



Non Small Cell Lung Cancer Molecular Alterations Impact on Brain Metastases Response to Gamma Knife Radiosurgery : Identification of Potential Radiosensitive Tumor Phenotypes

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Background

Scare and inconclusive data of radiosensitivity of Non Small Cell Lung Cancer (NSCLC) brain metastases (BM)

Molecular determinants of NSCLC radiosensitivity are largely unknown due to limitations current of in vitro and clinical models

Analysis of a prospective patient cohort of NSCLC patients harboring BMs treated by Gamma Knife radiosurgery and investigated whether the primary tumor molecular phenotype had an actual impact on BM radiosensitivity

Material and Methods

- **263 patients (January 2010 to April 2013)**
 => molecular profile available in 90 patients with BM
- **Anomalies screening in tumors :**
 - **EGFR mutation**
 - **KRAS mutation**
 - **PI3KCA mutation**
 - **ALK translocation**
 - **EML4 translocation**
 - **HER2 mutation**
 - **BRAF mutation**
- **Response evaluation => Radiological monitoring using multimodal MRI-scans**
 (undertaken every 3 months after radiosurgery)
- **Correlate molecular profile and other patient-, tumor-, treatment-related data to intracranial radiological control.**

Results

Patient and treatment characteristics

Characteristic	EGFR mutant	ALK translocation	KRAS mutant	Others*	All	<i>p</i>
Median followup (months)	5.8	5.0	6.2	7.8	5.9	
Age (yrs)						
≤ 60	8 (50%)	3 (100%)	12 (48%)	2 (50%)	25 (52.1%)	0.45
> 60	8 (50%)	0 (0%)	13 (52%)	2 (50%)	23 (47.9%)	
Sex						
Female	12 (75%)	3 (100%)	10 (40%)	2 (50%)	27 (56.3%)	0.05
Male	4 (25%)	0 (0%)	15 (60%)	2 (50%)	21 (43.7%)	
Number of lesions treated						
Median	2	3	1	2	2	0.69
Range	1-3	1-8	1-12	1-4	1-12	
Lesion diameter (mm)						
Median	9.7	16.3	13.1	11.5	12.6	0.13
SD	4.7	5.5	6.1	1.9	4.5	
Dose prescribed (Gy)						
Median	22	22	22	23	22	0.59
Range	18-24	20-24	18-24	22-24	18-24	
Previous radiotherapy	4 (57%)	1 (14%)	2 (29%)	0 (0%)	7 (15%)	0.22
Previous craniotomy	4 (33%)	1 (8.3%)	6 (50%)	1 (8.3%)	16 (25%)	0.48

* *BRAF, PI3KCA and HER2 mutations*

Results

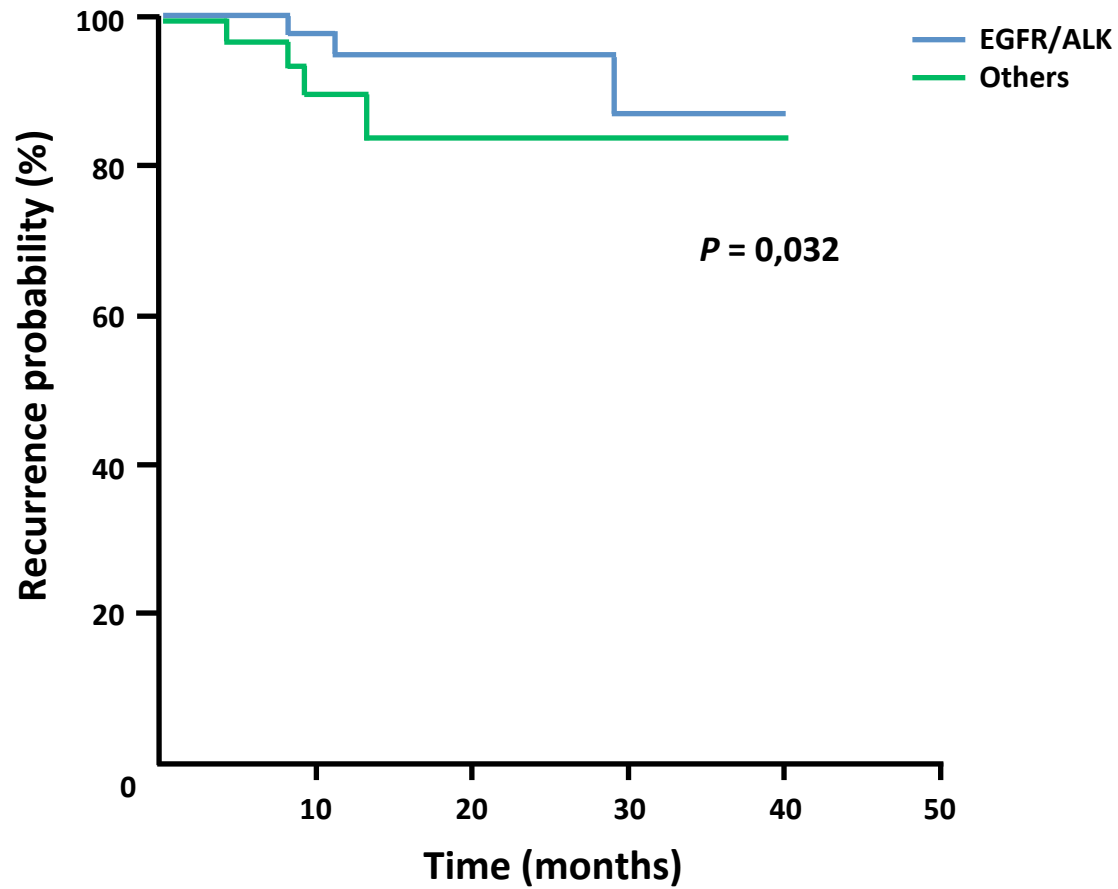
Absolute recurrence rates by molecular subtype and EGFR/ALK tumors versus others tumors

	EGFR mutated	ALK translocated	KRAS mutated	Others*	No Mutation	All
Per Patient						
In situ progression	0/16 (0%)	0/3 (0%)	1/25 (4%)	2/4 (50%)	4/42 (9,5%)	7/90 (4,4%)
Distant progression	8/16 (50%)	3/3 (100%)	16/25 (64%)	3/4 (75%)	21/42 (50%)	51/90 (56,6%)
Per Lesion	0/26 (0%)	0/11 (0%)	1/52 (1,9%)	2/7 (28,5%)	4/77 (5,1%)	7/173 (4%)
In situ progression						
	EGFR/ALK	Others**	P			
Per Patient						
In situ progression	0/19 (0%)	7/71 (9,8%)	0,0158			
Distant progression	11/19 (57,9%)	40/71 (56,3%)				
Per Lesion	0/37 (0%)	7/136 (5,1%)				
In situ progression						

* BRAF, PI3KCA and Her2 mutations ; ** KRAS, BRAF, PI3KCA , Her2 mutations and no mutations

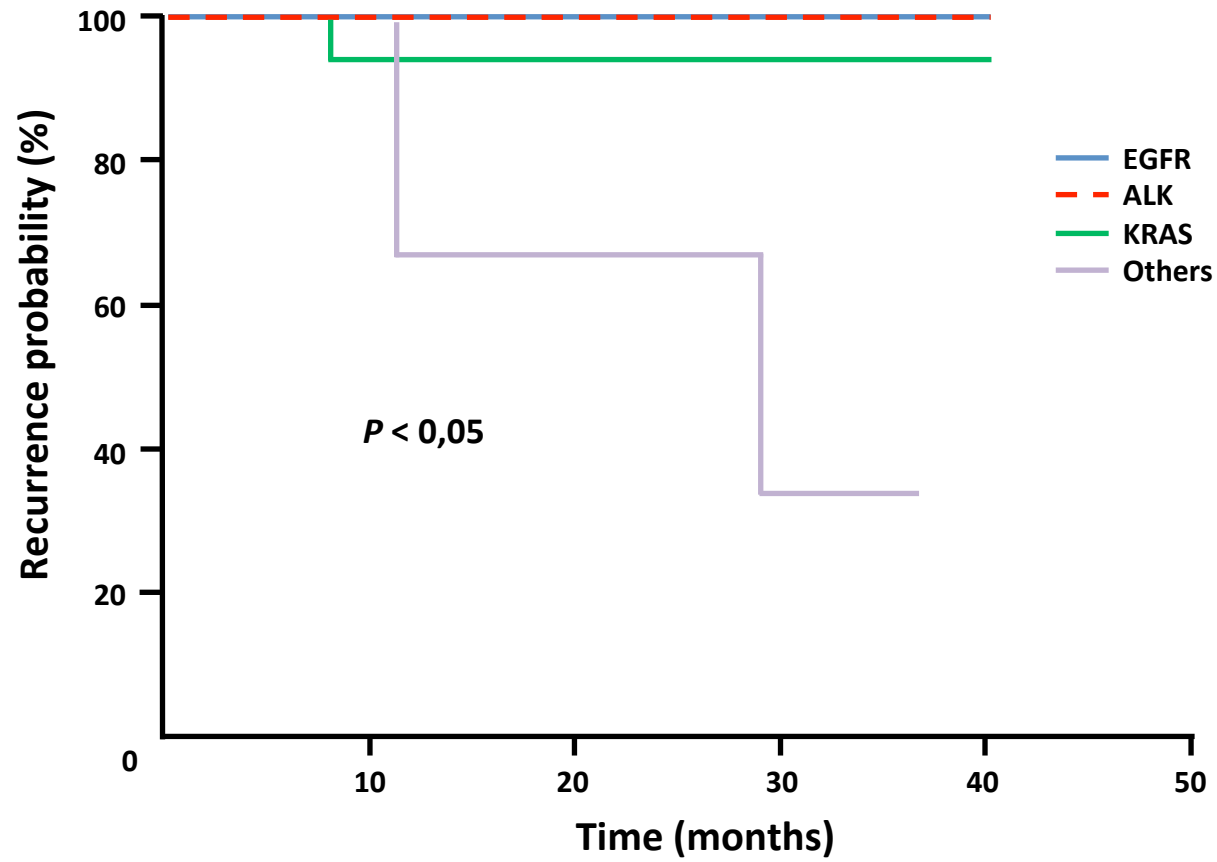
Results

In situ progression-free survival curve



Results

In situ progression-free survival curve



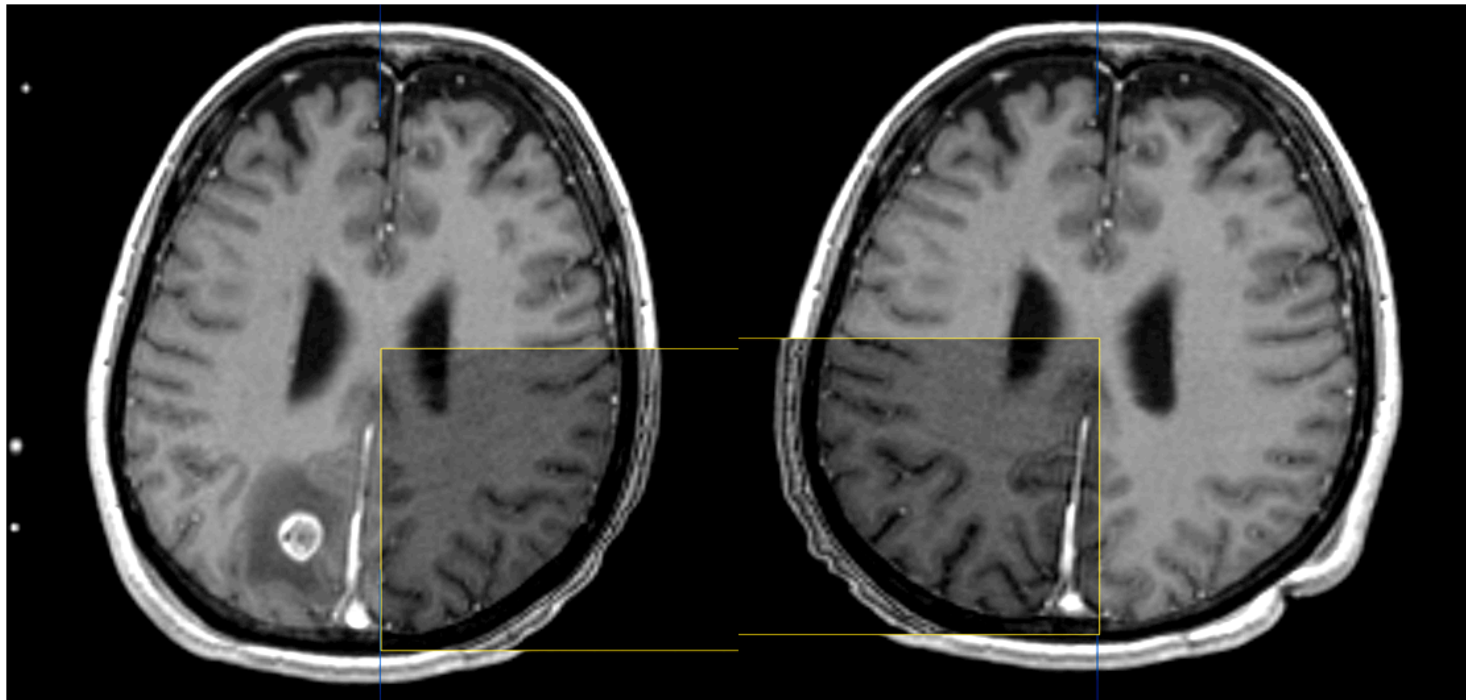
Results

Radiological monitoring : T1 post contrast MRI-scans

EGFR-mutant tumor

Pre - SRS

Post - SRS



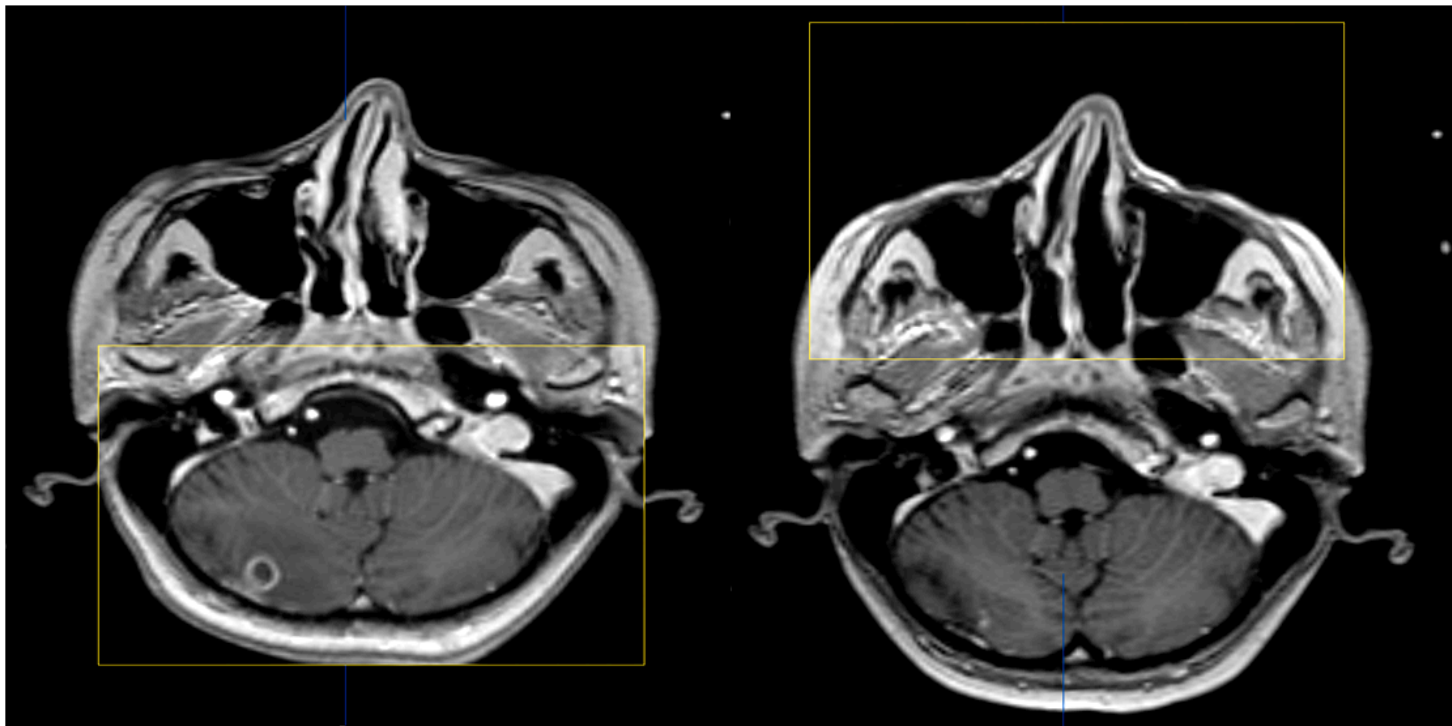
Results

Radiological monitoring : T1 post contrastMRI-scans

ALK-tranlocated tumor

Pre - SRS

Post - SRS



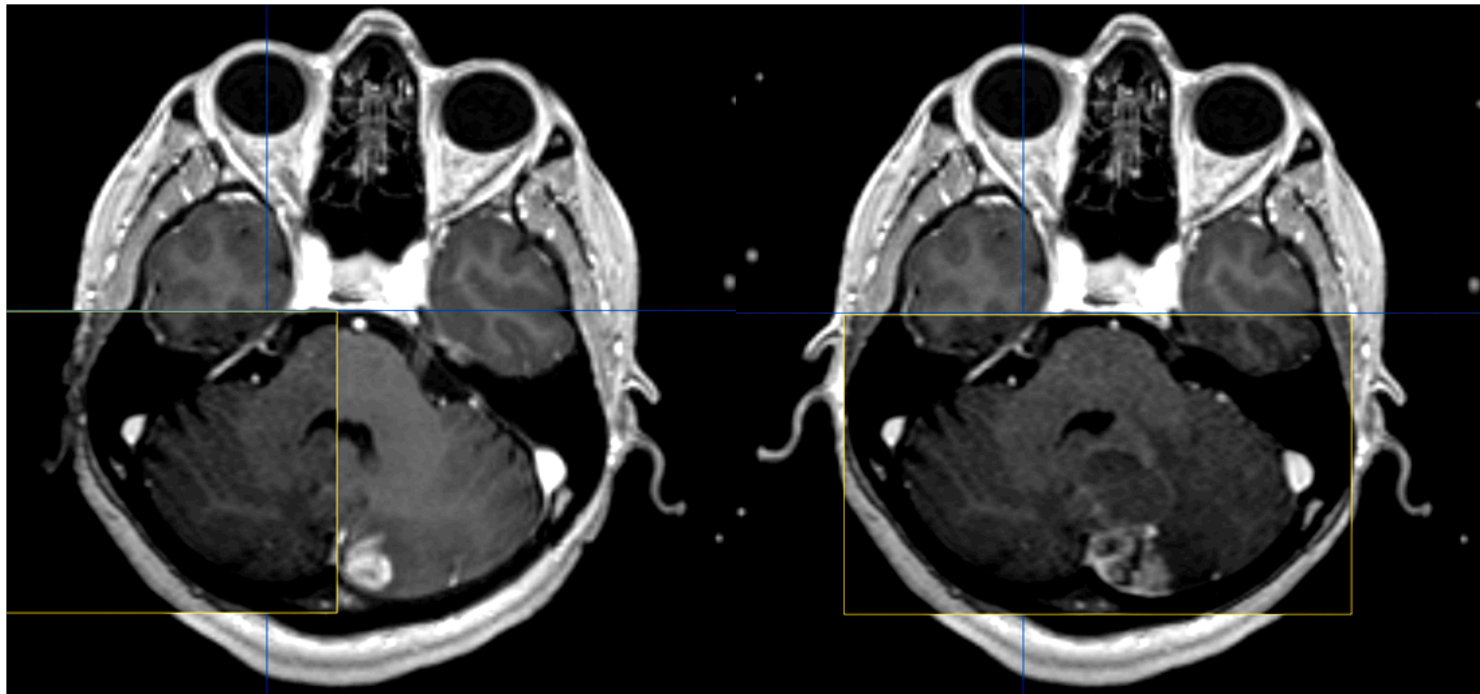
Results

Radiological monitoring : T1 contrast-enhanced MRI images

Progression in patient without mutation

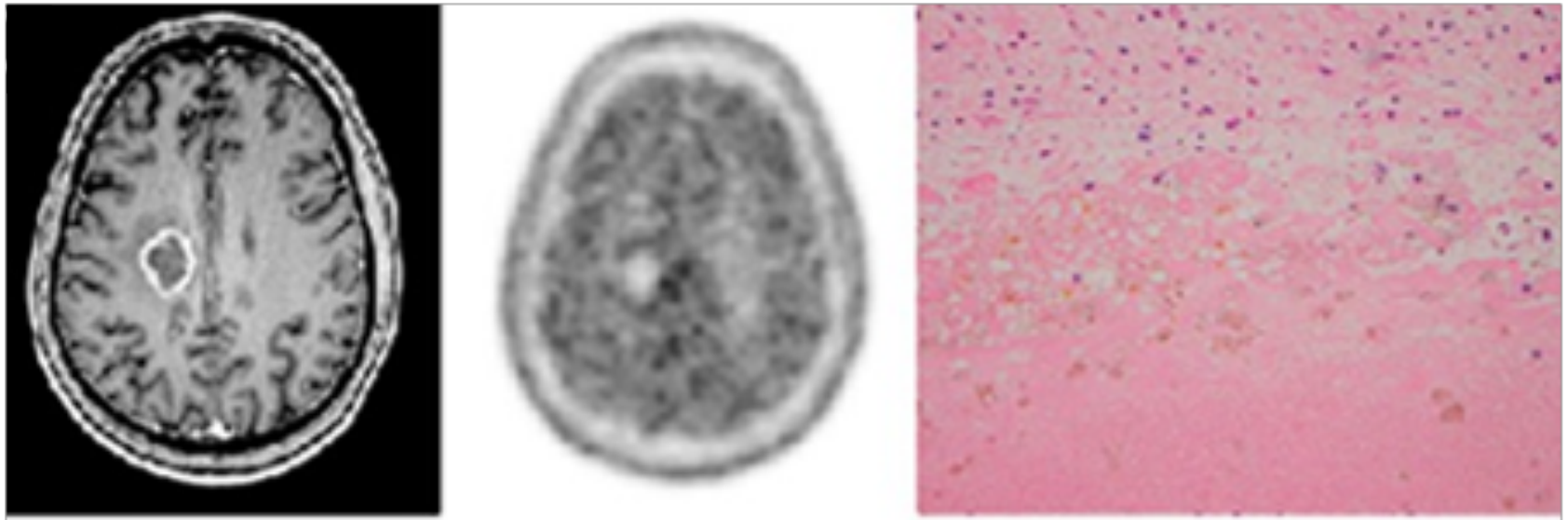
Pre - SRS

Post - SRS



Results

Radiological monitoring of a suspected progression in KRAS mutated patient
On T1 contrast-enhanced MRI images



Suspected progression

Negative F-DOPA PET
L/S 0,63

Histology
Inflammatory cells
Necrosis

Conclusion

EGFR mutation and ALK translocation are independent prognostic factors regarding local control after Gamma Knife radiosurgery in NSCLC patients with BM

Molecular profile of NSCLC patient might be taken into account in treatment decision strategy

Actual need to improve radiological assessment of progression after radiosurgery

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