Usefulness of Thallium-201 Single Photon Emission Computed Tomography to Quantify the Malignancy Grade of Brain Tumors

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Abstract

Preoperative thallium-201 (201Tl) single photon emission computed tomography (SPECT) was used to evaluate the histological malignancy in 24 patients with brain tumors. A corrected L/E ratio was calculated based on the ratio of thallium uptake in the tumor on early images versus the tumor in the delayed images (L/E ratio) corrected for thallium uptake in the contralateral cerebral hemisphere. The corrected L/E ratio in benign brain tumors was 0.79 ± 0.23, significantly different to 1.32 ± 0.25 in high grade astrocytomas (p < 0.01) and 1.19 ± 0.05 in metastatic brain tumors (p < 0.01), respectively. The corrected L/E ratio in low grade astrocytomas was 0.64 ± 0.32, significantly lower than that in high grade astrocytomas (p < 0.01) and metastatic brain tumors (p < 0.05). There was one false positive result among 24 patients using a threshold of 1.0 to separate malignant and benign tumors. 201Tl SPECT using the corrected L/E ratio is effective for determining the malignant viability of tumors.

Key words: thallium-201, single photon emission computed tomography, low grade astrocytoma, high grade astrocytoma, metastatic brain tumor, benign brain tumor

Introduction

Neuroradiological diagnosis of brain tumors has advanced considerably with computed tomography (CT) and magnetic resonance (MR) imaging. However, CT and MR imaging cannot provide good assessments of tumor viability.

Thallium-201 (201Tl) was introduced for myocardial imaging, but observations of uptake by lung carcinoma, and untreated lung, thyroid, liver, and esophageal cancers demonstrated that lesions could be visualized by 201Tl uptake, suggesting utility in the diagnosis of cerebral lesions. 201Tl single photon emission computed tomography (SPECT) is useful for assessment of the malignancy of tumors and the evaluation of therapeutic effects on brain tumors using parameters such as ratio of tumor to normal brain tissue uptake, ratio of tumor to myocardial uptake, and retention index calculated from uptake in tumor tissue in the early and delayed scans. Normal brain tissue demonstrates slight thallium uptake related to factors such as regional blood flow and blood-brain barrier (BBB) permeability, but there is considerable individual variation which depends on age. 201Tl SPECT has a poor resolution, suggesting that 201Tl counts in brain tissue also include artifacts caused by 201Tl in the surrounding tissue or error.

This study investigated whether 201Tl uptake in surrounding tissue affects 201Tl uptake in normal brain tissue, and analyzed two different 201Tl uptake indexes intended to provide better differentiation of the malignancy of brain tumors.

Clinical Materials and Methods

Preoperative 201Tl SPECT studies were performed in 24 patients with brain tumors: three with low grade astrocytoma (grades 1 and 2), 10 with high grade astrocytoma (grades 3 and 4), three with metastatic brain tumor, and eight with benign brain tumor including six meningiomas and two neurinomas. Histological type was confirmed by examination of surgi-
cal specimens in all patients. Preoperative CT scans and/or MR images were also carried out in all patients.

Each patient was injected with 74 MBq of $^{201}$Tl in isotonic sodium chloride. SPECT imaging was initiated 10 minutes (early images) and 2 hours (delayed images) after injection using a gamma view SPECT (Hitachi, Tokyo) filtered with a high resolution collimator. A 64 x 64 matrix with a Butterworth filter was used and images were reconstructed on the transverse plane to facilitate comparison with CT and MR imaging studies.

Regions of interest (ROIs) were drawn on the slice with the greatest tumor activity. Preoperative CT or MR images were used as anatomic guides. The tumor ROI measured 6 x 6 pixels. The control ROIs were the contralateral cerebral hemisphere and scalp, respectively.

**Results**

$^{201}$Tl counts in the contralateral cerebral hemisphere ranged from 1 to 1063. Significant individual differences were noted, but the $^{201}$Tl uptake on the delayed image tended to be greater compared to the $^{201}$Tl uptake on the early image (Fig. 2). The $^{201}$Tl uptake by the contralateral cerebral hemisphere and the contralateral scalp on the early and delayed image showed a significant correlation ($r^2 = 0.96$, $p < 0.001$) (Fig. 3).

The L/E ratio ranged from 0.45 to 1.11 (mean ± SD 0.88 ± 0.21) in the benign brain tumors, 0.83 and 1.00 (0.92 ± 0.09) in low grade astrocytomas, 1.02 to 1.72 (1.32 ± 0.25) in high grade astrocytomas, and 1.13 to 1.21 (1.16 ± 0.04) in metastatic brain tumors (Fig. 4). There was no significant difference in the L/E ratio between high grade astrocytomas and metastatic brain tumors, but the L/E ratio of benign brain tumors was significantly lower than that of high grade astrocytomas and metastatic brain tumors, and the L/E ratio of low grade astrocytomas was significantly lower than that of high grade astrocytomas. Using a cutoff point of 1.0 to distinguish benign brain tumors and malignant brain tumors (high grade astrocytomas and metastatic brain tumors), the histology of all 13 malignant brain tumors and of five of eight benign brain tumors could be correctly predicted, for an overall accuracy of 85.7%.

The corrected L/E ratio ranged from 0.41 to 1.09 (mean ± SD 0.79 ± 0.23) in benign brain tumors, 0.28 to 0.86 (0.64 ± 0.32) in low grade astrocytomas, 1.02 to 1.77 (1.32 ± 0.25) in high grade astrocytomas, and 1.13 to 1.22 (1.19 ± 0.05) in metastatic brain tumors.
brain tumors (Fig. 5). $^{201}$T1 uptake in the tumor tissue on the early image was slight in the low grade astrocytomas. There was a significant difference between benign brain tumors and malignant brain tumors, and low grade astrocytomas and malignant brain tumors, but there was no significant difference between high grade astrocytomas and metastatic brain tumors ($^*p < 0.05$, $^{**}p < 0.01$).

**Representative Cases**

**Case 1:** A 20-year-old male presented with a 1-month history of headache. $T_1$-weighted MR imaging demonstrated a low intensity mass and $T_2$-weighted MR imaging showed a high intensity mass in the left temporal lobe without enhancement by gadolinium (Gd), suggesting a low grade astrocytoma. However, the tumor showed notable uptake on $^{201}$T1 SPECT (Fig. 6), with a L/E ratio of 1.52 and corrected L/E ratio of 1.77, suggesting a malignant brain tumor. He underwent a biopsy of the tumor. Histological examination revealed astrocytoma grade 4.

**Case 2:** A 50-year-old male presented with epilepsy. MR imaging showed a left frontal tumor as a low intensity mass on $T_1$-weighted images and a high intensity mass on $T_2$-weighted images with slight enhancement by Gd, suggesting high grade astrocytoma. However, $^{201}$T1 SPECT showed no abnormal uptake (Fig. 7), with a L/E ratio of 0.95 and corrected L/E ratio of 0.88, suggesting benign brain tumor. Left frontal lobectomy was performed. The histological examination revealed astrocytoma grade 2.

**Case 3:** A 48-year-old male presented with a chronic occipitalgia. MR images revealed a markedly enhanced mass in the left occipital region. $^{201}$T1 SPECT showed high uptake on the early image and low uptake on the delayed image (Fig. 8). The L/E ratio...
was 0.82 and the corrected L/E ratio was 0.79, suggesting benign brain tumor. Total tumor extirpation was performed. Histological examination revealed meningothelial meningioma.

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Discussion

Contrast enhancement in CT or MR imaging is solely dependent on the breakdown of the BBB, but the distribution of $^{201}$TI is related to changes in BBB permeability, regional blood flow, and increased pumping of thallium, a potassium analogue, directly into the malignant tumor cells by the Na$^+$-K$^+$-adenosine triphosphatase (ATPase) pump. Because Na$^+$-K$^+$-ATPase in transformed cultured fibroblast is increased four- to five-fold compared with that in the normal fibroblasts, $^{201}$TI SPECT is thought to more accurately reflect the viable tumor burden than other neurological findings.

Black et al. reported that a $^{201}$TI index (ratio of uptake in tumor to contralateral normal brain) of less than 1.5 almost excludes malignant lesion. This study found that high $^{201}$TI uptake is not necessarily associated with malignant tumors, because $^{201}$TI uptake on the early image was considerable in such benign brain tumors as meningioma and neurinoma.

Our present study found marked individual differences in $^{201}$TI uptake by normal brain tissue, and a significant correlation between $^{201}$TI uptake by normal brain tissue and that by the surrounding scalp. These findings suggested that $^{201}$TI count in normal brain also includes artifacts caused by $^{201}$TI in the scalp.

Our corrected L/E ratio, based on subtraction of $^{201}$TI count in normal brain tissue from $^{201}$TI count in the brain tumor to reflect the $^{201}$TI actually incorporated into the brain tumor, was a better guide to malignancy than the L/E ratio. However, the corrected L/E ratio did not differentiate between high grade astrocytoma and metastatic brain tumor, as the corrected L/E ratios of all malignant brain tumors were higher than 1.0. Using a cutoff value of 1.0 can distinguish benign from malignant tumors, with false positive rate of only 1/24.

References


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Commentary

The authors examined the usefulness of thallium-201 (\(201\text{Tl}\)) single photon emission computed tomography (SPECT) in the preoperative evaluation of the malignancy of brain tumors. To eliminate the bias by the individual differences in \(201\text{Tl}\) uptake by normal brain tissue and reflect the \(201\text{Tl}\) actually incorporated into the brain tumor, they calculated a "corrected L/E ratio" based on the subtraction of \(201\text{Tl}\) counts in normal brain tissue from those in brain tumors. Apparently, there was little difference in the results between the conventional and corrected L/E ratio calculations. However, this study demonstrated that \(201\text{Tl}\) SPECT can clearly differentiate benign tumors or low grade gliomas from high grade gliomas or metastatic gliomas and is useful in the preoperative histological diagnosis. As \(201\text{Tl}\) is known to be incorporated into viable tumor cells, \(201\text{Tl}\) SPECT may also be useful in the differential diagnosis of recurrent gliomas and radiation necrosis.

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