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The retention indices of ^{201}Tl-SPECT in brain tumors

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Objective: The aim of this study was to assess the utility of ^{201}Tl SPECT in the differential diagnosis of intracranial tumors and to determine the relationship between ^{201}Tl uptake and histological types. ***Methods:*** Thirty-eight patients (19 males and 19 females) with thirty-eight brain tumors were evaluated with ^{201}Tl-SPECT. The early and delayed ^{201}Tl uptake ratio was calculated, and the retention index (RI) was applied as follows; RI = delayed uptake ratio/early uptake ratio. ***Results:*** The RI of malignant tumors was higher (0.72 ± 0.18) than that of benign tumors (0.50 ± 0.16) and the difference was statistically significant (p = 0.00045). The difference between high-grade glioma (0.80 ± 0.15) and metastatic tumors (0.64 ± 0.19) was statistically significant (p = 0.039). ***Conclusion:*** ^{201}Tl-SPECT may add useful biochemical information and could differentiate malignant brain tumors from benign lesions, but the RI of metastatic tumors varied depending on the organs with the primary lesion and histological types.

Key words: ^{201}Tl-SPECT, retention index, brain tumor, Gd-enhanced MRI

INTRODUCTION

Several imaging methods have been used in the differential diagnosis of intracranial tumors. Computed tomography (CT) and magnetic resonance imaging (MRI) are mainly used for this purpose. Nevertheless, it is often difficult to make a histopathological diagnosis from the degree of contrast-enhancement and the anatomical location only. Positron emission tomography (PET) and single photon emission computed tomography (SPECT) are considered to evaluate some tissue characterization and biochemical activities of the tumors. PET is not available in city hospitals. Thallium-201 (^{201}Tl) SPECT has been widely used in clinical oncology not only in brain tumors but also thyroid, lung and other tumors,[1–3] but the utility of ^{201}Tl SPECT in the differential diagnosis of brain tumors is still unclear. The aim of this study was to assess the utility of ^{201}Tl SPECT in the differential diagnosis of intracranial tumors and to determine the relationship between ^{201}Tl uptake and histological type.

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MATERIALS AND METHODS

Patients

The study population consisted of 38 patients with 38 brain tumors (19 males and 19 females, aged between 12 and 85 years old, mean 58.4 y.o.). Thirteen of 38 lesions were benign and 25 were malignant. All lesions were histologically confirmed in accordance with WHO directives.[4] Informed consent was obtained from all the study subjects.

^{201}Tl-SPECT

SPECT was performed 15 min (early) and 4 h (delayed) after the intravenous injection of 148 MBq ^{201}Tl-Cl by means of a three-head gamma camera (GCA-9300A/DI, TOSHIBA, Japan) The system was equipped with a low-energy, high-resolution collimator, interfaced with a computer. Data were obtained in a 64 × 64 matrix with 120 s/rot, 6 deg over 360°. A 20% symmetrical window at 74 keV photopeak was used. The data were reconstructed with a Butterworth prefilter with an initial frequency of 0.5 cm^{-1}, a power factor of 8 and backprojection with a Shepp & Logan filter. The axial, coronal and sagittal

views were reconstructed (without attenuation or scatter collection).

The ^{201}Tl uptake ratio (tumor to normal brain parenchymal uptake ratio) was calculated for both early and delayed images. Regions of interest (ROIs) of the tumors were manually placed over the area showing the greatest activity with MRI for reference. ROIs of normal brain parenchyma were placed over the contralateral regions. In the case of midline lesions, the ROIs of normal brain parenchyma were set in the anterior-posterior region in the same slice. We calculated the early and delayed ^{201}Tl uptake ratios, and the retention index (RI) was applied as follows:

RI = delayed uptake ratio/early uptake ratio

MRI

MRI was performed in all patients except one with a 1.0 or 1.5-Tesla scanner (MAGNETOM SP and Symphony, SIEMENS, Signa Advantage, GE). Spin-echo T1 weighted images with 5 mm thick axial slices were obtained pre- and post-intravenous administration of gadolinium-diethylenetriamine pentaacetic acid (Gd-DTPA). Two radiologists evaluated the scoring of the contrast enhancement of the tumors. A 4-point scale was used; 0 = none, 1 = slight, 2 = moderate, 3 = strong

Statistical analysis

Early uptake ratio, delayed uptake ratio and retention index values were compared by two-tailed Student's t-test. The level of statistical significance was set at 0.05.

Table 1 Summary of results in 38 patients with brain tumors

lesion	year	gender	diagnosis	RI	MRI
1	40	M	glioblastoma	0.66	1
2	45	M	glioblastoma	0.87	1
3	51	M	glioblastoma	0.65	0
4	70	M	glioblastoma	0.88	3 (PE)
5	70	M	glioblastoma	0.83	3 (PE)
6	77	M	glioblastoma	0.93	2
7	30	F	malignant astrocytoma	1.08	1
8	39	M	malignant astrocytoma	0.65	2
9	58	M	malignant astrocytoma	0.65	2
10	58	M	malignant oligodendroglioma	0.65	3
11	12	M	medulloblastoma	0.90	3
12	51	M	atypical meningioma	0.72	3
13	35	M	meta. (lung)	0.55	2
14	50	M	meta. (lung)	0.83	2
15	73	F	meta. (lung)	0.59	3
16	78	F	meta. (lung)	0.96	2
17	80	M	meta. (lung)	0.66	2
18	54	F	meta. (breast)	0.86	3
19	59	F	meta. (breast)	0.56	3 (PE)
20	61	F	meta. (breast)	0.56	3
21	52	M	meta. (kidney)	0.32	2
22	85	M	meta. (prostate)	0.46	3
23	71	M	meta. (malignant mesothelioma)	0.65	3
24	73	F	NHL	0.90	3
25	77	F	NHL	0.75	3
26	48	F	meningioma (meningotheliomatous)	0.48	2
27	49	F	meningioma (meningotheliomatous)	0.54	3
28	49	M	meningioma (meningotheliomatous)	0.70	1
29	50	F	meningioma (meningotheliomatous)	0.42	3
30	51	F	meningioma (meningotheliomatous)	0.35	1
31	56	F	meningioma (meningotheliomatous)	0.68	2
32	57	F	meningioma (meningotheliomatous)	0.56	(-)
33	65	F	meningioma (meningotheliomatous)	0.38	3
34	70	F	meningioma (meningotheliomatous)	0.39	3
35	78	F	meningioma (meningotheliomatous)	0.55	1 (PE)
36	75	M	meningioma (fibrous)	0.32	2
37	81	F	meningioma (transitional)	0.33	3
38	42	F	oligodendroglioma (grade 2)	0.81	1

PE; peripheral-dominant enhancement

RESULTS

The results are shown in Table 1 and Figures 1–5. The mean retention index of malignant tumors was higher than that of benign tumors and the difference was statistically significant ($p < 0.01$). The values for metastatic tumors were scattered (0.32–0.96, 0.32: renal cell carcinoma, 0.96: lung adenocarcinoma). The difference between high-grade gliomas and metastatic tumors was statistically significant. The difference between benign tumors and metastatic tumors was not statistically significant. The values for all high-grade gliomas were higher than 0.65. When early and delayed uptake ratios were separately examined, a significant difference was detected between benign tumors and high-grade gliomas only in the early uptake ratio.

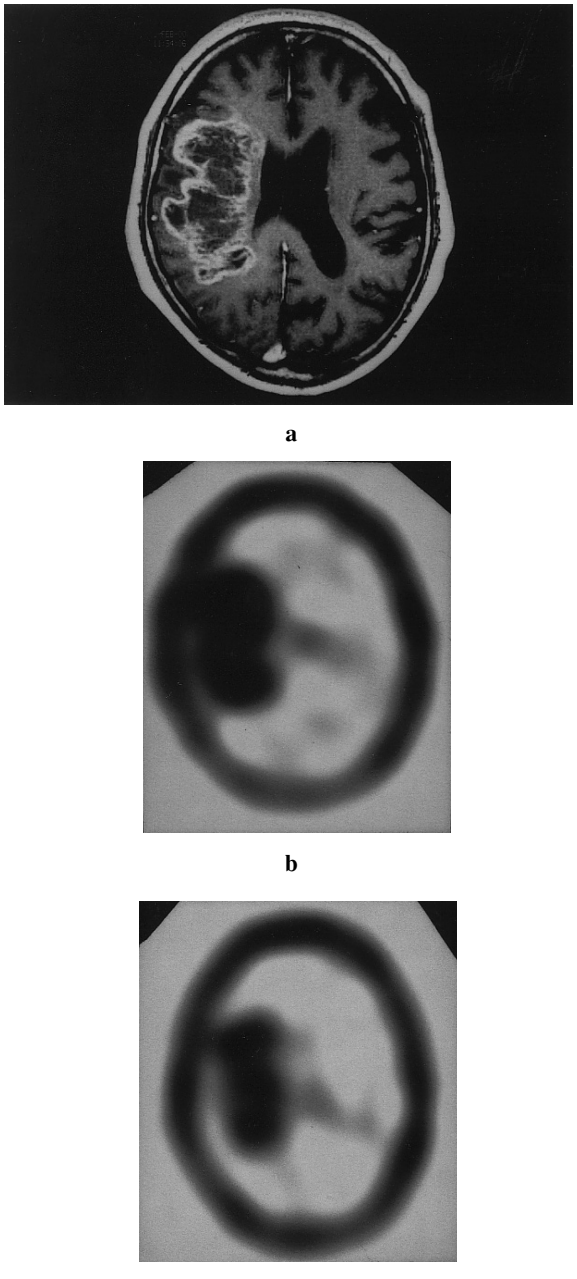

Fig. 1 A 70-year-old male with glioblastoma. a) The Gd-DTPA T1-weighted image shows a peripheral-dominant enhanced tumor. Early (b) and delayed (c) ^{201}Tl-SPECT shows high uptake in the tumor. The retention index is 0.83.

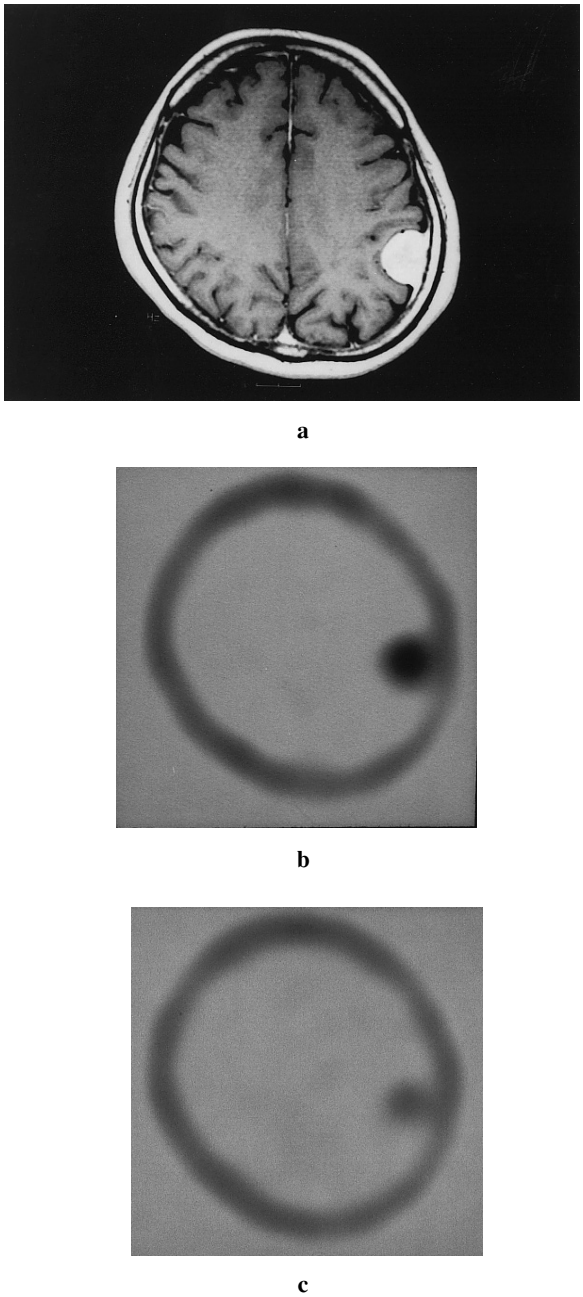

Fig. 2 A 49-year-old female with meningotheliomatous meningioma. a) The Gd-DTPA T1-weighted image shows a strongly enhanced tumor. b) Early ^{201}Tl-SPECT shows high uptake in the tumor. c) Delayed ^{201}Tl-SPECT shows rapid washout from the tumor. The retention index is 0.54.

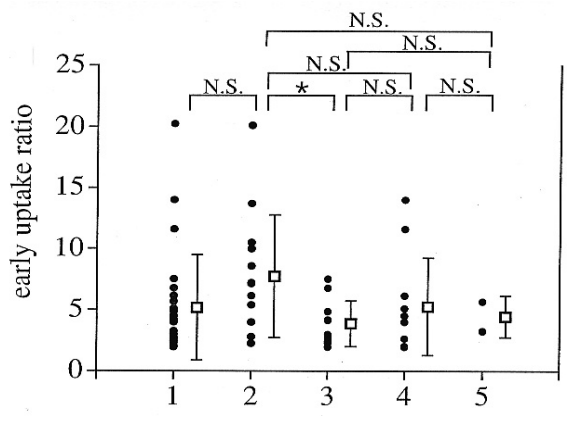

Fig. 3

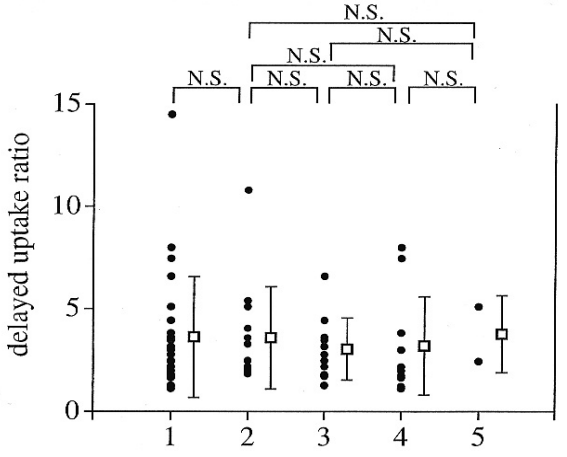

Fig. 4

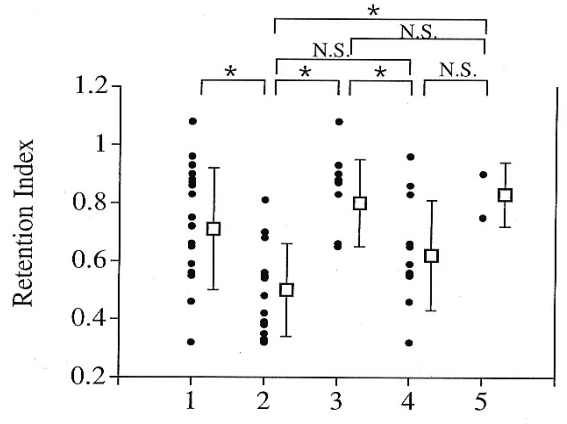

Fig. 5

Figs. 3–5 Early uptake ratio (Fig. 3). Delayed uptake ratio (Fig. 4). Retention index (Fig. 5).
1: Malignant tumors, 2: Benign tumors, 3: High-grade glioma, 4: Metastatic tumors, 5: Non-Hodgkin's lymphoma
●: each values, □: mean ± SD, *: statistically significant, N.S.: not significant

In enhanced-MRI of meningioma (including atypical meningioma), moderate or higher effects were observed in 9 patients, and slight effects in 3 patients. In metastatic tumors and non-Hodgkin's lymphoma (NHL), moderate or higher effects were obtained in all patients. In the patients with high grade glioma, the effects varied from none to strong, and peripheral dominant enhancement was observed in 2 patients.

DISCUSSION

Anatomical imaging methods such as CT and MRI can demonstrate brain tumors clearly and are useful in differential diagnosis by means of the signal intensity or enhancement pattern. ^{201}Tl-SPECT can add valuable biochemical information, and plays an important role in clinical oncology. Several factors are combined in the accumulation of ^{201}Tl in brain tumors, including the blood-brain barrier (BBB) permeability, regional blood flow, cell proliferation and Na-K ATPase. Gd-DTPA enhancement of MRI depends on BBB dysfunction, regional blood flow and tissue permeability. ^{201}Tl accumulation in the tumor has a similar mechanism in the early stage, and the early uptake ratio correlated well with the degree of enhancement on MRI. Dynamic ^{99m}Tc-ECD SPECT correlated well with ^{201}Tl indices and could differentiate benign tumors from malignant ones.[5] In high-grade gliomas, cell proliferation is high and the PCNA-LI (proliferating cell nuclear antigen labeling index), which is regarded as a parameter for tissue proliferating ability, has a higher value than that of low-grade glioma or meningioma.[6] In some literature, Na-K ATPase was involved in ^{201}Tl accumulation in glioblastoma.[7] Taki et al. reported that the ^{201}Tl retention index correlates with the histological grading.[8] In contrast, Hirano et al. found no statistically significant difference in ^{201}Tl uptake or washout on histological malignancy.[9] In our study, the RIs of malignant tumors were higher than those of benign tumors and the difference was statistically significant, but the retention indices of metastatic tumors ranged across various values because of the different primary lesions involved. Meningiomas, especially the meningotheliomatous type, show high early ^{201}Tl uptake and rapid washout. In 2 patients with NHL, the RI was high, and the tumor was clearly imaged by enhanced-MRI. It has been reported that ^{201}Tl-SPECT is useful for distinguishing whether intracranial lesions complicated with AIDS are NHL or other diseases.[10] If the primary lesion is identified and a number of tumors are observed in the skull, metastatic tumors are usually diagnosed and treatment is performed accordingly. In such cases ^{201}Tl-SPECT may not be useful as a method for distinguishing between benign and malignant tumors, but this method is very useful for the evaluation of treatment by chemotherapy and radiotherapy.[11] It is sometimes difficult to distinguish postoperative changes and recurrence by means of en-

hanced-MRI, and the usefulness of ^{201}Tl-SPECT in such cases has been reported.[12,13] We have examined some other ^{201}Tl studies, which remained unevaluated pathologically, but these lesions are suspected to be meningioma or metastatic tumors from the identified primary lesions. These lesions were excluded from this study.

The results of this study indicated that the retention index is useful for distinguishing between benign and malignant tumors, supporting the conclusions of other studies. Interestingly, there was a significant difference between high-grade gliomas and metastatic tumors in the retention index. Metastatic tumors would have different retention indices depending on the primary lesions, and the primary lesions were located in diverse regions in a limited number of patients. We are planning to continue this study with a large number of patients. Since the retention index is the ratio of the delayed uptake ratio to the early uptake ratio, it is easily affected if the latter is small. When early and delayed uptake ratios were separately examined, a significant difference was detected between benign tumors and high-grade gliomas only in the early uptake ratio. Among benign tumors ^{201}Tl accumulation in the early phase was low in oligodendroglioma, resulting in a small early uptake ratio and consequently a high retention index. This case indicated that it is important to evaluate the retention index by imaging not only the early phase but also the delayed phase. The partial and low MRI enhancement of solid components of oligodendroglioma and its cystic degeneration would have resulted in the low ^{201}Tl accumulation. Renal cell carcinoma is naturally a hypervascular tumor, and metastatic lesions in the brain are considered to reflect its characteristics. The metastatic lesions in the brain that we encountered were enhanced by enhanced-MRI and were accompanied by edema around the lesions, but hemorrhage was not noted. Interestingly, the retention index of this lesion was low, and the vascularity could be related to the ^{201}Tl washout rate. In 4 lesions, the periphery was enhanced by enhanced-MRI, and 3 of these lesions were malignant. The retention index of high-grade gliomas was higher than that of metastatic tumor (breast cancer), suggesting that the retention index could be used for the distinction. In all 4 lesions, internal degeneration/necrosis was observed, but hemorrhage was not. The enhanced volume and the percentage of solid tissues were not evaluated in this study.

In conclusion ^{201}Tl-SPECT may add useful biochemical information and could differentiate malignant brain tumors from benign lesions. The significant finding in this study was differences between metastatic tumors and high-grade gliomas in the retention index, but several factors are involved in the accumulation of ^{201}Tl in tumors, and the pattern of accumulation of ^{201}Tl in metastatic tumors varies depending on the organ with the primary lesion and the histological type. Further investigations are necessary to solve these problems.

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