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*Clinical Study*

# Quantitative measurement of quality outcome in malignant glioma patients using an independent living score (ILS)

*Assessment of a retrospective cohort*

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*Key words:* quality of life scale, malignant glioma, independent living scale

## Summary

*Purpose.* Although a number of tools have been developed to measure 'quality of life' in patients with malignant glioma, there remains no completely satisfactory technique that incorporates a quality of life measure into survival analysis. We propose that a patient's ability to maintain independent activity offers a way to accomplish this goal.

*Patients and methods.* An independent living score (ILS) is generated by awarding points on a monthly basis based on Karnofsky score and weighing the score based on the particular month of the clinical course. The ILS has a large range for any given survival, and can discriminate important treatment effects to which standard survival analyses are completely insensitive. Using this score and several variations, we were able to retrospectively analyze a patient cohort to assess what correlated with ILS.

*Results.* We found a strong correlation with survival of all the measures tested. Interestingly, we found that patients for whom a total resection was performed and those who were most intensively treated had significantly higher ILS values, suggesting that not only did more aggressive treatment improve survival but that it did not simply increase survival at the expense of the time a patient remained independent.

*Conclusion.* Since the general course for patients with malignant glioma is one of increasing disability and loss of independence, we feel that these measures can serve as a way to distinguish between those therapies that increase survival at the expense of quality of life *versus* those that do not. Consideration should be given to incorporating these measures into prospective trials.

Although survival remains the gold standard by which treatment efficacy in glioma patients is measured, there is an increasing emphasis on maintaining (or improving) quality of life. This becomes an especially important issue when discussing aggressive treatment regimens that may be associated with substantial morbidity. Thus, one possible effect of increasing treatment intensity might be an increased survival at a diminished capacity, resulting in an overall poor quality of life.

Cancer patient quality of life has been defined as the subjective sense of well-being as a whole and also as a multidimensional concept that encompasses physical, occupational, psychosocial and spiritual components [1]. Such a concept has many facets and is obviously very difficult to analyze. Several studies have tried to do this in brain tumor patients using patient self-reports [2], Barthel index [3] and various other types of questionnaires [4]. A more rigorous treatment incorporates the length of time spent in each of several clinical states and then weighted to give a quality-time survival metric (Q-TwiST). The Q-TwiST strategy has recently been applied to patients with brain metastases to determine the optimum dose of accelerated radiation therapy [5], and to patients with leptomeningeal cancer to select the optimum approach between two competing intrathecal chemotherapy regimens [6].

There are several potential drawbacks to each of these approaches. First, each strategy requires additional time of both the patient and investigator. Second, except for the Q-TwiST approach, each strategy is difficult to assess quantitatively, and tends to be dwarfed in importance by the objective survival numbers in assessing outcome. While the Q-TwiST technique is quantitative and fully integrates survival information, it does not consider the patient's baseline level of debility, and does not consider progressive loss of function not directly related to tumor progression – both critical issues in patients with nervous system cancer. What is needed, therefore, is a technique that quantitatively expresses both overall survival and quality of life as it evolves over time.

We propose that a useful way in which quality survival can be measured is to examine one global variable over time. This reductionist approach underestimates the complexity of this concept, but if the correct variable is chosen, it should reflect other aspects of quality of life. We propose that in brain tumor patients, an appropriate variable is the ability to live and perform independently. Thus, while this might not reflect the patient's mood or sense of well-being, it does correlate with disability and has economic ramifications as well. Furthermore, it can be estimated from any of the performance scores that are routinely used in following patients. Prior studies have successfully used Karnofsky scores to assess quality of life in brain tumor patients [7,8], although the score was not incorporated into survival. In addition, the KPS correlates very closely with more complex, independent measures of quality of life and with overall survival, while at the same time providing very good inter-rater reliability, ease and simplicity [9].

Patients with brain tumors tend to become more disabled as their tumors progress and this disability is reflected in a loss of independence. We hypothesized that a patient's ability to remain independent would therefore correlate with survival, but might be more affected than survival by the aggressiveness of therapy. To test this hypothesis, we retrospectively analyzed a cohort of patients for whom independence was measured prospectively throughout their clinical course; we also evaluated the effects of various patient variables on ability to maintain independence.

## Patients and methods

Seventy-five patients with malignant glioma enrolled in one of two early phase clinical trials [10,11] between 1992 and 1998 who survived at least 2 months after diagnosis and for whom monthly Karnofsky scores were available were accessed from one of the authors' (MG) personal database. Clinical data such as demographics, location, extent of surgery and further treatments were abstracted from medical records. Treatment intensity was estimated from 1 to 4+ according to whether the patient received only RT or one, two or more subsequent therapies. Extent of surgical resection was estimated from surgical records and post-operative imaging studies.

A patient was considered independent if his/her KPS was $\geq$70 for at least one half the month. Using monthly KPS as a guide, four calculations were made to assess independence (for a more detailed description, please refer to the Appendix):

Percent time independent (PTI) was derived from dividing the total number of months with KPS $\geq$ 70 over the total survival time.
The independent living score (ILS) was calculated by scoring 2 points for KPS $\geq$ 70, 1 point for KPS $\geq$ 50 (semi-independent) and no points for lower scores. Each monthly score was multiplied by a correction weighting factor equal to [(month graded in clinical course)/survival (months)] and then the products summed.
ILS $\times$ survival (ILS $\times$ surv) was calculated by multiplying the ILS times the months of survival.
$ILS/ILS_{max}$ was calculated by dividing the ILS by the theoretical maximal ILS (which represented the sum of the survival in months +1).

Data was analyzed using a SigmaStat Package, version 2.03. A Pearson Product Moment Correlation was used to calculate correlation coefficients between variables and a Spearman coefficient was used when non-parametric values such as treatment intensity were evaluated. $P$-values $\leq$0.05 were considered significant.

## Results

The patient cohort consisted of 35 men and 40 women with a mean patient age at time of diagnosis of 55.8 years (median 56; range 22–78). Sixty-six patients (88%) had a histologic diagnosis of GBM and nine tumors were anaplastic astrocytomas. Thirty patients (40%) presented with seizure.

The mean survival of the entire cohort was 13.1 months (95% CI: 2.7 months). The values for the measurement tools of independence are listed in Table 1. The median survival for all patients was

9 months (25–75%: 6–15 months). As adjudged by both PTI and $ILS/ILS_{max}$, approximately 60% of the survival was independent time. A similar value was noted for the ILS and ILS × surv scores. The ILS score of 6, for example, reflects 5 months of independent time (or 55% of the total survival), while a score of 66 for the ILS × surv is equivalent to between 7 and 8 months (one can arrive at this by solving the quadratic equation $x(x + 1) = 66$). Forty-three patients (57%) achieved an ILS × surv score of 42 (equivalent to 6 months of KPS $\geq$ 70), compared to 61 (80%) patients who survived this period. By 18 months, however, comparable percentages were only 17% and 20%; thus, virtually every patient who had survived to this longer time point was still independent at that time (Table 2).

In order to assess the correlation between survival and independence, we performed a Pearson Product Moment Correlation (Table 3). The correlation coefficients were all significant but the highest associations were between survival and ILS (0.961) and ILS × surv (0.911). Each score is plotted against survival in Figure 1. Interestingly, the $r^2$ values for ILS and ILS × surv (0.92 and 0.83, respectively) were much greater than those for $ILS/ILS_{max}$ and PTI (0.15 and 0.20, respectively).

As expected, patient age strongly correlated with survival in this series of patients ($r = -0.491$, $P < 0.000008$). Age also correlated strongly with all measures of independence with correlation coefficients ranging from −0.472 (ILS) to −0.309 ($ILS/ILS_{max}$). Independence, measured either as total months independent or as a percentage of the clinical course, decreased significantly with advancing age (Figure 2). Values for $r^2$ ranged from 0.106 for $ILS/ILS_{max}$ to 0.228 for ILS ($P < 0.005$ for all comparisons).

*Table 1.* Independence measures for the patient cohort ($n = 75$)

| | Mean | Median | Std. dev. | C.I. of mean |
|---|---|---|---|---|
| Survival (months) | 13.2 | 9.0 | 11.9 | 2.8 |
| PTI | 49.2 | 57.0 | 32.4 | 7.5 |
| ILS | 9.8 | 6.0 | 10.2 | 2.4 |
| ILS × surv | 246.1 | 66.0 | 608.8 | 140.1 |
| $ILS/ILS_{max}$ | 63.5 | 61.0 | 17.6 | 4.1 |

A one way ANOVA on ranks was used to assess potential effects of other prognostic variables. There was no significant correlation of either survival or any independence measurement with sex, side, location, histology or presentation with seizure. Extent of initial tumor resection was associated with differences in survival and independence. Patients who underwent a gross total resection ($n = 25$) survived longer (14 months) than patients ($n = 50$) with less than a gross total resection (8 months, $P = 0.001$, one way ANOVA on ranks). Patients who underwent a gross total resection were also independent for a greater percentage of their survival time and for a long absolute period as assessed by the four measures of independence (Figure 3). Using the ILS × surv value to estimate independent functioning, patients with total resections had a median time of independence of almost 1 year (score 147) compared to less than 6 months for those with less than total resections ($P < 0.001$, one way ANOVA on ranks). This effect was not confounded by the fact that younger patients were more likely to undergo gross total resections; the mean ages between the groups were not different (53 vs. 57 years, $P = 0.2$).

Although this analysis was retrospective, and patients were not treated in a uniform fashion, patients could be categorized on a 1–4 scale according to post-surgical treatment intensity as outlined in the Patients and method section. Using the Spearman Rank Order Correlation to assess this non-parametric value, we noted a strong correlation with survival ($r = 0.501$, $P < 0.0001$). Treatment intensity was also strongly and positively correlated with better ILS ($r = 0.581$, $P < 0.001$; Figure 4), ILS × surv ($r = 0.564$, $P = 0.001$), $ILS/ILS_{max}$ ($r = 0.539$, $P < 0.001$) and PTI ($r = 0.571$, $P < 0.001$).

## Discussion

Despite the development of many novel therapeutic approaches, survival for patients with malignant gliomas has not increased appreciably over the last two decades [12]. Moreover, the observation that many of

*Table 2.* Comparison of patient survival with ILS × surv scores for patient cohort

| Survival | | | ILS × surv | | |
|---|---|---|---|---|---|
| >6 months | >12 months | >18 months | >6 months | >12 months | >18 months |
| 61 pts (80%) | 31 pts (41%) | 15 pts (20%) | 43 pts (57%) | 21 pts (28%) | 13 pts (17%) |

these novel therapies produce significant toxicity raises the issue of whether the primary goal of therapy should be maximizing survival. If overall survival in patients with malignant gliomas cannot be appreciably increased with currently available therapies, then optimizing available survival time may be a more meaningful clinical outcome and a more logical endpoint for clinical trials. This concept of 'rectangularizing' the survival curve has been compellingly argued by Fries [12].

*Table 3.* Pearson Product Moment Correlations of independence measures with survival data for patient cohort

| | PTI | ILS | ILS × surv | $ILS/ILS_{max}$ |
|---|---|---|---|---|
| Survival | 0.452 | 0.961 | 0.911 | 0.386 |
| PTI | | 0.558 | 0.347 | 0.863 |
| ILS | | | 0.934 | 0.553 |
| ILS × surv | | | | 0.350 |
| $ILS/ILS_{max}$ | | | | |

If quality of life is going to be integrated with survival data, adequate measurement tools for 'quality' are needed. The Karnofsky scale provides one type of assessment [13]. By rating the patient's performance status based on particular capabilities, one can obtain a semi-quantitative idea of how far the patient's lifestyle has deviated from normal. The KPS is an approximate, non-parametric, score that may underestimate morbidity in brain tumor patients compared with more complex assessment tools [14]. Other tools have been developed that are more sensitive to neurologic disability, but such tools generally suffer from an inability to be quantitatively described in a simple fashion analagous to survival. Thus, while independence as interpreted by the KPS is not a perfect surrogate for quality of life, it is an easily assessable, and reliable clinical and research tool with good predictive validity in cancer patients [9].

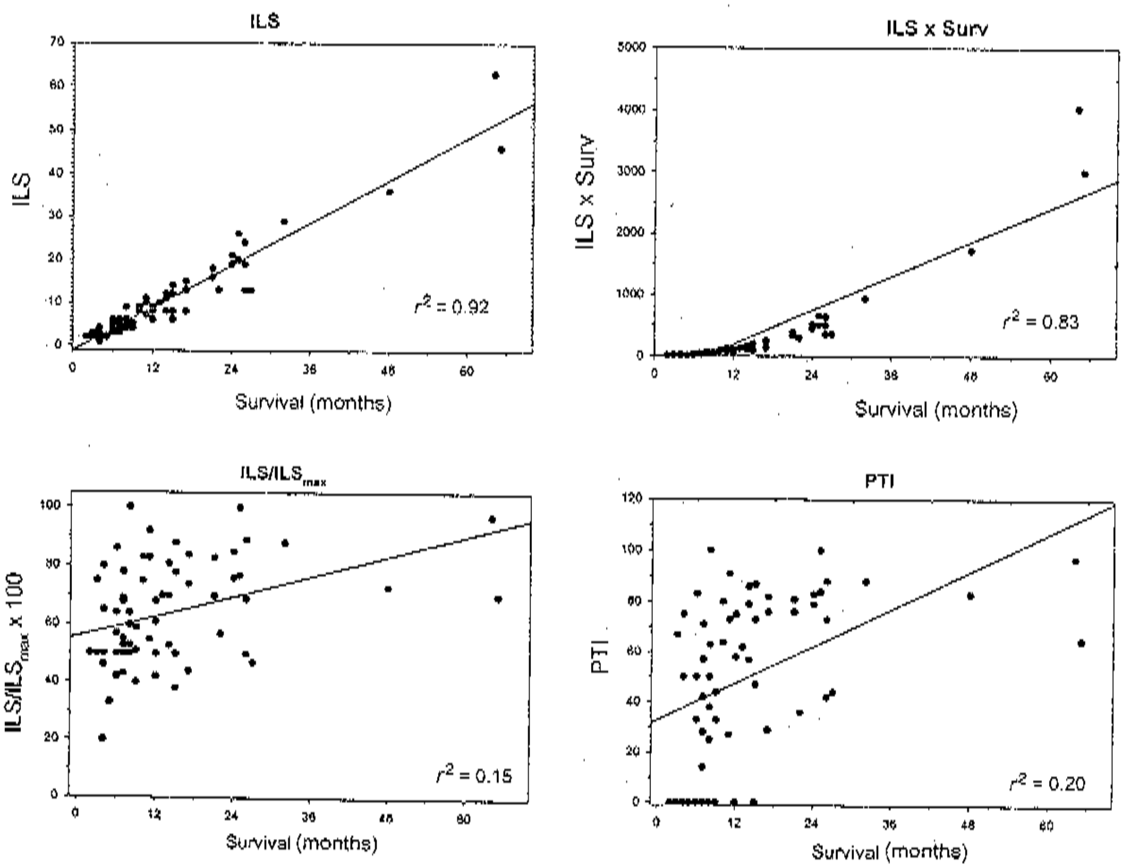


*Figure 1.* Analysis of independence measures as a function of survival for patient cohort.

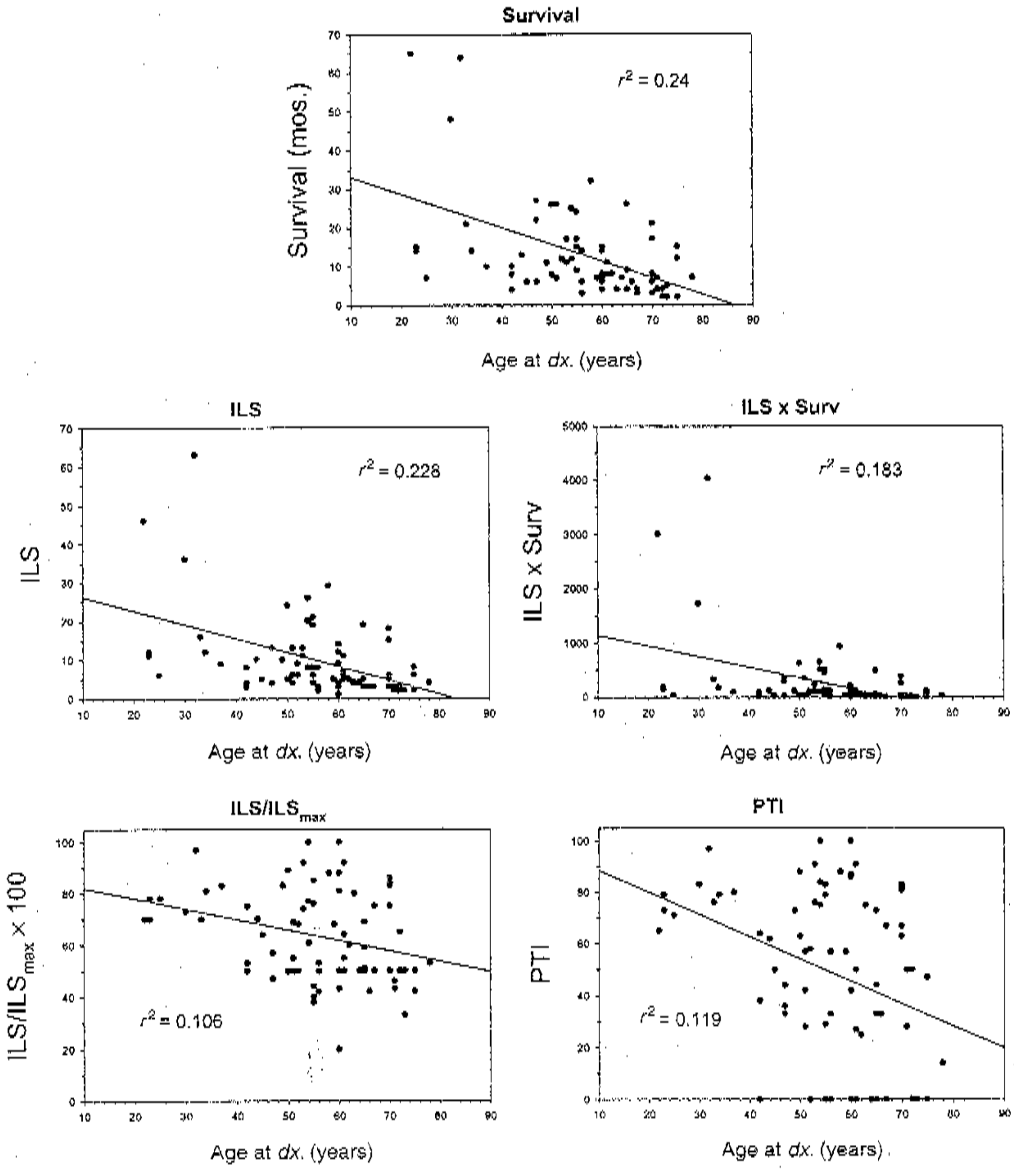


*Figure 2.* Survival and independence measures *versus* patient age at diagnosis.

Our method for quantifying independence (described in the Appendix) allows this variable to be incorporated into clinical studies. As is discussed in the Appendix, we feel that the ILS and ILS × surv measures will be much more useful measures for assessing those treatments that *increase* quality of life. For example, since the PTI or $ILS/ILS_{max}$ values are time dependent, a value of 1.00 has little

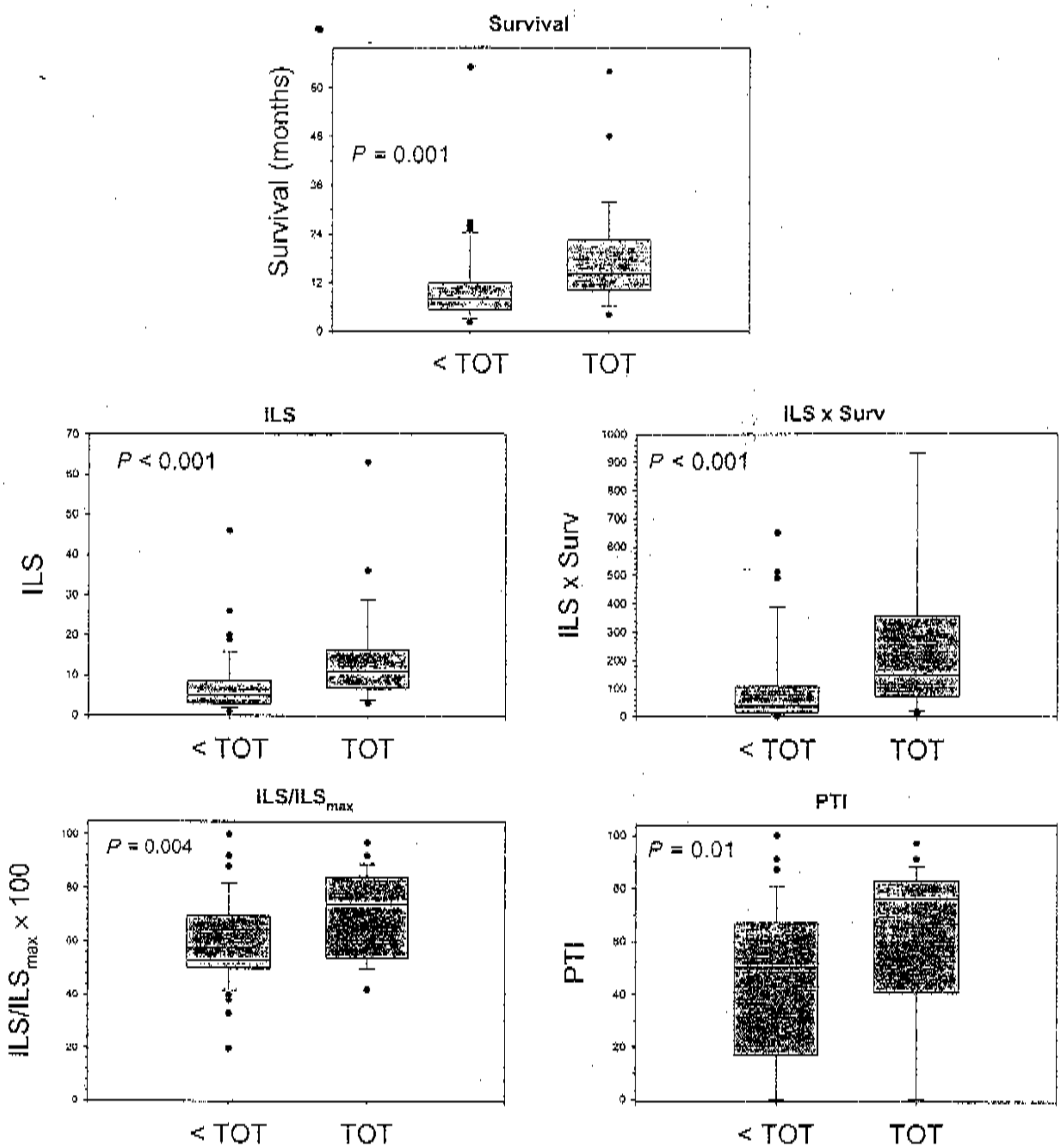


*Figure 3.* Outcome in terms of survival and various independence measures of patients undergoing either visually total ($n = 25$) or less than total ($n = 51$) resections.

meaning unless one knows the survival. By contrast, an ILS × surv score of 156 means that there has been the equivalent of 1 year of independent functioning.

Since data from a large randomized clinical trial was not available for analysis, we first sought to validate our technique using data prospectively collected from a cohort of patients initially enrolled in one of two successive early phase clinical trials. All the patients were cared for by one of the authors and received monthly Karnofsky scores. By awarding points based on independence per month, a monthly cumulative score could be calculated that could be expressed as an ordinal number. Our theoretical treatment of these measures (see Appendix) indicated that if two patients

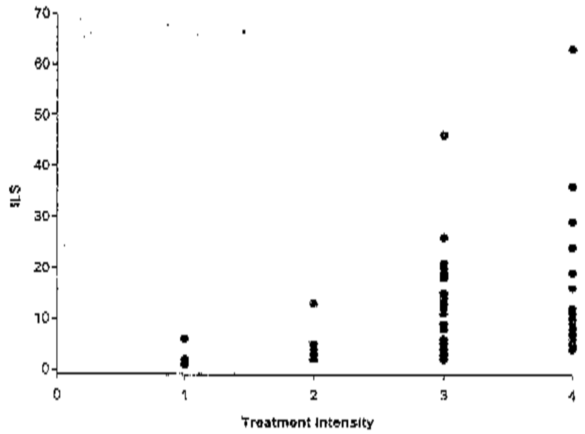


*Figure 4.* Vertical Line plot of ILS as a function of treatment intensity. The correlation coefficient in Spearman Rank Order test is 0.581 ($P < 0.0001$).

had equivalent survivals, there would still be a discrepancy in independence scores if one of the survivals were spent in a dependent state. Therefore, our intent in this small cohort of malignant glioma patients was to analyze whether treatment intensity was inversely correlated with independence scores.

We found that the amount of independent time closely correlated with survival. Patients on average were independent for approximately 60% of their clinical course, although the actual amount of independent time varied widely from patient to patient. The closer correlation between ILS and ILS × surv with survival compared to PTI and $ILS/ILS_{max}$ indicates that patients with longer survivals spent more time independent than those with shorter survivals. The close correlation between PTI and $ILS/ILS_{max}$ with ILS and ILS × surv is consistent with the observation that independent functioning typically occurs at the beginning of the clinical course and is lost at a later time.

A negative correlation between age and both survival and independence measures was also noted. Age is the most powerful predictor of survival in patients with GBM. Our data indicate that age is also an important determinant of length and percentage of time independent. No differences in any measure of independence was seen between patients with AA and GBM, probably reflecting the small number ($n = 9$) of patients with AA in this series.

Since this is a retrospective study, the analysis of treatment effects must be interpreted very cautiously. For instance, the better survival achieved by patients undergoing total resection might simply reflect the presence of a polar, accessible lesion that itself has a better prognosis. The relationship of tumor resection to survival in patients with malignant gliomas is poorly defined [15,16]; a recent study, for example, concludes that resection is only helpful in patients with pretreatment midline shift [17]. In the present cohort, not only was there an improvement in survival in those patients for whom a visually total resection was accomplished, but those patients remained independent for both a longer period and for a greater percentage of time. Thus, although a definite conclusion is difficult, there is no evidence that an aggressive tumor resection decreases quality time as measured by independence.

Similarly, the finding of a strong positive correlation between treatment intensity and both survival and independence may reflect an unintentional bias of the treating physician to more intensively treat those patients who were expected to do better. In addition, the longer a patient survives, the more likely that patient may be to receive further treatment. Nevertheless, the results do not support the contention that intensive treatment prolongs survival at the cost of increased disability and diminished functional status.

The close correlation of independence measures with survival in this retrospective analysis is not surprising. In the setting of a randomized clinical trial, however, these two measures could easily diverge, particularly if one treatment arm increased the percentage of independent time, or, more strikingly, allowed patients to regain independent function over time. The measures of independence discussed in this paper (especially the ILS) can detect differences between therapies that result in identical overall survivals (see Appendix). These measures are easy to calculate, and the data upon which they are based are simple to collect. Utilizing these measures in a prospective trial may enhance our ability to identify valuable treatments for patients with malignant gliomas.

## Appendix. Quantitating time of independence

Because the clinical course of patients with gliomas tends to be one of increasing impairments that decrease independent functioning, we propose that a simple way in which to measure 'quality time' is by quantifying the time a patient remains independent in his/her activities. Such a simple, measurable variable (independent/not independent) measured per time provides a readily reproducible number that can be used to compare treatments.

In order to describe the possible ways in which independence can be measured, consider the following case scenario:

> PT 1 is a 50 year old woman diagnosed with a GBM. Her post-operative KPS is 80. She is enrolled in an experimental protocol postoperatively and receives treatment without incident, being able to maintain independence. At a follow-up visit 7 months after diagnosis, her KPS continues to be rated 80. The next month, she develops a subacute hemiparesis. MR indicates recurrence. She responds incompletely to decadron and now needs some assistance with her daily activity (KPS = 60). When she is seen at month 11, she is wheelchair bound and requires total care (KPS = 40). She dies the next month, twelve months from time of diagnosis.

In this scenario, the patient remained independent for 8 months at which time she became semi-independent for two more months and then lost independence completely for the last 2 months of life. If one multiplies the arithmetic product of KPS at any given time point with survival, one could theoretically arrive at a score, but since it is a non-parametric number, it is unclear how to interpret the values. For example, should the time that the patient's KPS was 80 be rated double that when it was 40?

On the other hand, if one considers the variable of independence, one could calculate the percent time after diagnosis that she remained independent (which we will term PTI). Using this calculation, one arrives at a figure of 67% (8/12 months). However, this calculation considers semi-independence and dependence equal and does not distinguish the time in the course of the illness when the patient is independent. For instance, a patient who was not independent but who regains independence because of treatment would have the same score as one who was independent early in the course for an equal amount of time and then lost this ability later.

If one awards two points for a KPS $\geq$ 70 and one point for a KPS of 5–60 per month, a patient can then receive 2, 1 or 0 points per month of survival. One could then add the numbers to arrive at a score. However, this still does not distinguish the time in the course when the patient is independent. To address this, we propose adding a weighting factor to account for the time in the clinical course that the patient is independent. If the patient's independence level is plotted over time, the area under the curve (i.e. deriving the integral) would be one way in which to arrive at a quantitative number. A simple arithmetic way to describe this would be to draw rectangles that extended from consecutive points on the abscissa to the height of the curve between them and add their areas. Usually, these areas are simply summed (i.e. obey the commutative law); in order to weigh the score in favor of those patients who improve over time, however, we propose that each rectangle be multiplied by a correction factor equivalent to the month that is being measured over the total survival (i.e. for the sixth month in a 12 month course, you would multiply by 6/12). These monthly values can then be added to give a score, which we will term the ILS.

Let us return to the patient detailed above. Consider Table 4. Since we know her survival is 12 months, the correction factor is month/12 for each month. Retrospective analysis of her course then reveals an ILS score of 7.6. Note that because of the correction factor, the monthly scores decrease after month 8. If one works out the calculations, in fact, it can be seen that if the patient had died suddenly at month 8 when she remained completely independent, her ILS would have been 9.00; thus, 'the greater the fraction of time a patient remains independent during the entire clinical course, the higher the score'. If the patient continues to survive but is dependent, then the correction factor would decrease each month since the independent time would be decreasing as the survival increases. In this situation, the ILS would decrease monthly.

This ILS can be easily modified in two additional ways that might be useful for prospective and retrospective study. One way is to simply multiply ILS × surv. Thus, for this patient, ILS × surv would be

*Table 4.* Calculation of the ILS for PT 1

| Month | KPS | Independence score (0–2) | Correction factor | ILS |
|---|---|---|---|---|
| 1 | 80 | 2 | 1/12 | 0.16 |
| 2 | 80 | 2 | 2/12 | 0.33 |
| 3 | 80 | 2 | 3/12 | 0.50 |
| 4 | 80 | 2 | 4/12 | 0.67 |
| 5 | 80 | 2 | 5/12 | 0.83 |
| 6 | 80 | 2 | 6/12 | 1.00 |
| 7 | 80 | 2 | 7/12 | 1.17 |
| 8 | 80 | 2 | 8/12 | 1.33 |
| 9 | 60 | 1 | 9/12 | 0.75 |
| 10 | 60 | 1 | 10/12 | 0.83 |
| 11 | 40 | 0 | 11/12 | 0.00 |
| 12 | 40 | 0 | 12/12 | 0.00 |
| Score | | | | 7.57 |

*Table 5.* Range of independence measures for survivals of varying lengths

| Survival (months) | ILS range | ILS × surv range | $ILS/ILS_{max}$ range | PTI range |
|---|---|---|---|---|
| 6 | 0–7.0 | 0–42 | 0–100 | 0–100 |
| 12 | 0–13.0 | 0–156 | 0–100 | 0–100 |
| 18 | 0–19.0 | 0–342 | 0–100 | 0–100 |
| 24 | 0–25.0 | 0–600 | 0–100 | 0–100 |

91 (12 months × 7.6). Another way in which to express independence is to express ILS as a fraction of the maximal ILS ($ILS/ILS_{max}$). The maximal ILS will always be equal to the survival in months plus one; thus, it is easily calculated. For this patient, the $ILS/ILS_{max}$ score is 0.58 (7.6/13).

These calculations each reflect slightly different aspects of independence as it relates to survival. The PTI and $ILS/ILS_{max}$ both address the percentage of independent time. A similar result would be obtained for both a patient who has a 4-month survival with 3 months of independence and a 12 month survivor in which the independence time was 9 months. On the other hand, both the ILS and ILS × surv scores are cumulative and as such they are strongly linked to survival. Equivalent numbers for the 4 and 12-month survivors are 3 and 7.5 for the ILS and 12 and 90 for ILS × surv. This is illustrated in Table 5. The range of values for both PTI and $ILS/ILS_{max}$ vary between 0 and 100 for any survival length. By contrast, there is a definable range of values for both ILS and ILS × surv which is survival dependent. A patient who lives 6 months, for example, can never obtain a score higher than 7 and 42 for ILS and ILS × surv, respectively. Furthermore, the ILS × surv score might be best suited for prospective studies because independent survival is doubly rewarded (therefore it increases as a function of the square of survival) and will not change further once the patient becomes dependent.

The advantages of measuring independence can be illustrated by comparing the following two patient scenarios:

> PT 2 is diagnosed with a GBM and is enrolled in one arm of a study. After 8 months, he develops a complication that renders him unable to live independently and his KPS drops to 60. He continues at this level for six months after which he loses the ability to care for himself and requires placement in a nursing home. He then survives another 6 months.
>
> PT 3 is diagnosed with a GBM and is enrolled in the other arm of the study. She continues to function independently (KPS ≥ 70) until tumor progression is noted nineteen months later. She dies one month later.

*Table 6.* Independence measures for PT 2 and PT 3

| | PT 2 | PT 3 |
|---|---|---|
| ILS | 7.1 | 20.0 |
| ILS × surv | 141.0 | 400.0 |
| $ILS/ILS_{max}$ | 0.34 | 0.95 |
| PTI | 0.40 | 0.95 |

From the perspective of most treatment analyses that measure survival, these outcomes are equal in that both of these patients survived 20 months. However, most would agree that the functional results are different. Each of these measures emphasizes this difference; if one calculates the overall scores (Table 6), one can see a divergence so that PT 3's scores are at least twice as high as PT 2's using any of the scoring systems. Thus, a difference would be quantifiable despite the equal survival times and would indicate that the two treatments are not equivalent when assessed by these measures.

A clear superiority of any one of the independence measures over the others is not appreciable in the above case studies. However, a difference can be discerned when one considers the following slightly less realistic scenarios (by today's standards at least).

> PT 4 receives treatment for a GBM. His KPS at enrollment is 90. Six months after initiation, he develops a complication that decreases his KPS to 40. He survives another six months at that level of function.
>
> PT 5 also receives treatment for a GBM. Her KPS at enrollment is 40. Six months after initiation of treatment, she recovers function and her KPS increases to 90. She survives another six months at which time she dies of a myocardial infarction.

Again, although the survivals are equal, there does seem to be a difference in efficacy. PT 4 begins at a high level of independence but then becomes disabled for half her course. PT 5 begins treatment disabled but then recovers independence. This type of difference might be important to identify during a clinical study. If one grades independence using either PTI or $ILS/ILS_{max}$, however, the scores are equal (50 and 0.5, respectively) (Table 7) because there is no way to distinguish independent survival early and late in the

*Table 7*. Independence measures for PT 4 and PT 5

| | PT 4 | PT 5 |
|---|---|---|
| ILS | 3.5 | 9.5 |
| ILS × surv | 42.0 | 114.0 |
| $ILS/ILS_{max}$ | 0.50 | 0.50 |
| PTI | 0.50 | 0.50 |

*Table 8*. Comparison of treatments A and B

| | Relative to A | | | |
|---|---|---|---|---|
| | Surv | ILS | PTI | Comment |
| I | ⇑ | ⇑ | ⇑ | Increased survival, greater time independent |
| II | ⇑ | ⇓ | ⇓ | Increased survival, increased morbidity |
| III | 0 | ⇑ | ⇑ | No inc. survival, greater percentage time independent |
| IV | 0 | ⇑ | 0 | No inc. survival but pt improving toward end of course |

clinical course. Both the ILS and ILS × surv scores for the two patients are much different, however, because of the weighting factor alluded to above. Thus, even in this situation where there is identical survivals and amounts of independent time, there is still a marked difference in ratings.

If such measures are to be utilized in comparing treatments, the following possible positive results can be envisioned (Table 8): (1) a treatment increases survival, PTI ($ILS/ILS_{max}$) and ILS (ILS × surv). This indicates that this treatment improves both quality and quantity of survival; (2) a treatment increases survival but not PTI or ILS. This indicates that the treatment, while improving survival, is doing so at the cost of independence; (3) a treatment does not increase survival but does increase PTI and ILS. This indicates that the treatment results in a greater period of patient independence; (4) a treatment does not increase survival or PTI but does increase ILS. This indicates that the patient status is improving from non-independent to independent over the course of the treatment, even though the treatment itself is not improving survival.

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