REPORTS OF PRACTICAL ONCOLOGY AND RADIOTHERAPY 23 (2018) 215–219

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://www.elsevier.com/locate/rpor

Original research article

^{11}C-methionine positron emission tomography for target delineation of recurrent glioblastoma in re-irradiation planning

Hidekazu Tanaka[a,*], *Takahiro Yamaguchi*[a], *Kae Hachiya*[a], *Kazuhiro Miwa*[b], *Jun Shinoda*[b], *Masahide Hayashi*[c], *Shinichi Ogawa*[c], *Hironori Nishibori*[d], *Satoshi Goshima*[a], *Masayuki Matsuo*[a]

[a] *Department of Radiology, Gifu University Graduate School of Medicine, Yanagido 1-1, Gifu 501-1194, Japan*
[b] *Department of Neurosurgery, Chubu Medical Centre for Prolonged Traumatic Brain Dysfunction, Shimokobi 630, Kobicho, Minokamo 505-8503, Japan*
[c] *Department of Radiation Oncology, Kizawa Memorial Hospital, Shimokobi 590, Kobicho, Minokamo 505-8503, Japan*
[d] *Department of Radiology, Kizawa Memorial Hospital, Shimokobi 590, Kobicho, Minokamo 505-8503, Japan*

ARTICLE INFO

Article history:
Received 31 May 2017
Received in revised form
18 October 2017
Accepted 8 April 2018
Available online 25 April 2018

Keywords:
Glioblastoma
Radiation therapy
Magnetic resonance imaging
^{11}C methionine positron emission tomography

ABSTRACT

Aim: To define the optimal margin on MRI scans in the re-radiation planning of recurrent glioblastoma using methionine positron emission tomography (MET-PET).

Background: It would be very useful if the optimal margin on MRI to cover the uptake area on MET-PET is known.

Materials and Methods: CT, MRI, and MET-PET were performed separately over the course of 2 weeks. Among the MRI scans, we used the contrast-enhanced T1-weighted images (Gd-MRI) and T2-weighted images (T2-MRI). The Gd-MRI-based clinical target volume (CTV) (CTV-Gd) and the T2-MRI-based CTV (CTV-T2) were defined as the contrast-enhanced area on Gd-MRI and the high intensity area on T2-MRI, respectively. We defined CTV x mm (x = 5, 10, 15, 20) as x mm outside the CTV. MET-PET-based CTV (CTV-MPET) was defined as the area of accumulation of MET-PET. We calculated the sensitivity and specificity of CTV-Gd and CTV-T2 following comparison with CTV-MPET, which served as the gold standard in this study.

Results: The sensitivity of CTV-T2 5 mm (98%) was significantly higher than CTV-T2 (87%), and there was no significant difference in the sensitivity between CTV-T2 5 mm and CTV T2 10, 15, or 20 mm. The sensitivity of CTV-Gd 20 mm (97%) was lower than that of CTV-T2 5 mm (98%).

Conclusions: A margin of at least 5 mm around the high intensity area on T2-MRI is necessary in the target volume delineation of recurrent glioblastoma for the coverage of MET-PET findings in re-radiation therapy planning.

* *Corresponding author.*
E-mail address: htanaka-gif@umin.ac.jp (H. Tanaka).

https://doi.org/10.1016/j.rpor.2018.04.003

1. Background

Glioma is one of the common primary brain tumors. Glioblastoma (GBM) is the most common among the gliomas. A landmark trial by Stupp et al. led to the acceptance that maximum safe surgical excision followed by adjuvant chemoradiotherapy and adjuvant chemotherapy is the best standard care protocol.[1] Despite multidisciplinary treatment, early failure of local treatment is a common feature of this disease.[2,3] The median survival time is limited to approximately 10–15 months for GBM.[1,4] Most episodes of relapse occur within 2–3 cm of the margin of the original lesion.[5,6] The usefulness of hypofractionated stereotactic radiotherapy (SRT) was reported for recurrent GBM.[7–9] SRT is often used to irradiate the gadolinium (Gd)-contrasted tumor edge on magnetic resonance imaging (MRI) for recurrent GBM. However, GBM often exists beyond the Gd-enhanced lesion because of its infiltrative character.[10–12] Several articles reported that ^{11}C methionine positron emission tomography (MET-PET) has greater accuracy than MRI in correctly outlining the true extent of gliomas.[13–16] Grosu et al. reported that patients who received SRT planned with a biological imaging technique, such as MET-PET, survived longer compared to patients who received SRT planned with MRI.[17] Iuchi et al. reported that MET-PET could not only visualize the tumor extent but also predict the required irradiation dose to control tumors.[18] Moreover, Yoo et al. reported that usefulness of MET-PET as a prognostic factor for progression-free survival.[19] However, the number of institutes where MET-PET is available is limited.

2. Aim

It would be very useful if the optimal margin to add the target delineated on MRI to cover the uptake area on MET-PET is known. The purpose of this study was to investigate the recognition of the tumor extent and to define the optimal margin on MRI scans in the re-irradiation planning of recurrent GBM using MET-PET.

3. Materials and methods

3.1. *Patients*

A total of 25 patients participated in this study. All patients received an initial treatment consisting of surgery, adjuvant chemoradiotherapy, and adjuvant chemotherapy (temozolomide). The patient characteristics are shown in Table 1. This study was conducted with the approval of our institutional review board. Written informed consent was obtained from each patient before radiotherapy.

Table 1 – Patient characteristics.

		N (%)
Age (years)	≥50	14 (56)
	<50	11 (44)
Sex	Male	18 (72)
	Female	7 (28)
KPS	≥70	20 (80)
	<70	5 (20)

KPS: Karnofsky performance status.

3.2. *Images*

Computed tomography (CT), MRI and MET-PET were separately performed within a 2-week period. CT was performed using helical equipment (Light Speed; General Electric, Waukesha, WI). The head was immobilized in a commercially available stereotactic mask while acquiring CT images. The scan was performed with 2.5-mm slice-thickness, scanned without gaps.

MRI for radiation treatment planning was performed using a 1.5-T scanner (Genesis Signa; General Electric, Waukesha, WI). Images were acquired using a standard head coil without rigid immobilization. Axial, three-dimensional gradient echo T1-weighted native and after contrast administration (Gd-diethylenetriaminepentaacetic acid [Gd-DTPA; Magnevist, Schering, Berlin, Germany], 0.1 mmol/kg body weight) at 2.0-mm slice thickness were acquired from the foremen magnum to the vertex. The T2-weighted (2600/102 [effective]) images were acquired with a 512 × 224 matrix and a 24-cm field of view with a 6-mm slice thickness. We used contrast-enhanced T1-weighted images (Gd-MRI) and T2-weighted images (T2-MRI) for target delineation.

Patients fasted for at least 4 h before MET-PET to ensure standardized metabolic conditions. They were advised to have only a light breakfast on the morning of the examination day. The PET scanner used was an Advance NXi imaging system (General Electric Yokogawa Medical System, Hino-shi, Tokyo, Japan), which provides 35 axial images at 4.25 intervals. The crystal width is 4.0 mm (transaxial). The in-plane spatial resolution (full width at half-maximum) was 4.8 mm, and the standard 2-dimensional scan mode was used. Before the emission scans were performed, a 3-min transmission scan was performed to correct the photon attenuation, using a ring source containing 68 Ge. A dose of 7.0 MBq/kg ^{11}C methionine was injected intravenously, depending on the examination. Emission scans were acquired for 30 min, beginning 5 min after injection of ^{11}C methionine. During MET-PET data acquisition, the patient's head position was continuously monitored using laser beams projected onto ink markers drawn over the forehead skin, and the head position was corrected as necessary.

3.3. *Target delineation*

These images sets (CT/MRI and CT/MET-PET) were then fused utilizing the Pinnacle system. The MET-PET and MRI scans were analyzed separately in each patient. The target volumes were defined by three observers, including a neurosurgeon (JS), radiation oncologist (MM) and nuclear medicine specialist (HN). The Gd-MRI-based clinical target volume (CTV) (CTV-Gd) and the T2-MRI-based CTV (CTV-T2) were defined as the contrast-enhanced area on the Gd-MRI and high intensity area on the T2-MRI, respectively. We defined CTV *x* mm ($x = 5$, 10, 15, 20) as *x* mm outside the CTV. MET-PET-based CTV