

UNIVERSITY OF
BIRMINGHAM

 INSTITUTE OF
CANCER AND
GENOMIC SCIENCES



Advances in Neurosurgery

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University Hospitals
Birmingham 
NHS Foundation Trust

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Glioma: A Case of Unmet Need

- 250 000 malignant annually
- 77% are
- 40%-50% will have surgery - craniotomy
- 10% will have a biopsy
- 30-40 % will have no treatment - as factors such as multifocal disease or poor PS



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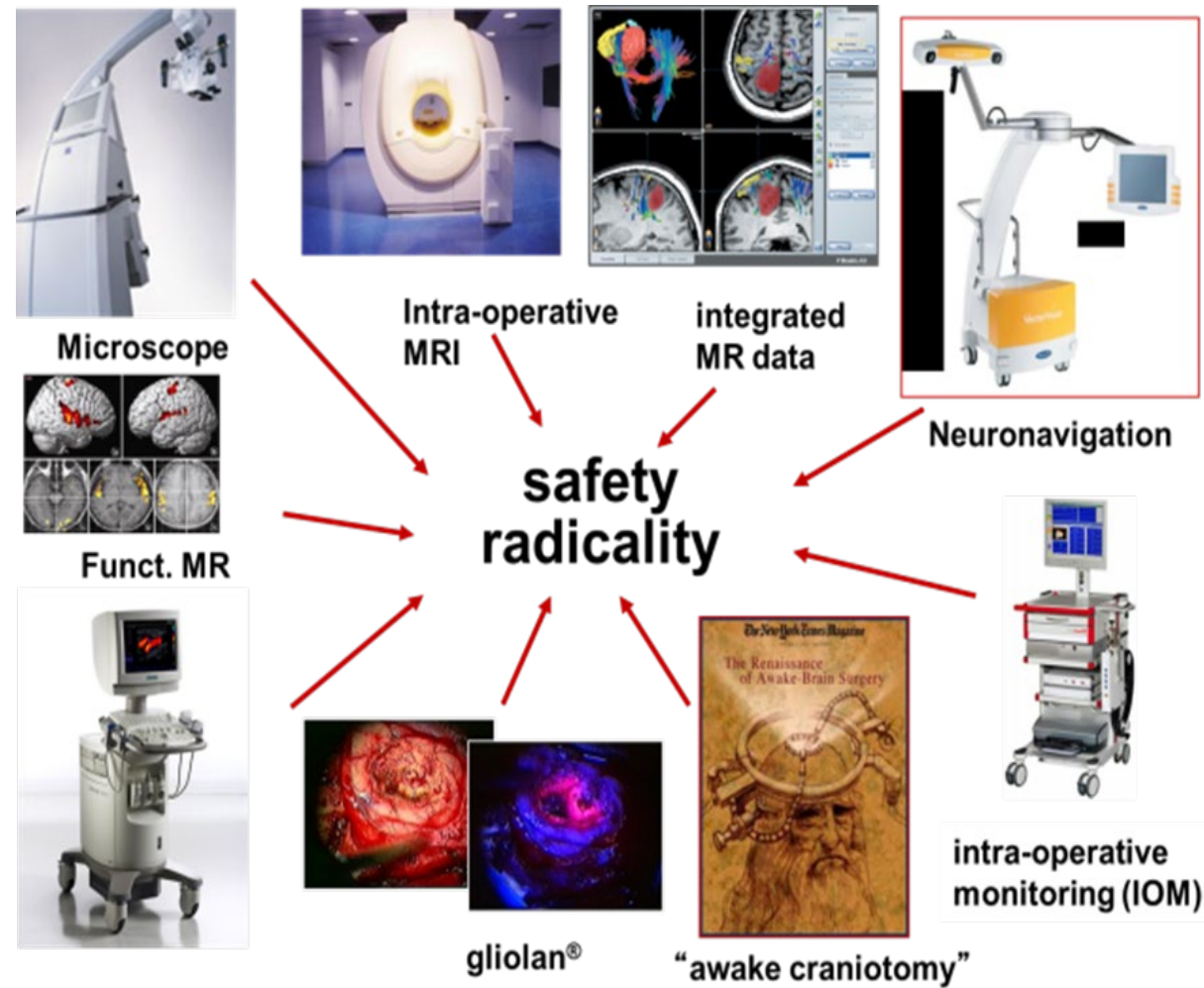
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Optimising resection is not
always the same as maximizing
resection

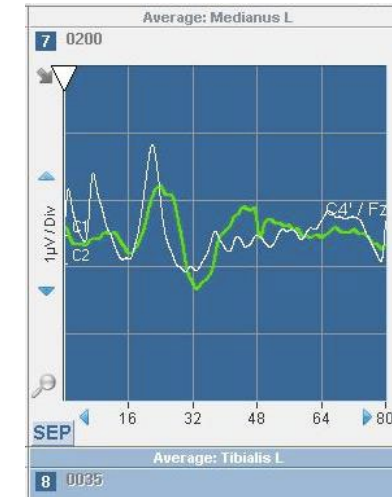
But more is generally better

Optimising resection of glioma requires a multimodal approach

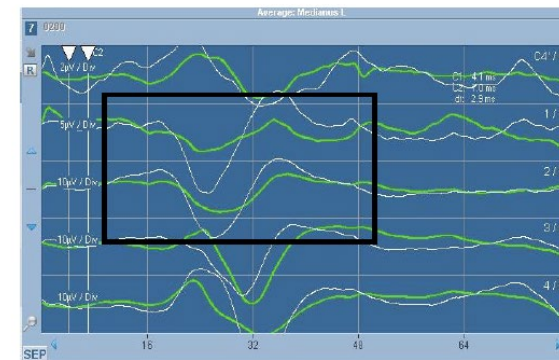


Individualised Surgical Strategy through a multimodal approach

- Precise determination of tumour margin
- Identification of eloquent brain
 - Neuronavigation
 - Awake surgery
 - Intra-operative monitoring
 - 5-ALA surgery
 - IO MRI
 - IO U/S



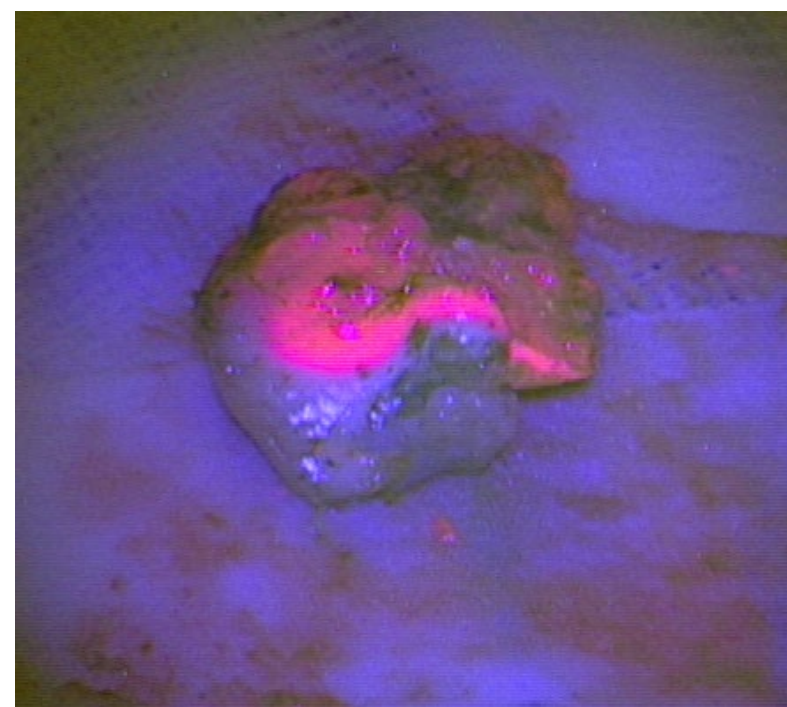
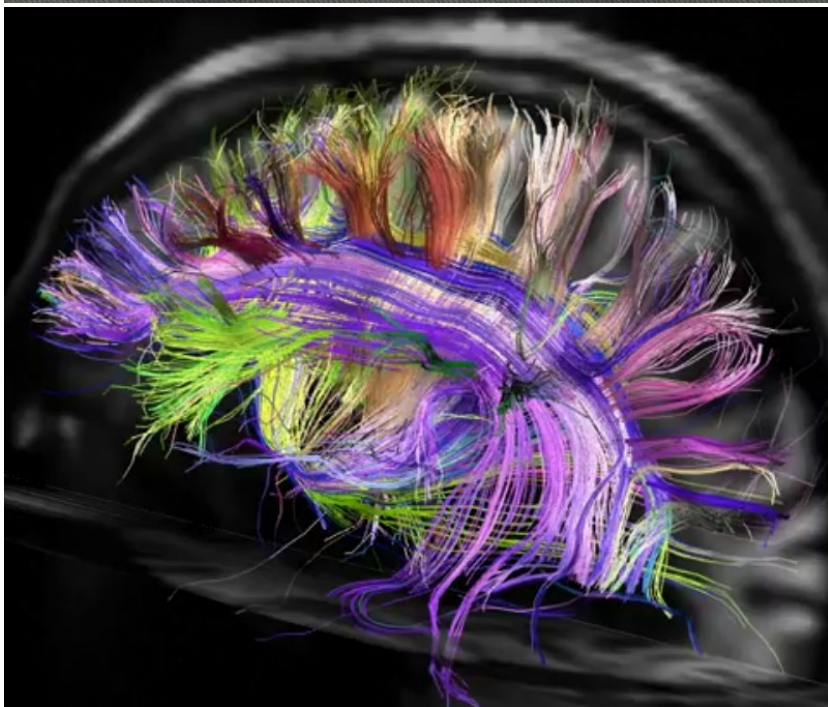
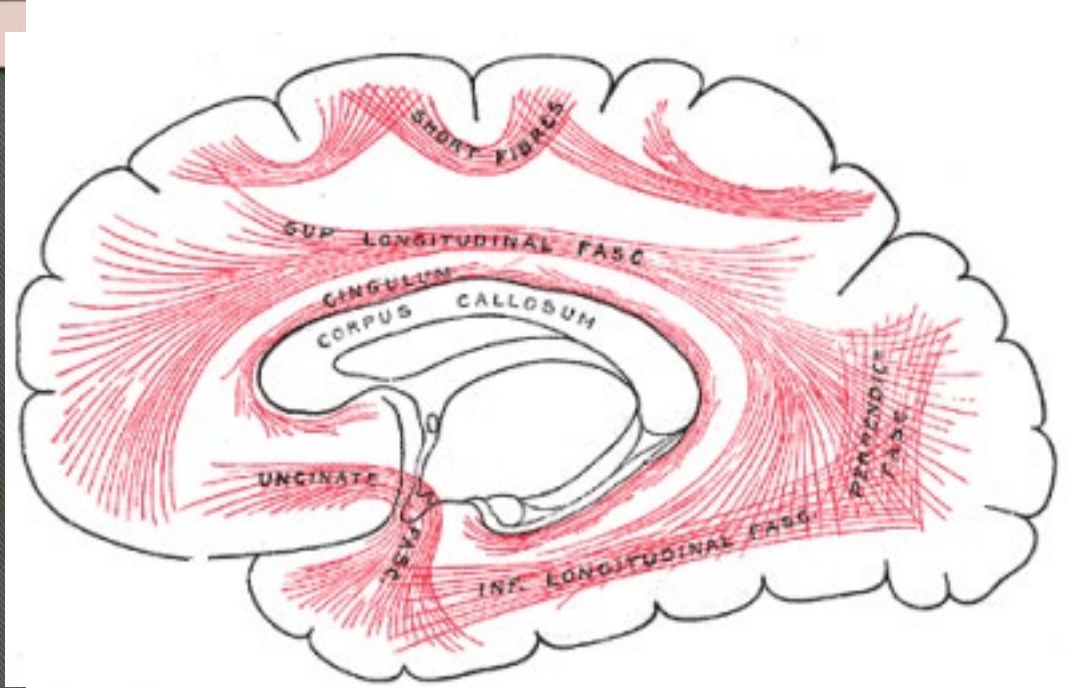
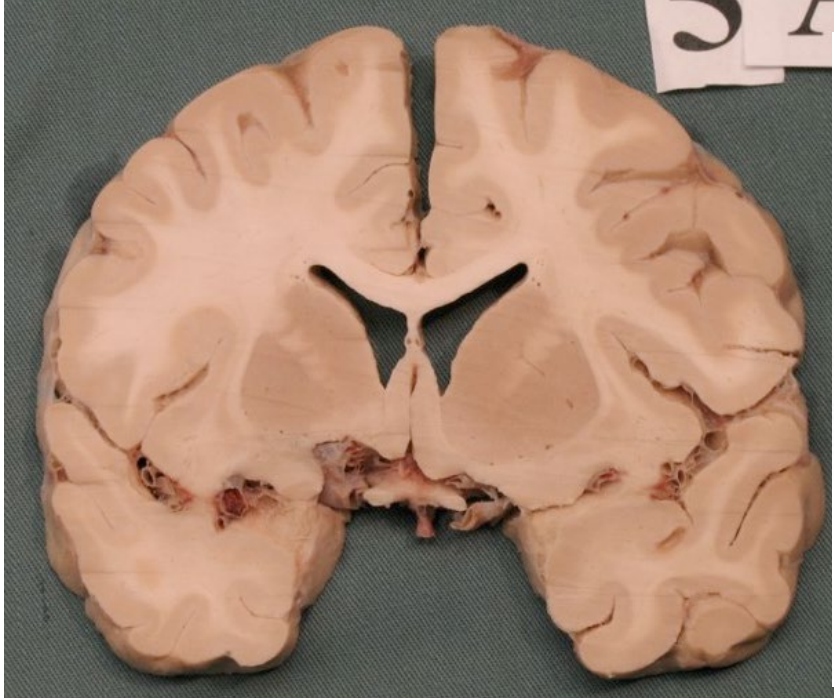
SSEP PHASE REVERSAL

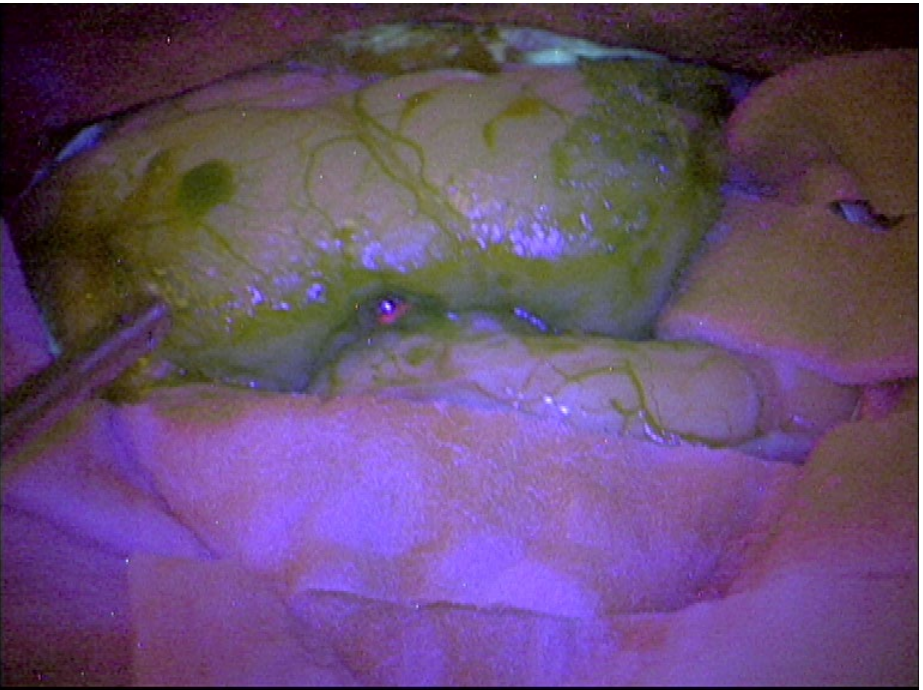
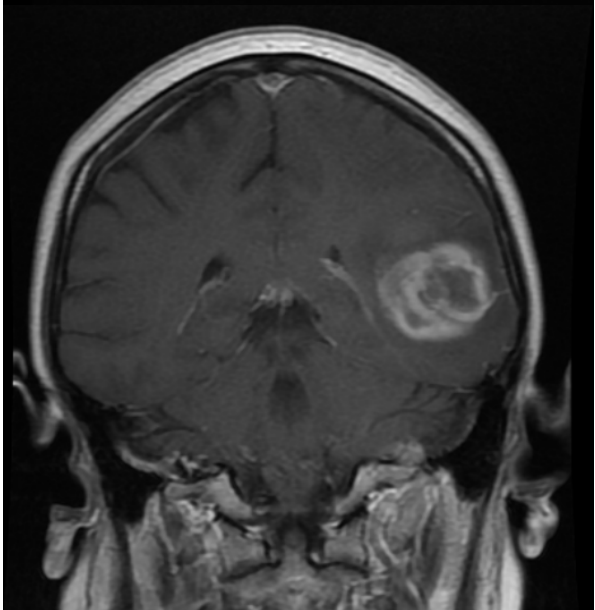
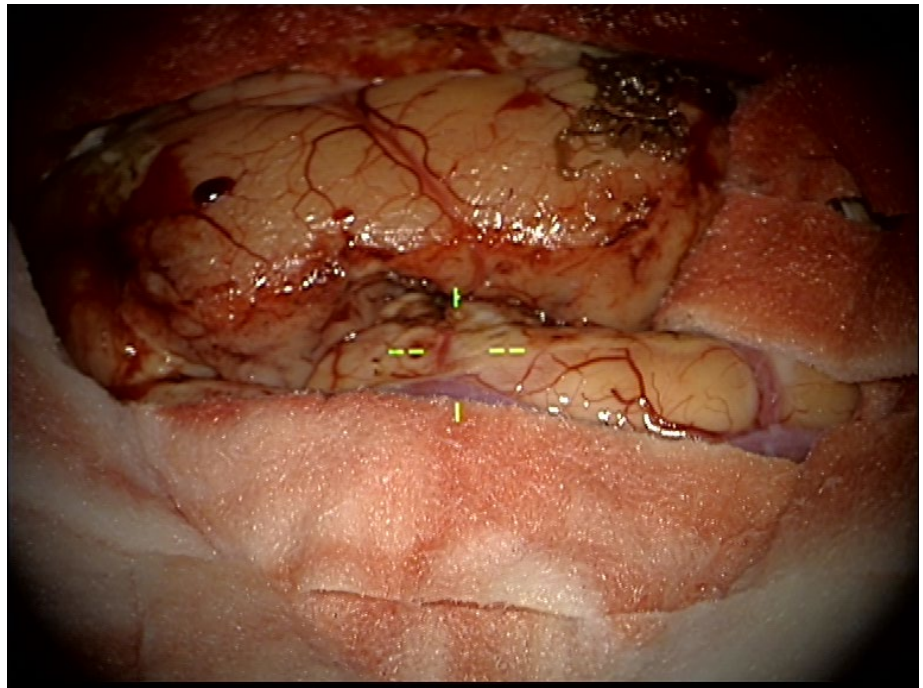
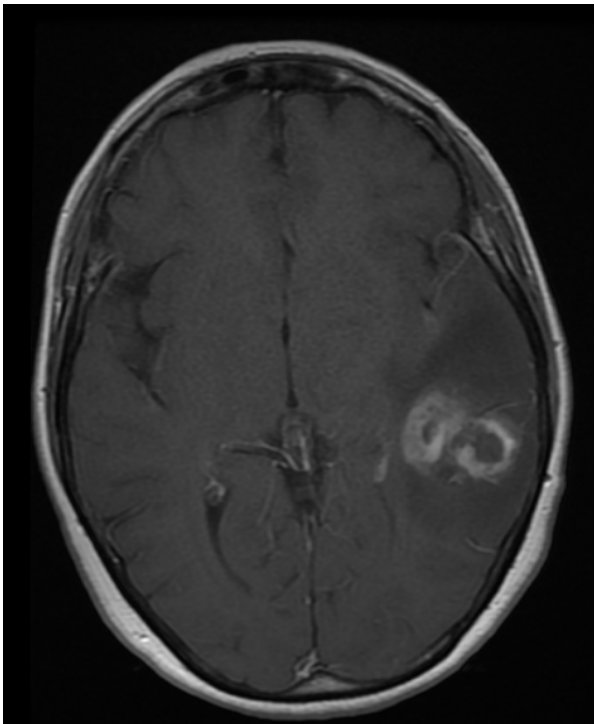


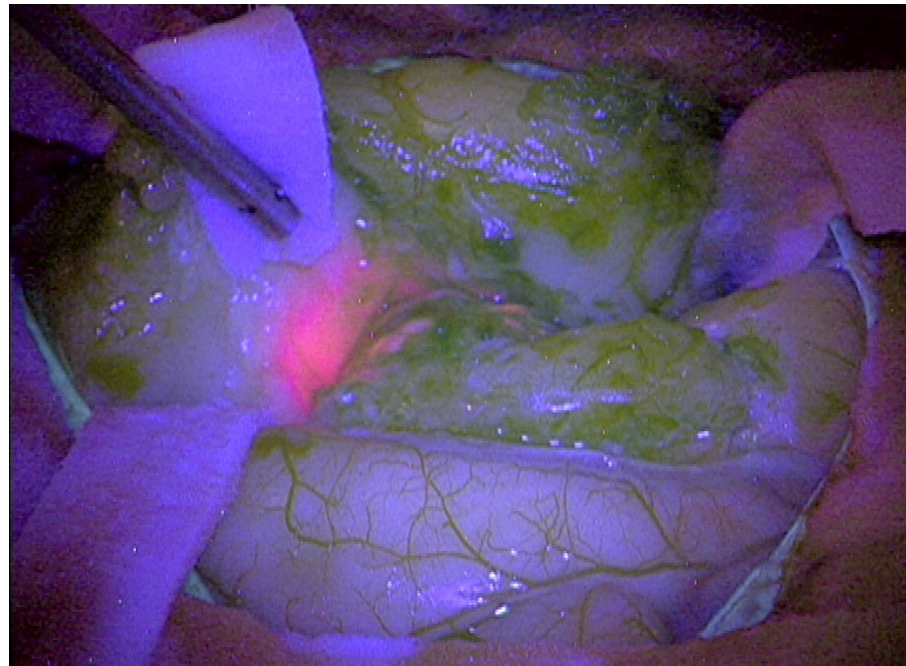
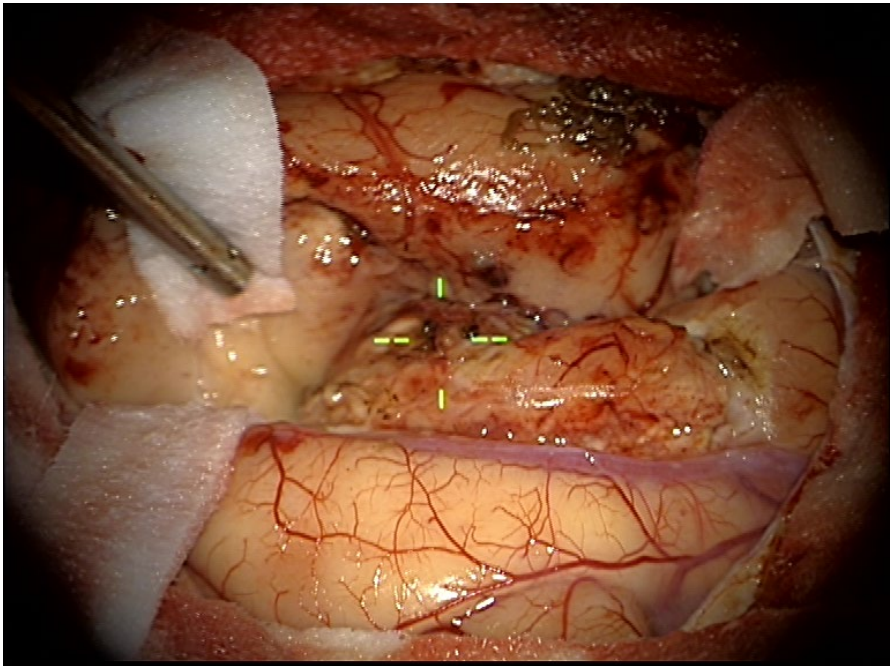
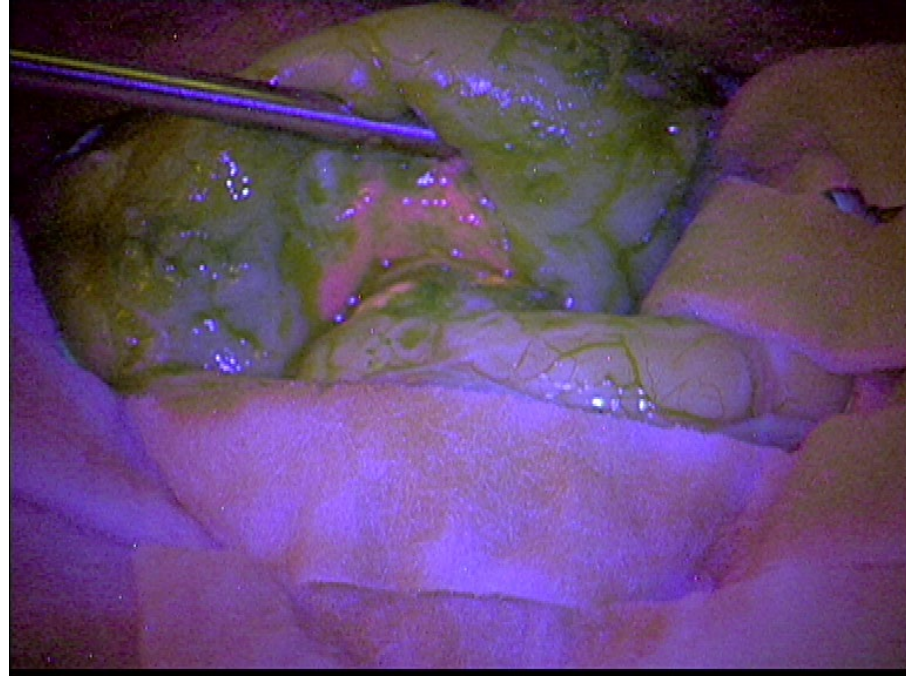
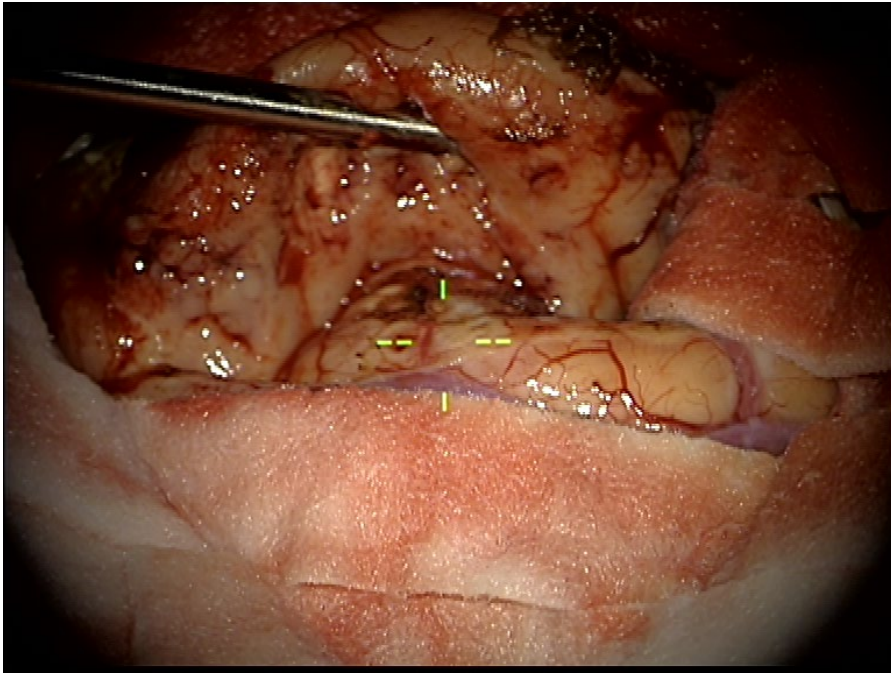
Scalp SEP:
N20 waveform

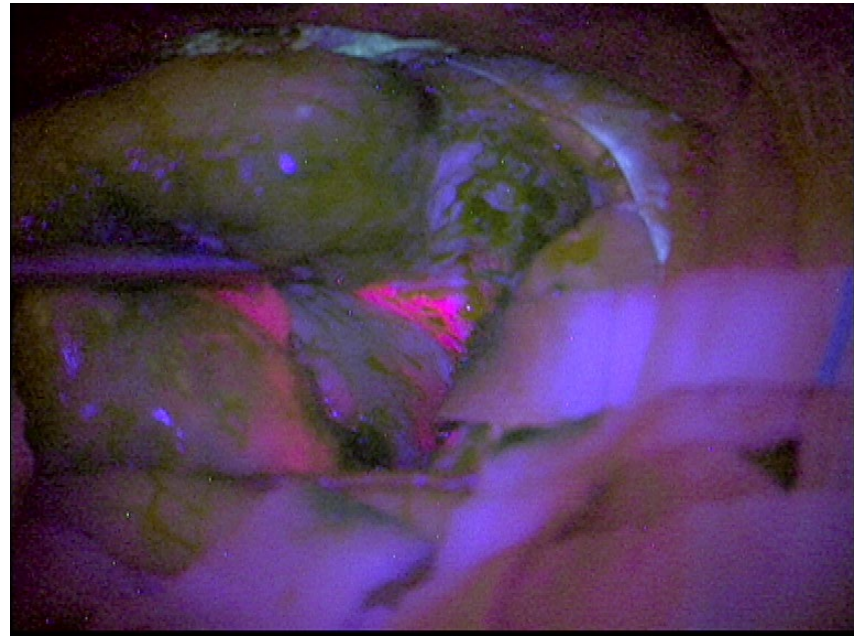
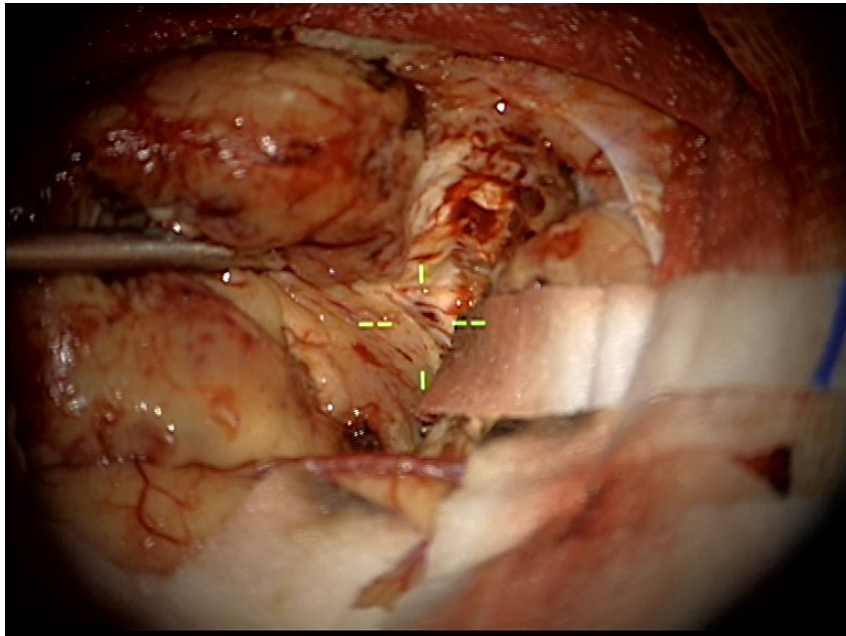
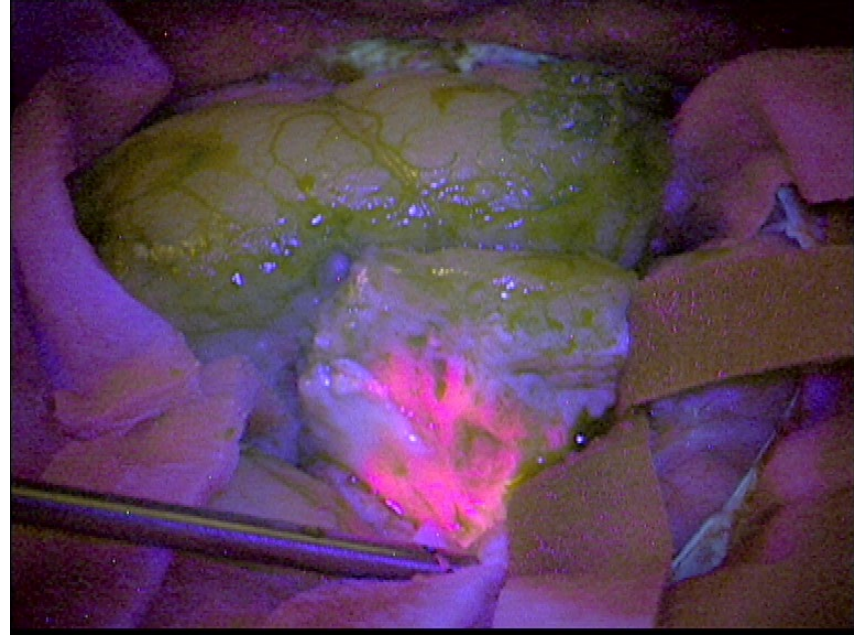
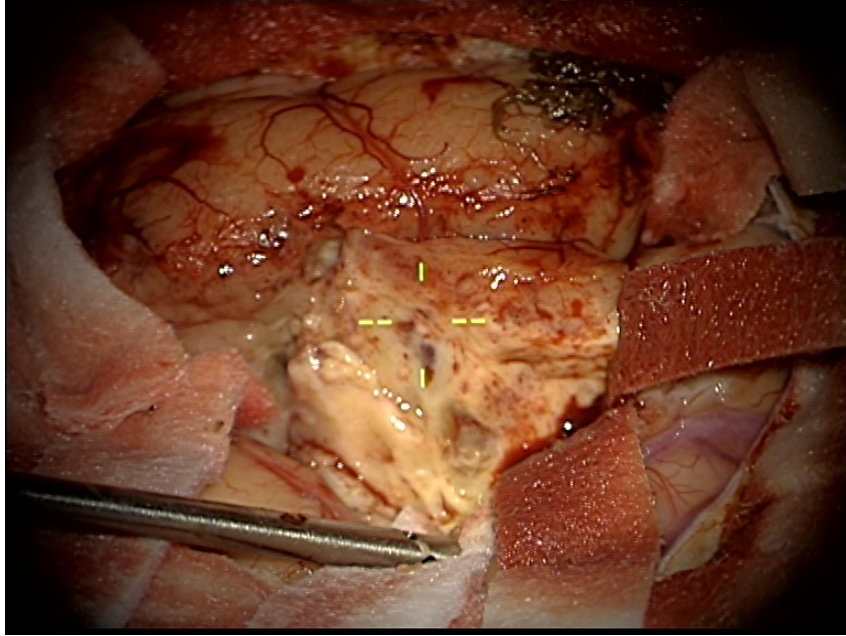
Contact 1, 2:
P20 waveforms
Motor strip

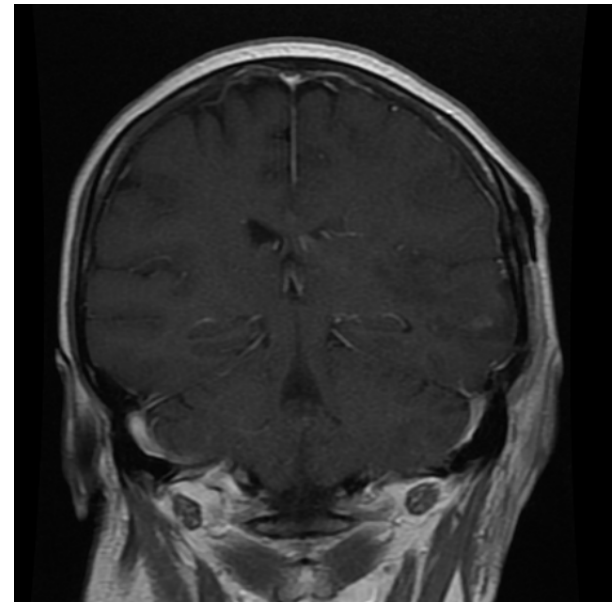
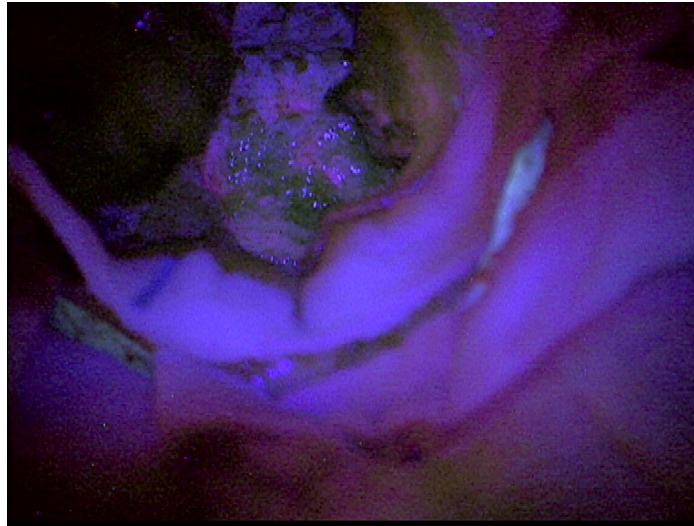
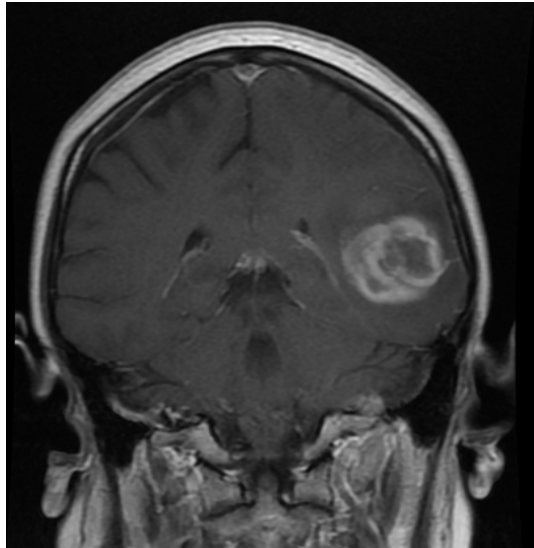
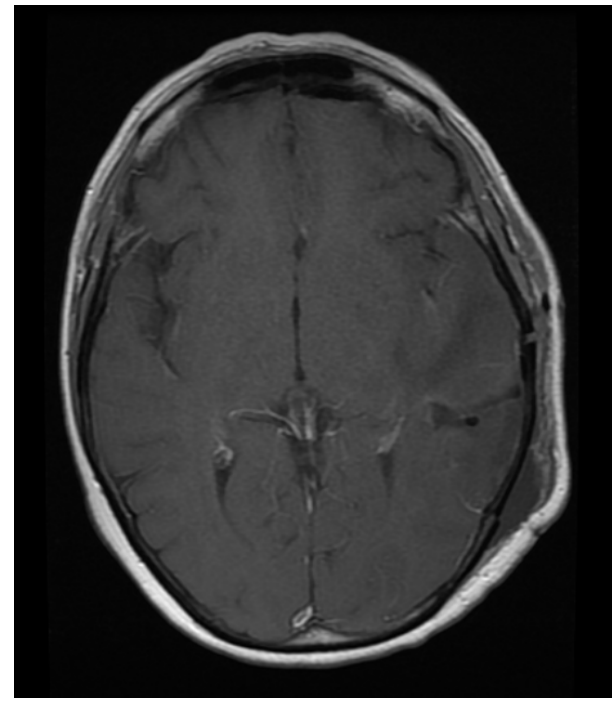
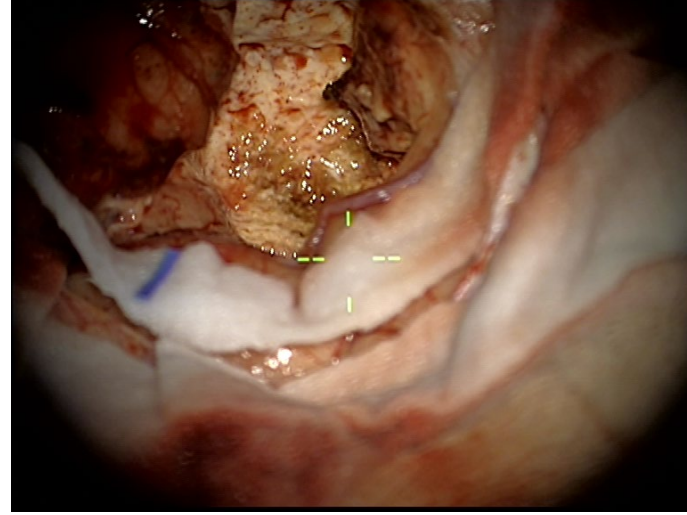
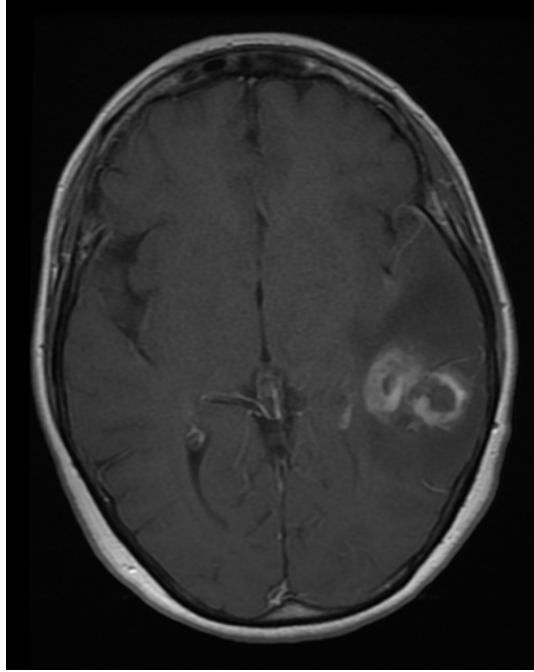
Contact 3, 4:
N20 waveforms
Sensory areas







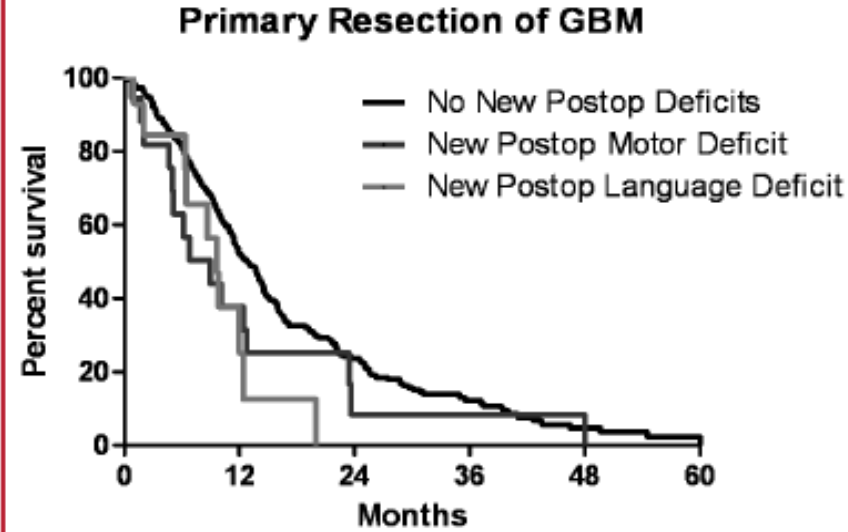




CLINICAL STUDIES

Matthew J. McGirt, M.D.

Department of Neurosurgery,
The Neuro-Oncology Surgical
Outcomes Research Laboratory,
The Johns Hopkins University
School of Medicine,
Baltimore, Maryland



ED MOTOR
L SURVIVAL
MULTIFORME

FIGURE 1. Kaplan-Meier plot demonstrating survival after resection of glioblastoma multiforme (GBM) in patients without a new postoperative (postop) neurological deficit, with a surgically acquired motor deficit, or with a surgically acquired language deficit. Patients with a new postoperative motor deficit ($P < 0.05$) or a new postoperative language deficit ($P < 0.05$) experienced decreased overall survival compared with patients without a new-onset perioperative neurological deficit.

Original Investigation

Association of the Extent of Resection With Survival in Glioblastoma

A Systematic Review and Meta-analysis

Timothy J. Brown, MD; Matthew C. Brennan, MD; Michael Li, MD, PhD; Ephraim W. Church, MD;
Nicholas J. Brandmeir, MD; Kevin L. Rakszawski, MD; Akshal S. Patel, MD; Elias B. Rizk, MD; Dima Suki, PhD;
Raymond Sawaya, MD; Michael Glantz, MD

“...but the quality of the supporting evidence is moderate to low”

3/ Studies

41117 patients

Decreased mortality for GTR compared to STR at 1 year (RR 0.63, 95% CI 0.56 - 0.69, NNT=9, $p < 0.001$)

Decreased mortality for GTR compared to STR at 2 year (RR 0.84, 95% CI 0.79-0.89, NNT=17, $p < 0.001$)

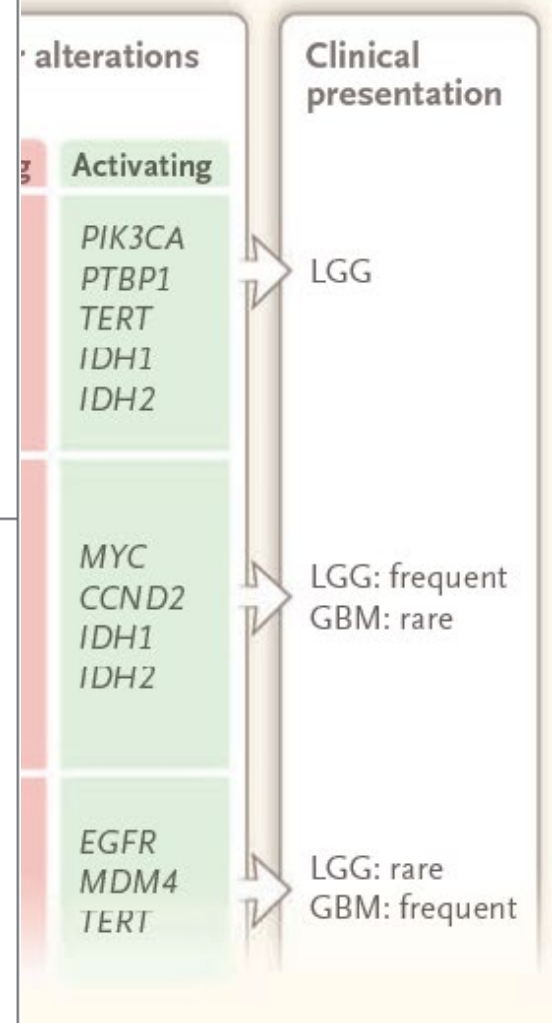
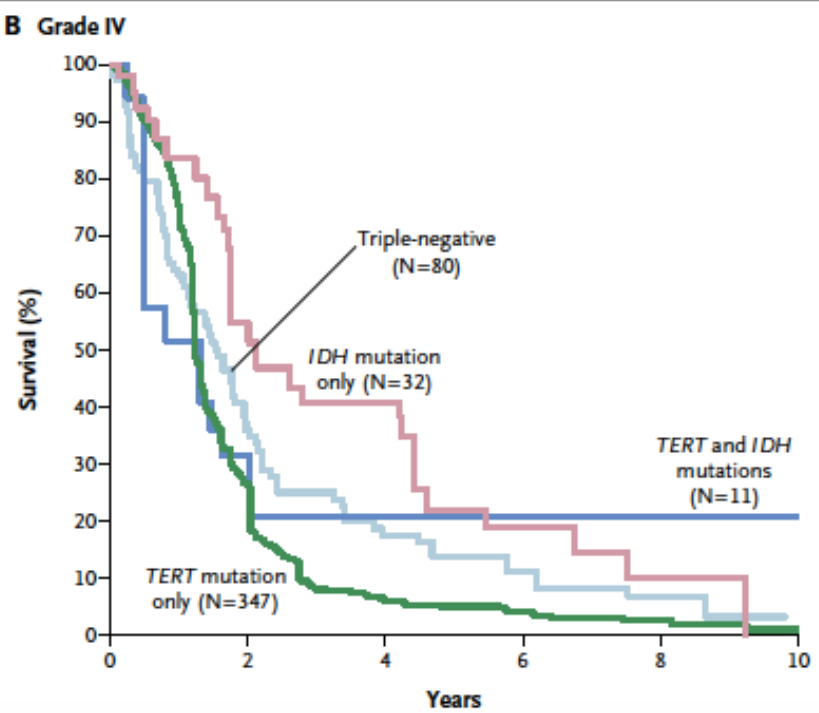
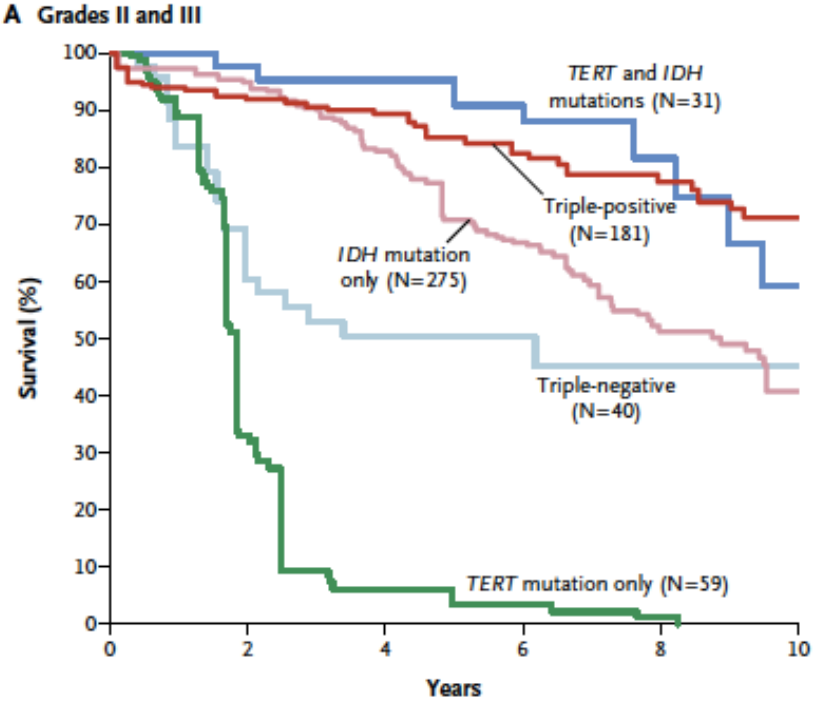
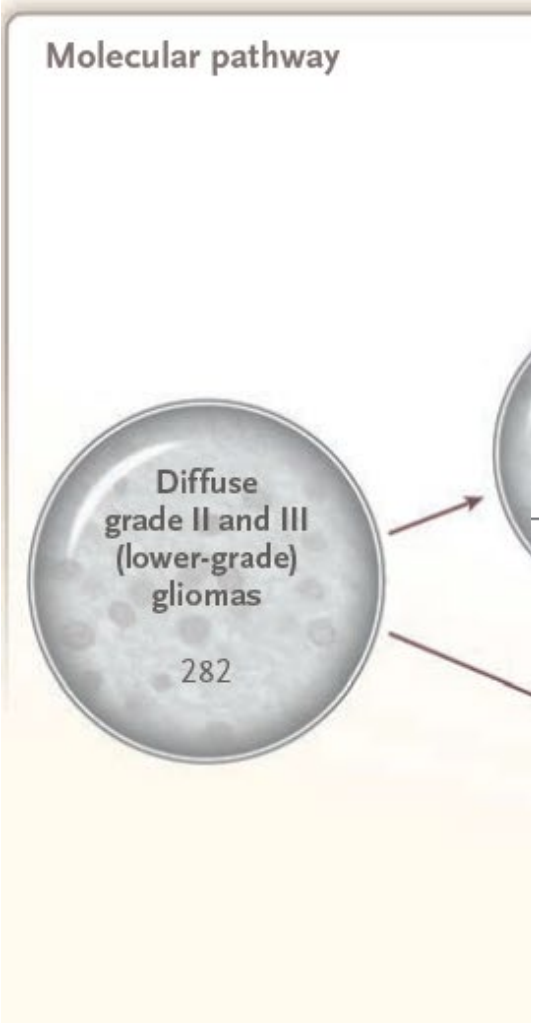
Likelihood of disease progression was decreased with GTR compared to STR at 1 year 95% CI, 0.43-0.99; $P < .001$; NNT, 26

Optimisation of the extent of resection
should be an integral part of the
multidisciplinary management of LGG

but

Surgical management must take account
of recent clinical trial data and emerging
biomarkers

Not all LGG will behave like LGG



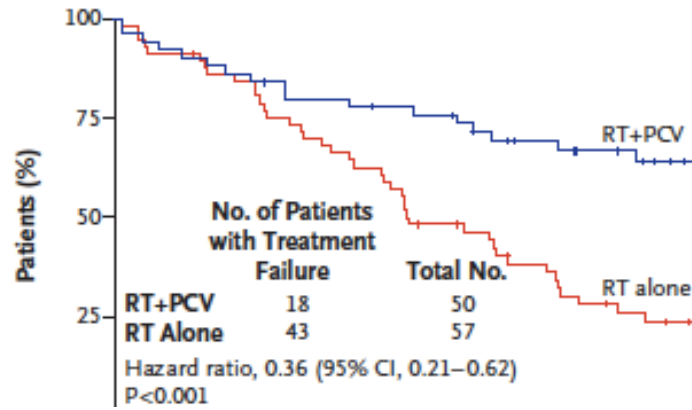
Radiation plus Procarbazine, CCNU, and Vincristine in Low-Grade Glioma

Jan C. Buckner, M.D., Edward G. Shaw, M.D., Stephanie L. Pugh, Ph.D.,
Arnab Chakravarti, M.D., Mark R. Gilbert, M.D., Geoffrey R. Barger, M.D.,
Stephen Coons, M.D., Peter Ricci, M.D., Dennis Bullard, M.D., Paul D. Brown, M.D.,
Keith Stelzer, M.D., David Brachman, M.D., John H. Suh, M.D.,
Christopher J. Schultz, M.D., Jean-Paul Bahary, M.D., Barbara J. Fisher, M.D.,
Harold Kim, M.D., Albert D. Murtha, M.D., Erica H. Bell, Ph.D.,
Minhee Won, M.A., Minesh P. Mehta, M.D., and Walter J. Curran, Jr., M.D.

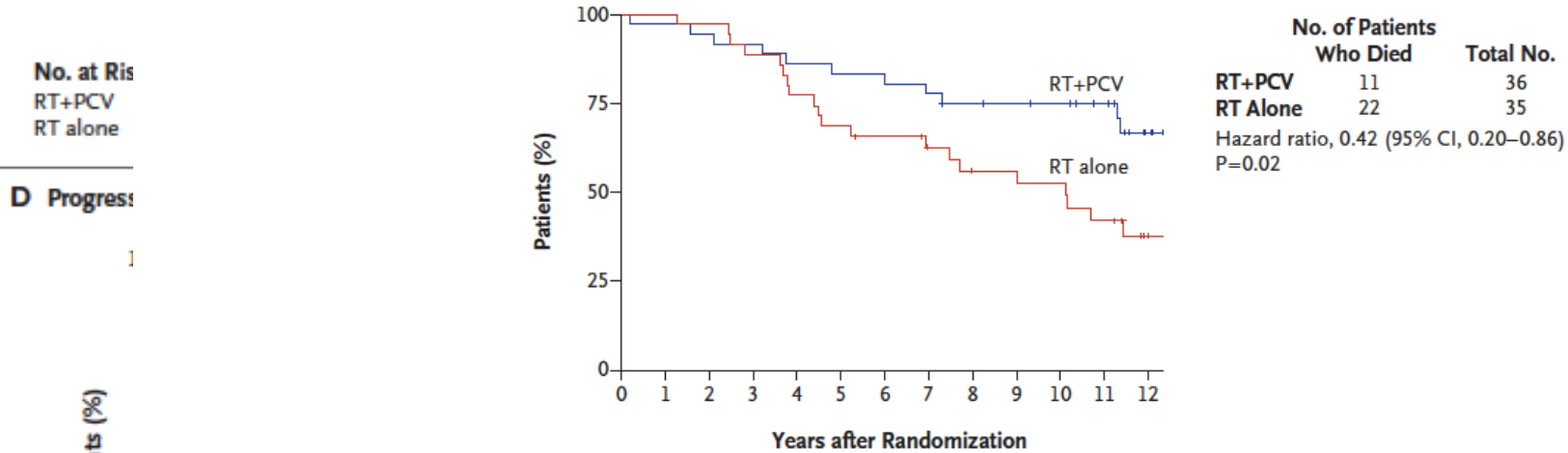
Incomplete resection

Age >40

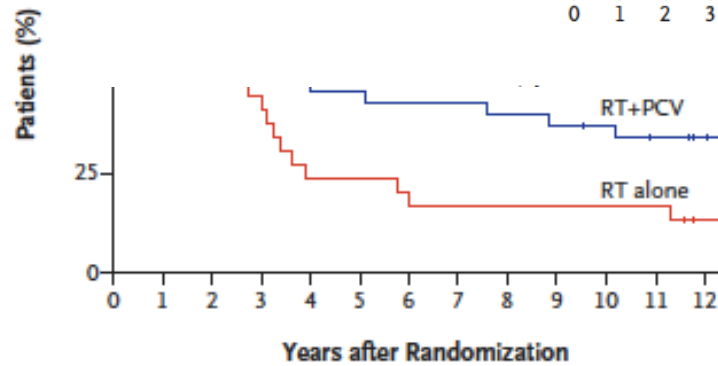
B Progression-free Survival, Grade 2 Oligodendroglioma



E Overall Survival among Patients with IDH1 R132H Mutation

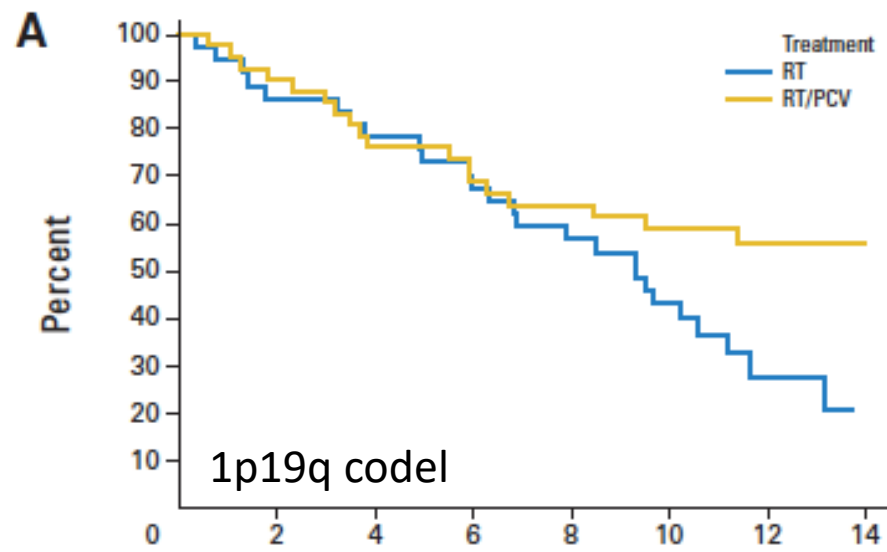


D Progression-free Survival



No. at Risk

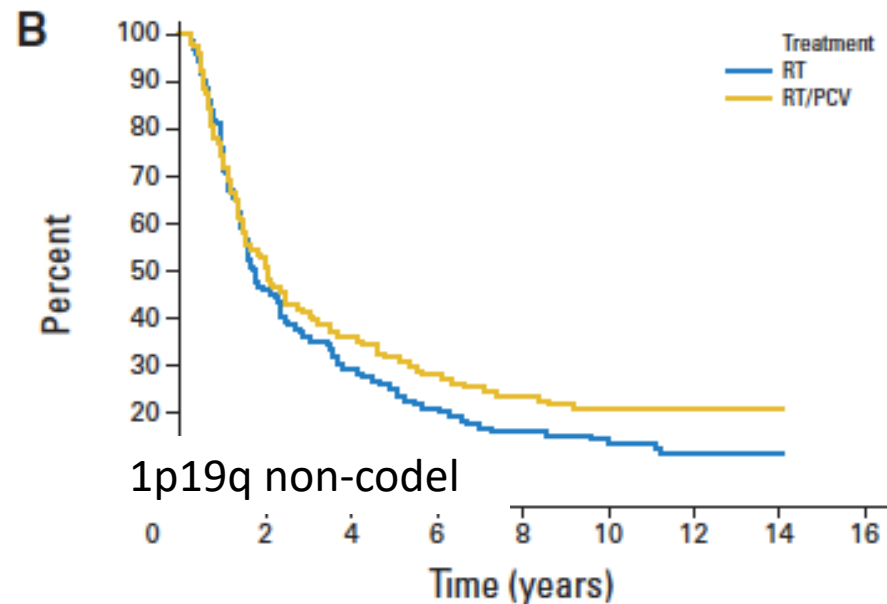
RT+PCV	36	22	20	18	17	16	15	15	14	13	12	11	8
RT alone	29	16	14	13	8	7	6	5	5	5	5	5	2



codeletion of 1p/19q was found. In these patients with codeleted tumors, OS was not reached in the RT/PCV group versus 112 months in the RT group (HR, 0.56; 95% CI, 0.31 to 1.03; Fig 3A). In the

and Vincristine
naplastic
ow-Up of EORTC

Kros, Mathilde C.M. Kouwenhoven, Wolfgang Grisold, László Sipos, Licht, Anouk Allgeier, Denis Lacombe,



No. at risk	0	N	2	4	6	8	10	12	14
RT	107	122	56	35	25	19	17	4	1
RT/PCV	90	114	60	41	31	26	22	12	1

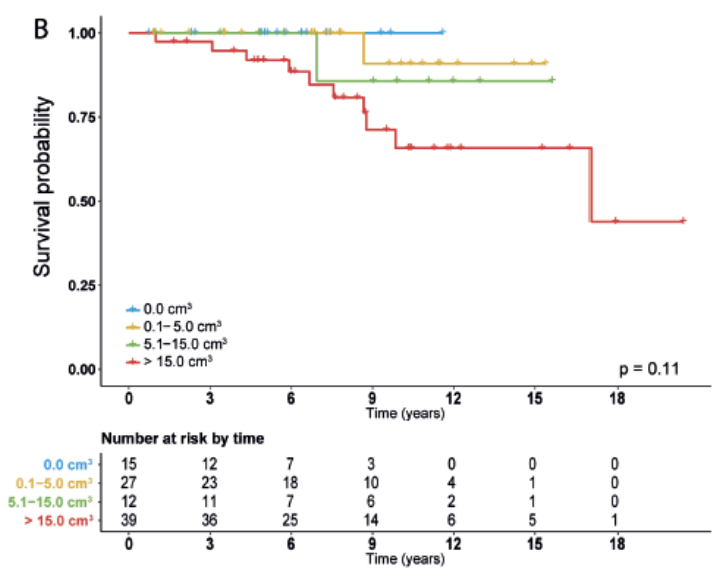
The impact of surgery in molecularly defined low-grade glioma: an integrated clinical, radiological, and molecular analysis

Maarten M. J. Wijnenga, Pim J. French, Hendrikus J. Dubbink, Winand N. M. Dinjens, Peggy N. Atmodimedjo, Johan M. Kros, Marion Smits, Renske Gahrmann, Geert-Jan Rutten, Jeroen B. Verheul, Ruth Fleischeuer, Clemens M. F. Dirven, Arnaud J. P. E. Vincent, and Martin J. van den Bent

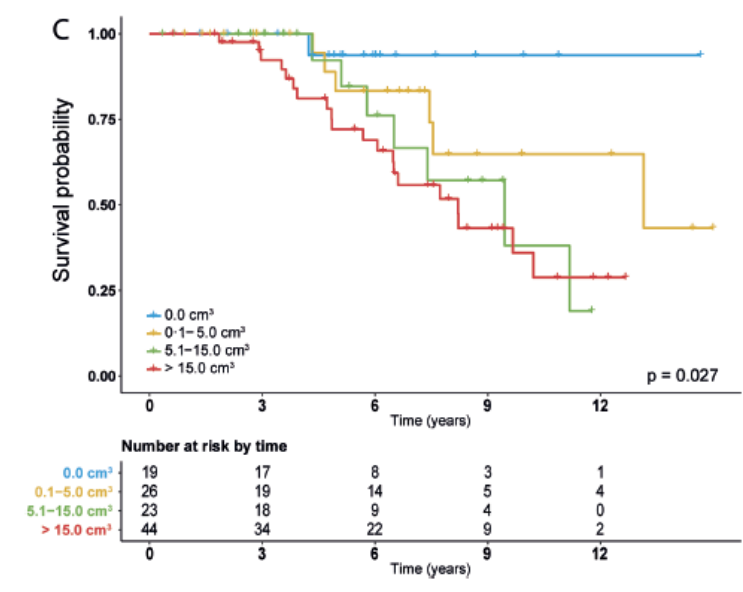
Department of Neurology, Erasmus University Medical Center (Erasmus MC) Cancer Institute, Rotterdam, the Netherlands (M.M.J.W., P.J.F., M.J.v.d.B.); Department of Pathology, Erasmus MC Cancer Institute, Rotterdam, the Netherlands (H.J.D., W.N.M.D., P.N.A., J.M.K.); Department of Radiology and Nuclear Medicine, Erasmus MC, Rotterdam, the Netherlands (M.S., R.G.); Department of Neurosurgery, St Elisabeth Hospital, Tilburg, the Netherlands (G.J.R., J.B.V.); Department of Pathology, St Elisabeth Hospital, Tilburg, the Netherlands (R.F.); Department of Neurosurgery, Erasmus MC Cancer Institute, Rotterdam, the Netherlands (C.M.F.D., A.J.P.E.V.)

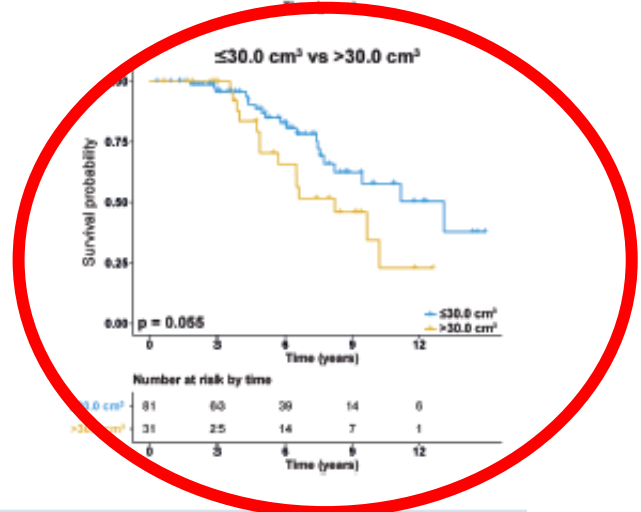
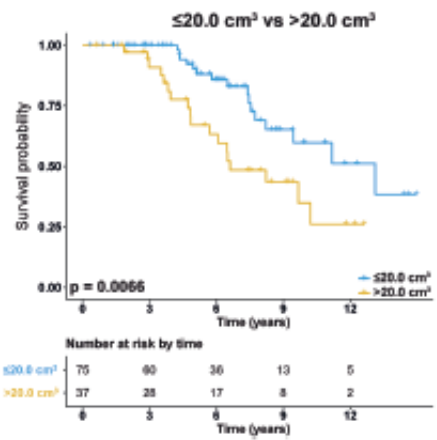
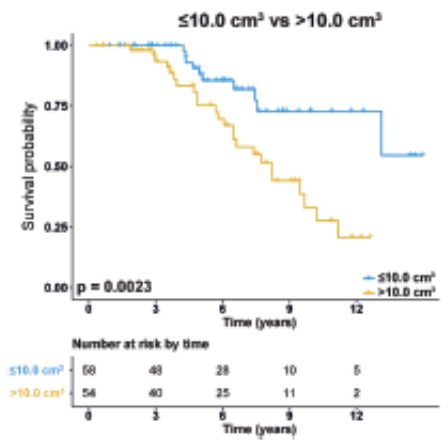
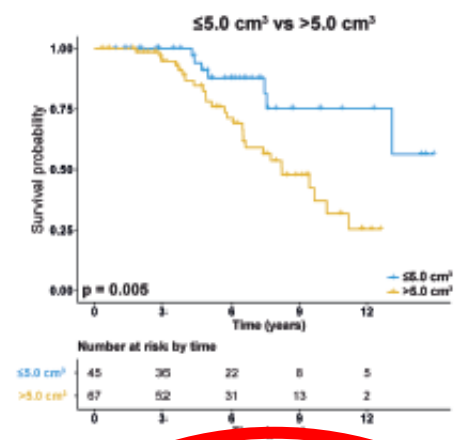
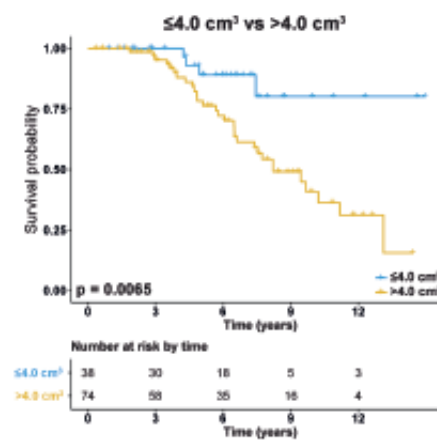
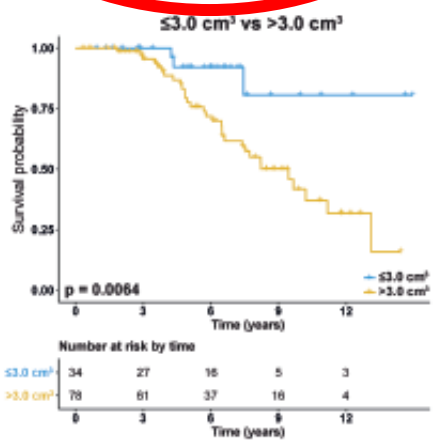
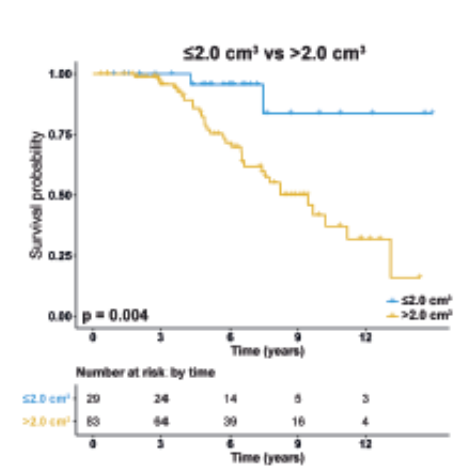
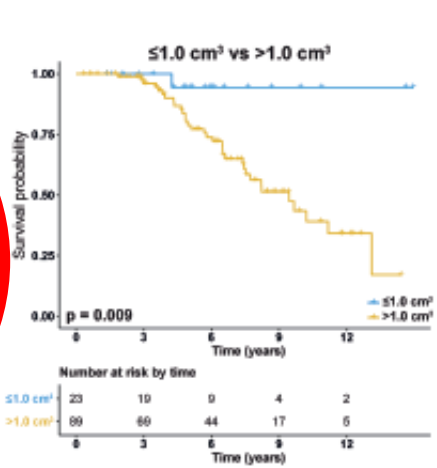
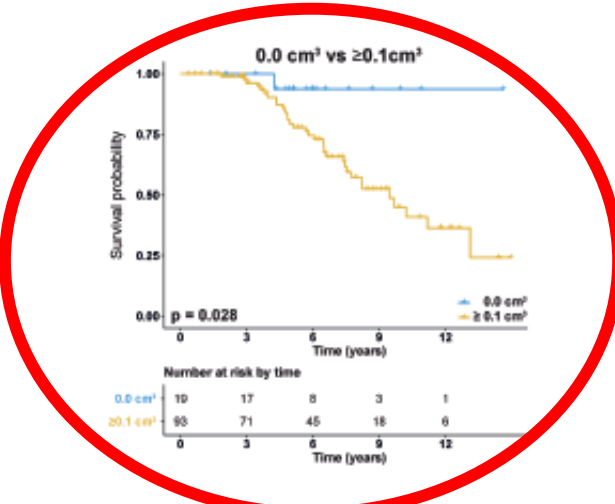
Corresponding Author: Martin J. van den Bent, Department of Neurology, Erasmus MC Cancer Institute, PO Box 5201, 3008AE Rotterdam, The Netherlands (m.vandenbent@erasmusmc.nl).

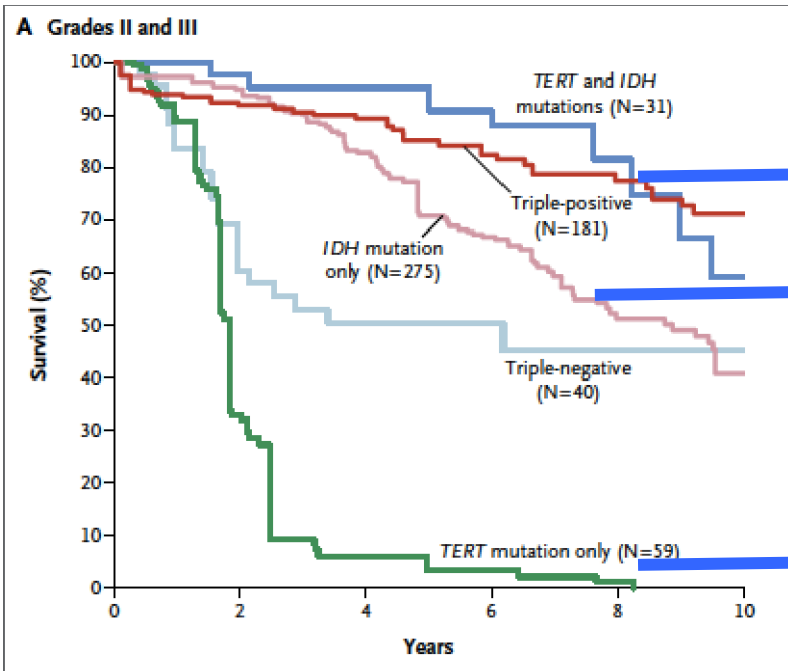
IDH^{mut} 1p19q codel



IDH^{mut} 1p19q intact





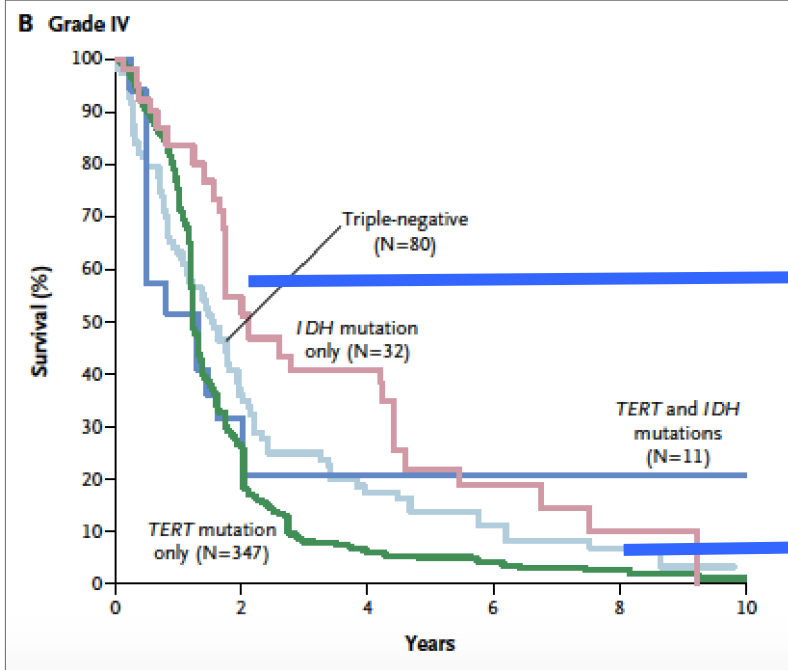


Oligos

IDH^m 90%

Astros

1° GBM?

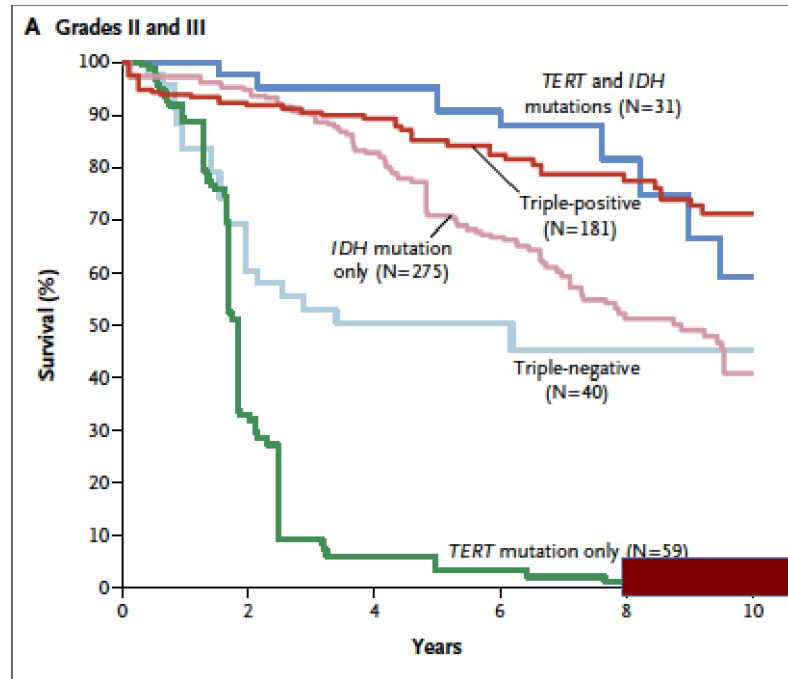


2° GBM

IDH^m 10%

1° GBM

Tailoring surgery to individual patients



De-escalate surgical aggression?

Maximal safe resection

Aim for GTR

So subtotal resection can matter

- For IDH^{mut} astrocytoma aim for maximal resection
- Consider early re-operation for residual disease
- Any cyto-reduction could be of benefit

- For IDH^{mut} oligodendroglioma aim for maximal resection
- Use RT + Chemo for residual disease
- Consider observation if GTR on FLAIR

The surgical issues around resection in glioma surgery are changing

- Should we be more aggressive if we know the patient has poor prognosis disease?
- Should we be more aggressive if we know the patient has good prognosis disease?
- Should surgical management become a 2-stage process?
- Should we consider neo-adjuvant chemotherapy?

Patients want quality not quantity
of survival

Thank you