7 Retrospective analysis of salvage surgery for local progression of brain metastasis previously treated by stereotactic irradiation

Mitsuya K, Hayashi N, Deguchi, S, Onoe T, Harada H, Nakasu Y *Divisions of Neurosurgery and Radiation and proton beam center, Shizuoka Cancer Center, JAPAN*

Background

■ Local progression after stereotactic irradiation (STI) for brain metastases is difficult to differentiate from radiation necrosis, and is difficult to treat. Just a few studies have clarified the prognosis and effectiveness of salvage surgery for progression after STI.

Objective

■ To evaluate functional outcomes and diagnostic value of the salvage surgery.

Methods

■ We retrospectively examined records of patients who underwent salvage surgery for local progression of brain metastases after STI (October 2002 to July 2019). Salvage surgery was indicated for post-STI local progression on MR imaging findings and/or clinical evidence associated with stable systemic disease. We employed two prospective strategies according to the eloquency of the lesions: complete resection with a safety margin utilizing a fence-post method for a non-eloquent lesion; minimal resection and postoperative STI for an eloquent lesion. Prognostic factors for survival were analyzed.

Conclusion

■ The salvage surgeries contributed to rapid improvement of neurological function and histological differentiation of tumor recurrence from radiation effect with minimal adverse effects. Salvage surgery is recommended for large lesions especially with surrounding edema either in eloquent or non-eloquent areas.

Patient characteristics

	No. (%)
Patients	48
Median overall survival from surgery (months)	20.2
Median age at surgery (years)	63.5
Median time from STI to surgery (months)	12
Gender	
Male	32 (66.7)
Female	16 (33.3)
Primary cancer	
Lung	31 (64.6)
Breast	9 (18.8)
Others	8 (16.6)

	No. (%)
Lesions	54
Location	
Supratentrial	47 (87)
Infratentrial	7 (13)
Neurological deficit	
Yes	36 (67)
No	18 (33)
RPA classification at surgery	
Class1	7 (13)
Class2	18 (33)
Class3	29 (53)
Radiotherapy before salvage surgery	
STI	46 (85)
SRS	24 (44.5)
SRT	17 (31.5)
Repeated STI	5 (9)
WBRT+STI	8 (15)
Surgical method	
Minimum resection	26 (48)
with radiotherapy	12 (22)
without radiotherapy	14 (26)
Resection with free margine	28 (52)
Pathological diagnosis	
Tumor recurrence + Necrosis	47 (87)
Radiation necrosis alone	7 (13)
Extent of resection	
Gross total removal	48 (89)
Subtotal removal	6 (11)
Radiotherapy after salvage surgery	
Yes	20 (37)
WBRT	10 (18.5)
STI	10 (18.5)
No	34 (63)

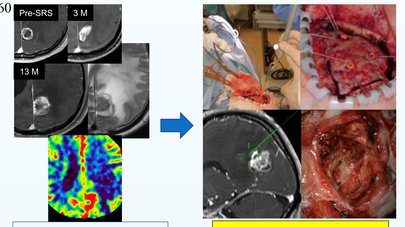
Results

Representative case

■ 67yo/M, Renal cell carcinoma (clear cell), Brain metastases 【2cm】

◆ After SRS (21Gy) 13M→ PD 【3cm】
✓ Rt. hemiparesis 4/5
✓ Extra CNS disease: good control
✓ KPS 60

✓ KPS 80
✓ Rapid improvement

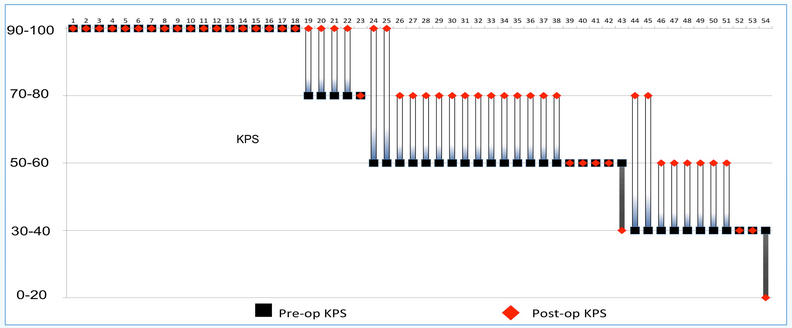


Perfusion study: rCBV↑ = Tumor Recurrence

Navigation guided fence post methods

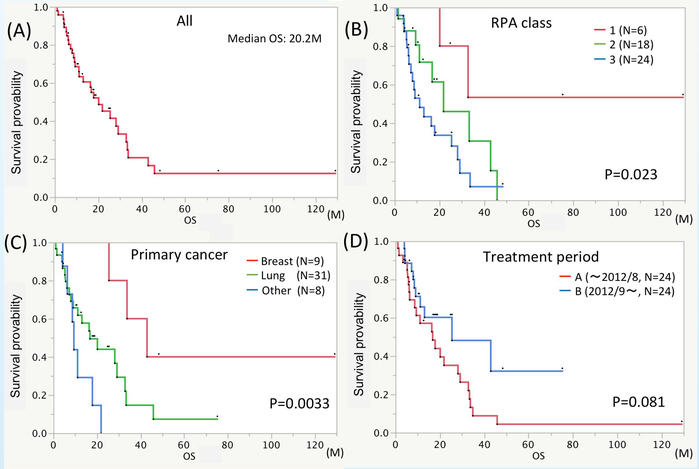
Unclear tumor margin: gliosis, viable tumor and necrosis

Improvement of KPS: pre- and post-surgery



Changes of KPS in individual cases. Among 36 cases having lower KPS due to neurological deficits before surgery, 27 (75%) cases showed improved KPS, seven (19.4%) showed no change, and two (5.6%) deteriorated.
＊analysis for each surgical cases (54 cases)

Overall survival from salvage surgery



Median OS was 20.2 months from salvage surgery (a). RPA classes (b) and primary cancer histology (c) showed a significant correlation with OS on univariate analysis. Patients showed a trend towards longer survival in recent years (d).
＊analysis for each patients (48patients; six patients with two surgical cases was analyzed from first surgery)

Surgical indications

1. MR and /or clinical evidence of lesion progression
2. Systemic disease: stable
3. Surgically resectable

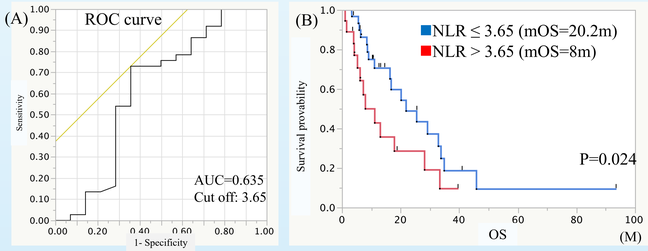
Surgical technique and outcome

＊Fisher's exact test

	All lesions	Minimum resection +/- SRT	Resection with free margin	P value
Number of lesions	54	26	28	
Local recurrence	13 /54 (24%)	9 /26 (34.6%)	4 /28 (14.3%)	0.07
Leptomeningeal Dissemination	3 /54 (5.6%)	3 /26 (11.5%)	0 /28 (0%)	0.105

＊analysis for each surgical lesions (54 lesions)

Neutrophil-lymphocyte ratio before salvage surgery and overall survival



NLR was evaluated by Receiver Operating Characteristic curves, showing a maximum area under the curve of 0.635 (a). Kaplan-Meier survival curves of patients with low preoperative NLR (≤ 3.65) were compared with those with a high NLR (> 3.65). The median OS was significantly longer in patients with a low NLR (25.5 months) than those with a high NLR (8 months) (b). ＊analysis for each patients (48 patients)

Univariate analysis of patient and treatment factors for survival

		Univariate	
Tested Variable	Number (%)	median OS (M)	P value
Age at surgery (median; 63.5)			
< 63-years	21 (43.8)	29.2	0.4
≥ 63-years	27 (56.2)	16.8	
Median time from STI to surgery (12mo)			
≥ 12 months	22 (45.8)	32.9	0.13
< 12 months	26 (54.2)	13.1	
Pathological diagnosis			
Radiation necrosis alone	6 (12.5)	22.8	0.76
Tumor recurrence + Necrosis	42 (87.5)	20.2	
Gender			
Female	16 (33.3)	29	0.11
Male	32 (66.7)	16.8	
Location			
Supratentrial	42 (87.5)	25.5	0.016
Infratentrial	6 (12.5)	9.1	
Primary cancer			
Breast	9 (18.8)	43	0.0033
Lung	31 (64.6)	16.8	
Others	8 (16.6)	9.4	
Neurological deficit			
No	15 (31.3)	21.9	0.56
Yes	33 (68.7)	16.8	
RPA			
Class 1	6 (12.5)	NR	0.023
Class 2	18 (37.5)	21.9	
Class 3	24 (50)	11.2	
Surgical technique			
Minimum resection	23 (48)	25.5	0.7
Resection with free margine	25 (52)	17.9	
Extent of resection			
Subtotal removal	6 (12.5)	28.2	0.98
Gross total removal	42 (87.5)	20.2	
Radiotherapy after salvage surgery			
Yes	15 (31.3)	20.2	0.38
No	33 (68.7)	16.8	

＊NR; not reached

Multivariate Cox regression model for OS

	HR	95% CI	P value
Supra- vs Infratentrial	0.54	0.19-1.79	0.3
Breast vs Lung	0.15	0.019-0.73	0.017
Breast vs Others	0.06	0.006-0.45	0.006
Lung vs Others	0.54	0.22-1.48	0.22
RPA Class 1 vs 3	0.1	0.014-0.47	0.002
RPA Class 2 vs 3	0.28	0.08-0.76	0.011
RPA Class 1 vs 2	0.38	0.04-2.31	0.31

I have no COI with regard to our presentation.