Update on management of metastatic brain disease

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Mount Vernon Cancer Centre
Northwood
UK

Incidence

- 15-30% of patients with solid tumours will develop brain metastases
- Most common primary sites are:
  - Lung
  - Breast
  - Melanoma
  - Renal
  - Colorectal

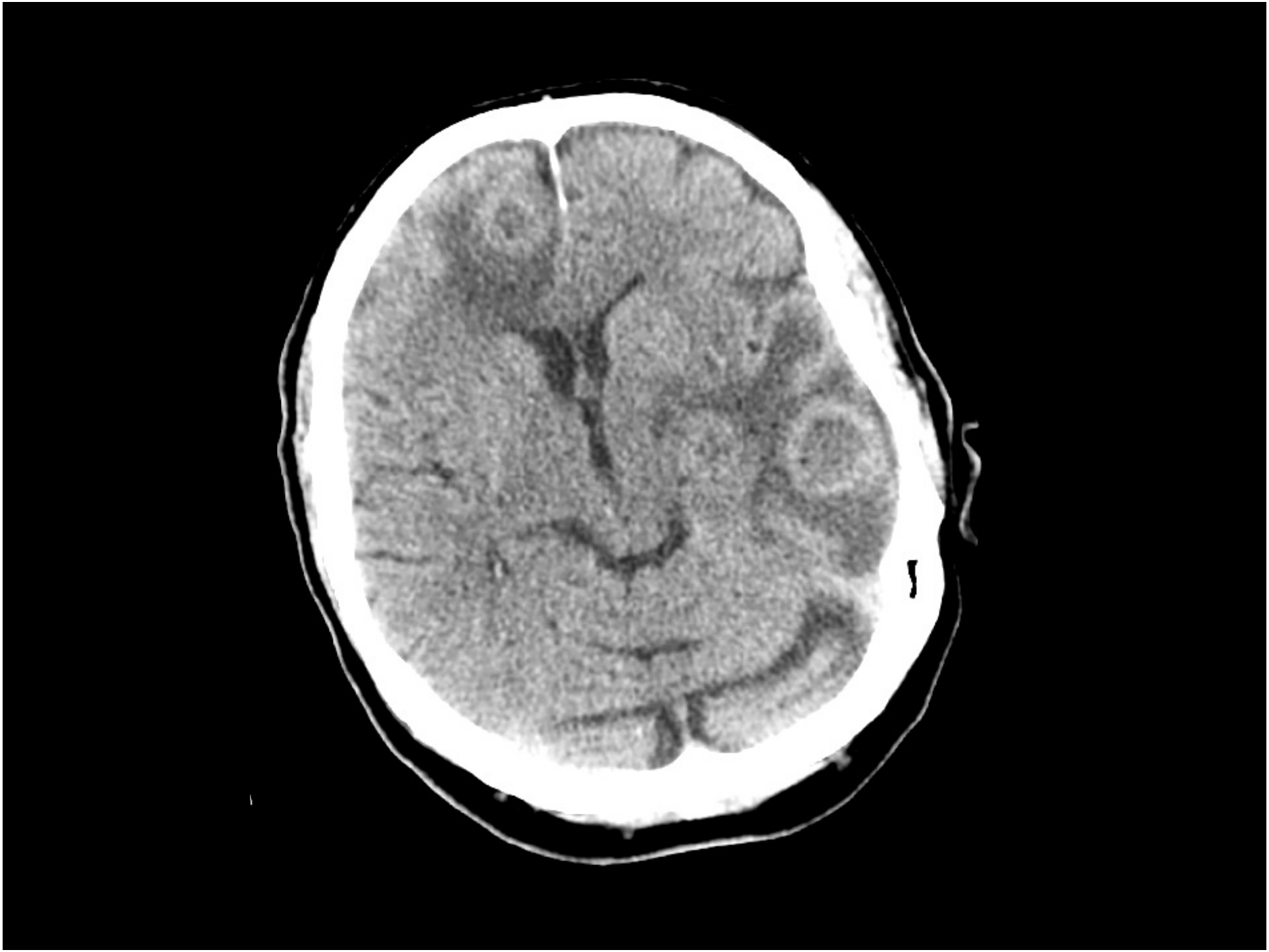
Changing pattern of brain metastases

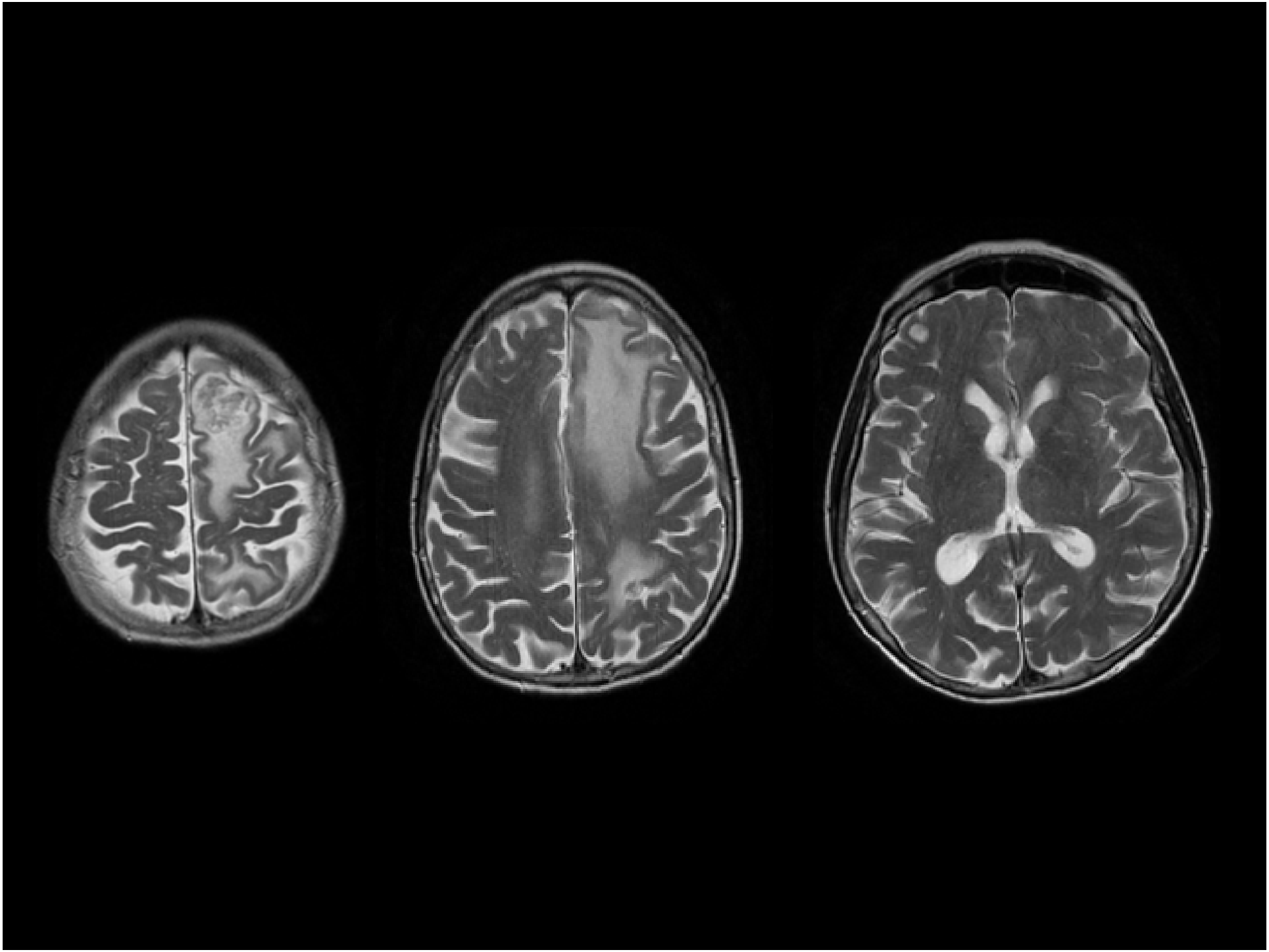
	1983-1989	2003-2009
Lung	52%	40%
Melanoma	5%	9%
Breast	17%	17%
Renal/ Colorectal	8%	24%

Neider et al 2011

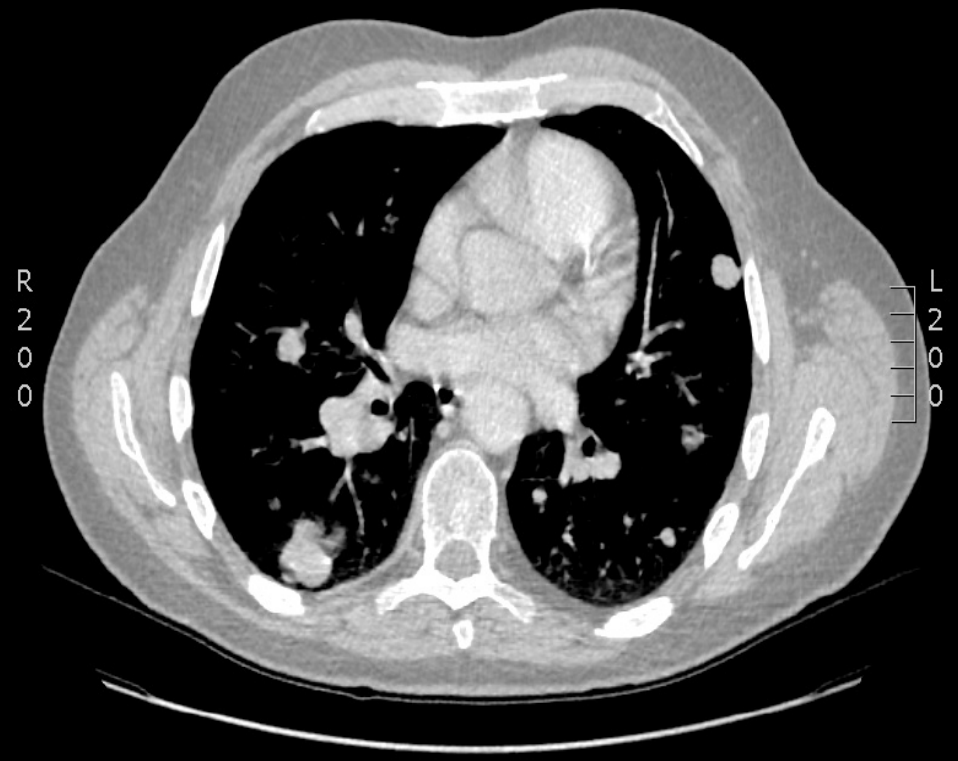
Diagnosis of brain metastases

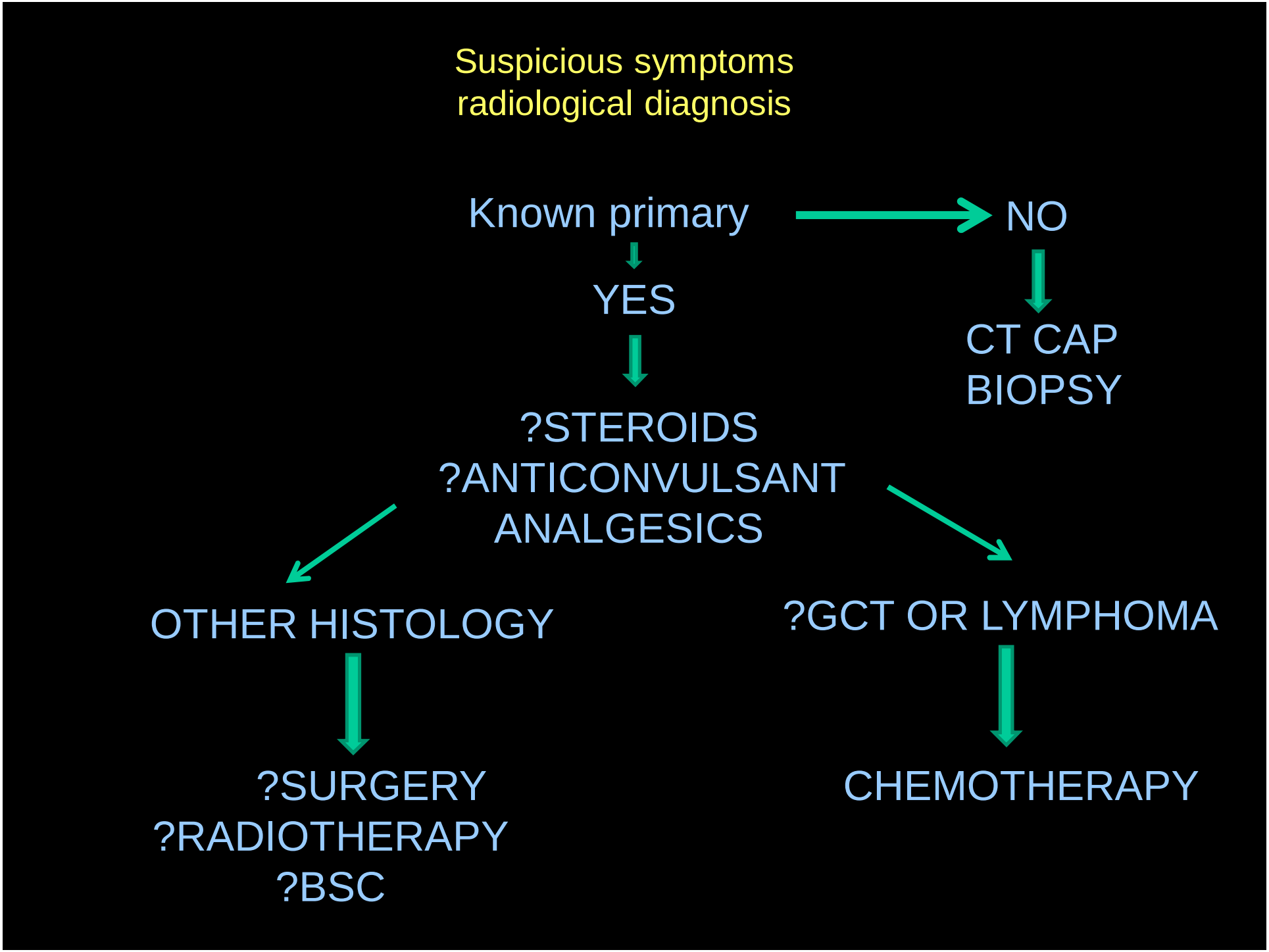
- CT scan: screening
  - Will detect lesions 3-4mm
  - Oedema may be prominent with midline shift
  - Lung and breast often similar to normal brain
  - Most enhance with IV contrast
  - On CT approximately 50% will be solitary
- MR scan: definitive
  - More sensitive
  - 10% have haemorrhage
  - Gadolinium enhanced MR will identify multiple metastases in 2-11% of CT defined solitary mets
  - Functional MR may have a role

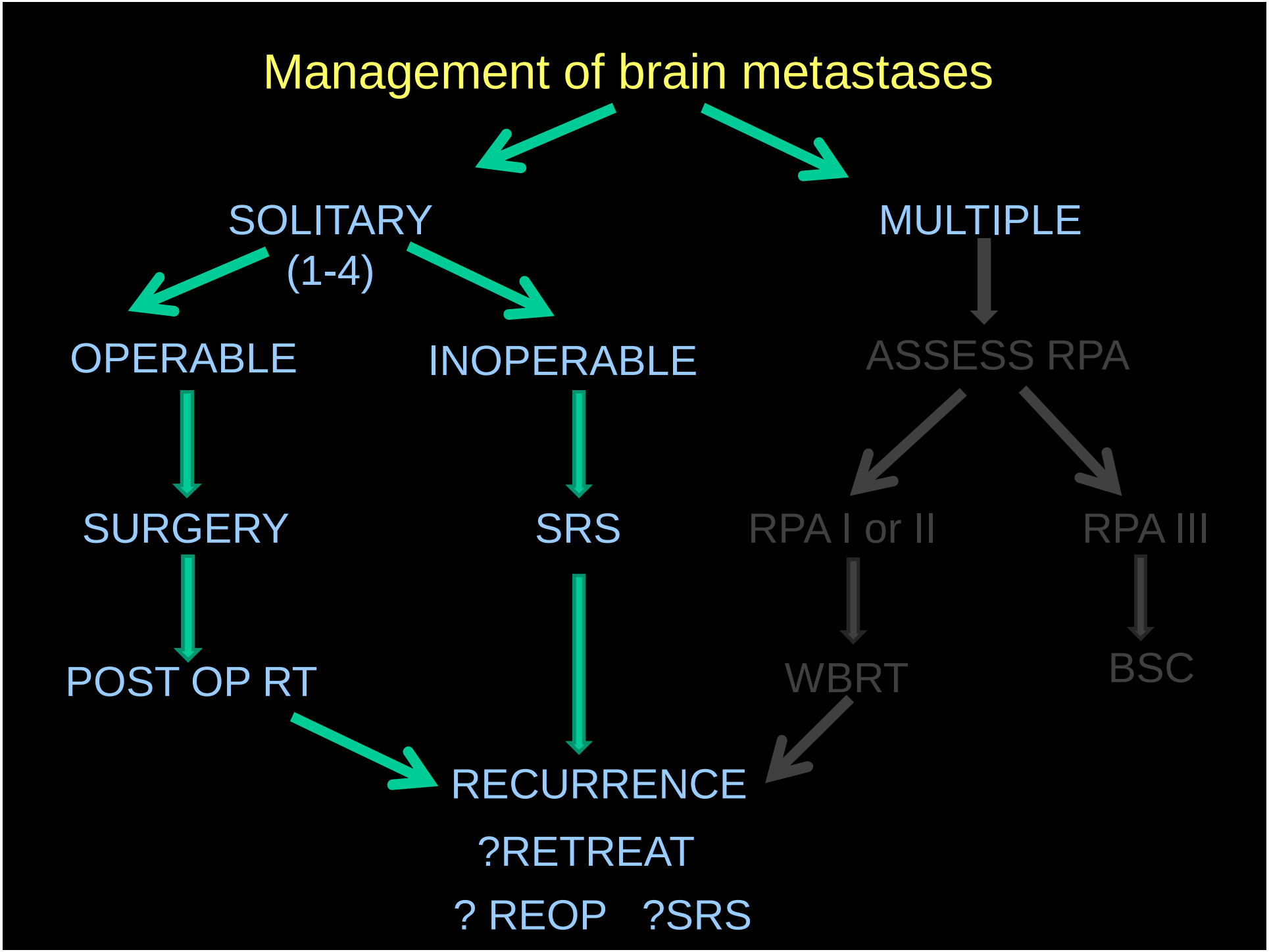




Management of brain metastases



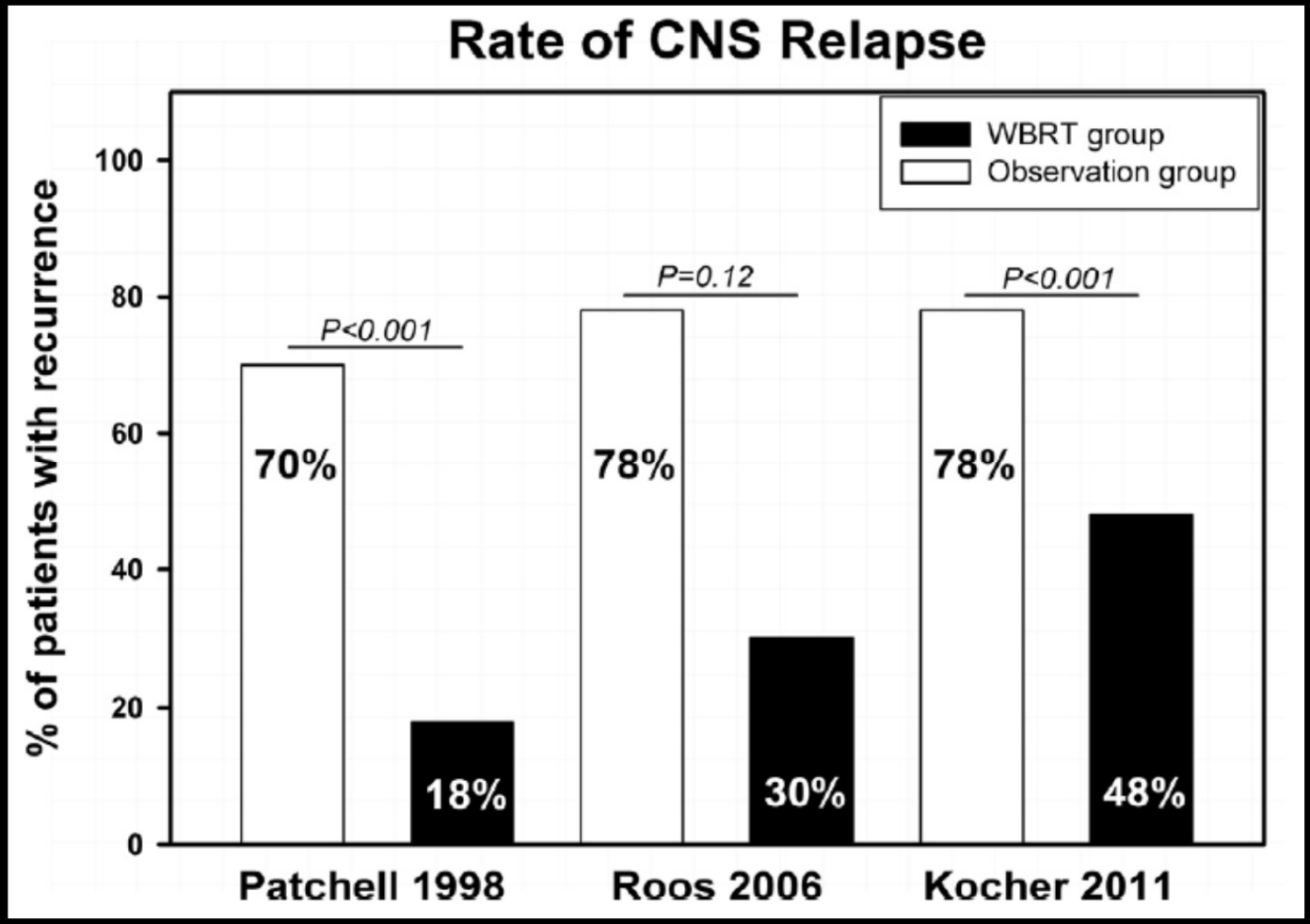

Suspicious symptoms
radiological diagnosis
Known primary
NO
YES
CT CAP
BIOPSY
?STEROIDS
?ANTICONVULSANT
ANALGESICS
OTHER HISTOLOGY
?GCT OR LYMPHOMA
?SURGERY
?RADIOTHERAPY
?BSC
CHEMOTHERAPY


Management of brain metastases
SOLITARY
(1-4)
MULTIPLE
OPERABLE
INOPERABLE
ASSESS RPA
SURGERY
SRS
RPA I or II
RPA III
POST OP RT
WBRT
BSC
RECURRENCE
?RETREAT
? REOP ?SRS

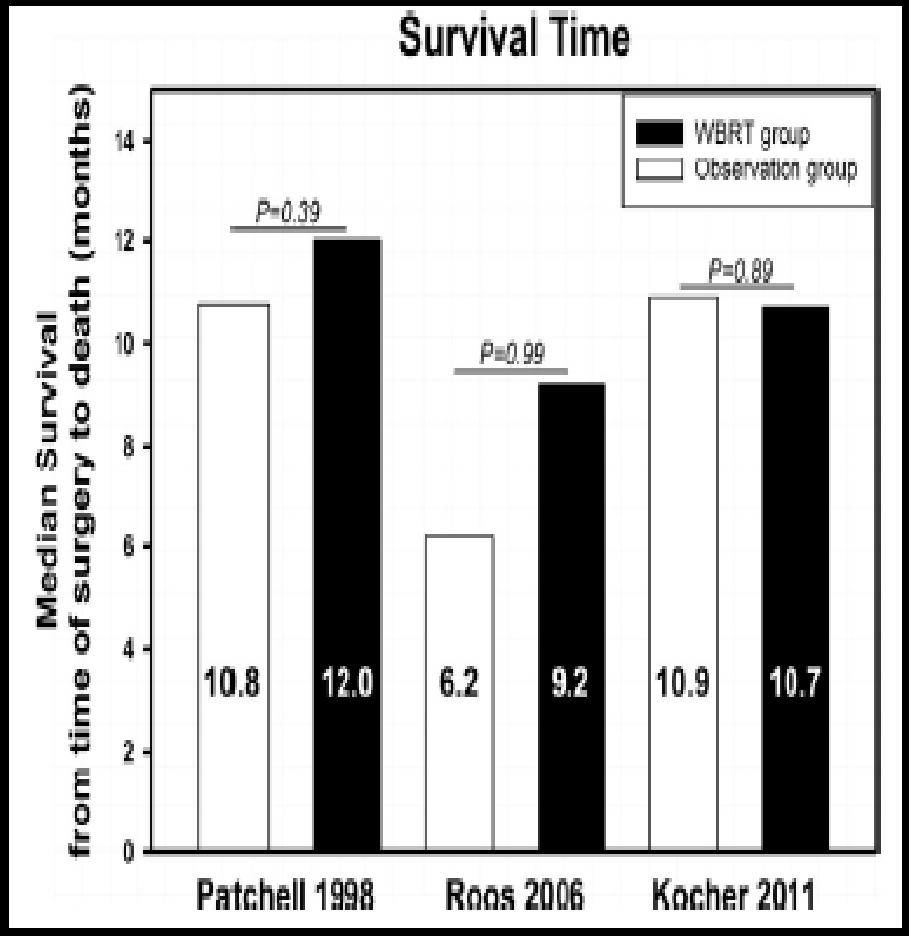
Solitary metastases

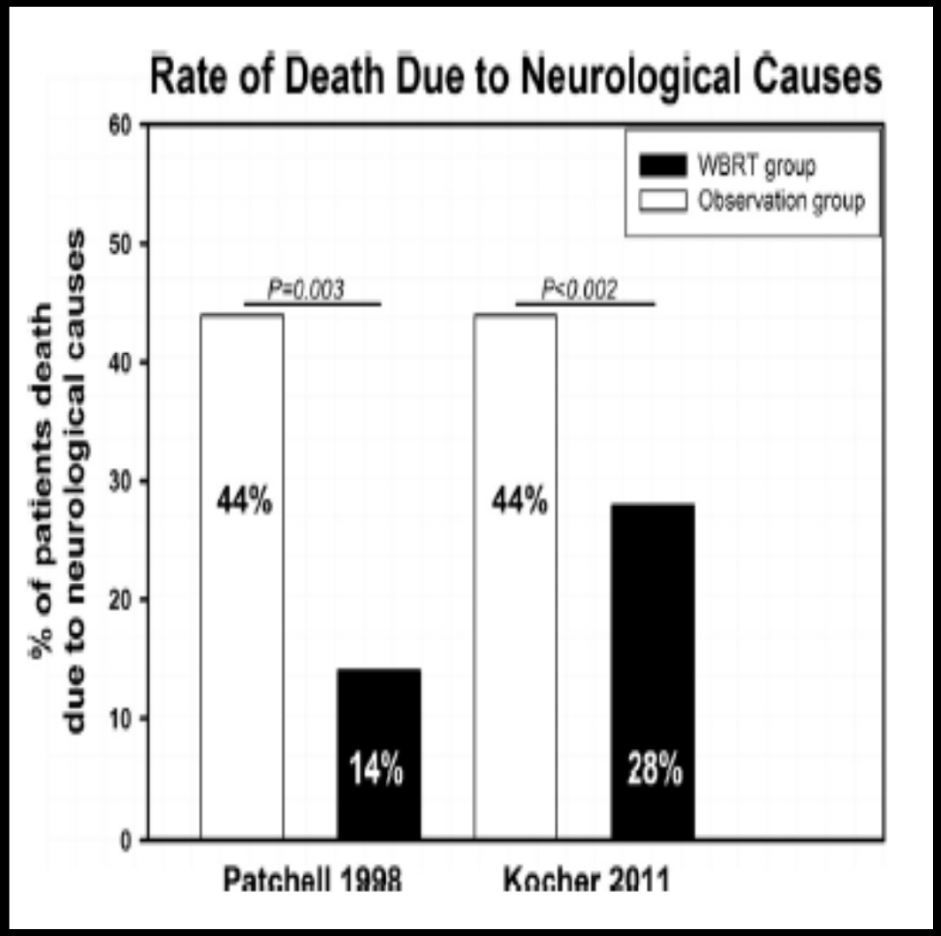
- Surgery alone
- Surgery + post op radiotherapy
  - + WBRT
  - + SRS
- RT alone
  - Whole brain radiotherapy
  - Radiosurgery

Surgery + post op radiotherapy



Surgery + post op radiotherapy



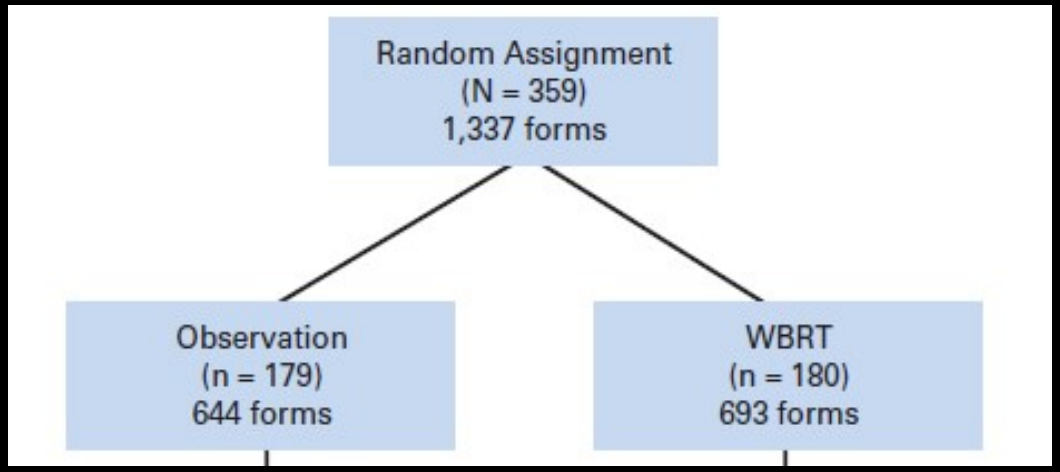


A European Organisation for Research and Treatment of Cancer Phase III Trial of Adjuvant Whole-Brain Radiotherapy Versus Observation in Patients With One to Three Brain Metastases From Solid Tumors After Surgical Resection or Radiosurgery: Quality-of-Life Results

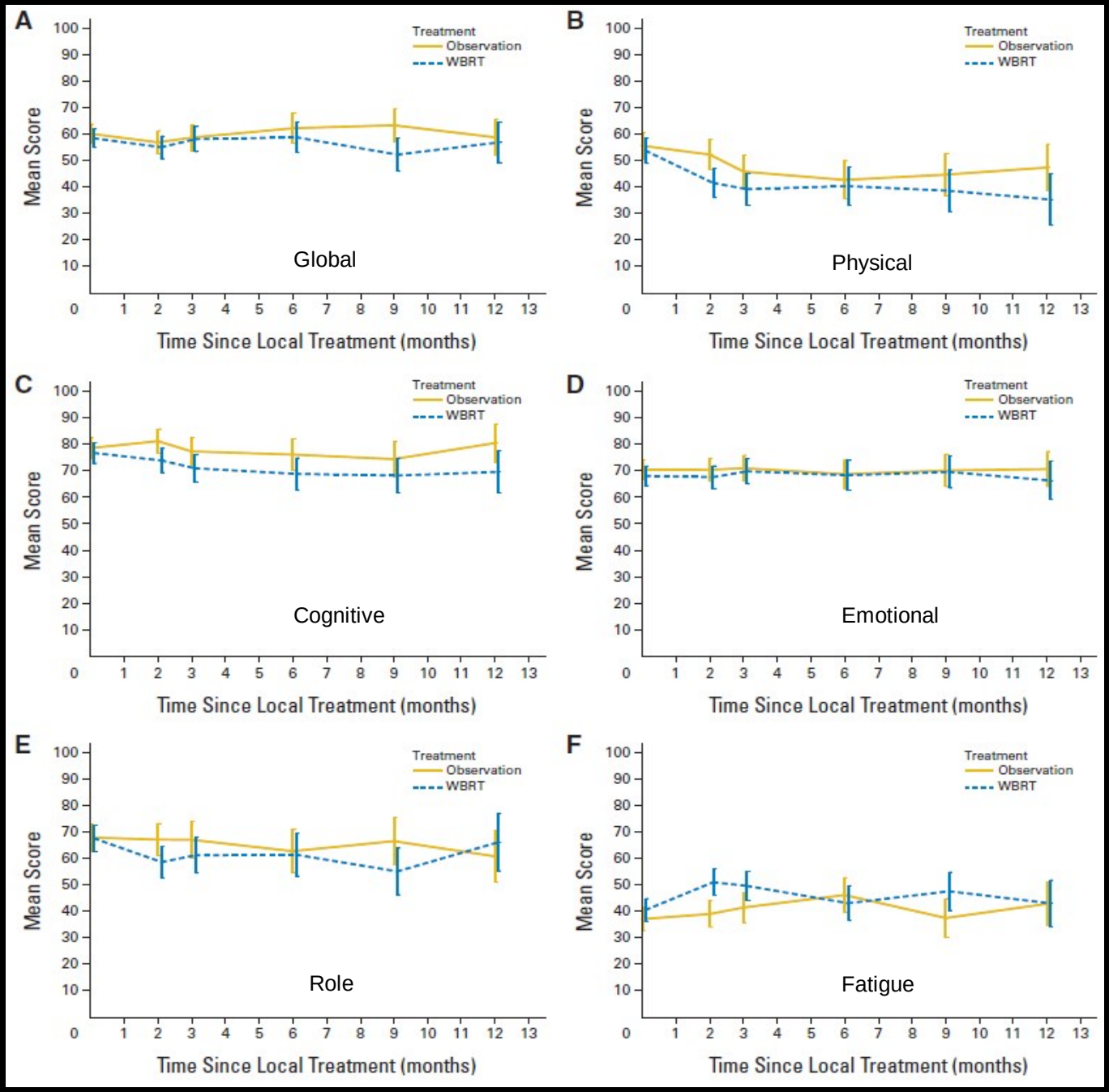
Riccardo Soffietti, Martin Kocher, Ufuk M. Abacioglu, Salvador Villa, François Fauchon, Brigitta G. Baumert,

J Clin Oncol 31:65-72. © 2012

Radiosurgery or Surgery
for 1-3 metastases



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



J Clin Oncol 31:65-72. © 2012

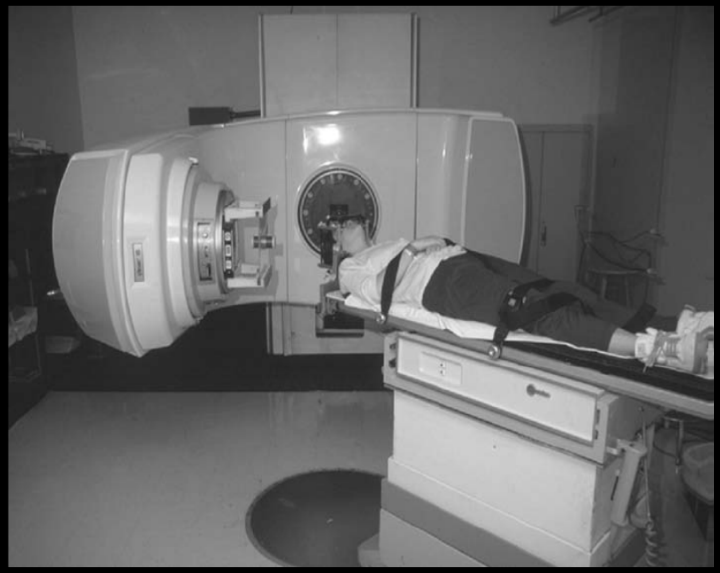
Solitary metastases

- Surgery alone
- Surgery + post op radiotherapy
- **RT alone**
  - **Whole brain radiotherapy**
  - **Radiosurgery**

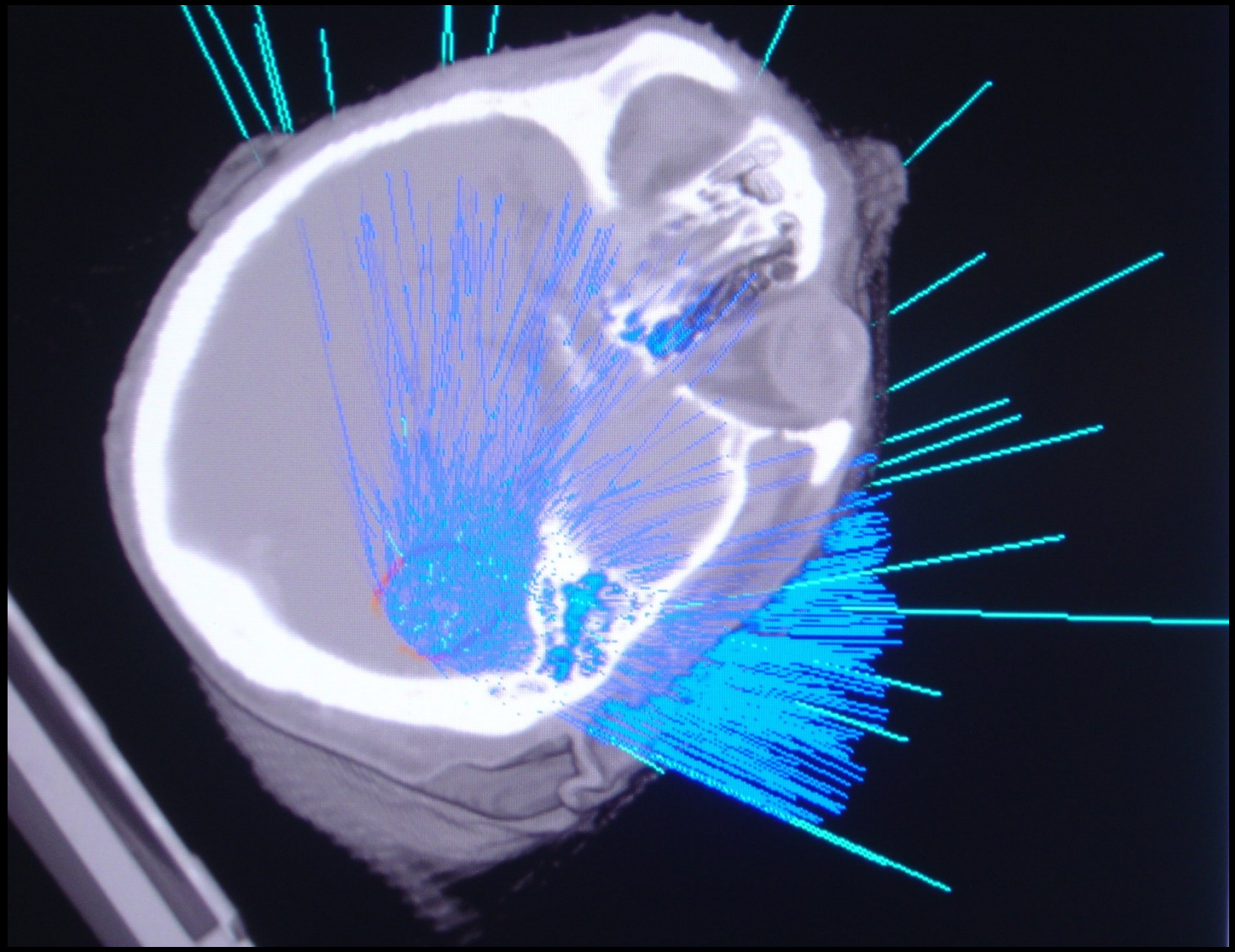
Solitary brain metastases: RadioSurgery

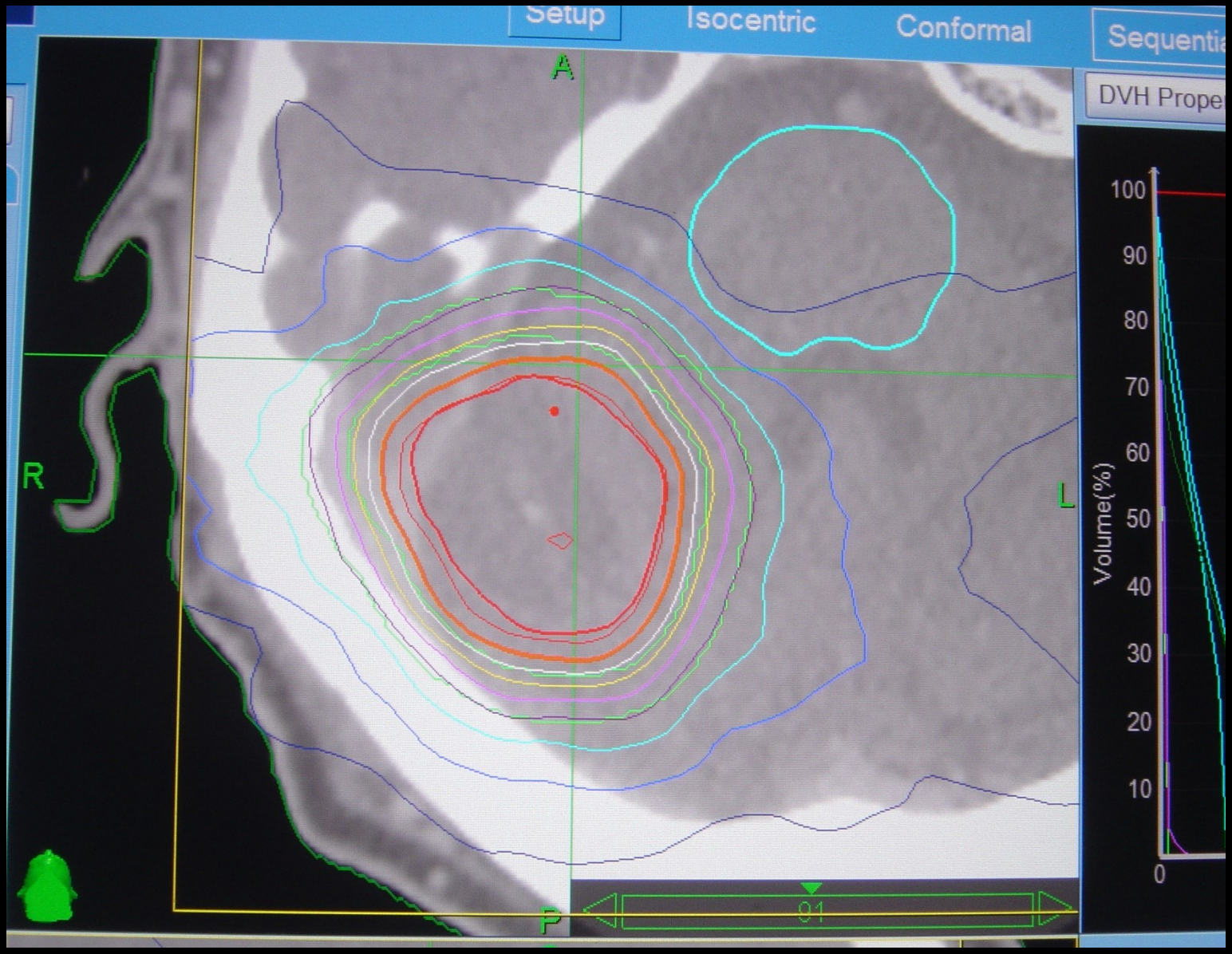
- Gammaknife

- Stereotactic linear accelerator techniques




CyberKnife

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80
70
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30
20
10
0
Volume(%)

Surgery vs SRS

- No RCT: three retrospective analyses

Muacevic	Schoggl	McNeil
n=108	n=133	n=97

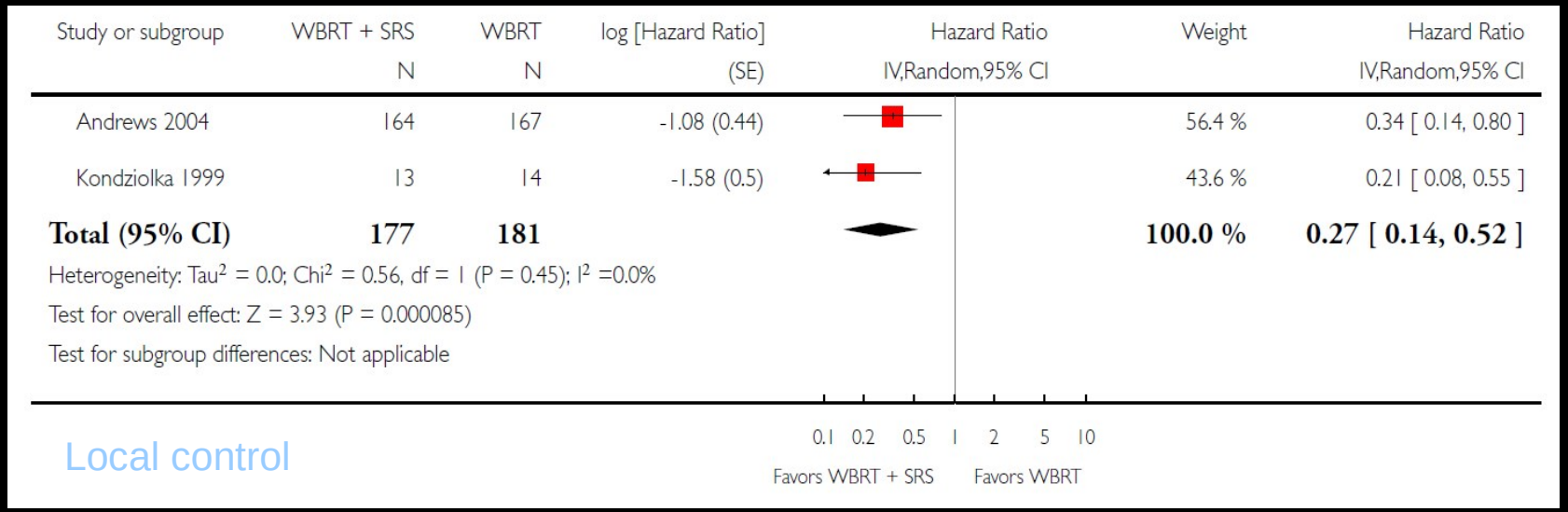
All subject to selection bias
No difference for survival
or Local control shown

Randomised trials of SRS vs WBRT + SRS

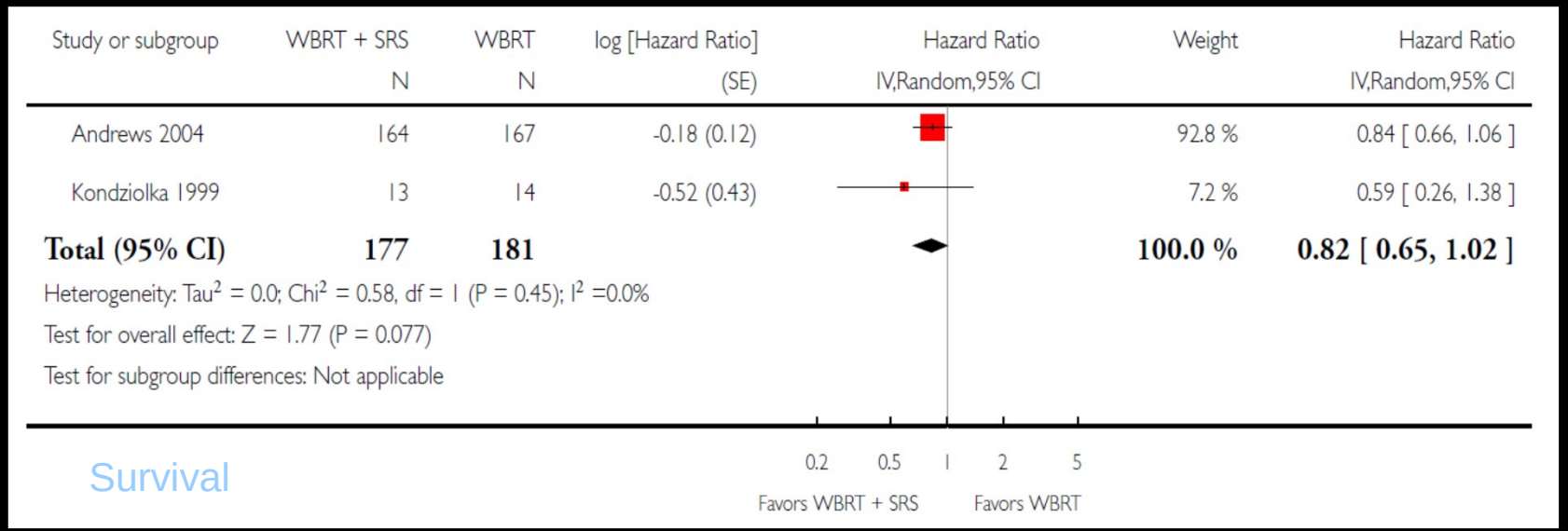
	N	Number of lesions	12-month local tumour control	12-month brain tumour recurrence	Median survival (months)
Radiation Therapy Oncology Group 95-08[2] (N=331)					
Whole-brain radiotherapy plus stereotactic radiosurgery	164	1–3	82%	25%	6·5
Whole-brain radiotherapy alone	167	1–3	71%	30%	5·7
Japanese Radiation Oncology Study Group 99-1[22] (N=132)					
Stereotactic radiosurgery plus whole-brain radiotherapy	65	1–4	88·7%	47%	7·5
Stereotactic radiosurgery alone	67	1–4	72·5%	76%	8·0
M D Anderson Cancer Center (N=58)					
Stereotactic radiosurgery plus whole-brain radiotherapy	28	1–3	100%	27%	5·7
Stereotactic radiosurgery alone	30	1–3	67%	73%	15·2

Whole brain radiation therapy (WBRT) alone versus WBRT and radiosurgery for the treatment of brain metastases

Patil CG, Pricola K, Sarmiento JM, Garg SK, Bryant A, Black KL



Local control



Survival

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

Probability of significant neurocognitive decline

	Stereotactic radiosurgery plus whole-brain radiotherapy (N=11)	Stereotactic radiosurgery alone (N=20)
Total recall	52%	24%
Delayed recall	22%	6%
Delayed recognition	11%	0%

Neurocognitive functioning and health-related quality of life in patients treated with stereotactic radiotherapy for brain metastases: a prospective study

Neuro-Oncology 2015; **0**, 1–10, doi:10.1093/neuonc/nov186

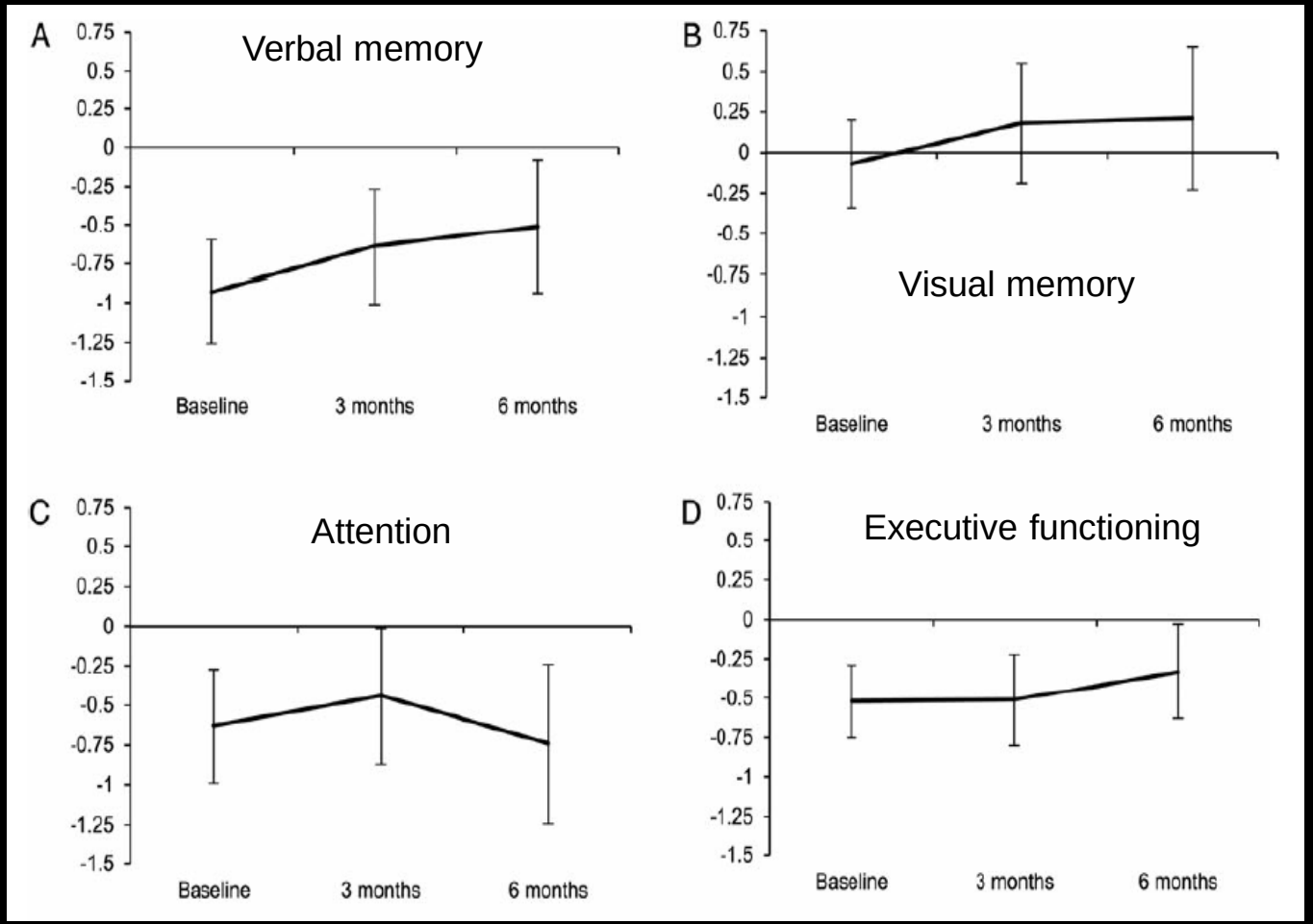
Esther J.J. Habets, Linda Dirven, Ruud G. Wiggenraad, Antoinette Verbeek-de Kanter, et al

N=97

Median survival :7.7mo
1yr survival: 30%

Pre SRS:
53% below expected in at least 1 domain

Compliance:
84% at 6months



Stereotactic radiosurgery for multiple brain metastases

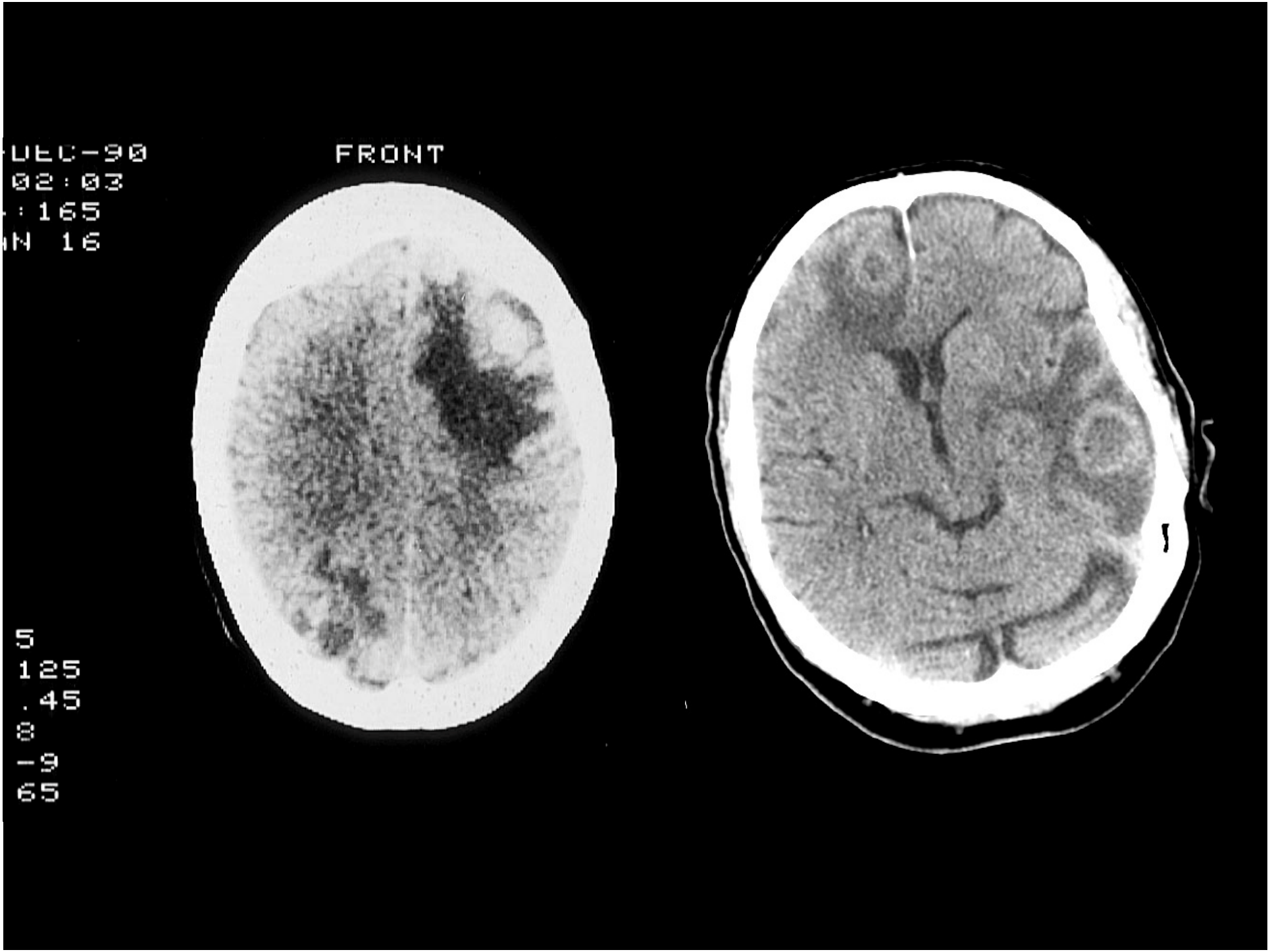
Expert Rev. Anticancer Ther. Early online, 1–20 (2014)

Tai-Chung Lam[1], Arjun Sahgal[2], Eric L Chang[3] and Simon S Lo*[4]

- Stereotactic radiosurgery (SRS) for brain metastases gives consistently high local control rates of approximately 70–90% at 1 year, with minimal acute side effects and a low risk of symptomatic radiation necrosis (<10%).
- Efficacy of SRS is considered to be equivalent to neurosurgical excision in lesions smaller than 3 cm in diameter.
- SRS alone for newly diagnosed, limited brain metastases (1–4) is associated with better preserved neurocognitive function and quality of life compared to SRS plus upfront WBRT.
- Patients who receive radiation treatments for brain metastases must be followed up by close surveillance with MRI as distant intracranial recurrence rates are high – consistently approximately 30–50% at 1 year. Repeating focal treatment either with SRS or surgical treatment was feasible in selected patients.
- Salvage treatment for symptomatic recurrence after SRS alone treatment is associated with worse outcomes than asymptomatic recurrence.
- There is adequately powered level II evidence showing that OS of patients with 2–4 brain metastases is similar to 5–10 metastases after SRS alone treatment, provided that the total tumor volume is less than 15 ml, the largest tumor is less than 10 ml or less than 3 cm in diameter, performance status of patients is ≥70 and there is no evidence of leptomeningeal metastases.

Solitary brain metastases

- Operable single lesions: surgery
- Postop radiotherapy recommended
  - SRS
- Inoperable 1-4 lesions: SRS alone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65

Multiple brain metastases

- Radiotherapy
  - Dose fractionation
  - Patient selection
- Chemotherapy
  - Patient selection

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

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

Dose >30Gy/10f vs 30Gy/10f control

SURVIVAL

Study or subgroup	log [Hazard Ratio] (SE)	Hazard Ratio IV,Fixed,95% CI	Weight	Hazard Ratio IV,Fixed,95% CI
Chatani 1985	-0.7487 (0.2907)		6.9 %	0.47 [0.27, 0.84]
Chatani 1994	0.0435 (0.2169)		12.4 %	1.04 [0.68, 1.60]
Kurtz 1981	-0.0747 (0.1367)		31.2 %	0.93 [0.71, 1.21]
Murray 1997	0.0698 (0.1085)		49.5 %	1.07 [0.87, 1.33]
Total (95% CI)			**100.0 %**	**0.97 [0.83, 1.12]**

Dose <30Gy/10f vs 30Gy/10f control

Study or subgroup	log [Hazard Ratio] (SE)	Hazard Ratio IV,Fixed,95% CI	Weight	Hazard Ratio IV,Fixed,95% CI
Chatani 1994	0.0171 (0.239)		10.0 %	1.02 [0.64, 1.63]
Harwood 1977	0.3461 (0.199)		14.4 %	1.41 [0.96, 2.09]
Priestman 1996	0.179 (0.087)		75.5 %	1.20 [1.01, 1.42]
Total (95% CI)			**100.0 %**	**1.21 [1.04, 1.40]**

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

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

Dose >30Gy/10f vs 30Gy/10f control

NEUROLOGICAL FUNCTION

Study or subgroup	Higher dose n/N	Control dose n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Borgelt 1980	346/741	156/359		74.1 %	1.14 [0.88, 1.47]
Chatani 1985	25/34	26/35		4.1 %	0.96 [0.33, 2.82]
Chatani 1994	32/46	57/81		7.7 %	0.96 [0.44, 2.12]
Kurtz 1981	45/86	44/98		14.1 %	1.35 [0.75, 2.41]
Total (95% CI)	**907**	**573**		**100.0 %**	**1.14 [0.92, 1.42]**

Dose <30Gy/10f vs 30Gy/10f control

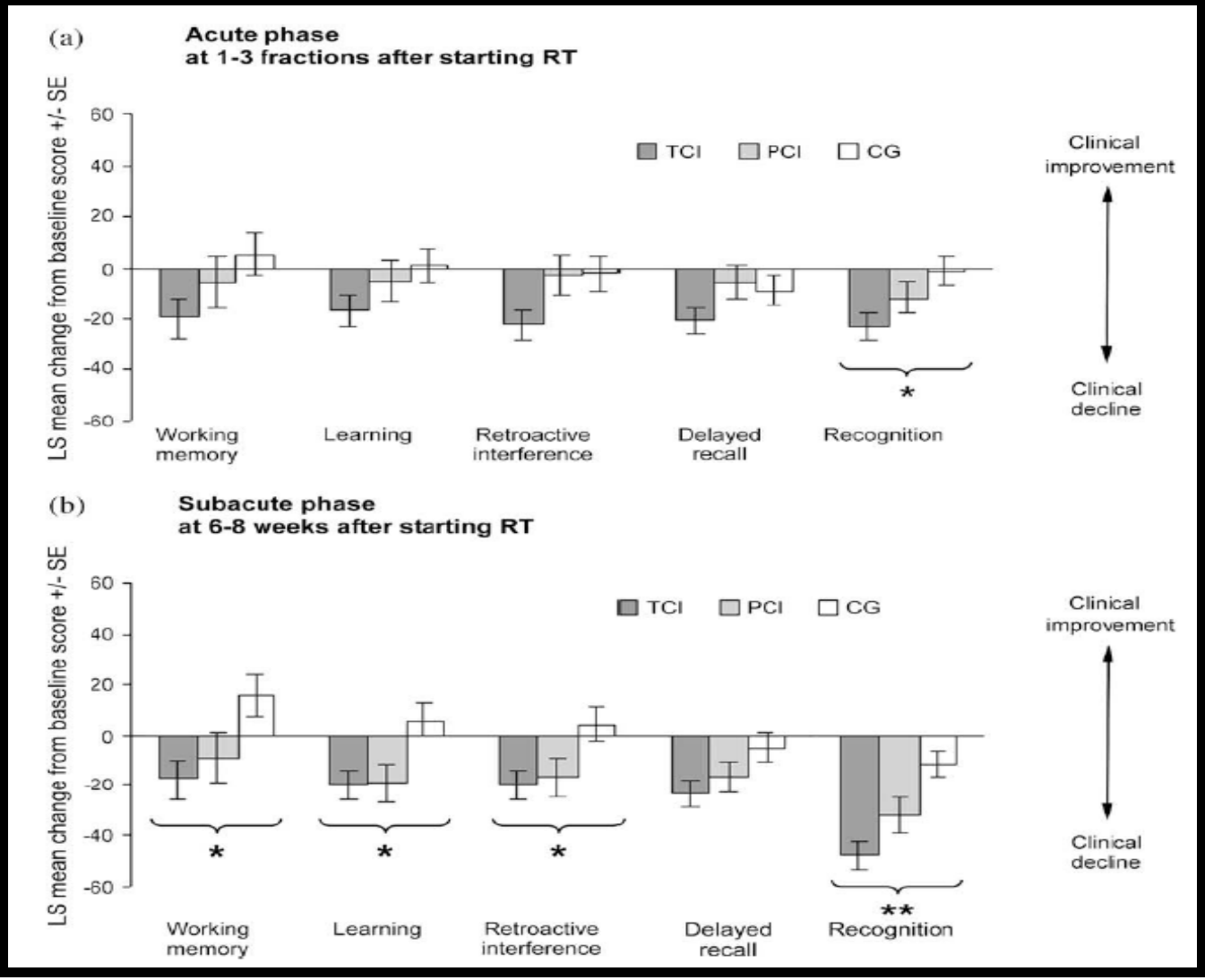
Study or subgroup	Lower dose n/N	Control dose n/N	Odds Ratio M-H,Random,95% CI	Weight	Odds Ratio M-H,Random,95% CI
Harwood 1977	22/51	18/50		16.3 %	1.35 [0.61, 3.00]
Borgelt 1980	250/353	156/359		25.9 %	3.16 [2.32, 4.31]
Borgelt 1981	38/68	41/82		19.3 %	1.27 [0.66, 2.42]
Chatani 1994	29/35	57/81		13.1 %	2.04 [0.75, 5.53]
Priestman 1996	163/270	142/263		25.3 %	1.30 [0.92, 1.83]
Total (95% CI)	**777**	**835**		**100.0 %**	**1.74 [1.06, 2.84]**

MEMORY FUNCTION BEFORE AND AFTER WHOLE BRAIN RADIOTHERAPY IN PATIENTS WITH AND WITHOUT BRAIN METASTASES

GRIT WELZEL, M.SC.,* KATHARINA FLECKENSTEIN, M.D.,*† JÖRG SCHAEFER, M.D.,* BRIGITTE HERMANN, M.D.,* UTA KRAUS-TIEFENBACHER, M.D.,* SABINE K. MAI, M.D.,* AND FREDERIK WENZ, M.D.*

* Department of Radiation Oncology, University Medical Center Mannheim, University of Heidelberg, Mannheim, Germany; and † Department of Radiation Oncology, Duke University Medical Center, Durham, NC

Int. J. Radiation Oncology Biol. Phys., Vol. 72, No. 5, pp. 1311–1318, 2008

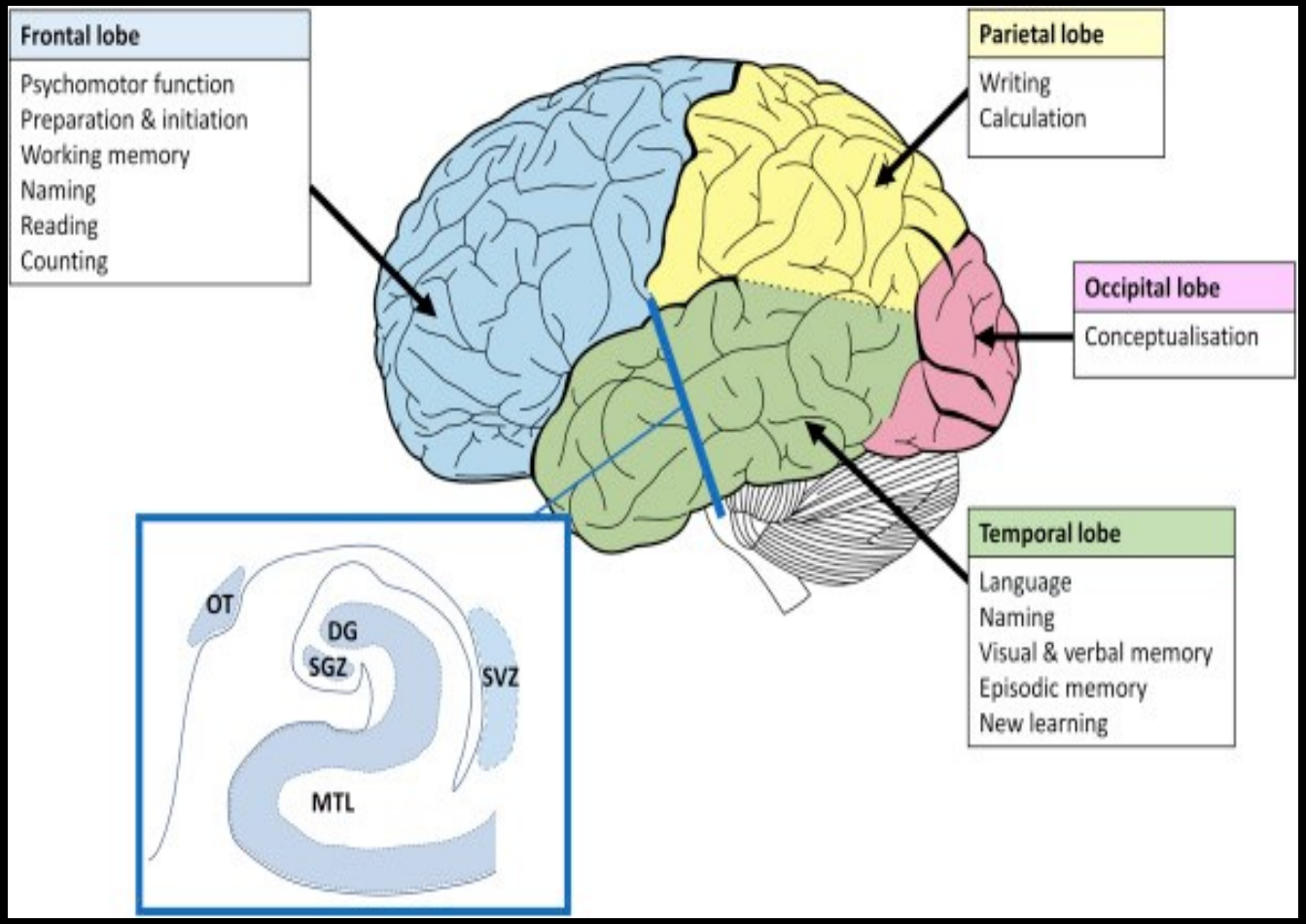


Neurocognitive Effects Following Cranial Irradiation for Brain Metastases

Clinical Oncology 27 (2015) 630–639

M.B. Pinkham *†, P. Sanghera ‡, G.K. Wall §, B.D. Dawson §, G.A. Whitfield *

Hippocampal sparing



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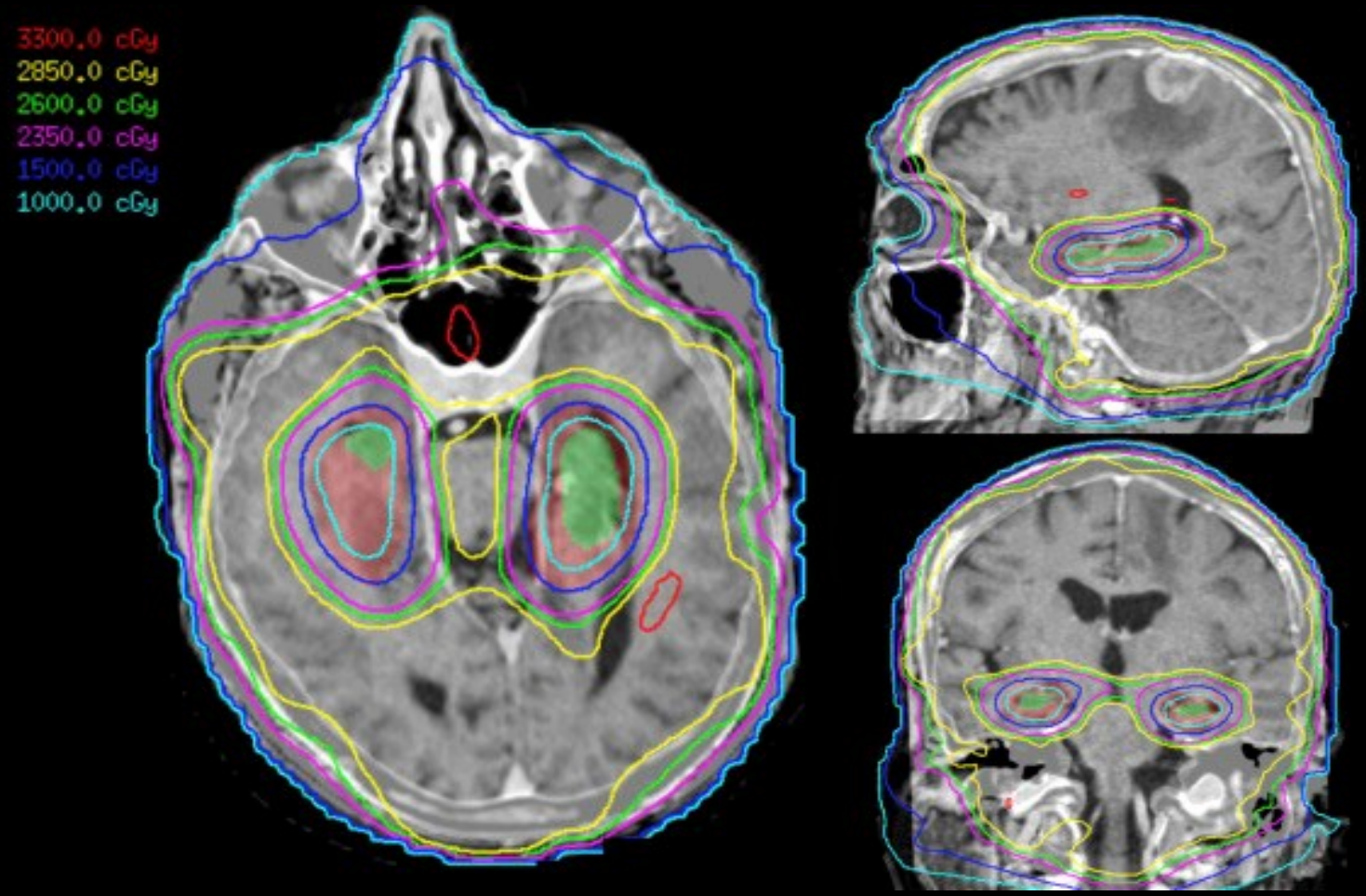
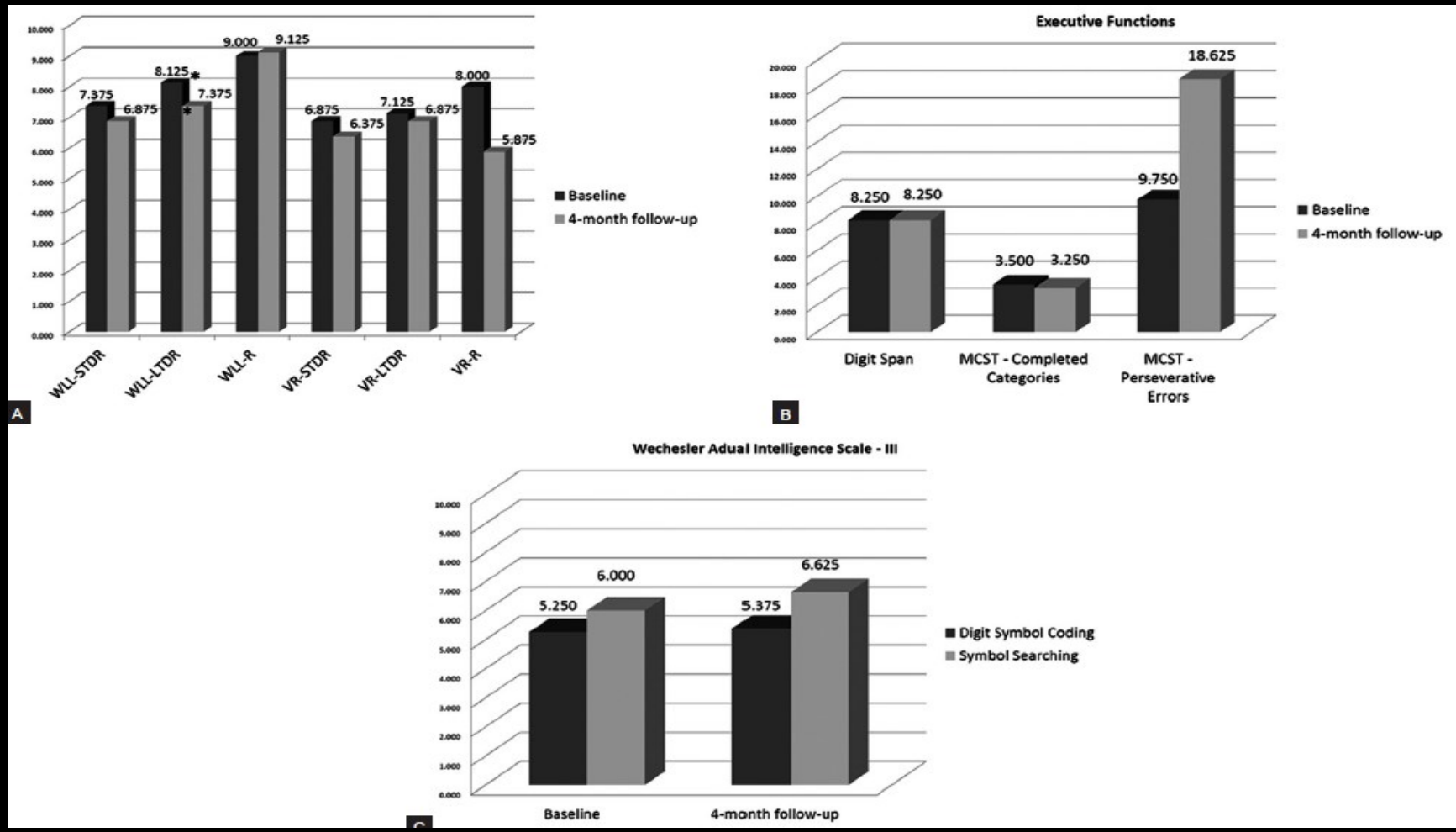


Evaluating the Impact of Hippocampal Sparing During Whole Brain Radiotherapy on Neurocognitive Functions: A Preliminary Report of a Prospective Phase II Study

(Biomed J 2015;38:439-449)

Shinn-Yn Lin[1,2,3], Chi-Cheng Yang[4], Yi-Ming Wu[5], Chen-Kan Tseng[1,2], Kuo-Chen Wei[6], Yi-Chuan Chu[7], Hsiang-Yao Hsieh[7], Tung-Ho Wu[1,2], Ping-Ching Pai[1,2], Peng-Wei Hsu[6], Chi-Cheng Chuang[6]



Chemotherapy for brain metastases

- Highly chemosensitive tumours:
  - Germ cell, Lymphoma
- Moderate chemosensitive tumour:
  - SCLC
  - Breast

Chemotherapy for brain metastases: Choriocarcinoma Rustin et al

- 25 patients: 22 on CT (18 solitary)
  3 raised CSF HCG

- EMA CO:
  - 18 primary presentation: 13/18 CR
  - 7 recurrences: 2/7 CR

Chemotherapy for brain metastases: Germ cell

• Fossa et al:	56	45% CSS
• Bokemeyer et al:	18	33% survived
• Lester et al:	5	80% survival
• Rustin et al:	10	80% survival

Systemic treatments for brain metastases from breast cancer, non-small cell lung cancer, melanoma and renal cell carcinoma: An overview of the literature

Cancer Treatment Reviews 40 (2014) 951–959

Breast

Author	PTS	Regimen	RR (%)	PFS (ms)	OS (ms)
Cytotoxic drugs					
Freedman et al. [7]	15	Sagopilone	13.3	1.4	5.3
Siena et al. [5]	51	Temozolomide	4	1.9	NR
Cassier et al. [3]	25	Cisplatin + vinorelbine + RT	76	3.7	6.5
Rivera et al. [6]	24	Capecitabine + temozolomide	18	12 wks	NA
Franciosi et al. [4]	56	Cisplatin + etoposide	38	4	8
Targeted therapies					
Brufsky et al. [8]	258	Trastuzumab vs. no use	NA	NA	17.5 vs. 3.9
Lin et al. [11]	39	Lapatinib	2.6	3	NR
	242	Lapatinib	6	2.4	6.4
Lin et al. [12]	(50)	(Lapatinib + capecitabine)	(20)	(3.6)	
Lin et al. [13]	22	Lapatinib + capecitabine vs. lapatinib + topotecan	38 vs. 0	NA	NA
Bachelot et al. [14]	44	Lapatinib + capecitabine	66	5.5	17
Lin et al. [15]	35	Lapatinib + RT	79	4.8	19

Lung

Author	PTS	Regimen	RR (%)	mPFS (ms)	OS (ms)
Franciosi et al. [4]	43	Cisplatin–etoposide	30	4	8
Cortes et al. [20]	26	Cisplatin–taxol	38	3.2	5.3
Cotto et al. [77]	31	Cisplatin–fotemustine	23	5	4
Fujita et al. [78]	30	Cisplatine–ifosfamide–CPT11	50	4.6	12
Dinglin et al. [19]	42	Pemetrexed–cisplatin	68	10.6	12.6
Kleisbauer et al. [21]	24	Cisplatin	30	NA	NA
Siena et al. [5]	53	TMZ	NA	66 days	172 days
Giorgio et al. [24]	30	TMZ	10	3.6 ms	6 ms
Quantin et al. [22]	23	RT + vinorelbine–ifosfamide–cisplatin	30	NA	7.6

Systemic treatments for brain metastases from breast cancer, non-small cell lung cancer, melanoma and renal cell carcinoma: An overview of the literature

Cancer Treatment Reviews 40 (2014) 951–959

Melanoma

Author	PTS	Regimen	RR (%)	mPFS (wks)	mOS (wks)
Jacquillat et al. [39]	36	Fotemustine	25	NA	NA
Avril et al. [40]	22	Fotemustine	5.9	NA	NA
Mornex et al. [41]	37	Fotemustine + RT	10	8	15
Margolin et al. [42]	31	Temozolomide + RT	9	8	24
Atkins et al. [43]	39	Temozolomide + RT + Talidomide	7.6	7	16
Margolin et al. [50]	51	Ipilimumab	16	10.7	28
Queirolo et al. [51]	146	Ipilimumab	11	11.2	17.2
Falchook et al. [54]	10	Dabrafenib	90	16.8	32
Dummer et al. [56]	24	Vemurafenib	52	16	30

Lung

Author	PTS	Regimen	RR (%)	mPFS (ms)	OS (ms)
Ceresoli et al. [32]	41	Gefitinib	10	3	5
Chiu et al. [26]	21	Gefitinib	76	5	9.9
Wu et al. [33]	44	Gefitinib	38	9	13
Kim et al [25]	23	Gefitinib/ erlotinib	69	7.1	18.8
Welsh et al. [30]	40	Erlotinib + RT	86	NA	19.1

Renal

Authors	PTS	Regimen	RR (%)	mPFS (ms)	mOS (ms)
Gore et al. [66]	213	Sunitinib	12	5.6	9.2
Stadler et al. [68]	70	Sorafenib	4	NA	NA
Zustovich et al. [76]	4	Bevacizumab	75	26.3*	33.2*

Recommendations on Disease Management for Patients With Advanced Human Epidermal Growth Factor Receptor 2–Positive Breast Cancer and Brain Metastases: American Society of Clinical Oncology Clinical Practice Guideline

J Clin Oncol 32:2100-2108. © 2014

Key Recommendations

- For patients with a favorable prognosis for survival and a single brain metastasis, treatment options include surgery with postoperative radiation, stereotactic radiosurgery (SRS), whole-brain radiotherapy (WBRT; ± SRS), fractionated stereotactic radiotherapy (FSRT), and SRS (± WBRT), depending on metastasis size, resectability, and symptoms. After treatment, serial imaging every 2 to 4 months may be used to monitor for local and distant brain failure.
- For patients with a favorable prognosis for survival and limited (two to four) metastases, treatment options include resection for large symptomatic lesion(s) plus postoperative radiotherapy, SRS for additional smaller lesions, WBRT (± SRS), SRS (± WBRT), and FSRT for metastases > 3 to 4 cm. For metastases < 3 to 4 cm, treatment options include resection with postoperative radiotherapy. In both cases, available options depend on resectability and symptoms.

Targeting brain metastases in *ALK*-rearranged non-small-cell lung cancer

Isabella Zhang, Nicholas G Zaorsky, Joshua D Palmer, Ranee Mehra, Bo Lu

Lancet Oncol 2015; 16: e510–21

25 case reports!

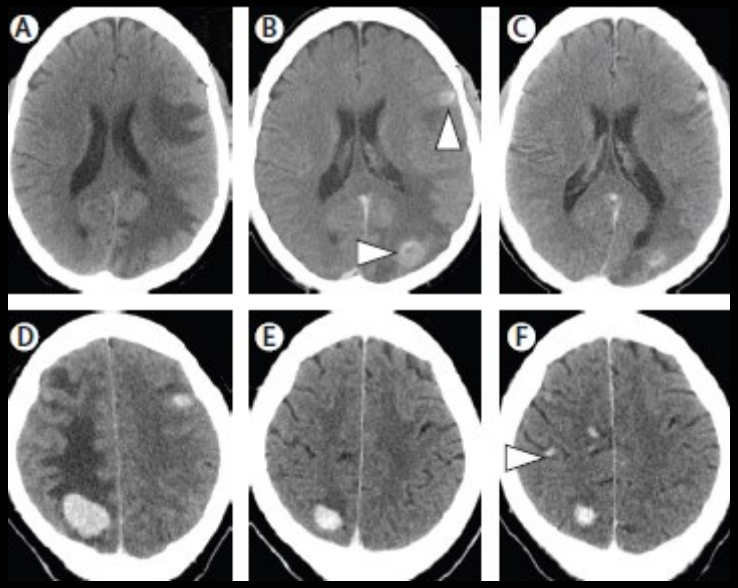
Evolving treatment options for melanoma brain metastases

Thankamma Ajithkumar, Christine Parkinson, Kate Fife, Pippa Corrie, Sarah Jefferies

Lancet Oncol 2015; 16: e486–97

Ipilimumab

Venmurafenib



13 open trials
15 published

Modern systemic therapies for metastatic melanoma have proven effective even when no brain involvement exists. For patients with *BRAF*-mutant melanoma, BRAF-targeted agents could be used preferentially to radiotherapy while the potential benefits and risks of the combination of radiotherapy and immunotherapy are still being studied (figure 2).

Multiple brain metastases

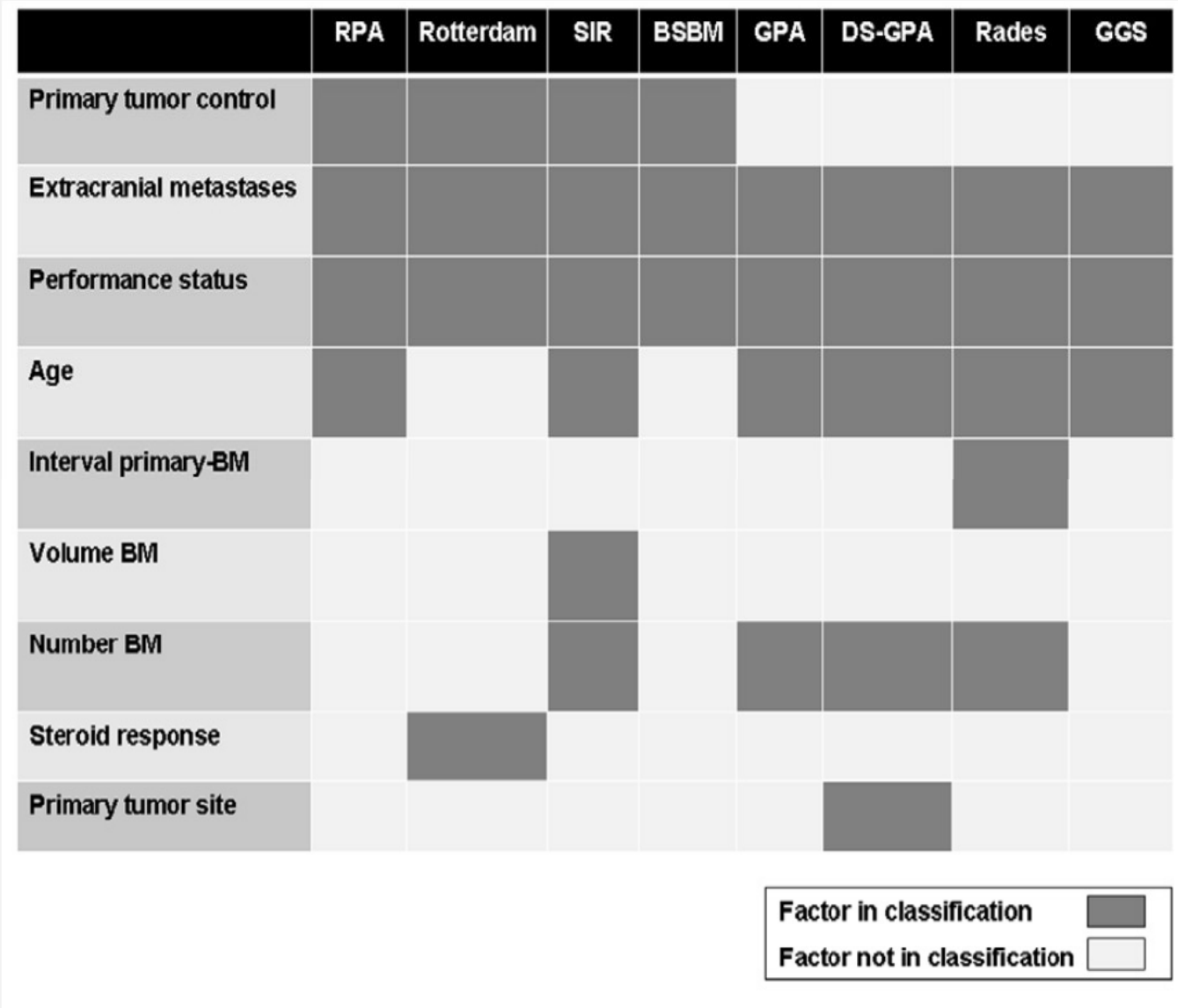
- Radiotherapy
  - Dose fractionation
  - Patient selection
- Chemotherapy
  - Patient selection

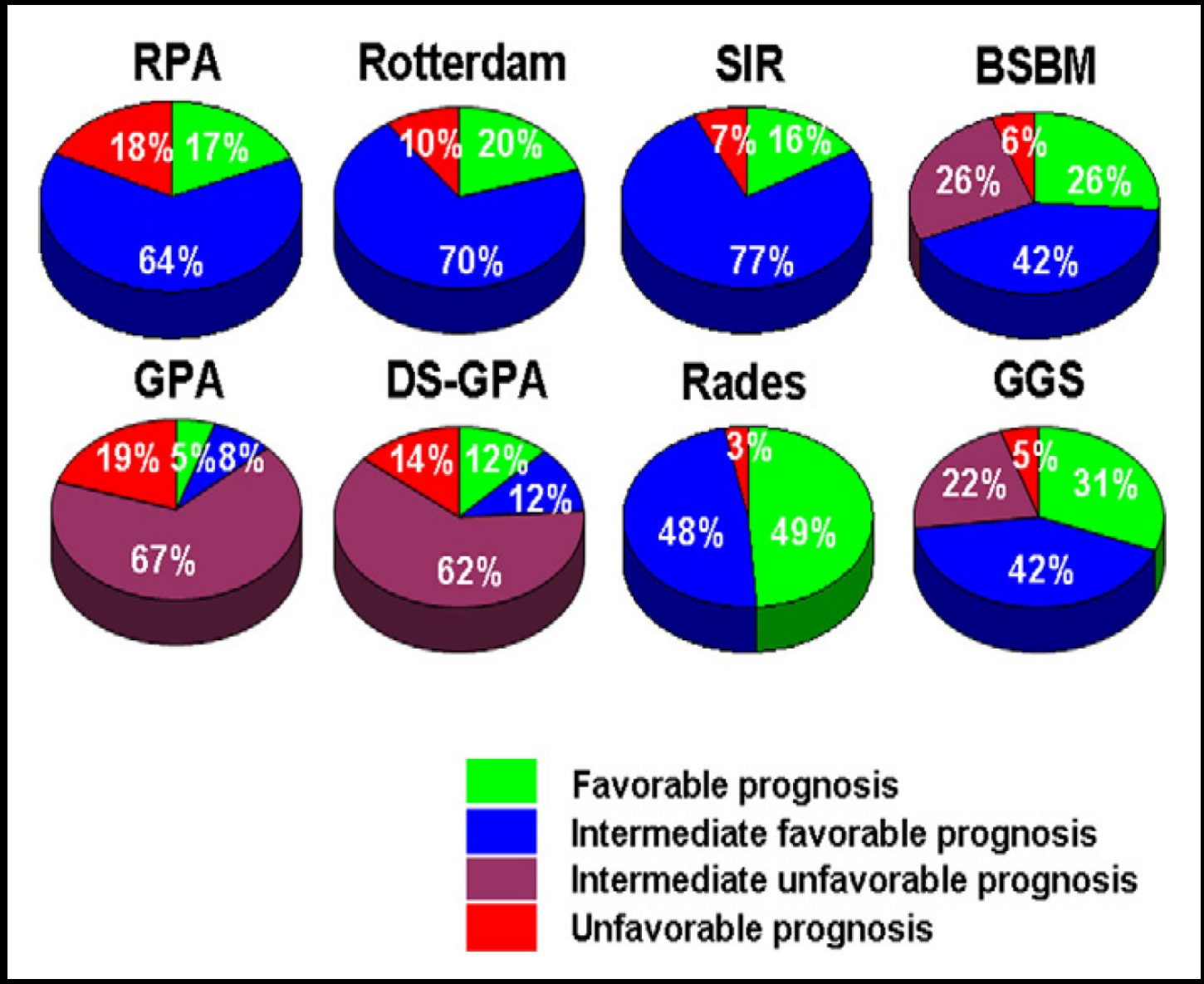
The clinical utility of prognostic scoring systems in patients with brain metastases treated with radiosurgery

Jaap D. Zindler[a], George Rodrigues[b], Cornelis J.A. Haasbeek[a], Patricia F. De Haan[a], Otto W.M. Meijer[a], Ben J. Slotman[a], Frank J. Lagerwaard[a,*]

Radiotherapy and Oncology 106 (2013) 370–374

Baseline characteristics included in various prognostic scoring systems for patients with brain metastases.



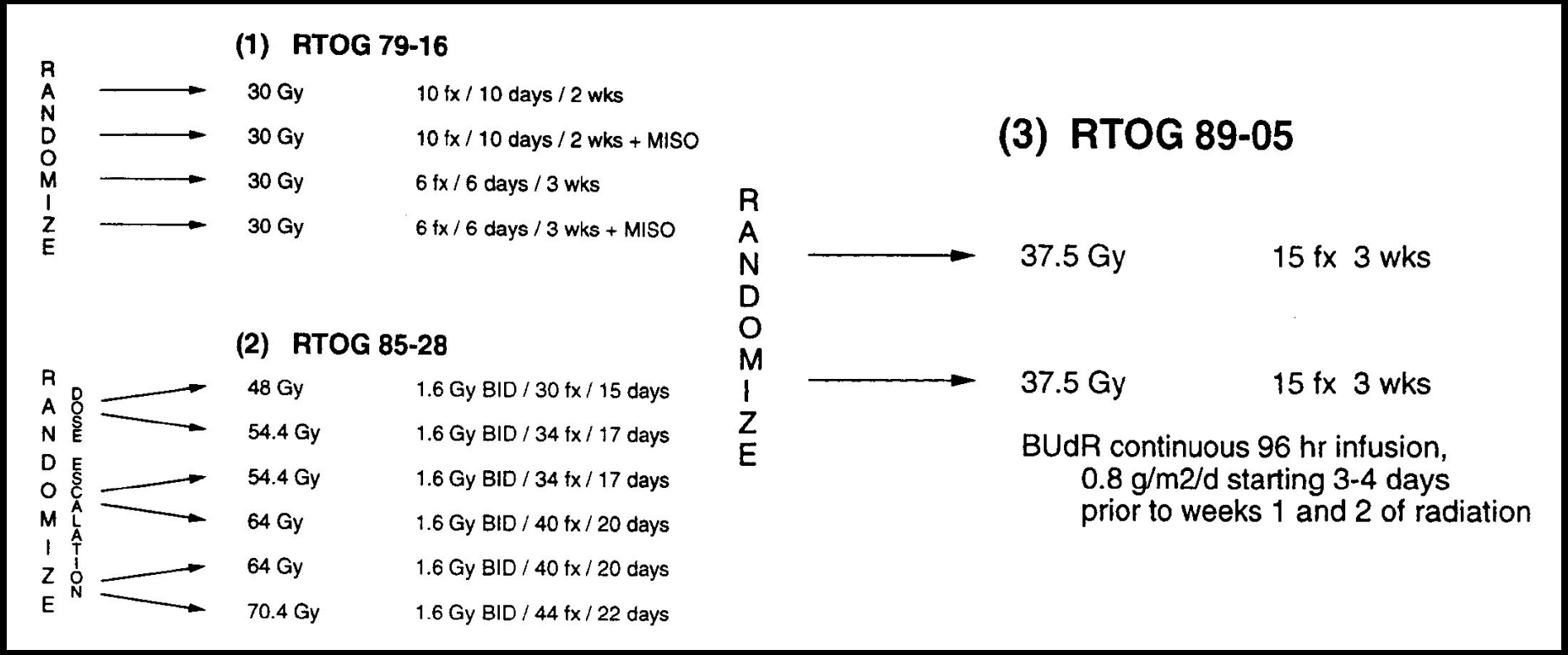


Zindler et al

Radiotherapy and Oncology 106 (2013) 370–374

Recursive partitioning of prognostic factors in RTOG trial

1200 patients



Recursive partitioning of prognostic factors in RTOG trial

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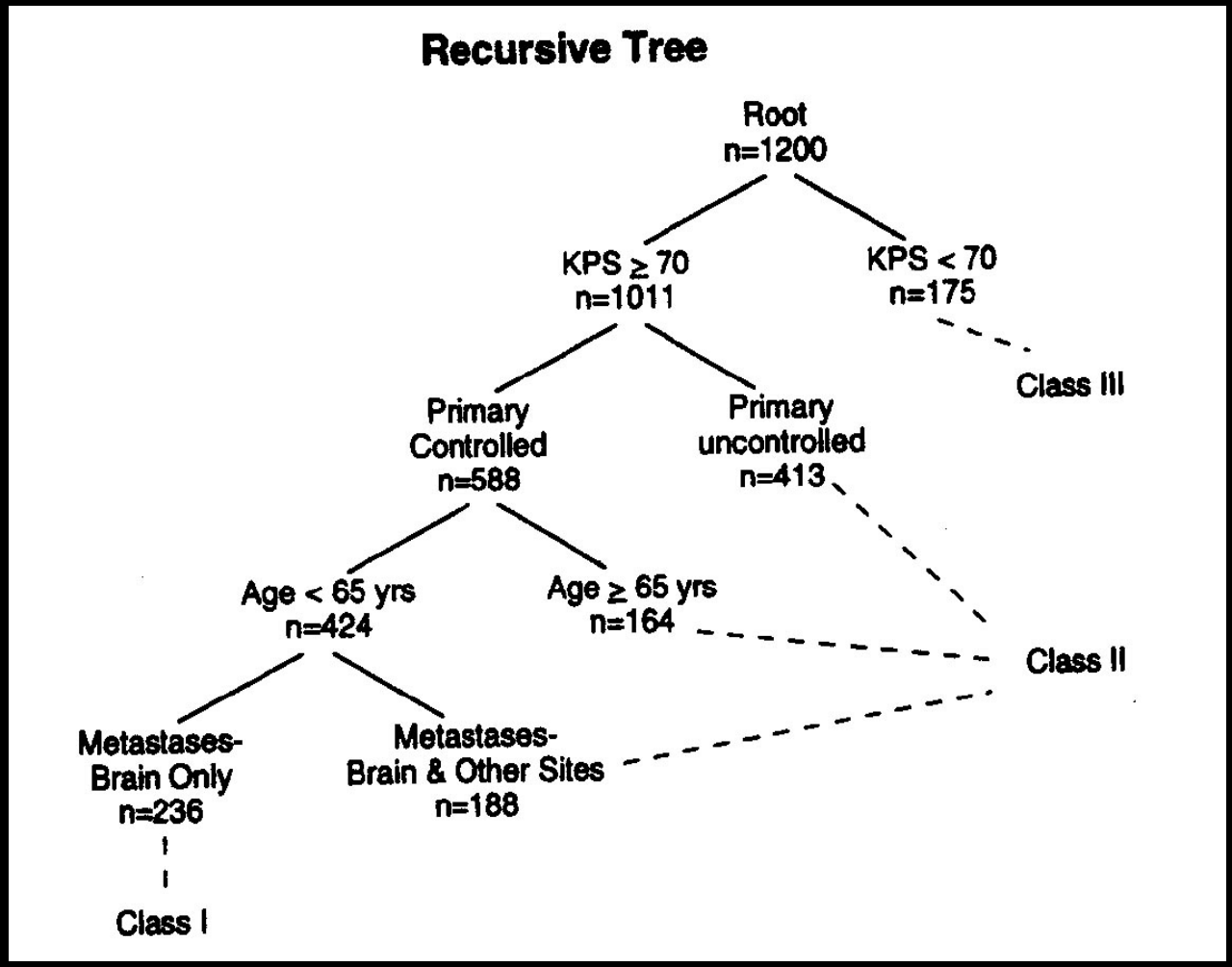

Recursive partitioning of prognostic factors in RTOG trial

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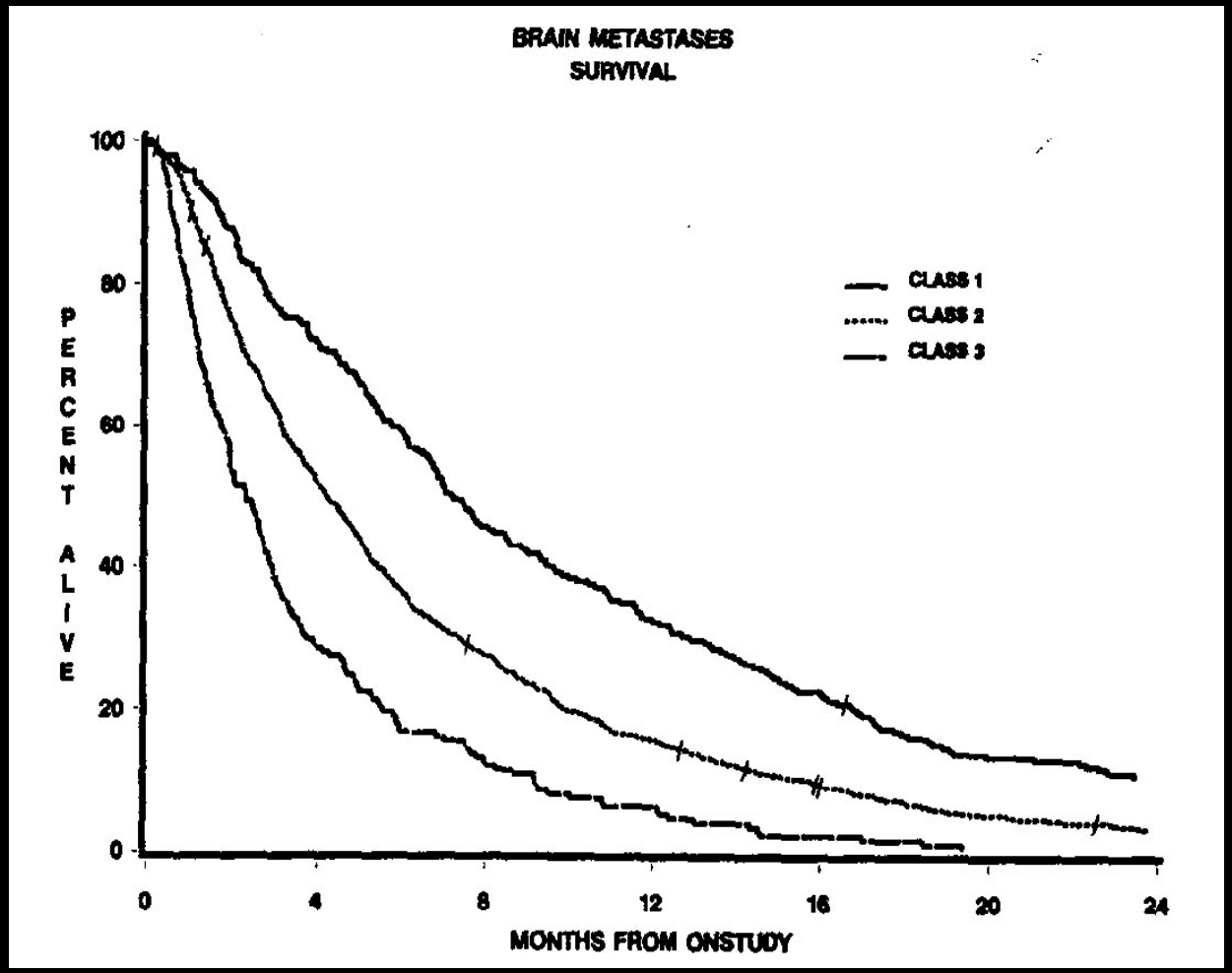


Prognosis of Patients With Brain Metastases by Diagnosis-Specific Graded Prognostic Assessment (DS-GPA) Score

Lung Cancer	GPA Scoring Criteria		
Prognostic Factor	0	0.5	1.0
Age, years	> 60	50–60	< 50
KPS	< 70	70–80	90–100
ECM	+	n/a	–
No. of BM	> 3	2–3	1

Total Score = _____ →

Melanoma	GPA Scoring Criteria		
Prognostic Factor	0	1.0	2.0
KPS	< 70	70–80	90–100
No. of BM	> 3	2-3	1

Total Score = _____ →

Breast Cancer	GPA Scoring Criteria				
Prognostic Factor	0	0.5	1.0	1.5	2.0
KPS	≤ 50	60	70–80	90–100	n/a
Subtype	Basal	n/a	LumA	HER2	LumB
Age, years	≥ 60	< 60	n/a	n/a	n/a

Total Score = _____ →

Renal Cell Carcinoma	GPA Scoring Criteria		
Prognostic Factor	0	1.0	2.0
KPS	< 70	70–80	90–100
No. of BM	> 3	2–3	1

Total Score = _____ →

GI Cancers	GPA Scoring Criteria				
Prognostic Factor	0	1	2	3	4
KPS	< 70	70	80	90	100

Total Score = _____ →

Total Score	Median Survival Time in Months (95% CI)	
Lung Cancer	NSCLC	SCLC
0–1.0	3.02 (2.63 to 3.84)	2.79 (1.83 to 3.12)
1.5–2.0	5.49 (4.83 to 6.40)	4.90 (4.04 to 6.51)
2.5–3.0	9.43 (8.38 to 10.80)	7.67 (6.27 to 9.13)
3.5–4.0	14.78 (11.80 to 18.80)	17.05 (4.70 to 27.43)

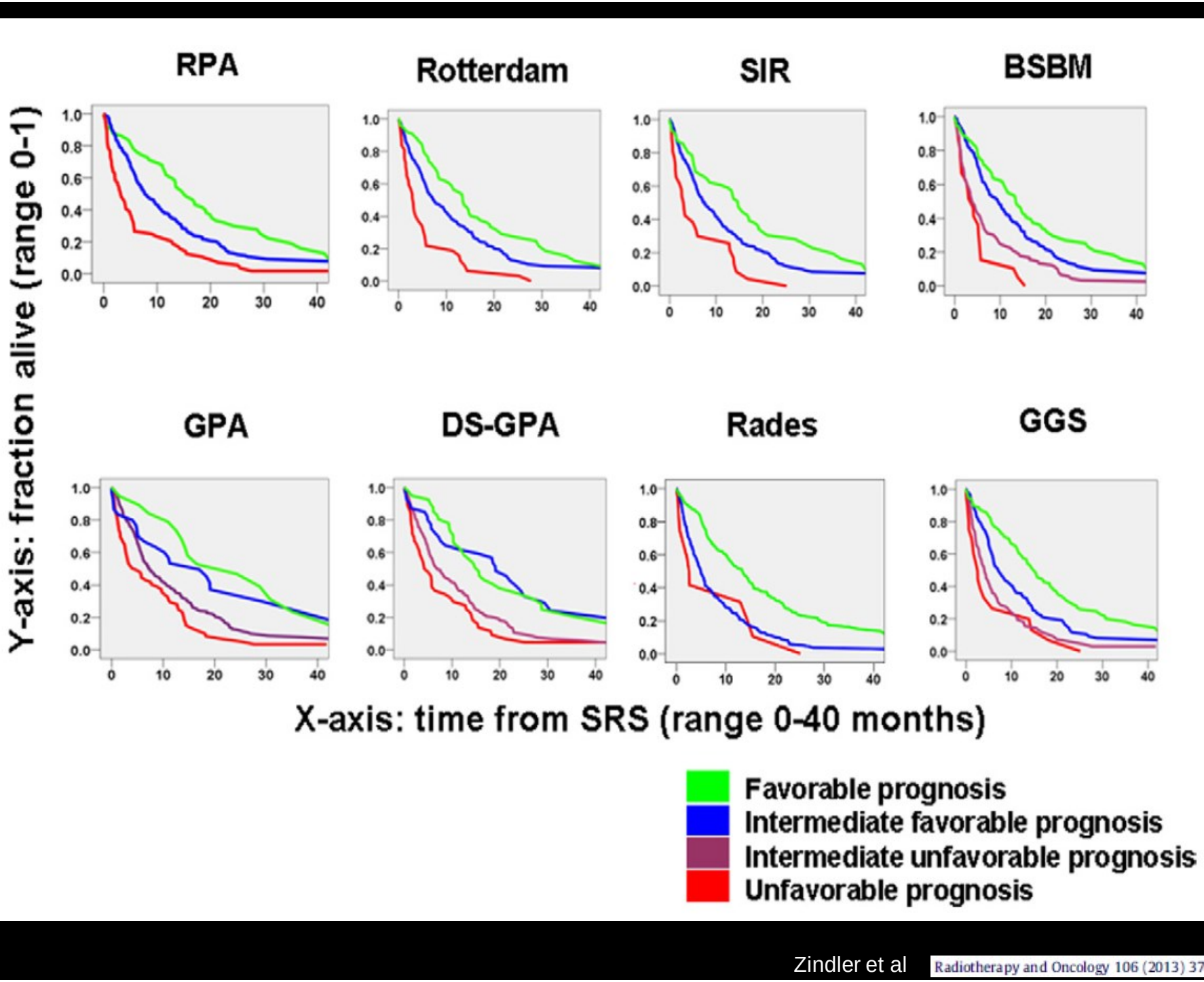
Melanoma	
0–1.0	3.38 (2.53 to 4.27)
1.5–2.0	4.70 (4.07 to 5.39)
2.5–3.0	8.77 (6.74 to 10.77)
3.5–4.0	13.23 (9.13 to 15.64)

Breast Cancer	
0–1.0	3.35 (3.13 to 3.78)
1.5–2.0	7.70 (5.62 to 8.74)
2.5–3.0	15.07 (12.94 to 15.87)
3.5–4.0	25.30 (23.10 to 26.51)

Renal Cell Carcinoma	
0–1.0	3.27 (2.04 to 5.10)
1.5–2.0	7.29 (3.73 to 10.91)
2.5–3.0	11.27 (8.80 to 14.80)
3.5–4.0	14.77 (9.73 to 19.79)

GI Cancers	
0–1.0	3.13 (2.37 to 4.57)
1.5–2.0	4.40 (3.37 to 6.53)
2.5–3.0	6.87 (4.86 to 11.63)
3.5–4.0	13.54 (9.76 to 27.12)

Xuling Lin and Lisa M. DeAngelis
J Clin Oncol 33:3475-3484. © 2015



Zindler et al Radiotherapy and Oncology 106 (2013) 370–374

Prognostic Indexes for Brain Metastases: Which Is the Most Powerful?

Int J Radiation Oncol Biol Phys, Vol. 83, No. 3, pp. e325–e330, 2012

Gustavo Arruda Viani, M.D., Lucas Godói Bernardes da Silva, M.D., and Eduardo Jose Stefano, M.D.

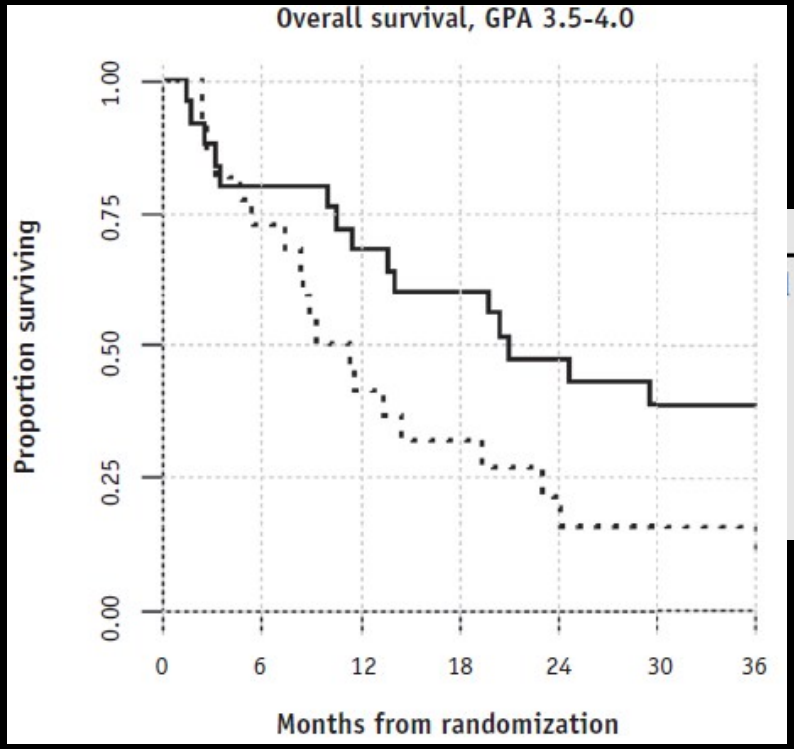
Variable	Overall survival at 1 y (%)	*p* (log-rank test)
Rotterdam score		.001
Class I	31	
Class II	18	
Class III	11	
BSBM		.002
Class I	26	
Class II	17	
Class III	13	
Class IV	8	
Germany score		<.0001
Class I	42	
Class II	35	
Class III	26	
Class IV	14	
RPA		<.0001
Class I	44	
Class II	30	
Class III	16	
GPA		<.0001
Class I	49	
Class II	27	
Class III	13	
Class IV	9	

Abbreviations: BSBM = basic score for brain metastases; RPA = recursive partitioning analysis; GPA = graded prognostic assessment.

Secondary Analysis of RTOG 9508, a Phase 3 Randomized Trial of Whole-Brain Radiation Therapy Versus WBRT Plus Stereotactic Radiosurgery in Patients With 1-3 Brain Metastases; Poststratified by the Graded Prognostic Assessment (GPA)

Paul W. Sperduto, MD, MPP, FASTRO,* Ryan Shanley, MS,† et al

Int J Radiation Oncol Biol Phys, Vol. 90, No. 3, pp. 526–531, 2014



Prognostic factor	GPA Scoring Criteria		
	0	0.5	1.0
Age	>60	50-60	<50
KPS	<70	70-80	90-100
ECM	Present	-	Absent
No. of BM	>3	2-3	1

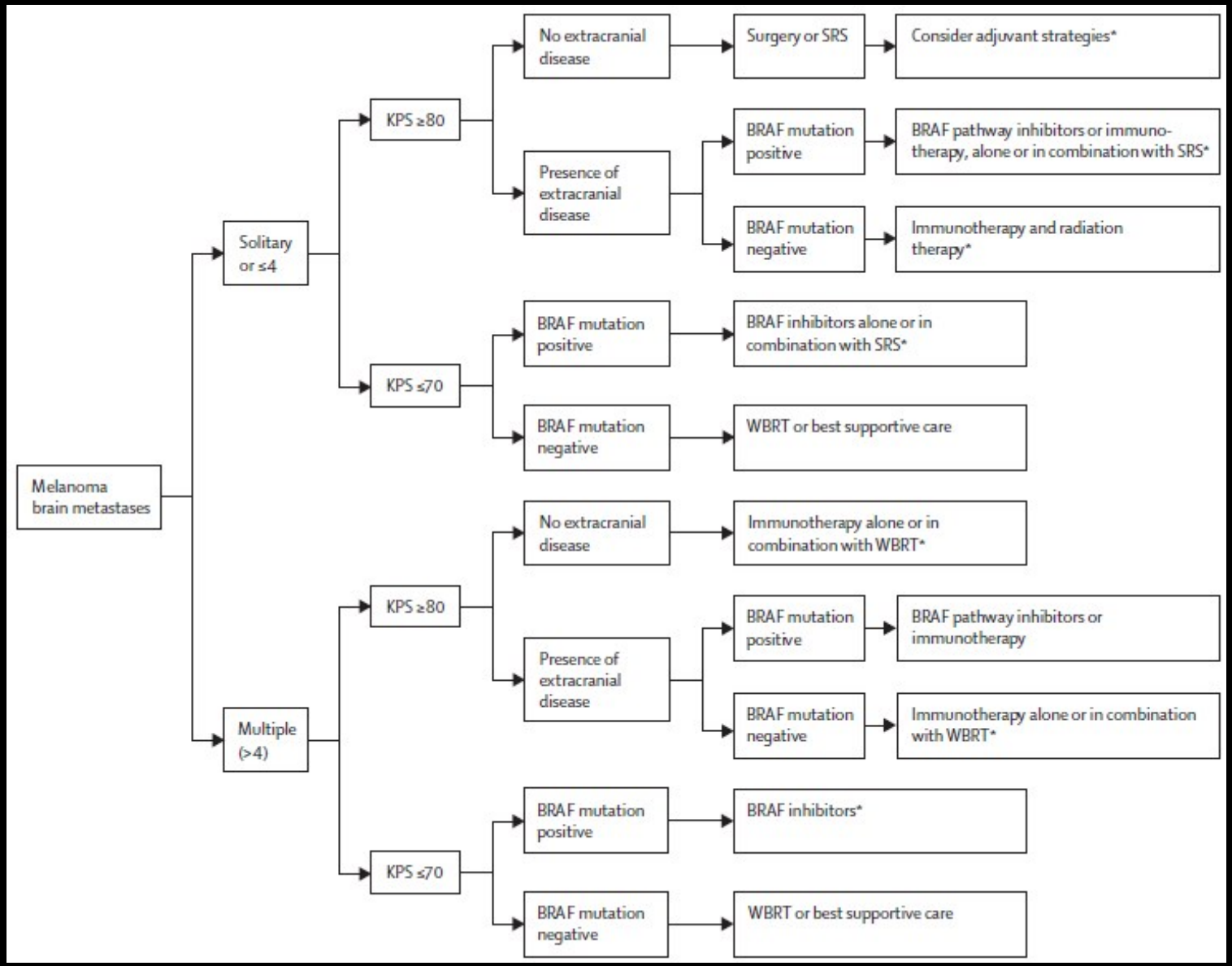
If the only tool you have is a hammer then you tend to see every problem as a nail’

Abraham Maslow

Evolving treatment options for melanoma brain metastases

Thankamma Ajithkumar, Christine Parkinson, Kate Fife, Pippa Corrie, Sarah Jefferies

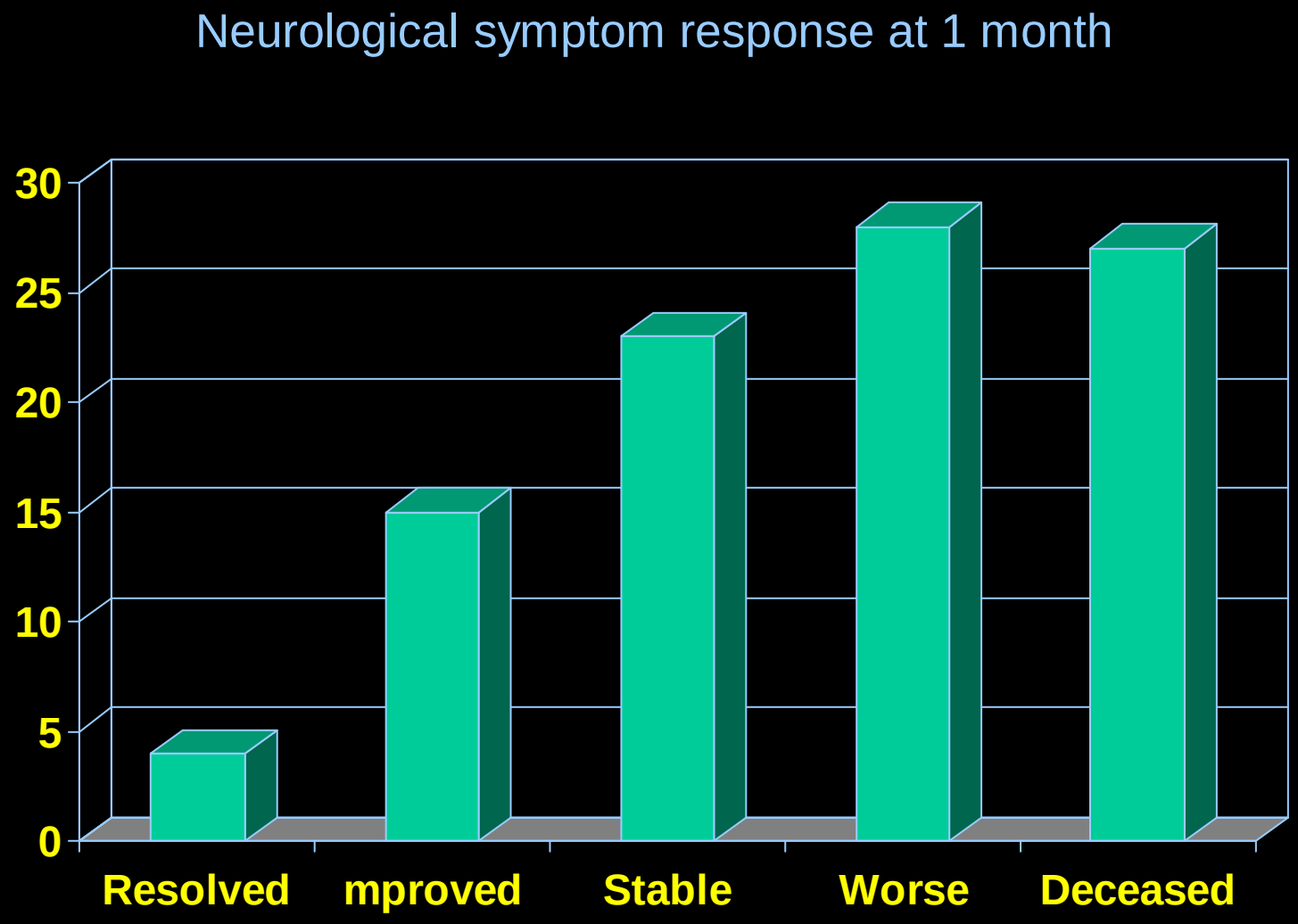
Lancet Oncol 2015; 16: e486–97



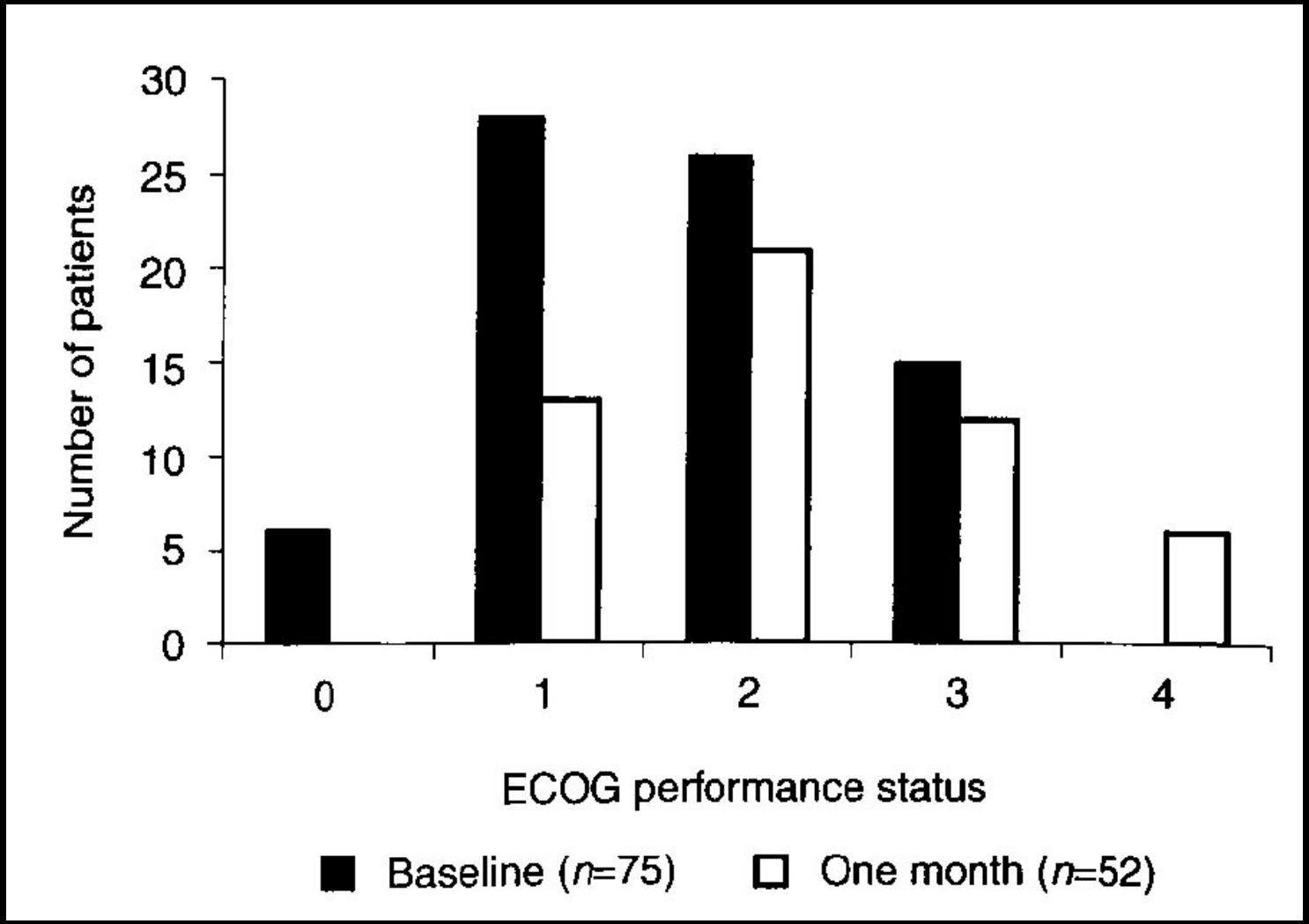
Supportive care management of brain metastases: what is known and what we need to know [Tsao et al 2003]

‘the optimal management of brain metastases remains elusive. The magnitude of benefit of using WBRT above supportive care alone is uncertain’

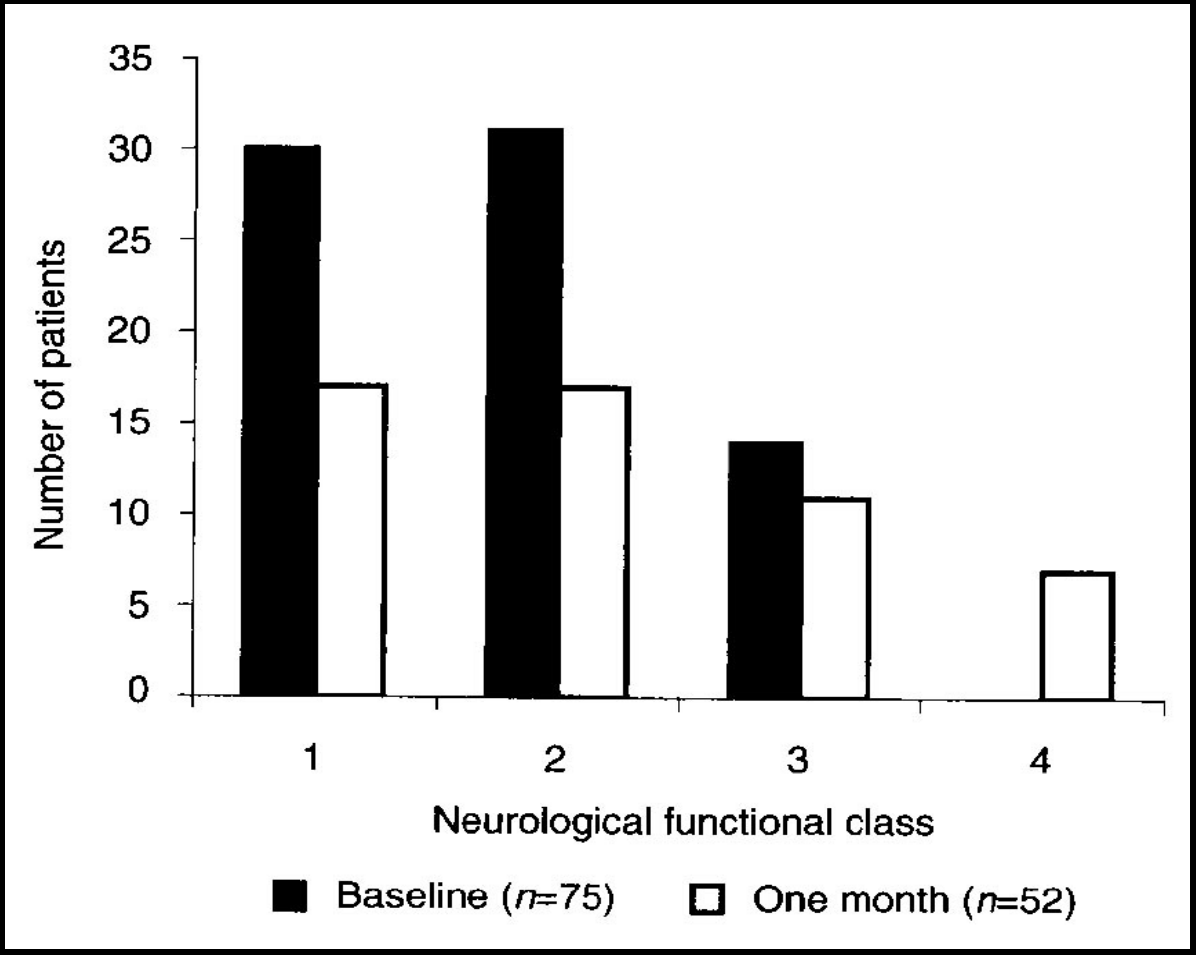
Symptom response after palliative radiotherapy for patients with brain metastases [Bezjak et al 2002]



Symptom response after palliative radiotherapy for patients with brain metastases [Bezjak et al 2002]

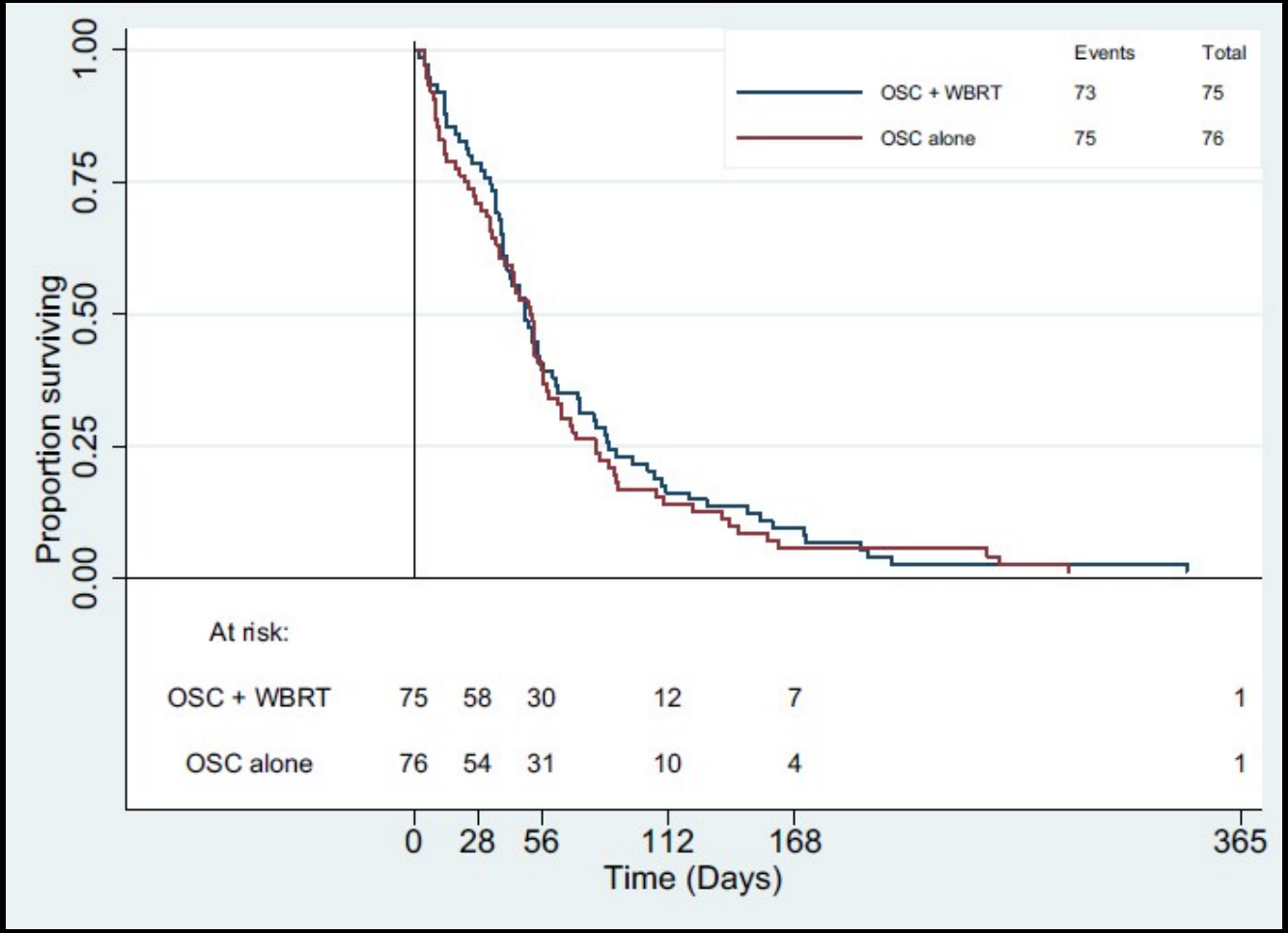


Symptom response after palliative radiotherapy for patients with brain metastases [Bezjak et al 2002]



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?

Clinical Oncology 25 (2013) e23–e30



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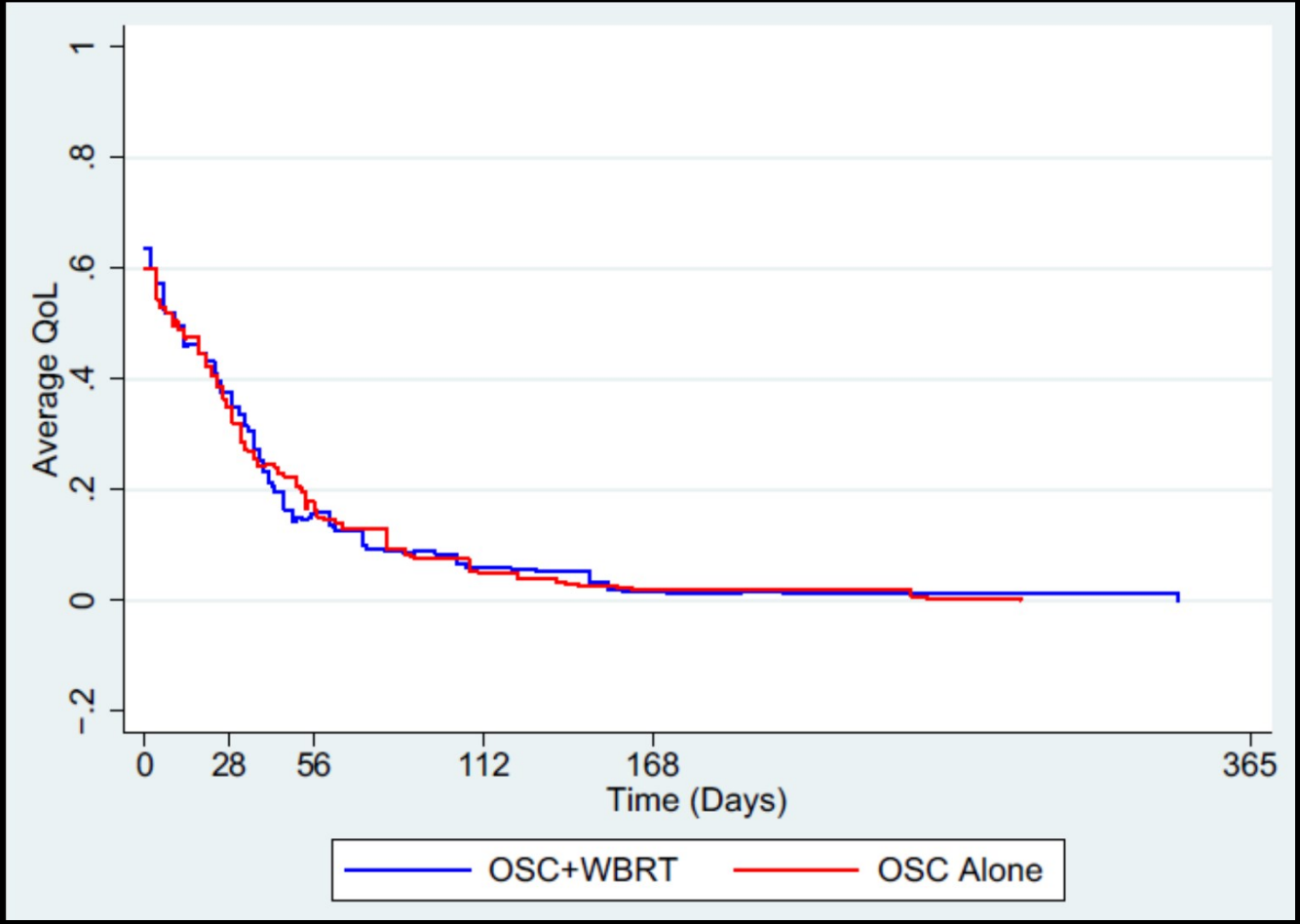
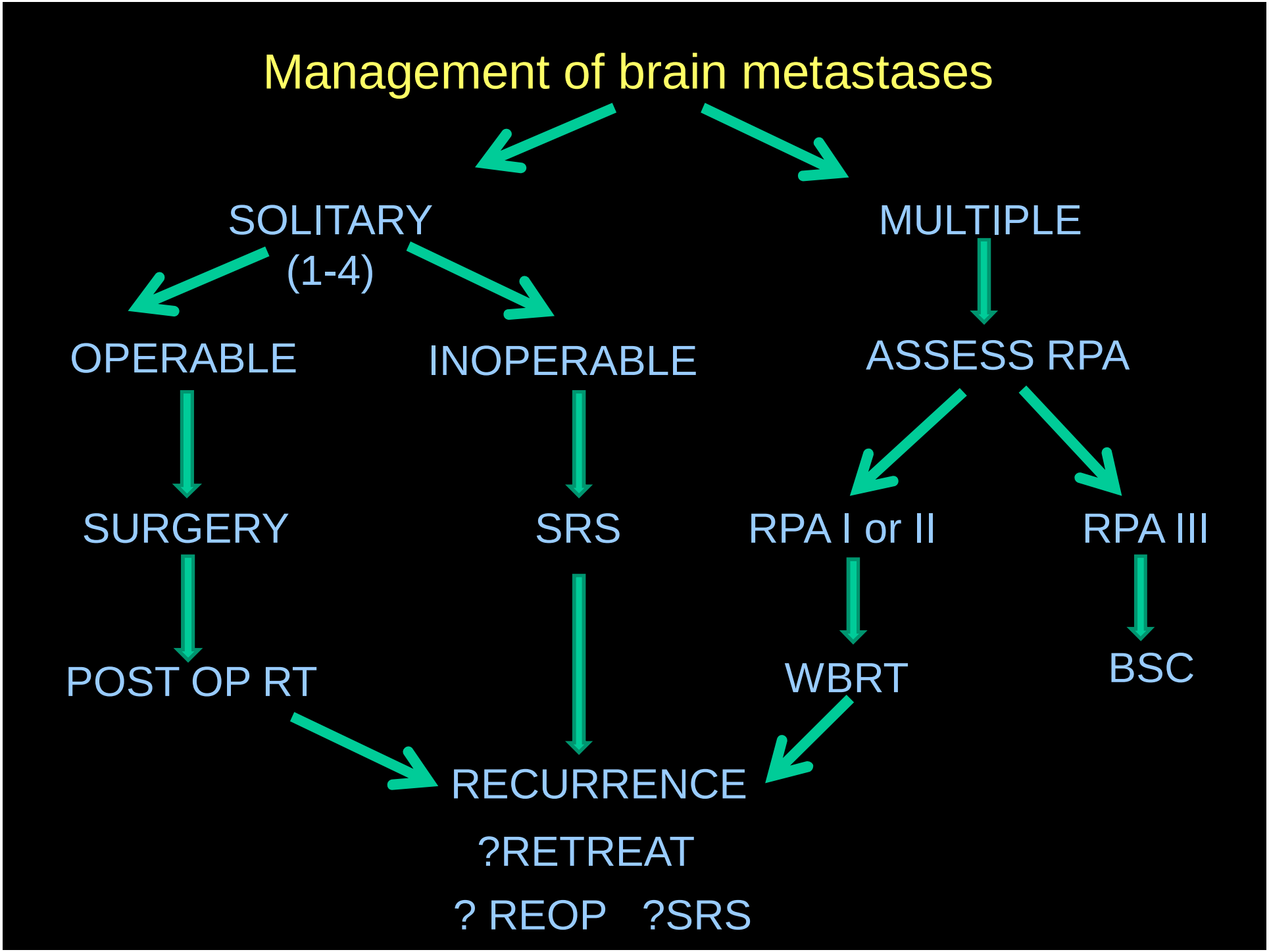
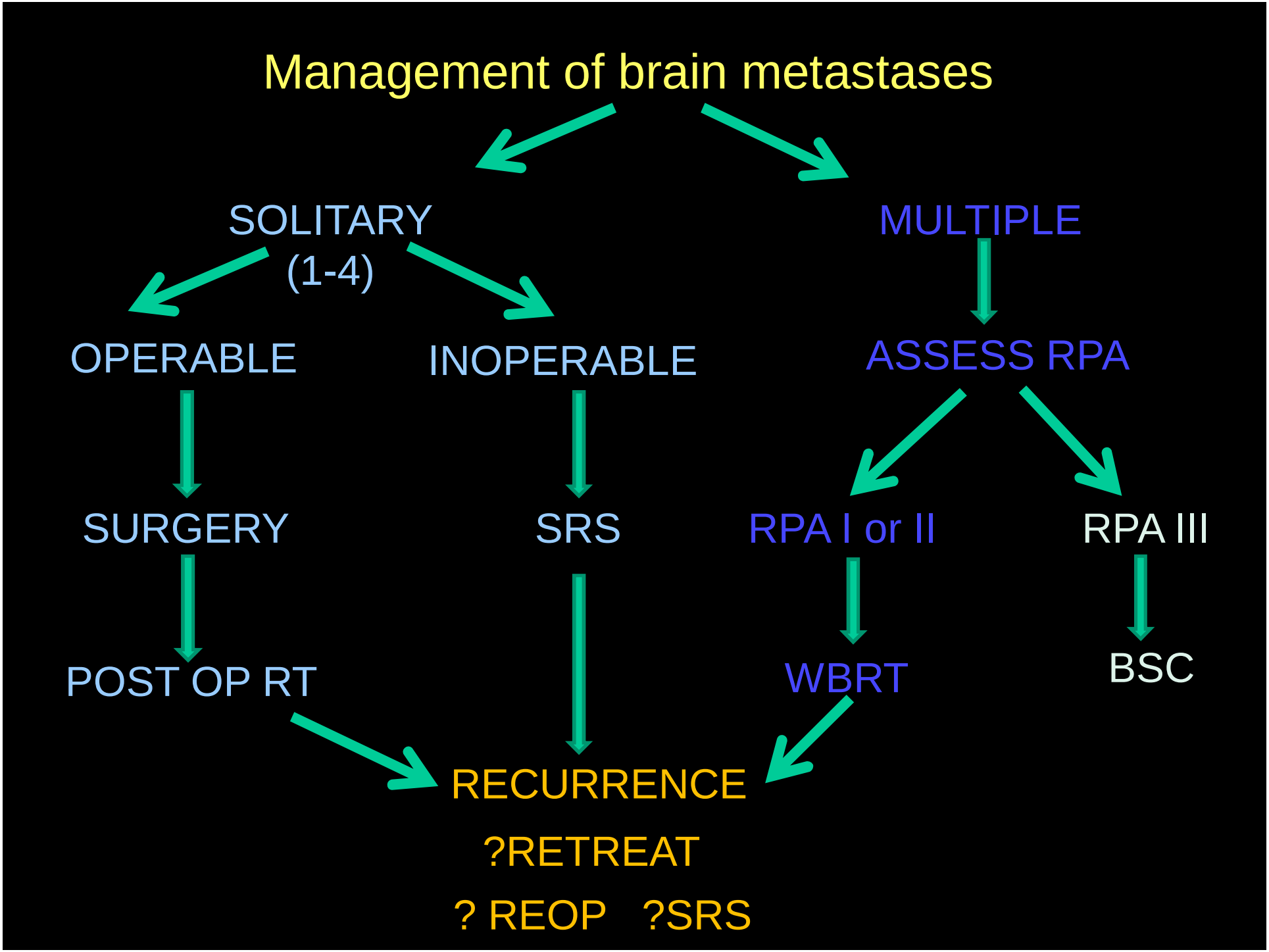


Cochrane meta-analysis 2007 & 2012

Supportive care versus whole brain radiotherapy

- There is a lack of high quality randomized evidence to clarify the value of WBRT versus supportive care alone
- Supportive care alone is an option (for example, for patients with poor performance status or widely disseminated cancer based on short life expectancy).
- There is lack of contemporary high quality trials to guide practitioners as to which subsets of patients with brain metastases should be managed with supportive care alone without whole brain radiotherapy.


Management of brain metastases
SOLITARY
(1-4)
MULTIPLE
OPERABLE
INOPERABLE
ASSESS RPA
SURGERY
SRS
RPA I or II
RPA III
POST OP RT
WBRT
BSC
RECURRENCE
?RETREAT
? REOP ?SRS


Management of brain metastases
SOLITARY
(1-4)
MULTIPLE
OPERABLE
INOPERABLE
ASSESS RPA
SURGERY
SRS
RPA I or II
RPA III
POST OP RT
WBRT
BSC
RECURRENCE
?RETREAT
? REOP ?SRS

Conclusion

- SOLITARY (1-4)
  - SURGERY + SRS
  - SRS alone
- MULTIPLE
  - CHEMOTHERAPY for
    - GCT, LYMPHOMA
    - ?breast, SCLC,
    - ??ALK+ve NSCLC, B-RAF+ve melanoma
  - WBRT
    - RPA I/II
  - BSC
    - RPA III