

**Original article** **The impact of modern neurosurgical approaches and extent of resection on patient outcome**

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**SUMMARY:** Despite advances in preoperative imaging, intraoperative techniques, and postoperative care, it remains unclear whether greater glioma resection affects patient survival. Although the available evidence supports the utility of surgery for diagnosis and decompression, there is controversy as to whether a greater extent of resection can influence outcome. We have reviewed every major clinical publication since 1990 that comments on the role of greater resection in changing survival. This review of the modern neurosurgical literature has identified 37 manuscripts in total. These studies were evaluated in terms of design, statistics, and raw data. Overall, their cumulative findings underscore the value of a greater extent of resection, which is not only associated with improved survival, but also may delay the malignant transformation of low grade tumors. Although we still lack incontrovertible evidence in favour of extent of resection, the entire body of literature in the modern neurosurgery still supports its survival benefit for glioma patients.

**KEY WORDS:** Glioma, Modern neurosurgery, Outcome, Resection extent.

 **L'impatto dei moderni approcci neurochirurgici e dell'estensione della resezione chirurgica sulla sopravvivenza del paziente**

**RIASSUNTO:** Nonostante i miglioramenti dell'imaging preoperatorio, delle tecniche intraoperatorie e dell'assistenza postoperatoria, rimane non chiaro se una maggiore resezione del glioma possa migliorare le prospettive di vita del paziente. Malgrado l'evidenza scientifica sostenga l'utilità della chirurgia per la diagnosi e la decompressione, è ancora controverso se resezioni più ampie possono influenzare l'outcome. Abbiamo eseguito una revisione di tutta la maggiore letteratura clinica pubblicata a partire dal 1990 che valuta il ruolo di una maggiore resezione sulle prospettive di sopravvivenza. Questa revisione della letteratura della moderna neurochirurgia ha evidenziato in tutto 37 pubblicazioni, che sono state valutate in termini di progettazione dello studio, qualità dei dati statistici e dei dati grezzi. In generale, i risultati sottolineano l'importanza di una maggiore estensione della resezione, che non solo è associata ad un livello di sopravvivenza più elevato, ma anche alla possibilità di ritardare la trasformazione maligna di tumori di basso grado. Anche se ancora oggi mancano dati certi sull'efficacia dell'estensione della resezione chirurgica, tutta la letteratura della moderna neurochirurgia sostiene l'efficacia di questa tecnica chirurgica nel migliorare le prospettive di vita dei pazienti affetti da glioma.

**PAROLE CHIAVE:** Glioma, Neurochirurgia moderna, Esito, Estensione della resezione.

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## □ INTRODUCTION

Central nervous system tumors are a major cause of morbidity and mortality with approximately 18,000 new cases of primary intracranial tumors diagnosed each year in the United States. This represents approximately 2% of all adult tumors in this country. More than half of these are high grade gliomas. These lesions are extremely aggressive and the vast majority of patients invariably have tumor recurrence, with the median survival time ranging from 1 to 3 years after initial diagnosis. Despite facing a better prognosis when compared to higher grade glial tumors, 50 to 75% of patients harboring low grade gliomas eventually die of their disease. Median survival times have been reported to range between 5 years and 10 years, and estimates of 10-year survival rates range from 5 to 50%.

Controversy persists regarding prognostic factors and treatment options for both low and high grade hemispheric gliomas. Among the various tumor- and treatment-related parameters, including tumor volume, neurological status, timing of surgical intervention, and the use of adjuvant therapy, only age and tumor histology have been identified as reliable predictors of patient prognosis. Importantly, despite significant advances in operative technology and preoperative planning, the effect of glioma extent of resection in prolonging tumor-free progression and/or survival remains unknown.

While the importance of glioma resection in obtaining tissue diagnosis and decompressing mass effect are unquestionable, a lack of class I evidence prevents similar certainty in assessing the influence of extent of resection. Although low grade and high grade gliomas are distinct in their biologies, clinical behaviors, and outcomes, understanding the effect of surgery remains equally important for both. With this in mind, we have examined every major clinical publication since 1990 that reports on the role of extent of resection in affecting outcome in glioma patients.

## □ CLINICAL MATERIAL AND METHODS

A literature search of the PubMed database from January 1990 to September 2006 was conducted using the following key words: "high grade glioma", "low grade glioma", "astrocytoma", "anaplastic astrocytoma", "oligodendrogloma", "oligoastrocytoma", and "glioblastoma".

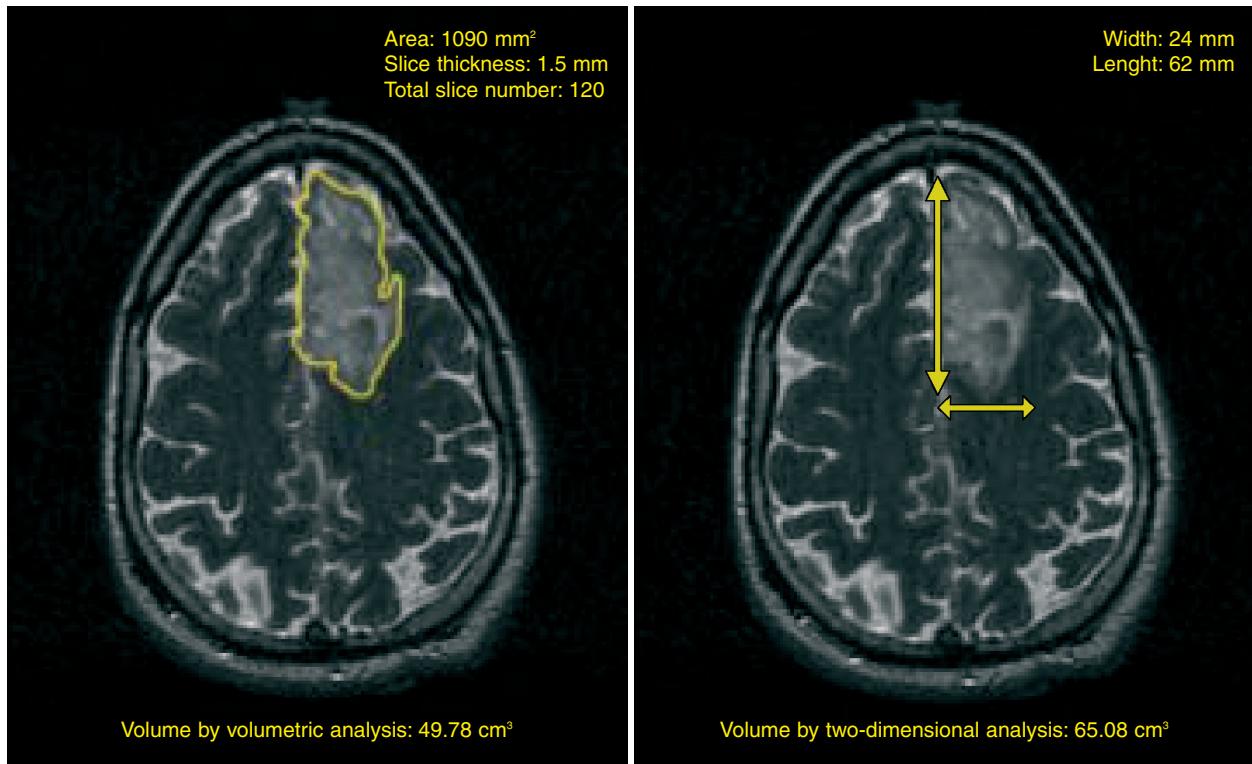
Series including adult patients with hemispheric gliomas were identified. Reports written in languages other than English and studies in which researchers mainly focused on non-hemispheric gliomas were excluded, as were paediatric series. Before analyzing the resultant studies in detail, we conducted additional screening. Because children with hemispheric gliomas can have distinct clinical courses from adults, we excluded series that had both adult and paediatric patients if the adult patients had not been analyzed separately. Similarly, studies including pilocytic and gemistocytic astrocytomas, in which data regarding patients with these tumor histologies could not be separated from other low grade gliomas, were also eliminated. Series with small numbers of patients (< 75) or small numbers of events (i.e.: deaths for survival studies) were also excluded from analysis. Based upon these criteria, we found 27 studies examining extent of resection for high grade gliomas and 19 studies examining extent of resection for low grade gliomas. For these remaining studies, we considered the statistical issues that affected interpretation of data. These covered both possible methodological flaws and information that was omitted from the paper. The methodological aspects we evaluated included choice of statistical tests and adjustment of confounding variables.

The specific information that we searched for consisted of discussion of possible sources of bias in selection of cases, number of events (deaths), length of follow up for patients without events (i.e.: survivors), hazard ratios, and confidence intervals.

We also looked for a specific statement of how the multivariate analysis, if any, was conducted. Of particular interest was whether a stepwise forward or backward method was used and which variables were considered for inclusion. Because none of these studies were randomized trials, we looked for an indication of how many patients were in each of the subsets, because that affects the statistical power required to detect any differences.

We also looked for information on the extent to which possible predictors were confounded. As an extreme example, it would be possible that all patients in whom a subtotal resection was achieved underwent radiation therapy and that none of those in whom a total resection was achieved underwent radiation therapy. Clearly, this would have an impact on the interpretation of the data, although it could be difficult to discern from a review of the paper.

Preoperative and postoperative tumor volumes, from



**Figure 1.** Volumetric *versus* two-dimensional postoperative magnetic resonance imaging analysis.

which the extent of resection is calculated, have been considered as possible prognostic factors. We therefore identified references, including those with end points other than overall survival, to find studies that included evaluations of the effects of preoperative and residual tumor volumes on outcome. Studies using volumetric tumor analysis were evaluated separately, as this method can dramatically affect extent of resection calculations (Figure 1).

## □ RESULTS

■ **NON-VOLUMETRIC AND VOLUMETRIC LOW GRADE GLIOMA EXTENT OF RESECTION STUDIES.** Nineteen studies<sup>(2,5,11,13,14,20,22-24,26-28,33,35-37,43,45,46)</sup> since 1990 have applied statistical analysis to examine the efficacy of extent of resection in improving survival and delaying tumor progression among low grade glioma patients (Table 1).

Prognostic effect	Authors and year		
	1990-1995	1996-2000	2000-2006
Statistics favor more extensive resections	North <i>et al.</i> , 1990 <sup>(28)</sup> Philippon <i>et al.</i> , 1993 <sup>(28)</sup> Ito <i>et al.</i> , 1994 <sup>(11)</sup> Rajan <i>et al.</i> , 1994 <sup>(33)</sup> Nicolato <i>et al.</i> , 1995 <sup>(24)</sup>	Karim <i>et al.</i> , 1996 <sup>(14)</sup> (volumetric) Scerrati <i>et al.</i> , 1996 <sup>(35)</sup> Leighton <i>et al.</i> , 1997 <sup>(20)</sup> Lote <i>et al.</i> , 1997 <sup>(22)</sup> Peraud <i>et al.</i> , 1998 <sup>(27)</sup> van Veelen <i>et al.</i> , 1998 <sup>(43)</sup> (volumetric)	Nakamura <i>et al.</i> , 2000 <sup>(23)</sup> Shaw <i>et al.</i> , 2002 <sup>(36)</sup> Claus <i>et al.</i> , 2005 <sup>(5)</sup> (volumetric) Yeh <i>et al.</i> , 2005 <sup>(46)</sup>
Statistics do not favor any resection group	Whitton <i>et al.</i> , 1990 <sup>(45)</sup> Shibamoto <i>et al.</i> , 1993 <sup>(37)</sup> (volumetric)	Bauman <i>et al.</i> , 1999 <sup>(2)</sup>	Johannesen <i>et al.</i> , 2003 <sup>(13)</sup>

**Table 1.** Low grade gliomas studies using statistical analysis to examine the efficacy of extent of resection in improving survival and delaying tumor progression.

Authors and year	Grade(s)	No. of patients	Extent of resection (No. of patients)	5-Year progression-free survival			5-Year survival		
				5-Year progression free survival (%)	Univariate p value	Multivariate p value	5-Year survival (%)	Univariate p value	Multivariate p value
North et al., 1990 <sup>(26)</sup>	II	77	GTR (8) STR (43) Biopsy (26)	NA	NA	NA	85% 64% 43%	0.013	0.002
Philippone et al., 1993 <sup>(28)</sup>	II	179	GTR (45) STR (95) Biopsy (39)	NA	NA	NA	80% 50% 45%	0.0002	< 0.01
Ito et al., 1994 <sup>(11)</sup>	II	87	GTR (19) STR (51) Biopsy (17)	NA	NA	NA	NA	NA	0.0011
Rajan et al., 1994 <sup>(33)</sup>	II	82	GTR (11) STR (30) PR (22) Biopsy (19)	NA	NA	NA	90% 52% 50% 42%	< 0.05	NS
Nicolato et al., 1995 <sup>(24)</sup>	II	75	GTR (16) PR (58)	NA	NA	NA	87% 26%	0.0001	< 0.05
Scerrati et al., 1996 <sup>(35)</sup>	II	131	GTR (76) STR (31) PR (24)	NA	NA	NA	100% 93.7% 91.7%	0.0005	0.001
Leighton et al., 1997 <sup>(20)</sup>	II	167	GTR (85) STR (23)	NA	NA	NA	82% 64%	0.008	0.006
Lote et al., 1997 <sup>(22)</sup>	II	97	GTR (77) Biopsy (20)	NA	NA	NA	NA	< 0.03	NS
Peraud et al., 1998 <sup>(27)</sup>	II	75	GTR (40) STR (35)	NA	NA	NA	96% 64%	0.01	NA
Nakamura et al., 2000 <sup>(23)</sup>	II	88	Radical (43) Non radical (45)	NA	NA	NA	NA	< 0.001	< 0.001
Shaw et al., 2002 <sup>(36)</sup>	II	203	GTR (29) STR (71) Biopsy (103)	NA	0.0137	NS	88% 56% 71%	0.0116	0.0349
Yeh et al., 2005 <sup>(46)</sup>	II	93	GTR (13) STR (71) Biopsy (9)	NA	0.0073	0.002	92% 52% 52%	0.0349	0.016

**Table 2.** Positive non-volumetric low grade glioma studies using statistical analysis to examine the efficacy of extent of resection in improving survival and delaying tumor progression. Legend: GTR = Gross Total Resection; NA = Not Available; NS = Not Specified; PR = Partial Resection; STR = SubTotal Resection.

Authors and year	Grade(s)	No. of patients	Extent of resection (No. of patients)	5-Year progression-free survival			5-Year survival		
				5-Year progression free survival (%)	Univariate p value	Multivariate p value	5-Year survival (%)	Univariate p value	Multivariate p value
Whitton et al., 1990 <sup>(45)</sup>	II	88	GTR (6) STR (33) PR(28) Biopsy (27)	NA	NA	NA	NA	NS	NA
Bauman et al., 1999 <sup>(2)</sup>	II	401	GTR (277) STR (124)	NA	NA	NA	NA	NS	NS
Johannesen et al., 2003 <sup>(13)</sup>	II	993	GTR (173) STR (689) Biopsy (131)	NA	NA	NA	NA	NS	NS

**Table 3.** Negative non-volumetric low grade glioma studies using statistical analysis to examine the efficacy of extent of resection in improving survival and delaying tumor progression. Legend: GTR = Gross Total Resection; NA = Not Available; NS = Not Specified; PR = Partial Resection; STR = SubTotal Resection.

Authors and year	Grade(s)	No. of patients	Extent of resection (No. of patients)	5-Year progression-free survival			5-Year survival		
				5-Year progression free survival (%)	Univariate p value	Multivariate p value	5-Year survival (%)	Univariate p value	Multivariate p value
Shibamoto et al., 1990 <sup>(37)</sup>	II	101	> 80% < 80%	NA	NA	NA	64% 59%	NS	NS
Karim et al., 1996 <sup>(14)</sup>	II	343	90-100% (84) 50-89% (103) < 50% (156)	NA	NA	NA	NA	< 0.01	< 0.05
van Veelen et al., 1998 <sup>(43)</sup>	II	90	> 75% (13) < 75% (59)	NA	NA	NA	62% 18%	0.002	0.04
Claus et al., 2005 <sup>(5)</sup>	II	156	100% (56) < 100 (100)	NA	NA	NA	98.2% 92.0%	0.05	<0.05

**Table 4.** Volumetric low grade glioma studies using statistical analysis to examine the efficacy of extent of resection in improving survival and delaying tumor progression. Legend: NA = Not Available; NS = Not Specified.

Four of these studies included volumetric analysis of extent of resection<sup>(5,14,37,43)</sup>. Of the non-volumetric studies, 12 demonstrated evidence supporting extent of resection as a statistically significant predictor of either 5-year survival or 5-year progression free survival (Table 2). These studies were published from 1990 to 2005 and most commonly employed a combination of multivariate and univariate analyses to determine statistical significance.

In most instances, extent of resection was defined on the basis of gross total versus subtotal resection. Interestingly, only 3 non-volumetric studies did not support extent of resection as a predictor of patient outcome. However, none of these reports evaluated progression free survival, but instead focused solely

on 5-year survival (Table 3). Of the 4 volumetric low grade glioma studies reviewed, 3 demonstrated statistical significance based upon 5-year survival (Table 4). For their statistical analyses, each study divided the extent of resection percentages into two categories, although the cut-off threshold was different in each publication and varied from 75% to 100%.

■ **NON-VOLUMETRIC AND VOLUMETRIC HIGH GRADE GLIOMA EXTENT OF RESECTION STUDIES.** Twenty-seven studies<sup>(1,3,4,6-10,12,15-19,21,25,29-32,34,38-42,44)</sup> since 1990 have applied statistical analysis to examine the efficacy of extent of resection in improving survival and delaying tumor progression among high grade glioma patients (Table 5).

Four of these studies included volumetric analysis of

Prognostic effect	Authors and year		
	1990-1995	1996-2000	2000-2006
Statistics favor more extensive resections	Shibamoto et al., 1990 <sup>(37)</sup> Vecht et al., 1990 <sup>(44)</sup> Curran et al., 1992 <sup>(6)</sup> Simpson et al., 1992 <sup>(39)</sup> Dinapoli et al., 1993 <sup>(7)</sup> Jeremic et al., 1994 <sup>(12)</sup> Nitta et al., 1995 <sup>(25)</sup>	Barker et al., 1996 <sup>(1)</sup> Keles et al., 1999 (volumetric) <sup>(16)</sup>	Buckner et al., 2001 <sup>(4)</sup> Lacroix et al., 2001 (volumetric) <sup>(18)</sup> Lamborn et al., 2004 <sup>(19)</sup> Brown et al., 2005 <sup>(3)</sup> Stark et al., 2005 <sup>(40)</sup> Ushio et al., 2005 <sup>(42)</sup>
Statistics do not favor any resection group	Hollerhage et al., 1991 <sup>(9)</sup> Phillips et al., 1991 <sup>(29)</sup> Sandberg-Wollheim et al., 1991 <sup>(34)</sup> Duncan et al., 1992 <sup>(8)</sup> Prados et al., 1992 <sup>(31)</sup> Huber et al., 1993 <sup>(10)</sup>	Kowalcuk et al., 1997 <sup>(17)</sup>	Levin et al., 2002 <sup>(21)</sup> Puduvalli et al., 2003 <sup>(32)</sup> Tortosa et al., 2003 <sup>(41)</sup> Pope et al., 2005 (volumetric) <sup>(30)</sup> Keles et al., 2006 (volumetric) <sup>(15)</sup>

**Table 5.** High grade glioma studies using statistical analysis to examine the efficacy of extent of resection in improving survival and delaying tumor progression.

Authors and year	Grade(s)	No. of patients	Extent of resection (No. of patients)	Time to tumor progression			Survival			XRT	Chemo
				Mean time to tumor progression (months)	Univariate p value	Multivariate p value	Mean survival (months)	Univariate p value	Multivariate p value		
Shibamoto et al., 1990 <sup>(2)</sup>	IV	135	GTR + STR (50) PR+ Biopsy (85)	NA	NA	NA	15 11	< 0.05	NA	135 (100%)	67 (49.6%)
Vecht et al., 1990 <sup>(44)</sup>	III and IV	243	Total (15) Large (15) Small (57) Decompression (139) Biopsy (17)	NA	NA	NA	NA	NA	0.001	NA	NA
Curran et al., 1992 <sup>(6)</sup>	III	103	GTR (14) PR (58) Biopsy (31)	NA	NA	NA	49.3 49.3 18.3	0.0023	NS	103 (100%)	103 (100%)
Simpson et al., 1992 <sup>(8)</sup>	IV	645	Total (123) Partial (413) Biopsy (109)	NA	NA	NA	11.3 10.4 6.6	< 0.001	< 0.001	645 (100%)	NA
Dinapoli et al., 1993 <sup>(7)</sup>	III and IV	346	GTR+STR (246) Biopsy (25)	NA	NA	NA	NA	0.0375	0.0046	346 (100%)	334 (96.5%)
Jeremic et al., 1994 <sup>(12)</sup>	IV	86	GTR+STR (61) Biopsy (25)	8.3 5.3	0.00001	0.0045	14 7.3	0.0000	0.00030	86 (100%)	86 (100%)
Nitta et al., 1995 <sup>(25)</sup>	III and IV	101	GTR (26) STR (36) PR (39)	NA	NA	NA	20 12 11	< 0.01	NA	101 (100%)	101 (100%)
Barker et al., 1996 <sup>(1)</sup>	IV	222	GTR (28) STR (165) Biopsy (13)	NA	NA	NA	NA	< 0.001	0.04	222 (100%)	NA
Buckner et al., 2001 <sup>(4)</sup>	III and IV	275	GTR (99) STR (169) Biopsy (92)	NA	0.54	0.0002	NA	0.54	0.0002	275 (100%)	275 (100%)
Lamborn et al., 2005 <sup>(9)</sup>	IV	832	GTR (101) STR (469) Biopsy (86)	NA	NA	NA	NA	< 0.001	832 (100%)	832 (100%)	832 (100%)
Brown et al., 2005 <sup>(3)</sup>	III and IV	124	GTR (49) STR (53) Biopsy (22)	NA	NA	NA	NA	NS	< 0.001	124 (100%)	124 (100%)
Stark et al., 2005 <sup>(40)</sup>	IV	267	GTR (167) STR (80) PR (14)	NA	NA	NA	NA	0.014	NA	222 (83.1%)	57 (21.3%)
Ushio et al., 2005 <sup>(42)</sup>	IV	105	GTR (35) PR (57) Biopsy (13)	10.3 5.2 3.6	0.017	0.0042	20 14.2 8.3	0.0048	0.018	105 (100%)	105 (100%)

**Table 6.** Positive non-volumetric high grade glioma studies using statistical analysis to examine the efficacy of extent of resection in improving survival and delaying tumor progression. Legend: GTR = Gross Total Resection; NA = Not Available; NS = Not Specified; PR = Partial Resection; STR = SubTotal Resection; XRT = Radiation Therapy.

extent of resection<sup>(15,16,18,30)</sup>. Of the non-volumetric studies, 13 demonstrated evidence supporting extent of resection as a statistically significant predictor of either time to tumor progression or overall survival (Table 6).

Although some of these reports showed extent of resection to significantly affect both tumor progression and overall survival, every study showed a survival benefit. Ten studies, however, demonstrated no sig-

nificant benefit based upon extent of resection (Table 7). Notably, the distribution of adjuvant chemotherapy and radiation treatment was comparable among all high grade glioma extent of resection studies (Figure 2).

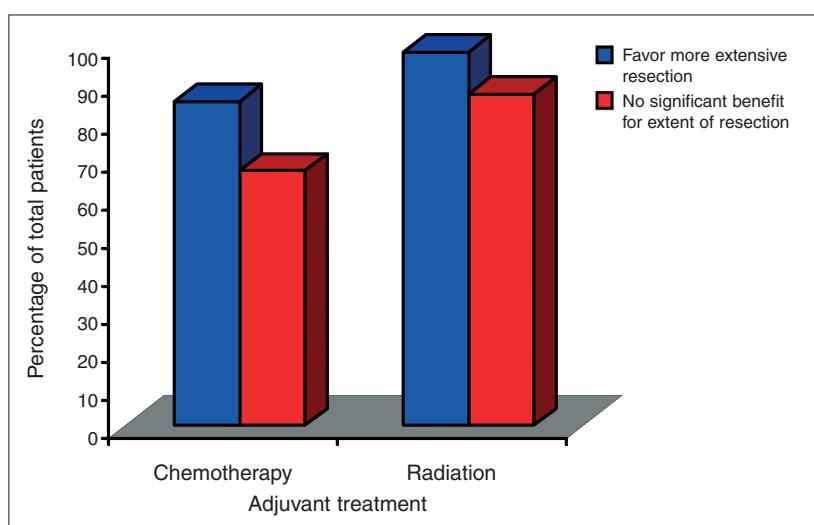
Echoing the non-volumetric study results, half of all high grade volumetric studies showed a significant survival advantage with greater extent of resection (Table 8).

Authors and year	Grade(s)	No. of patients	Extent of resection (No. of patients)	Time to tumor progression			Survival			XRT	Chemo
				Mean time to tumor progression (months)	Univariate p value	Multivariate p value	Mean survival (months)	Univariate p value	Multivariate p value		
Hollerage et al., 1991 <sup>(9)</sup>	IV	118	NA	NA	NA	NA	NA	NS	NS	NA	NA
Phillips et al., 1991 <sup>(25)</sup>	IV	173	GTR (28) STR (137) Biopsy (8)	NA	NS	NS	NA	NS	NS	173 (100%)	173 (100%)
Sandberg-Wolfeim et al., 1991 <sup>(34)</sup>	III and IV	171	GTR (59) STR (112)	5.5 5.3	NS	NS	13.5 12.8	NS	NS	84 (49.1%)	171 (100%)
Duncan et al., 1992 <sup>(8)</sup>	III and IV	235	GTR (39) STR (121) Biopsy (75)	NA	NS	NS	NA	NS	NS	235 (100%)	0 (0%)
Prados et al., 1992 <sup>(31)</sup>	III	357	NA	NA	NA	NS	NA	NA	NS	357 (100%)	337 (94.4%)
Huber et al., 1993 <sup>(10)</sup>	III and IV	163	NA	NA	NA	NA	NA	NS	NS	NA	NA
Kowalcuk et al., 1997 <sup>(7)</sup>	III and IV	75	GTR (30) STR (32) Biopsy (13)	NA	NA	NA	NA	NS	NS	67 (89.3%)	49 (65.3%)
Levin et al., 2002 <sup>(21)</sup>	III	92	GTR (20) STR (45) Biopsy (25)	NA	NA	NA	NA	NA	NS	92 (100%)	92 (100%)
Puduvali et al., 2003 <sup>(33)</sup>	III	106	GTR (30) STR (61) Biopsy (14)	NA	NA	NS	NA 80.4 33.6	NS	NS	90 (84.9%)	45 (42.4%)
Tortosa et al., 2003 <sup>(41)</sup>	III	95	GTR (33) PR (33) Biopsy (29)	NA	NA	NA	NA	NS	NS	87 (90.6%)	76 (80%)

**Table 7.** Positive non-volumetric high grade glioma studies using statistical analysis to examine the efficacy of extent of resection in improving survival and delaying tumor progression. Legend: GTR = Gross Total Resection; NA = Not Available; NS = Not Specified; PR = Partial Resection; STR = SubTotal Resection; XRT = Radiation Therapy.

Although the high grade studies reviewed were all modern series conducted by expert neurosurgeons with access to comparable operative technologies, it remains difficult to define the many inherent disparities between the cases described that may have biased the reported findings.

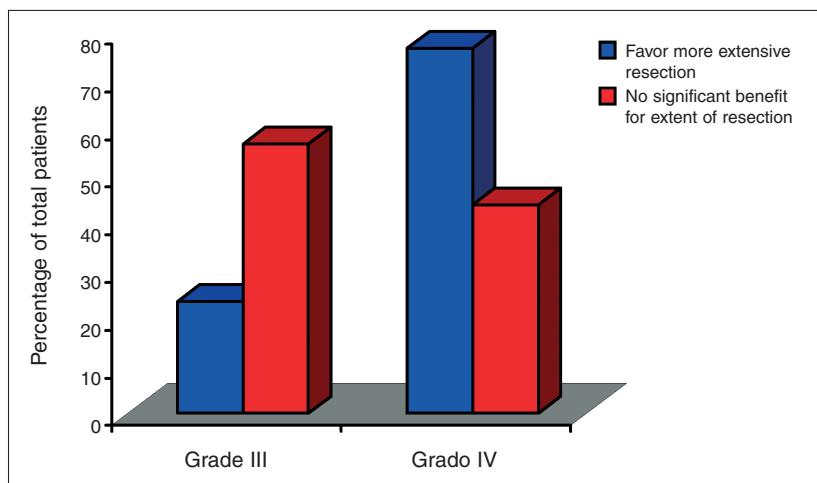
One factor that may distinguish various high grade glioma studies from one another is the distribution of WHO grade III and IV histologies among the study patients. After quantifying this parameter in each publication, it remains difficult



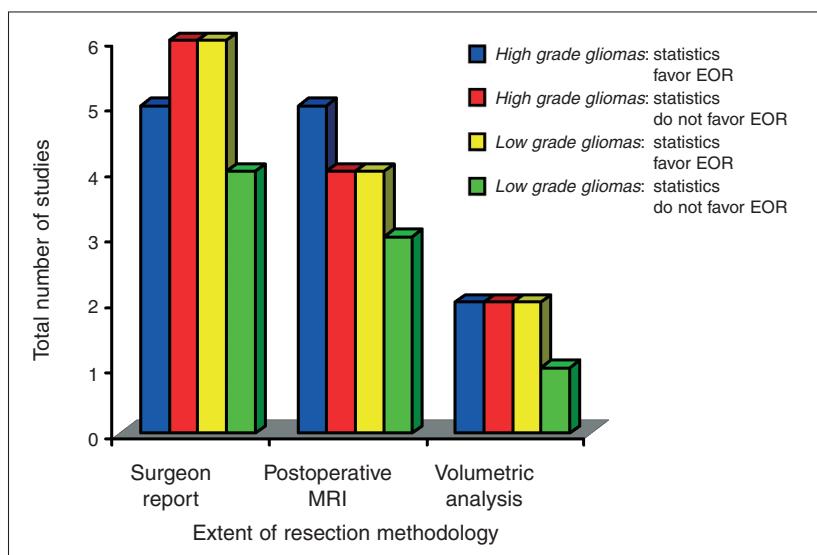
**Figure 2.** The use of adjuvant chemo- and radiation therapy in high grade glioma extent or resection analyses.

Authors and year	Grade(s)	No. of patients	Extent of resection (No. of patients)	Time to tumor progression			Survival			XRT	Chemo
				Mean time to tumor progression (months)	Univariate p value	Multivariate p value	Mean survival (months)	Univariate p value	Multivariate p value		
Keles et al., 1990 <sup>19</sup>	IV	107	< 25% (25) 25-49% (21) 50-74% (18) 75-99% (20) 100% (23)	3.6 6.0 8.0 11.5 13.3	NA	< 0.0001	8.0 14.2 15.7 22.1 23.3	NA	< 0.0005	107 (100%)	77 (84%)
Lacroix et al., 2001 <sup>18</sup>	IV	416	< 98% ≥ 98%	NA	NA	NA	8.8 13.0	< 0.0001	< 0.0001	416 (100%)	NA
Pope et al., 2005 <sup>20</sup>	IV	110	< 20% 20-89% 90-99% 100%	NA	NA	NA	27.4 11.1 17.1 22.1	NS	NS	110 (100%)	Most
Keles et al., 2006 <sup>19</sup>	III	102	0-100%	26.0	0.015	NS	41.0	NS	NS	102 (100%)	96 (94%)

**Table 8.** Volumetric high grade glioma studies using statistical analysis to examine the efficacy of extent of resection in improving survival and delaying tumor progression. Legend: NA = Not Available; NS = Not Specified; XRT = Radiation Therapy.



**Figure 3.** Relative distribution of histologic grades in extent of resection analyses of high grade gliomas.



**Figure 4.** Distribution of extent of resection methodologies by tumor grade and statistical analysis results. Legend: EOR = Extend Of Resection; MRI = Magnetic Resonance Imaging.

to draw any firm conclusions regarding causality (Figure 3). Another dimension of extent of resection analysis that can greatly affect the reported findings is the method with which the extent of resection is calculated. Although volumetric MRI analysis is now the gold-standard, many Centers still rely upon the surgeon's report or two-dimensional analysis based upon postoperative MR imaging. When we examined the distribution of extent of resection methodologies and compare them to the findings for both low grade and high grade gliomas, there does not appear to be any identifiable trend, as there was a relatively even distribution of techniques for each study category (Figure 4).

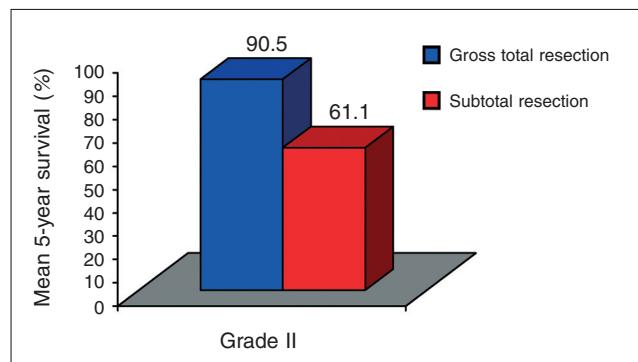
#### QUANTIFICATION OF IMPROVEMENT IN PATIENT OUTCOME

For both low and high grade gliomas, we sought to define the mean survival time associated with subtotal *versus* gross total resection. Although the level of evidence available for each tumor category does not permit a statistical meta-analysis, this measurement provides an overall estimation of the additional survival time these studies suggest may be gained through a greater extent of resection.

Not surprisingly, the effect of a greater extent of resection was more pronounced in the low grade glioma studies, where the mean survival was extended from 61.1 to 90 months (Figure 5). Among the high grade gliomas, the improvement was more modest, with an increase from 64.9 to 75.2 months in WHO grade III gliomas and from 11.3 to 14.5 months in WHO grade IV gliomas (Figure 6).

#### CONCLUSIONS

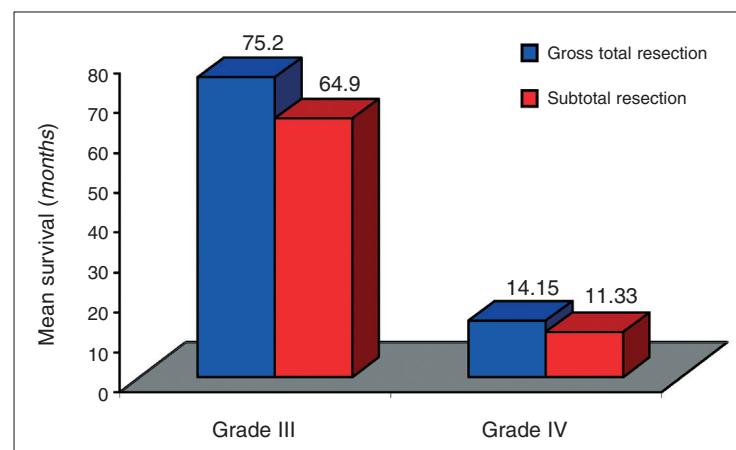
Our review of the available studies for both low grade and high grade hemispheric gliomas in adults indicates that there continues to be limitations in the quality of data examining the effect of extent of resection on patient survival. There is growing evidence, however, that a more exten-



**Figure 5.** Mean 5-year survival percentage by extent of resection in all low grade glioma studies.

sive surgical resection may be associated with a more favorable life expectancy for both low grade and high grade glioma patients.

In addition to providing longer overall survival, more aggressive resections for low grade gliomas may also affect the risk of malignant transformation among low grade gliomas, as well as take advantage of an opportunity to treat the disease when the neoplasm is at its earliest stage of evolution. Because no class I evidence exists to support a particular management paradigm, the optimal combination of surgery, a chemotherapeutic agent, and radiation therapy remains unknown. Since it is unlikely that a prospective, randomized study will be designed to address these issues, we believe retrospective, matched studies or prospective observational trials may be a more practical solution.



**Figure 6.** Mean survival time by extent of resection in all high grade glioma studies.

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