Focal treatments versus whole brain irradiation for patients with brain metastases

Alba Fiorentino
Radioterapia Oncologica
Ospedale Sacro Cuore Don Calabria, Negrar –Verona
Direttore: Dott. F. Alongi

Brain metastases

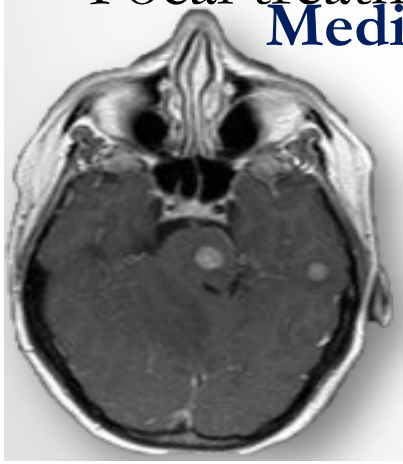
20-40% of cancer patients

Median Overall survival (without therapies): 1 month

Focal treatments versus whole brain irradiation for patients with brain metastases

Median Overall survival (with therapies): 3-6 months

2-yr OS: 10 %

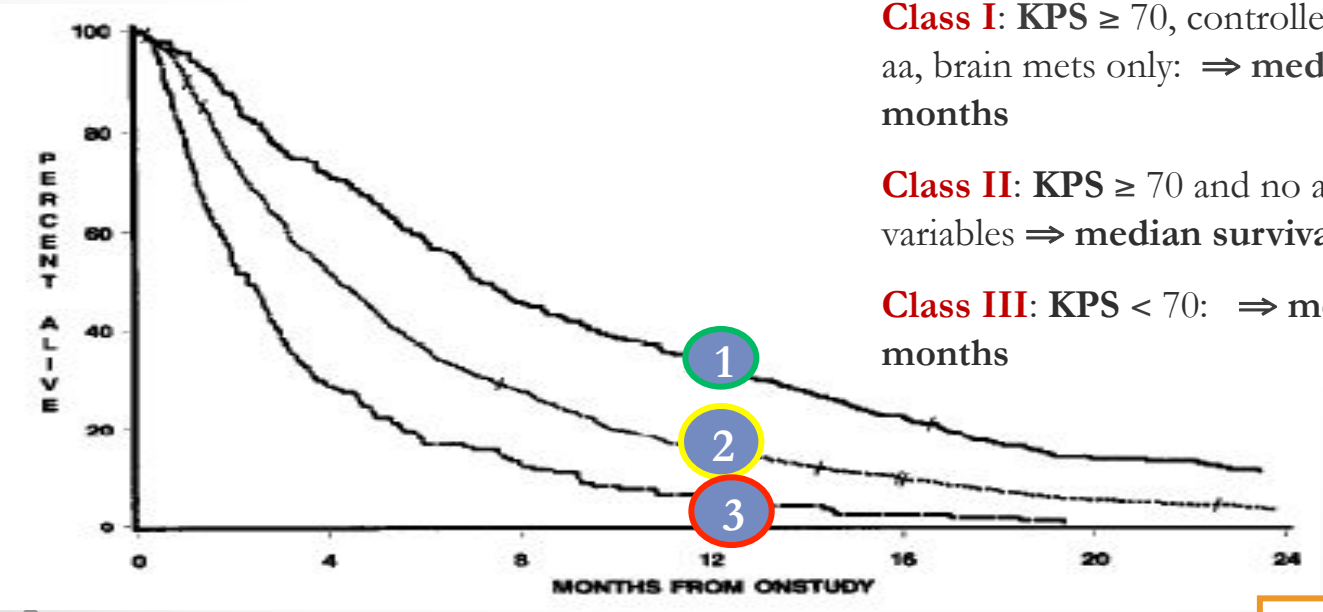


Baisden J. M., Neurosurg Focus 22 (3): 1, 2007

Focal treatments versus whole brain irradiation for patients with brain metastases

Prognosis

RTOG Recursive Partitioning Analysis (RPA)



Class I: **KPS** ≥ 70, controlled primary, year < 65 aa, brain mets only: ⇒ **median survival: 7.1 months**

Class II: **KPS** ≥ 70 and no above mentioned variables ⇒ **median survival: 4.2 months**

Class III: **KPS** < 70: ⇒ **median survival: 2.3 months**

Gaspar L. et al. IJROBP, '97

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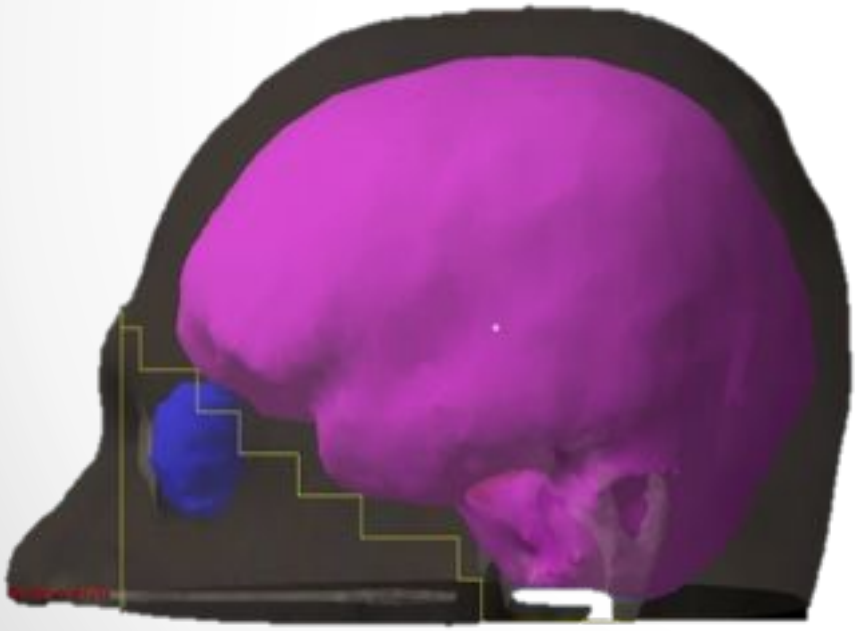
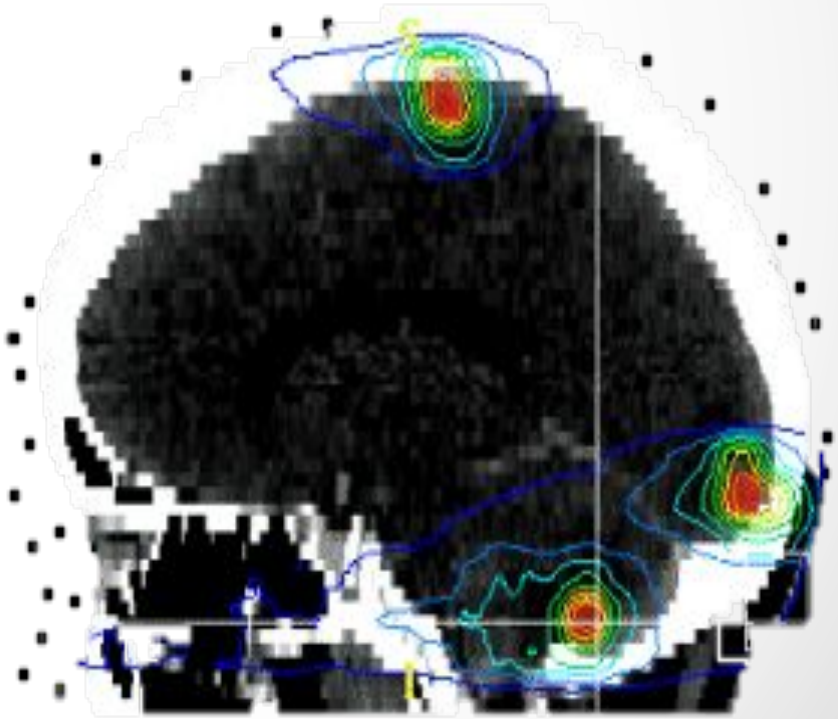
Focal treatments versus whole brain irradiation for patients with brain metastases

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2014
Limited (1-3) Metastatic Lesions

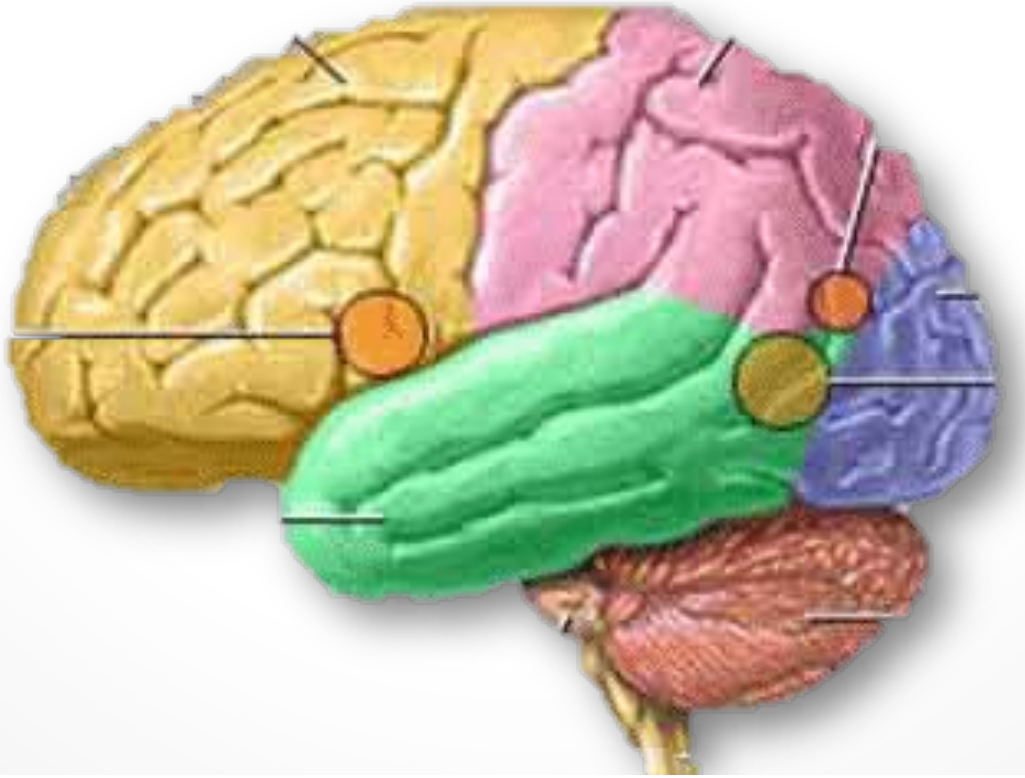
Purpose





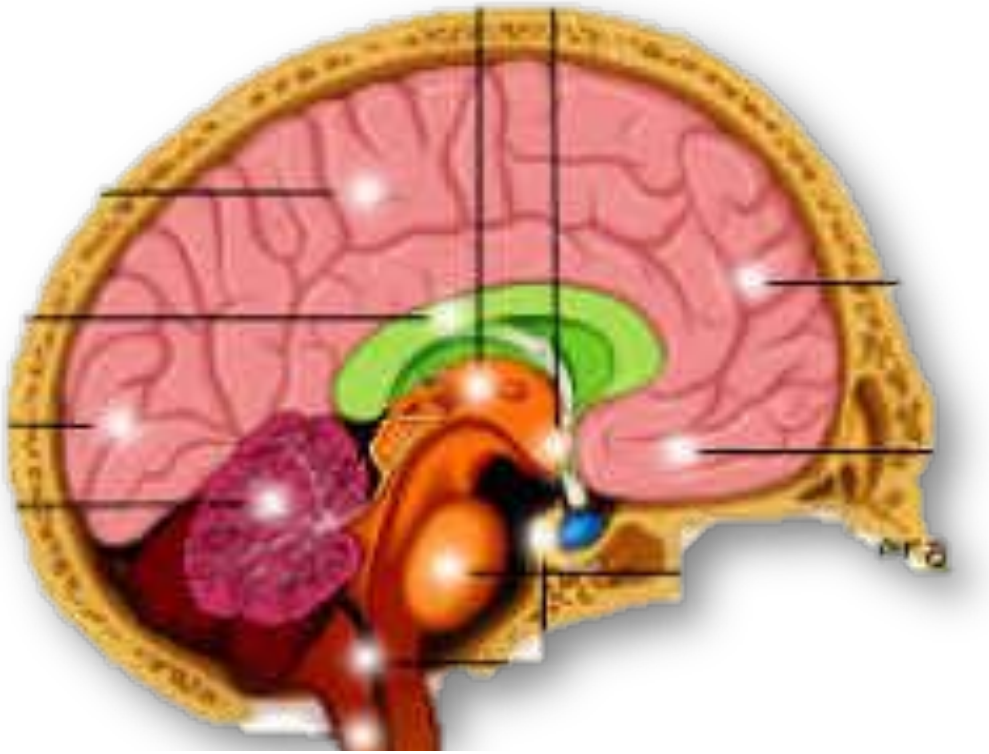
Focal treatments versus whole brain irradiation for patients with brain metastases

Purpose
SRS-SRT



Focal treatments versus whole brain irradiation for patients with brain metastases

Purpose
+ WBRT



Focal treatments versus whole brain irradiation for patients with brain metastases

SRS + WBRT

VS

SRS alone + F-U

Overall survival

Progression free survival

Toxicity

Focal treatments versus whole brain irradiation for patients with brain metastases

SRS + WBRT

Or

SRS alone + Follow-UP

PROS

Focal treatments versus whole brain irradiation for patients with brain metastases

SRS + WBRT

Or

SRS alone + Follow-UP

PROS

XXIV CONGRESSO NAZIONALE AIRO 2014

Focal treatments versus whole brain irradiation for patients with brain metastases

SRS + WBRT

VS

SRS alone + F-U

Overall survival

Focal treatments versus whole brain irradiation for patients with brain metastases

Randomized phase III trials: SRS vs SRS + WBRT

	# of patients	Overall survival (months)
Aoyama 2006	**132** **(67 SRS vs 65 SRS+WBRT)**	**No difference**
Chang 2009	**58** **(30 SRS vs 28 SRS+ WBRT)**	
Kocher & Soffietti 2010	**359** **(179 SRS/Surg. vs 180 SRS/ Surg + WBRT)**	

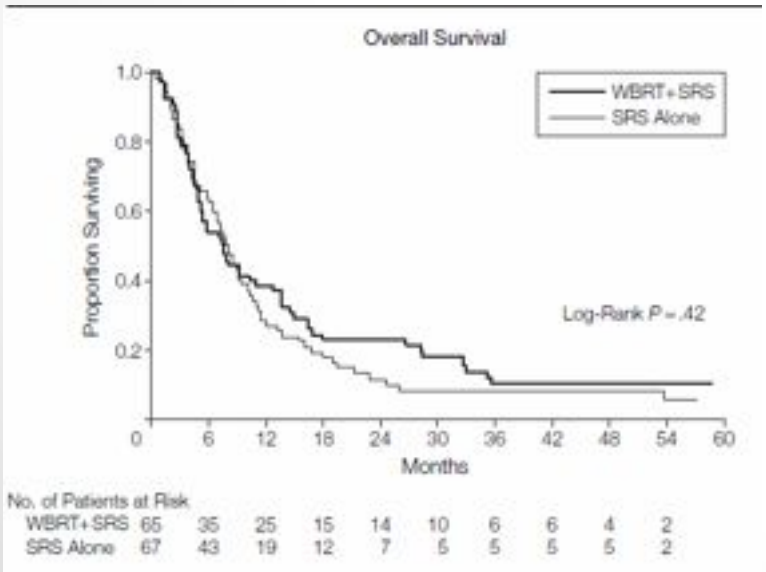
Focal treatments versus whole brain irradiation for patients with brain metastases

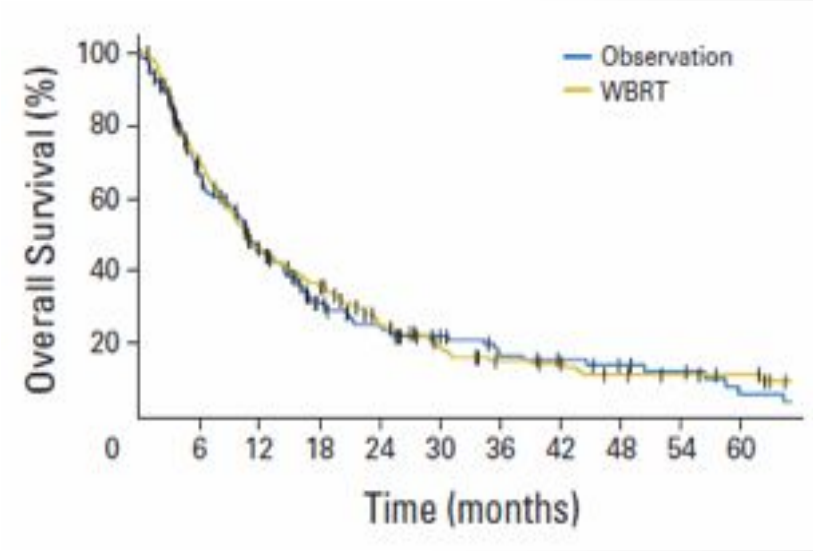
Stereotactic Radiosurgery Plus Whole-Brain Radiation Therapy vs Stereotactic Radiosurgery Alone for Treatment of Brain Metastases

A Randomized Controlled Trial

Hidefumi Aoyama, MD, PhD

Context In patients with brain metastases, it is unclear whether adding up-front whole-





Adjuvant Whole-Brain Radiotherapy Versus Observation After Radiosurgery or Surgical Resection of One to Three Cerebral Metastases: Results of the EORTC 22952-26001 Study

Martin Kocher, Riccardo Soffietti, Ufuk Abacioglu, Salvador Villà, Francois Fauchon, Brigitta G. Baumert, Laura Fariselli, Tzahala Tzuk-Shina, Rolf-Dieter Kortmann, Christian Carrie, Mohamed Ben Hassel, Mauri Kouri, Egils Valeinis, Dirk van den Berge, Sandra Collette, Laurence Collette, and Rolf-Peter Mueller

Focal treatments versus whole brain irradiation for patients with brain metastases

A Meta-Analysis Evaluating Stereotactic Radiosurgery, Whole-Brain Radiotherapy, or Both for Patients Presenting with a Limited Number of Brain Metastases

May Tsao, MD[1]; Wei Xu, PhD[2]; and Arjun Sahgal, MD[1,3]

Cancer 2012;118:2486-93.

Study or Subgroup	log[Hazard Ratio]	SE	Weight	Hazard Ratio IV, Fixed, 95% CI
Aoyama 2006	0.315	0.193	72.2%	1.37 [0.94, 2.00]
Chang 2009	-0.904	0.311	27.8%	0.40 [0.22, 0.74]
Total (95% CI)			**100.0%**	**0.98 [0.71, 1.35]**

Heterogeneity: Chi² = 11.09, df = 1 (P = 0.0009); I² = 91%
Test for overall effect: Z = 0.15 (P = 0.88)

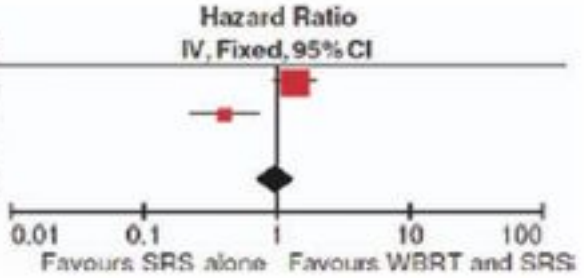


Figure 3. OS: SRS alone versus WBRT plus SRS boost.

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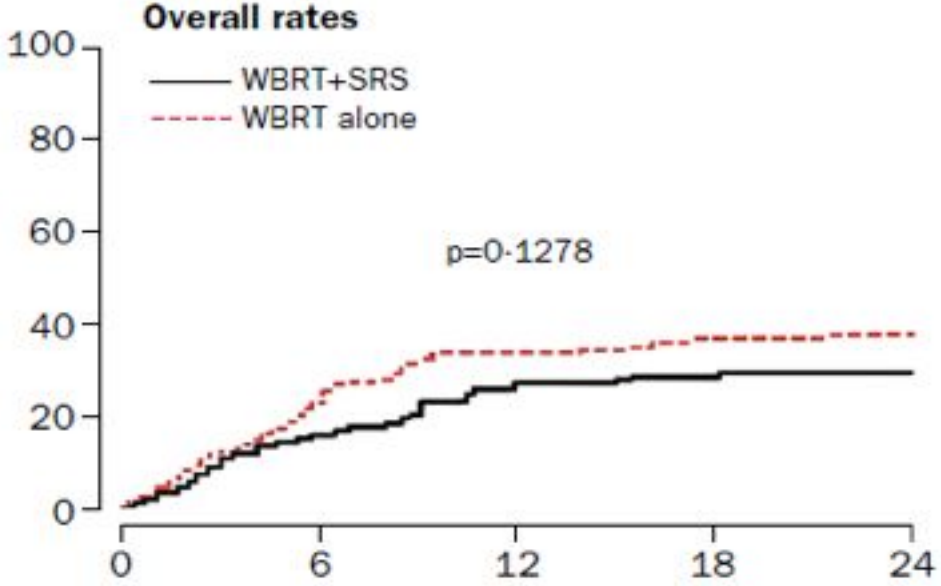
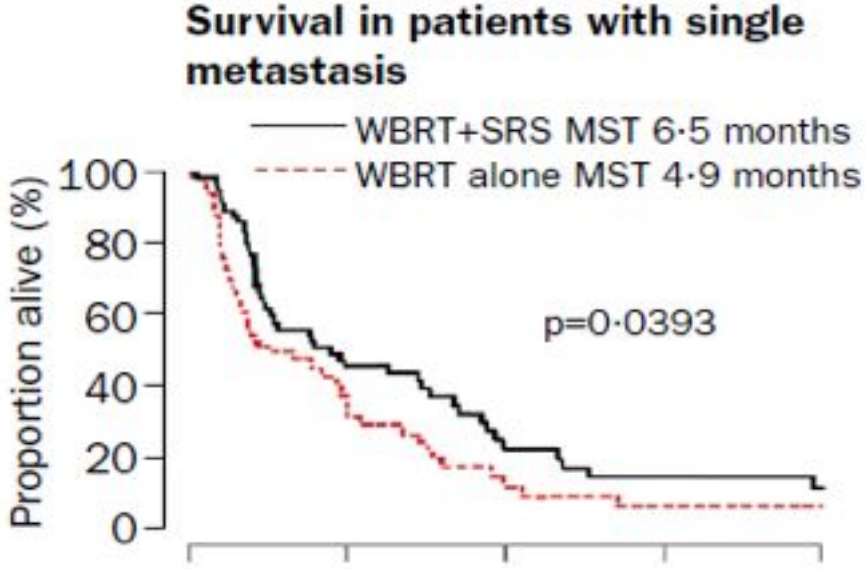
Focal treatments versus whole brain irradiation for patients with brain metastases

Whole brain radiation therapy with or without stereotactic radiosurgery boost for patients with one to three brain metastases: phase III results of the RTOG 9508 randomised trial

David W Andrews, Charles B Scott, Paul W Sperduto, Adam E Flanders, Laurie E Gaspar, Michael C Schell, Maria Werner-Wasik, William Demas, Janice Ryu, Jean-Paul Bahary, Luis Souhami, Marvin Rotman, Minesh P Mehta, Walter J Curran Jr

WBRT 37,5Gy in 15fr
SRS 15-24Gy





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Focal treatments versus whole brain irradiation for patients with brain metastases

El Gantery *et al. Radiation Oncology* 2014, **9**:116

Management of brain metastases with stereotactic radiosurgery alone versus whole brain irradiation alone versus both

RADIATION ONCOLOGY

Subgroup analysis indicated that WBRT plus SRS provided survival benefit to patients whose largest brain metastasis was 3 cm in diameter (median survival was 15 months vs 8 months vs 5 months for WBRT + SRS vs SRS vs WBRT, respectively with statistically significant *P value = 0.002*), also subgroup analysis showed that patients with controlled primary who recieved WBRT plus SRS had survival benefit compared to SRS vs WBRT (median survival was 12 months vs 8 months vs 5.5 months for WBRT + SRS vs SRS vs WBRT, respectively with statistically significant *P value = 0.027*).

Focal treatments versus whole brain irradiation for patients with brain metastases

WBRT: is necessary in Brain metastases, yet?

. . .

Improving OS

NO ?

80% of patients died for the primay disease.

Focal treatments versus whole brain irradiation for patients with brain metastases

	Surgery	Surgery +WBRT	Δ	*p*
Patiens number	46	49	-	-
% Brain Recurrence	70	18	52	<0.001
(%) Recurrence at the site of the original metastasis	46	10	36	<0.001
% Neurological death	44	14	39	<0.003
Median SVV (wks)	48	43	6	0.39

Patchell *JAMA* 1998

Focal treatments versus whole brain irradiation for patients with brain metastases

SRS + WBRT

VS

SRS alone + F-U

Progression free survival

Focal treatments versus whole brain irradiation for patients with brain metastases

Randomized phase III trials: SRS vs SRS + WBRT

	# of patients	Intracranial progression free survival (1 yr)
Aoyama 2006	132 (67 SRS vs 65 SRS+WBRT)	Favour to SRS + WBRT
Chang 2009	58 (30 SRS vs 28 SRS+ WBRT)	
Kocher & Soffietti 2010	359 (179 SRS/Surg. vs 180 SRS/ Surg + WBRT)	

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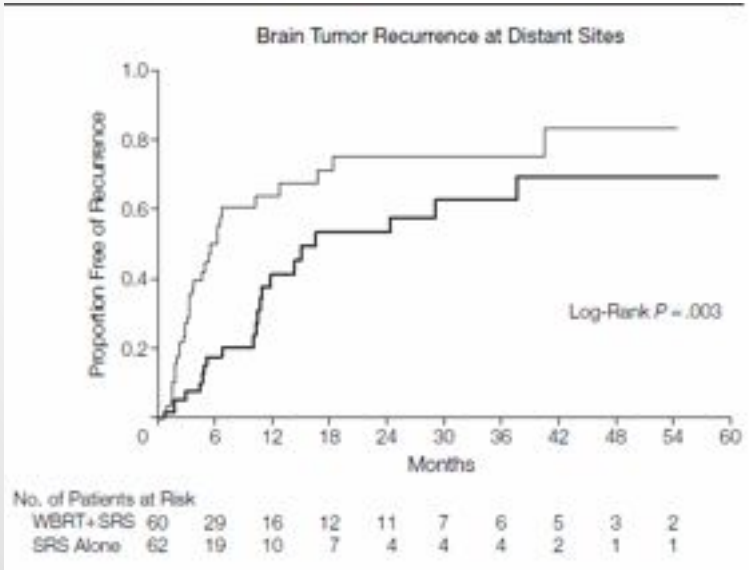

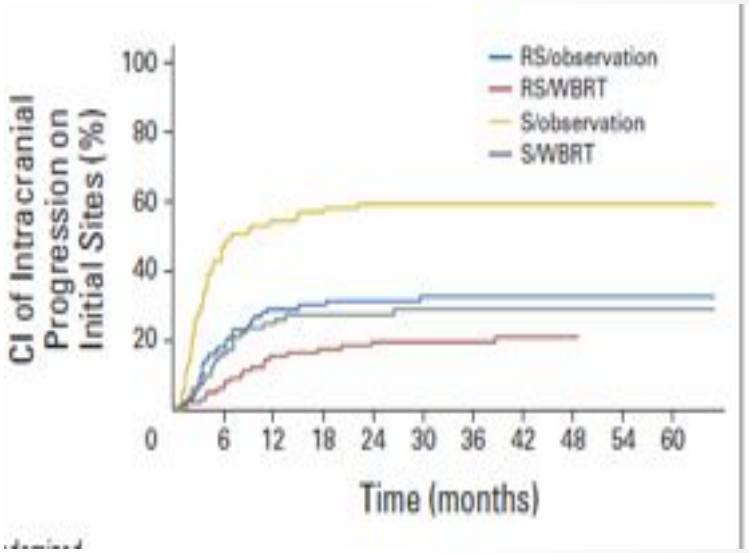

Adjuvant Whole-Brain Radiotherapy Versus Observation After Radiosurgery or Surgical Resection of One to Three Cerebral Metastases: Results of the EORTC 22952-26001 Study

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SRS + WBRT
Or
SRS alone + Follow-UP
PROS

Focal treatments versus whole brain irradiation for patients with brain metastases

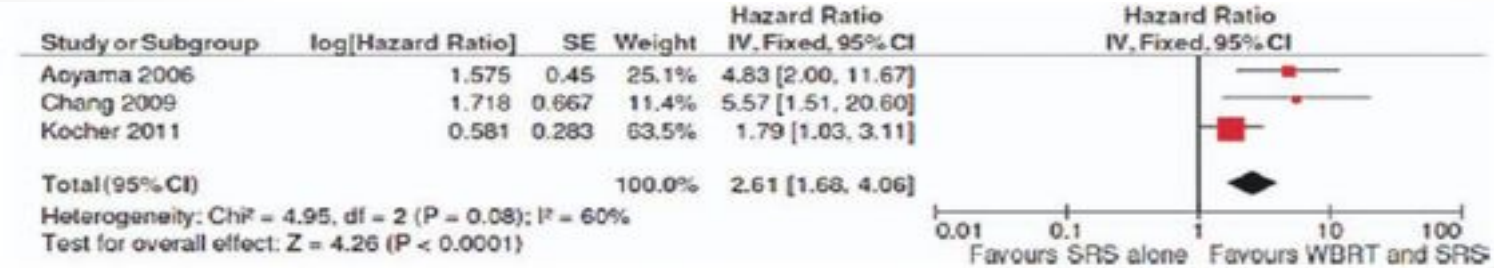

Figure 4. Local Control SRS alone versus WBRT plus SRS boost.

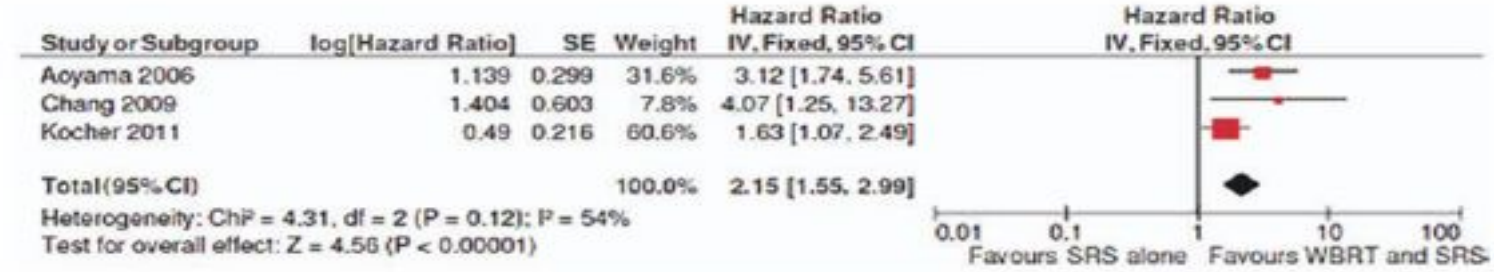

Figure 5. Distant brain control: SRS alone versus WBRT plus SRS boost.

Focal treatments versus whole brain irradiation for patients with brain metastases

Stereotactic Radiosurgery Plus Whole-Brain Radiation Therapy vs Stereotactic Radiosurgery Alone for Treatment of Brain Metastases

A Randomized Controlled Trial

Aoyama, JAMA 2006-vol 295, no 21

	SRS	SRS+WBRT	p
Median SVV (mts)	8	7.5	NS
12-mts Brain Recurrence (%)	76.4	46.8	0.001
Salvatage Brain Treatment (%)	43.2	15.4	0.001

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Focal treatments versus whole brain irradiation for patients with brain metastases

Article in Press

Patterns of distant brain recurrences after radiosurgery alone for newly diagnosed brain metastases: Implications for salvage therapy

Jaap D. Zindler[1], Ben J. Slotman, Frank J. Lagerwaard
Department of Radiation Oncology, VU University Medical Center, Amsterdam, The Netherlands
[1] Current working address: Department of Radiation Oncology, Maastro Clinic, Maastricht, The Netherlands.

Radiotherapy & Oncology
European Society of Radiotherapy and Oncology

Conclusions

In this study of patients treated with RS alone, only 25% of treated patients needed salvage treatment for DBR, and ultimately only 18% of all patients underwent WBRT at any time during follow-up. A three-monthly MRI follow-up scheme identifies DBR at an early stage with respect to size and number of lesions, and most patients were asymptomatic at radiological diagnosis.

?

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Radiotherapy &Oncology
European Society of Radiotherapy and Oncology

Results

Actuarial DBR rates at 6, 12 and 24 months in the remaining 423 patients were 21%, 41% and 54%, respectively, with a median time to DBR of 5.6 months. In 42% of DBR, a single new lesion was seen, in 70% there were ≤3 new lesions. Median diameter of the DBR was 6 mm; 97% of lesions were ≤30 mm. Salvage therapy was delivered in 82% of DBR patients, consisting of WBRT (46%), repeated RS (27%), or systemic treatment (9%). A RPA classification system (DBR-RPA), based on WHO performance status and interval between initial RS and diagnosis of DBR, was developed to estimate life expectancy after the development of DBR, which can be used to guide salvage therapy.

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Focal treatments versus whole brain irradiation for patients with brain metastases

Journal of Neuro-Oncology
June 2014, Volume 118, Issue 2, pp 329-334

Date: 10 Apr 2014

Whole brain reirradiation and concurrent temozolomide in patients with brain metastases

Giuseppe Minniti, Claudia Scaringi, Gaetano Lanzetta, Alessandro Bozzao, Andrea Romano, Vitaliana De Sanctis, Maurizio Valeriani, Mattia Osti, Riccardo Maurizi Enrici

27 pts
Re-WBRT:
25Gy in 10 fr

The median overall survival after the second course of WBRT was 6.2 months and the median time to progression was 5.5 months. Eight patients experienced complete resolution of symptoms, 9 patients had a significant improvement, and 6 patients had no change in their neurologic function. Four patients had further deterioration after reirradiation. Overall, 85 % of patients improved or maintained their neurologic status. No severe acute toxicity during or after the second course of WBRT reirradiation was observed. On multivariate analysis with the Cox proportional hazards model, stable or absent extracranial metastases ($p = 0.005$) and response to treatment ($p = 0.01$) were independent favorable prognostic factors for survival. The median and 12-month survival rates were 12 months and 50 % in patients with stable or absent extracranial disease and 4.6 months and 7 % in those with progressive extracranial disease ($p = 0.001$).

Focal treatments versus whole brain irradiation for patients with brain metastases

WBRT: is necessary in Brain metastases, yet?

. . .

Improving PFS

SI

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Focal treatments versus whole brain irradiation for patients with brain metastases

SRS + WBRT

VS

SRS alone + F-U

Overall survival

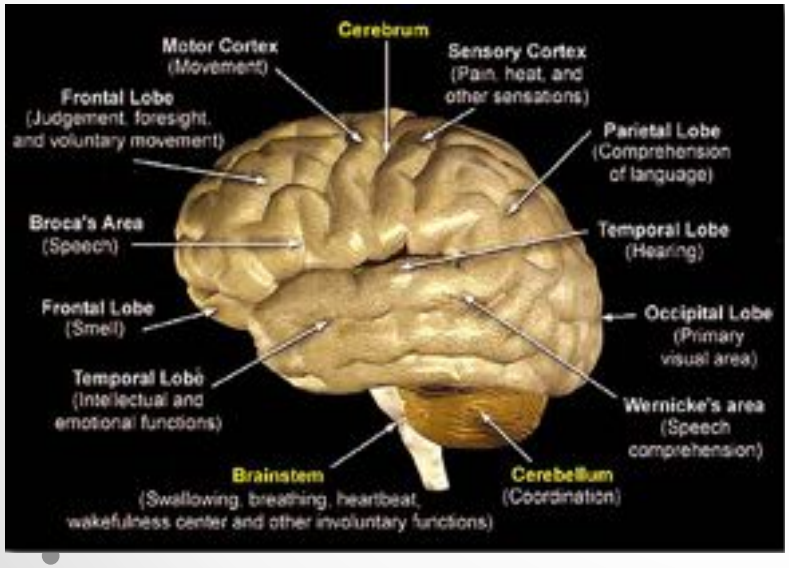
Progression free survival

Toxicity

Focal treatments versus whole brain irradiation for patients with brain metastases

WBRT and Neurocognitive Disorders

The patogenesis of irradiation-induced neurocognitive dysfunction is related to:



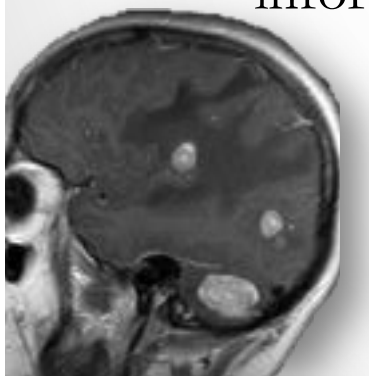
- Microvascular ischemia or infarct
- Alteration of synaptic composition
- Depletion of stem-cell necessary for neurogenesis

Shill L., IJROBP 71(2): 526, 2008

Focal treatments versus whole brain irradiation for patients with brain metastases

WBRT and Neurocognitive Disorders

- Cognitive decline occurse in 50% of pts who lives longer than 6 mts after treatment (RPA class I: median OS 7.1 mts)
- Neurocognitive decline is secondary also to chemotherapy, surgery, concurrent medical illness and neuropathologic comorbility
- Hippocampal-dependent functions of learning, memory and spatial informations processing are preferentially affected by radiotherapy



Abayomi O.K., Acta Oncol 35: 659, 1996
Laack N.N., Sem Oncol 31: 702, 2004
Shill L., IJROBP 71(2): 526, 2008

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Focal treatments versus whole brain irradiation for patients with brain metastases

Stereotactic Radiosurgery Plus Whole-Brain Radiation Therapy vs Stereotactic Radiosurgery Alone for Treatment of Brain Metastases — A Randomized Controlled Trial — Aoyama, 2006	Actuarial Free Rate of the 3-point drop in the MMSE (%)			Average duration until Deterioration (mts.)
	12	24	36	
WBRT+SRS	76.1	68.5	14.7	16.5*
SRS ALONE	59.3	51.9	51.9	7.6*

P=0.05

- **Only MMSE (Mini Mental State Examination)!**
- **Pretreatment MMSE available for only 99 pts (total 132)**
- **Author's CONCLUSION … However, the long-term adverse effects of WBRT on neurocognitive function might not be negligible.**

Focal treatments versus whole brain irradiation for patients with brain metastases

Decline in cognitive function (verbal memory)

	probability of decline in cognitive function (%)	
ψ* test	***+ whole brain RT***	***- whole brain RT***
total recall	**57%** (7/11)	**24%** (4/20)
delayed recall	**22%**	**6%**
delayed recognition	**11%**	**0%**

**ψ test* - Hopkins verbal learning test
- decline defined as change in >5 points on verbal memory test at 4 months

31/58 patients with 1-3 brain metastases tested

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Focal treatments versus whole brain irradiation for patients with brain metastases

	# of patients	Intracranial progression free survival (months)	
Chang 2009	58 (30 SRS vs 28 SRS+ WBRT)	at 1 year: 27% vs 73% (p = 0.0003)	?

Current Treatment Options in Oncology
DOI 10.1007/s11864-014-0307-3

Neuro-oncology (GJ Lesser, Section Editor)

Treatment of Radiation-Induced Cognitive Decline

On study

Hopkins Verbal Learning Test (HVLT) (Benedict RHB, 2007)—memorization of a list of words in consecutive trials tests the ability to recall the words (immediate recall), and ability to recall the words after a 20-minute delay (delayed recall).

SRS + WBRT
Or
SRS alone + Follow-UP
PROS

Focal treatments versus whole brain irradiation for patients with brain metastases

VOLUME 25 · NUMBER 10 · APRIL 1 2007
JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Regression After Whole-Brain Radiation Therapy for Brain Metastases Correlates With Survival and Improved Neurocognitive Function

Jing Li, Soren M. Bentzen, Markus Renschler, and Minesh P. Mehta

Conclusion

WBRT-induce
is stable or in
than WBRT d
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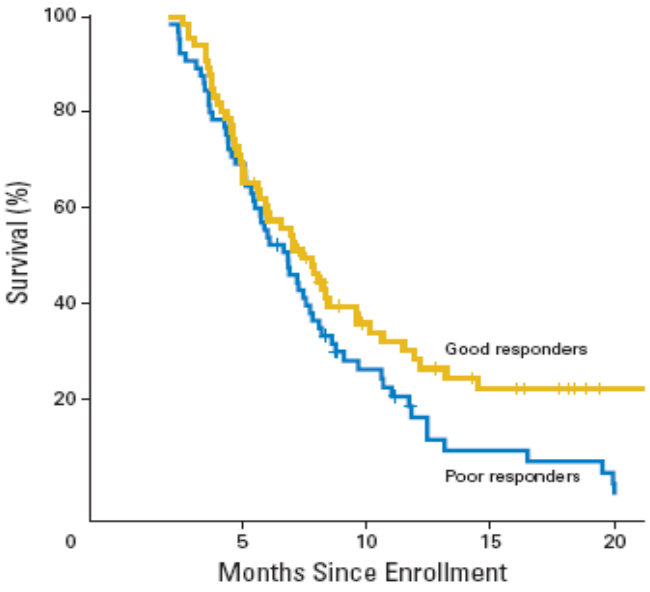

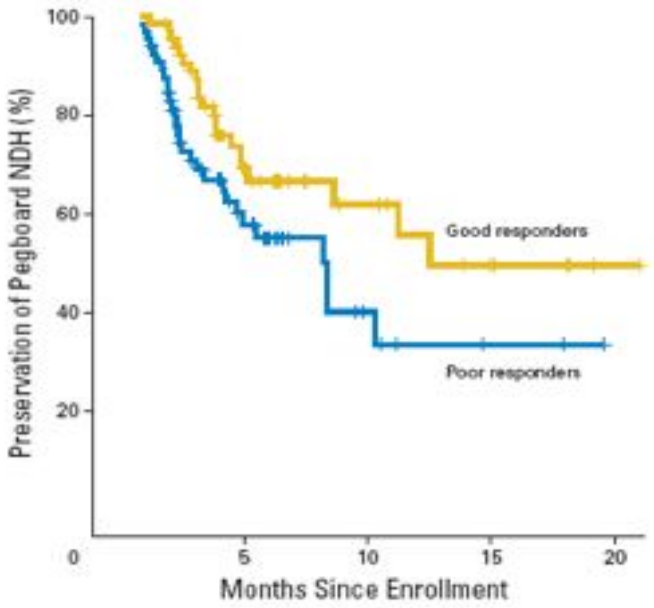

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SRS alone + Follow-UP

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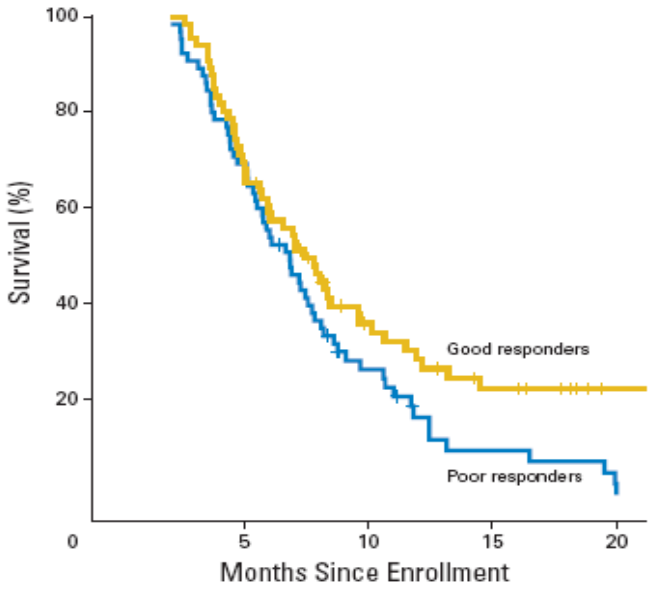
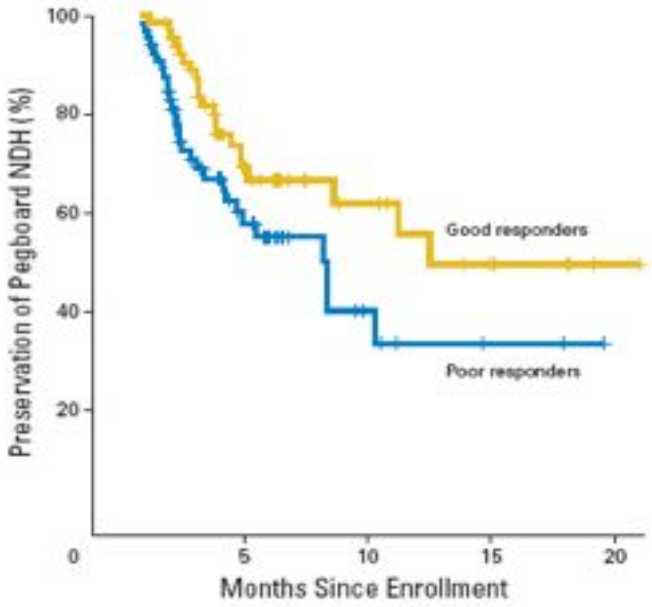




Memory Deficits both in good and poor responders !

SRS alone + Follow-UP

PROS

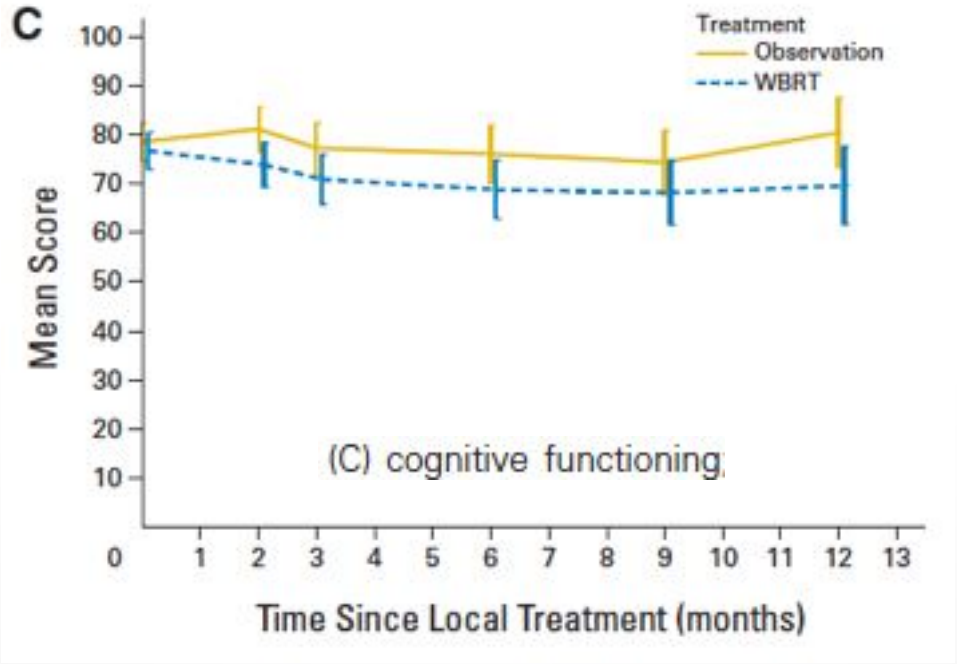
Focal treatments versus whole brain irradiation for patients with brain metastases

VOLUME 31 · NUMBER 1 · JANUARY 1 2013

JOURNAL OF CLINICAL ONCOLOGY

Riccardo Soffietti, Martin Kocher,

A European Organisation for Research and Treatment of Cancer Phase III Trial of Adjuvant Whole-Brain Radiotherapy Versus Observation in Patients With One to Three Brain Metastases From Solid Tumors After Surgical Resection or Radiosurgery: Quality-of-Life Results



Focal treatments versus whole brain irradiation for patients with brain metastases

VOLUME 31 · NUMBER 1 · JANUARY 1 2013
JOURNAL OF CLINICAL ONCOLOGY

Riccardo Soffietti, Martin Kocher,

A European Organisation for Research and Treatment of Cancer Phase III Trial of Adjuvant Whole-Brain Radiotherapy Versus Observation in Patients With One to Three Brain Metastases From Solid Tumors After Surgical Resection or Radiosurgery: Quality-of-Life Results

Table 1. Compliance With Health-Related Quality-of-Life Assessments

Assessment Time	No. of Forms Received	No. of Forms Expected	Compliance Rate (%)
Baseline	317	359	88.3
WBRT	162	180	90.0
OBS	155	179	86.6
8 weeks	206	333	61.9
WBRT	105	169	62.1
OBS	101	164	61.6
3 months	156	262	59.5
WBRT	81	133	60.9
OBS	75	129	58.1
6 months	107	210	51.0
WBRT	53	105	50.5
OBS	54	105	51.4
9 months	88	170	51.8
WBRT	45	87	51.7
OBS	43	83	51.8
12 months	65	144	45.1
WBRT	29	73	39.7
OBS	36	71	50.7

Another limitation of this study is that, although we assessed cognitive functioning with the EORTC QLQ-C30, we did not assess cognitive function with cognitive test batteries, and it is known that the self-report of cognitive functioning and formal neurocognitive testing may be poorly correlated. In patients with brain metastases, neurocog-

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Focal treatments versus whole brain irradiation for patients with brain metastases

Treatment of Radiation-Induced Cognitive Decline

Albert Attia, MD[1]
Brandi R. Page, MD[2]
Glenn J. Lesser, MD[3]
Michael Chan, MD[2,*]

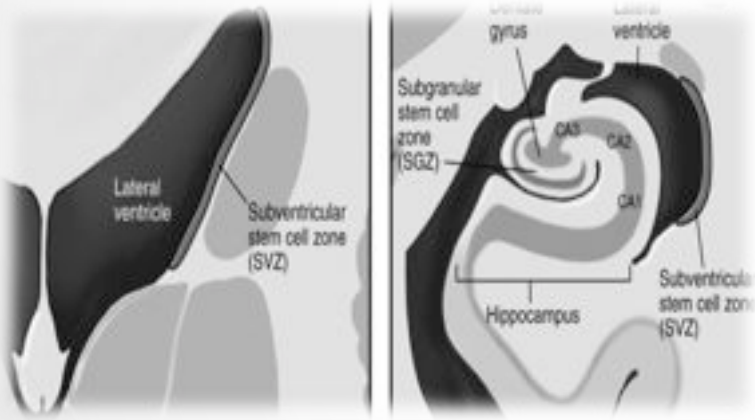
Current Treatment Options in Oncology
DOI 10.1007/s11864-014-0307-3

Memantine

Memantine, an N-methyl-D-aspartate (NMDA) receptor antagonist is often used to treat vascular dementia. The NMDA receptor is thought to be involved in learning and memory [23]. Ischemic events in the brain can induce excessive

Focal treatments versus whole brain irradiation for patients with brain metastases

NSCs (Neural Stem cells)



Barani et all. IJROBP 68,4, 978–985, 2007

Adult NSCs are relatively quiescent, with cell-cycle time of 28 days. This small population of cells generates transiently dividing progenitor cells that are characterized by a cell-cycle time of 12 h.

The resulting daughter cells then migrate throughout the brain parenchyma and integrate as interneurons in the cortical layers.

The ganglionic eminence(s) in the embryo, and both the subventricular zone (SVZ) of the lateral ventricles and the subgranular zone (SGZ) of the hippocampal dentate gyrus in adults, were consistently shown to represent major germinal niches, containing cells capable of driving neurogenesis and gliogenesis.

These processes are thought to be central to nervous-system repair and the preservation or reconstitution of function.

Int. J. Radiation Oncology Biol. Phys., Vol. 68, No. 4, pp. 971–977, 2007

Focal treatments versus whole brain irradiation for patients with brain metastases

DISTRIBUTION OF BRAIN METASTASES IN RELATION TO THE HIPPOCAMPUS: IMPLICATIONS FOR NEUROCOGNITIVE FUNCTIONAL PRESERVATION

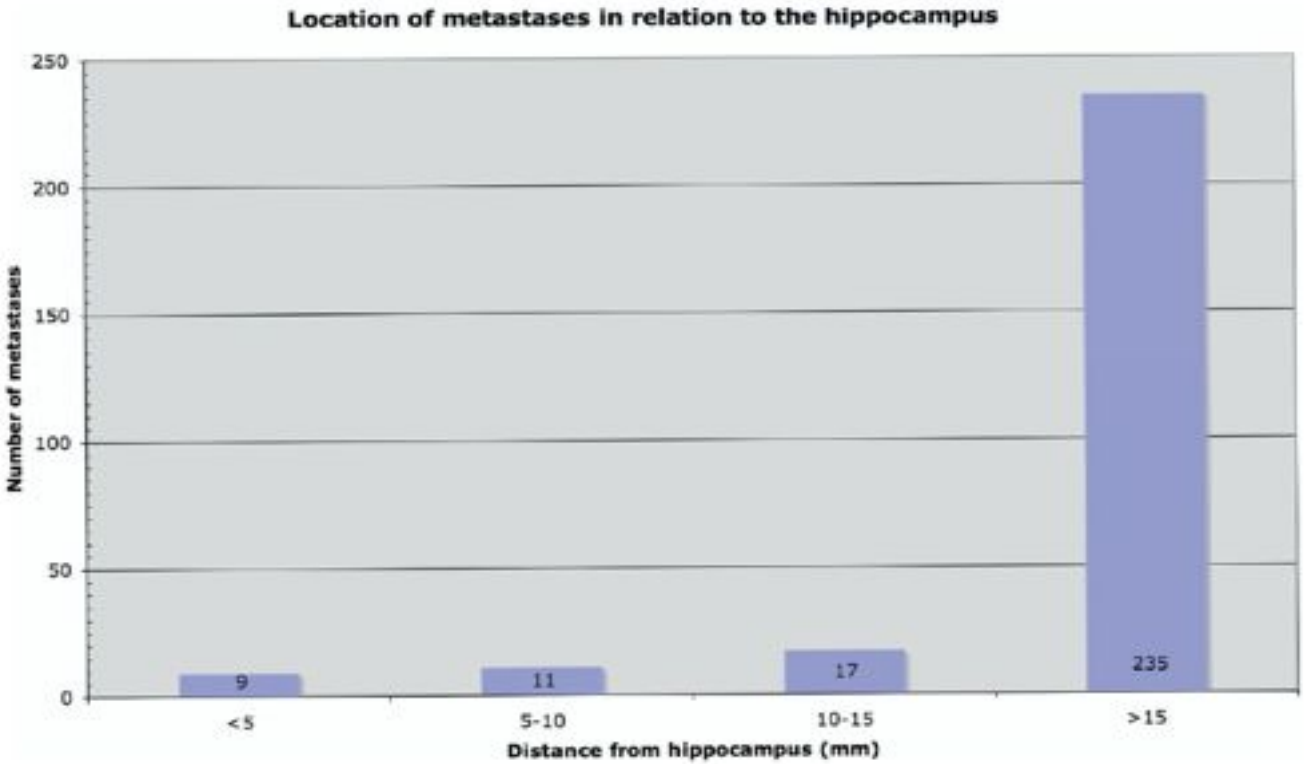


Fig. 1. Location of brain metastasis as a function of distance from the hippocampus.

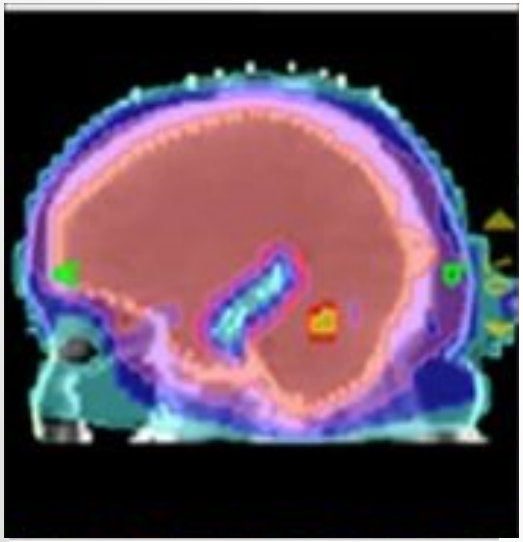
100 pts

Focal treatments versus whole brain irradiation for patients with brain metastases

Current Treatment Options in Oncology
DOI 10.1007/s11864-014-0307-3

Treatment of Radiation-Induced Cognitive Decline

Hippocampal sparing IMRT



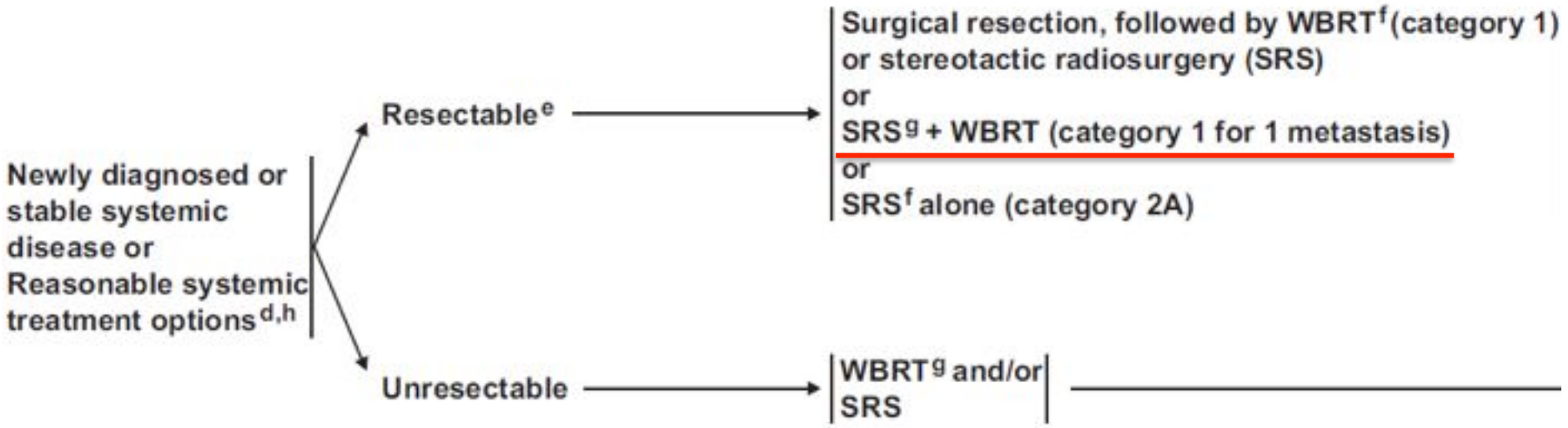
Given preclinical data [45, 46] and retrospective analyses [47] that suggested that the hippocampi are targets of radiation injury that lead to cognitive decline, the RTOG embarked on a single-arm, phase II study utilizing hippocampal sparing intensity-modulated radiotherapy (IMRT) where the results were compared with historical controls in patients who received standard WBRT [48]. The findings of this study were presented at the 2013 National Meeting of the American Society for Radiation Oncology (ASTRO). The study enrolled 113 adult patients who had brain metastasis outside a 5-mm margin around the hippocampi. All patients were treated to 30 Gy in 10 fractions. The maximum dose to the hippocampus was limited to 17 Gy. A statistically significant difference was noted when compared with historical controls in the decline in HVLT-DR. Although the results are promising, hippocampal sparing whole brain IMRT is still an investigational technique given the lack of randomized phase III studies demonstrating benefit. Several phase III studies are currently being planned.

Focal treatments versus whole brain irradiation for patients with brain metastases

Take home message

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2013
Limited (1-3) Metastatic Lesions



Focal treatments versus whole brain irradiation for patients with brain metastases

Radiothe … or newly diagnose… Society for Radi… time

Table 1 Single brain metastasis—initial management

Prognostic category (a)	Other features	Treatment options (evidence grade) references	Clinical benefit S	LC	WB control
Good prognosis Expected survival 3 mo or more	Complete resection possible	If brain metastasis ≤3-4 cm: • Surgery and WBRT (level 1)[10,11,22,23,42,43,b]	✓	✓	✓
		• Radiosurgery and WBRT (level 1)[51,53]	✓	✓	✓
		• Radiosurgery alone (Level 1)[23,54]		✓	
		• Surgery with radiosurgery/radiation boost to the resection cavity with or without WBRT (level 3)[26-41,b]		✓	✓ (with WBRT)
		If brain metastasis >3-4 cm: • Surgery and WBRT (level 1)[10,11,22,23,42,43,b]	✓	✓	✓
		• Surgery with radiosurgery/radiation boost to the resection cavity with or without WBRT (level 3)[26-41,b]		✓	✓ (with WBRT)
Good prognosis Expected survival 3 mo or more	Not resectable	If brain metastasis ≤3-4 cm: • Radiosurgery and WBRT (level 1)[51,53]	✓	✓	✓
		• Radiosurgery alone (level 1)[23,54]		✓	
		If brain metastasis >3-4 cm: • WBRT (level 3), with consideration of biopsy, if primary unknown[59,85,86]	✓	✓	✓
Poor prognosis Expected survival less than 3 mo		• WBRT (level 3)[59,85]		✓	✓
		• Palliative care without WBRT (level 3)[59,85]			

(2012) **2**, 210–225

XXIV CONGRESSO NAZIONALE AIRO 2014

Focal treatments versus whole brain irradiation for patients with brain metastases

- **Don't routinely add adjuvant whole brain radiation therapy to stereotactic radiosurgery for limited brain metastases.**

  Randomized studies have demonstrated no overall survival benefit from the addition of adjuvant whole brain radiation therapy (WBRT) to stereotactic radiosurgery (SRS) in the management of selected patients with good performance status and brain metastases from solid tumors. The addition of WBRT to SRS is associated with diminished cognitive function and worse patient-reported fatigue and quality of life. These results are consistent with the worsened, self-reported cognitive function and diminished verbal skills observed in randomized studies of prophylactic cranial irradiation for small cell or non-small cell lung cancer. Patients treated with radiosurgery for brain metastases can develop metastases elsewhere in the brain. Careful surveillance and the judicious use of salvage therapy at the time of brain relapse allow appropriate patients to enjoy the highest quality of life without a detriment in overall survival. Patients should discuss these options with their radiation oncologist.

Focal treatments versus whole brain irradiation for patients with brain metastases

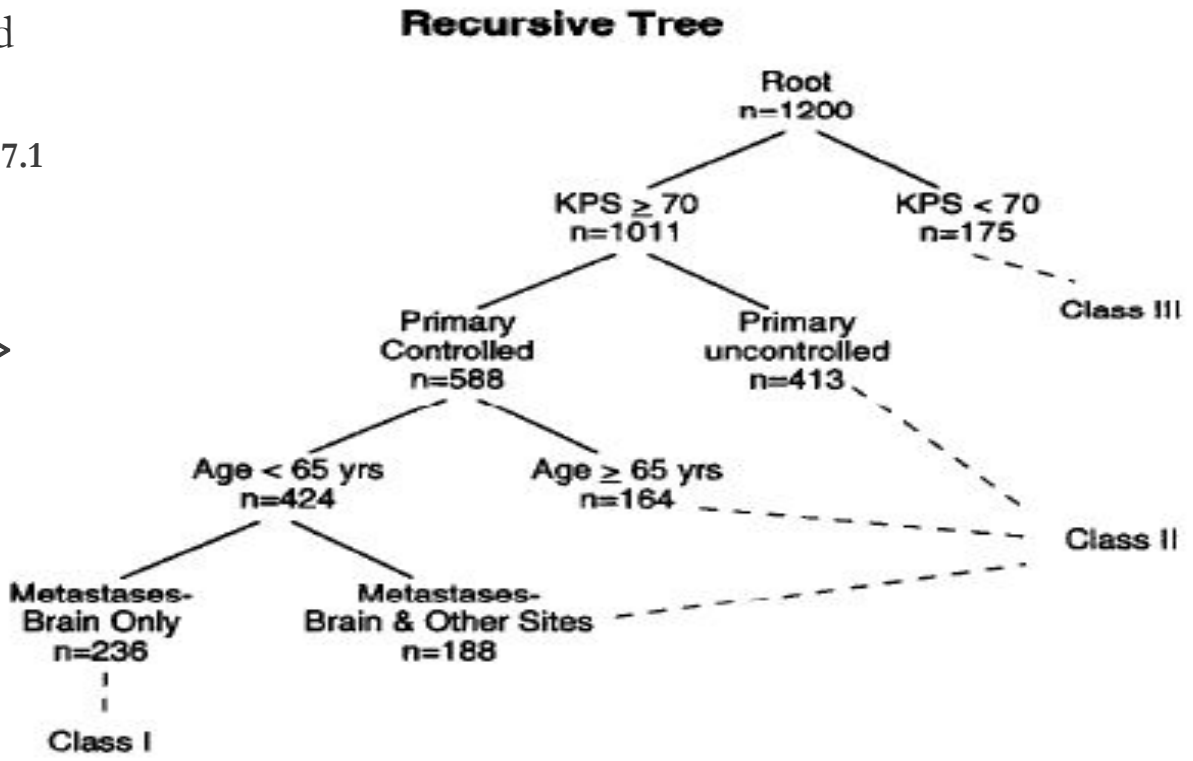
Proper patient
for
Proper therapy

Focal treatments versus whole brain irradiation for patients with brain metastases

Classe I: **KPS** ≥ 70, controlled primary, year < 65 aa, brain mets only: ⇒ **median survival: 7.1 months**

Classe II: **KPS** ≥ 70 and no above mentioned variables ⇒ **median survival: 4.2 months**

Classe III: **KPS** < 70: ⇒ **median survival: 2.3 months**



Gaspar IJRBP Vol. 37, No. 4, pp. 745-751, 1997

Focal treatments versus whole brain irradiation for patients with brain metastases

A NEW PROGNOSTIC INDEX AND COMPARISON TO THREE OTHER INDICES FOR PATIENTS WITH BRAIN METASTASES: AN ANALYSIS OF 1,960 PATIENTS IN THE RTOG DATABASE

Paul W. Sperduto, M.D.,* Brian Berkey, M.S.,† Laurie E. Gaspar, M.D.,‡ Minesh Mehta, M.D.,§ and Walter Curran, M.D.‖

Table 4. Graded Prognostic Assessment

	Score		
	0	0.5	1.0
Age	>60	50–59	<50
KPS	<70	70–80	90–100
No. of CNS metastases	>3	2–3	1
Extracranial metastases	Present	—	None

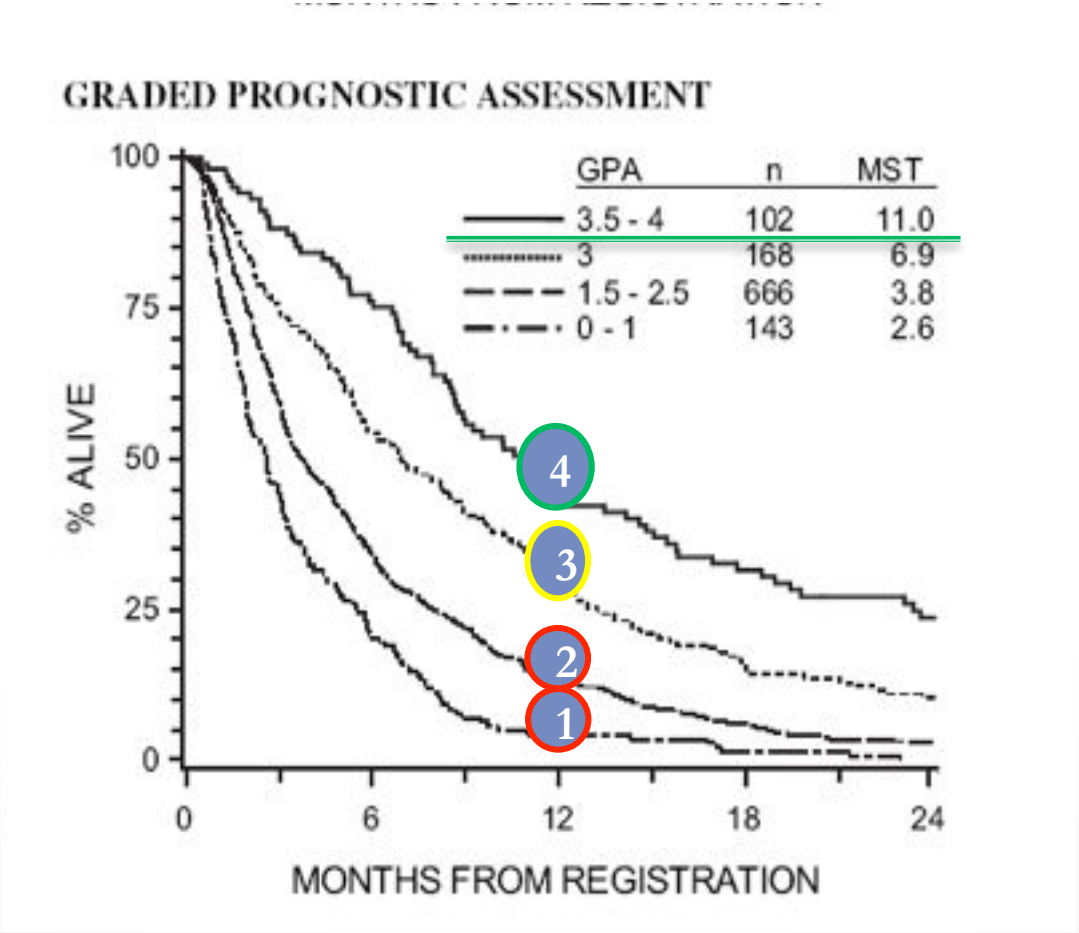
GPA:
number of metastases

Table 1. Recursive partitioning analysis

Class I:	Age <65 y, KPS ≥ 70, controlled primary tumor, no extracranial metastases
Class II:	All patients not in Class I or III
Class III:	KPS < 70

Int. J. Radiation Oncology Biol. Phys., Vol. 70, No. 2, pp. 510–514, 2008

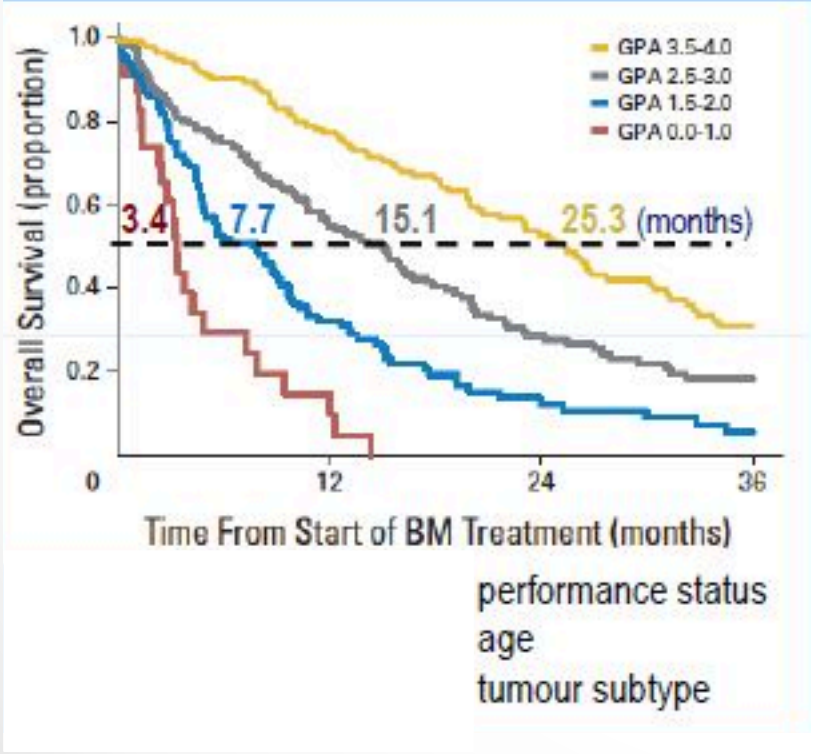
Focal treatments versus whole brain irradiation for patients with brain metastases



Int. J. Radiation Oncology Biol. Phys., Vol. 70, No. 2, pp. 510–514, 2008

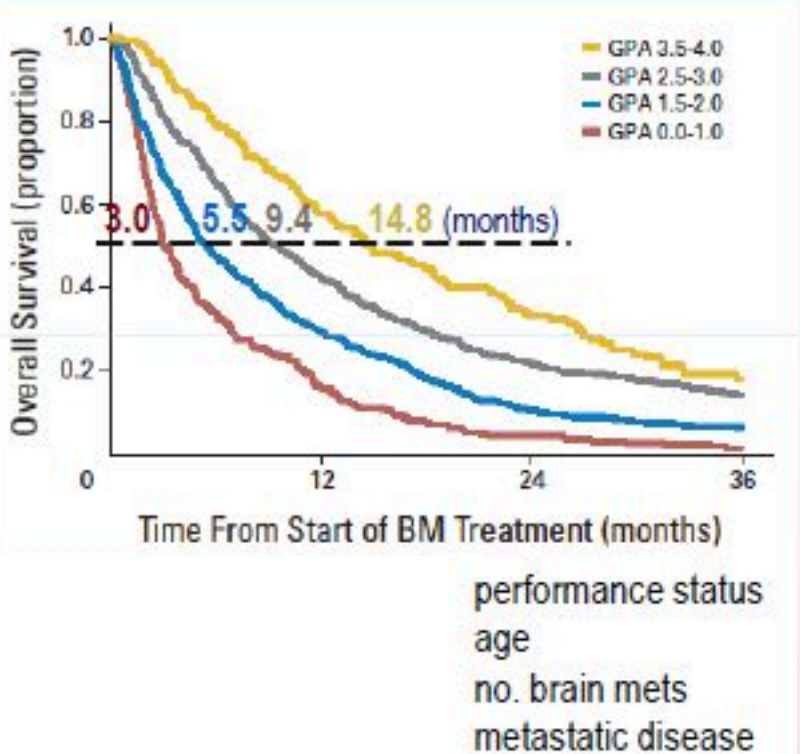
Focal treatments versus whole brain irradiation for patients with brain metastases

Breast



performance status
age
tumour subtype

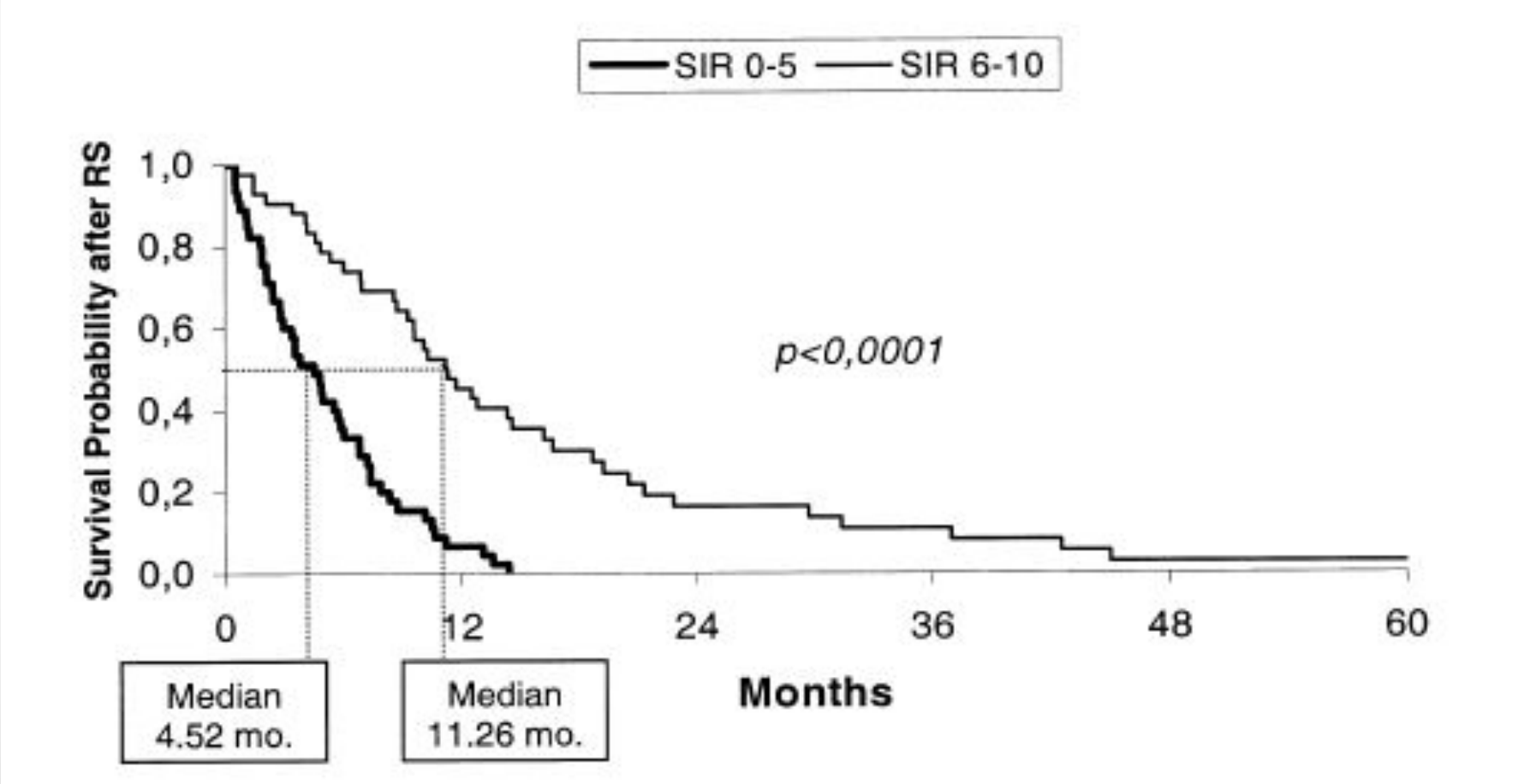
NSCLC



performance status
age
no. brain mets
metastatic disease

Sperduto et al J Clin Oncol 2012, 30: 419 - 425

Focal treatments versus whole brain irradiation for patients with brain metastases



- **Weltman et all. IJROBP Vol. 51, No. 5, pp. 1320–1327, 2001**

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AIRO 2014

Focal treatments versus whole brain irradiation for patients with brain metastases

Targ Oncol
DOI 10.1007/s11523-014-0326-9

DAY-TO-DAY PRACTICE

Erlotinib in combination with pemetrexed/cisplatin for leptomeningeal metastases and cerebrospinal fluid drug concentrations in lung adenocarcinoma patients after gefitinib faliure

Article in Press

Safety and Efficacy of Targeted Therapy for Renal Cell Carcinoma With Brain Metastasis

CLINICAL Genitourinary Cancer
Prostate, Kidney, & Bladder

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Focal treatments versus whole brain irradiation for patients with brain metastases

Stereotactic radiosurgery for patients with multiple brain metastases (JLGK0901): a multi-institutional prospective observational study

Published online March 10, 2014 http://dx.doi.org/10.1016/S1470-2045(14)70061-0

Total (n=1194)	1 tumour (n=455)	2–4 tumours (n=531)	5–10 tumours (n=208)

THE LANCET Oncology

Stereotactic radiosurgery for patients with brain metastases

*Filippo Alongi, *Alba Fiorentino, Pierina Navarria, Lorenzo Bello, Marta Scorsetti.*

Correspondence THELANCETONCOLOGY-D-14-00420

S1470-2045(14)70151-2

In conclusion, despite the relevance of Yamamoto and colleagues' study, its messages need to be interpreted carefully. Oversimplification of oncological treatment should be avoided.

Focal treatments versus whole brain irradiation for patients with brain metastases

SRS + WBRT: improve local control

Selection of patients: DS-GPA

WBRT and neurocognitive function: more trials with cognitive test batteries

WBRT sparing hippocampi: ongoing

Discuss with patients

Thanks for the attention