typically 1-1.5cm Around The Tumor Bed).**
High Risk And Very High Risk Disease	**Irradiation Of The Entire Posterior Fossa Is Presently Recommended**

Posterior Fossa Boost

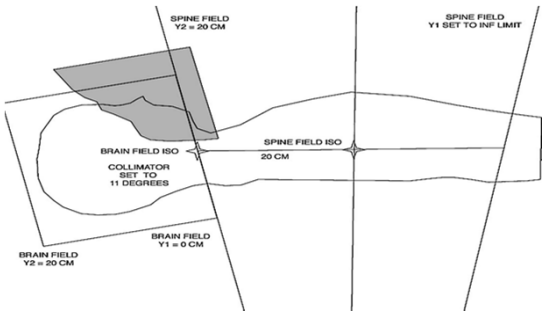




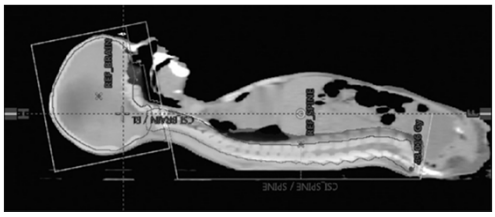
CSI and boost plans be summated to produce a composite treatment plan and final dose-distribution.

3DCRT with multileaf collimtors → **IMRT**

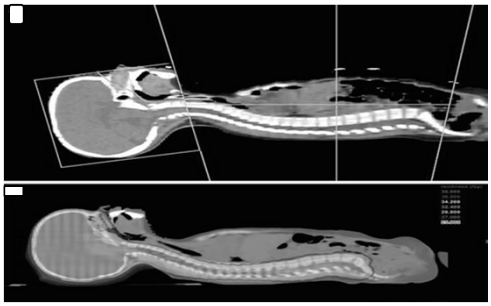
CSI in supine position



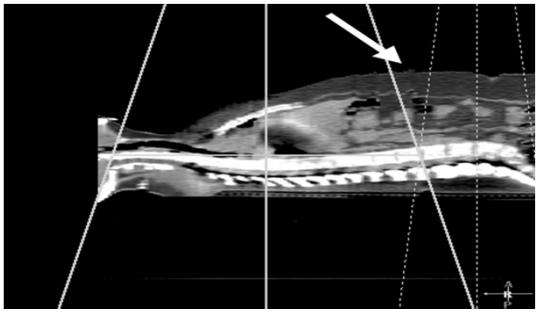
Fixed-field geometry for supine craniospinal irradiation with set-up isocentre fixed at mid-body of C2-vertebra.



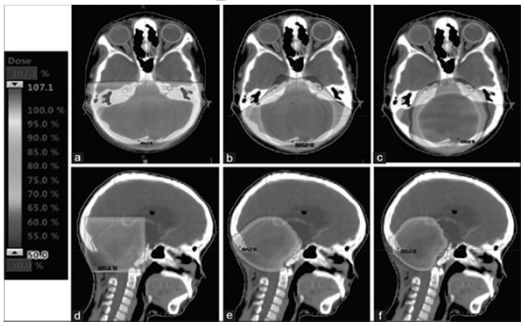
The field junction over the cervical cord usually is moved weekly ("feathered") to avoid over- or underdosage.



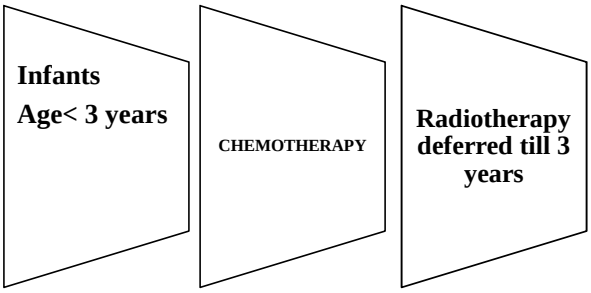
The anterior fields are shown and the gap can be measured directly from the image.



Tumor-bed Boost Following Craniospinal Irradiation



Radiotherapy prescription



ISNO guidelines

NCG Guidelines

Children 3- 18 years

Low Risk Disease	**Reduced dose of CSI** **Reduced chemotherapy intensity**
Standard Risk Disease	**Reduced dose CSI weekly VCR** **CSI: 23.4Gy/13#/3wks** **PF Boost : 12.6 Gy/7#/1.5 wks** **Tx Bed boost: 18 Gy/10#/2wks** **Followed by 6 cycles of adjuvant chemotherapy**
	HFRT **CSI: 36Gy/36# 1GyB.I.D** **(6-8 hrs gap in between 2 daily fractions)**
	Tx Bed Boost: 32 Gy/32# 1GyB.I.D

High Risk Disease/Very High Risk Disease	**Standard CSI 35Gy/21#/4week concurrent carboplatin during CSI and tumor bed boost : 19.8Gy/11#/2.5wks**
	Boost to gross metastatic deposit: 5.4-9Gy/3-5#

Journal of Cancer Research and Therapeutics

The official publication of Association of Radiation Oncologists of India (AROI)

ORIGINAL ARTICLE

Ahead of Print

A dosimetric comparison between three-dimensional conformal radiation therapy and intensity-modulated radiation therapy in the treatment of posterior fossa boost in medulloblastoma

Meenu Gupta[1], Ravi Kant[1], Vipul Nautiyal[1], Jyoti Bisht[1], Shailndra Raghuvanshi[2], Manju Saini[2], BP Kalra[3], Mushtaq Ahmad[1]

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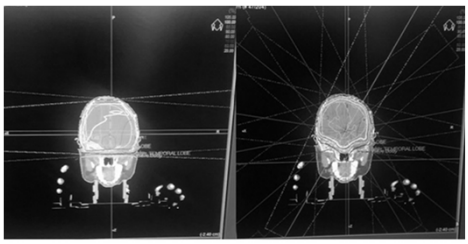
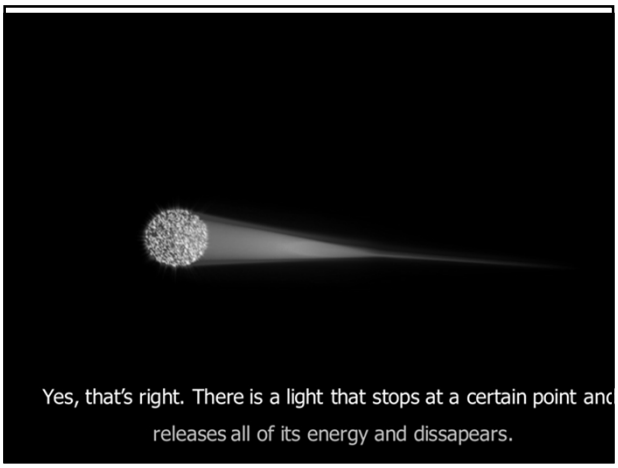
Source of Support: None, Conflict of Interest: None

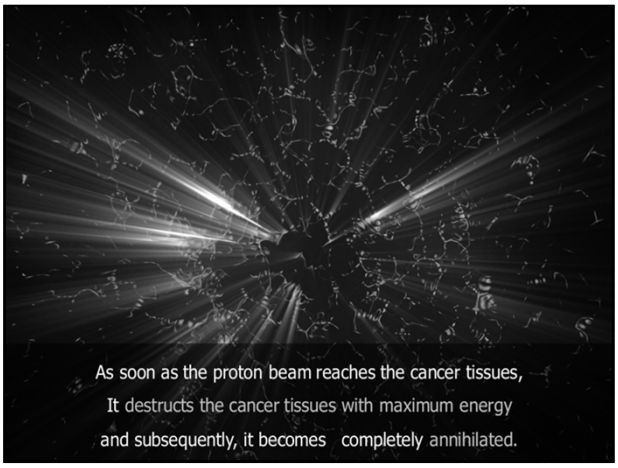
Mid-axial dose distributions with (a) 3DCRT (b) IMRT for one of the representative cases. Yellow represents 100%, Red 95% and Blue 70% of the isodose lines. 3DCRT, Three Dimensional Conformal Radiotherapy; IMRT, Intensity Modulated Radiotherapy.

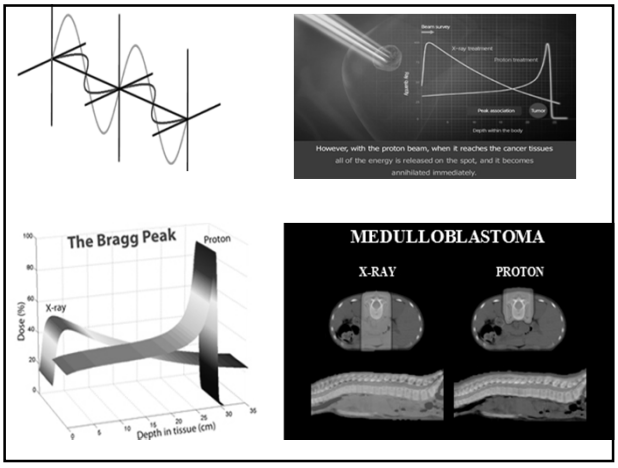


(a) (b)

Results: Mean values of planning target volume (PTV); PTV95% and PTV5% in IMRT were 97.19% and 106.07% and for 3DCRT were 96.57% and 106.33%, respectively. The dose homogeneity was better in IMRT (1.091) as compared to 3DCRT (1.100), but was not statistically significant (P = 0.341). Conformity index was comparable in both the plans, i.e., 3DCRT (0.979) and IMRT (0.976) with P = 0.819. **IMRT plan provided reduced mean dose to cochlea relative to the 3DCRT plans with P = 0.032 for the right cochlea and 0.020 for the left cochlea.** IMRT showed no advantage over 3DCRT in sparing the anterior cranial structures where mean doses to the right and left lens were 0.61 Gy and 0.56 Gy for IMRT and 0.16 Gy and 0.09 Gy for 3DCRT, respectively. Conclusions: IMRT technique was able to improve homogeneity index, spare the cochleae, but 3DCRT plans were superior in sparing anterior cranial structures without compromising the dose to PF.


Yes, that's right. There is a light that stops at a certain point and
releases all of its energy and dissapears.


As soon as the proton beam reaches the cancer tissues,
It destructs the cancer tissues with maximum energy
and subsequently, it becomes completely annihilated.


However, with the proton beam, when it reaches the cancer tissues
all of the energy is released on the spot, and it becomes
annihilated immediately.
The Bragg Peak
Proton
X-ray
Dose (%)
Depth in tissue (cm)
MEDULLOBLASTOMA
X-RAY
PROTON

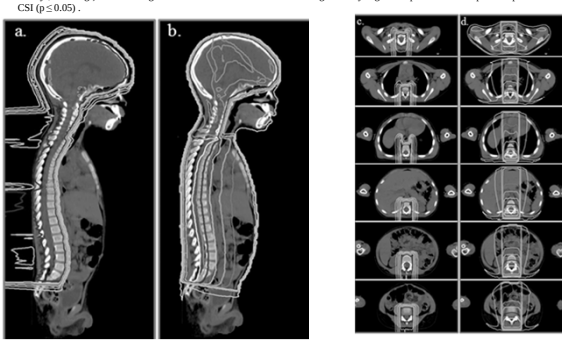
Proton Craniospinal Radiation Therapy: Rationale and Clinical Evidence
Anita Mahajan, MD University of Texas MD Anderson Cancer Center, Houston, TX, USA

Abstract Purpose: To review the existing evidence that supports the use of proton craniospinal irradiation (p-CSI) in pediatric patients.

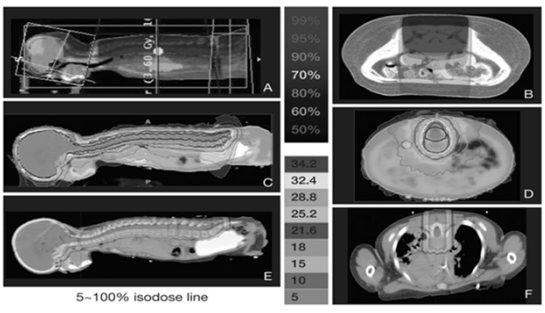
Conclusions: Based on the theoretical and early clinical outcomes, p-CSI appears to provide equal tumor control with potentially reduced risk of side effects when compared with data. Ongoing efforts will continue to evaluate these advantages.

Comparison of therapeutic dosimetric data from passively scattered proton and photon craniospinal irradiations for medulloblastoma. **Rebecca M Howell,Anita et al. M.D Anderson cancer centre**.

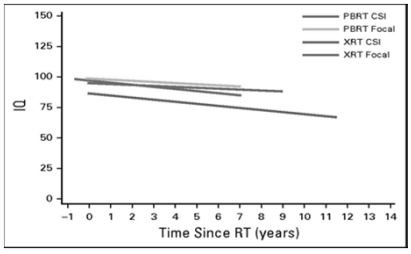
Proton CSI improved normal tissue sparing while also providing more homogeneous target coverage than photon CSI for patients across a wide age and BMI spectrum. Of the 24 parameters (V_5, V_{10}, V_{15}, and V_{20} in the esophagus, heart, liver, thyroid, kidneys, and lungs) Wilcoxon signed rank test results indicated 20 were significantly higher for photon CSI compared to proton CSI ($p \leq 0.05$) .



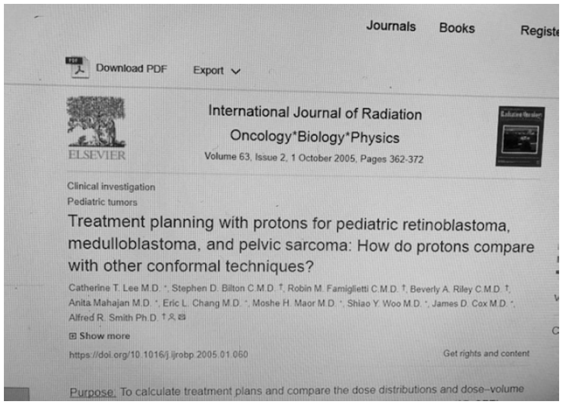
Technology comparison



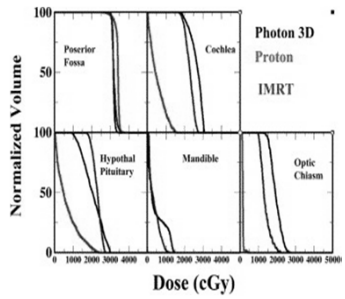
IQ Change Over Time by RT Group



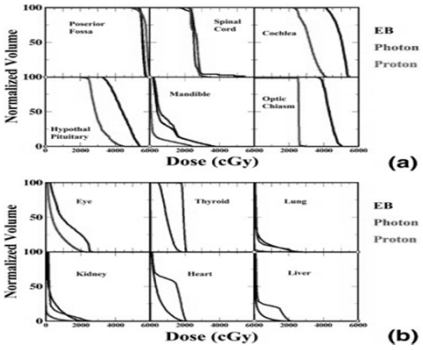
Regression lines of IQ change over time since RT for each RT group and by CSI/focal RT, CSI, craniospinal irradiation; IQ, intelligence quotient; PBRT, proton beam radiation therapy; RT, radiation therapy; XRT, photon radiation therapy.



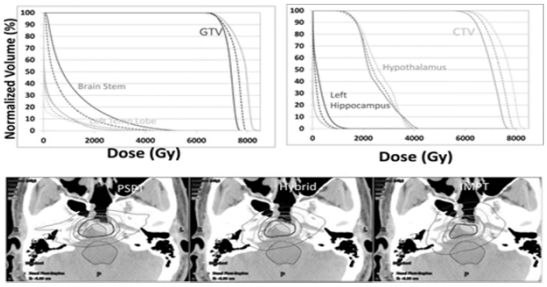
Medulloblastoma, posterior fossa irradiation alone: Dose–volume histogram comparisons across treatment modalities. (3D = three-dimensional; IMRT = intensity-modulated radiation therapy.)



Medulloblastoma, composite of craniospinal plus posterior fossa



Novel Hybrid Scattering- and Scanning-Beam Proton Therapy Approach



The solid, dashed, and dotted lines denote intensity-modulated proton therapy, hybrid, and passive scattered proton therapy plans.

Chemotherapy

- Adjuvant chemotherapy following RT
- Adjuvant chemotherapy following surgery in infant medulloblastoma (<3-years)
- Pre-irradiation chemotherapy in infant medulloblastoma to defer RT (till 3-years)
- High-dose chemotherapy with autologous stem-cell rescue
- Concurrent chemotherapy with RTSalvage therapy in relapsed/recurrent medulloblastoma.