

What type of radiotherapy is indicated in brain metastasis?

Anthony Chalmers

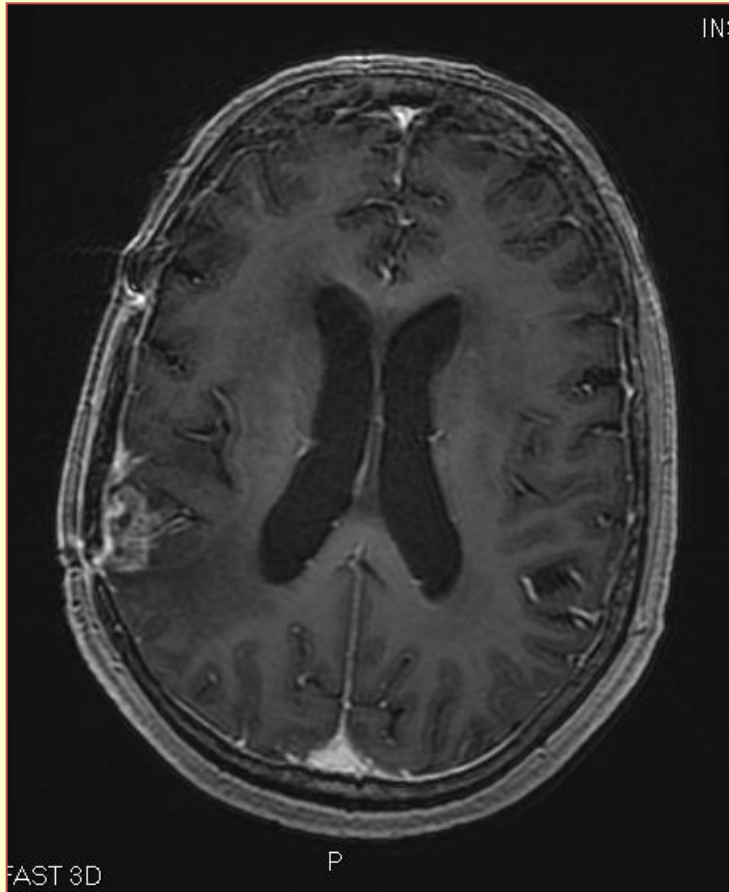
University of Glasgow

ESMO 2014

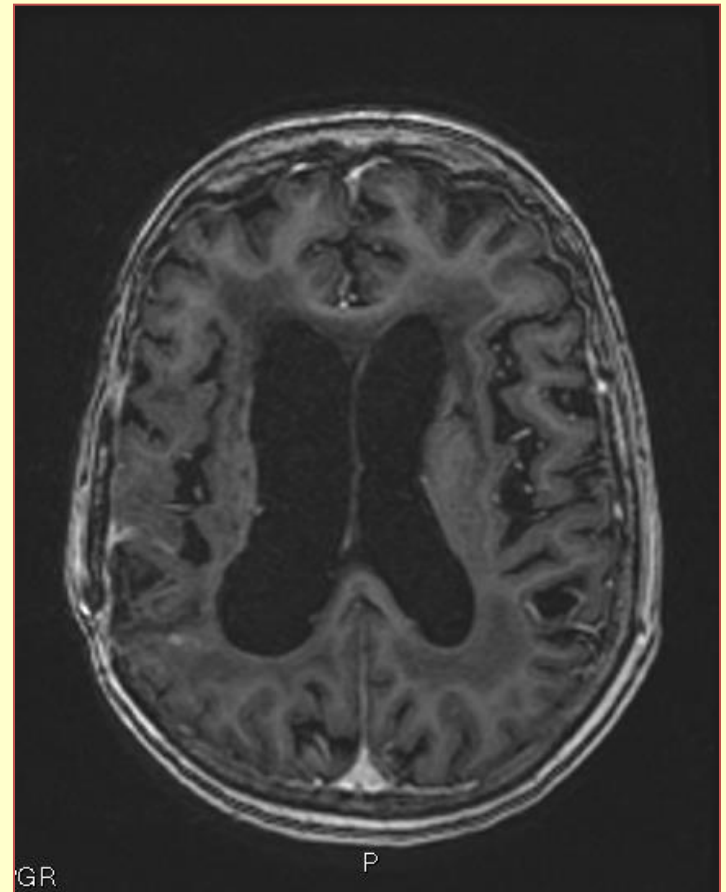
The evidence base is poor:

- Highly heterogenous group of patients:
 - Number and volume of mets
 - Histology, extracranial disease, systemic and primary treatment
 - Performance status
- Difficult patient group for clinical trials
- Historical nihilism
- Rapid evolution of radiotherapy technology

WBRT is a potentially toxic treatment

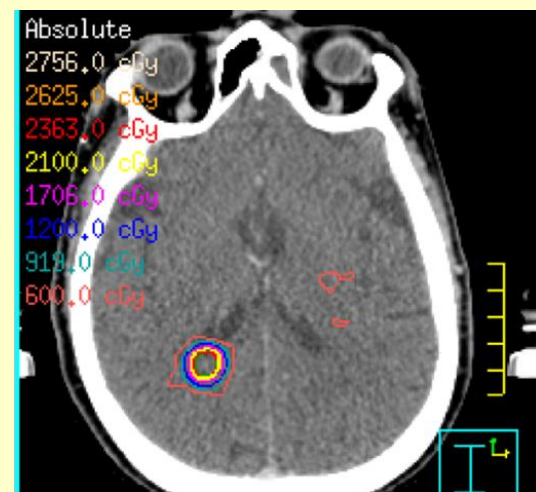
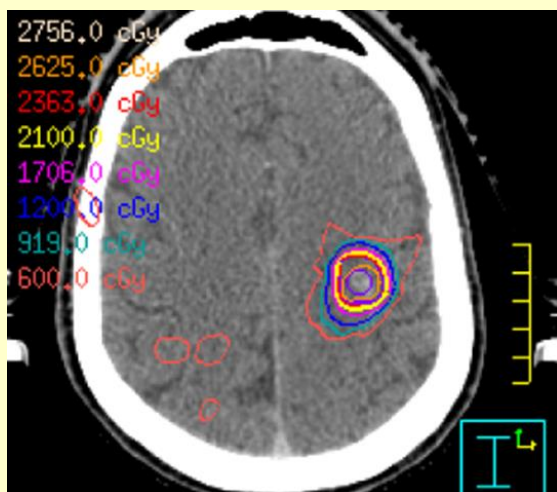
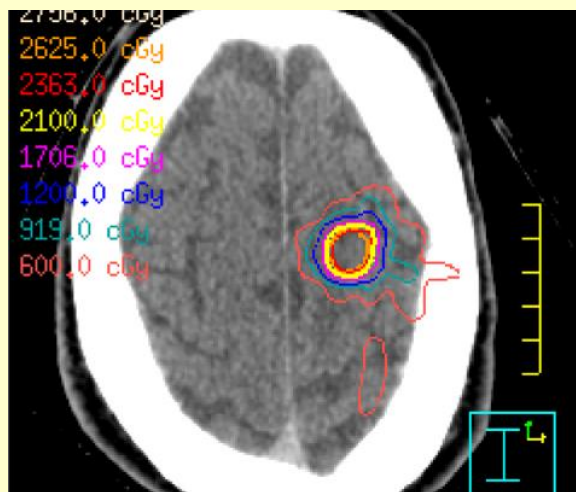
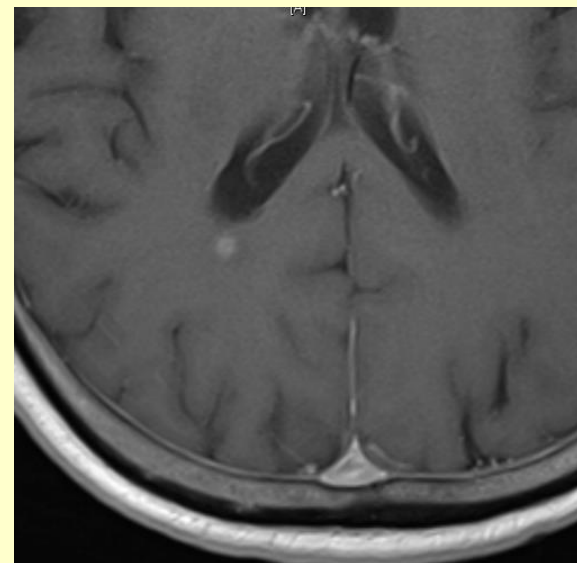
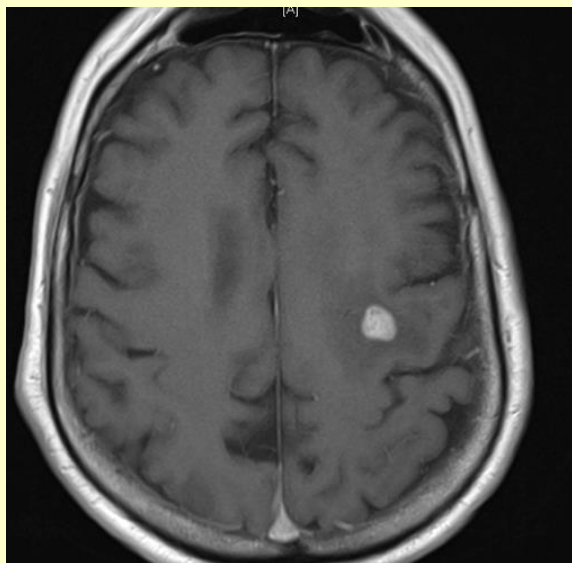
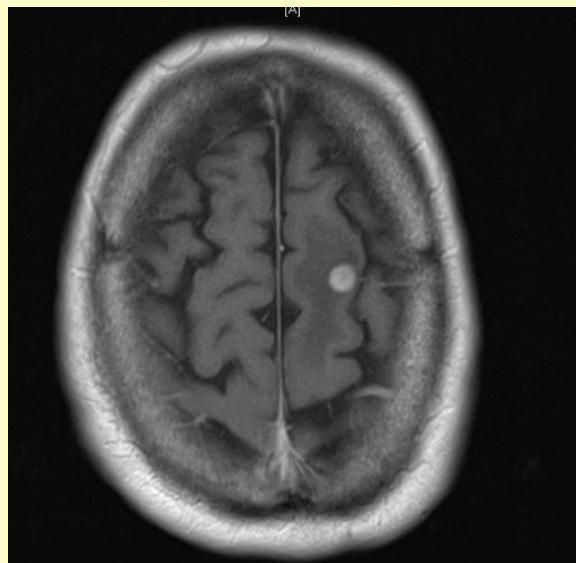


Pre-radiation

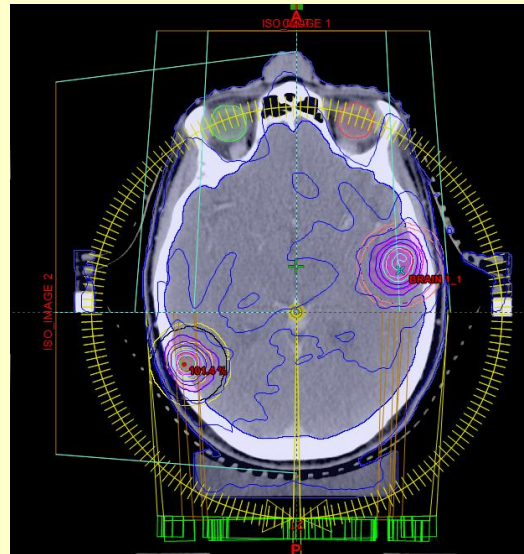
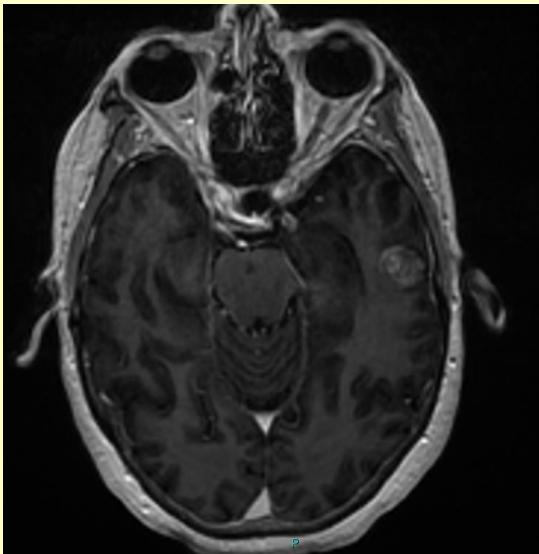
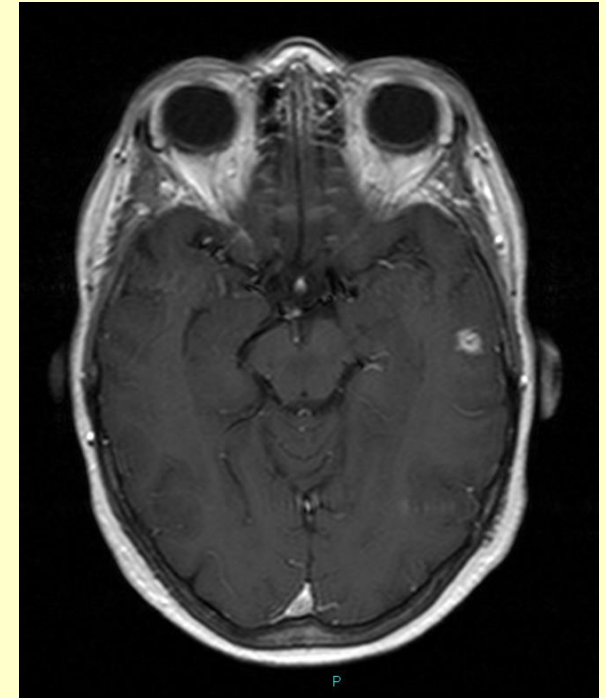
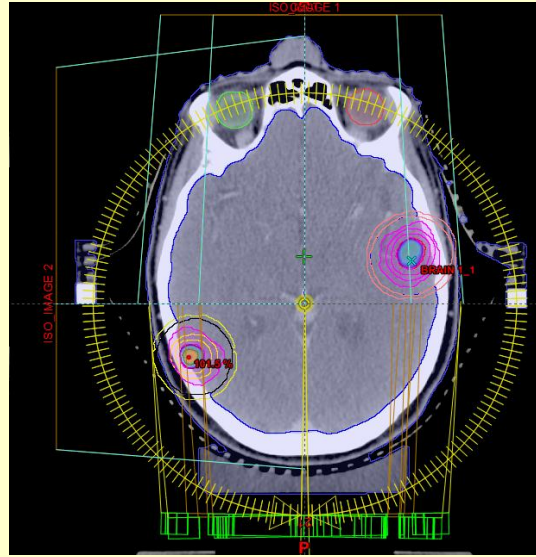
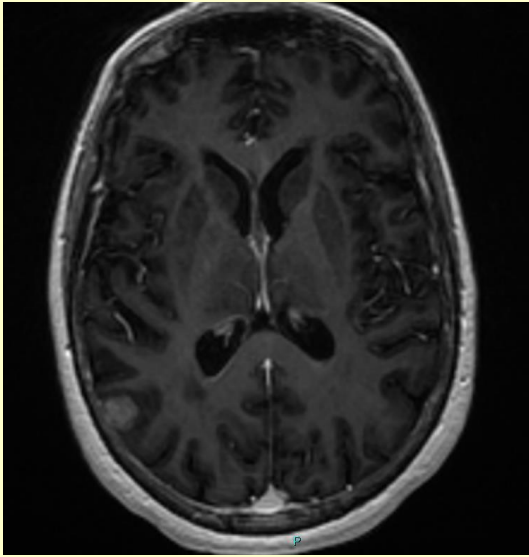


18 months
post-radiation

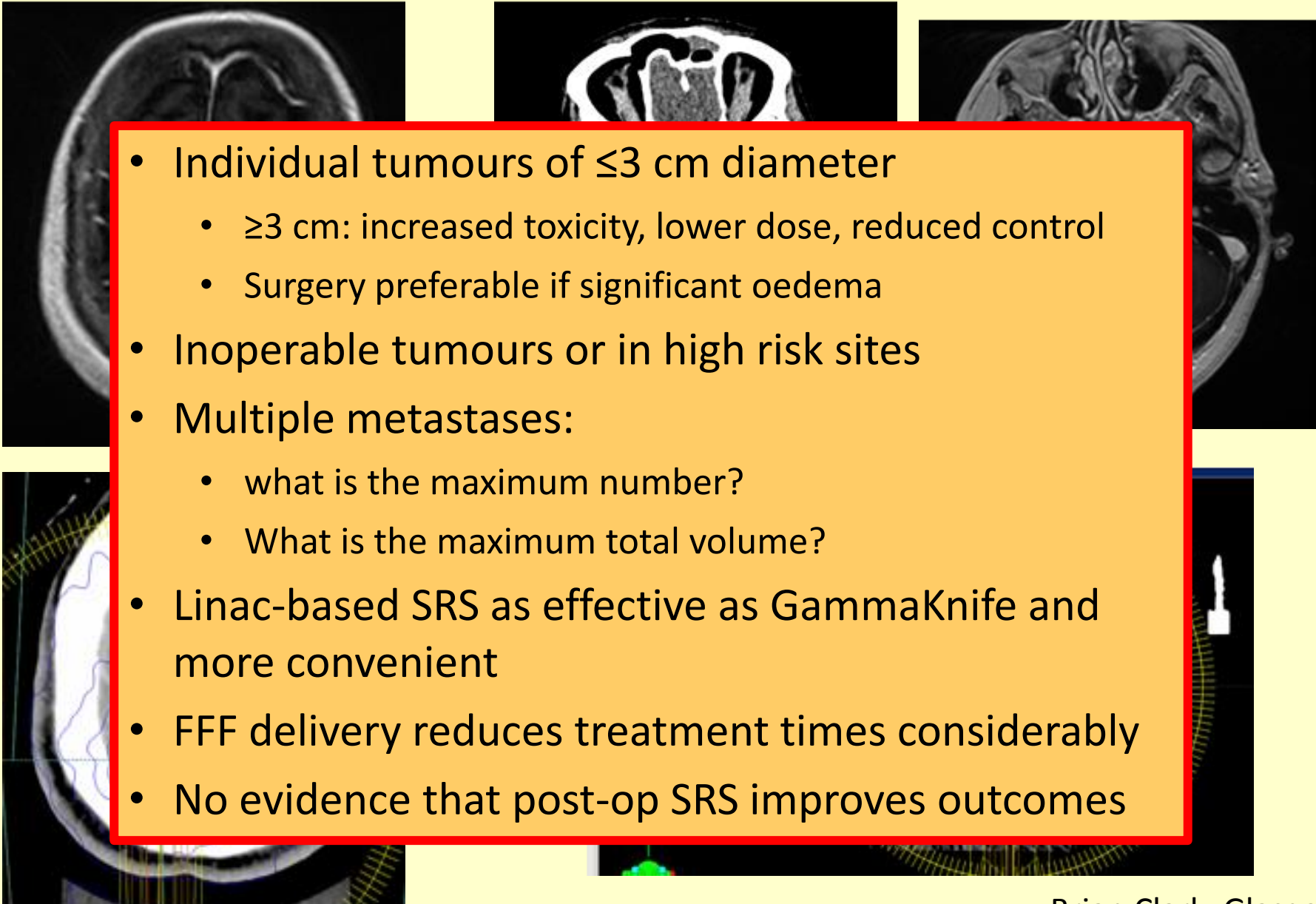
SRS is increasingly available, convenient and flexible



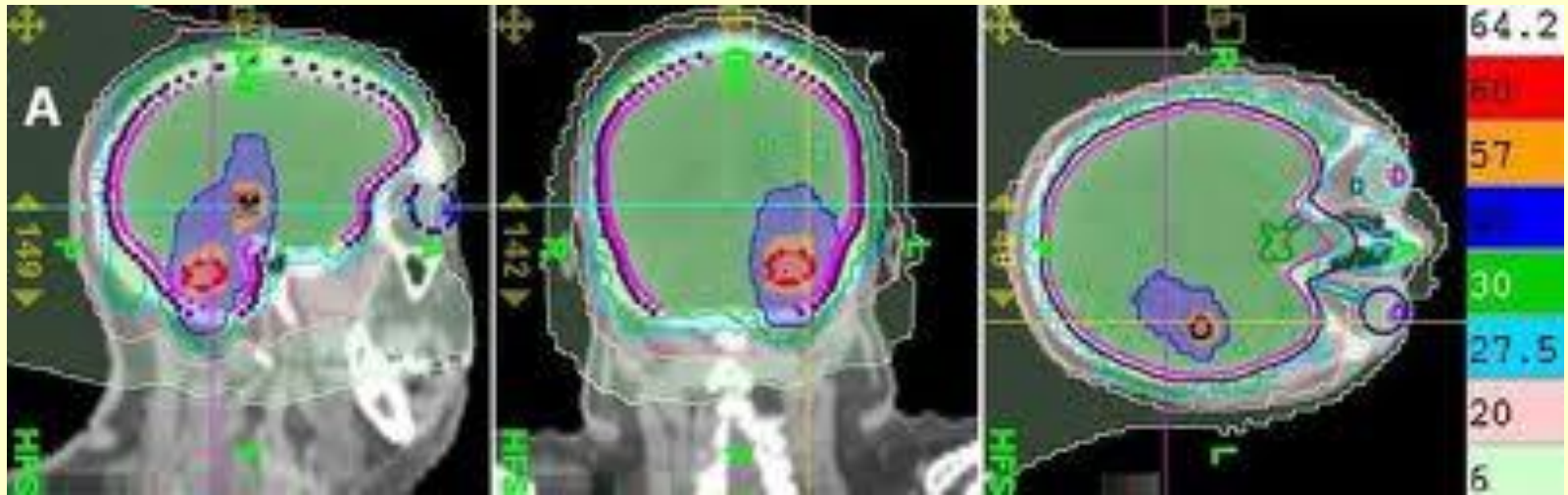
SRS is increasingly available, convenient and flexible



SRS is a good alternative (and adjunct?) to surgery


- 
- Individual tumours of ≤ 3 cm diameter
 - ≥ 3 cm: increased toxicity, lower dose, reduced control
 - Surgery preferable if significant oedema
 - Inoperable tumours or in high risk sites
 - Multiple metastases:
 - what is the maximum number?
 - What is the maximum total volume?
 - Linac-based SRS as effective as GammaKnife and more convenient
 - FFF delivery reduces treatment times considerably
 - No evidence that post-op SRS improves outcomes

WBRT plus simultaneous integrated boost...



...and hippocampal sparing


WBRT as sole treatment



Contents lists available at SciVerse ScienceDirect

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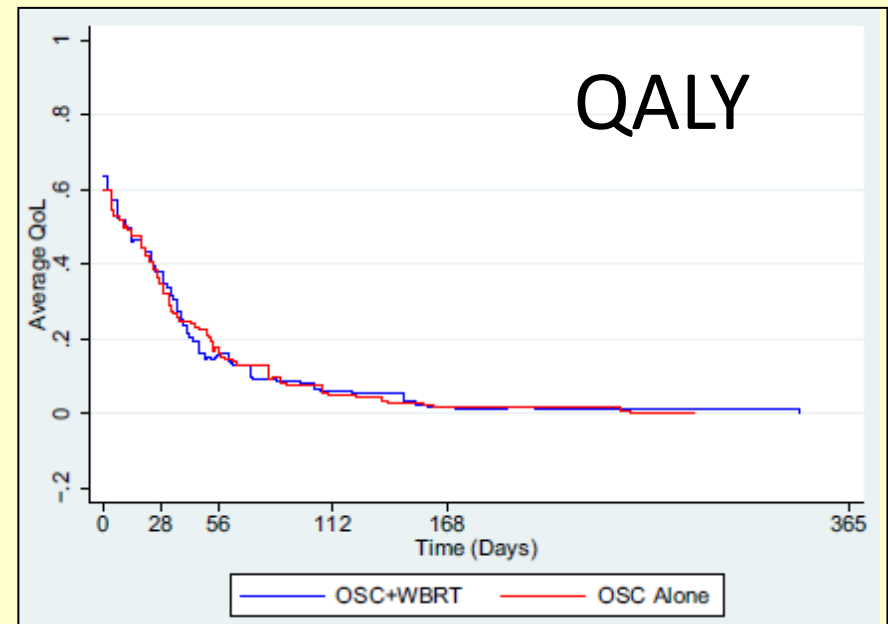
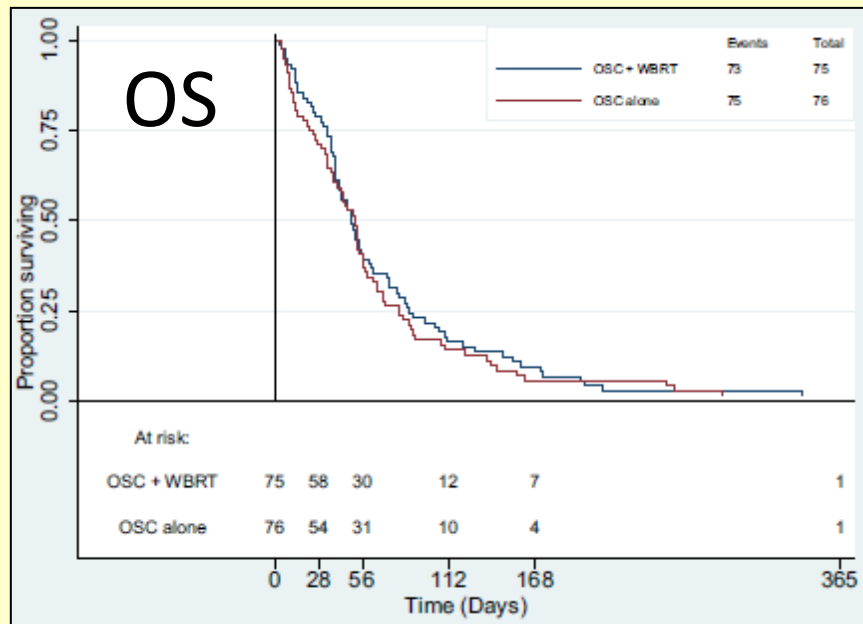
journal homepage: www.clinicaloncologyonline.net



Original Article

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



WBRT as sole treatment



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

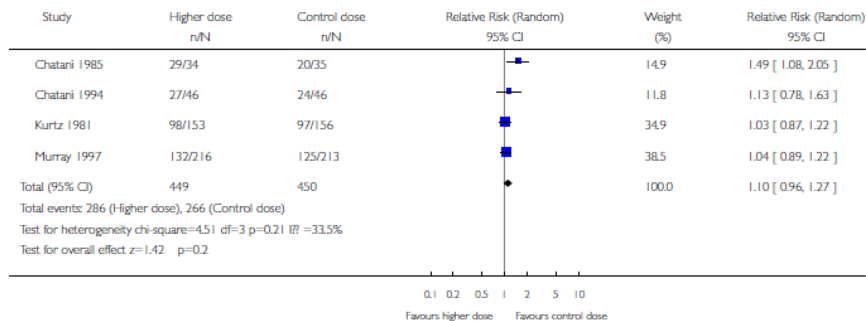
Tsao MN, Lloyd N, Wong R, Chow E, Rakovitch E, Laperriere N

Analysis 01.02. Comparison 01 Altered WBRT fractionation schedules versus WBRT control (3000 cGy/ 10 fractions): mortality, Outcome 02 Mortality at six months: higher dose WBRT versus control dose WBRT (3000 cGy/ 10 fractions)

Review: Whole brain radiotherapy for the treatment of multiple brain metastases

Comparison: 01 Altered WBRT fractionation schedules versus WBRT control (3000 cGy/ 10 fractions): mortality

Outcome: 02 Mortality at six months: higher dose WBRT versus control dose WBRT (3000 cGy/ 10 fractions)



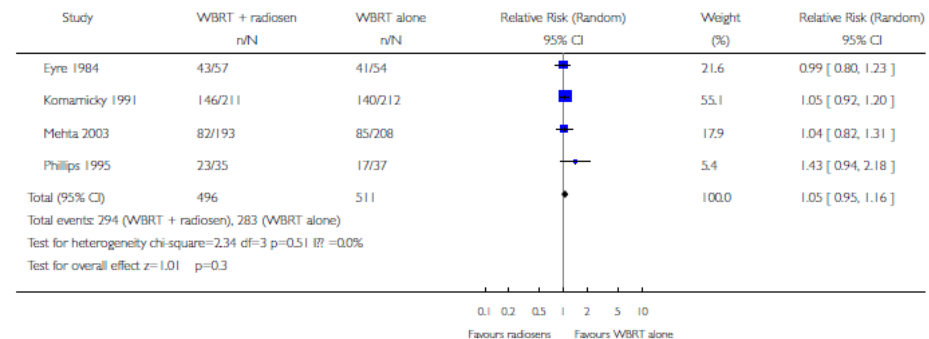
No effect of dose

Analysis 03.01. Comparison 03 WBRT with radiosensitizers (radiosen) versus WBRT alone, Outcome 01 Mortality at six months

Review: Whole brain radiotherapy for the treatment of multiple brain metastases

Comparison: 03 WBRT with radiosensitizers (radiosen) versus WBRT alone

Outcome: 01 Mortality at six months



No effect of radiosensitisers

Adding SRS to WBRT improves local control and PS;
also improves survival if single metastasis or RPA class I



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

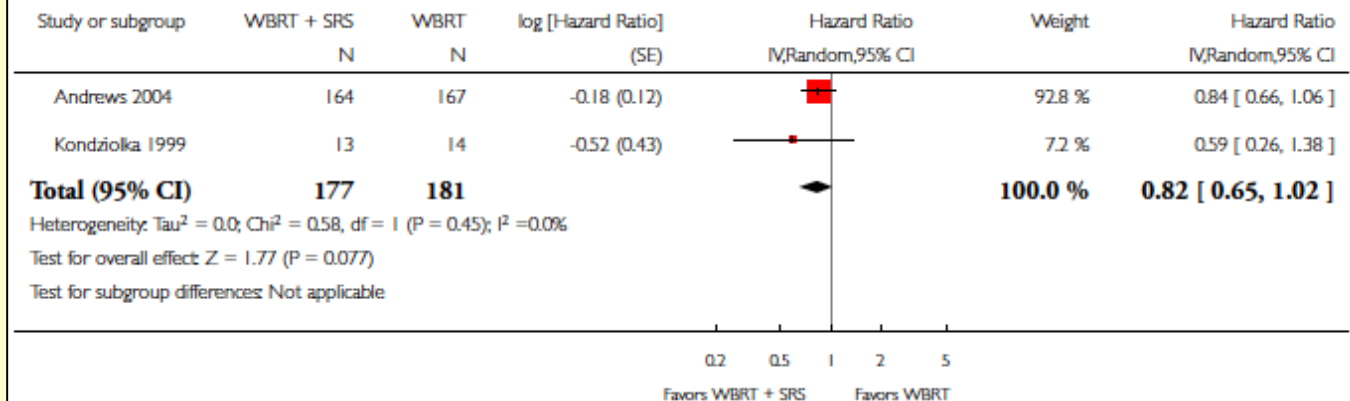
Patil CG, Pricola K, Sarmiento JM, Garg SK, Bryant A, Black KL

Analysis 1.1. Comparison 1 WBRT plus radiosurgery versus WBRT, Outcome 1 Overall survival.

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

Comparison: 1 WBRT plus radiosurgery versus WBRT

Outcome: 1 Overall survival



Adding WBRT to focal treatment does not improve survival....



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

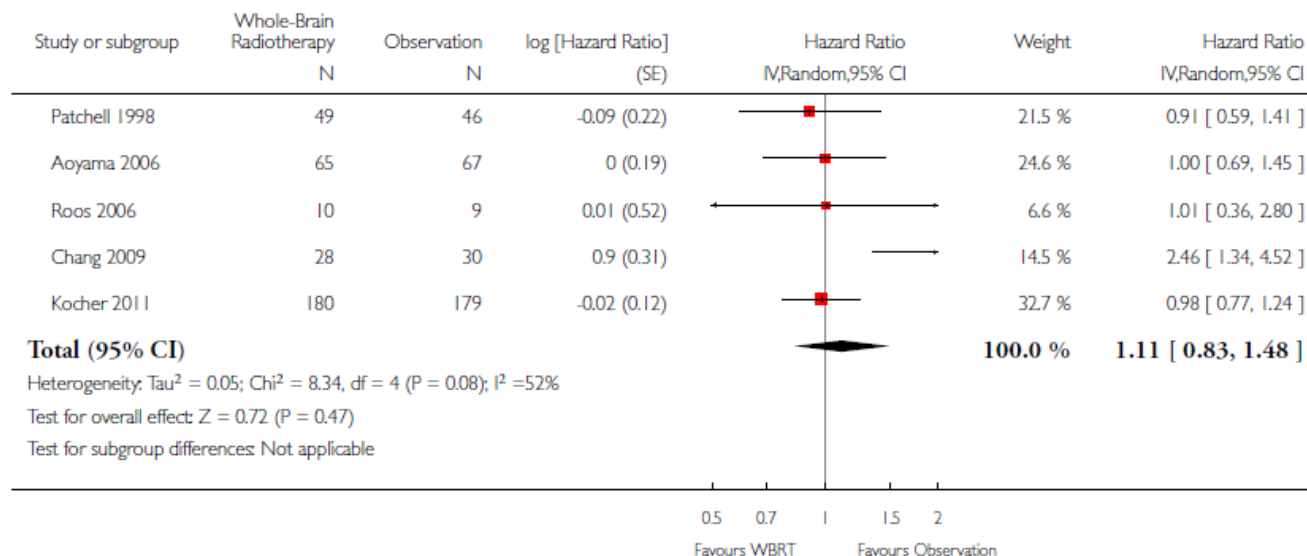
Soon YY, Tham IWK, Lim KH, Koh WY, Lu JJ

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



...but improves intracranial disease control



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

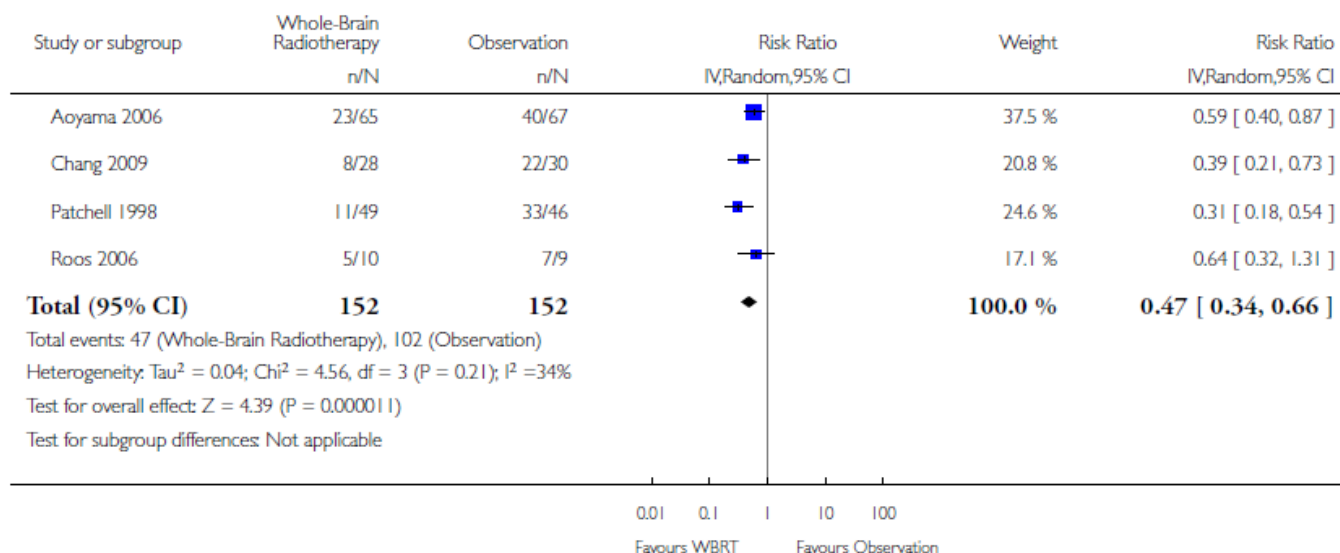
Soon YY, Tham IWK, Lim KH, Koh WY, Lu JJ

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



No effect of:

- surgery v SRS
- single v multiple
- scheduling
- WBRT dose

Does toxicity of WBRT outweigh adverse effects of disease progression?

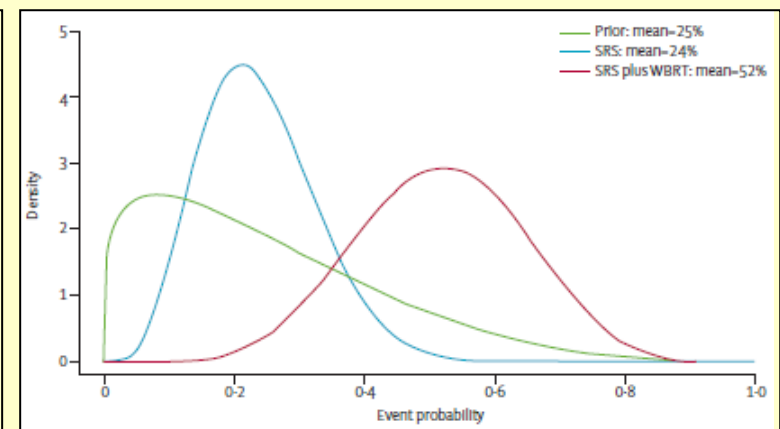
Neurocognition in patients with brain metastases treated with radiosurgery or radiosurgery plus whole-brain irradiation: a randomised controlled trial

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

	Stereotactic radiosurgery plus whole-brain radiotherapy (N=11)	Stereotactic radiosurgery alone (N=20)	p (A>B)
Total recall	52%	24%	96%
Delayed recall	22%	6%	86%
Delayed recognition	11%	0%	86%

p (A>B)—Bayesian probability that the proportion with a significant neurocognitive worsening is higher in stereotactic radiosurgery plus whole-brain radiotherapy than stereotactic radiosurgery alone.

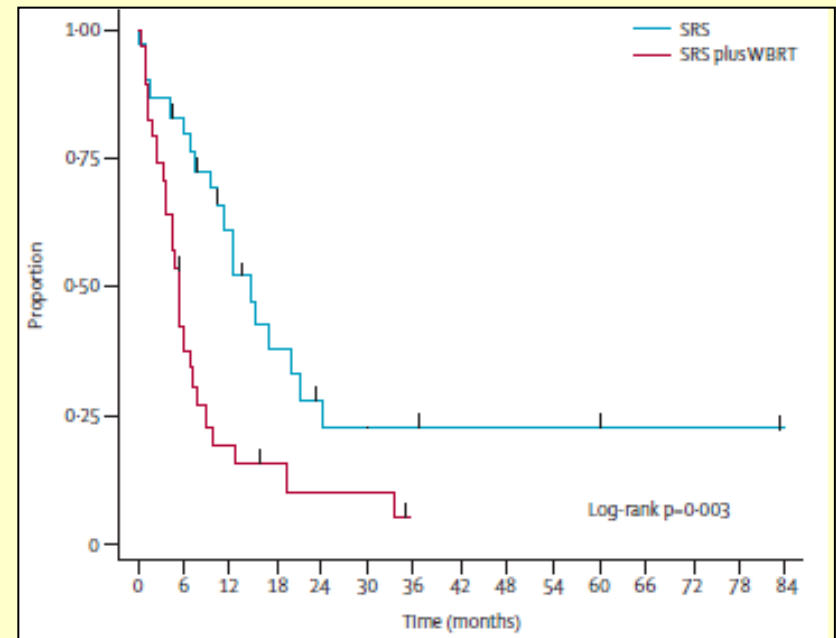
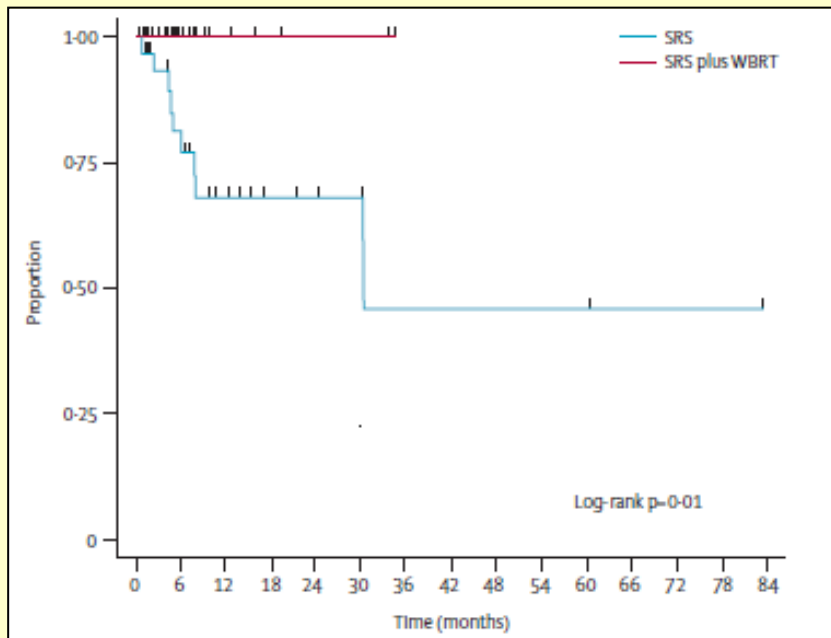
Table 3: Bayesian posterior mean probability of significant neurocognitive decline at 4 months by treatment group, by Hopkins Verbal Learning Test—Revised



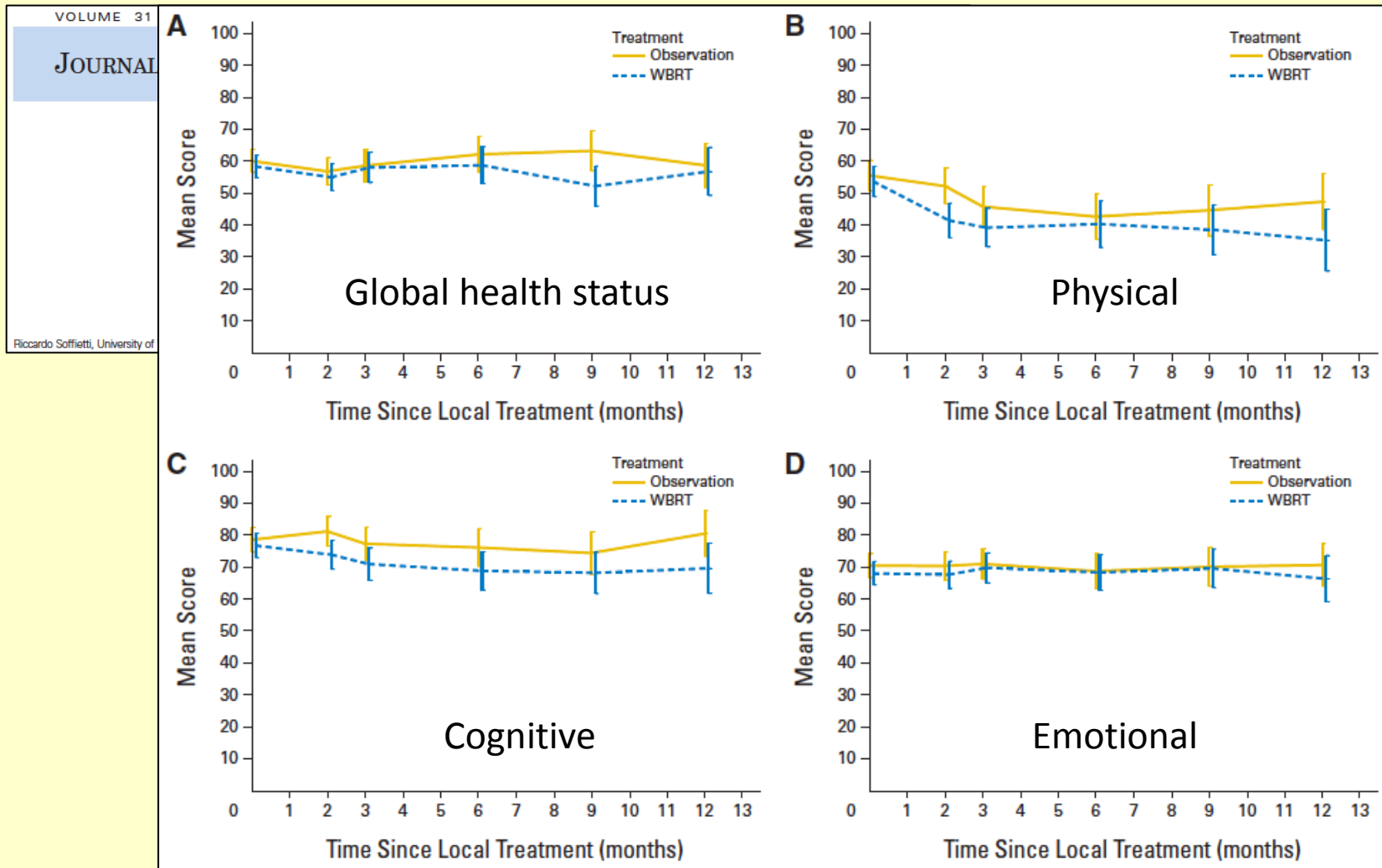
Does toxicity of WBRT outweigh adverse effects of disease progression?

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

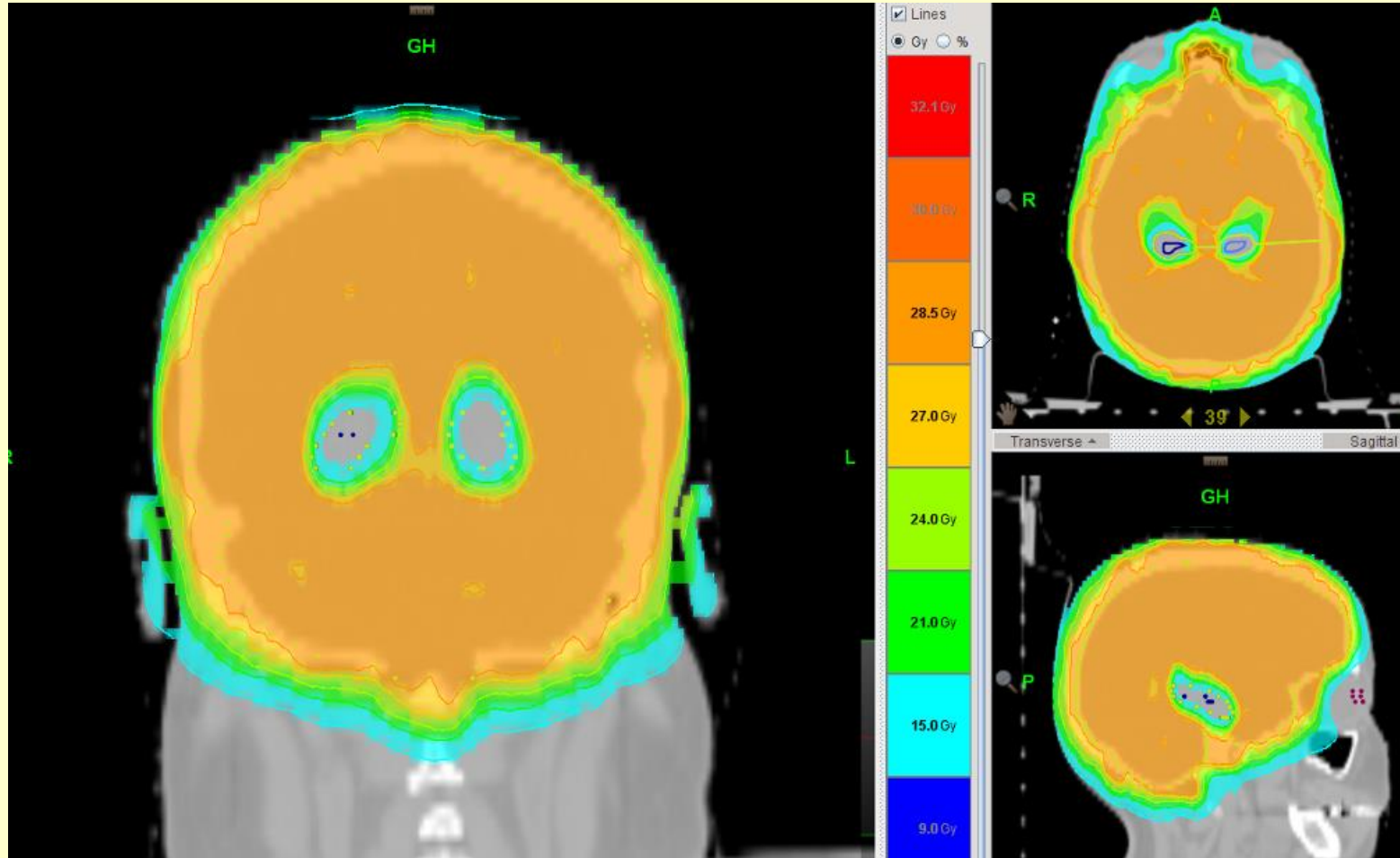
Eric L Chang, Jeffrey S Wefel, Kenneth R Hess, Pamela K Allen, Frederick F Lang, David G Kornguth, Rebecca B Arbuckle, J Michael Swint, Almon S Shiu, Moshe H Maor, Christina A Meyers



Does toxicity of WBRT outweigh adverse effects of disease progression?



Does hippocampal sparing reduce toxicity without compromising disease control?



2013 American Society for Radiation Oncology (ASTRO) 55th Annual Meeting

News Briefing, Monday, September 23, 2013, 8:30 a.m. Eastern time

Scientific Session: Monday, September 23, 2013, 2:00 – 3:10 pm ET, Georgia World Congress Center

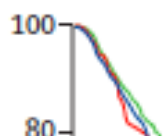
LBA1 Memory Preservation with Conformal Avoidance of the Hippocampus during Whole-Brain Radiotherapy (WBRT) for Patients with Brain Metastases: Primary Endpoint Results of RTOG 0933

V. Gondi^{1,2}, M. P. Mehta^{*3}, S. Pugh^{*4}, W. A. Tome^{*5}, A. Kanner^{*6}, C. Caine^{*7}, H. Rowley^{*8}, V. Kundapur^{*9}, J. N. Greenspoon^{*10}, L. Kachnic^{*11}.

- 113 patients received 30 Gy in 10f with hippocampal sparing by IMRT
- 42 patients evaluable at 4 months, median OS 6.8 months
- Mean relative decline in HVLt-DR 7% v. 30% in historical controls (p=0.0003)
- 3 patients relapsed in hippocampal avoidance region
- Randomised phase III study in development

Is SRS feasible for patients with >4 metastases?

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



	Univariable		Multivariable	
	HR (95% CI)	p value	HR (95% CI)*	p value
Age, years (≥ 65 vs <65)	1.412 (1.229–1.622)	<0.0001	1.351 (1.174–1.554)	<0.0001
Sex (male vs female)	1.427 (1.242–1.655)	<0.0001	1.377 (1.179–1.608)	<0.0001
KPS (≤ 70 vs ≥ 80)	2.079 (1.729–2.500)	<0.0001	1.529 (1.240–1.886)	<0.0001
Number of tumours				
2–4 vs 1	1.313 (1.131–1.525)	0.0001	1.328 (1.141–1.546)	0.0003
5–10 vs 2–4	0.974 (0.806–1.177)	0.78	0.993 (0.819–1.204)	0.94
Maximum diameter of largest tumour (≥ 1.6 cm vs <1.6 cm)	1.431 (1.249–1.638)	<0.0001	1.006 (0.771–1.314)	0.92
Cumulative tumour volume (≥ 1.9 mL vs <1.9 mL)	1.503 (1.313–1.721)	<0.0001	1.172 (0.899–1.530)	0.24

Number at risk

1 tumour	455	234	97	22
2–4 tumours	531	215	61	16
5–10 tumours	208	84	31	1

What type of radiotherapy is indicated in brain metastasis; a personal view:

- Neurosurgery has an important role
- SRS is the best option for small and/or unresectable mets $\leq 3\text{cm}$
- Probably safe and effective to treat up to 10 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
- Individualise treatment!

Treat the individual

