Usefulness of Intraoperative Computed Tomography in Surgery for Low-Grade Gliomas: a Comparative Study Between Two Series Without and With Intraoperative Computed Tomography

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Abstract

We have routinely used an intraoperative CT (i-CT) system in over 800 neurosurgical procedures since 1997. To investigate the utility of i-CT in low-grade glioma (LGG) surgery, we investigated whether i-CT improved the extent of tumor resection and prognosis in 46 patients with histologically confirmed LGG consisting of 27 patients with World Health Organization grade II astrocytoma, 12 with oligodendroglioma, and 7 with oligoastrocytoma. The patients were divided into two groups, 23 who underwent tumor resection without i-CT (non i-CT group) and 23 who underwent surgery using i-CT (i-CT group). We investigated the extent of tumor resection, pre- and postoperative Karnofsky performance status scores, and overall survival in each group. The extent of tumor resection was biopsy 26.1%, partial resection 60.9%, subtotal resection 13.0%, and gross total resection 0% in the non i-CT group, and 4.4%, 21.7%, 34.8%, and 39.1%, respectively, in the i-CT group. The i-CT group showed significantly longer overall survival than the non i-CT group among patients with astrocytoma (p < 0.05) and oligodendroglioma or oligoastrocytoma (p < 0.005). Prolonged survival was related to the extent of resection. There were no significant differences between pre- and postoperative Karnofsky performance status scores between the groups. Surgical resection using i-CT may improve the outcomes of patients with LGG. Additional resection or emergency treatment can be quickly performed as the surgical results are confirmed intraoperatorically or immediately after the operation using i-CT.

Key words: intraoperative computed tomography, low-grade glioma, extent of resection, prognosis

Introduction

The management of patients with intracerebral glioma generally focuses on the selection of intraoperative treatment modalities such as awake surgery and electrophysiological monitoring, which prolong survival while minimizing the risk of complications and maintaining an adequate quality of life. Recent series have suggested a survival advantage in patients with gliomas that undergo more extensive surgery.1,6,8,11–13,15,17) However, the significance of the data from these retrospective investigations is limited due to the small number of patients, short follow-up time, and/or variations in patient profiles and histology.7,12) In addition, most of these studies did not evaluate the extent of surgery intra- or postoperatively with a standardized imaging method. Recently, 5-aminolevulinic acid fluorescence-guided resections were suggested to be useful for extensive resections and improved the outcome of patients with glioblastomas.10) However, low-grade gliomas (LGG) are difficult to discriminate from normal neural tissue using fluorescent imaging. Intraoperative imaging techniques may also be useful in the treatment of LGG such as ultrasonic imaging, magnetic resonance (MR) imaging, and computed tomography (CT).2,9,16) For the past quarter of a century, the treatment strategy for patients with LGG in our department has been extensive surgical resection if allowed by the location of the tumor. An intraoperative CT (i-CT) system with a sliding gantry on a railtrack was installed in our neurosurgical operating room.
in April 1997, and we have routinely used this system in neurosurgical procedures for over 800 patients. No adverse events have been encountered in connection with the use of i-CT. i-CT is considered to be helpful in skull base and spinal surgery because these procedures mainly involve osseous structures.\textsuperscript{10} However, the usefulness of i-CT is controversial especially in gliomas.

The present study examined the utility of i-CT in surgery for LGG, and investigated whether i-CT improved the extent of tumor resection and prognosis in patients with LGG.

**Patients and Methods**

The i-CT system consists of a high-speed helical CT scanner (X vision/SP; Toshiba Corp., Tokyo) and a specially designed neurosurgical operating table (MST-7200BXD; Mizuho Co., Ltd., Nagoya, Aichi). The CT gantry is fixed on a motorized carrier that is moved along a railtrack under the control of a digital operating system. The operating table, which can be tilted or rotated to obtain any neurosurgical operating position, can also be moved by the operating system to a pre-memorized position, based on preoperative CT scans taken to determine the desired surgical level before the operation. The initial CT scanning position is then memorized and so can be reestablished accurately for repeated i-CT scans. In our hospital, all staff move into an adjoining remote control room during CT scanning, where the CT scan workstation and patient physiological monitor are installed. The preparation and scanning between surgical procedures requires a maximum of 15 minutes. We have routinely used this system for neurosurgical procedures since April 1997. In this time, no patients have developed neurological complications or infections attributable to use of the i-CT system.

We performed a retrospective analysis of 46 patients with supratentorial LGG who were treated surgically and followed up at our department between April 1984 and March 2007. All patients who underwent biopsy or resection were histologically confirmed to have World Health Organization (WHO) grade II astrocytoma, oligodendroglioma, or oligoastrocytoma. These patients consisted of 27 with astrocytoma and 19 with oligodendroglial tumors (12 with oligodendroglioma and 7 with oligoastrocytoma), and were divided into two groups: the non i-CT group of 23 patients who underwent tumor resection without i-CT, 16 men and 7 women aged from 13 to 65 years (mean 39.5 years); and the i-CT group of 23 patients who underwent surgery using i-CT, 7 men and 16 women aged from 16 to 64 years (mean 42.0 years). The extent of tumor resection, pre- (on admission) and postoperative (on discharge) Karnofsky performance status (KPS) scores, and overall survival using the Kaplan-Meier method were investigated.

The extent of tumor resection was determined by pre- and postoperative (within the first 28 days after surgery) CT with contrast medium. For tumors without contrast enhancement, areas showing abnormal density on CT were segmented. For tumors with contrast enhancement, areas of contrast enhancement were also segmented. Volumetric assessment of the tumors was conducted using three-dimensional analysis with the Ziosation software (version 1.3.0.0; Ziosoft, Inc., Tokyo). The CT area corresponding to the tumor was manually segmented across all sections. Manual segmentation was performed by at least two neurosurgeons or neuroradiologists. The extent of tumor reduction was defined as follows: biopsy, less than 10%; partial resection (PR), from 10% or greater to less than 50%; subtotal resection (STR), from 50% or greater to less than 90%; and gross total resection (GTR), 90% or greater tumor resection.

Operative strategy of LGG remained the same during this study (from 1984 to 2007). The target was resection of areas showing abnormal density on CT. No navigation system was used in this study. Postoperative treatment strategy of LGG in our department also remained the same as follows: GTR, observation without radiotherapy or chemotherapy; biopsy, PR, and STR, radiotherapy (50–60 Gy) and combined chemotherapy with nimustine hydrochloride (ACNU), carboplatin, and etoposide.

Overall survival was defined as the time from diagnosis to death or the last follow-up examination. Survival curves were calculated by the Kaplan-Meier method and analyzed with the log-rank test. Statistical significance was defined as $p < 0.05$.

**Results**

Additional resection could be performed in 11 of the 23 patients (47.8%) in the i-CT group, as i-CT revealed residual tumors after the initial tumor resection (Table 1). The extent of tumor resection in all 46 patients with LGG was biopsy 6/23 (26.1%), PR 14 (60.9%), STR 3 (13.0%), and GTR 0 (0%) in the non i-CT group, and 1/23 (4.4%), 5 (21.7%), 8 (34.8%), and 9 (39.1%), respectively, in the i-CT group. Among all patients with LGG, the pre- and postoperative KPS scores were $81.4 \pm 24.4$, respectively, in the non i-CT group, with no significant difference compared to $89.5 \pm 11.7$ and $91.7 \pm 10.3$, respectively, in the

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Table 1 Clinical characteristics of the study population

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<tr>
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<th>Non i-CT group</th>
<th>i-CT group</th>
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<tr>
<td></td>
<td>Astrocytoma</td>
<td>Oligodendroglial tumors</td>
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<tr>
<td>Age (yrs)</td>
<td>38.5 ± 19.9</td>
<td>41.5 ± 12.0</td>
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<tr>
<td>Sex (male:female)</td>
<td>11:4</td>
<td>5:3</td>
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<tr>
<td>Extent of resection</td>
<td>biopsy (&lt;10%)</td>
<td>6 (26.1%)</td>
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<tr>
<td></td>
<td>PR (&lt;50%)</td>
<td>14 (60.9%)</td>
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<tr>
<td></td>
<td>STR (&lt;90%)</td>
<td>3 (13.0%)</td>
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<tr>
<td></td>
<td>GTR (≥90%)</td>
<td>0</td>
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<td></td>
<td>Additional resection</td>
<td>0</td>
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<tr>
<td></td>
<td>KPS score</td>
<td>preoperative</td>
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<tr>
<td></td>
<td>on discharge</td>
<td>78.6 ± 24.4</td>
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<td>Five-year survival rate</td>
<td>5 (33.3%)</td>
<td>8 (100%)</td>
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i-CT group. There were no significant differences in the pre- and postoperative KPS scores between the i-CT group and the non i-CT group among patients with astrocytoma or oligodendroglial tumors.

Kaplan-Meier survival curves revealed that the i-CT group showed significantly longer overall survival than the non i-CT group among all patients with LGG (p < 0.005), astrocytoma (p < 0.05), and oligodendroglial tumors (p < 0.005) (Fig. 1). Among all patients with LGG, the 5-year survival rates were 13/23 (56.5%) in the non i-CT group and 20/23 (87.0%) in the i-CT group (p < 0.0001).

The patients treated with GTR were all alive at the end of this study. The patients who underwent STR showed significantly longer overall survival than those who underwent PR (p < 0.005) or biopsy (p < 0.005) (Fig. 2). Histologically, the overall survival of the patients with astrocytoma was significantly shorter than that of the patients with oligodendroglial tumors (p < 0.001).

Illustrative Case

A 64-year-old man with a right insular protoplasmic astrocytoma without contrast enhancement on preoperative CT (Fig. 3A) underwent tumor resection with i-CT. After the first resection attempt, i-CT revealed residual tumor (Fig. 3B). Further resection of the residual tumor was performed, and second i-CT demonstrated residual tumor in the medial posterior region (Fig. 3C). Thereafter, additional resection was performed with cortical motor evoked electrical stimulation, and the operation was terminated.

Discussion

The recent trend toward more aggressive surgery is supported by recent evidence suggesting that more radical surgery increases the accuracy of diagnosis. In two cases of our study, the histological diagnosis of the specimens obtained by biopsy was diffuse astrocytoma (WHO grade 2), but the patients died within 3 months after surgery due to the aggressive growth of the tumors. These tumors may have originally been malignant or malignant transformation may have occurred following biopsy. In addition, the radicality of tumor removal in patients with glioma is considered to be an important factor for longer survival. However, no randomized trials have analyzed the extent of surgical resection and the outcomes in patients with LGG. The utility of i-CT in the resection of gliomas has previously been reported. The use of i-CT leads to the extension of resection as a means of improving the quality of tumor resection and survival.

An i-CT system with a mobile CT gantry mounted on a railtrack is available and can be used in all operative positions such as the prone or park bench position. The advantages of i-CT are as follows: No adverse events were encountered when using the i-CT; The extent of tumor removal can be evaluated during tumor resection, when the surgical field remains open, and additional resection can be quickly resumed in less than 15 minutes; Surgical complications such as intracranial hematomas and hy-
Fig. 1 Kaplan-Meier survival curves of the patients who underwent tumor resection with and without intraoperative computed tomography (i-CT). A: 46 patients with low-grade gliomas (total), B: 27 patients with astrocytoma, C: 19 patients with oligodendrogial tumors. *p < 0.05, **p < 0.005.

Fig. 2 Kaplan-Meier survival curves demonstrating significant differences in overall survival between biopsy, partial resection (PR), subtotal resection (STR), and gross total resection (GTR) in all 46 patients with low-grade gliomas. The patients treated with GTR were all alive at the end of this study. The patients treated with STR showed longer survival than the patients treated with PR or biopsy (*p < 0.005).

Hydrocephalus are immediately recognized during or after the operation. i-CT is also useful for resecting deep-seated tumors as the surgical orientation can be reconfirmed during tumor resection. This real-time CT helps neurosurgeons when disorientation occurs during the operation. Our present study may contribute to improving the effectiveness of glioma resection, especially of LGG. The development of intraoperative imaging has made it possible to visualize changes in brain structures during surgery and may allow the intraoperative discrimination of normal and abnormal tissue. This gives the neurosurgeon greater confidence to proceed with more extensive resection while decreasing postoperative morbidity. i-CT allows more informed decisions to be made about the appropriate course of action for tumor margins that were adjacent to vital structures.

Recently, intraoperative MR imaging with an integrated navigation system have been used in a few specialized hospitals. Intraoperative MR imaging may have advantages with regard to operative modality and image quality over i-CT. However, the installation and maintenance of such equipment is expensive, few of these machines are available, and applications are mainly limited to resect brain tumor. In addition, the imaging procedure is complex and time-consuming, and requires special personnel in the operating room. Recently, i-CT imaging and updating of the neurosurgical navigation system can be performed at any time during
Fig. 3 A: Preoperative computed tomography (CT) scan with contrast medium showing a non-enhanced tumor located in the right insula that extends into the caudate head and basal ganglia. B: Intraoperative CT scan obtained after the first attempt at tumor removal showing residual tumor. C: Intraoperative CT scan obtained after the second attempt at residual tumor resection showing residual tumor adjacent to the resection cavity (arrow) with surgical cotton containing radiopaque marker (arrowhead).

Surgery.10) Intraoperative updating of the CT images used by the neuronavigation system may also resolve the problems caused by intraoperative brain shifts.

Tumor histopathology is a prognostic factor in gliomas. Oligodendrogliomas often have sharp radiographic borders and are therefore more amenable to extensive resection than fibrillary astrocytomas, have a better natural history, and are more sensitive to radiochemotherapy than astrocytomas.8,12) Therefore, surgical resection using i-CT may be more beneficial for patients with astrocytic tumors.

i-CT allows more extensive resection and improves the surgical outcome in patients with LGG. Neurosurgeons are always concerned about the extent of tumor resection and the occurrence of surgical complications after the operation. Occasionally, disorientation occurs during the operation, even when a navigation system is used. These problems may be resolved by i-CT or MR imaging. We have derived a sense of confidence from the use of i-CT during surgery and think that this may be the most useful aspect of i-CT.

References

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