



**UNIKLINIK  
KÖLN**

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Neurosurgery**

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# Hypofractionated Stereotactic Radiosurgery as Salvage Treatment of Brain Metastases

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# Objectives: SRS in brain metastasis

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- SRS is part of standard care in brain metastasis
- Limitations of single-fraction SRS:
  - large volume of lesions (e.g. diameter > 3 cm)
  - close proximity to critical structures (i.e. pontine)

# Objectives: Hypofractionation

Fractionated Radiotherapy


Single fraction radiosurgery

preservation by  
fractionation

preservation by  
conformal target  
definition

**Hypofractionated radiosurgery (hSRS)**

# Objectives: Current studies



Clinical Oncology  
journal homepage: [www.clinicaloncologyonline.net](http://www.clinicaloncologyonline.net)

Original Article

Fractionated Stereotactic Radiotherapy using CyberKnife for the Treatment of Large Brain Metastases

T. Murai<sup>\*†</sup>, H. Ogino<sup>‡</sup>, Y. Manabe<sup>\*</sup>, M. H. Suzuki<sup>§</sup>, Y. Shibamoto<sup>\*</sup>

J Neurooncol (2012) 106:601–610  
DOI 10.1007/s11060-011-0697-z

Inoue et al. *Radiation Oncology* 2014, 9:231  
<http://www.ro-journal.com/content/9/1/231>



**RESEARCH** Open Access

## Optimal hypofractionated conformal radiotherapy for large brain metastases in patients with high risk factors: a single-institutional prospective study

Hiroshi K Inoue<sup>1,2\*</sup>, Hiro Sato<sup>1</sup>, Yoshiyuki Suzuki<sup>3</sup>, Jun-ichi Saitoh<sup>4</sup>, Shin-ei Noda<sup>4</sup>, Ken-ichi Seto<sup>1</sup>, Kota Torikai<sup>5</sup>, Hideyuki Sakurai<sup>6</sup> and Takashi Nakano<sup>4</sup>

## Cyberknife hypofractionated stereotactic radiosurgery (HSRS) of resection cavity after excision of large cerebral metastasis: efficacy and safety of an 800 cGy × 3 daily fractions regimen

Lesueur et al. *Radiation Oncology* (2018) 13:138  
<https://doi.org/10.1186/s13014-018-1083-1>

Radiation Oncology

**RESEARCH**

Open Access

## Radiosurgery or hypofractionated stereotactic radiotherapy for brain metastases from radioresistant primaries (melanoma and renal cancer)

Paul Lesueur<sup>1,2,7\*</sup>, Justine Lequesne<sup>3</sup>, Victor Barraux<sup>4</sup>, William Kao<sup>1</sup>, Julien Geffrelot<sup>1</sup>, Jean-Michel Grellard<sup>3</sup>, Jean-Louis Habrand<sup>1,7</sup>, Evelyne Emery<sup>5,7</sup>, Brigitte Marie<sup>6</sup>, Juliette Thariat<sup>1,7</sup> and Dinu Stefan<sup>1</sup>

*Journal of Radiation Research*, 2017, pp. 1–6  
doi: 10.1093/jrr/rrx042  
Regular Paper

Journal of  
Radiation  
Research

OXFORD

## Investigation of the efficacy and safety of CyberKnife hypofractionated stereotactic radiotherapy for brainstem metastases using a new evaluation criterion: ‘symptomatic control’

Masaki Nakamura<sup>1,\*</sup>, Hideki Nishimura<sup>1</sup>, Hiroshi Mayahara<sup>1</sup>, Haruka Uezono<sup>1</sup>, Aya Harada<sup>1</sup>, Naoki Hashimoto<sup>1</sup>, Yasuo Ejima<sup>2</sup>, Takeaki Ishihara<sup>2</sup>,

# Objectives: Summary of current studies

Authors	n (patients/ tumors)	median Tumor Volume (cm <sup>3</sup> )	Radiation schedule	median Follow-up (mo)	6 mos LC %	6 mos OS %	median OS (mo)
<b>Lesueur et al, 2018</b>	35/106	4.2	27-33Gy/3 fr. IDL: 80%	7.4	83	69	9.6
<b>Nakamura et al., 2017</b>	20 / 26	0.3	18–30 Gy / 3-5 fr. IDL 70–80%	6.5	100	72	17
<b>Murai et al., 2014</b>	54 / 61	≥ 8 - < 33 ≥ 33	18-30Gy / 3 fract. 21-35Gy / 5 fract.	-	77	52	6
<b>Inoue et al., 2014</b>	88 / 92	10 – 74.6 (median 16.2)	25-40Gy / 3-10 fr. IDL 57-55%	7	90.2	62	9
<b>Wang et al., 2012</b>	37 / 37	11.07–81.04 (mean 28.84±16)	8 Gy x 3 fr. IDL 74–91%	5.5	80	-	5.5

# Methods: Cologne protocol for hSRS of brain metastasis

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- **Dose prescription:** 27 Gy / 3 fractions / 65% isodose
- **PTV = CTV** (GTV + 1-2 mm)
- **Follow-up interval:** MRI every 3 months
- **Local control failure:**
  - RANO Brain Metastases Criteria (2015)
  - Contrast Enhancement  $\geq 30\%$
  - preferably proven by FET-PET / biopsy

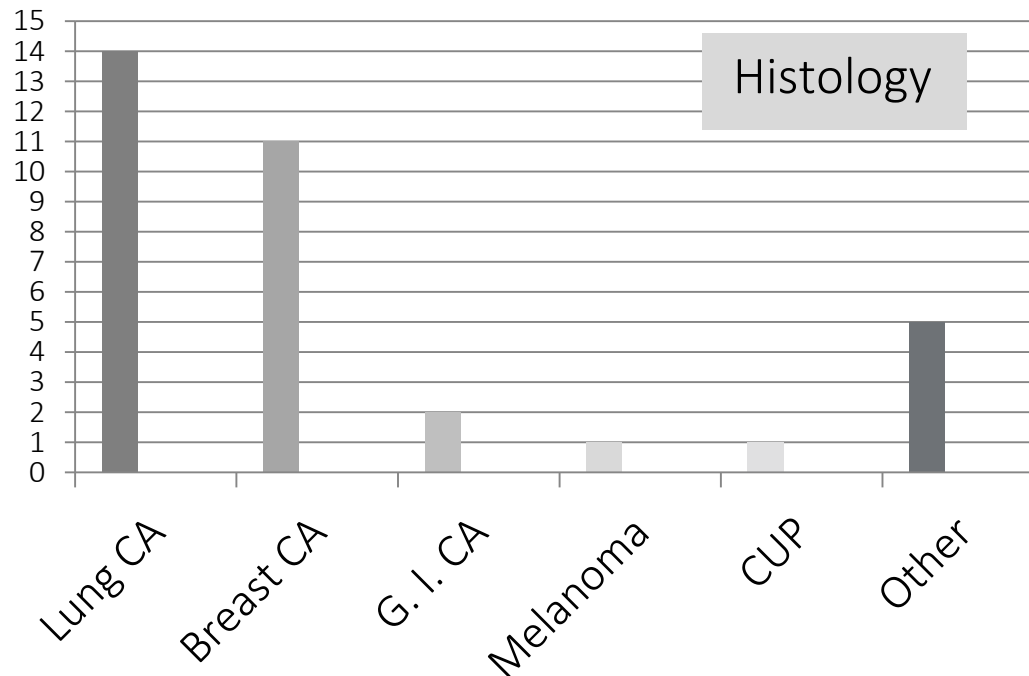
# Results: Patient characteristics

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■ total no. of treated patients	<b>34</b>
■ 1 brain metastasis	16
■ 2 brain metastases	6
■ 3 brain metastases	5
■ 4 brain metastases	3
■ 5 brain metastases	4
■ gender (m : f)	<b>13 : 21</b>
■ median age (range, years)	<b>55.5 (35 – 84)</b>
■ median follow-up (range, months)	<b>8.0 (3 – 28)</b>

# Results: Tumor characteristics

- total no. of tumors **75**
- median tumor vol. (range, cm<sup>3</sup>) **4.6 (0.03 - 24.8)**
- median diameter (range, cm) **2.0 (0.4 – 4.3)**





# Results: Indications for hSRS of brain metastasis

Indications	n (patients)	%
Brain metastases ( $\geq 3$ cm)	18	53
Eloquent localization (close to critical structures)	14	41
Shortening irradiation after surgery	1	2.9
Multiple lesion with confluent isodose	1	2.9
	<b>34</b>	<b>100</b>

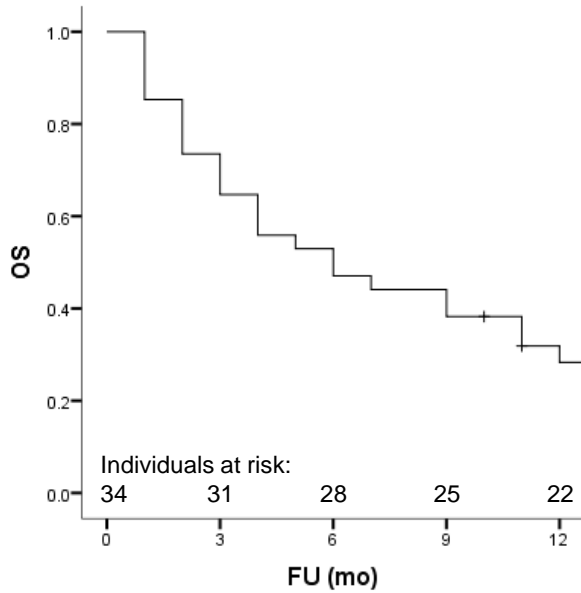
# Results: hSRS as salvage treatment

- hSRS as salvage treatment in 29.5% (n=10)

Pre-treatment modality	n (lesions)	%	n (patients)	%
Progressiv & new lesions after WBRT	24	32	8	23.5
Recurrence after SRS	1	1.3	1	3
Recurrence after 125-Iodine Seed Brachytherapy	1	1.3	1	3
	<b>26</b>	<b>34.6</b>	<b>10</b>	<b>29.5</b>

# Results: Kaplan-Meier analysis

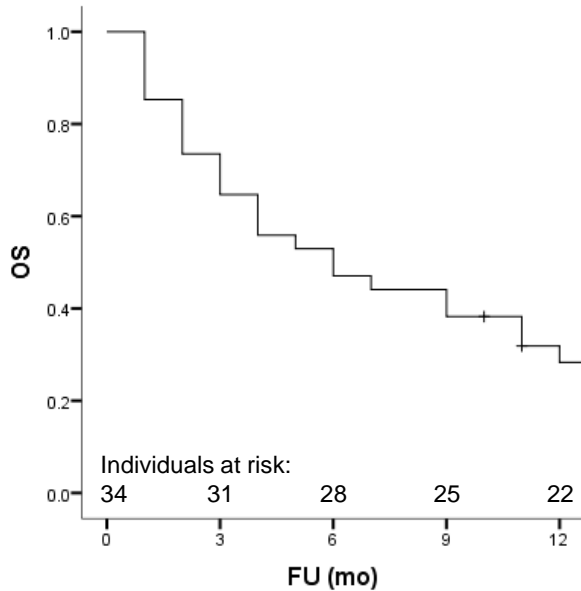
Overall survival (OS):



- 3 mo = 64%
- 6 mo = 43%
- 12 mo = 28%

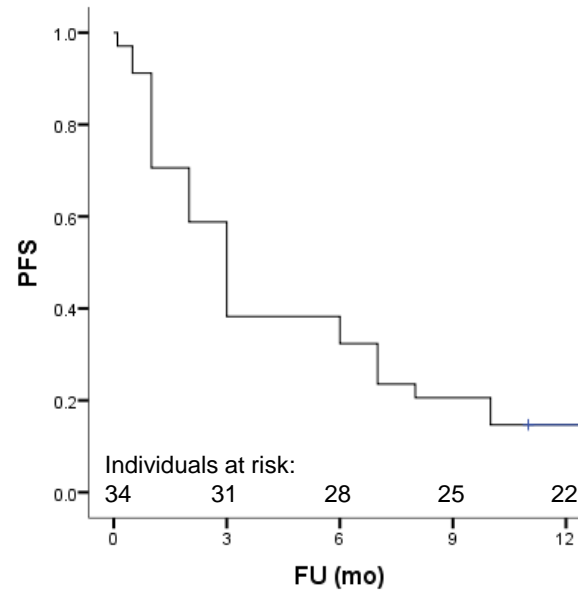
# Results: Kaplan-Meier analysis

Overall survival (OS):



- 3 mo = 64%
- 6 mo = 43%
- 12 mo = 28%

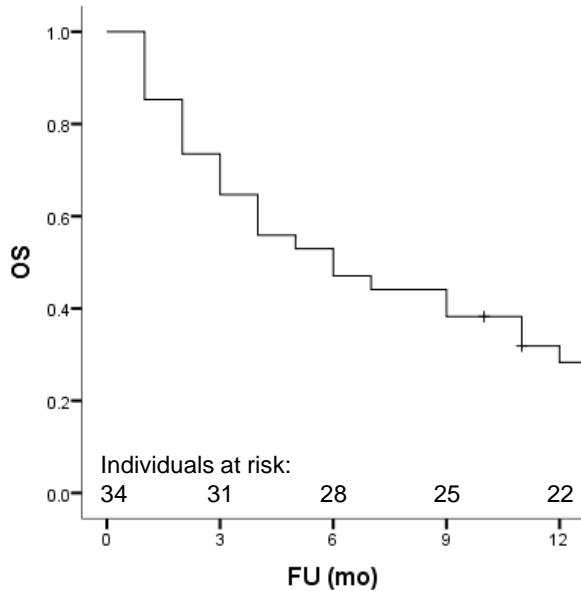
Progression free survival (PFS):



- 3 mo = 36%
- 6 mo = 28%
- 12 mo = 17%

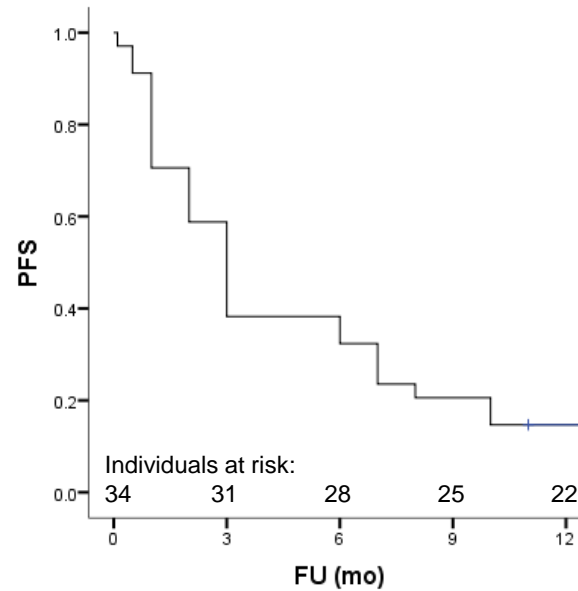
# Results: Kaplan-Meier analysis

Overall survival (OS):



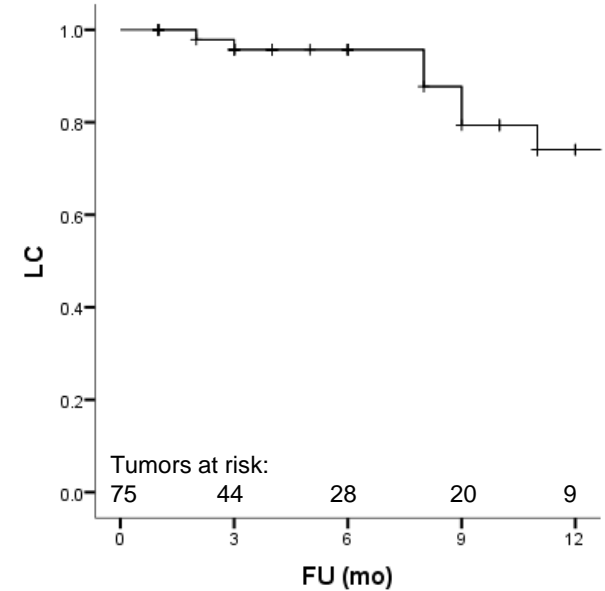
- 3 mo = 64%
- 6 mo = 43%
- 12 mo = 28%

Progression free survival (PFS):



- 3 mo = 36%
- 6 mo = 28%
- 12 mo = 17%

Local control rate (LC):



- 3 mo = 93%
- 6 mo = 84%
- 12 mo = 75%

# Results: Complications

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- Radiogenic edema (CTCAE Grade 1-3) **3/34 (9%)**
- Expansion of tumor cyst / stereotactic puncture (CTCAE Grade 3) **3/34 (9%)**

# Results: Comparison with literature

Authors	n (patients/ tumors)	median Tumor Volume (cm <sup>3</sup> )	Radiation Schedule	median Follow-up (mo)	LC 6 mo (%)	median OS (mo)
Cologne hSRS data 2014-2017	34/75	4.6	27Gy/3 fr. IDL: 65%	7.4	84	6
Cited studies 2012-2018	234 / 322	12.3 (0.3 – 81.0)	18–40 Gy / 3-10 fr. IDL: 55–91%	6.6 (5.5-7.4)	86 (77-100)	9.4 (5.5-17)

# Conclusion

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- reasonable results for local tumor control
- promising salvage treatment option for brain metastasis:
  - with large volumes
  - in eloquent areas
  - after irradiation





Thank you for  
your attention!