# 2

# Gamma Knife Treatment for Patient Harboring Brain Metastases: How to Estimate Patient Eligibility and Survival?

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## 1. Introduction

Gamma Knife radiosurgery is a well validated option for the treatment of brain metastases existing solid evidence reinforcing his role in the management of these tumors.

The result achieved with this technique in terms of tumor control and survival is comparable to results obtained with surgery plus whole brain irradiation. Radiosurgery has the advantages of lower complications; allow treatment of multiple lesions, permits treatment of lesions deeply located or in high functional zones, rapid recovery and lower cost.

Although radiosurgery could be useful for tumor control, increase survival and improved quality of life, there are some clinical situations where the treatment can be considered applicable and justified and others where radiosurgery could not be recommended.

For the estimation of survival many variables have been identified, the most important seem to be the Karnofsky performance status, control of the cancer disease either at the primary site as well as at the systemic level (dissemination) and the number of brain metastases.

Regarding the different variables studied in the present chapter, each variable was arranged in 1 of 5 powered categories according to the number of publications and the agreement of their findings.

1. **Consistent agreement:** there are clear coincidental conclusions among the publications, without controversial findings. In this category is highly possible that the conclusion is right.
2. **Reasonable agreement:** there are more coincidental conclusions among the publications, but with some controversial findings. In this category is quite possible that the conclusion is right.
3. **Some agreement with a trend:** there are less coincidental conclusions among the publications, more controversial findings but a trend is observed. In this category the conclusion could be right but more information is recommended.

4. **Scarce information with a trend:** A trend is observed, but because the small quantity of data more information is recommended for definitive conclusions.
5. **Scarce information with no clear trend or controversial findings:** In these cases more information is absolutely needed for having any conclusion.

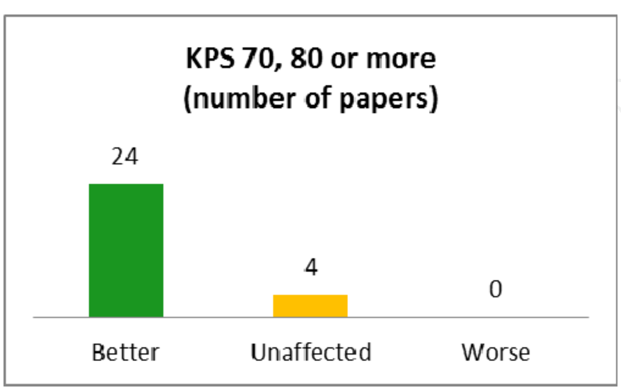
Two plots for each variable were built. The first plot represents the number of publications (papers) supporting the prognostic value of the variable and the second plot shows the number of patients enrolled in such studies: better (variable is a positive prognostic factor), unaffected (variable is not a prognostic factor) and worse (variable is a negative prognostic factor).

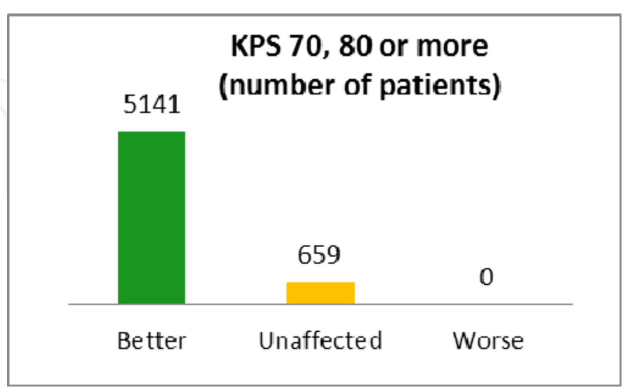
Integrating these variables many stratification systems have been proposed for survival estimation: "Recursive Partitioning Analysis", "Score Index for Radiosurgery in Brain Metastases", Basic Score for Brain Metastases" and "Graded Prognostic Assessment Index". All of these stratifications systems allow estimating survival for a particular patient. In this chapter some more details will be given concerning the most used systems.

## 2. Prognostic factors for survival

### 2.1 Karnofsky performance status (KPS)

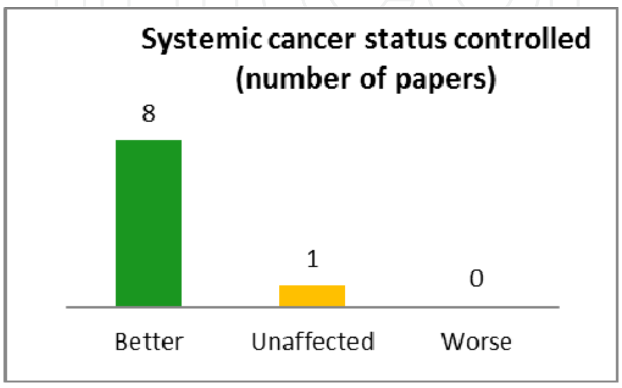
This variable represents the most powerful prognostic factor for survival. The majority of studies show significant influence of KPS in multivariate analysis (Simonová, 2000); Sneed, 2002; Petrovich, 2002; Wowra, 2002; Schoeggl, 2002; Hasegawa, 2003; Muacevic, 2004; Serizawa, 2005; Pan, 2006; Gaudy, 2006; Rades, 2007; Matuiew, 2007; Golden, 2008; Kased, 2009; Da Silva, 2009; Aba cioglu, 2010; Kondziolka 2011; Matsunaga 2011; Liew, 2011). Others authors have communicated significance in univariate studies (Chidel, 2000; Amendola, 2002; Lorenzoni, 2004; Frazier, 2010; Skeie, 2011). A few studies found no influence of KPS in survival (Vesagas, 2002; Hernandez, 2002; Flannery, 2003; Gerosa, 2005), nevertheless, three of these four studies have a small number of patients. A favorable Karnofsky performance status (≥70 or 80) influences positively the survival with "**consistent agreement".**

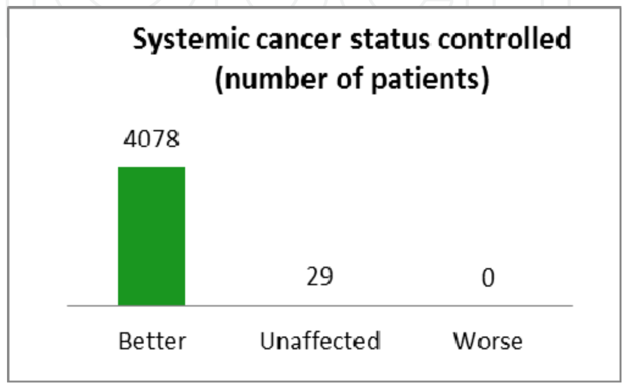



### 2.2 Systemic cancer control status

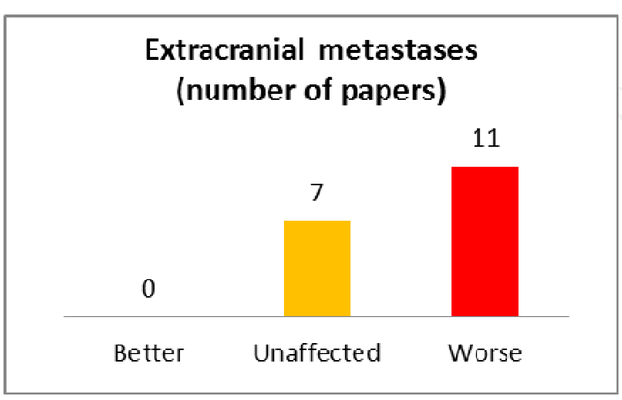
This variable is used for many authors as an evaluation tool for the systemic extracranial integrated situation of the cancer progression, taking into account at once the control of the primary tumor site as well as the existence of extracranial metastases. Others authors prefer to study separately the primary tumor control and the extracranial dissemination. Considering the systemic "extracranial" cancer status, there is also predominance of multivariate analysis proving its positive influence on survival (Petrovich, 2002; Serizawa, 2005; Mathiew, 2007; Kondziolka, 2011; Liew, 2011). In univariate studies 3 communications show this influence too (Hasegawa, 2003; Yu, 2005; Karlsson , 2009). Just one publication (Hernández 2002) found no influence of this variable on survival; this is a publication reporting 29 patients with renal cell carcinoma. The present study found a positive influence of Systemic cancer control status on survival with "**consistent agreement**".

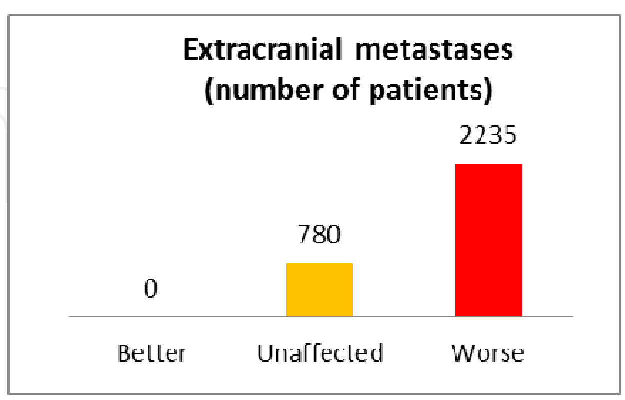



## 2.3 Extracranial metastases

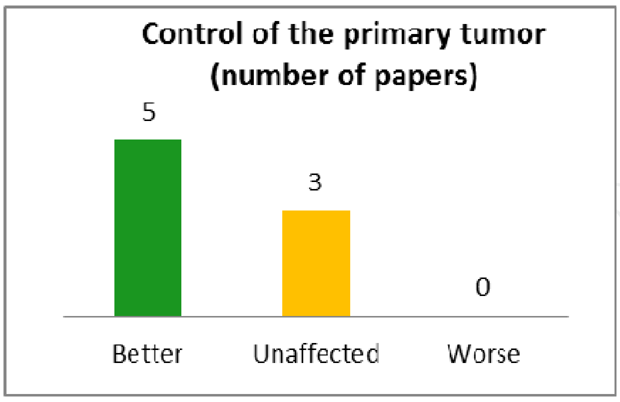
The existence of extracranial metastatic disease has been identified as a negative prognostic factor for survival by the majority of authors either in multivariate studies (Simonová, 2000; Sneed, 2002; Rades, 2007; Golden, 2008; Matsunaga, 2011; Skeie, 2011) and in univariate studies (Chidel, 2000; Wowra, 2002; Lorenzoni, 2004; Yu, 2005; Pan, 2005). Some others manuscripts have shown no influence of this variable on survival (Hernández, 2002; Schoeggl, 2002; Jawahar, 2004; Gaudy, 2006; Kased, 2009; Da Silva, 2009; Kondziolka, 2011). Concerning the existence of extracranial metastases a negative influence on survival was found with "**reasonable agreement**".

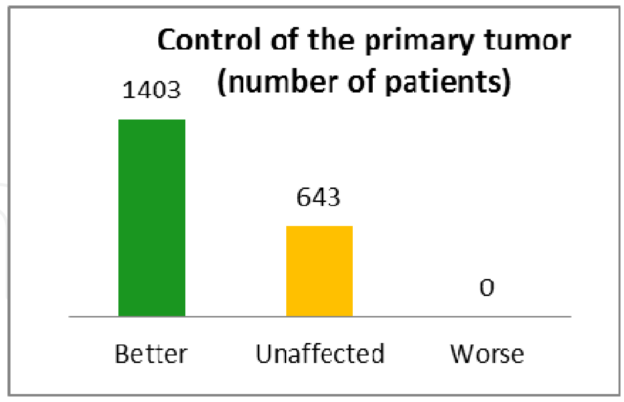



## 2.4 Control of the primary tumor

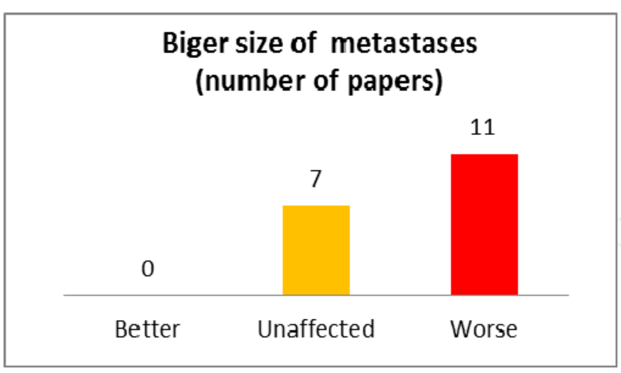
Positive influence of controlled primary site has been reported in multivariate study (Sneed, 2002) and in univariate studies (Lorenzoni, 2004; Jawahar, 2004; Pan, 2005; Kased, 2009). Some studies did not find significant influence (Chidel, 2000; Hernández, 2002; Golden, 2008). A positive effect on survival of the control of the primary tumor was observed with **"reasonable agreement".**

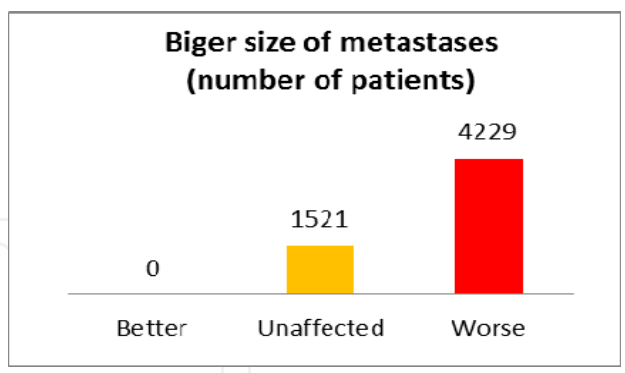



### 2.5 Bigger size of brain metastases

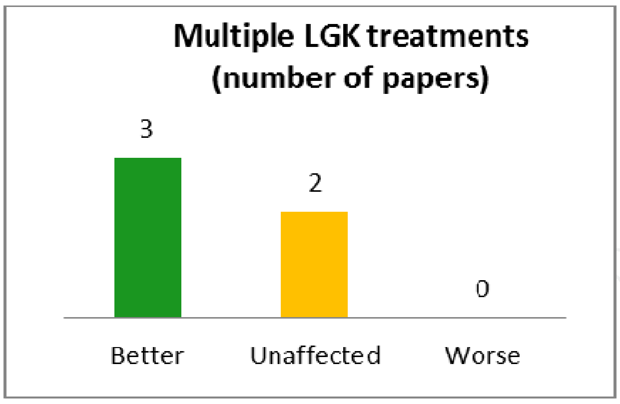
Gamma Knife radiosurgery in general indicated to patients with brain metastases with a diameter up to 3 centimeters or a volume up to 13 cubic centimeters. Some authors consider the diameter of the lesions; others consider volume and others take into account the addition of the volume of all lesions when multiple metastases are treated. An unfavorable influence of larger size of lesions have been reported in multivariate studies (Petrovich, 2002; Gaudy, 2006; Abacioglu, 2010, Kondziolka, 2011; Skeie, 2011) and in univariate studies (Simonová, 2000; Nam, 2005; Feigl, 2006; Karlsson, 2009; Kased, 2009; Frazier, 2010; Liew, 2011). No influence was communicated too (Hernández, 2002; Hasegawa, 2003; Lorenzoni, 2004; Serizawa, 2005; Yu, 2005; Gerosa, 2005; Da Silva, 2009). With regard the size of metastases a bigger size or total tumoral volume was associated with a poor survival with "**reasonable agreement".**

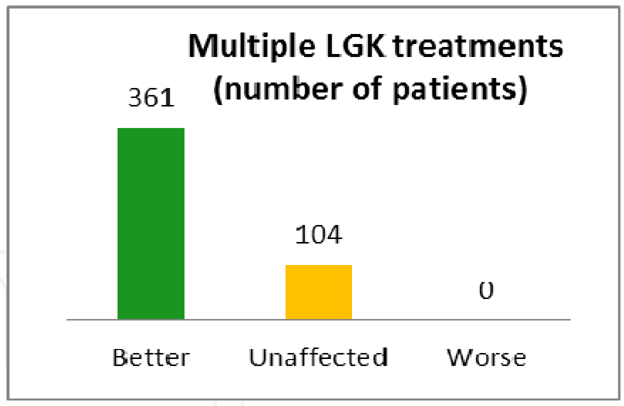



### 2.6 Multiple LGK treatments

After a Gamma Knife treatment for brain metastases, along the time new metastases can develop, in such situations a new Gamma Knife treatment can be offered to these patients, Pan (Pan, 2005) found a positive influence on survival the realization of a new treatments in multivariate analysis. Vesagas (Vesagas, 2002) and Yu (Yu, 2005) found benefice in univariate studies. Conversely, two authors (Hernández, 2002; Wowra, 2002) did not find any effect. Concerning new Gamma Knife treatments, a positive effect on survival has been observed with "**scarce information with a trend".**




### 2.7 Number of brain metastases

The study of this variable is nowadays a challenge and not definitive conclusions have been stated concerning the maximal number of lesions that is reasonable to treat. A negative influence on survival of larger number of metastases have been found in multivariate analysis (Sneed, 2002; Gudy, 2006; Mathiew, 2007; Golden, 2008; Abacioglu, 2010; Liew, 2011) and in univariate ones (Vesagas, 2002; Wowra, 2002; Radbill, 2004; Nam, 2005; Serizawa, 2005; Gerosa, 2005; Feigl, 2006; Karlsson, 2009; Kondziolka, 2011; Matsunaga, 2011). Others investigators on the other hand have informed no influence of this factor on survival (Chidel, 2000; Petrivich, 2002; Hernández, 2002; Schoeggl, 2002; Hasegawa, 2003; Lorenzoni, 2004; Jawahar, 2004; Muacevic, 2004; Yu, 2005; Rades, 2007; Kased, 2009; Frazier, 2010; Skeie, 2011). When on observe the number of patients reported in the papers, it is possible to recognize that in average those manuscripts showing no influence of this variable on survival have less number of patients (put in evidence in the plot dealing with the number of patients). It seems that a higher number of brain metastases affect negatively the survival with "**reasonable agreement".**

With regard the number of brain metastases that is reasonable to treat, the higher level of evidence recommends to treat up four lesions, based in three prospective, randomized studies (Metha, 2005), nevertheless, these 3 studies included patients with a maximum of 3 or 4 lesions, then, patients with higher number of metastases were not studied.

Nam (Nam, 2005) compared a group of 84 patients with up to three brain metastases with 46 harboring 4 or more lesions. The survival of the second group (26 weeks) was significantly less than 48 weeks in the group with up to 3 metastases, Nevertheless when a multivariate analysis was done, only the RPA stratification system was the independent factor affecting survival. The author concluded that the Karnofsky performance status and the RPA stratification should be considered as the most important factors and multiplicity of the lesions alone should not be a reason for withholding Gamma Knife treatment.

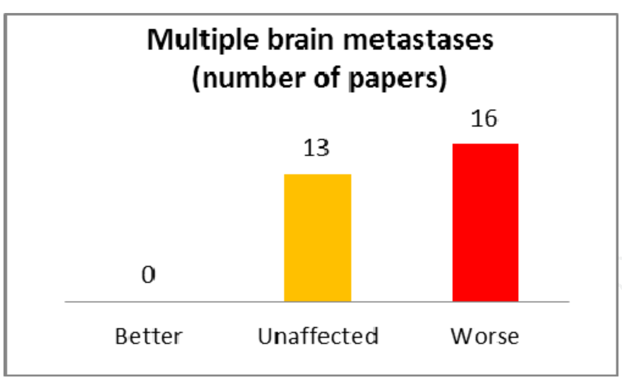
Karlsson (Karlsson, 2009) in a multicentric retrospective study involving 1855 patients found no difference on survival among patients with single or multiple metastases when the the systemic status of the cancer was controlled. Moreover, there was no difference in overall survival comparing patients harboring 2 metastases, 3 to4 metastases, 5-8 metastases or ≥9 metastases.

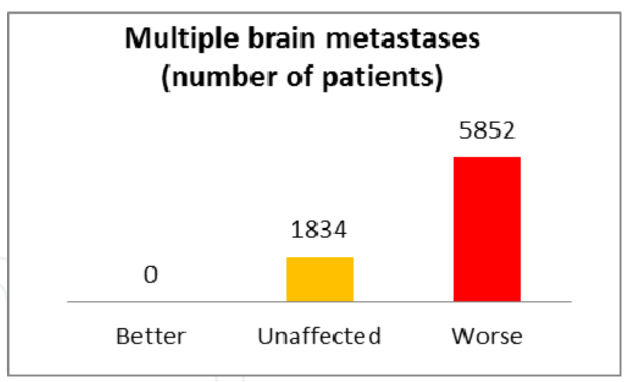
Chang (Chang, 2010), in a series of 323 patients studied the influence on survival of the number of brain metastases. The survivals were not significantly different between patient with 1 to 5 lesions (10 months), 6 to 10 lesions (10 months), 11 to 15 lesions (13 months) and ≥15 lesions (8 months). The author concluded that Gamma Knife radiosurgery may be a good treatment option for local control of metastatic lesions and for improved survival in patients with multiple metastatic brain lesions, even those patients who harbor more than 15 brain metastases.

Serizawa (Serizawa, 2010) studied 778 patients with the following 6 inclusion criteria: newly diagnosed brain metastases, one to 10 lesions, up to 10cc of maximal volume of the larger metastasis, less than 15cc of total intracranial tumoral volume, No evidence on magnetic resonance of meningeal tumor dissemination and a KPS ≥70. There was no upfront use of whole brain irradiation. The overall survival was 8.6 months (0.72 years). There were not differences in survival between patients with single, two, 3 to 4, 5 to 6 and 7 to 10 brain metastases. The study conclusion was that the brain lesion number has no effect on survival.

Some concerns could exist in relation to the total integral dose received by the normal brain when numerous lesions are treated; Yamamoto (Yamamoto, 2002) studied the safety of this treatment situation in 80 patients with 10 or more brain lesion that underwent Gamma Knife treatment. The conclusion was that the cumulative whole brain irradiation was not exceeding the threshold level of normal brain necrosis.

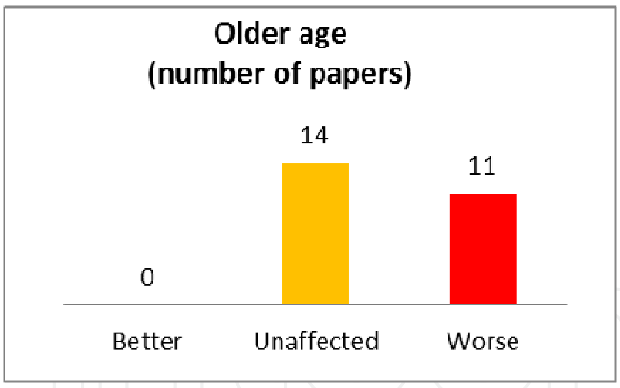
With regard the number of brain metastases it seems that selecting patients with favorable Karnofsky performance status and having a controlled cancer, up to 10 or even up to 15 brain metastases could be reasonable treated, nevertheless, prospective randomized trials are desirable.

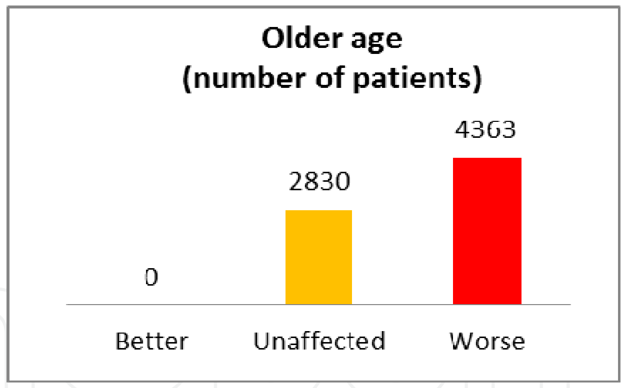



### 2.8 Older age

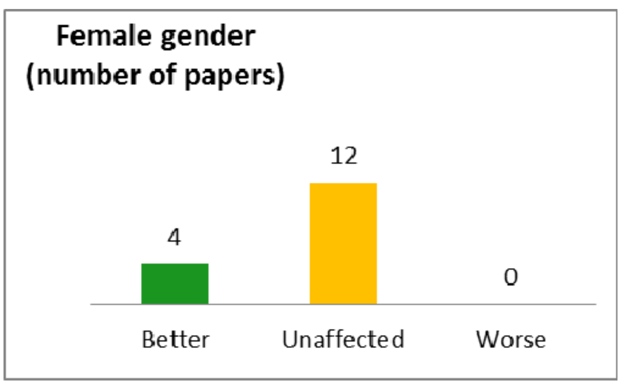
Most manuscripts show no influence of this factor on survival (Simonová, 2000; Petrovich, 2002; Hernández, 2002; Wowra, 2002; Schoeggl, 2002; Lorenzoni, 2004; Jawahar, 2004; Nam, 2005; Serizawa, 2005; Yu, 2005; Gerosa, 2005; Da Silva, 2009; Kondziolka, 2011; Matsunaga, 2011), nevertheless, when the number of patients enrolled in such studies is observed, bigger studies report a negative influence of an older age on survival in multivariate studies (Hasegawa, 2003; Pan, 2006; Gaudy, 2006; Rades, 2007; Golden 2008) as well as univariate ones (Sneed, 2002; Muacevic, 2004; Karlsson, 2009; Kased, 2009; Frazier, 2010; Liew, 2011). Older age influences negatively the survival with **“some agreement with a trend”.**

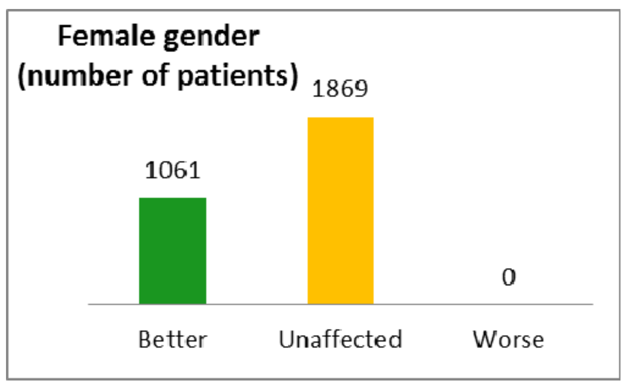



### 2.9 Female gender

Most studies have shown that gender is not a prognostic factor for survival (Wowra, 2002; Schoeggl, 2002; Hasegawa, 2003; Flannery, 2003; Lorenzoni, 2004; Jawahar, 2004; Nam, 2005; Rades, 2007; Mathiew, 2007; Frazier, 2010; Matsunaga, 2011), a few reports have shown positive influence of female gender on survival in multivariate analysis (Serizawa, 2005) and in univariate analysis (Amendola, 2002; Gaudy, 2006; Liew, 2011). It appears that gender do not affect survival with **"Some agreement with a trend".**




### 2.10 Location or histology of the primary tumor

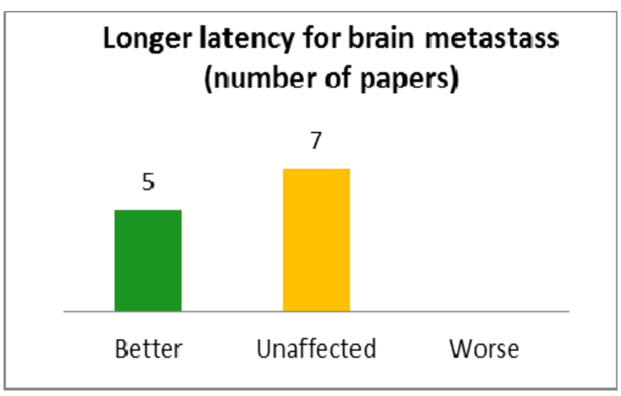
No influence on survival of the primary tumor have been reported (Lorenzoni, 2004; Nam, 2005; Rades, 2007; Frazier, 2010), on the other hand other studies have demonstrated significant association of this variable with survival: Hasegawa (Hasegawa, 2003), in the multivariate analysis found significant lower survival in patients harboring malignant melanoma. In multivariate studies Simonová (Simonová, 2000) reported better survival in patients with breast or renal cancer, Petrovich (Petrovich, 2002) found worse survival in patients with Melanoma and colon cancer and better survival in patients with breast cancer. Vesagas (Vesagas, 2002) communicated better survival in patients with breast carcinoma. "**Scarce information with a trend"** could suggest that primary melanoma or colon cancer could be a negative prognosric factors for survival, and breast could be a positive prognostic factor.

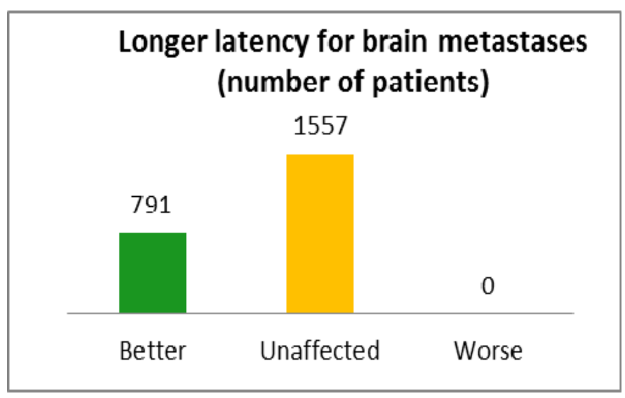
### 2.11 Location of the brain metastases

Kondziolka (Kondziolka, 2011) in a series of 350 patients with breast cancer found a negative influence on survival of the brainstem location in multivariate analysis and a deep brain location of lesions in the univariate study. Gaudy-Marqueste (Gaudy-Marqueste, 2006) found worse survival in a multivariate study in patients harboring deep location of the lesions in a series of 106 patients with melanoma brain metastases. Others authors (Mathiew, 2007, Liew, 2011) have found in multivariate analysis that cerebellar tumor location was associated to poorer survival. Regarding tumor location, **"scarce information with a trend"** suggests that brainstem location, deep brain location and cerebellar location of a melanoma metastasis could be negative prognostic factors.

### 2.12 Latency period to brain metastases diagnose

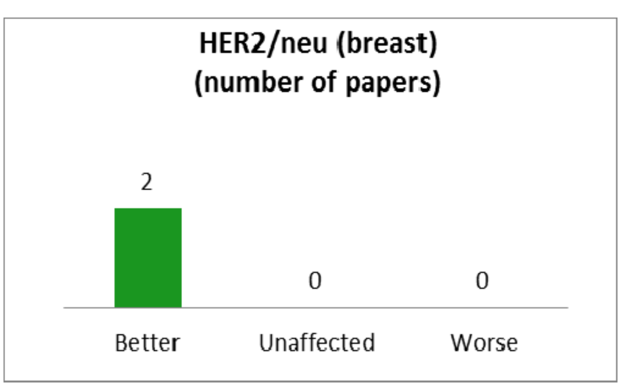
The time elapsed between the diagnosis of the cancer and the moment of the apparition of brain metastases has been propose as a prognostic factor, two studies have shown this association on multivariate analysis (Flanery, 2003; Rades, 2007) and 3 studied on univariate analysis (Yu, 2005; Kased, 2009; Liew, 2011). Seven investigators did not found this influence (Wowra, 2002; Schoeggl, 2002; Muacevic, 2004; Serizawa, 2005; mathiew, 2007; Kondziolka, 2011; Matsunaga, 2011). "**some agreement with a trend"** could suggest that a longer latency period could be associated with longer survival.

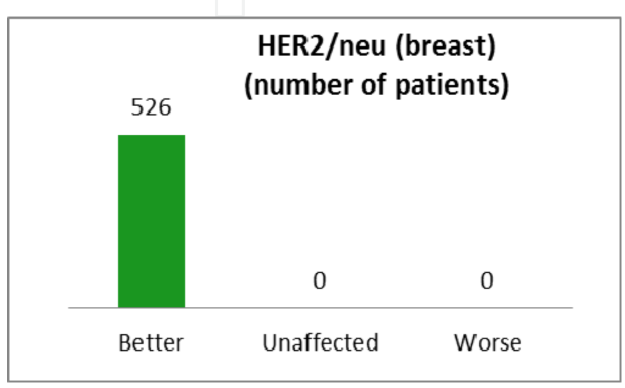



### 2.13 HER2/neu receptors (breast)

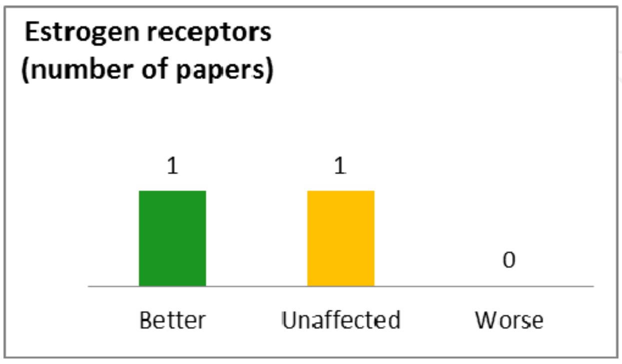
The two publications revised (Kassed, 2009; Kondziolka, 2011) have shown on multivariate analysis a positive association of the existence of the HER2/neu receptors with a favorable survival. In spite of the strong association, it was considered that **"scarce information with a trend"** support this finding.

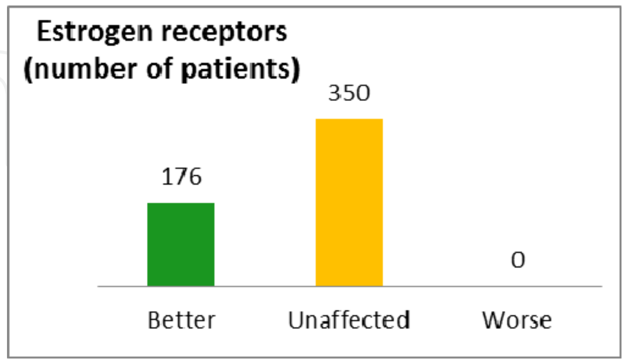


### 2.14 Estrogen receptors (breast)

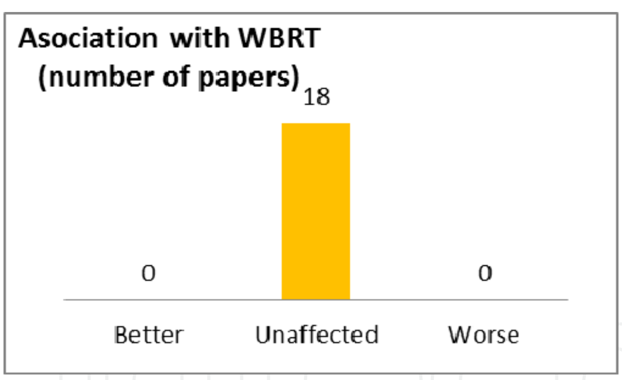
Among two publications revised, one found positive influence of the existence of estrogen receptors on survival (Kassed, 2009). Kondziolka (Kondziolka, 2011) on the other hand, report no influence of this variable on survival. **"Scarce information with a trend"** could suggest that the presence of estrogen receptors could be associates with a longer survival.

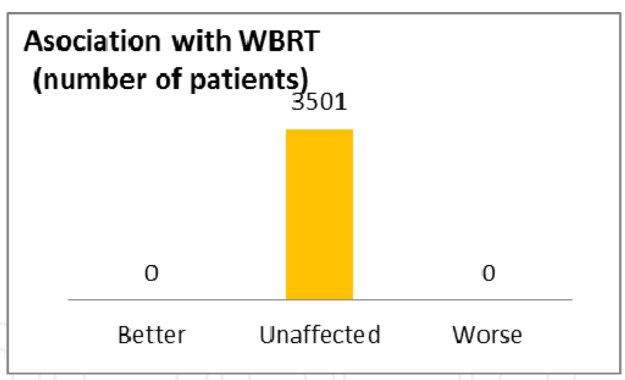



### 2.15 Whole brain radiotherapy

This was the only prognostic factor in the present study where after the analysis of many manuscripts absolute **"consistent agreement"** exists. All the articles revised report no benefit in terms of survival when whole brain radiotherapy is added to Gamma Knife radiosurgery (Chidel, 2000; Sneed, 2002; Petrovich, 2002; Jawahar, 2002; Vesagas, 2002; Schoeggl, 2002; Flannery, 2003; Lorenzoni, 2004; Muacevic, 2004; Nam, 2005; Gerosa, 2005; Pan, 2005; Mathiew, 2007; Da Silva, 2009; Frazier, 2010, Abacioglu, 2010; Liew, 2011; Skeie, 2011).




## 3. Stratification systems used in radiosurgery

The combination and integration of some of the strongest prognostic factors allow creating score systems or stratification systems as tools for patient survival estimation. Many of these have been proposed and all of them have shown to be reliable:

### 3.1 Recursive Partitioning Analysis (RPA)

This system is the most used and widely known. It was proposed initially for patients treated with whole brain radiotherapy (Gaspar, 1997; Gaspar, 2000) and subsequently tested and used for radiosurgery (Sanghavi, 2001; Lorenzoni, 2004; Nieder, 2009). It considers Karnofsky, age, the control of the primary tumor and the existence of extracranial metastases (table 1).

In the study of Sanghavi (Sanghavi, 2001) the median survival for patients in cathegories I, II and III were 16.1, 10.3 and 8.7 months respectively. Subsequently, in the study of Lorenzoni (Lorenzoni 2004) the survival were 27.6, 10.7 and 2.8 months for classes I, II and III respectively. This score system has not good specificity for detecting patients with short survival. In the study of Lorenzoni (Lorenzoni, 2004) the maximal survival reached by patients in the poorer category (RPA III) was 11 months. The advantage of RPA is to be a reliable and easy system. As a disadvantage it could be considered the heterogeneity of the category II and as it was mentioned before it´s relative reduced capacity for detecting patients with very short survival.

| | |
|---|---|
| RPA I: | Karnofsky ≥ 70<br>Age less than 65 years<br>Primary tumor controlled<br>No extracranial metastases |
| RPA II: | Karnofsky ≥ 70<br>Do not fulfill criteria for RPA I |
| RPA III: | Karnofsky < 70 |

Table 1. RPA.

### 3.2 Score Index for Rradiosurgery in brain metastases (SIR)

The "Score index for radiosurgery in brain metastases" (SIR) was described by Weltman (Weltman, 2000; Weltman, 2001) and validated afterwards (Lorenzoni, 2004). It uses five prognostic factors: Age, Karnofsky, systemic disease status, the size and the number of lesions (table 2).

In the article of Weltman (Weltman, 2000), the survivals for patients with scores 8-10, 4-7 and 1-3 were 31.4, 7 and 2.9 months respectively. In the study of Lorenzoni (Lorenzoni, 2004), the survivals were 27.7, 10.8, 4.6 and 2.4 for patients with scores 8-10, 5-7, 4 and 1-3 respectively. In the study of Lorenzoni SIR was the best system according to statistic significance. This score system represents quite a good specificity for detecting patients with short survival; in the study of Lorenzoni (Lorenzoni, 2004) the maximal survival reached by patients in the poorer category was 7 months. SIR has a more complex format what could be considered a relative disadvantage.

| Variable | 0 | 1 | 2 |
|---|---|---|---|
| Age | ≥60 | 51-59 | ≤50 |
| Karnofsky | ≥50 | 60-70 | ≥80 |
| Systemic disease status | PD | PR-SD | CR-NED |
| Large lesión volume (cc) | >13 | 5-13 | <5 |
| Number of lesions | ≥3 | 2 | 1 |
| | | (Range: 0 to 10 points) | |

PD: progressive disease, PR: partial remission, SD: stable disease, CR: complete remission, NED: no evidence of disease.

Table 2. SIR.

### 3.3 Basic Score for Brain Metastases (BSBM)

The Basic score for brain metastases was described by Lorenzoni (Lorenzoni, 2004; Lorenzoni, 2009). It was conceived as an attempt to develop a score system with a good balance between reliability and simplicity. It takes into account the three most powerful prognostic factors for survival (karnofsky, Control of the primary tumor and the existence of extracranial metastases), assigning on point for each factor (Table 3). Additionally, when associations of variables were analyzed in the original study (Lorenzoni, 2004), an "intrinsic" representation of other two linked variables (number of lesions and size of lesions) was demonstrated: 1- The number of lesions is represented by the existence of extracranial metastases (60% of patients with 3 or more brain metastases had extracranial metastases versus just 36% of patients with one or two brain metastases, p=0.04) and 2- The maximal size of lesions is represented by the Karnofsky (50% of patients with a brain metastasis volume ≥ 9 cc had an unfavorable Karnofsky index versus just 16% of patients with a maximal volume less than 9cc, p=0.01). This system does not take into account the patient age.

In the original manuscript of Lorenzoni (Lorenzoni, 2004), the survival was undefined (more than 50% of patients alive at 32 months) in patients with scores 3, 13.1 months for score 2, 3.3 months for score 1 and 1.9 months for score 0. This score system presented the best specificity for detecting patients with short survival: the maximal survival reached by any patient in the poorer category (score 0) was only 4 months. The main advantages of BSBM is it extreme simplicity and as it was mentioned, the high capacity for detecting patients with a very poor life expectancy.

| | |
|---|---|
| Karnofsky ≥ 80 | 1 point |
| Primary tumor controlled | 1 point |
| No extracranial metastases | 1 point |
| | (Range: 0 to 3 points) |

Table 3. BSBM.

### 3.4 Others score systems for radiosurgery

Some other authors have proposed systems such as GGS (Golden, 2008), and a Melanoma-specific system, MM.GKR (Gaudy-Marqueste, 2006).

## 4. Stratification systems tested with whole brain radiotherapy databases

Some systems have been developed recently based on databases of patients treated with fractionated whole brain irradiation but not jet tested for stereotactic radiosurgery. The graded prognostic assessment index (GPA) and some primary tumor-specific scores are the most common. All of these systems could be useful for patients treated with radiosurgery but its efficiency must be proved. Some differences could be found with regard to statistical testing, in fact, the survival of patients treated with radiosurgery could be twice compared with the survival of patients treated with whole brain radiotherapy (Sanghavi, 2001).

### 4.1 Graded Prognostic Assessment Index (GPA)

Proposed by Sperduto (Sperduto, 2008) using the RTOG database of 1960 patients treated with whole brain radiotherapy from five randomized prospective trials. It considers four prognostic factors: Age, Karnofsky, number of lesions and the existence of extracranial metastases (figure 4). GPA has also a more complex format that could be considered a relative disadvantage.

In the original article of Sperduto (Sperduto, 2008), in addition to the description of the GPA, the author performed a study using also others pre-existing score systems (RPA, SIR and BSBM). According to RPA, the survivals reported were 7.7, 4.5 and 2.3 months for patients in the categories I, II and III respectively.

Using SIR, the survivals were 8.8, 6 and 2.1 months for the scores 8-10, 4-7 and 1-3 respectively. With regard BSBM, the survivals were 7, 5.1, 3.4 and 2.2 months for scores 3, 2, 1, and 0 respectively.

In the GPA proposed the survivals were 11, 6.9, 3.8 and 2.6 months for patients with scores 3.5-4, 3, 1.5-2.5 and 0-1.

Nieder (Nieder, 2008) tested this score in 232 patients treated with whole brain radiotherapy. According to RPA, the survivals reported were 10.8, 3.2 and 2 months for patients in the categories I, II and III respectively. Using SIR, the survivals were 8.7, 4.1 and 1.7 months for the scores 8-10, 4-7 and 1-3 respectively. With regard BSBM, the survivals were 11.5, 3.9, 2.4 and 1.9 months for scores 3, 2, 1, and 0 respectively. In the GPA proposed the survivals were 10.3, 5.6, 3.5 and 1.9 months for patients with scores 3.5-4, 3, 1.5-2.5 and 0-1.

Concerning the capacity for detecting patients with the poorer survival, the most efficient system was the "basic score for brain metastases" (BSBM) (Nieder, 2010; Villà, 2011).

| Variable | 0 | 0.5 | 1 |
|---|---|---|---|
| Age | ≥60 | 51-59 | ≤50 |
| Karnofsky | <70 | 70-80 | 90-100 |
| Number of lesions | >3 | 2-3 | 1 |
| Extracranial metastases | yes | - | No |
| | | (Range: 0 to 4 points) | |

Table 4. GPA.

### 4.2 Others primary tumor-specific score systems tested for whole brain radiotherapy

Other authors have proposed primary-specific systems, such as Breast cancer-specific score (Nieder, 2009), Breast-GPA (Sperduto, 2011), and Melanoma-GPA (Sperduto, 2010) among others.

## 5. Conclusions

Gamma Knife radiosurgery is a highly effective method for controlling brain metastases and it can be useful and safely offered to those patients that fulfill the following conditions:

1. Karnofsky performance status ≥ 70,
2. Tumors with a maximum diameter of 3 centimeters or a maximum volume of 13 cubic centimeters.
3. No significant mass effect and absence of intracranial hypertension.
4. No evidence of leptomeningeal dissemination.
5. Up to 10 to 15 brain lesions (more recent observational non randomized studies) or up to 4 brain lesions (prospective randomized trials).
6. Up to 15 cubic centimeters of total tumor mass.
7. Systemic cancer diseases well controlled (desirable but not excluding condition).

Many prognostic factors for survival have been identified, among them, Karnofsky performance status (KPS) have been considered the most powerful followed by the status of the cancer disease (overall systemic cancer status or a separate analysis of the control of the primary site and the existence of extracranial metastases).

The integration of many prognostic factors has originated score systems for survival estimation, all of these scores are reliable, and the election of one of them should be according with the best compromise with reliability and simplicity. Some scores must be proved for radiosurgery and probably in the future new or improved specific scores will be available and tested for stereotactic radiosurgery.

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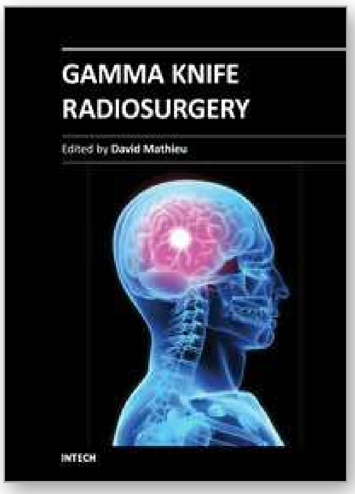


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Gamma knife radiosurgery is a minimally-invasive treatment alternative for intracranial disorders, including tumors, vascular malformations, facial pain and epilepsy. This book will allow the reader to learn when gamma knife radiosurgery is appropriate and what to expect as treatment results.