Controversy session

Brain metastases:

Is WBRT indicated for most patients?

"Contra"

Yoko Nakasu, MD
Division of Neurosurgery
Shizuoka Cancer Centre, Japan

ESMO Asia Singapore 20/Dec/2015

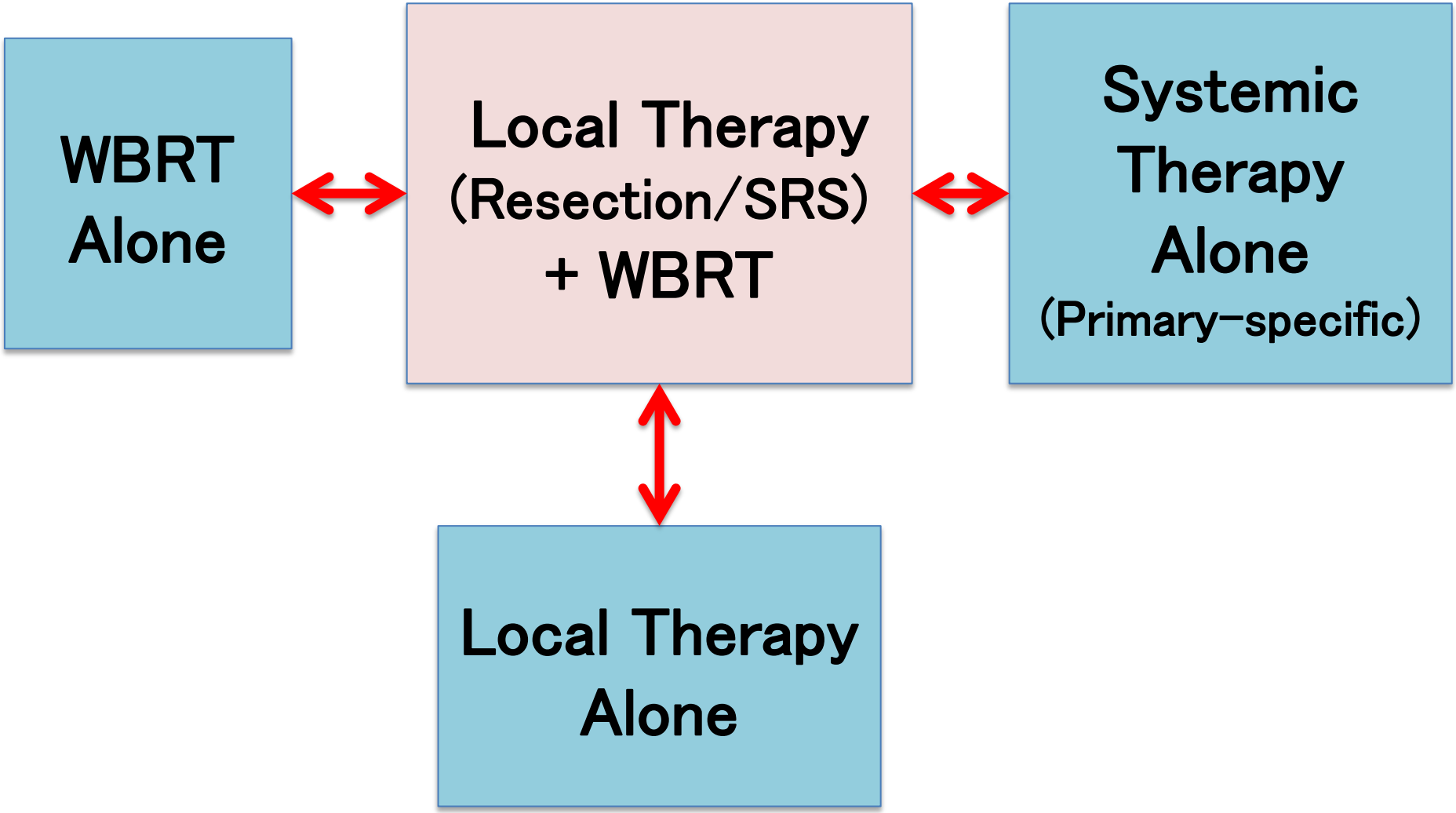
No conflict of interest

Yoko Nakasu, MD
Division of Neurosurgery
Shizuoka Cancer Centre, Japan

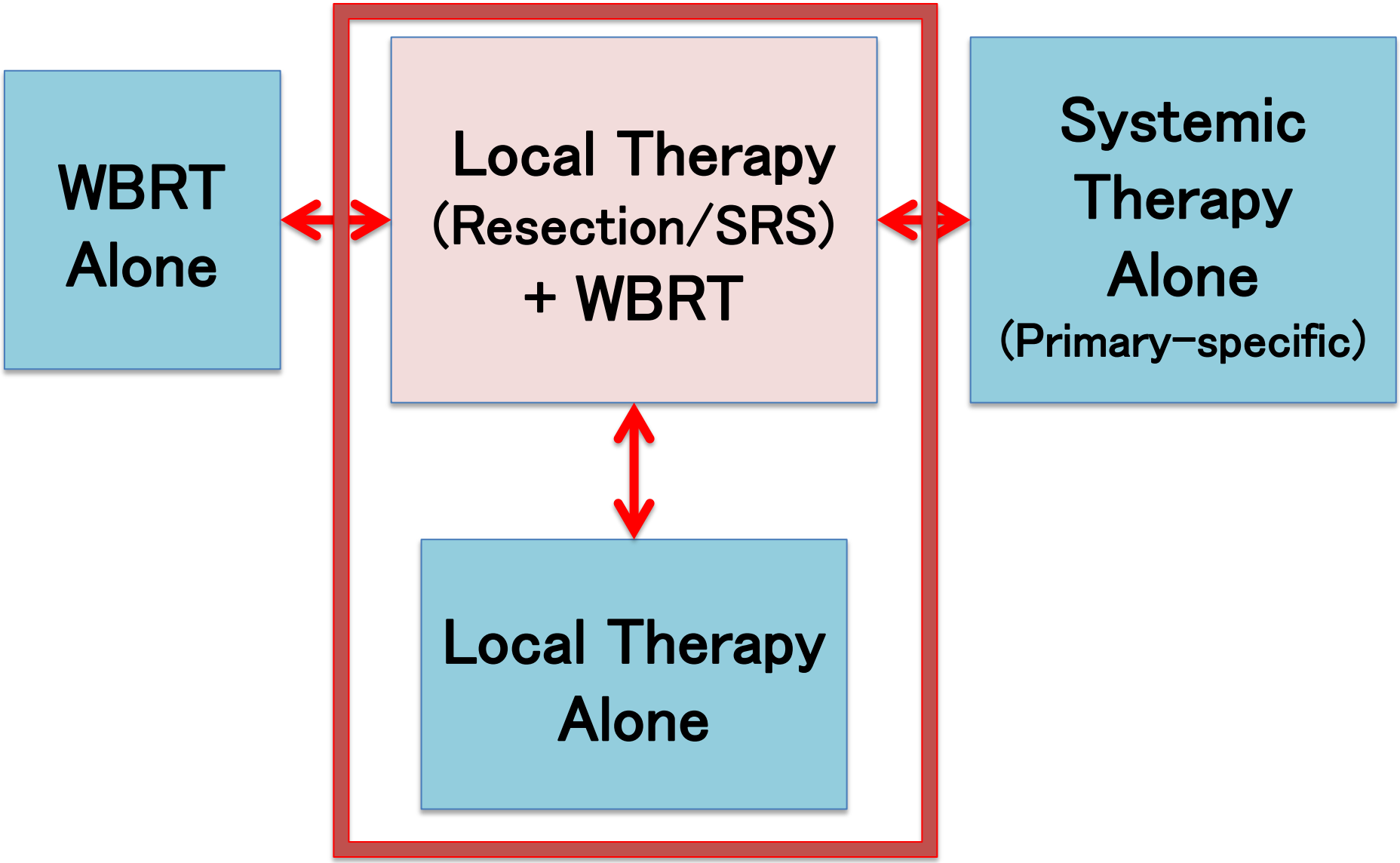
Brain metastases: Is WBRT indicated for most patients? “Contra”

ESMO Asia Singapore 2015

RCT: Metastatic Brain Tumours



RCT: Metastatic Brain Tumours



Brain Metastases:

Plus WBRT vs Local Therapy Alone

1. Survival
2. Local/Distant CNS Control
3. Cognition, Health-related QOL
4. Time, Cost

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VOLUME 29 · NUMBER 2 · JANUARY 10 2011
JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

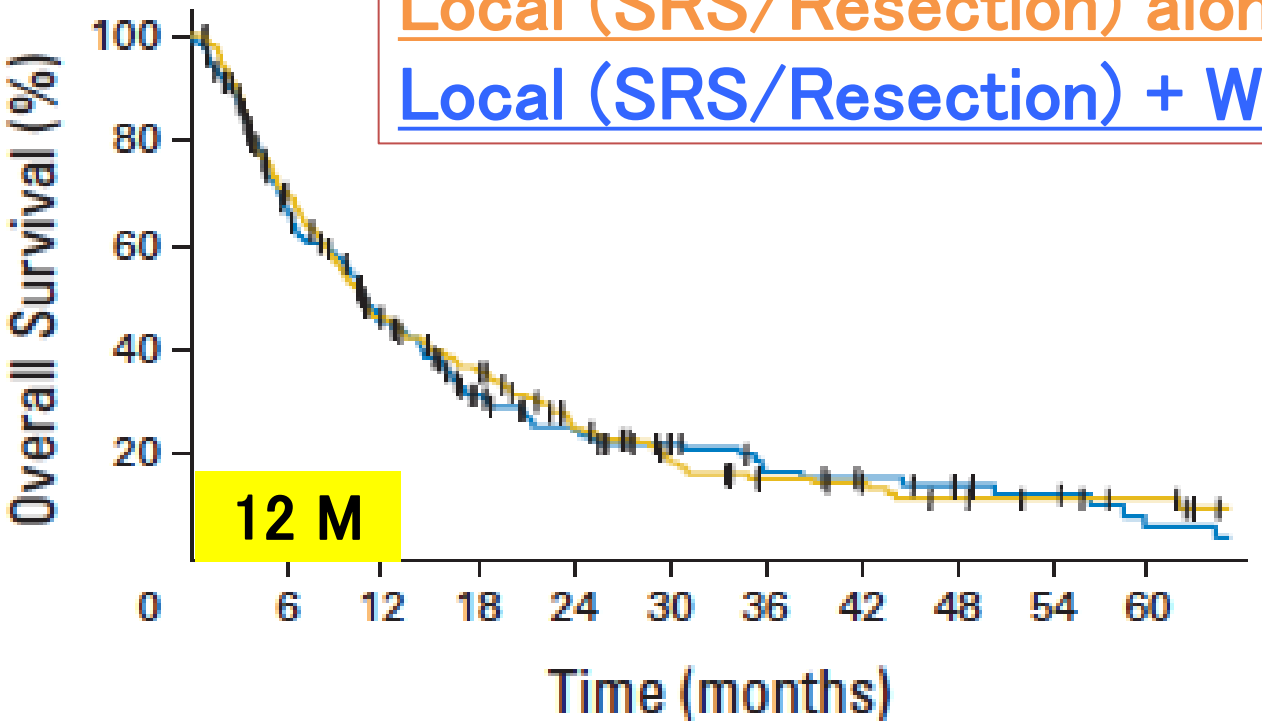
OS

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

B

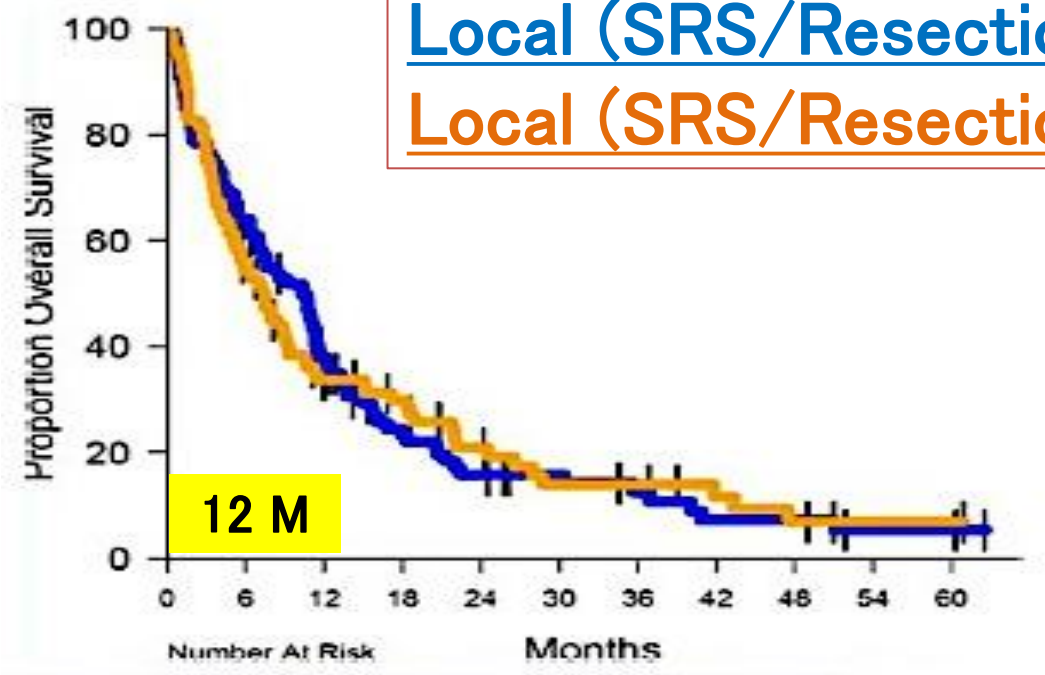
Local (SRS/Resection) alone
Local (SRS/Resection) + WBRT



Randomized treatment	0	N	No. of patients at risk									
Observation	143	179	117	75	44	31	22	15	12	9	7	3
WBRT	149	180	124	80	61	38	25	18	15	11	9	7

ASCO 2015
NCCTG N0574: A phase-3 RCT of WBRT in addition to SRS in patients with 1 to 3 metastases

OS



By the courtesy of Dr H. Okamoto, Yokohama Municipal Hosp, Japan

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Local Control

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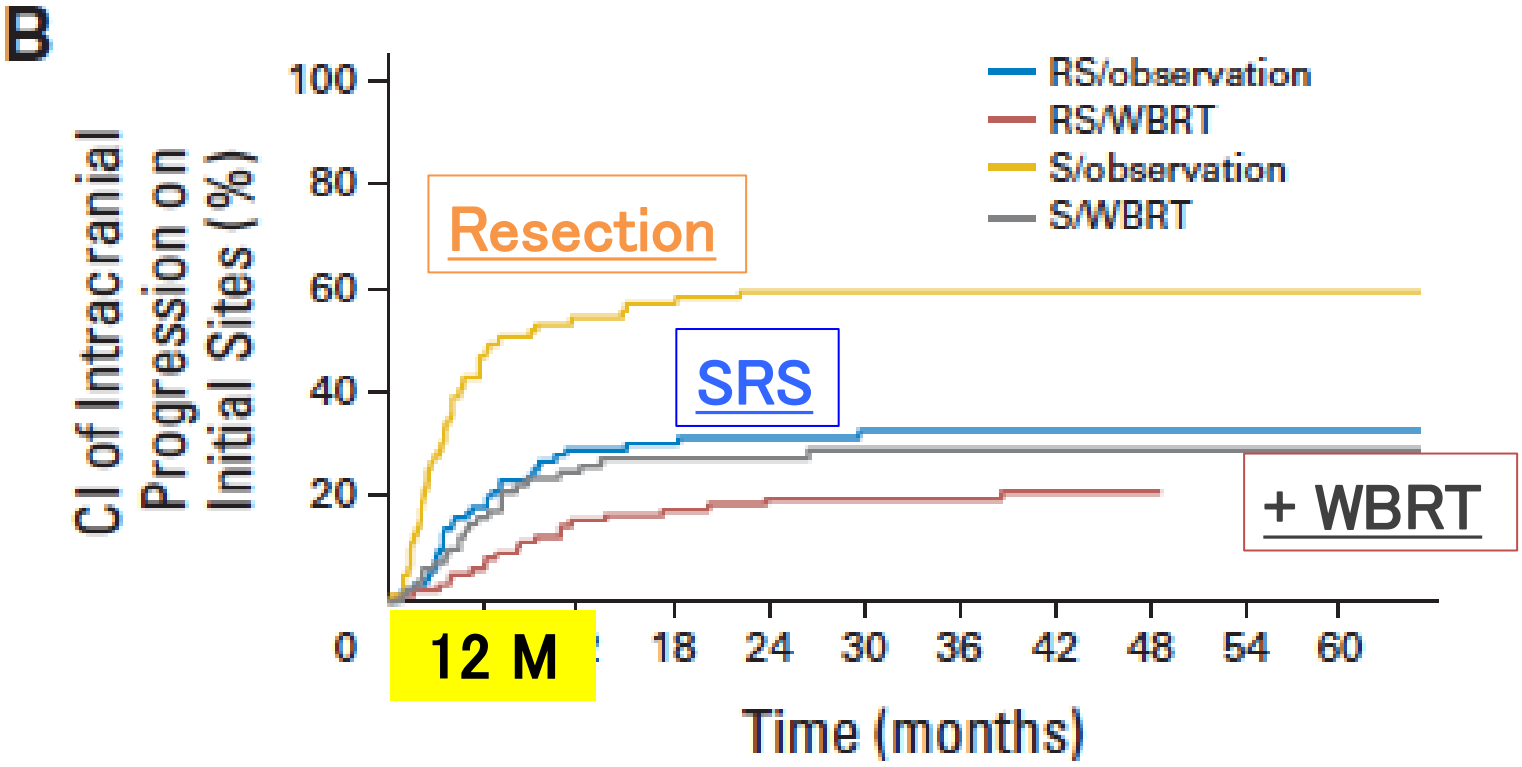
Martin Kocher, Riccardo Soffietti, Ufuk Abacioglu, Salvador Villà, Francois Fauchon, Brigitta G. Baumert, Laura Fariselli, Tzahala Tzuk-Shina, Rolf-Dieter Kortmann, Christian Carrie, Mohamed Ben Hassel, Mauri Kouri, Egils Valeinis, Dirk van den Berge, Sandra Collette, Laurence Collette, and Rolf-Peter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



Randomized treatment	0	N	No. of patients at risk									
RS/observation	32	100	43	16	9	6	3	3	2	2	1	1
RS/WBRT	20	99	59	26	16	10	7	5	3	1	0	0
S/observation	47	79	23	15	10	7	4	3	3	1	1	1
S/WBRT	23	81	47	30	23	11	9	8	8	7	6	4

VOLUME 29 · NUMBER 2 · JANUARY 10 2011

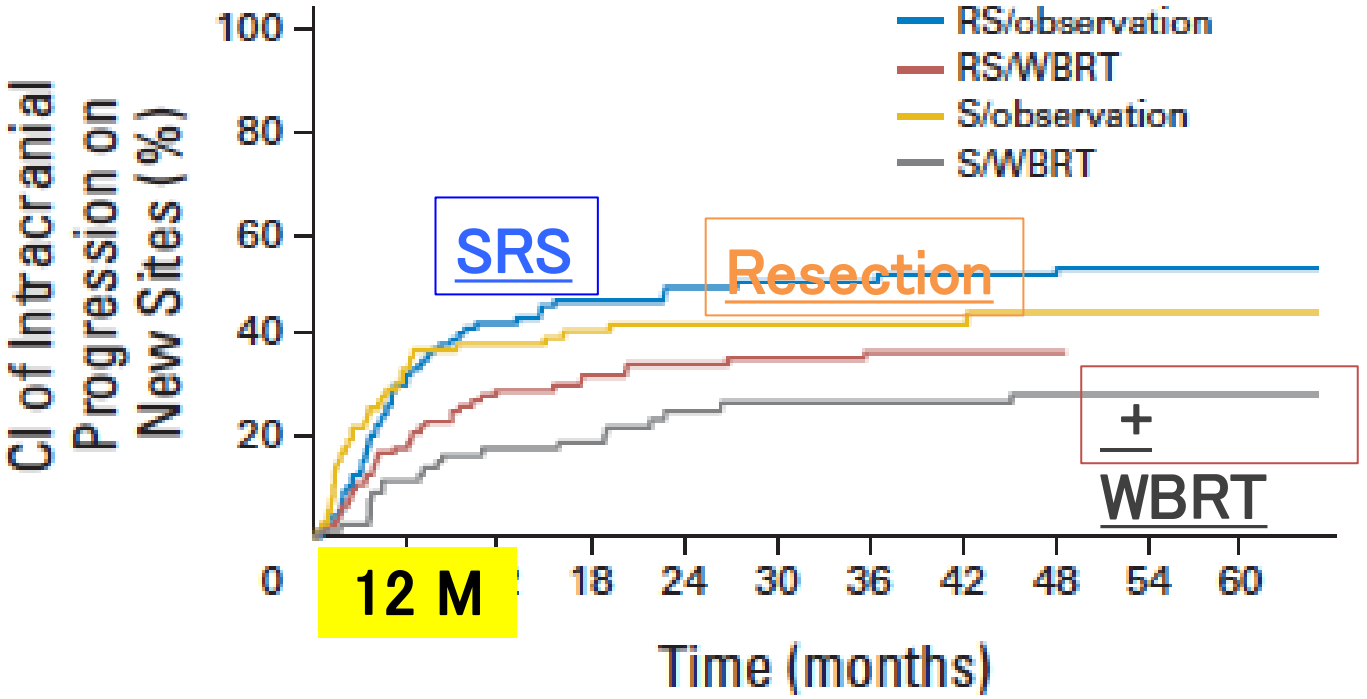
JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Distant Control

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

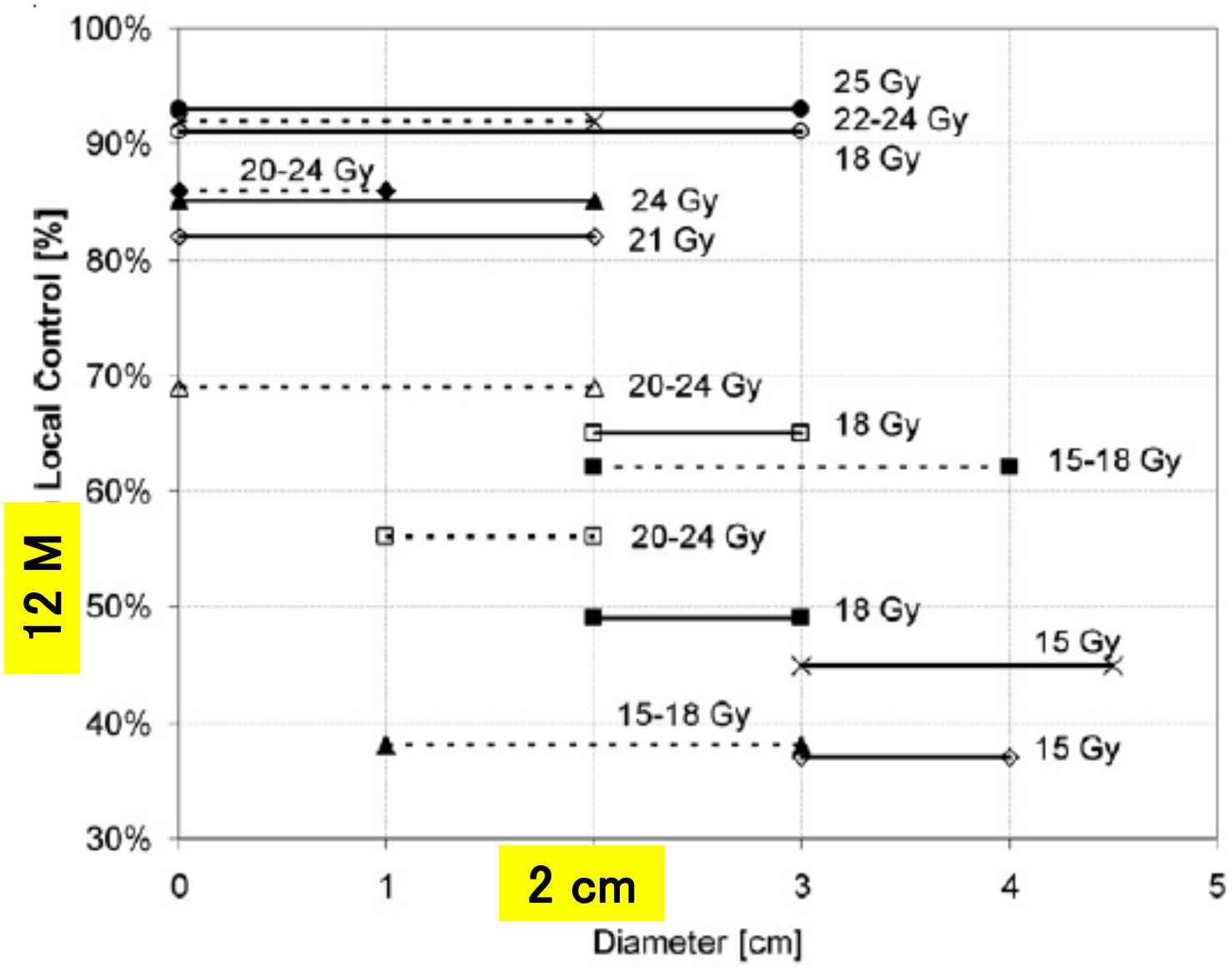
Martin Kocher, Riccardo Soffietti, Ufuk Abacioglu, Salvador Villà, Francois Fauchon, Brigitta G. Baumert, Laura Fariselli, Tzahala Tzuk-Shina, Rolf-Dieter Kortmann, Christian Carrie, Mohamed Ben Hassel, Mauri Kouri, Egils Valeinis, Dirk van den Berge, Sandra Collette, Laurence Collette, and Rolf-Peter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

A



Randomized treatment	0	N	No. of patients at risk									
RS/observation	51	100	43	16	9	6	3	3	2	2	1	1
RS/WBRT	35	99	59	26	16	10	7	5	3	1	0	0
S/observation	34	79	23	15	10	7	4	3	3	1	1	1
S/WBRT	21	81	47	30	23	11	9	8	8	7	6	4

Local control rates by SRS



Brain Metastases:

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4. Time, Cost

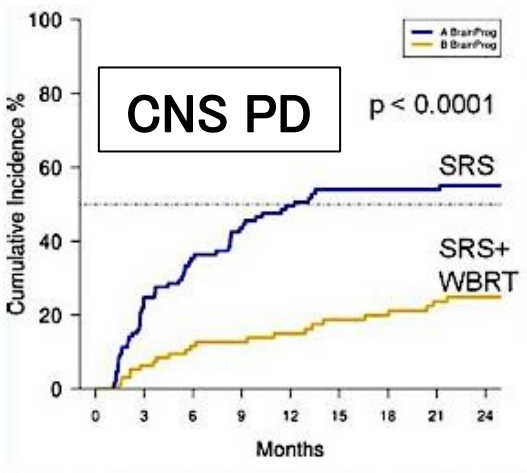
Radiation-induced dementia in patients cured of brain metastases

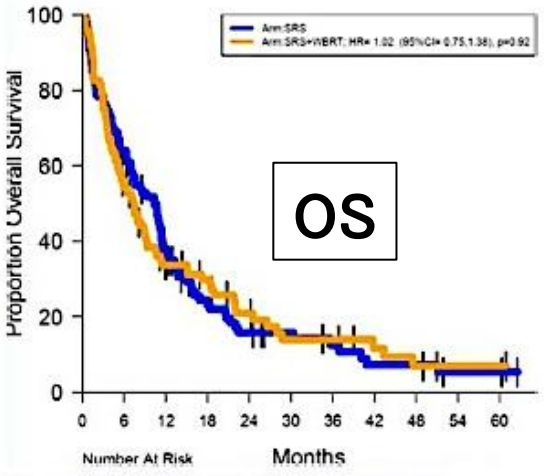
Lisa M. DeAngelis, MD; Jean-Yves Delattre, MD; and Jerome B. Posner, MD

Article abstract—When a patient with cancer develops a brain metastasis, death is usually imminent, but aggressive treatment in some patients with limited or no systemic disease yields long-term survival. In such patients, delayed deleterious effects of therapy are particularly tragic. We report 12 patients who developed delayed complications of whole brain radiotherapy (WBRT) given as sole treatment (4 patients) or in combination with surgical resection (8 patients). Within 5 to 36 months (median, 14) all patients developed progressive dementia, ataxia, and urinary incontinence causing severe disability in all and leading to death in 7. No patient had tumor recurrence when neurologic symptoms began. Cortical atrophy and hypodense white matter were identified by CT in all. Contrast-enhancing lesions were seen in 3 patients; 2 of the lesions yielded radionecrosis on biopsy. Autopsies on 2 patients revealed diffuse chronic edema of the hemispheric white matter in the absence of tumor recurrence. Corticosteroids and ventriculoperitoneal shunt offered significant but incomplete improvement in some patients. The total dose of WBRT was only 2,500 to 3,900 cGy, but daily fractions of 300 to 600 cGy were employed. We believe that these fractionation schedules, several of which are used commonly, predispose to delayed neurologic toxicity, and that more protracted schedules should be employed for the safe and efficacious treatment of good-risk patients with brain metastases. The incidence of WBRT-induced dementia was only 1.9 to 5.1% in the 2 populations reviewed here; however, this underestimates the incidence because only severely affected patients could be identified from chart review.

NEUROLOGY 1989;39:789-796

ASCO 2015
NCCTG N0574: A phase-3 RCT of WBRT in addition to SRS in patients with 1 to 3 metastases





	No (Lung)	PS 0-1	3M -Cognition Worse	6M-CNS PD	OS(M)
SRS	111 (72%)	91%	63.5%	35.4%	10.4
SRS + WBRT	102 (65%)	92%	91.7%	11.6%	7.4
			p=.0007	*p<.0001*	*p=.93*

By the courtesy of Dr H. Okamoto, Yokohama Municipal Hosp, Japan

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

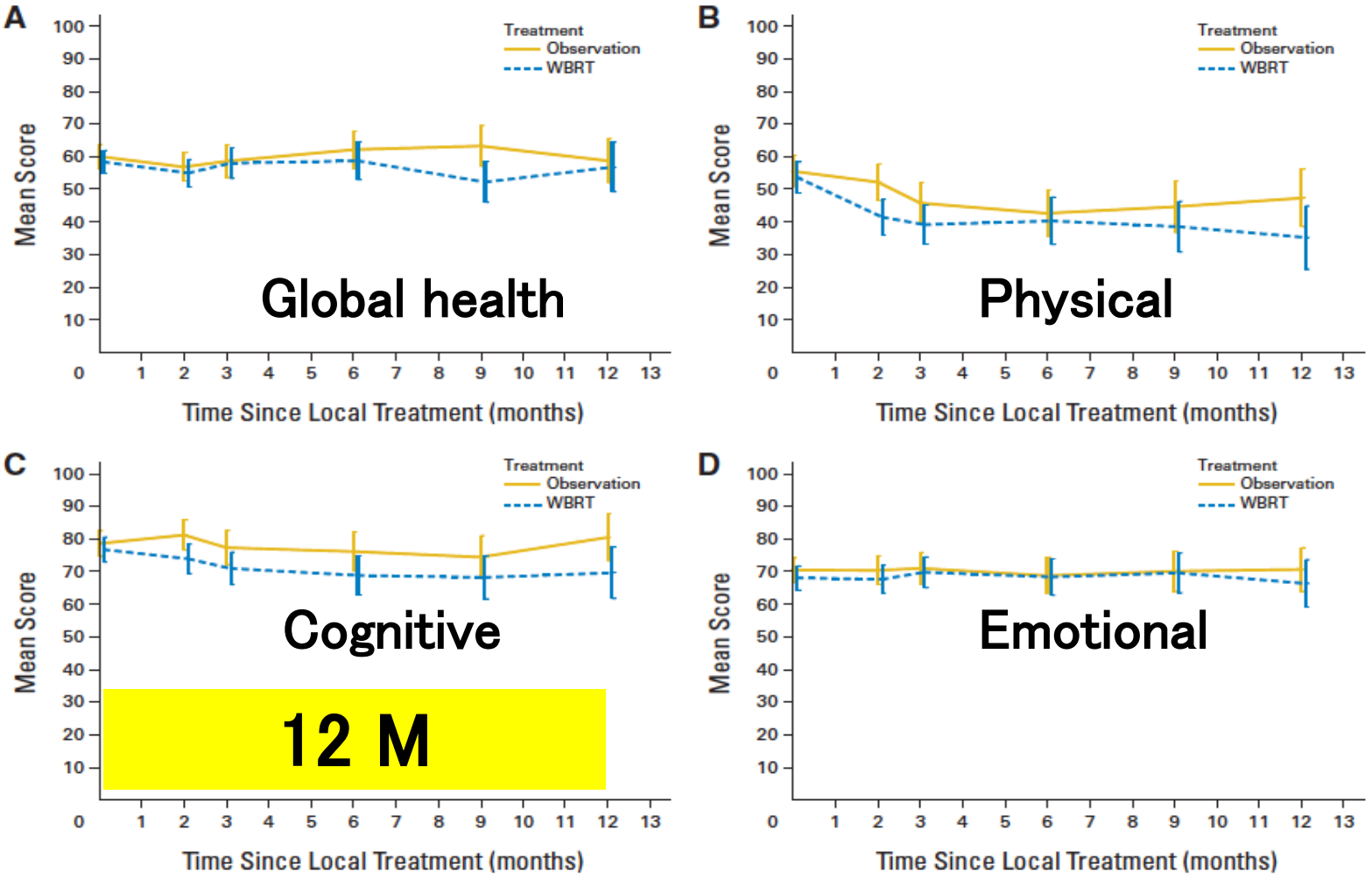
A European Organisation for Research and Treatment of Cancer Phase III Trial of Adjuvant Whole-Brain Radiotherapy Versus Observation in Patients With One to Three Brain Metastases From Solid Tumors After Surgical Resection or Radiosurgery: Quality-of-Life Results

Riccardo Soffietti, Martin Kocher, Ufuk M. Abacioglu, Salvador Villa, François 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, Rolf-Peter Mueller, Gloria Tridello, Laurence Collette, and Andrew Bottomley

Riccardo Soffietti, University of Torino and San Giovanni Battista Hospital, Turin; Laura Fariselli, Fondazione Istituto Neurologico "Carlo Besta," Milan; Gloria Tridello, Azienda Ospedaliera Universitaria Verona, Verona, Italy; Martin Kocher and Rolf-Peter Mueller, University of Cologne, Cologne;

Local (SRS/Resection) alone

Local (SRS/Resection) + WBRT



Int. J. Radiation Oncology Biol. Phys., Vol. 68, No. 5, pp. 1388–1395, 2007
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0360-3016/07/$–see front matter

ELSEVIER

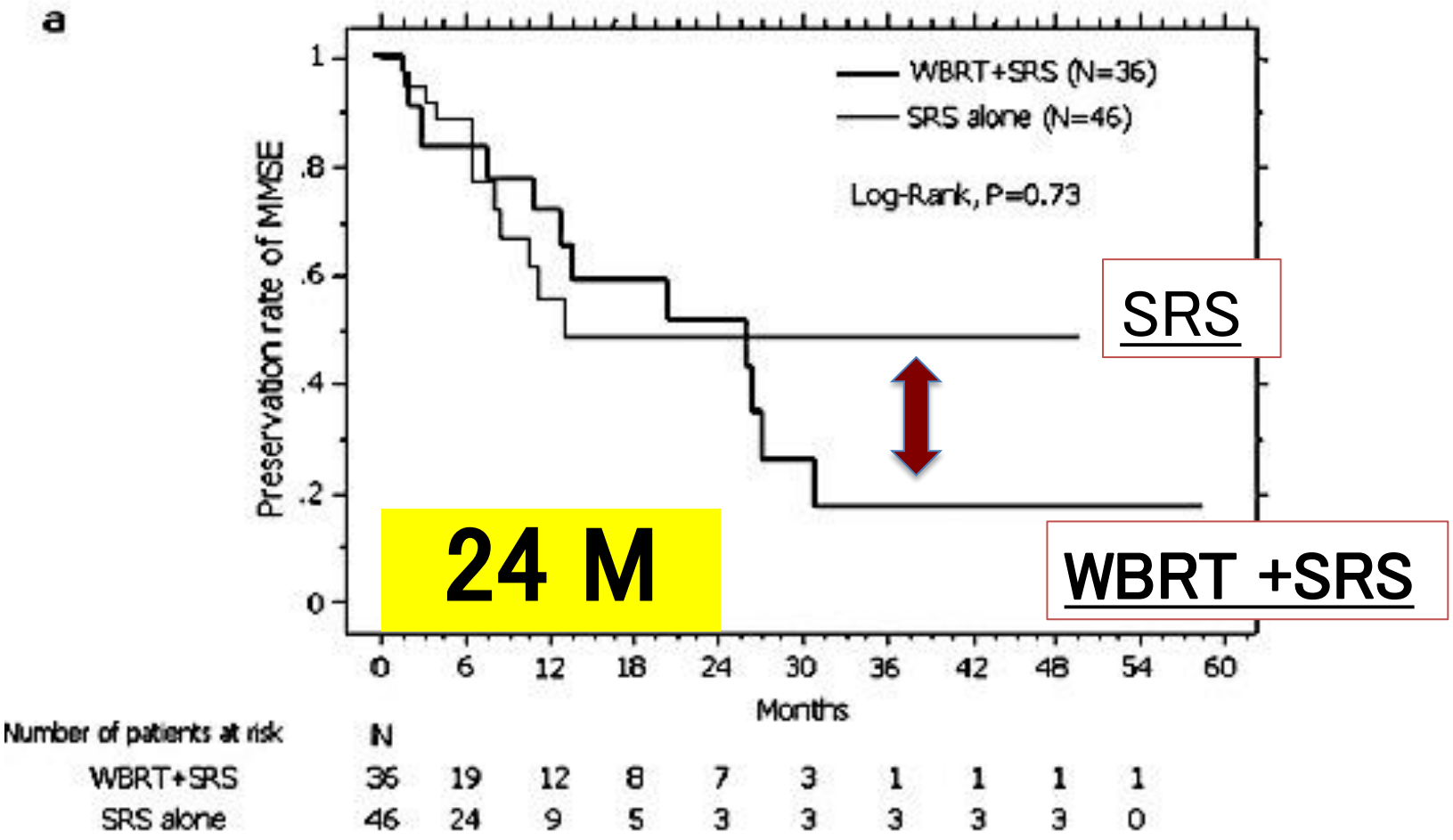
doi:10.1016/j.ijrobp.2007.03.048

CLINICAL INVESTIGATION **Brain**

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]

Reservation of MMSE score



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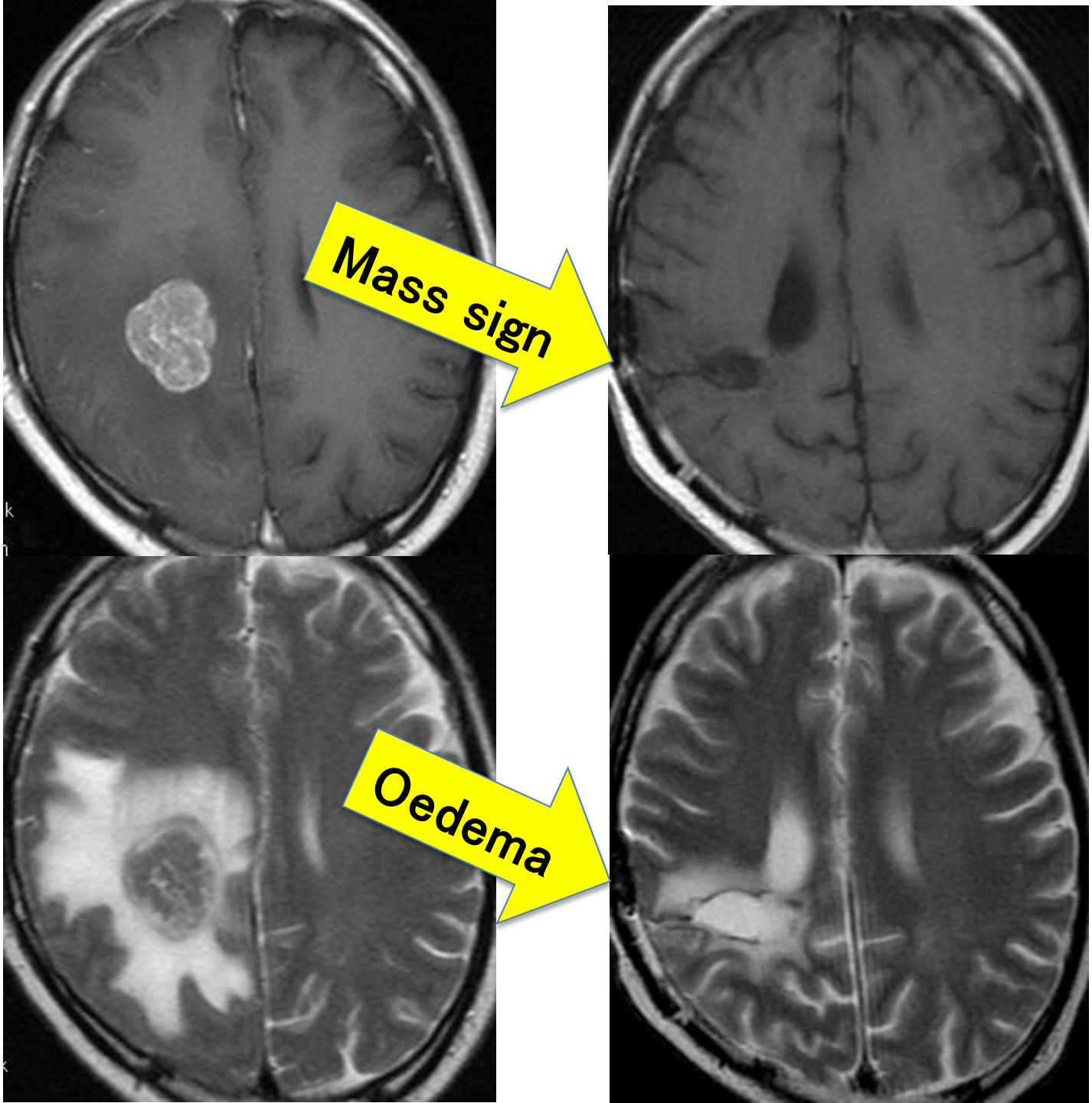
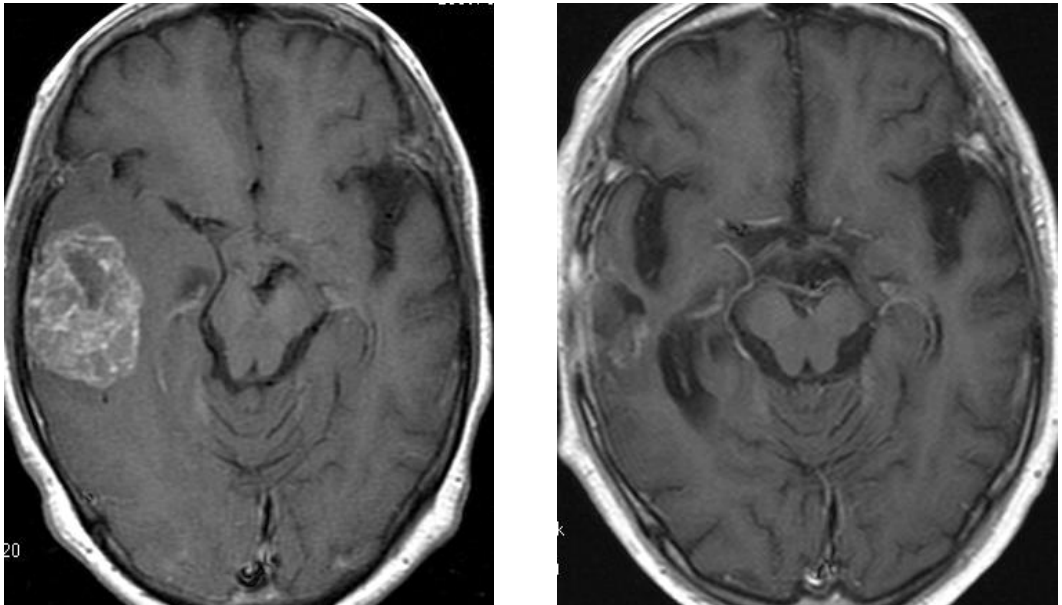
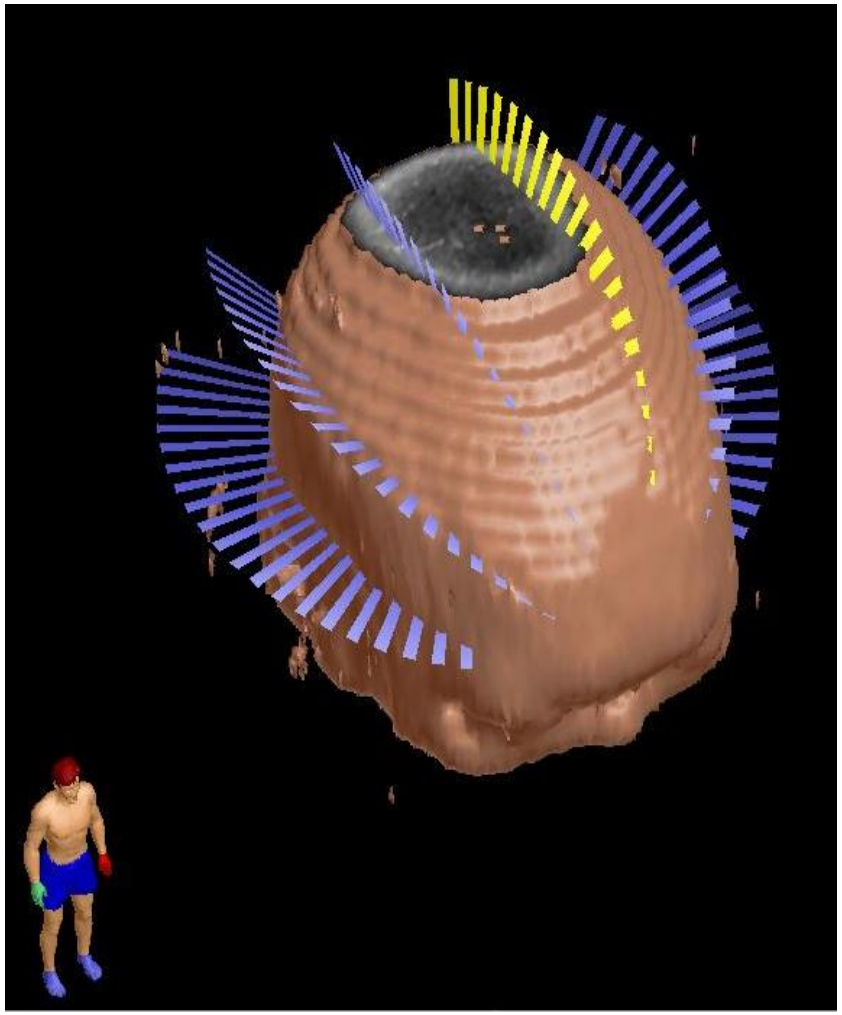

Mass sign
Oedema

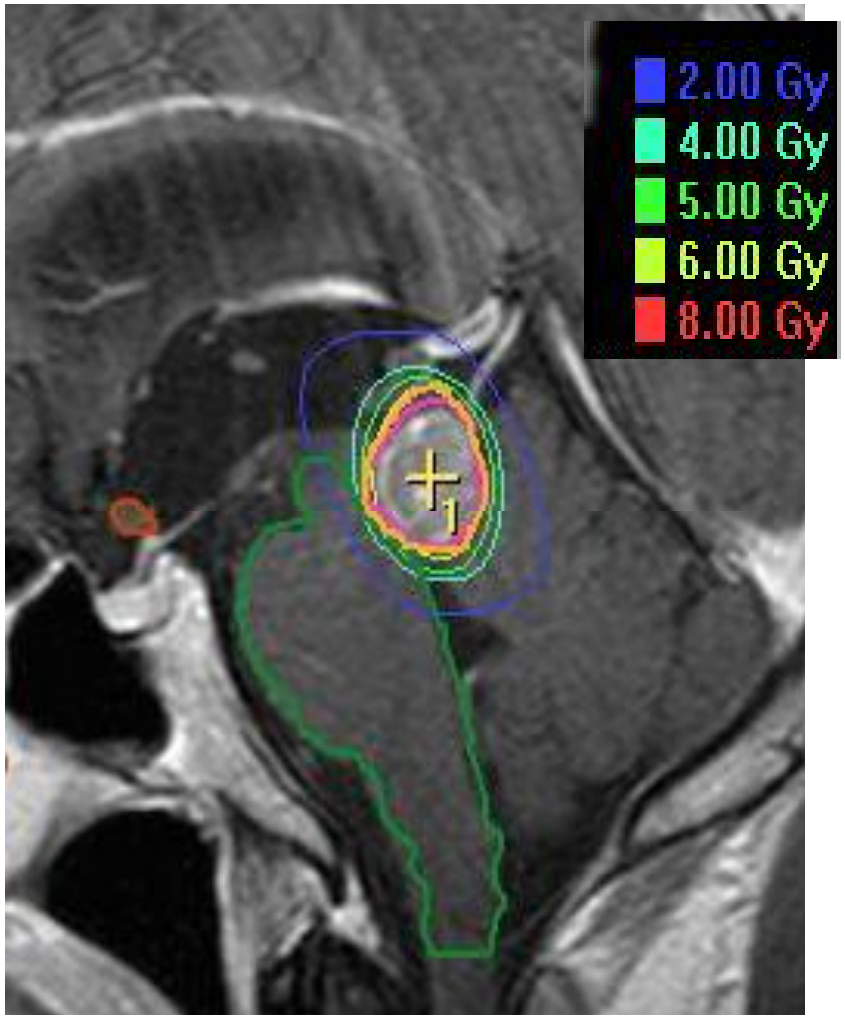
Resection

= Prompt recovery in neurological deficits

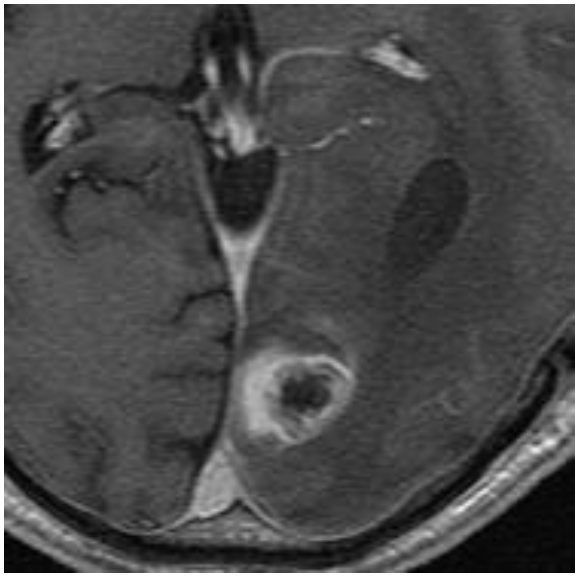


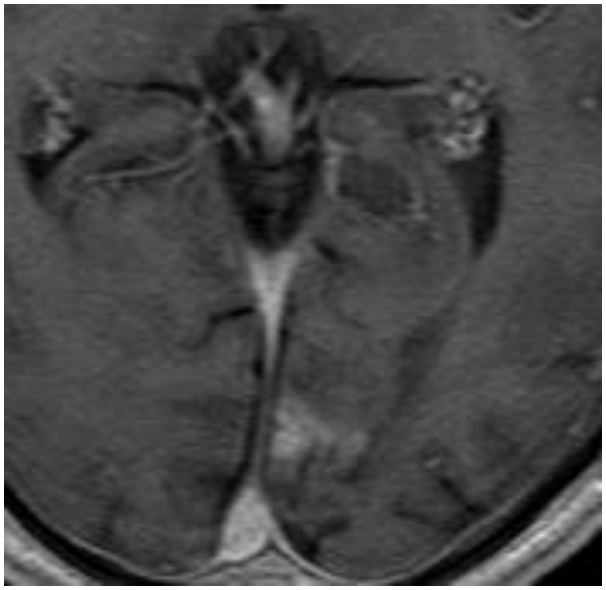
SRT





SRS/SRT
= 1- to 5-Day session





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

Masaaki Yamamoto*, Toru Serizawa*, Takashi Shuto, Atsuya Akabane, Yoshinori Higuchi, Jun Kawagishi, Kazuhiro Yamanaka, Yasunori Sato, Hidefumi Jokura, Shoji Yomo, Osamu Nagano, Hiroyuki Kenai, Akihito Moriki, Satoshi Suzuki, Yoshihisa Kida, Yoshiyasu Iwai, Motohiro Hayashi, Hiroaki Onishi, Masazumi Gondo, Mitsuya Sato, Tomohide Akimitsu, Kenji Kubo, Yasuhiro Kikuchi, Toru Shibasaki, Tomoaki Goto, Masami Takanashi, Yoshimasa Mori, Kintomo Takakura, Naokatsu Saeki, Etsuo Kunieda, Hidefumi Aoyama, Suketaka Momoshima, Kazuhiro Tsuchiya

Lancet Oncology
2014:15:387–95

	Total (n=1194)
Died	850 (71%)
Neurological death*	71 (8%)
Deterioration of neurological function	146 (12%)
Local recurrence†	138 (13%)
New lesions†	625 (58%)
Leptomeningeal dissemination†	144 (13%)
Leukoencephalopathy†	9 (1%)
Salvage SRS procedures	459 (38%)
1	256 (21%)
2	113 (9%)
≥3	90 (8%)
Salvage WBRT	107 (9%)
Salvage surgery	23 (2%)
Systemic anticancer agents	861 (72%)
Molecularly targeted agents	356 (30%)

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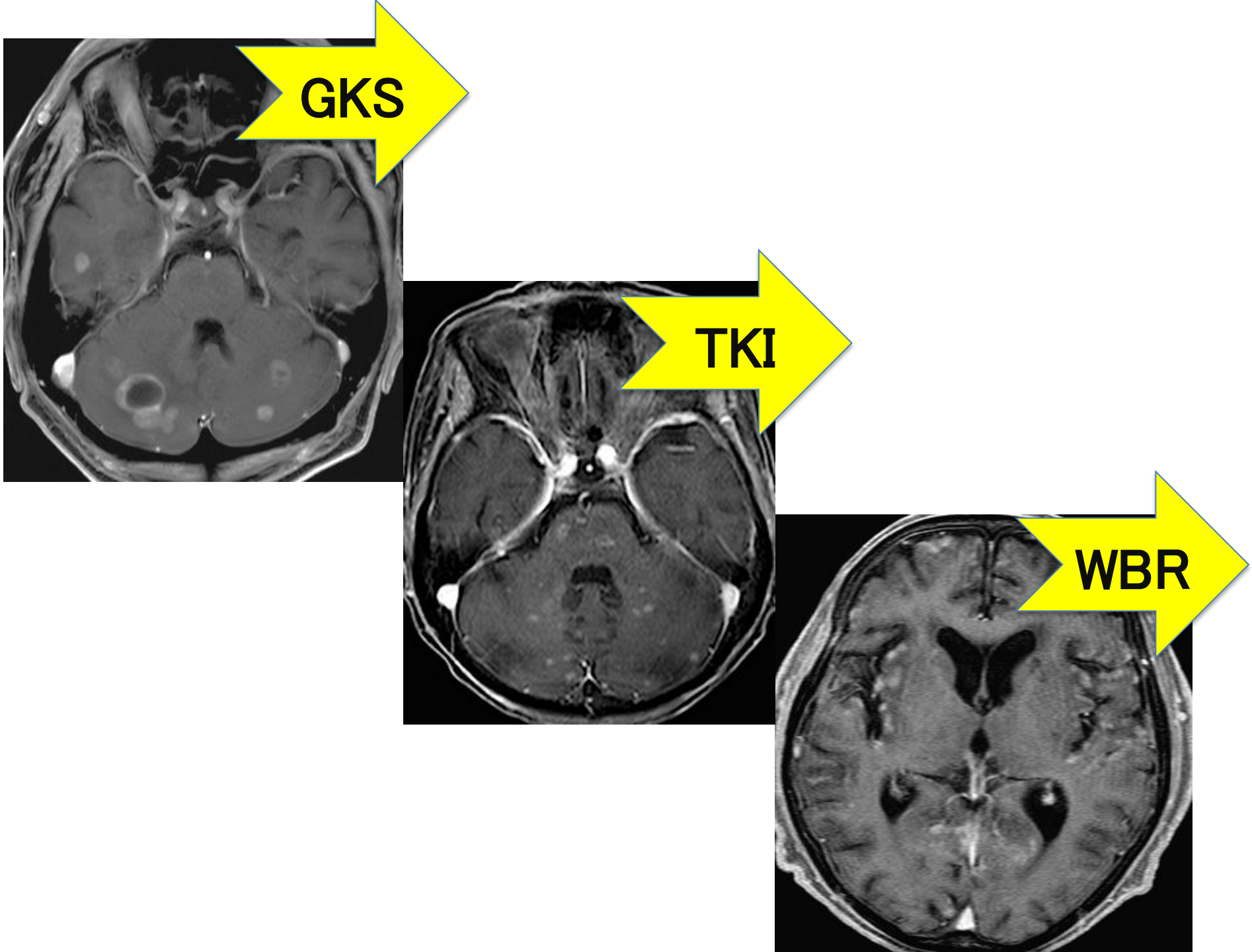
GKS
TKI
WBR

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4. Time, Cost

WBRT is not indicated for most patients.