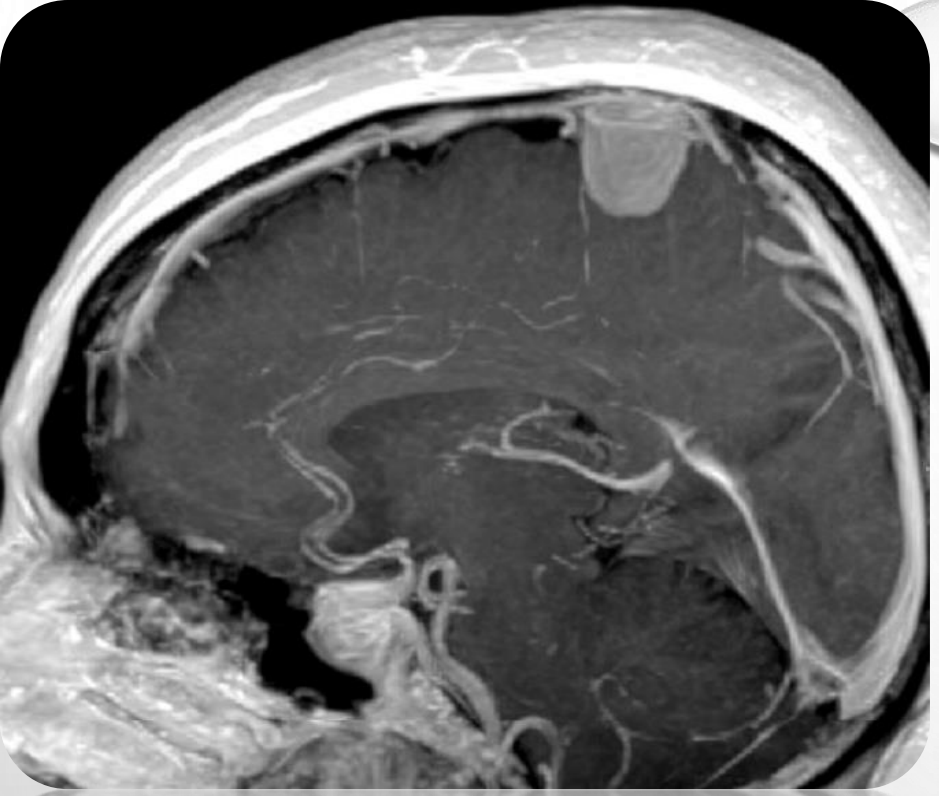


MENINGIOMI INTRACRANICI & RADIOTERAPIA

A.O.U. "Città della Salute e della Scienza di Torino"

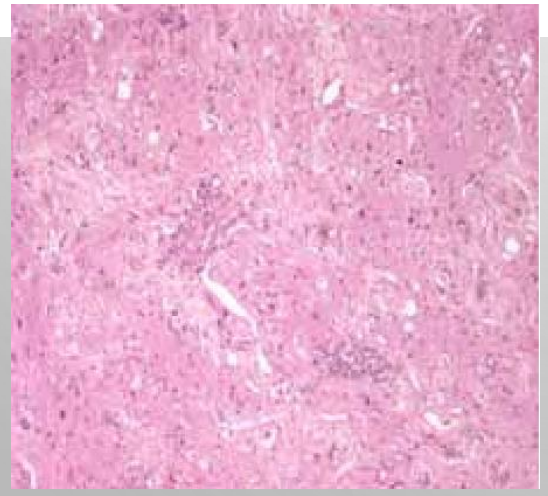
P.O. Sant'Anna – Radioterapia

Sergio Gribaudo

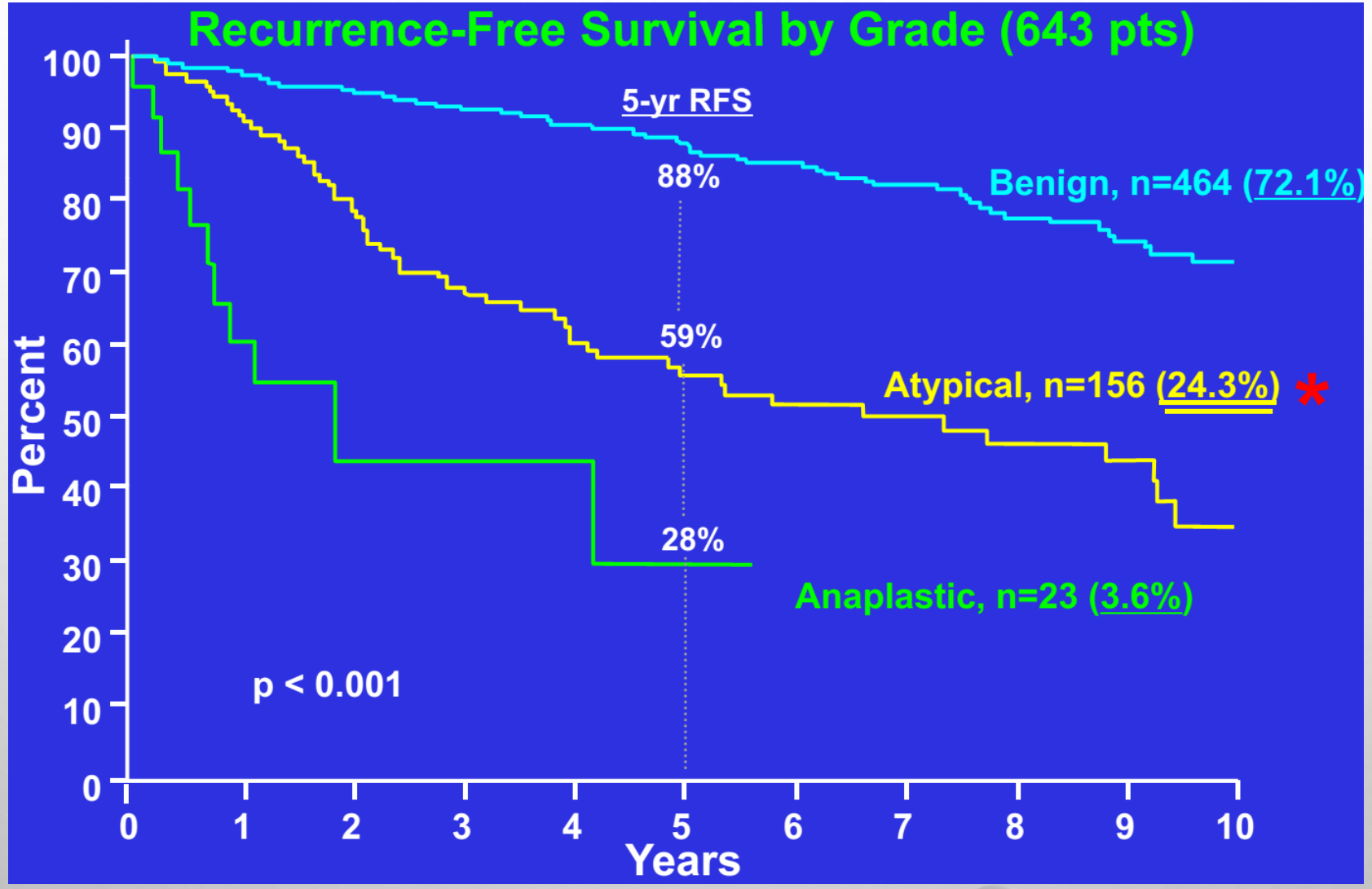
WHO GRADING OF MENINGIOMA

WHO Grade	Criterion
I	Meningioma variants: meningothelial, fibrous (fibroblastic), transitional (mixed), psammomatous, angiomatous, microcystic, secretory, clear cell, chordoid, lymphoplasmacyte-rich, and metaplastic subtypes
II	Atypical meningioma
III	Anaplastic (malignant) meningioma

Grade	Incidence (%)
Benign	90
Atypical	5
Malignant	3-5

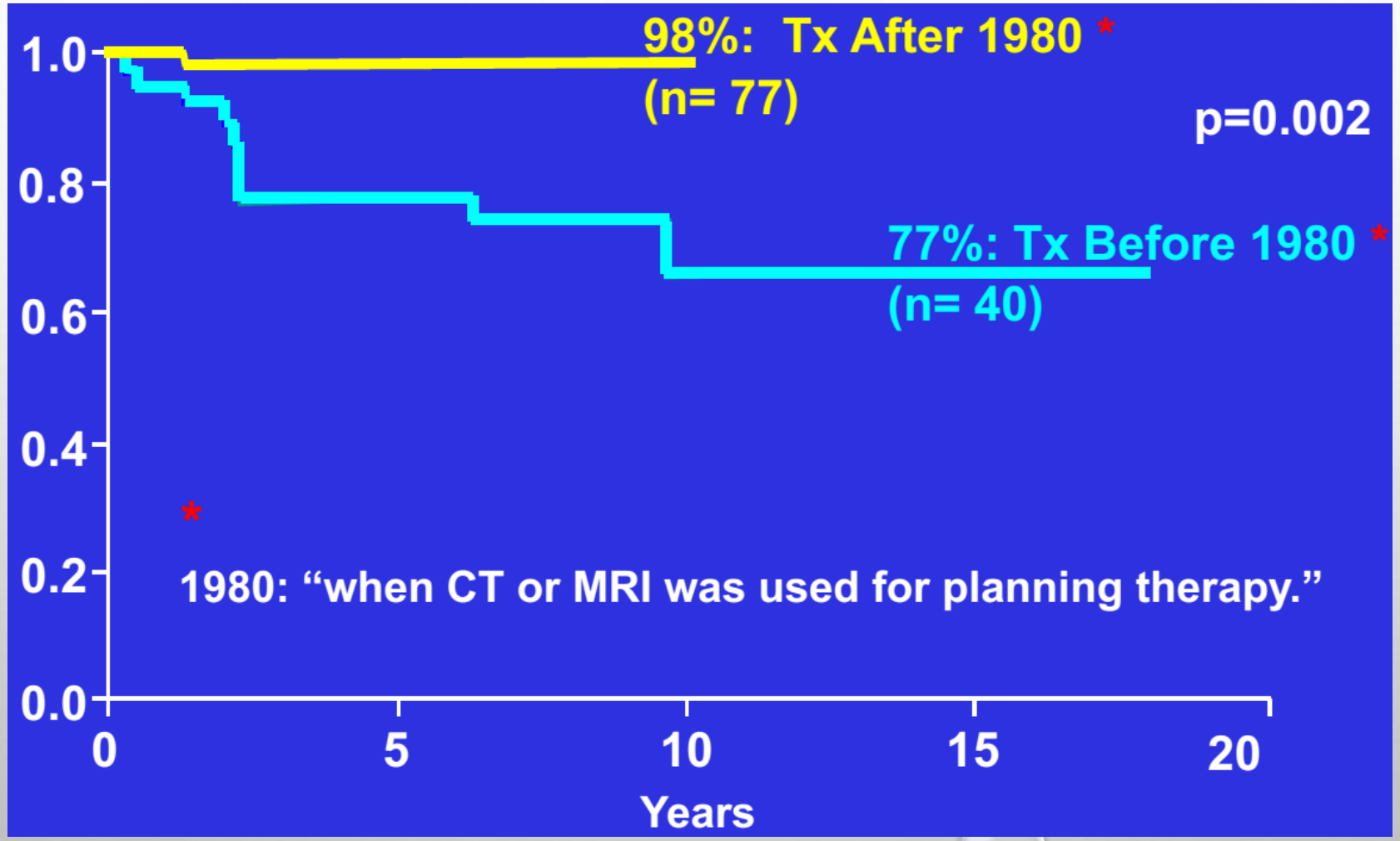


Claus EB, et al. Neurosurg 57:1088–1095, 2005



Arie Perryet al, Am J Surg Pathol 21: 1455-1465, 1997
Cancer 85: 2046-2056, 1999

MENINGIOMA
PFS by treatment era
STR (sub total resection) + post op EBRT



Goldsmith et al, J Neurosurg 80: 195-201, 1994

SIMPSON CRITERIA

Degree of Resection	Recurrence rate %
Complete resection with dural margin	9
Complete resection with coagulation of dura	19
Complete resection (no treatment of dura)	29
Partial removal leaving tumor in situ	40
Decompression	NA

LIMITATION OF SURGERY

- RECUR DESPITE “COMPLETE RESECTION”
- EVEN WITH GROSS TOTAL RESECTION, TUMOR RECURRENCE RATES CAN RANGE FROM 18–25 % AT 10 YEARS
- SURGICALLY INACCESSIBLE
- INVASION OF NORMAL NEURAL OR VASCULAR STRUCTURES
- HIGHER GRADE LESION HAVE A MORE AGGRESSIVE CLINICAL COURSE
- RISK OF HISTOLOGICAL DEDIFFERENTIATION

Benign meningioma
Results from retrospective studies

Total excision

Study (year)	5 years % recurrence	10 years % recurrence
NCDB (1998)	20,5	-
Mirimanoff (1985)	7	20
Mahmood (1993)	2	-
Jaaskelainen (1986)	3	-

- A dose-response relationship has not been identified between 50 and 75 Gy (Carella, 1982)
- The majority of favourable results in the retrospective series have been achieved with doses in the 50-60 Gy range
- Improved RT techniques lead to improved outcome (98% vs 77% FFP at 10 years in the UCSF series)

Subtotal excision

Study (year)	5 years % recurrence	10 years % recurrence
Taylor (1988)	-	82
Mirimanoff (1985)	37	55
Barbaro (1987)	-	60
Stafford (1998)	-	61

Subtotal excision + RT

Study (year)	10 years % recurrence
Goldsmith (1994)	2
Taylor (1988)	18
Barbaro (1987)	32
Miralbell (1992)	12

Neuro-Oncology

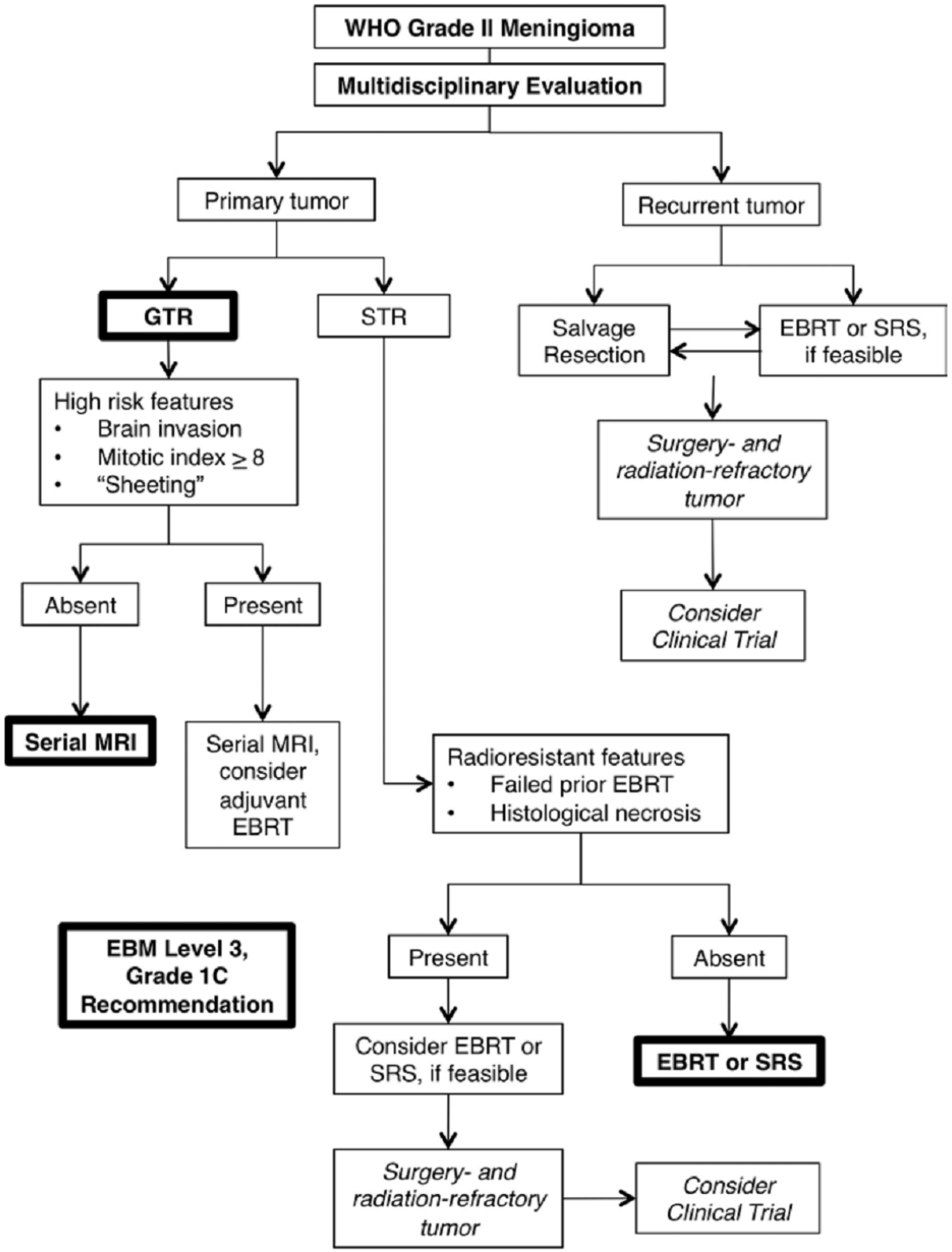
Neuro-Oncology 16(5), 628–636, 2014
doi:10.1093/neuonc/nou025

Adjuvant radiotherapy for atypical and malignant meningiomas: a systematic review

Gurvinder Kaur, Eli T. Sayegh, Andrew Larson, Orin Bloch, Michelle Madden, Matthew Z. Sun, Igor J. Barani, C. David James, and Andrew T. Parsa

Department of Neurological Surgery, Northwestern University, Chicago, Illinois (G.K., E.T.S., O.B., A.T.P.); Department of Pathology, University of California, San Francisco, California (M.M.); Department of Neurological Surgery, University of California, San Francisco, California (A.L., M.Z.S., C.D.J.); Department of Radiation Oncology, University of California, San Francisco, California (I.J.B.)

Controversy exists as to the role and prognostic impact of RT as an adjuvant to surgical resection, especially for sub totally resected AM. This systematic review demonstrates that adjuvant RT significantly improves local control of AM and MM, especially in patients with STR, and produces modest treatment toxicity. Furthermore, the extent of surgical resection and radiation dose are positively correlated with the clinical outcome in RT patients. Although the studies in this review were unable to establish a statistically significant correlation between adjuvant RT and improved prognosis in completely excised AMs, these studies were fraught with several limitations, including the lack of a non irradiated control group and inadequate sample sizes to detect statistically significant risk reductions, among others.

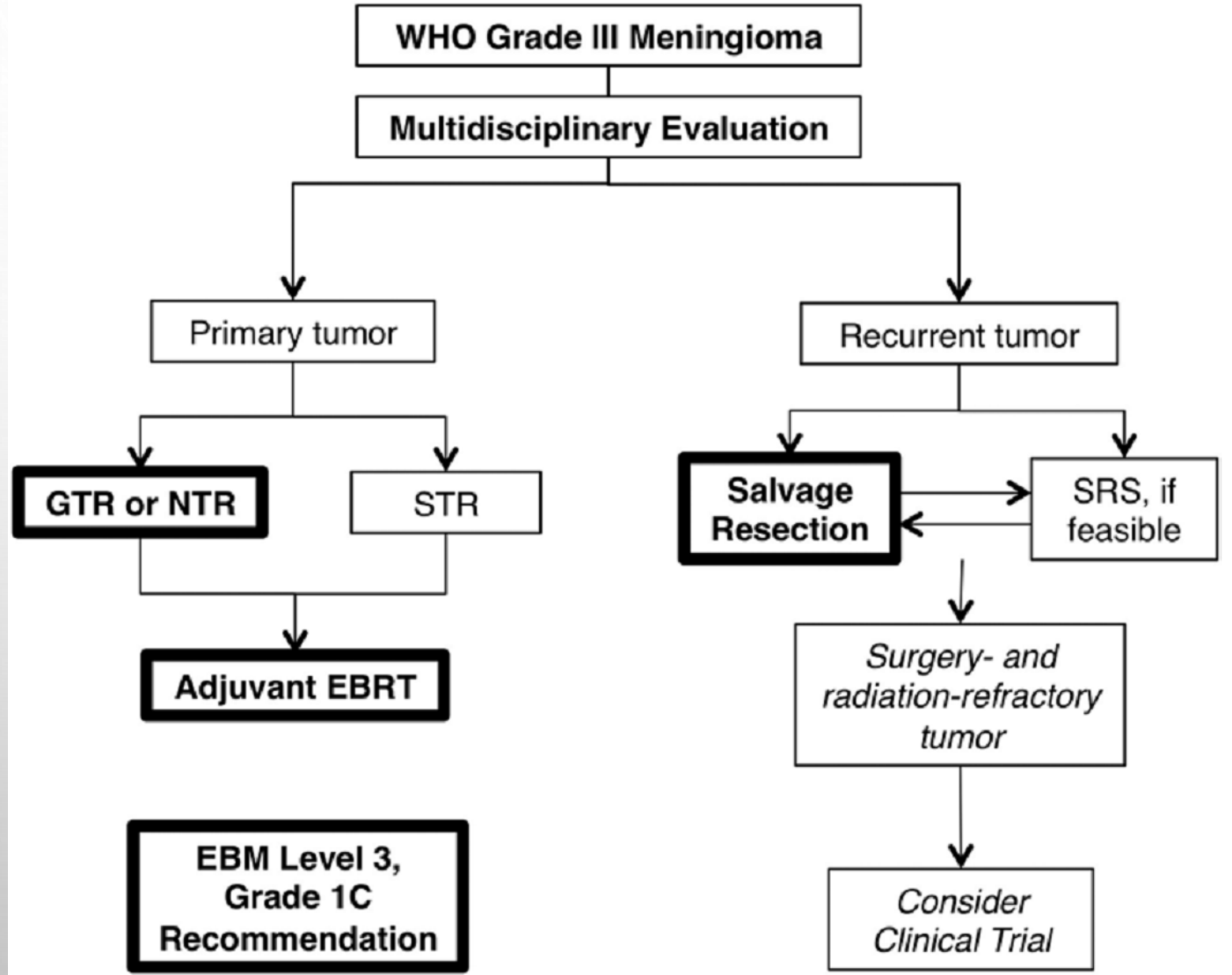


NEUROSURGICAL FOCUS
Neurosurg Focus 38 (3):E3, 2015

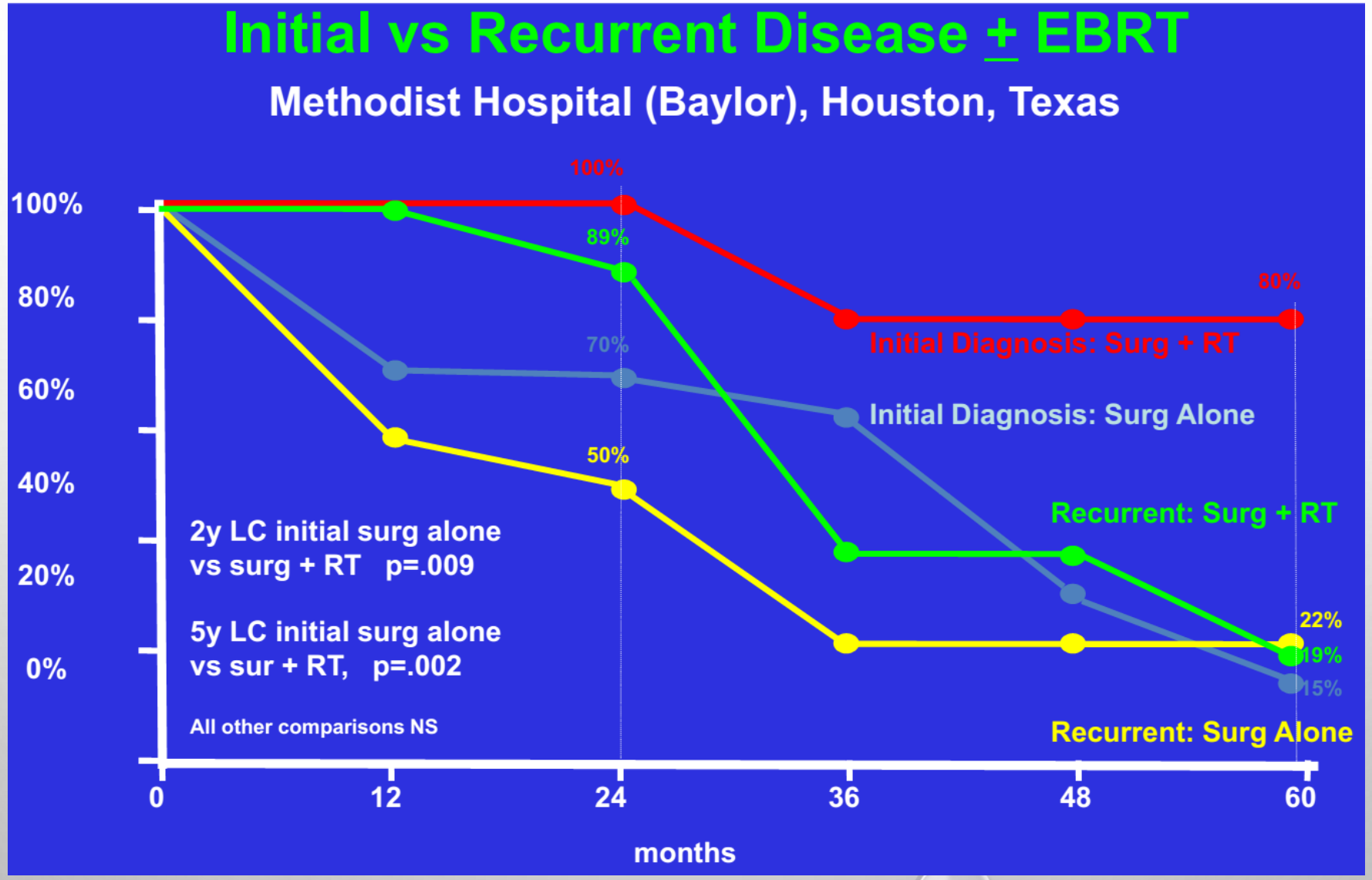
An evidence-based treatment algorithm for the management of WHO Grade II and III meningiomas

*Sam Q. Sun, BS,[1] Ammar H. Hawasli, MD, PhD,[2] Jiayi Huang, MD,[3] Michael R. Chicoine, MD,[2] and Albert H. Kim, MD, PhD[2]

[1]Washington University School of Medicine; and Departments of [2]Neurosurgery and [3]Radiation Oncology, Washington University School of Medicine in St. Louis, Missouri



ANAPLASTIC MENINGIOMA



Dziuk TW, Woo S, Butler EB, et al. Malignant meningioma: an indication for initial aggressive surgery and adjuvant radiotherapy. JNO 1998; 37:177-188

RTOG – 0539 SCHEMA

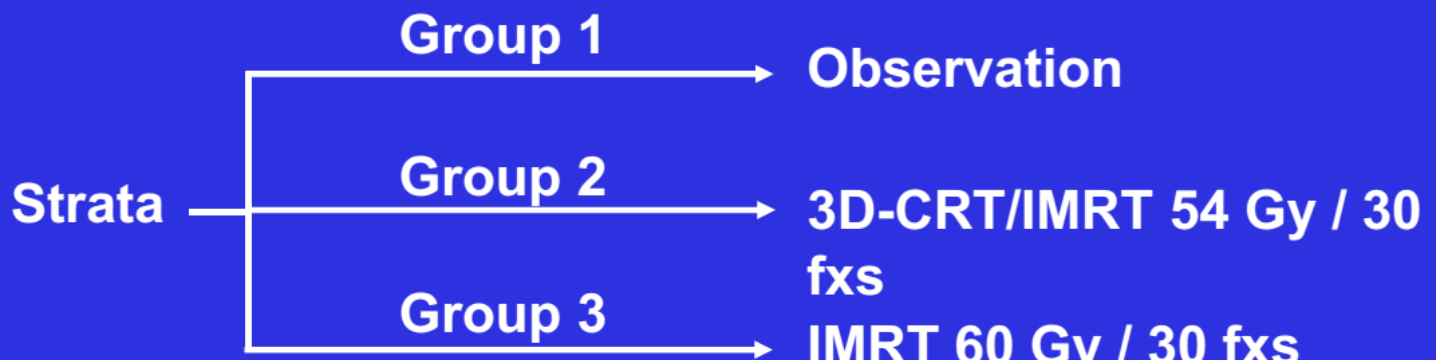
Phase II Study of IMRT for Intermediate and High Risk Meningiomas, and Observation for Low Risk Meningiomas

Group 1 (Low Risk): New Grade 1, GTR or STR

Group 2 (Interm Risk): Recurrent Grade 1, GTR or STR
New Grade 2, GTR

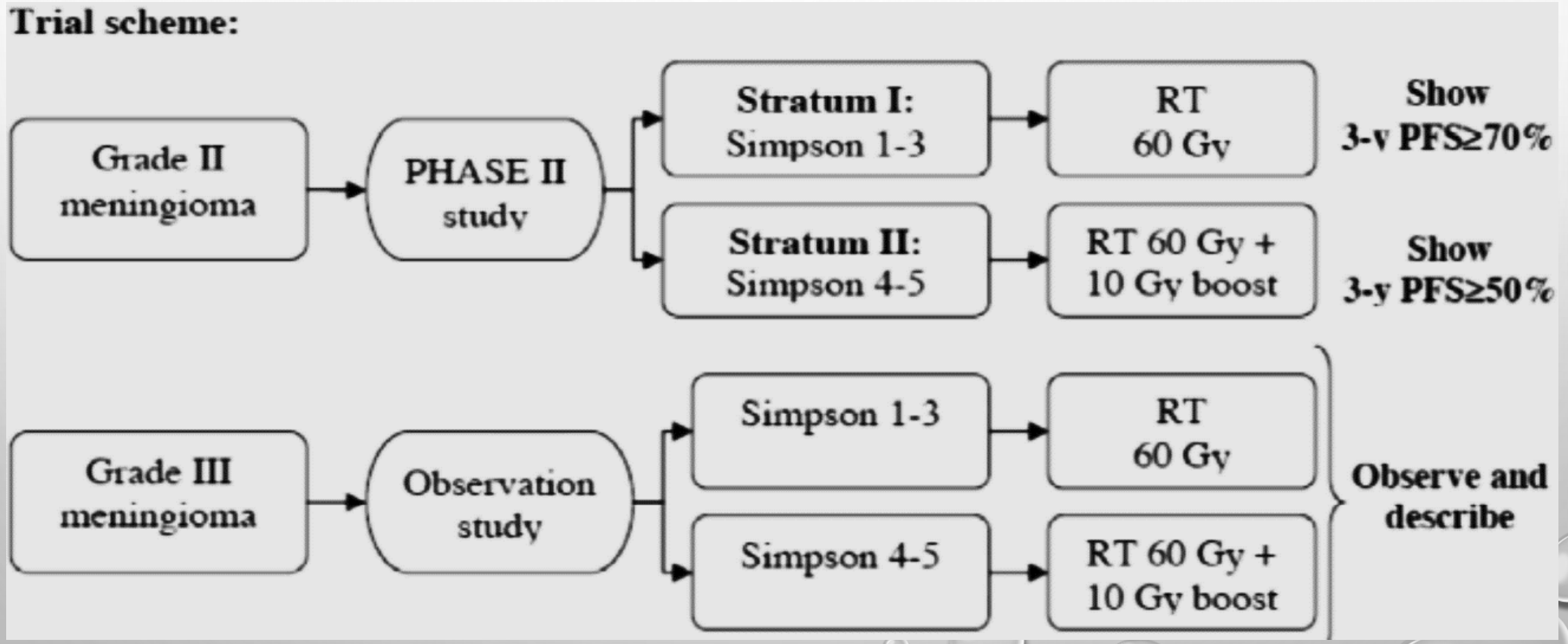
Group 3 (High Risk): Any Grade 3
Recurrent Grade 2
New Grade 2, STR

Primary endpoint: 3 yr PFS



CURRENT EORTC 22042-26042 TRIAL

ADJUVANT POSTOPERATIVE HIGH-DOSE RADIOTHERAPY FOR ATYPICAL AND MALIGNANT MENINGIOMA: A PHASE II AND OBSERVATION STUDY



INDICATIONS FOR RADIOSURGERY

- NEWLY DIAGNOSED PATIENTS
  - SKULL BASE
  - CONVEXITY
  - PARASAGITTAL
  - NOT USED FOR OPTIC NERVE SHEATH TUMOURS
- RECURRENT TUMOURS
- RESIDUAL TUMOUR AFTER RESECTION

RESPONSE ASSESSMENT IN NEURO-ONCOLOGY (RANO)

JNS

LITERATURE REVIEW

J Neurosurg 122:4–23, 2015

Meningiomas: knowledge base, treatment outcomes, and uncertainties. A RANO review

Leland Rogers, MD,[1] Igor Barani, MD,[2] Marc Chamberlain, MD,[3] Thomas J. Kaley, MD,[4] Michael McDermott, MD,[5] Jeffrey Raizer, MD,[6] David Schiff, MD,[7] Damien C. Weber, MD,[8] Patrick Y. Wen, MD,[9] and Michael A. Vogelbaum, MD, PhD[10]

[1]GammaWest Cancer Services, Radiation Oncology, Salt Lake City, Utah; [2]Department of Radiation Oncology, University of California, San Francisco, California; [3]Department of Neurology, University of Washington, Fred Hutchinson Cancer Research Center, Seattle, Washington; [4]Division of Neuro-Oncology, Memorial Sloan–Kettering Cancer Center, New York, New York; [5]Department of Neurosurgery, University of California, San Francisco, California; [6]Department of Neurology, Northwestern University, Chicago, Illinois; [7]Neuro-Oncology Center, University of Virginia, Charlottesville, Virginia; [8]Radiation Oncology, Geneva University Hospital, Geneva, Switzerland; [9]Center for Neuro-Oncology, Dana-Farber/Brigham and Women's Center, Boston, Massachusetts; and [10]Brain Tumor and NeuroOncology Center and Department of Neurosurgery, Cleveland Clinic, Cleveland, Ohio

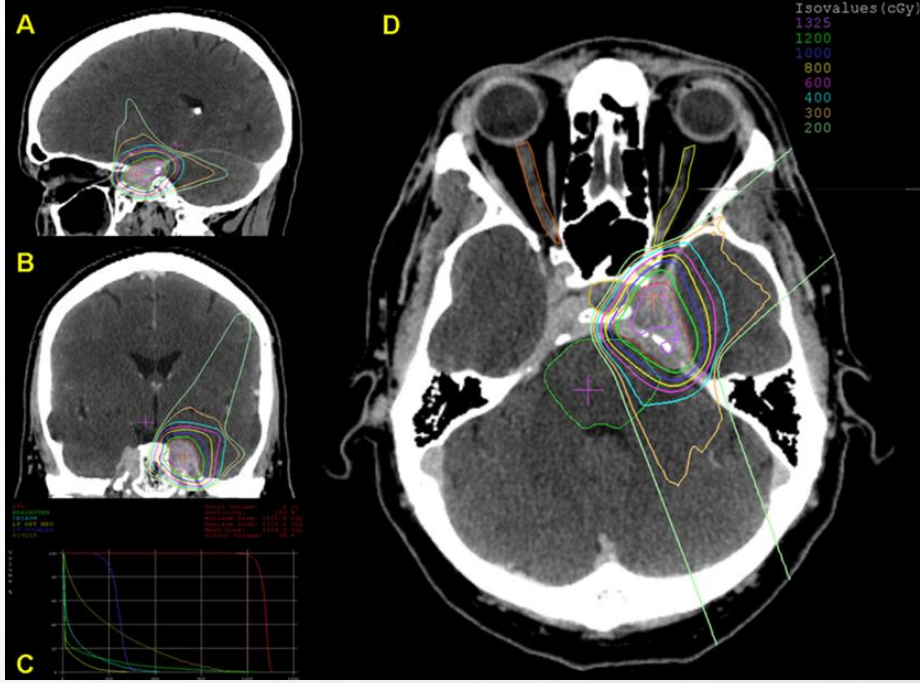
Amichetti *et al. Radiation Oncology* 2012, **7**:210
http://www.ro-journal.com/content/7/1/210

RADIATION ONCOLOGY

REVIEW Open Access

Radiosurgery with photons or protons for benign and malignant tumours of the skull base: a review

Maurizio Amichetti[1*], Dante Amelio[1] and Giuseppe Minniti[2,3]



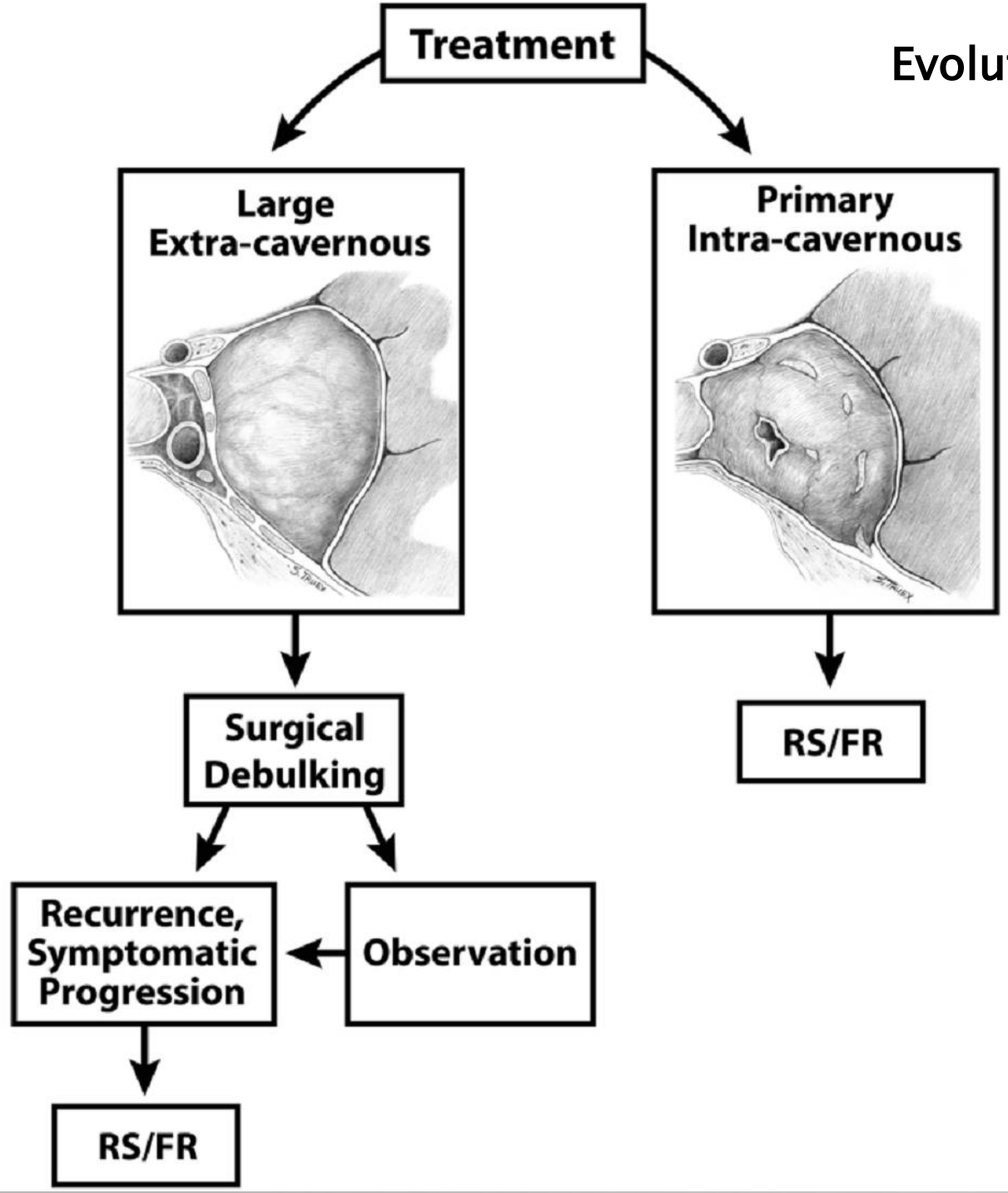
Stereotactic radiosurgery (SRS) is an important treatment option for intracranial lesions. Many studies have shown the effectiveness of photon-SRS for the treatment of skull base (SB) tumours; however, limited data are available for proton-SRS.

Several photon-SRS techniques, including Gamma Knife, modified linear accelerators (Linac) and CyberKnife, have been developed and several studies have compared treatment plan characteristics between protons and photons.

The principles of classical radiobiology are similar for protons and photons even though they differ in terms of physical properties and interaction with matter resulting in different dose distributions.

Protons have special characteristics that allow normal tissues to be spared better than with the use of photons, although their potential clinical superiority remains to be demonstrated.

Evolution in treatment of cavernous sinus meningiomas



The goal of modern therapy for CSMs should be maximizing tumor growth control while minimizing tumor-related and treatment related morbidity. This goal requires a multidisciplinary strategy, involving neurosurgery and radiation oncology, which is individualized to the patient's clinical status, tumor histology, and tumor anatomy

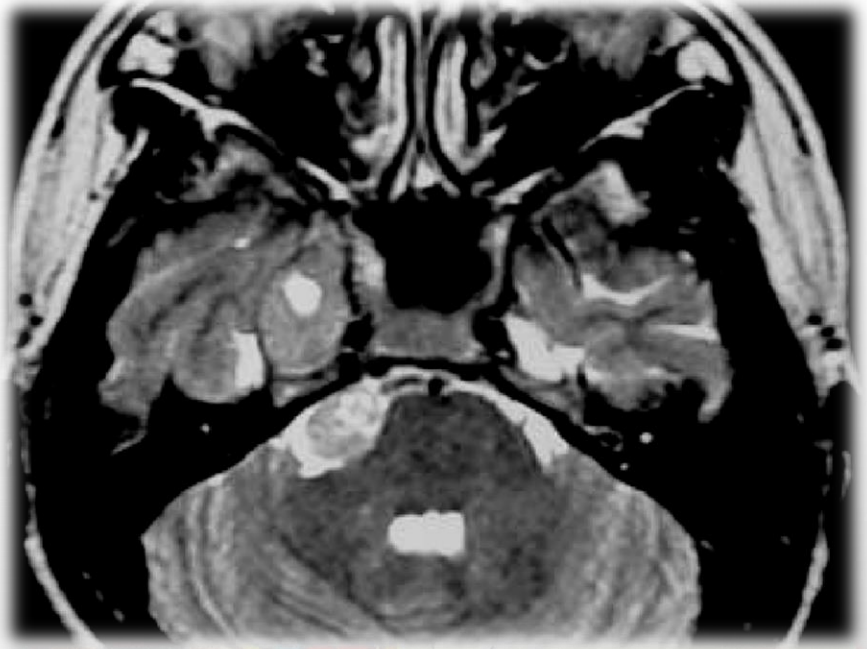
Neurosurg Focus 35 (6):E8, 2013

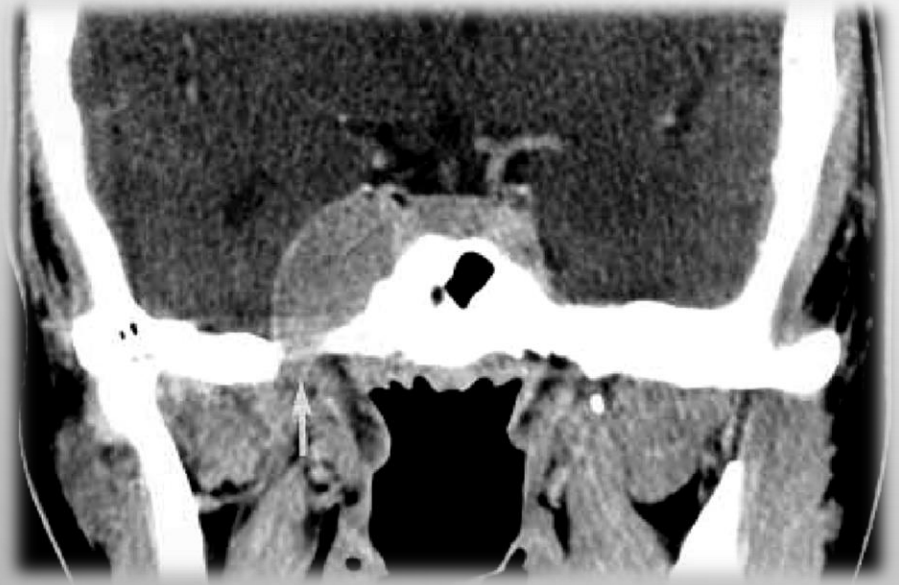
The treatment of cavernous sinus meningiomas: evolution of a modern approach

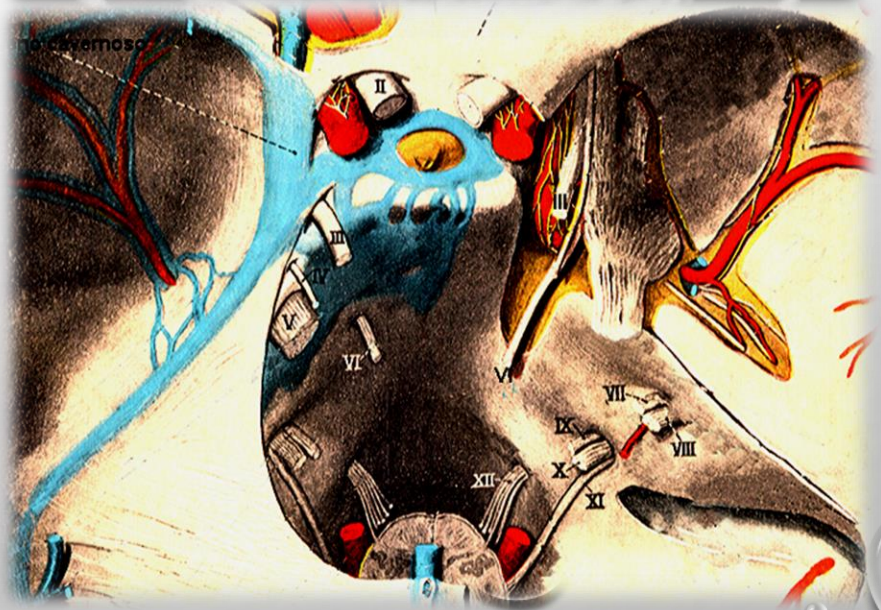
DANIEL R. KLINGER, M.D., BRUNO C. FLORES, M.D., JEREMY J. LEWIS, M.D., AND SAMUEL L. BARNETT, M.D.

Department of Neurological Surgery, University of Texas Southwestern Medical Center, Dallas, Texas

Meningiomas of the skull base

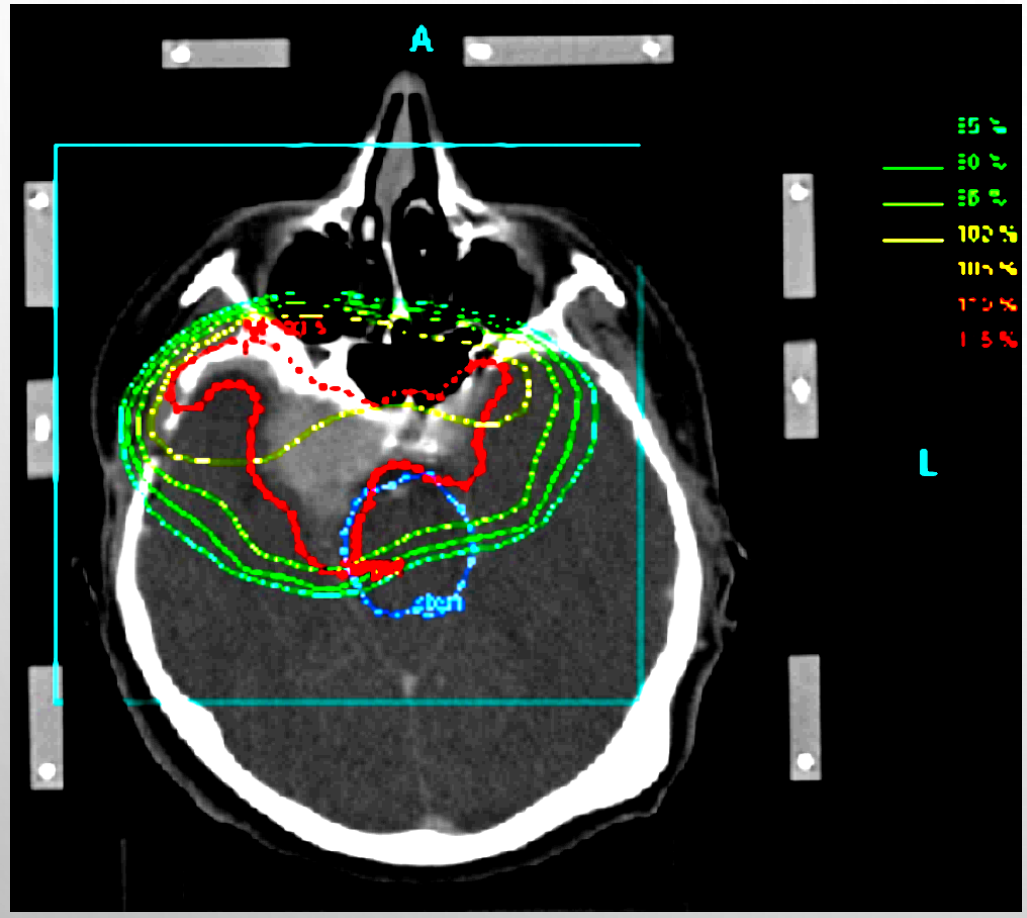


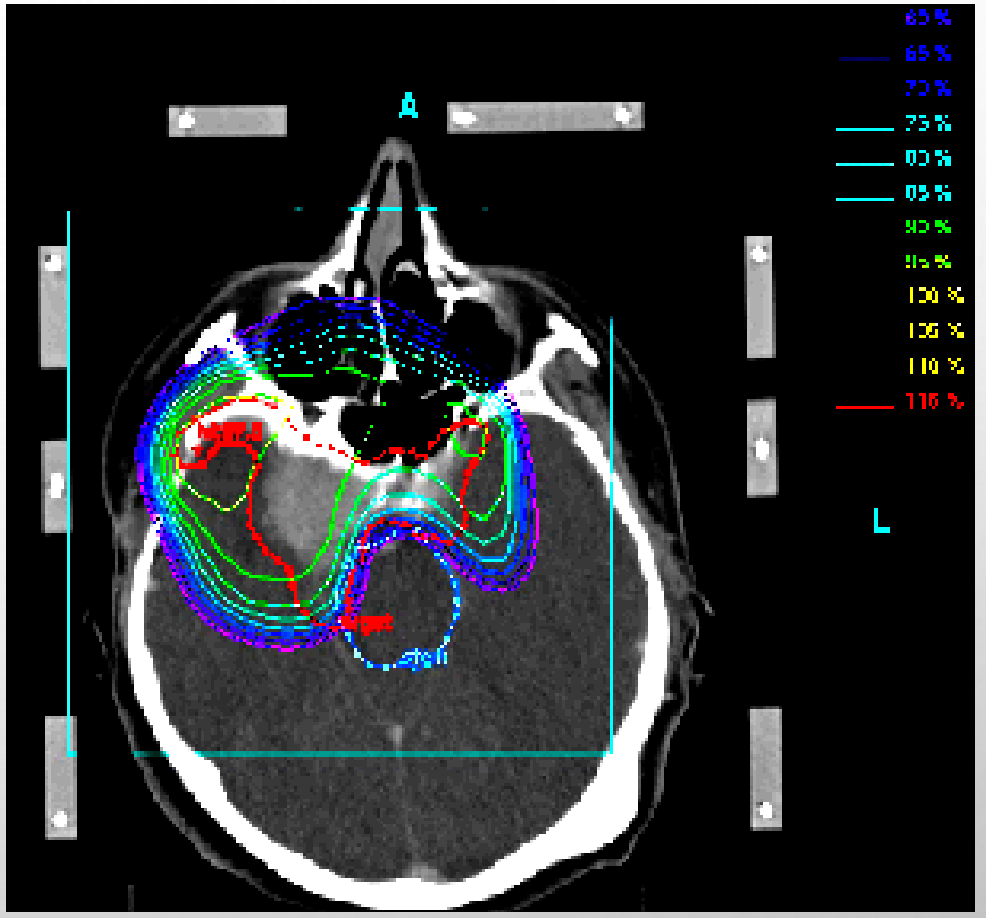




Dynamic Multileaf Collimator

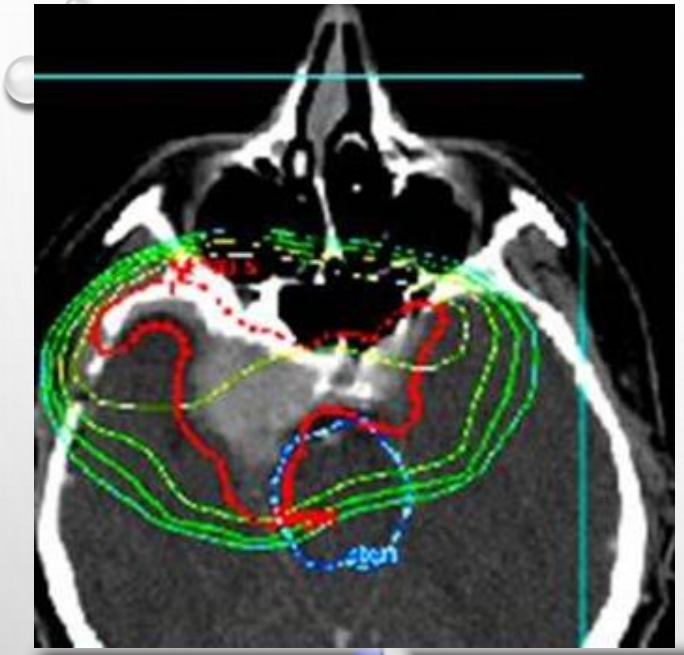
Meningioma of the sphenoid ridge: effects of arc modulation on dose distribution with arc therapy

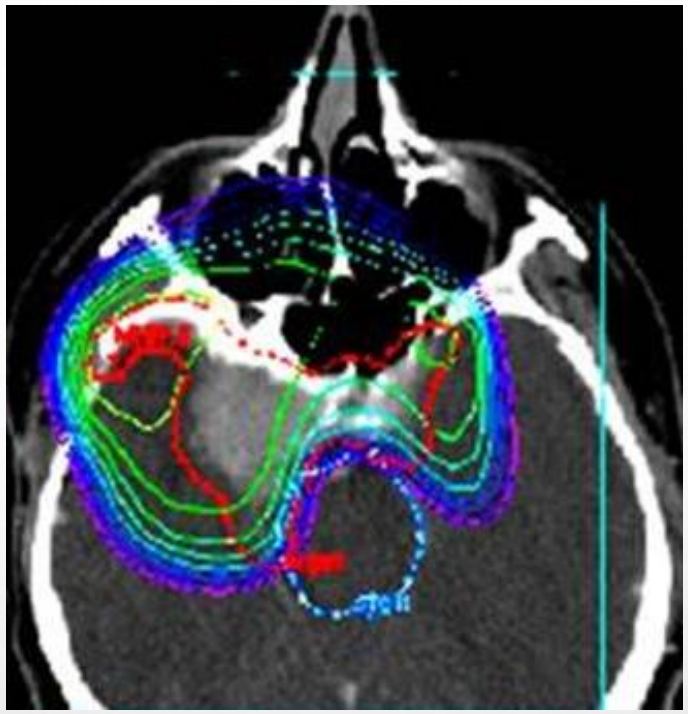




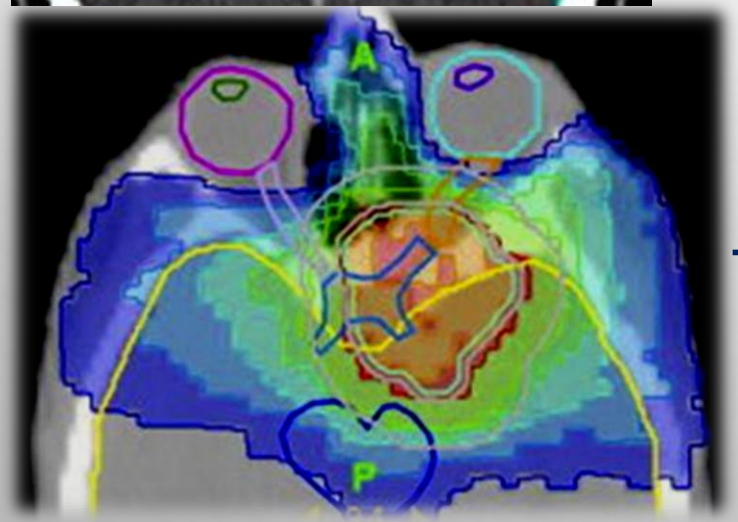
EFFECTS OF ARC MODULATION ON DOSE DISTRIBUTION

Dynamic arc therapy

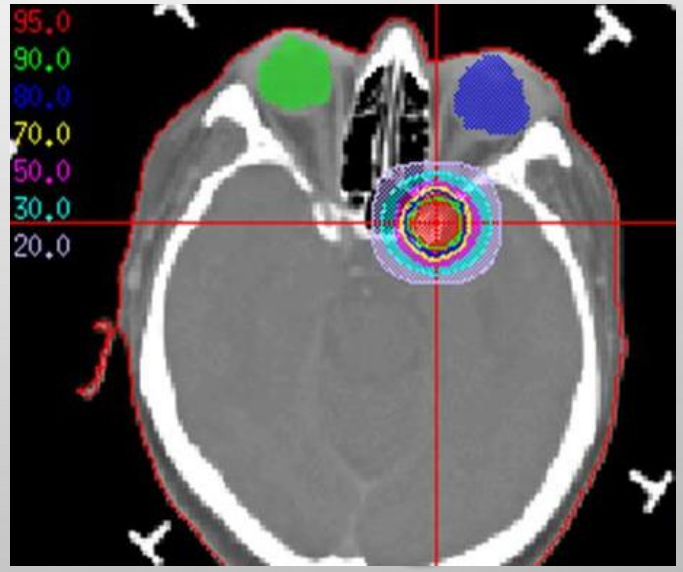




Intensity modulated arc therapy



Tomotherapy



SRS

fSRT DEI MENINGIOMI DELLA BASE CRANICA
Indicazioni al trattamento

- RESEZIONE INCOMPLETA: 16
- NON OPERATI: 41
- RECIDIVE: 6

- TOTALE: 63

fSRT DEI MENINGIOMI DELLA BASE CRANICA
Caratteristiche tecniche

Volume GTV/CTV	Mediana 24.3 ml (range: 4.8–93.2)
PTV	CTV + 2 mm margine
3D CRT	n = 29
IMAT	n = 34
TC	n = 26
TC/RM (fusione)	n = 37
Dose Totale (Gy)	54 ± 1.8
Dose Frazione (Gy)	1.8
N° frazioni	30 ± 1

RESULTS

- MEDIAN FOLLOW-UP MONTHS: RANGE 14-136
- IMPROVED SYMPTOMS: 65.7%
- UNCHANGED SYMPTOMS: 28.9%
- WORSENED SYMPTOMS: 1.5%
- NEW SYMPTOMS: 0%
- TUMOUR SHRINKAGE: 16.9%
- UNCHANGED VOLUME: 80.8%
- INCREASED VOLUME: 2.2%
- CEREBRAL OEDEMA: 0%
- 5 YEARS SURVIVAL: 100%
- 5 YEARS DFS: 98.5%

CONCLUSIONI

- LA RADIOTERAPIA STEREOTASSICA CON ARCHI DINAMICI CONFORMATI È UN TRATTAMENTO EFFICACE PER I MENINGIOMI DELLA BASE CRANICA
- LA TOSSICITÀ È TRASCURABILE
- LA MODULAZIONE DELL'INTENSITÀ DI DOSE LUNGO GLI ARCHI MIGLIORA LA CONFORMALITÀ E RIDUCE LA DOSE AGLI ORGANI CRITICI

EFFICACIA DELLA RADIOTERAPIA NEL TRATTAMENTO DEI MENINGIOMI: 12 ANNI DI ESPERIENZA DI TRE CENTRI

EFFICACY OF RADIATION THERAPY IN THE TREATMENT OF MENINGIOMAS: A 12 YEAR EXPERIENCE OF THREE CENTERS

S.GRIBAUDO*, A. ROSSI°, R. PANAIA§, E. MADON*, V. RICHETTO*, S. SALA°, P. GABRIELE§, G. MALINVERNI° AND A. URGESI*

*S.C. RADIOTERAPIA AO CITTÀ DELLA SALUTE E DELLA SCIENZA – OSPEDALE S. ANNA, TORINO

°S.C. RADIOTERAPIA AO MAURIZIANO UMBERTO I, TORINO

§ S.C. RADIOTERAPIA IRCC-FPO, CANDIOLO

Sergio Gribaudo E-mail: sergio_gribaudo@hotmail.com

Purpose

Meningiomas are the most common primary brain tumors in adults. Histological features are used to classify meningiomas into one of three World Health Organization (WHO) grades. About 90% of tumors are WHO grade I (benign). About 5% to 7% are classified as WHO grade II (atypical), and less than 3% are WHO grade III (malignant or anaplastic). Surgical resection is curative when complete removal of a benign meningioma is possible. Incompletely resected tumors and high-grade lesions are frequently treated with fractionated radiotherapy or stereotactic radio-surgery. When it is not possible to perform a resection (olfactory groove, lateral ventricle, orbit, suprasellar region, sphenoid ridge, cerebello-pontine angle, cavernous sinus, foramen magnum, and clivus), highly conformal techniques are mandatory if long term control with minimal risk of adverse effects is to be achieved by radiotherapy.

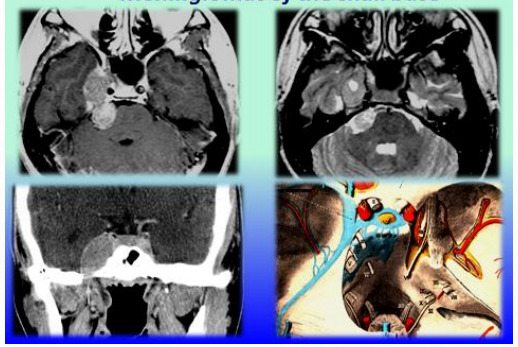
Patients and method

136 patients with meningiomas were treated with 3D-CRT, fSRT (Intensity Modulated Arc Therapy - IMAT), SRS and Tomotherapy between 1998 and 2010. Patients received radiotherapy either as primary treatment (n = 96), or after incomplete resection (n = 28) or recurrence (n = 12). The median target volume was 25.3 mL (range, 4.8 to 96.2 mL). 39 patients were treated with a single isocenter whit simple 3D conformation in the earlier years of the study, 65 with multiple converging arcs (3-9) with a dynamic micro-multileaf collimator (leaf width at isocenter 5 mm) and 33 with SRS circular collimators. Amplitude and dose-rate modulation were used in 34 patients treated between 2001 and 2010. GTV was defined as the contrast enhancing area, CTV was considered equivalent to GTV and PTV encompassed the GTV with a 2 mm margin; when a dural tail was present, no systematic attempt to include it in the PTV was done. MRI followed by image co-registration and fusion with CT was used for planning in 81 patients while CT only was used in 55. The mean radiation dose in fractionated RT was 54 Gy/30 fractions (1.8 Gy/1 fraction), in SRS was 15 Gy at isocenter. Evaluation of treatment plans was done using indexes of target coverage, dose conformality and homogeneity and outcome measurements. Follow-up examinations, including magnetic resonance imaging, were performed at 6 month intervals for the first 3 years and yearly thereafter. Median follow-up was 72 months (range 14-136).

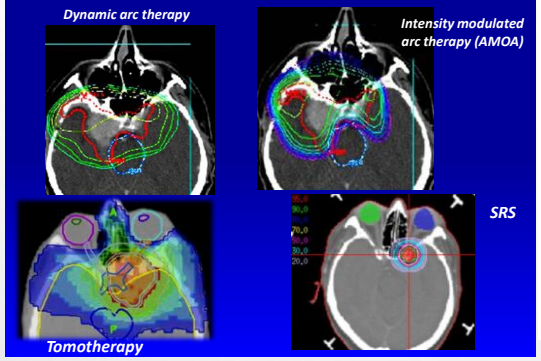
Rationale for RT in meningiomas of the skull base

- Unsatisfactory control rates with surgery (44% - 90%)
- High surgical risk (54 –60%) of neurologic morbidity
- High recurrence rate after surgery
- Risk of histological dedifferentiation

Meningiomas of the skull base



Effects of arc modulation on dose distribution



Results

- *Median follow-up months: range 14-136*
- *Improved symptoms: 65.7%*
- *Unchanged symptoms: 28.9%*
- *Worsened symptoms: 1.5%*
- *New symptoms: 0%*
- *Tumour shrinkage: 16.9%*
- *Unchanged volume: 80.8%*
- *Increased volume: 2.2%*
- *Cerebral oedema: 0%*
- *5 years survival: 100%*
- *5 years DFS: 98.5%*

Results

Patients treated with modulated techniques had better target coverage and conformality with slightly higher target dose heterogeneity; doses to optic nerve, chiasm, and brain stem were lower and NTCPs were better with arc modulation. Pre-existing neurologic symptoms were present in 38 patients, were improved in 25 (65.7%), remained unchanged in 11 (28.9%) and worsened in 2; no patient developed new symptoms. Tumour shrinkage was observed in 23 patients (16.9%) while volume remained unchanged in 110 (80.8%) and increased in 3 (2.2%). Overall survival at 5 years was 98.5% and progression-free survival was 96.3%. No patient developed treatment-related oedema or other toxicities.

Conclusions

3D-CRT, SRS, fSRT (IMAT) and tomotherapy are a safe and effective treatment for meningiomas. Particularly arc modulation and tomotherapy increases conformality and reduces the dose to critical structures in the base of skull meningiomas.