

Title Page

Title: Safety and Efficacy of Hypofractionated Stereotactic Radiosurgery for High-grade Gliomas at First Recurrence: A Single-Center Experience

Running Title: CyberKnife for Recurrent High-grade Gliomas

Authors: Yun Guan^{1234*} MD, Ji Xiong⁵ MD, Mingyuan Pan^{1234*} M.S., Wenyin Shi⁶ PhD, Jing Li¹²³⁴ MD, Huaguang Zhu¹²³⁴ MD, Xiu Gong¹²³⁴ MD, Chao Li¹²³⁴ MD, Guanghai Mei¹²³⁴ MD, Xiaoxia Liu¹²³⁴ MD, Li Pan¹²³⁴ MD, Jiazhong Dai¹²³⁴ MD, Yang Wang¹²³⁴ MD, Enmin Wang^{1234&} MD, Xin Wang^{1234&} MD

1 CyberKnife Center, Department of Neurosurgery, Huashan Hospital, Fudan University, 12 Wulumuqi Road (M), Shanghai, 200040, China.

2 Neurosurgical Institute of Fudan University, 12 Wulumuqi Road (M), Shanghai, 200040, China.

3 Shanghai Clinical Medical Center of Neurosurgery, 12 Wulumuqi Road (M), Shanghai, 200040, China.

4 Shanghai Key Laboratory of Brain Function and Restoration and Neural Regeneration, 12 Wulumuqi Road (M), Shanghai, 200040, China.

5 Department of pathology, Huashan Hospital, Fudan University, 12 Wulumuqi Road (M), Shanghai, 200040, China.

6 Department of Radiation Oncology, Thomas Jefferson University, Philadelphia, PA,
USA.

&Corresponding author:

Xin Wang, MD

E-mail: wangxinck@fudan.edu.cn

Tel: +86-13120557273

Address: CyberKnife Center, Department of Neurosurgery, Huashan Hospital, Fudan
University, 12 Wulumuqi Road (M), Shanghai, 200040, China.

Enmin Wang, MD

E-mail: emwang@fudan.edu.cn

Tel: +86-13671727320

Address: CyberKnife Center, Department of Neurosurgery, Huashan Hospital, Fudan
University, 12 Wulumuqi Road (M), Shanghai, 200040, China.

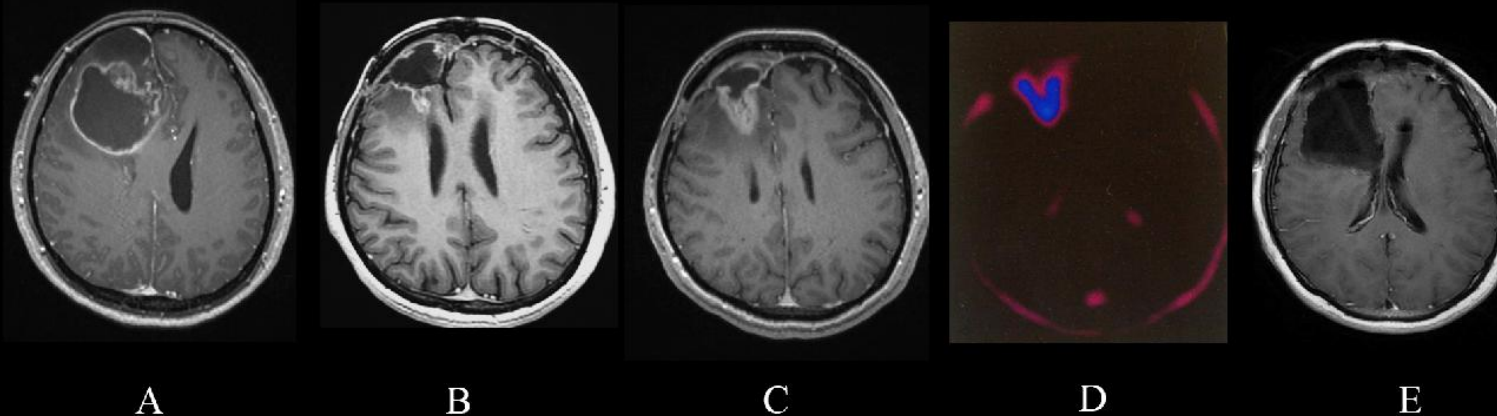
Additional file 1. Treatment of progression after CyberKnife radiosurgery

Treatment	No. of Patients	Percentage %
Surgery	2	3
Radiotherapy		
IMRT*	1	1
CyberKnife	13	19
TTF†	2	3
Systemic therapy		
Anti-PD-1	3*	4
Anlotinib	2	3
Bevacizumab	1	1
Temozolomide	1	1
BSC‡	46	65

Abbreviations: IMRT = Intensity-modulated radiation therapy ; TTF = Tumor Treatment Field; BSC = Best Supportive Care.

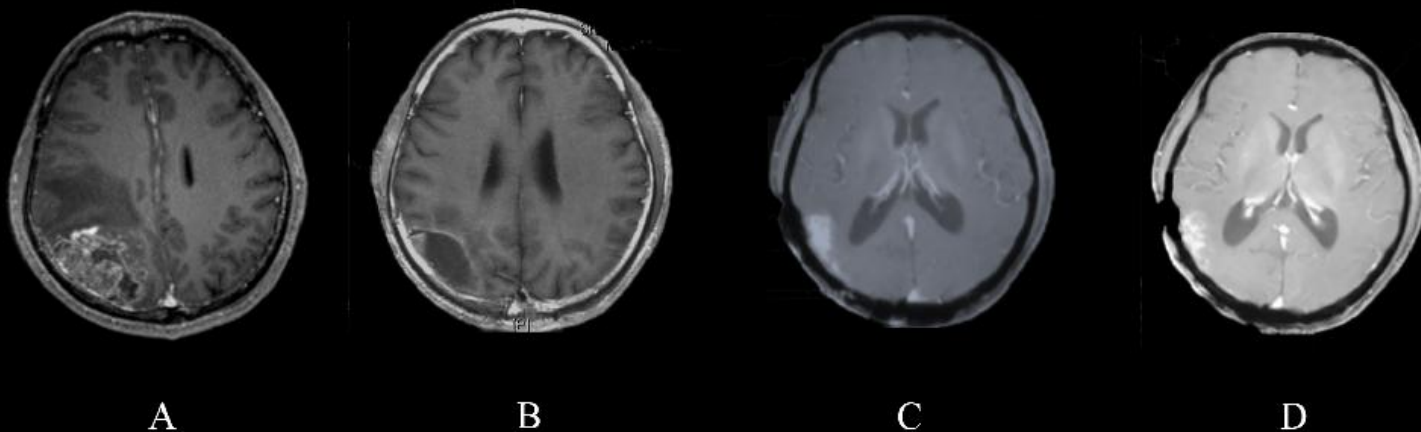
* One patient had CyberKnife with anti-PD-1 treatment.

Additional file 2. The dilemma of diagnosis of the LR and RN



Case 1.

- A. Forty-year-old female, presented with headache and dizziness. Histological-proven glioblastoma, MGMT (-), IDH1(+), 1p19q (-).
- B. RANO criteria diagnosed recurrence. Seventeen months after surgery and adjuvant chemoradiation IMRT 56Gy/28fx and temozolomide.
- C, D. Recurrence diagnosed by RANO criteria and 11C-methionine PET. Six months after CyberKnife 20Gy/5fx with concurrent bevacizumab.
- E. Histological-proven radiation necrosis after gross total resection.



Case 2.

- A. Fifty-eight years old male. Histological-proven glioblastoma, MGMT (-), IDH1(-), 1p19q (-), TERT (+).
- B. Treated with surgery and adjuvant chemoradiation IMRT 60Gy/30fx plus temozolomide and TTF. Four months after initial diagnosis.
- C. Twelve months after surgery, RANO criteria diagnosed recurrence.
- D. Three months follow-up after CyberKnife 25Gy/5fx with concurrent bevacizumab.

