Radioterapia panencefalica

Umberto Ricardi

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Background

- Systemic disease to the brain is unfortunately a quite common event
- Radiotherapy, especially with the great technical development during the past decades, represents a cornerstone of current treatment options
- Despite advances in treatment options, the prognosis is still poor

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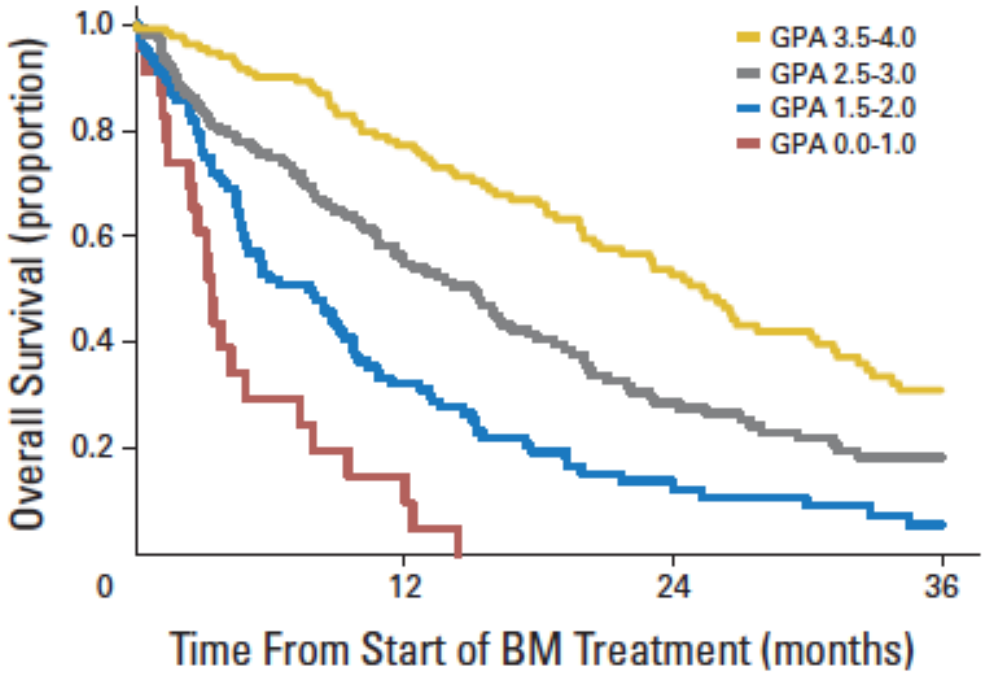
JOURNAL OF CLINICAL ONCOLOGY

	KPS	Age	Number of mets	Extra - cranial mets	Tumour subtype
Lung	✔	✔	✔	✔	-
Breast	✔	✔	-	-	✔
Melanoma	✔	-	✔	-	-
Renal	✔	-	✔	-	-
GI	✔	-	-	-	-

A

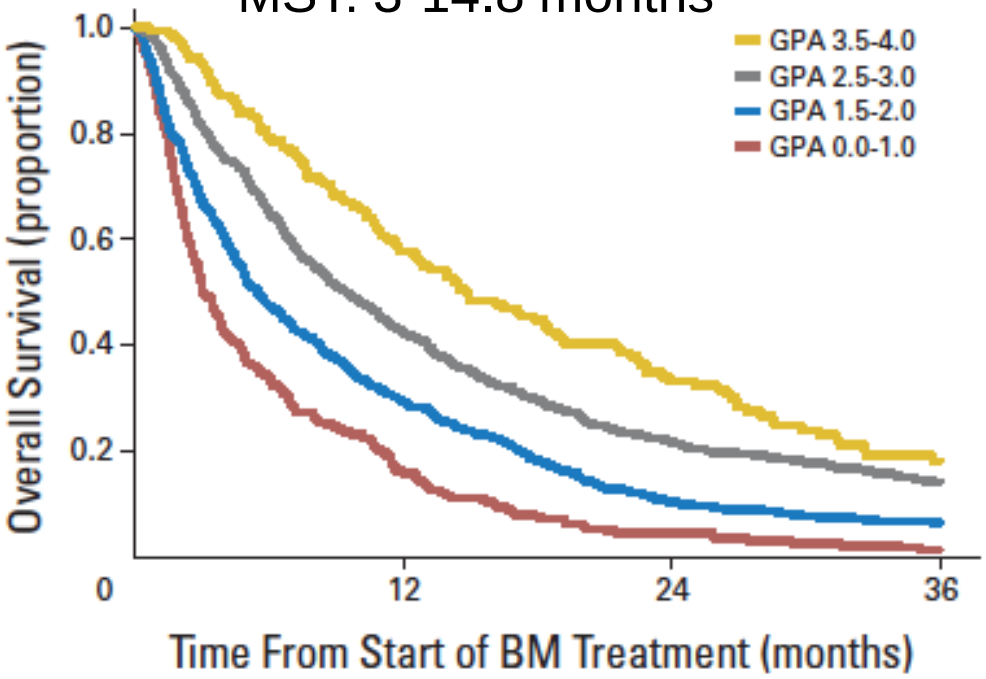
MST: 3.4-25.3 months



Breast cancer

B

MST: 3-14.8 months



NSCLC

Diagnosis-specific GPA

Sperduto et al.

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Brain metastases: background

- Many patients affected with brain metastases die as a result of extra-cranial disease progression
- A substantial number of brain metastases patients suffer from the local tumor progression in the CNS
- Optimising local control is thus of paramount importance

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Brain metastases: background

Corollary:

- development of symptomatic brain metastases has a substantial impact on patient's quality of life (QoL) and neuro-cognitive function

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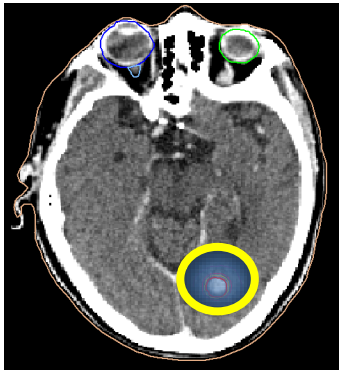
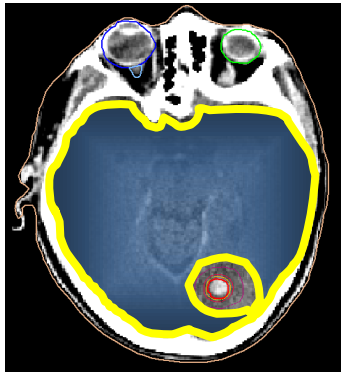
Brain metastases: clinical endpoints



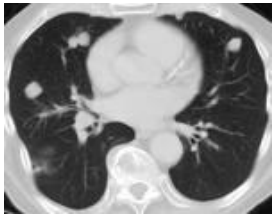


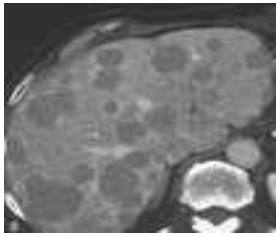
Local control

Regional control:
Freedom from new brain metastases

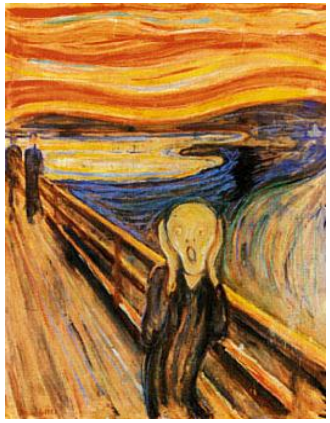
Brain tumor control

Extracranial disease control





Survival



Quality of Life

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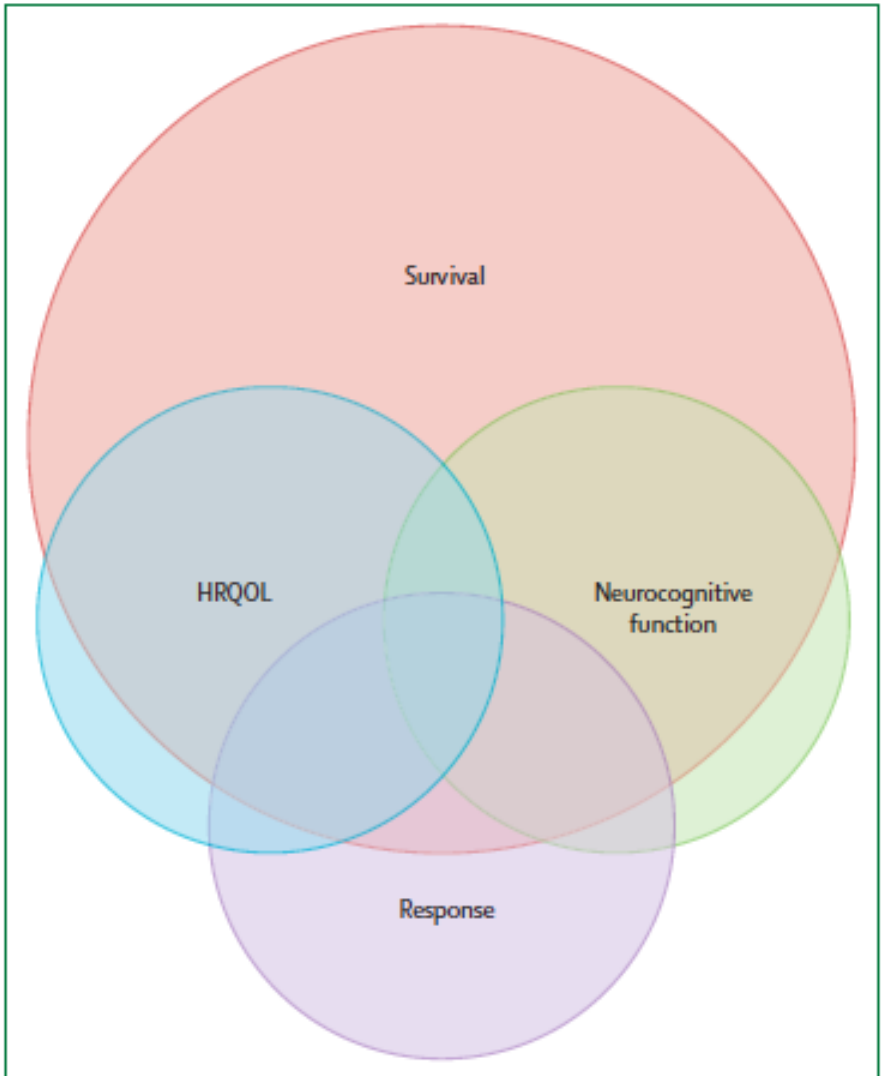
Challenges relating to solid tumour brain metastases in clinical trials, part 2: neurocognitive, neurological, and quality-of-life outcomes. A report from the RANO group

Nancy U Lin, Jeffrey S Wefel, Eudocia Q Lee, David Schiff, Martin J van den Bent, Riccardo Soffietti, John H Suh, Michael A Vogelbaum, Minesh P Mehta, Janet Dancey, Mark E Linskey, D Ross Camidge, Hidefumi Aoyama, Paul D Brown, Susan M Chang, Steven N Kalkanis, Igor J Barani, Brigitta G Baumert, Laurie E Gaspar, F Stephen Hodi, David R Macdonald, Patrick Y Wen, for the Response Assessment in Neuro-Oncology (RANO) group

Lancet Oncol 2013; 14: e407–16

Possible endpoints in clinical trials



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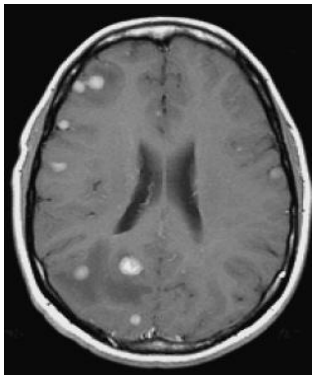
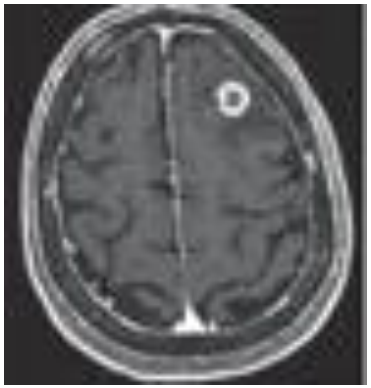
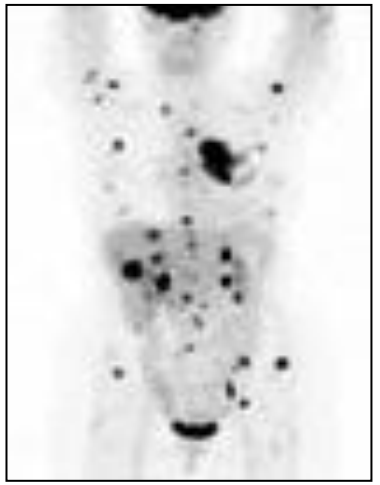


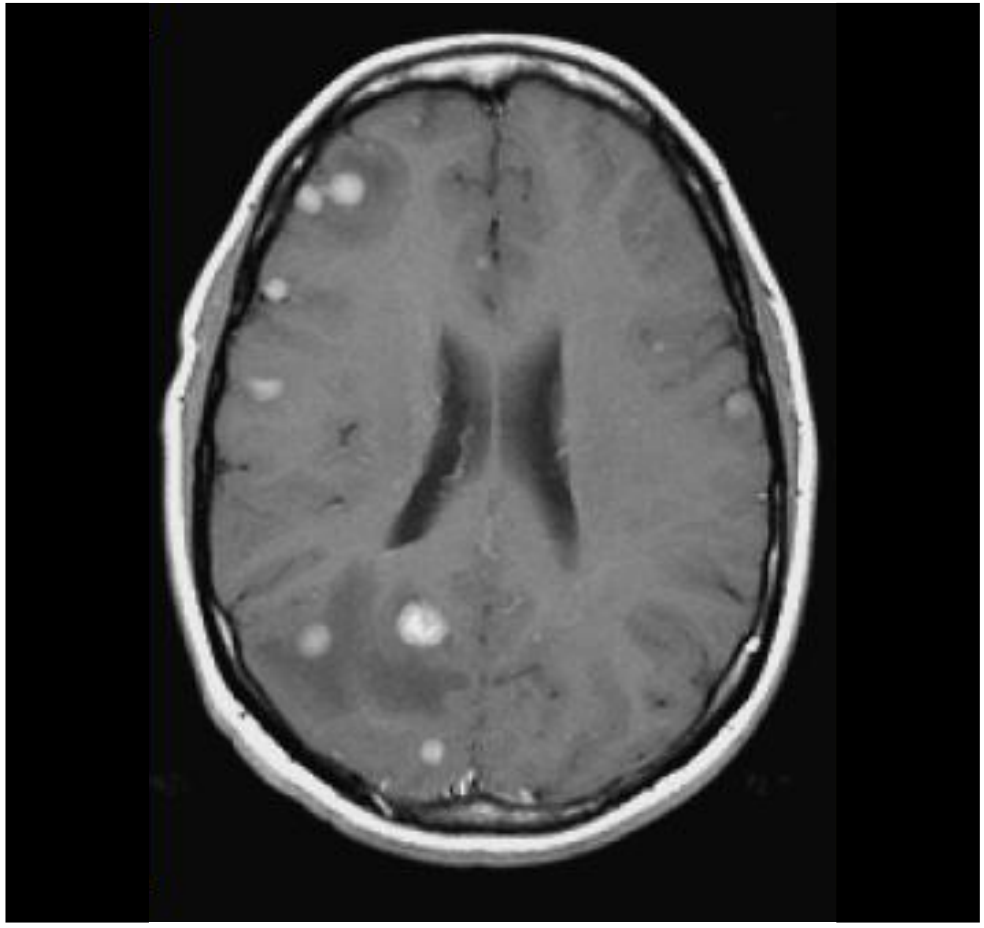




- Treatment decisions must be individualized based on a complex array of both **patient-specific** and **tumor-specific** characteristics

Multiple Brain Metastases

Whole Brain Radiotherapy



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WBI for Multiple Brain Metastases

- WBI is the conventional treatment for majority of patients affected with (symptomatic) brain mets

- Typical radiation schedule:
  - 30 Gy/10 fr
  - 20 Gy/5 fr
  - 37.5 Gy/15 fr

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WBRT: Schedule

Whole brain radiotherapy for the treatment of newly diagnosed multiple brain metastases (Review)

2012

Tsao MN, Lloyd N, Wong RKS, Chow E, Rakovitch E, Laperriere N, Xu W, Sahgal A

THE COCHRANE COLLABORATION®

"In summary, none of the randomized controlled trials have found a benefit (in terms of overall survival or neurologic function) with altered dose-fractionation schedules as compared to standard (3000 cGy/10 or 2000 cGy/5 daily fractions)."

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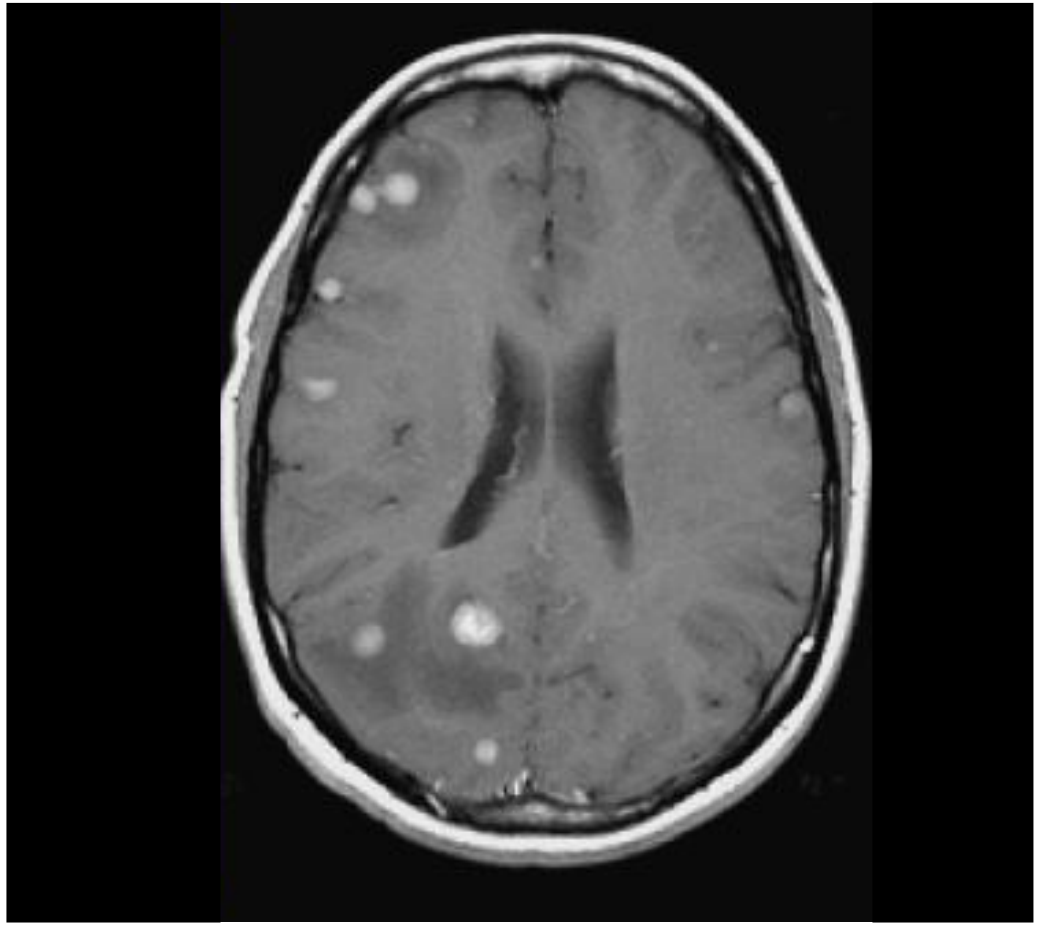
Multiple Brain Metastases

Whole Brain Radiotherapy



How to improve the efficacy of RT?

Phase III Trial: WBRT +/- RSR-13

- 538 patients enrolled

  WBRT and Supplemental O2 +/- RSR-13

No survival advantage: 5.3 vs 4.5 mo *(p=0.17)*

- In subset of 111 pts with breast cancer:
  - Control (n=52): 4.6 mo
  - RSR-13 (n=59): 8.7 mo

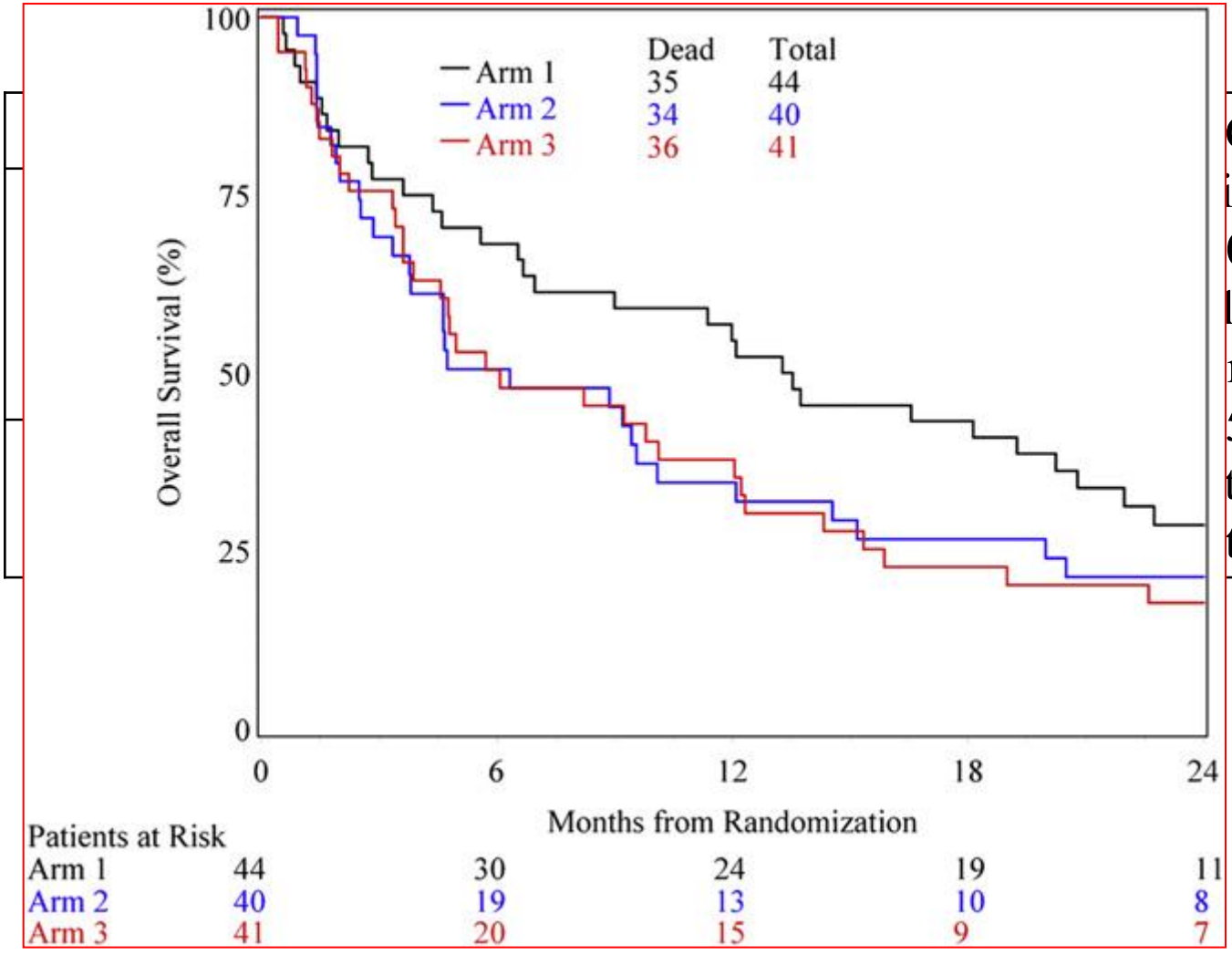
Pts with metastatic breast cancer to the brain also sustained a statistically significant increase in RR

A confirmatory phase III trial is underway

RCT to improve WBRT-SRS outcome

A Phase 3 Trial of Whole Brain Radiation Therapy and Stereotactic Radiosurgery Alone Versus WBRT and SRS With Temozolomide or Erlotinib for Non-Small Cell Lung Cancer and 1 to 3 Brain Metastases: Radiation Therapy Oncology Group 0320

Paul W. Sperduto, MD, MPP,* Meihua Wang, PhD,† H. Ian Robins, MD, PhD,‡ Michael C. Schell, PhD,§ Maria Werner-Wasik, MD,‖ Ritsuko Komaki, MD,¶ Luis Souhami, MD,# Mark K. Buyyounouski, MD,** Deepak Khuntia, MD,†† William Demas, MD,‡‡ Sunjay A. Shah, MD,§§ Lucien A. Nedzi, MD,‖‖ Gad Perry, MD,¶¶ John H. Suh, MD,## and Minesh P. Mehta, MD***



C with 1-3 brain metastasis
ize ≤ 4 cm
0-100
lass I-II
ranial disease stable
5
ty ≥ G3 in 11%, 41% and 49%
tively (p <0.001)

Sperduto et al., 2013

RADIATION THERAPY ONCOLOGY GROUP

RTOG 1119

PHASE II RANDOMIZED STUDY OF WHOLE BRAIN RADIOTHERAPY IN COMBINATION WITH CONCURRENT LAPATINIB IN PATIENTS WITH BRAIN METASTASIS FROM HER2-POSITIVE BREAST CANCER – A COLLABORATIVE STUDY OF RTOG AND KROG

SCHEMA

STRATIFY	Graded Prognostic Assessment (GPA) Score: 1.5-2 vs. 2.5-3 vs. 3.5-4 Use of Non-CNS–Penetrating HER2 Blockade at Study Entry: No vs. Yes: trastuzumab ± pertuzumab Previous Stereotactic Radiosurgery (SRS) or Surgical Resection: Yes vs. No	**RANDOMIZE**	**Arm A** WBRT: 37.5 Gy in 15 fx for 3 wks Versus **Arm B** WBRT: 37.5 Gy in 15 fx for 3 wks Plus Lapatinib: Once daily starting up to 1 day before the first day of WBRT and continuing until 21 days after the final day of WBRT

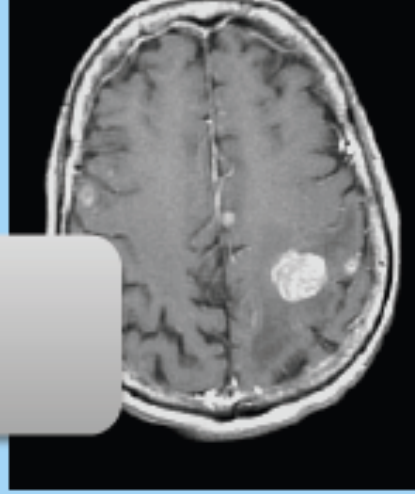
See Section 6.0 for details of radiation therapy and Section 7.0 for details of drug therapy.

Patient Population: (See Section 3.0 for Eligibility)
Pathologically (histologically or cytologically) proven diagnosis of invasive HER2-overexpressing breast cancer (3+ staining by immunohistochemistry or HER2 gene amplification by FISH or SISH ≥ 2.2). At least one measurable, unirradiated parenchymal brain lesion (≥ 10 mm on T1-weighted gadolinium enhanced MRI).

Required Sample Size: 143

Document History

	Version/Update Date	Broadcast Date
Update	October 8, 2012	October 8, 2012
Update	July 26, 2012	July 26, 2012
Activation	**July 19, 2012**	July 26, 2012

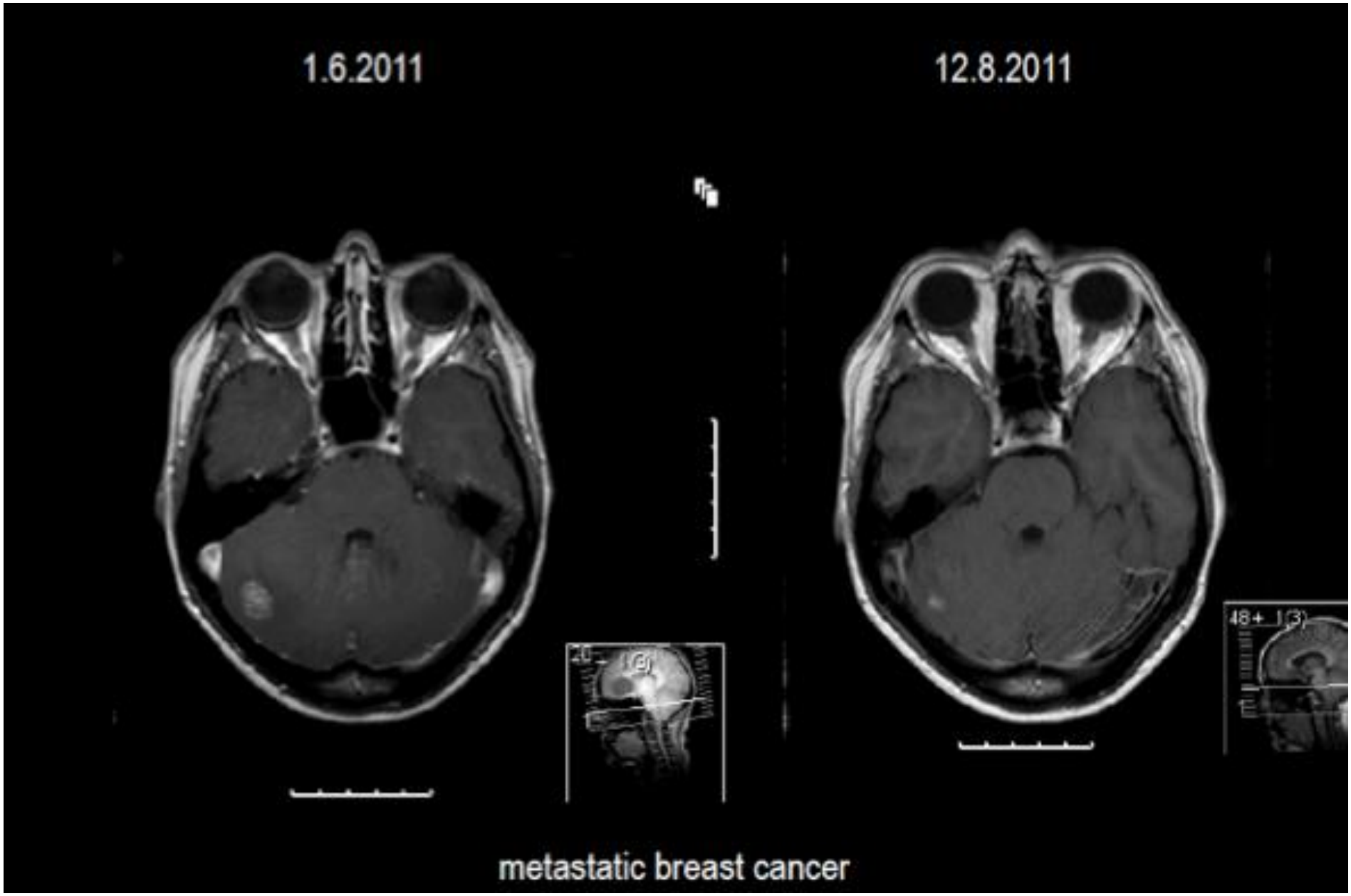


incidental asymptomatic brain metastases

chemoresponsive

poor prognosis

Diminishing role of radiotherapy



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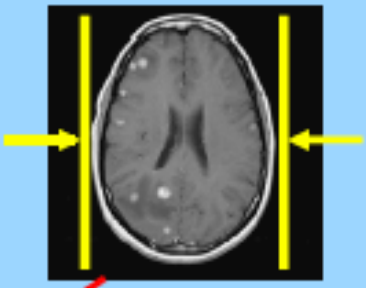
whole brain radiotherapy and survival



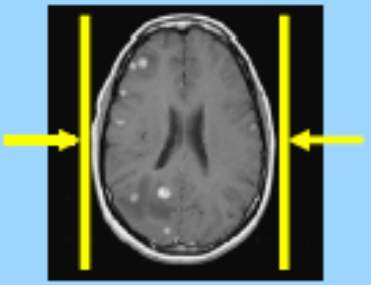
patients with brain metastases
randomize

supportive care

palliative radiotherapy
& supportive care

Effect of whole brain radiotherapy on survival

QUARTZ UK NCRI trial



brain metastases in NSCLC
& poor prognostic factors

supportive care

palliative radiotherapy
& supportive care

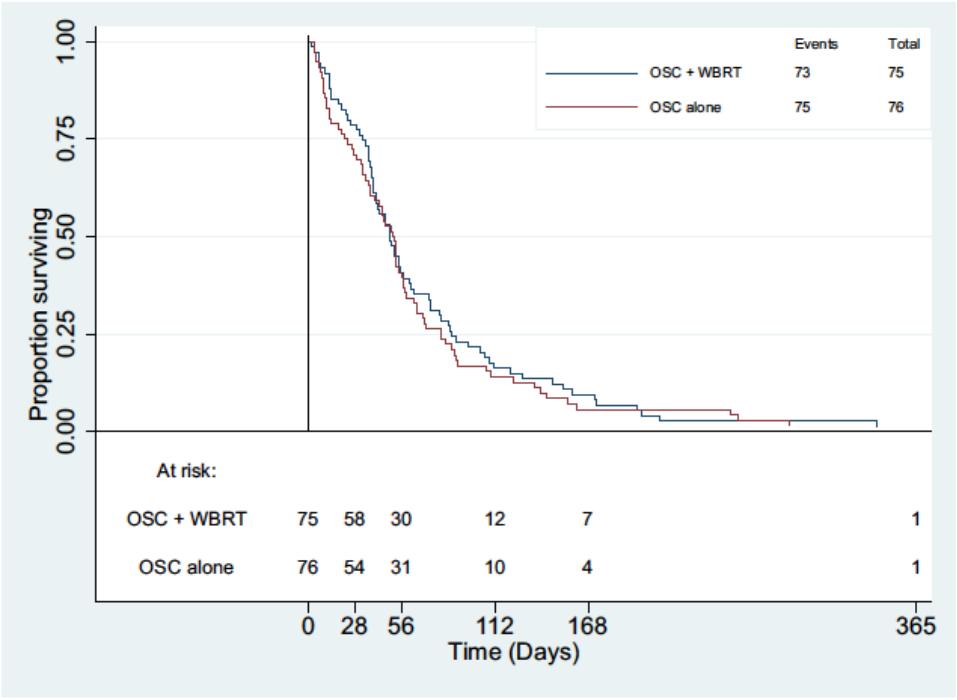
endpoints: palliative efficacy (QOL, Barthel),
survival free of neurological progression,
survival

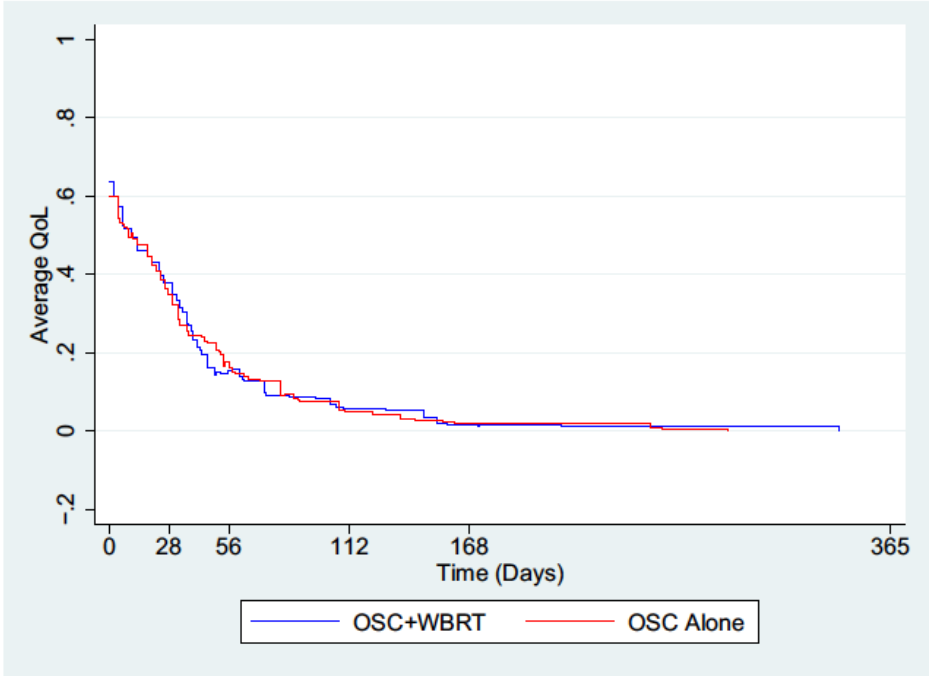
Effect of whole brain radiotherapy on survival & QOL

Interim Data from the Medical Research Council QUARTZ Trial: Does Whole Brain Radiotherapy Affect the Survival and Quality of Life of Patients with Brain Metastases from Non-small Cell Lung Cancer?

R.E. Langley *, R.J. Stephens *, M. Nankivell *, C. Pugh *, B. Moore †, N. Navani *,‡, P. Wilson §, C. Faivre-Finn ¶, R. Barton ||, M.K.B. Parmar *, P.M. Mulvenna **on behalf of the QUARTZ Investigators

Clinical Oncology 25 (2013) e23–e30





One of the main barriers to recruitment seemed to be a lack of any preliminary randomised data to support the trial's hypothesis (that omitting WBRT would not be detrimental)

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Evolving issues in Radiotherapy for brain mets:

Survival/Brain Tumor control/QoL/Cognitive Function

Patients selection

- ✓ prognostic scores only validated for OS

New Strategies:

1. **Radiosurgery instead of Whole Brain Radiotherapy**

2. **Partial Brain Radiotherapy**

3. **Specific dosimetry for WBRT**

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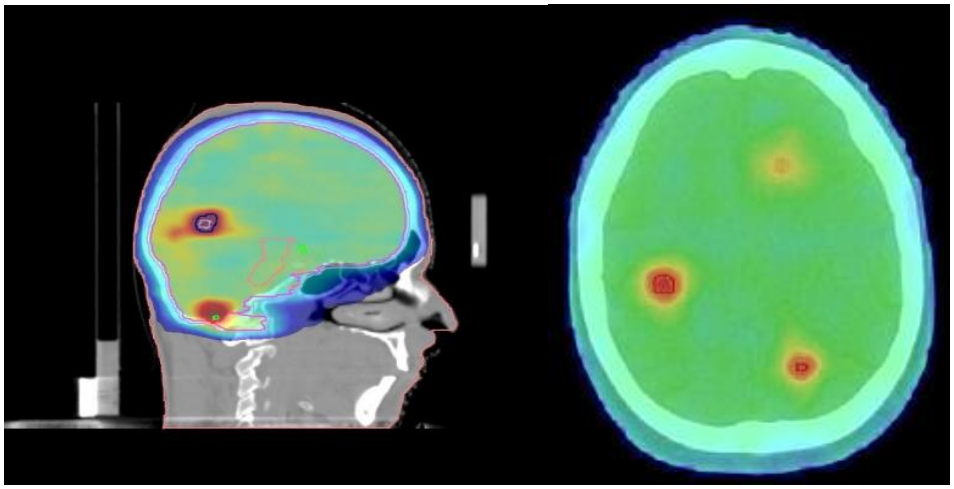
Specific dosimetry for WBRT



Integrated WBRT + boost (VMAT)

New delivery techniques allow for more complex tailored planning, including Simultaneous Integrated Boost (SIB) on oligomets

20 Gy/5 fr WBRT; 40 Gy/5 fr SIB

- Dosimetric advantages (steeper dose gradients)
- Logistic advantages (no separate procedures)
- Patient tolerance advantages (outpatient, frameless, delivery ~5 minutes)

Is radiation dose escalation clinically relevant in patients with multiple BM?

Toxicity? Efficacy?

EORTC
The future of cancer therapy

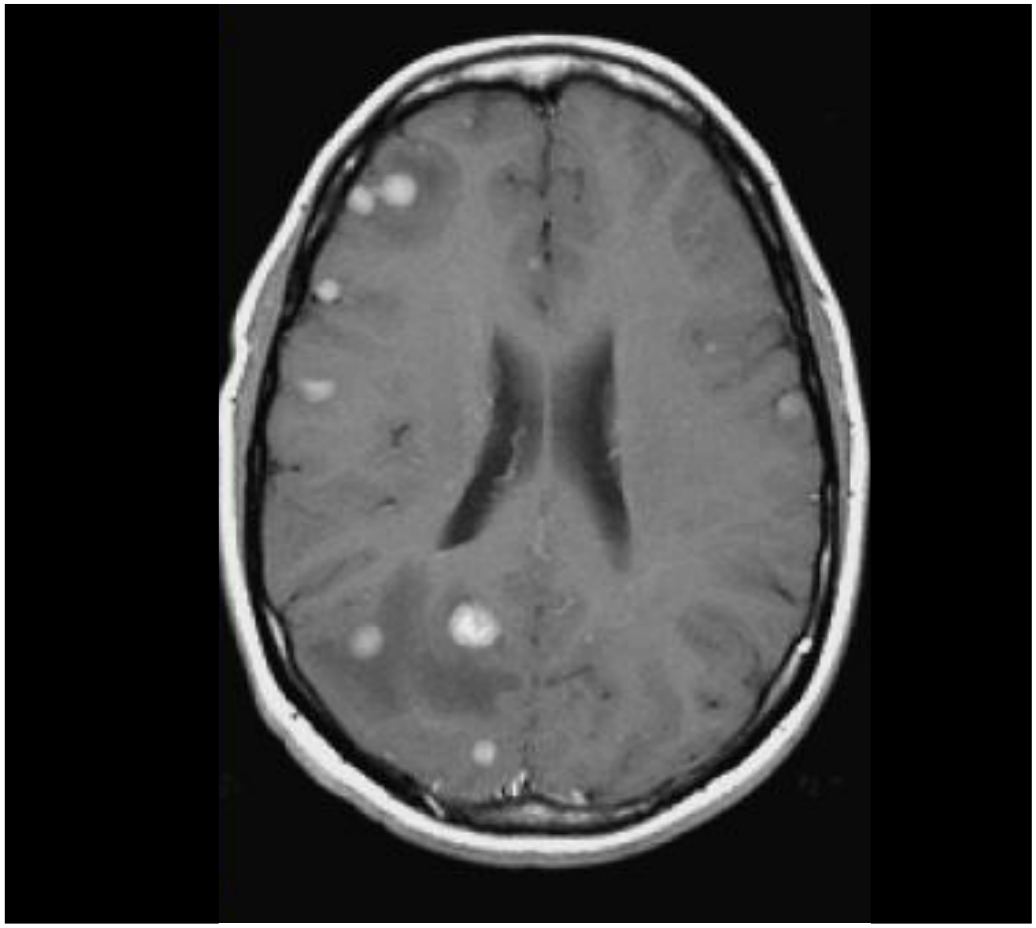
EORTC 22111-26111

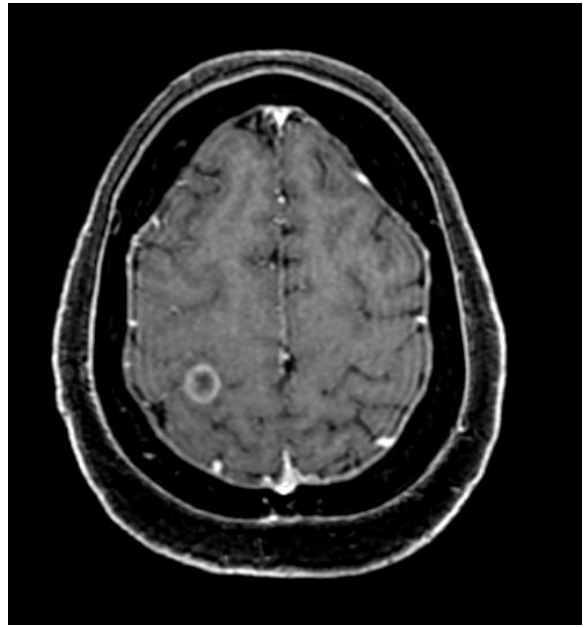
Whole brain radiotherapy with or without synchronous integrated boost in patients with 2 to 5 brain metastases. A randomized Phase III Study of the EORTC ROG and BTG

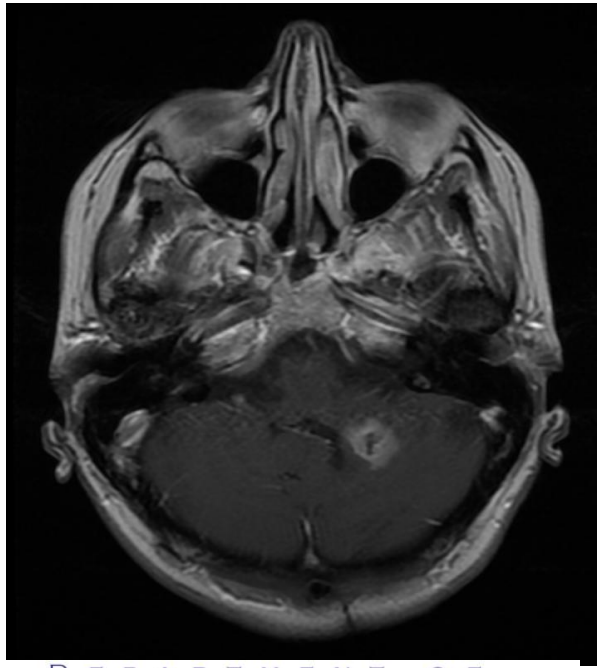
PI: B. Baumert, S. Erridge, F. Lagerwaard
Initiating end of 2012

Indications to WBRT

Role of adjuvant WBRT







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RCT in oligometastatic patients

Exclusive local treatment (surgery or radiosurgery) vs WBRT + local treatment (surgery or radiosurgery)

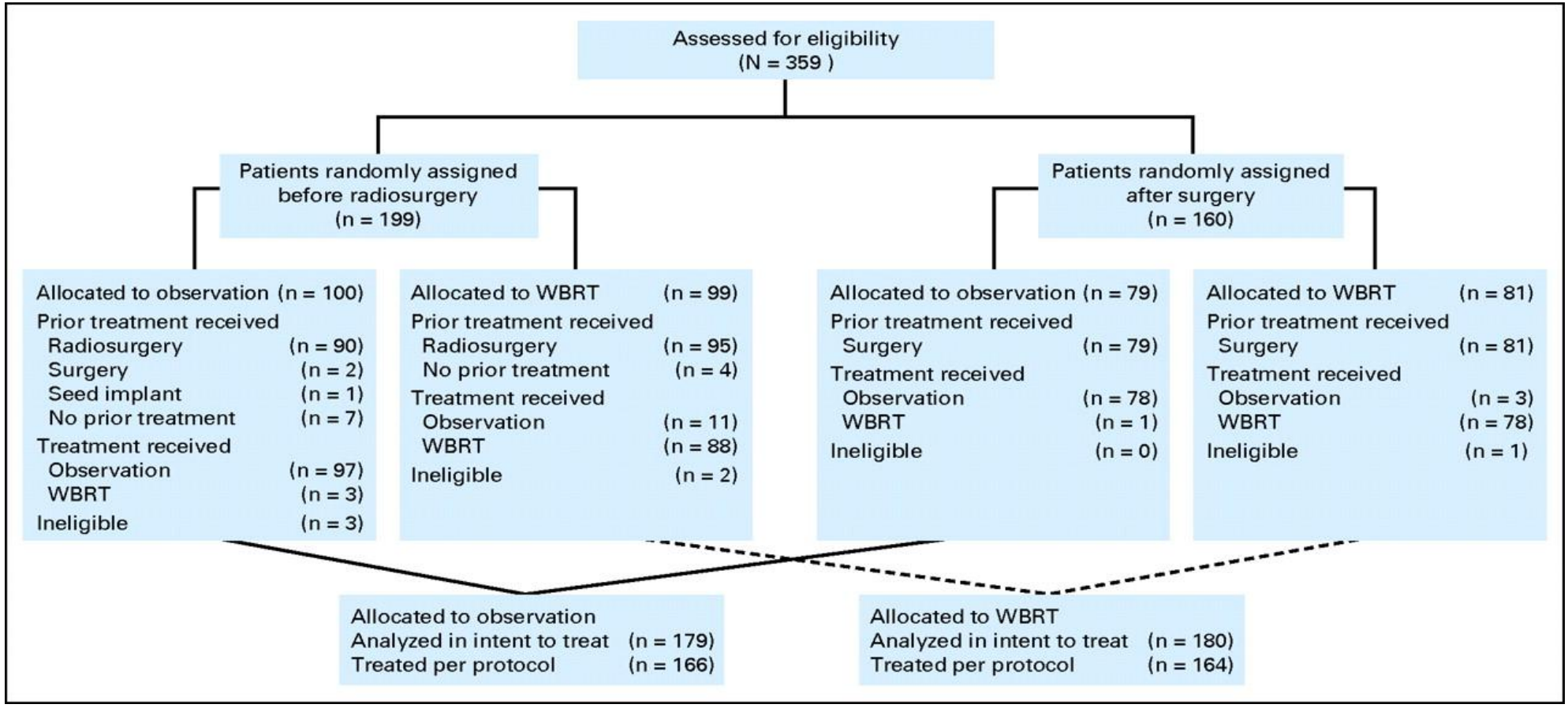
Trials comparing exclusive local therapy vs. (whole brain radiotherapy + local treatment.

Author	Treatment arms	Prescribed dose	*n*	Inclusion criteria	Local control	Freedom from new brain metastases	Brain tumor control	Neurologic death rate	Survival
Patchell [14]	S	–	95	Single lesion	54.0%	63.0%	30.0%	44.0%	NS
	S + WBRT	WBRT: 50,4 Gy in 28 fr		All the primaries	90.0%	86.0%	82.0%	14.0%	
Aoyama [15]	RS	RS:⩽2 cm: 22–25 Gy;>2 cm: 18–20 Gy	132	1–4 lesions	72.5% @ 1 y	36.3% @ 1 y	23.6% @ 1 y	NS	NS
	RS + WBRT	RS: dose reduction by 30% WBRT: 30 Gy in 10 fr or 12 fr		All the primaries	88.7% @ 1 y	58.5% @ 1 y	53.2% @ 1 y		
Chang [16]	RS	RS:<2 cm: 18 Gy; 2–3 cm: 15 Gy; 3–4 cm: 12 Gy	58	1–3 lesions	67.0% @ 1y	45.0% @ 1y	27.0% @ 1y	NS	15.2 m
	RS + WBRT	RS:<2 cm: 18 Gy; 2–3 cm: 15 Gy; 3–4 cm: 12 Gy WBRT: 30 Gy in 12 fr		All the primaries	100.0% @ 1y	73.0% @ 1y	73.0% @ 1y		5.7 m
Mueller and Kocher [20,21]	RS or S	RS: 20 Gy	359	1–3 lesions	68.7% @ 2 y	67.6% @ 2 y	46% @ 2y	44.0%	NS
	RS or S + WBRT	RS: 20 GyWBRT: 30 Gy in 10 fr		All the primaries	83.6% @ 2 y	82.4% @ 2 y	68.6% @ 2 y	28.0%	
Roos [22]	RS or S	RS: n.a.	19	Single lesion	n.a.	n.a.	NS	n.a.	NS
	RS or S + WBRT	WBRT: 36 Gy in 18 fror 30 Gy in 10 fr		All the primaries					

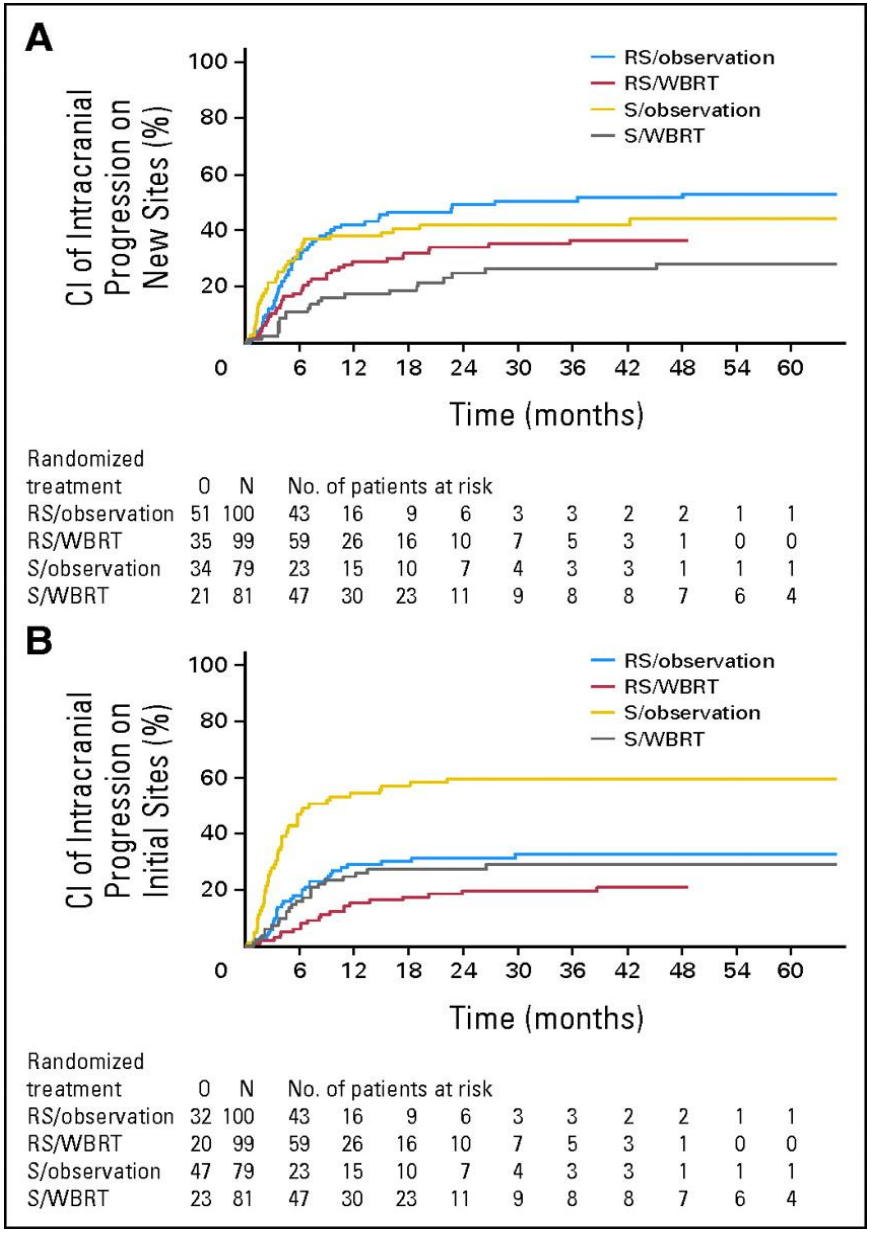
S, surgery; WBRT, whole brain radiotherapy; RS, radiosurgery; fr, fractions; w, weeks; m, months; y, year; n.a., not available; NS, not statistically significant difference.

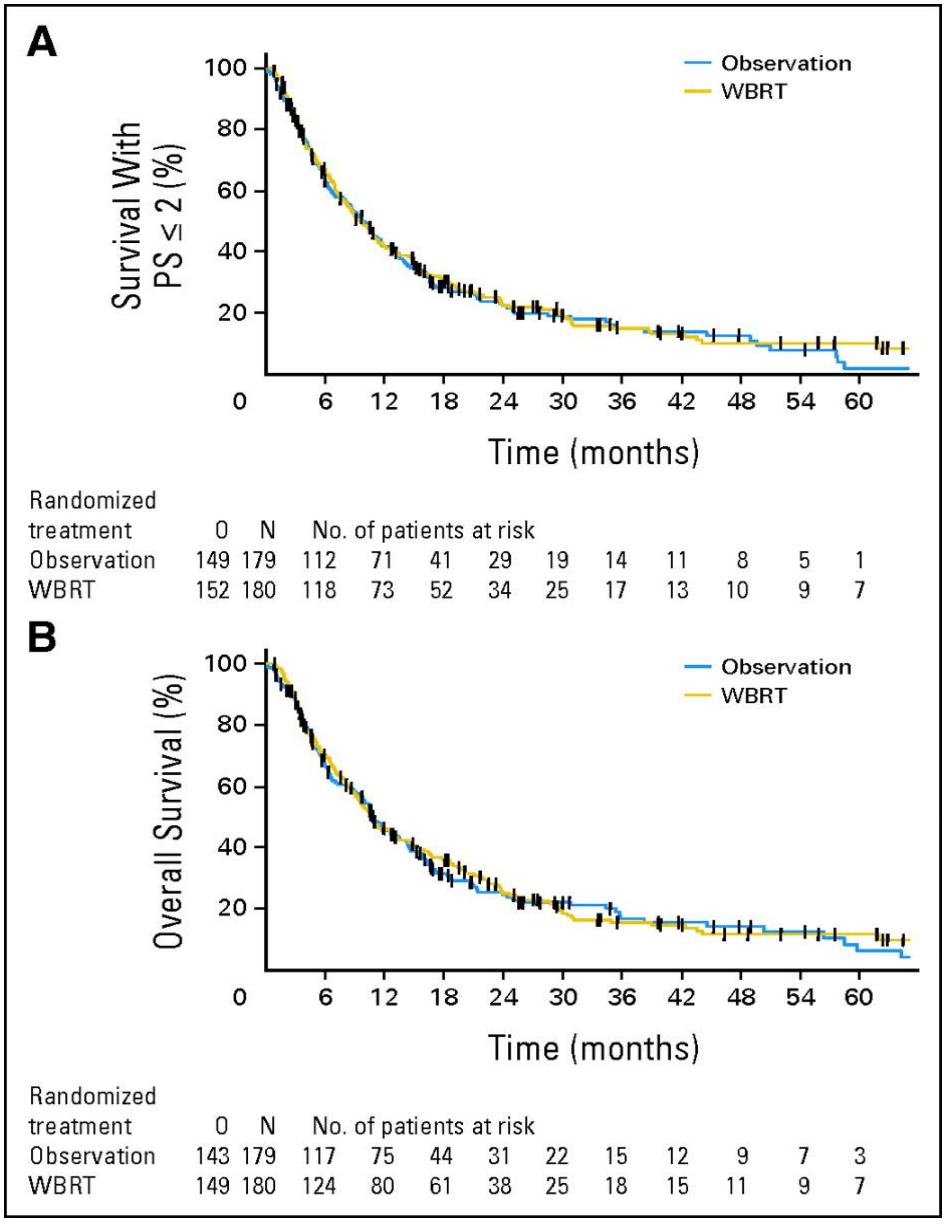
S. Scoccianti and U. Ricardi, Radiother Oncol 2011

Adjuvant Whole-Brain Radiotherapy Versus Observation After Radiosurgery or Surgical Resection of One to Three Cerebral Metastases: Results of the EORTC 22952-26001 Study; Kocher et al. 2011 JCO



Results of the EORTC 22952-26001 Study; Kocher et al. 2011 JCO





Neurocognition Balance

- WBRT reduces intracranial relapse and prolongs time to relapse
  - This should preserve NCF or slow down its decline, as tumor progression is associated with NCF decline
- WBRT damages the brain
  - This should cause an early decline in brain function

So, where is the balance

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Neurocognition: The Elephant in the Room

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NEUROCOGNITIVE FUNCTION OF PATIENTS WITH BRAIN METASTASIS WHO RECEIVED EITHER WHOLE BRAIN RADIOTHERAPY PLUS STEREOTACTIC RADIOSURGERY OR RADIOSURGERY ALONE

HIDEFUMI AOYAMA, M.D., PH.D.,[a] MASAO TAGO, M.D., PH.D.,[b] NORIO KATO, M.D.,[a] TATSUYA TOYODA, M.D., PH.D.,[c] MASAHIRO KENJYO, M.D., PH.D.,[d] SAEKO HIROTA, M.D., PH.D.,[e] HIROKI SHIOURA, M.D., PH.D.,[f] TAISUKE INOMATA, M.D., PH.D.,[g] ETSUO KUNIEDA, M.D., PH.D.,[h] KAZUSHIGE HAYAKAWA, M.D., PH.D.,[i] KEIICHI NAKAGAWA, M.D., PH.D.,[b] GEN KOBASHI, M.D., PH.D.,[j] AND HIROKI SHIRATO, M.D., PH.D.[a]

[a]Department of Radiology, Hokkaido University Graduate School of Medicine, Sapporo; [b]Department of Radiology, University of Tokyo Hospital, Tokyo; [c]Department of Radiology, Kanto Medical Center Nippon Telegraph and Telephone East Corporation, Tokyo; [d]Department of Radiology, Hiroshima University School of Medicine, Hiroshima; [e]Department of Radiology, Hyogo Medical Center for Adults, Akashi; [f]Department of Radiology, Izumisano General Hospital, Izumisano; [g]Department of Radiology, Osaka Medical College, Osaka; [h]Department of Radiology, Keio University School of Medicine, Tokyo; [i]Department of Radiology, Kitasato University School of Medicine, Sagamihara; and [j]Department of Global Health and Epidemiology, Division of Preventive Medicine, Hokkaido University Graduate School of Medicine, Sapporo, Japan

Int. J. Radiation Oncology Biol. Phys., Vol. 68, No. 5, pp. 1388–1395, 2007

Radiosurgery(RS) maximum diameter ≤2cm:22-25 Gy; >2cm:18-20 Gy	•1-4 lesions •Maximum diameter ≤ 3 cm •All the primaries •RPA class I and II
Radiosurgery (RS) dose reduction by 30% **+ WBRT** 30 Gy in 10 #	•n=92/132 underwent the follow-up Mini-Mental State Examination (MMSE)

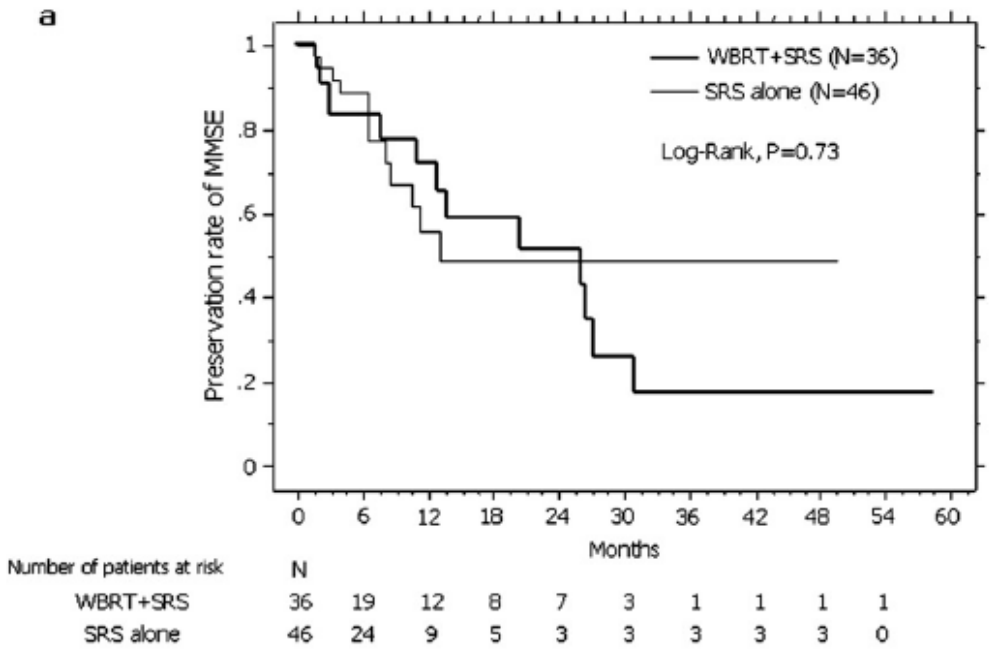

Fig. 2. (a) Actuarial curves of subjects free from 3-point decrease in Mini-Mental State Examination (MMSE). (b) Actuarial curves of subjects free from second 3-point decrease in MMSE. (c) Actuarial rate of subjects free from decrease of MMSE to ≤26. WBRT = whole brain radiotherapy; SRS = stereotactic radiosurgery.

- Control of the brain tumor is the most important factor for stabilizing neurocognitive function

- However, the long-term adverse effects of WBRT on neurocognition might not be negligible

Criticism: MMSE, used as the sole measurement of neurocognitive function, has been criticized for having low specificity and sensitivity

Neurocognition in patients with brain metastases treated with radiosurgery or radiosurgery plus whole-brain irradiation: a randomised controlled trial

Eric L Chang, Jeffrey S Wefel, Kenneth R Hess, Pamela K Allen, Frederick F Lang, David G Kornguth, Rebecca B Arbuckle, J Michael Swint, Almon S Shiu, Moshe H Maor, Christina A Meyers

Lancet Oncol 2009; 10: 1037–44

Radiosurgery (RS) maximum diameter <2cm: 18 Gy; 2-3cm: 15 Gy; 3-4cm: 12 Gy	•1-3 lesions •All the primaries •RPA class I and II
Radiosurgery (RS) **+ WBRT** 30 Gy in12 #	•n=58

Patients treated with WBRT were at a greater risk of a significant decline in learning and memory function as measured with the Hopkins Verbal Learning Test – Revised [HVLT-R] total recall at 4 months

MDACCC: Cognitive Decline (HVLT @ 4 mo)

Modality	Mean Probability of NCF decline @ 4 months
SRS	23%
SRS+WBRT	49%

Chang Lancet 2009

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Shortcomings of this study

1) Neurocognitive function was assessed at a single time point of 4 months (it is known that WBRT may have a transient effect on memory measured by verbal learning tests)

2) The combined therapy group had a greater burden in terms of disease volume (median tumor volume 2.3 vs 1.4) and worse RPA class distribution. It is therefore unsurprising that baseline neurocognitive function was worse in this group

3) Authors failed to account for many medications, including opioids, sedatives, anticonvulsivant and steroids that are known to cause neurocognitive dysfunction

Longitudinal Assessment of Chemotherapy-Induced Alterations in Brain Activation During Multitasking and Its Relation With Cognitive Complaints

Sabine Deprez, Mathieu Vandenbulcke, Ronald Peeters, Louise Emsell, Ann Smeets, Marie-Rose Christiaens, Frederic Amant, and Stefan Sunaert

J Clin Oncol 32. © 2014

Results

Voxel-based paired *t* tests revealed significantly decreased activation ($P < .05$) from t1 to t2 at matched performance in the multitasking network of chemotherapy-treated patients, whereas no changes were noted in either of the control groups. At baseline, there were no differences between the groups. Furthermore, in contrast to controls, the chemotherapy-treated patients reported a significant increase in cognitive complaints ($P < .05$) at t2. Significant ($P < .05$) correlations were found between these increases and decreases in multitasking-related brain activation. Moreover, a significant group-by-time interaction ($P < .05$) was found whereby chemotherapy-treated patients showed decreased activation and healthy controls did not.

Conclusion

These results suggest that changes in brain activity may underlie chemotherapy-induced cognitive complaints. The observed changes might be related to chemotherapy-induced damage to the brain or reduced connectivity between brain regions rather than to changes in effort or changes in functional strategy. To the best of our knowledge, this is the first longitudinal study providing evidence for a relationship between longitudinal changes in cognitive complaints and changes in brain activation after chemotherapy.

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JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

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

Soffietti et al., 2013

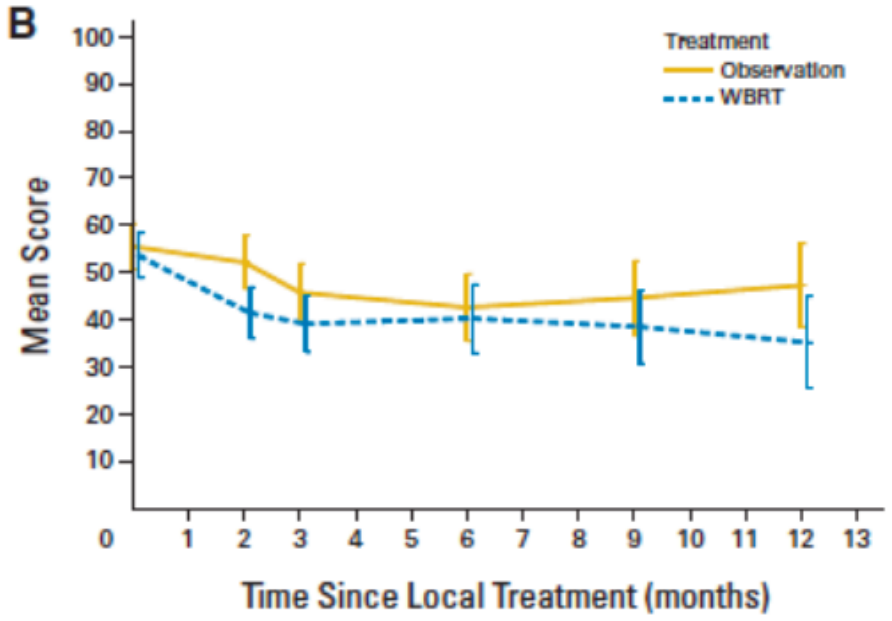


Table 2. Global Quality-of-Life Results With Cut Off at 12 Months

Time Point	WBRT Mean Score*	WBRT SD	Observation Mean Score*	Observation SD	*P* for Treatment Difference
Overall postbaseline test†					.1
Baseline	58.3	1.8	60.0	1.8	.5
8 weeks	54.9	2.1	56.8	2.2	.5
3 months	58.0	2.4	58.6	2.5	.9
6 months	58.7	2.9	62.1	2.9	.4
9 months	52.2	3.2	63.2	3.2	.01
12 months	56.8	3.9	58.7	3.5	.7

Conclusion

This study shows that adjuvant WBRT after surgery or radiosurgery of a limited number of brain metastases from solid tumors may negatively impact some aspects of HRQOL, even if these effects are transitory. Consequently, observation with close monitoring with magnetic resonance imaging (as done in the EORTC trial) is not detrimental for HRQOL.

Surgery or radiosurgery plus whole brain radiotherapy versus surgery or radiosurgery alone for brain metastases (Review)

Soon YY, Tham IWK, Lim KH, Koh WY, Lu JJ

THE COCHRANE COLLABORATION®

Analysis 1.1. Comparison 1 Whole-Brain Radiotherapy versus Observation, Outcome 1 Overall Survival.

Review: Surgery or radiosurgery plus whole brain radiotherapy versus surgery or radiosurgery alone for brain metastases

Comparison: 1 Whole-Brain Radiotherapy versus Observation

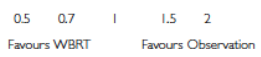
Outcome: 1 Overall Survival

Study or subgroup	Whole-Brain Radiotherapy N	Observation N	log [Hazard Ratio] (SE)	Hazard Ratio IV,Random,95% CI	Weight	Hazard Ratio IV,Random,95% CI
Patchell 1998	49	46	-0.09 (0.22)		21.5 %	0.91 [0.59, 1.41]
Aoyama 2006	65	67	0 (0.19)		24.6 %	1.00 [0.69, 1.45]
Roos 2006	10	9	0.01 (0.52)		6.6 %	1.01 [0.36, 2.80]
Chang 2009	28	30	0.9 (0.31)		14.5 %	2.46 [1.34, 4.52]
Kocher 2011	180	179	-0.02 (0.12)		32.7 %	0.98 [0.77, 1.24]
Total (95% CI)					**100.0 %**	**1.11 [0.83, 1.48]**

Heterogeneity: $Tau^2 = 0.05$; $Chi^2 = 8.34$, df = 4 (P = 0.08); $I^2 = 52\%$

Test for overall effect: Z = 0.72 (P = 0.47)

Test for subgroup differences: Not applicable



Analysis 1.3. Comparison 1 Whole-Brain Radiotherapy versus Observation, Outcome 3 Any intracranial disease progression at one year.

Review: Surgery or radiosurgery plus whole brain radiotherapy versus surgery or radiosurgery alone for brain metastases

Comparison: 1 Whole-Brain Radiotherapy versus Observation

Outcome: 3 Any intracranial disease progression at one year

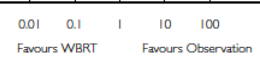
Study or subgroup	Whole-Brain Radiotherapy n/N	Observation n/N	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
Aoyama 2006	23/65	40/67		37.5 %	0.59 [0.40, 0.87]
Chang 2009	8/28	22/30		20.8 %	0.39 [0.21, 0.73]
Patchell 1998	11/49	33/46		24.6 %	0.31 [0.18, 0.54]
Roos 2006	5/10	7/9		17.1 %	0.64 [0.32, 1.31]
Total (95% CI)	**152**	**152**		**100.0 %**	**0.47 [0.34, 0.66]**

Total events: 47 (Whole-Brain Radiotherapy), 102 (Observation)

Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 4.56$, df = 3 (P = 0.21); $I^2 = 34\%$

Test for overall effect: Z = 4.39 (P = 0.000011)

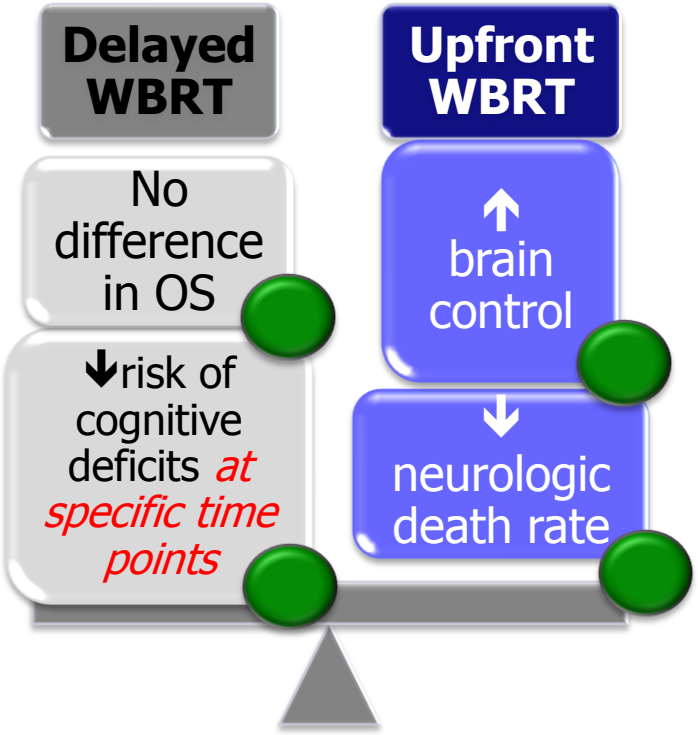
Test for subgroup differences: Not applicable



There is low quality evidence that adding upfront WBRT to surgery or SRS decreases any intracranial disease progression at one year. There was no clear evidence of an effect on overall and progression free survival. The impact of upfront WBRT on neurocognitive function, health related quality of life and neurological adverse events was undetermined due to the high risk of performance and detection bias, and inconsistency in the instruments and methods used to measure and report results across studies

Upfront or delayed WBRT

Brain oligometastatic patients

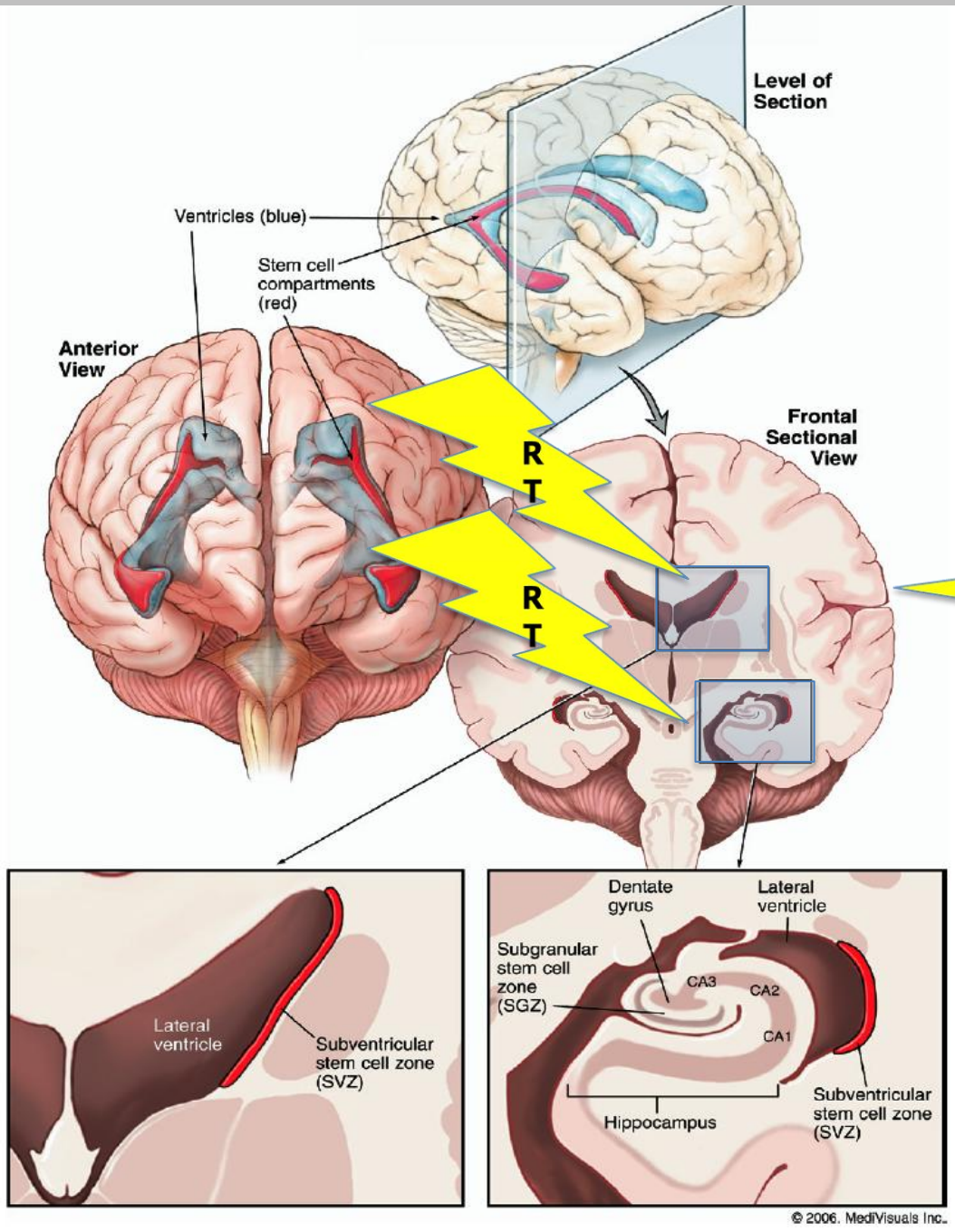


based on Phase III trials

Less toxic radiotherapy

Selection of patients for RT withdrawal

Radiation induced neurotoxicity

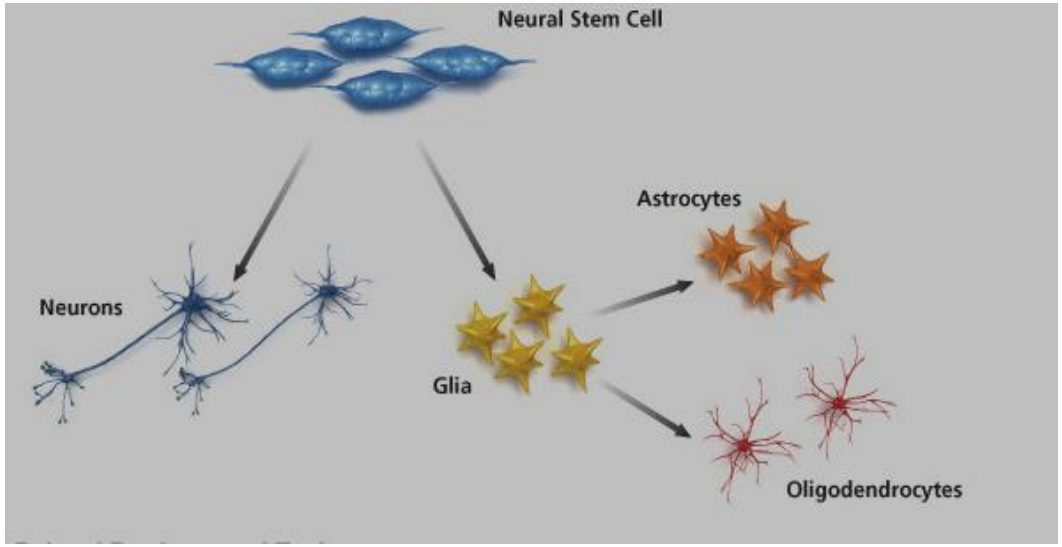


Injury to neural stem cells

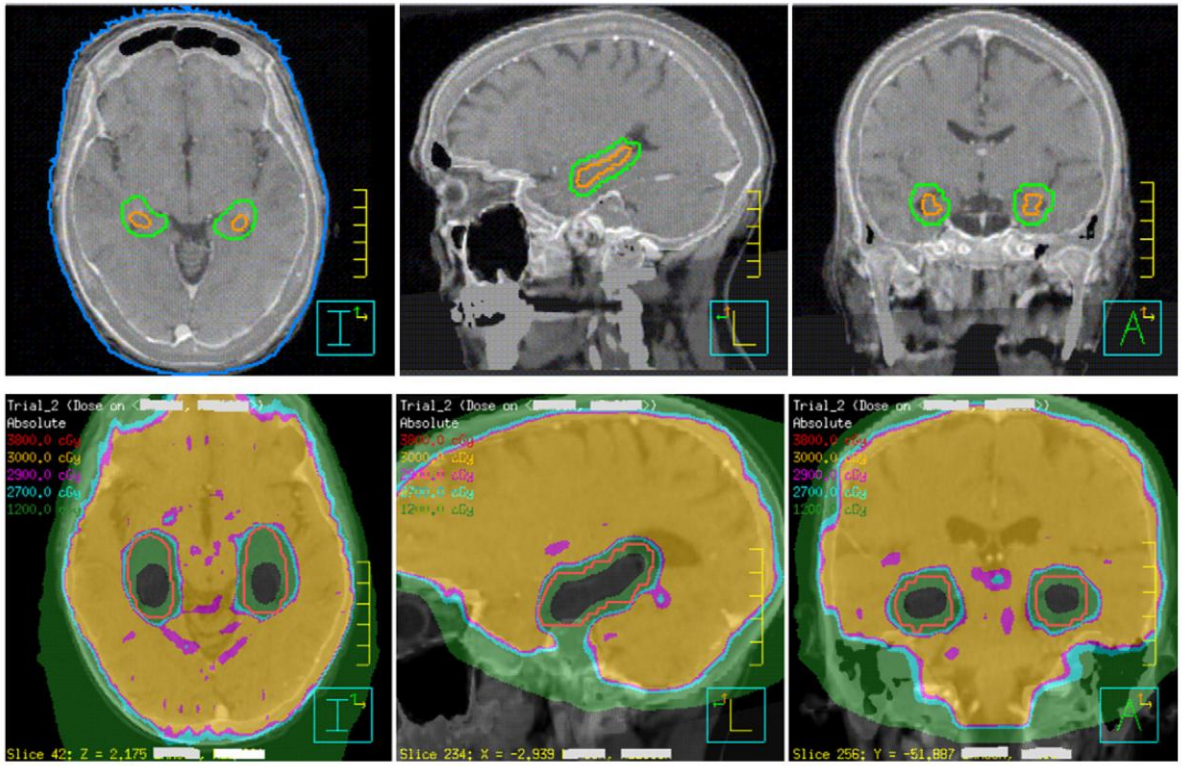
Radiotherapy

Chemotherapy

Shors, Nature 2001



Hippocampal avoidance and WBI



Review

Why avoid the hippocampus? A comprehensive review

Vinai Gondi [a,*], Wolfgang A. Tomé [a,b], Minesh P. Mehta [a]

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RADIATION THERAPY ONCOLOGY GROUP

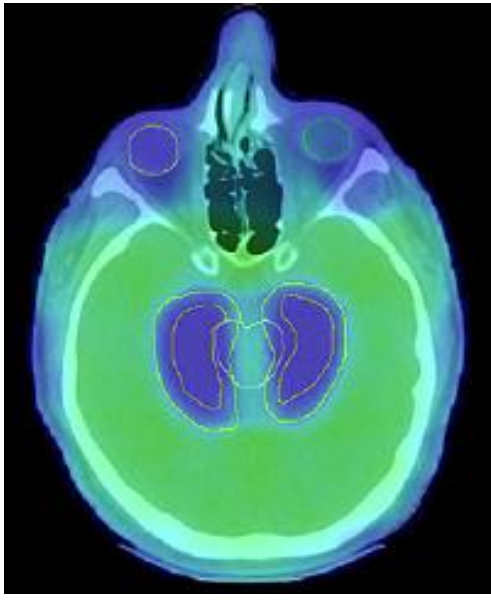
RTOG 0933

A PHASE II TRIAL OF HIPPOCAMPAL AVOIDANCE DURING WHOLE BRAIN RADIOTHERAPY FOR BRAIN METASTASES

SCHEMA (12/5/11)

For Patients with MRI Evidence of Brain Metastasis Within 1 Month Prior to Registration

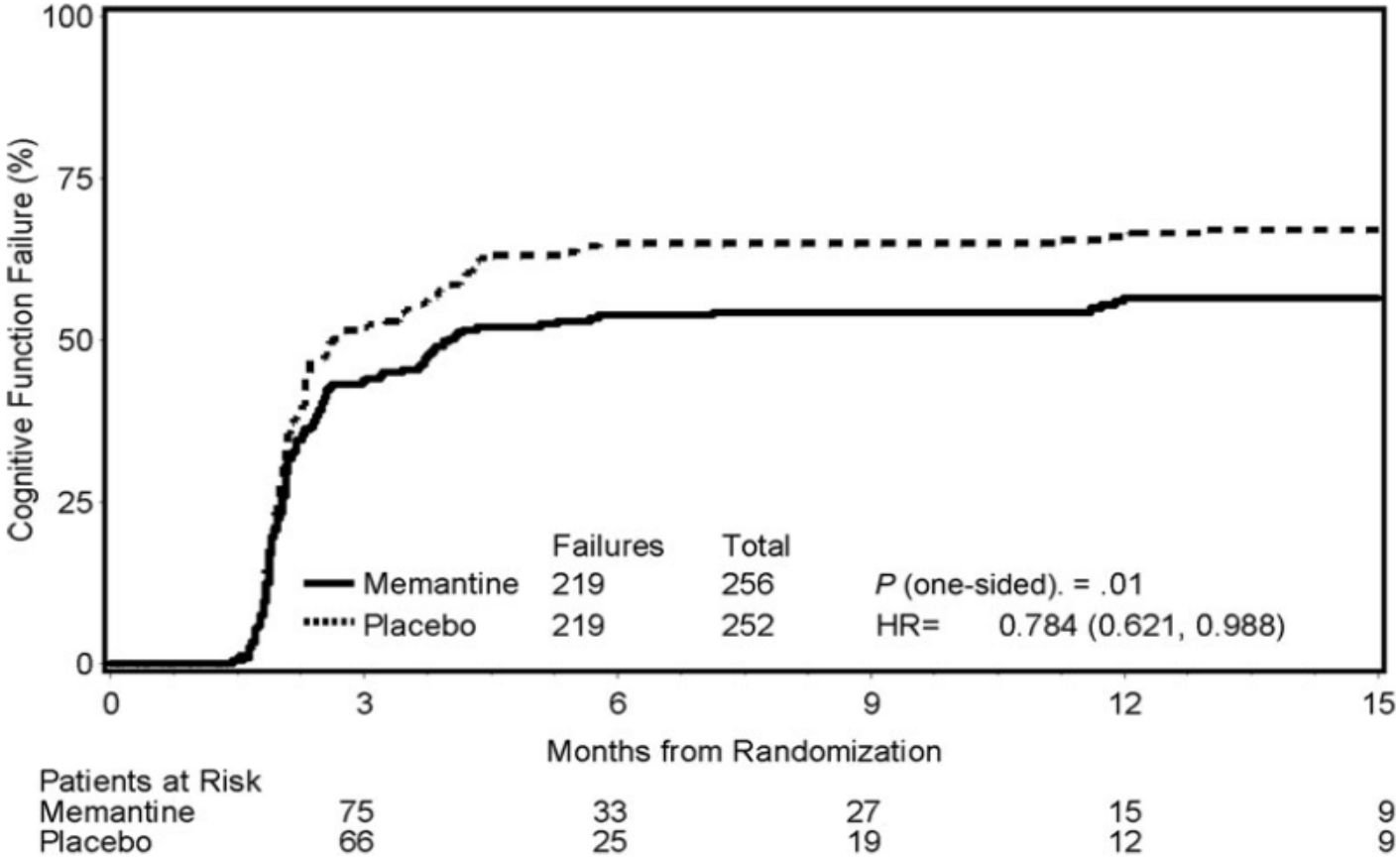
	Prior to Treatment Start	Radiation Therapy
REGISTER[1]	1. MRI with Fused CT Simulation[2] 2. Neurocognitive Function Testing 3. Quality of Life Assessment 4. Rapid Central Review of Hippocampal Contours and HA-WBRT Treatment Plan[3]	WBRT with Hippocampal Avoidance using IMRT (30 Gy in 10 Fractions)



Memantine for the prevention of cognitive dysfunction in patients receiving whole-brain radiotherapy: a randomized, double-blind, placebo-controlled trial

Paul D. Brown

Neuro-Oncology 15(10):1429–1437, 2013



Evolving issues in Radiotherapy for brain mets:

Survival/Brain Tumor control/QoL/Cognitive Function

Patients selection

- ✓ prognostic scores only validated for OS

New Strategies:

- ✓ **Radiosurgery instead of Whole Brain Radiotherapy**
- ✓ **Partial Brain Radiotherapy**
- ✓ **Specific dosimetry for WBRT**

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SRS vs WBRT:

it’s not a numbers game !

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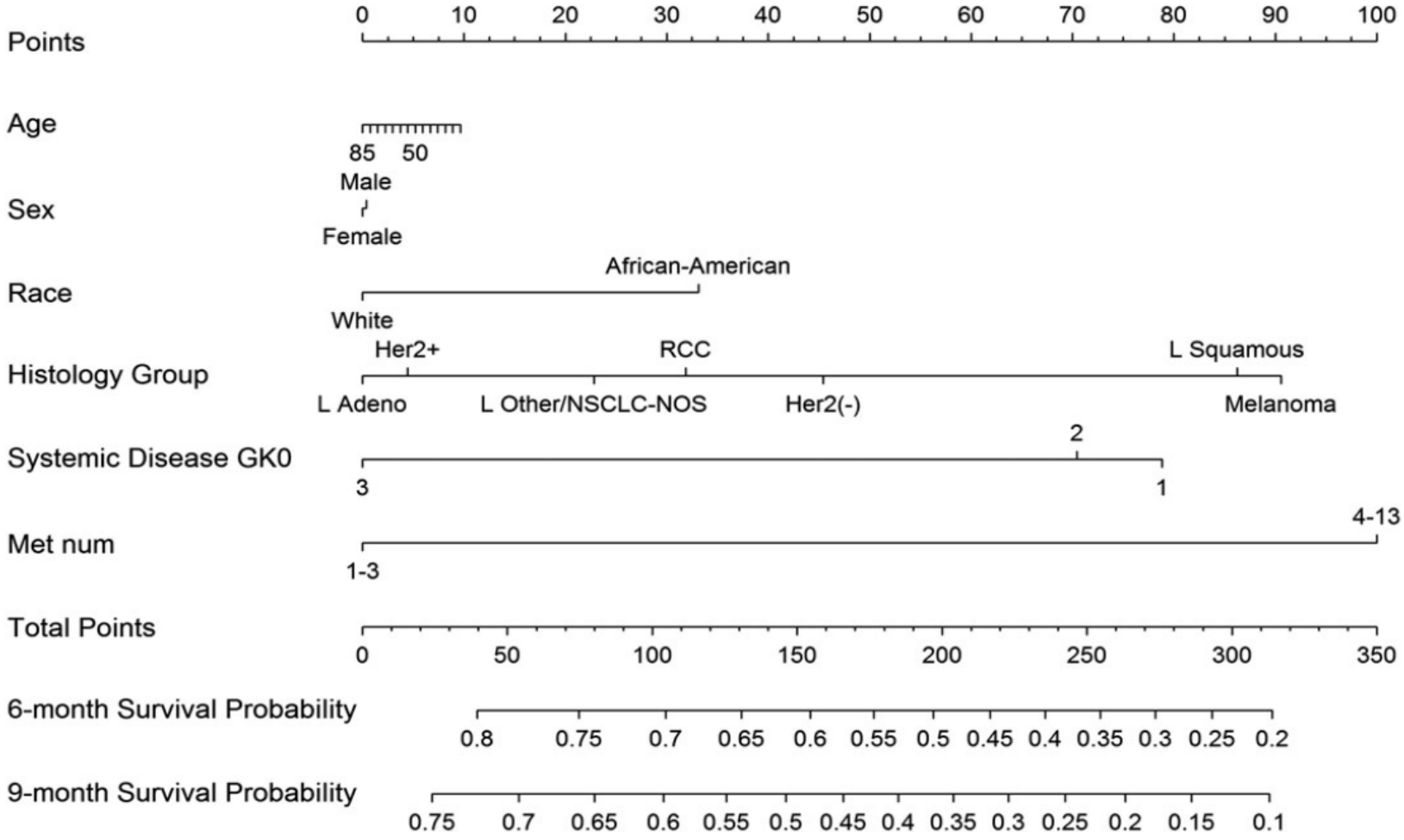
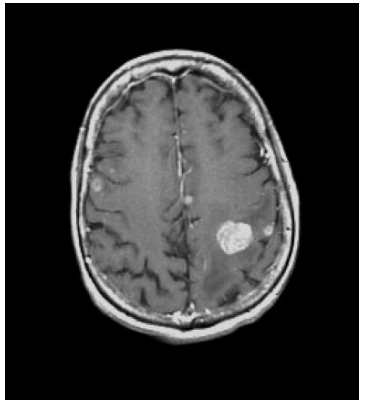
A nomogram for predicting distant brain failure in patients treated with gamma knife stereotactic radiosurgery without whole brain radiotherapy

Diandra N. Ayala-Peacock

Neuro-Oncology 16(9), 1283–1288, 2014



Brain mets in HER2-overexpressing breast cancer: conclusions



- Multiple symptomatic brain mets: WBI (space for anti-HER2 therapies)

- Oligometastatic disease (1-4; now: 1-…?): Sx and/or SRS ("regional" adjuvant treatment to be discussed)

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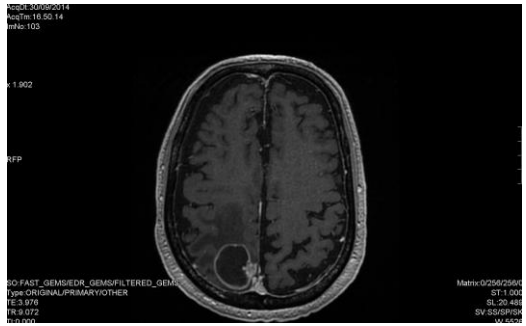
What type of radiotherapy is indicated in brain metastases? A personal view



- Neurosurgery has an important role
- SRS is the best option for small and/or unresectable mets (≤ 3 cm)
- Probably safe and effective to treat multiple small deposits
- WBRT with hippocampal sparing may be useful for multiple mets where SRS not feasible
- WBRT with SIB not yet shown to improve outcomes but has potential
- No evidence that post-op SRS improves outcome
- Individualise treatment !!! And: **MDT evaluation**

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