

# First Report of Staged Adaptive Frameless Stereotactic Radiosurgery in 3 “Pulses” to Salvage Brain Metastases that Failed Prior Radiosurgery



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**OBJECTIVE**

- To report outcomes of novel 3-fraction staged stereotactic radiosurgery (St-SRS) regimen aimed at salvaging previously irradiated brain metastases which are at a high risk of radiation necrosis.

**MATERIALS AND METHODS**

- 50 patients with 89 lesions previously treated with SRS, received 3 fraction St-SRS re-irradiation course (8Gy, 8Gy, 4Gy every 2 weeks).
- Prior to each fraction, all patients had adaptive re-planning with a new planning MRI.
- The primary endpoint was the rate of radiation necrosis (RN). Secondary end points were local failure (LF) and overall survival (OS).

**RESULTS**

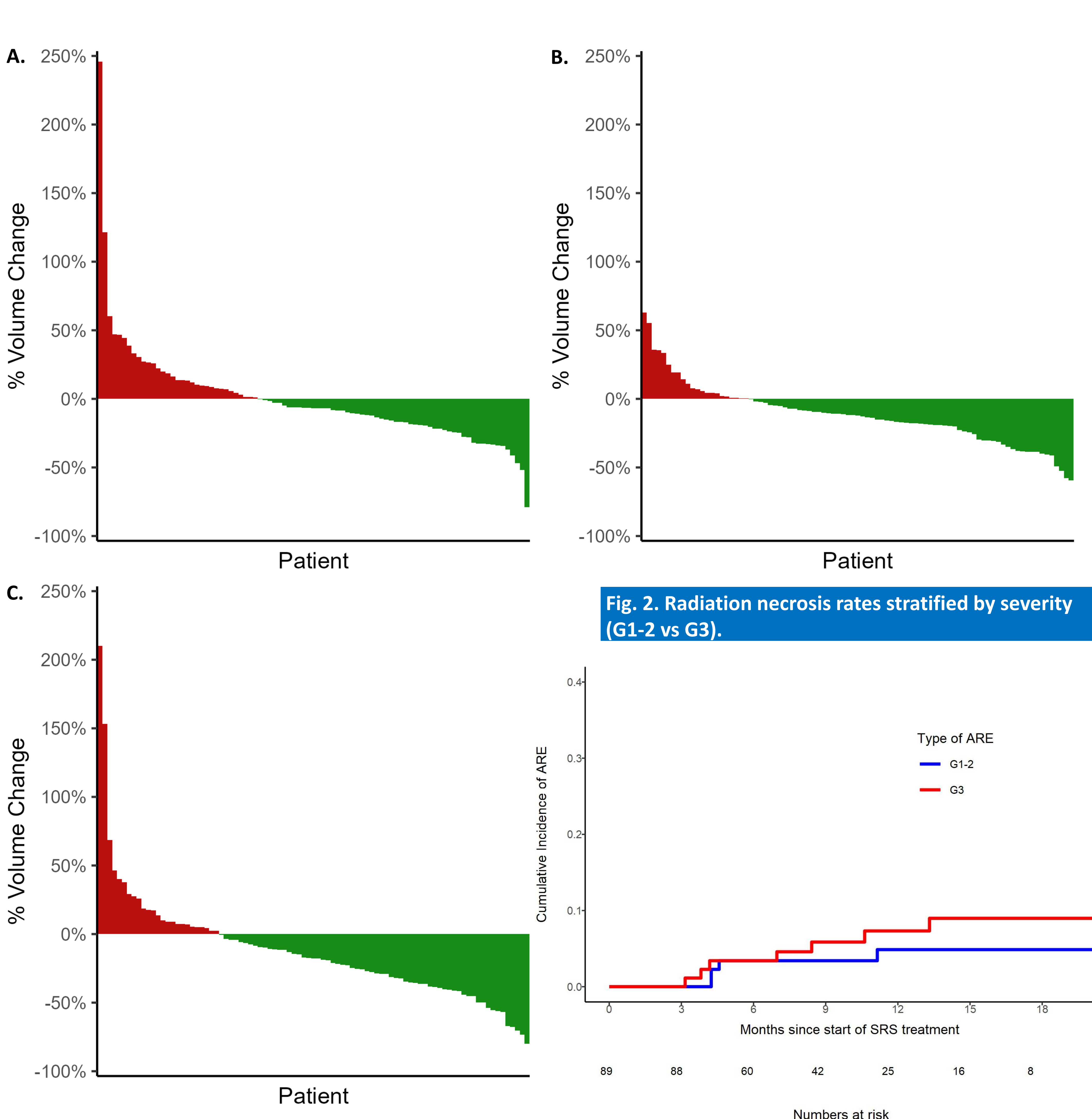
- Median follow-up: 9.6 months (range: 2.6-43.9) (Table 1).
- 34.8% had primary breast cancer and 41.6% lung ca.
- 22.5% had radioresistant primaries.
- Reduction in target volume was observed in 63% and 75% of all treated lesions between fractions 1 to 2 and 2 to 3 (Figure 1).
- Radiation necrosis rates at 6, 12 and 18 months were 6.8%, 12.4% and 13.8%. At 1 year, 4.5% RN events were Grade 1 or 2, and 7.9% were Grade 3 (Figure 2).
- LF and OS rates at 6, 12 and 18 months were 16.1%, 28%, 30.8%, and 81.6%, 60.4%, 42.3% (Figure 3).
- Multivariable analysis:
  - i) Predictive for RN: Maximum dose within the target lesion as a weighted average (HR=1.14 per additional Gy, p=0.048).
  - ii) Predictive for OS: KPS ≤70 (HR 14.7, p<0.001) and more lesions treated (HR 1.38 per additional lesion, p=0.006).

**Table 1. Patient, tumor and dosimetric characteristics**

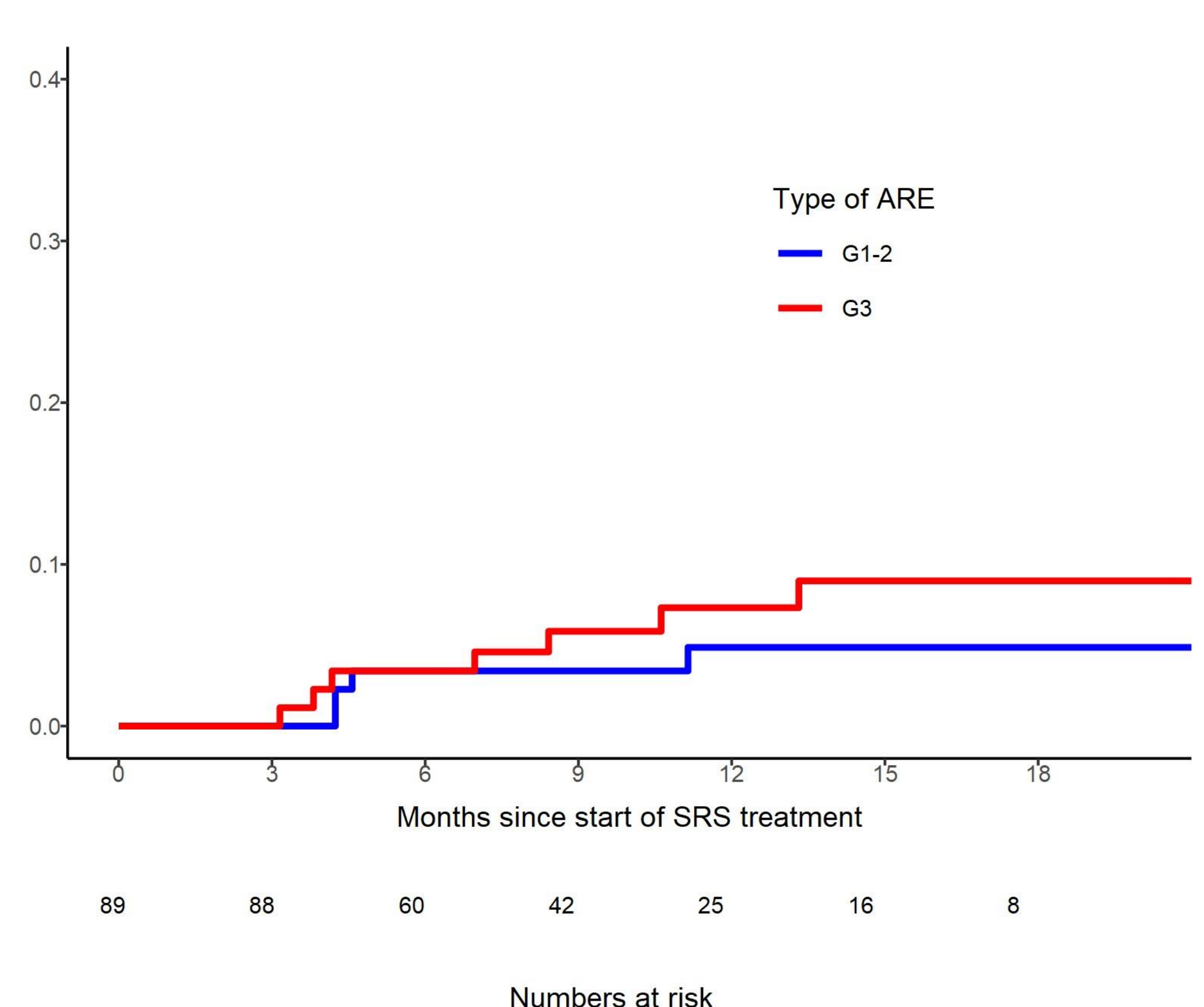
Patient factors, per patient (N=50)	Value
Age (years) Median (range)	61.6 (32.2, 84.0)
Gender	
Female	31 (62%)
KPS	
≤70	4 (8%)
>=90	26 (52%)
Median number of active brain metastases at baseline (range)	1.5 (1.0, 23.0)
Median number of Brain Metastases Treated During Staged course (range)	1 (1-8)
Extracranial disease	
Yes and controlled	12 (24%)
Yes and not controlled	6 (12%)
Oligometastatic Disease	28 (56%)
Concomitant CNS-active drugs	9 (18%)
<b>Tumor factors, per lesion (N=89)</b>	
Primary Site	
Breast	31 (34.8%)
Colorectal	2 (2.2%)
Lung	37 (41.6%)
Melanoma	8 (9%)
Renal	5 (5.6%)
Histology	
Radiosensitive	69 (77.5%)
Radioresistant*	20 (22.5%)
Location of target lesion	
Brainstem	4 (4.5%)
Infratentorium	26 (29.2%)
Supratentorium	59 (66.3%)
Previous surgery at target site	8 (9%)
Previous SRS	
Single fraction	48 (53.9%)
Multi fraction	41 (46.1%)
Prior WBRT	30 (33.7%)
<b>Dosimetry, per lesion (N=89), Median (Range)</b>	
Weighted average mean dose to target (EQD2)	15.4 (2.4, 44.7)
Weighted average max dose to target (EQD2)	23.4 (3.4, 78.5)
% coverage of target	100 (100, 100)
Paddic conformity index	0.8 (0.0, 0.9)

\*Radioresistant= gastrointestinal, melanoma, renal cell, sarcoma or thyroid cancer

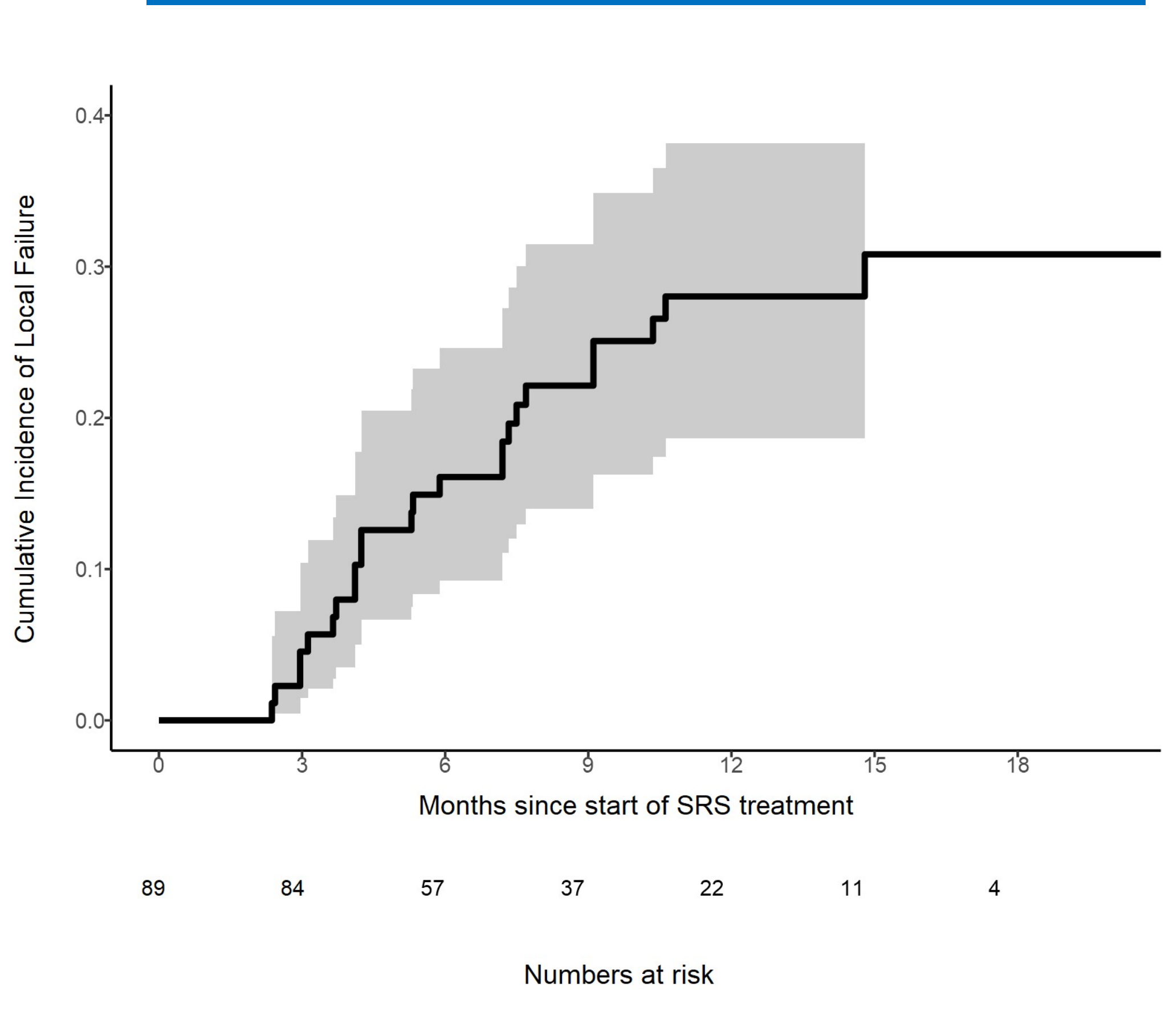
**Fig 1. Waterfall plots of relative volume change of lesions over the course of treatment**  
A) from fraction 1 to 2, B) from fraction 2 to 3, C) from fraction 1 to 3.



**Fig 2. Radiation necrosis rates stratified by severity (G1-2 vs G3).**



**Fig 3. Local failure in the overall cohort.**



**CONCLUSION**

- St-SRS is an effective and well-tolerated adaptive treatment for re-irradiation of brain metastases with a favorable RN profile.
- Modified regimen of 8Gy/8Gy/6Gy is being investigated for radioresistant tumours to further optimize the therapeutic ratio.
- Lengthening the interval between staged fractions may improve inter-fractional response further, while allowing concomitant CNS-active drugs to be given.

