



# Local tumor progression as risk factor for postoperative seizures in patients with brain metastasis

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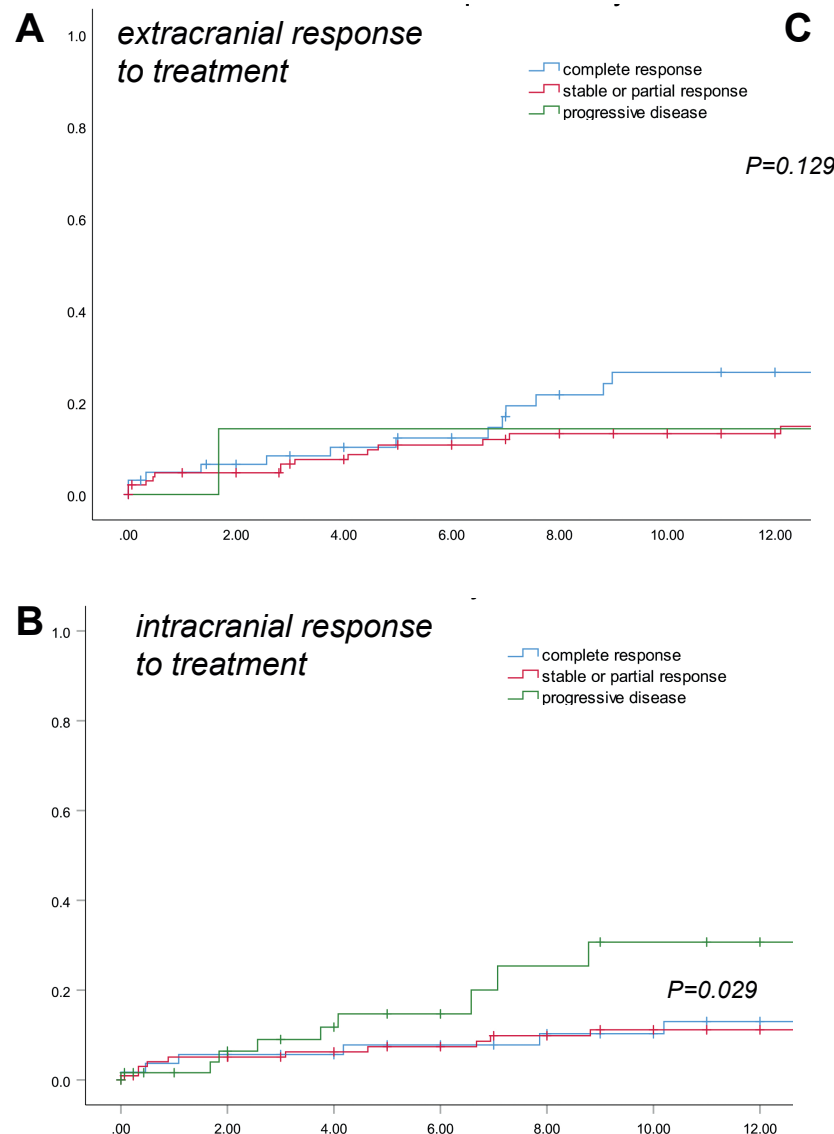
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## Background

Brain tumor-related epilepsy (BTRE) occurs in 20-35% of patients with brain metastases (BM) (1-3) and influences morbidity, mortality as well as quality of life (2). Several factors associated with seizure risk have been identified, including incomplete resection and supratentorial localization of BM (2,3). In primary brain tumors like lower grade glioma, tumor growth is associated with seizures (4). However, it remains to be elucidated whether this holds also true for patients with BM. Here we assess.....

	All patients (n=305)	No seizures (n=254, 83.3%)	Seizures (n=51, 16.7%)
<b>Sex, m/f</b>	151/154	130/124	21/30
<b>Age, median (range)</b>	60.5 (20.5-90.1)	60.9 (20.5-90.1)	58.4 (26.6-84.9)
<b>Number of BM, median (range)</b>	2 (1-64)	2 (1-64)	1 (1-20)
<b>KPS, median (range)</b>	80 (20-100)	80 (30-100)	80 (20-100)
<b>Primary tumor, n (%)</b>			
unknown	19 (6.2)	16 (84.2)	3 (15.8)
lung cancer	114 (37.4)	95 (83.3)	19 (16.7)
melanoma	58 (19.0)	49 (84.5)	9 (15.5)
breast cancer	42 (13.8)	36 (85.7)	6 (14.3)
renal cell cancer	11 (3.6)	10 (90.9)	1 (9.1)
gastrointestinal	30 (9.8)	25 (83.3)	5 (16.7)
other	31 (10.2)	23 (74.2)	8 (25.8)
<b>Localiation of BM, n (%)</b>			
infratentorial	42 (25.5)	40 (95.2)	2 (4.8)
supratentorial	123 (74.5)	98 (79.7)	25 (20.3)
Multiple BM		132	
Incomplete file		8	
<b>Extent of resection</b>			
biopsy	2 (0.8)	1 (50.0)	1 (50.0)
partial resection	161 (65.2)	125 (77.6)	36 (22.4)
total resection	84 (34.0)	77 (91.7)	7 (8.3)
no post-op MRI		58	
<b>Treatment after first BM resection, n (%)</b>			
Chemotherapy	167 (54.9)	142 (85.0)	25 (15.0)
No Chemo	137 (45.1)	111 (81.0)	26 (19.0)
Incomplete file		1	
Radiotherapy	268 (91.2)	219 (81.7)	49 (18.3)
No Radiotherapy	26 (8.8)	25 (96.2)	1 (3.8)
Incomplete file		11	

**Table 1.** Patient characteristics stratified for absence versus presence of BTRE. The first column depicts characteristics item, with main items in bold letters and sub-characters in normal letters. The second column shows absolute values for all patients as indicated and percentages in brackets. The third and fourth columns show the fraction of patients without and with seizures as indicated above.



**Figure 1:** Seizure risk and tumor progression. A-C. The Kaplan-Meier curve shows time-dependent seizure rates for different subgroups, in (A) dependent on extracranial and in (B) on intracranial response. In (C), seizure rates are shown for patients with local (green line), distant (orange), stable disease (red line) and unknown pattern of progression (blue line). The log-rank test was used for statistical evaluation, p values are provided in italic letters. Legends indicate different types of progression according to color code, with the y-axis marking percentage of patients with onset of post-operative seizures and the x-axis time in months.

Candidate factor	p=	Hazard Ratio	95% CI	
			Lower	Upper
<b>Supratentorial localization</b>	0.043	4.5	1.1	19.3
<b>Incomplete resection</b>	0.018	3.7	1.4	10.9
<b>Intracranial progression</b>	0.038	1.4	1.4	5.8
<b>Extracranial progression</b>	0.729	0.9	0.4	1.7

**Table 1:** Multivariate testing of candidate risk factors for postoperative seizures are shown. A Cox Hazards model was employed. First column: candidate factor, second column two-sided p-values, third to fifth column Hazard Ratios following 95% CI. Supratentorial BM, incomplete resection and intra- but noch extracranial progression show an independent association with postoperative seizures.

## Conclusion and outlook

- intra- but not extracranial tumor progression is associated with postoperative seizures in BM patients
- patients with local progression of BM are more prone to seizures than those with new, distant BM lesions
- Patients with local tumor recurrence are patients at high risk and might be candidates for primary prophylaxis with antiepileptic drugs

## References

- (1) van Breemen et al., Lancet Neurol. 2007 May;6(5):421-30.
- (2) Wolpert et al., Neuro Oncol. 2020 May 15;22(5):718-728.
- (3) Wu et al., World Neurosurg. 2017 Aug;104:120-128.
- (4) Avila et al., Neuro Oncol. 2017 Jan;19(1):12-21.