Preoperative Grading of Glioma Malignancy with Thallium-201 Single-Photon Emission CT: Comparison with Conventional CT

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PURPOSE: To compare thallium-201 single-photon emission CT with conventional CT in grading the malignancy of gliomas and to determine the reliability of each in tumor assessment. **METHODS:** We studied 37 patients who had gliomas (31 high grade and 6 low grade) and compared the CT findings with the thallium-201 index, which we defined as tumor uptake relative to the uptake in the contralateral hemisphere. **RESULTS:** Among the high-grade gliomas, we observed a significant correlation between breakdown volume of the blood-brain barrier and thallium-201 uptake. However, 8 of the high-grade gliomas had low thallium-201 uptake, in the same range as the low-grade gliomas. Of these, 2 were nonenhancing and the other 6 showed ring enhancement on CT scans. Analysis of variance showed no significant difference in thallium-201 indexes between low-grade gliomas and highly malignant (grade II–III) gliomas. Accuracy of thallium-201 imaging was lower (78%) than that of CT (84%) in identifying high-grade gliomas. **CONCLUSIONS:** Damage to the blood-brain barrier is a prerequisite for uptake of thallium-201 in gliomas. Tumors with central necrotic areas and moderate ring enhancement tend to be underestimated when evaluated by means of thallium-201 scintigraphy. The results indicate a need for caution when interpreting findings on images obtained with thallium-201 single-photon emission CT in preoperative evaluation of brain tumors.

Index terms: Brain neoplasms, computed tomography; Glioma; Single-photon emission computed tomography

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In the treatment of gliomas it is essential to define accurately the grade of malignancy, since the approach differs for low-grade and high-grade gliomas. Diagnostic procedures currently used include computed tomography (CT) or magnetic resonance (MR) imaging followed by tumor resection or brain biopsy and histologic staging. The imaging characteristics seen on CT scans enable tumor staging to some extent (1). Damage to the blood-brain barrier is considered a reliable marker of high-grade malignancy, but as stated by Chamberlain et al (2), nonenhancing tumors are rather frequent among the moderately malignant anaplastic astrocytomas (ie, high-grade malignant gliomas as defined histologically, also known as Kernohan grade III gliomas).

Thallium-201 single-photon emission CT (SPECT) has been introduced as a promising diagnostic tool for guiding the management of gliomas, because thallium is taken up by malignant glioma cells (3, 4). This technique is also said to be an instrument in preoperative assessment, since its prediction accuracy is high (89%), and there is a strong statistical difference between the thallium index in high-grade gliomas versus that in low-grade gliomas (5, 6) (the thallium index is defined as tumor uptake relative to the uptake in the contralateral hemisphere). Since thallium-201 uptake is not solely dependent on breakdown of the blood-brain barrier, as are contrast agents, but is also related to cell growth rate, some authors have postulated a better correlation between the thallium uptake index and grade of tumor malig-

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nancy than between CT findings and histologic staging (7–11). Because thallium-201 is an ionized particle and should not be able to pass through an intact blood-brain barrier, it is hard to conceive that thallium-201 SPECT could add to the classification of nonenhancing malignant gliomas. The aim of this study was to compare CT findings, thallium-201 uptake indexes, and histologic tumor staging in cerebral gliomas and to evaluate the reliability of these two preoperative assessment methods.

Subjects and Methods

Patients

Over a 3-year interval, 67 patients with suspected malignant glioma as judged from CT scans underwent thallium-201 SPECT imaging of the brain. Thirty-seven patients were included in this study; the age range was 10 to 75 years (median, 55 years), and 15 patients were female and 22 were male. All patients were imaged before surgery. Patients who had had tumor resection or biopsy before their thallium-201 study were excluded, because thallium uptake may be influenced by prior surgical intervention. Of the 37 patients, 7 had had diagnostic biopsy and 30 had had tumor resection. The time interval between the thallium study and the surgery never exceeded 35 days (median, 12 days). All patients with primary brain tumor other than glioma were excluded. The histologic classification method of Kernohan was used (12). This system includes four grades of primary astrocytoma, oligodendroglioma, or mixed oligoastrocytoma (I, II, III, IV), but gliomas with heterogeneous growth and areas of varying grades of malignancy are common. Grade I and grade II tumors were grouped together as low-grade gliomas; grade II–III, grade III, and/or grade IV were grouped together as high-grade gliomas. With reference to the World Health Organization classification (13), this means that high-grade gliomas in this study comprised anaplastic astrocytomas and oligodendrogliomas and glioblastomas; all other tumors were considered low-grade gliomas. One patient was excluded from the study because the primary histologic diagnosis was considered to be erroneous owing to a sampling error. His preoperative CT scan showed a thin ring of enhancement; his survival time turned out to be 2 months, and autopsy data showed grade II–III glioma.

Techniques

Thallium-201 measurements were made with the use of a SPECT scanner dedicated to brain imaging. Each patient was given an intravenous injection of 75 MBq thallium-201 in isotonic sodium chloride (thallous chloride Tl 201). Children received 1 MBq thallium-201 per kilogram of body weight. The patients were positioned in the SPECT scanner 5 minutes after thallium administration. The thallium uptake was recorded in 10 transaxial contiguous 1-cm-thick sections from 1 cm below the orbitomeatal line and superiorly. The intrasection resolution was about 1 cm full width half maximum. Images were acquired with 3 turns per minute in continuous rotation for 5 minutes. We used a 47 to 87 keV energy window around the 70 keV photon peak. The images were reconstructed in a 64 × 64 image matrix with filter back projection and linear attenuation correction in the axial plane. The attenuation coefficient was 16%.

Preoperative CT scans served as an anatomic guide. The thallium uptake was measured in the section corresponding to the location of tumor changes identified on CT scans. Without knowledge of the histology of the lesion, a cross-section profile was drawn through the part of the tumor with the highest thallium uptake. The average value of the three adjacent pixels with the highest thallium uptake was used. For each patient we determined a thallium index of the uptake within the tumor relative to the mean of three homologous pixels in the contralateral side (thallium index tumor uptake/contralateral uptake). In one case, the lesion was in the midline and consequently the thallium index was 1.0. In that case, thallium uptake in the tumor was compared with that in a low-uptake region in the lateral part of one hemisphere.

All patients had a preoperative CT examination before and after administration of contrast material. Different CT scanners were used. The time interval between the SPECT and CT examinations never exceeded 6 weeks (median, 13 days). The sections were parallel to the orbitomeatal line and the thickness varied from 4 mm to 10 mm in the posterior fossa and from 8 mm to 10 mm supratentorially. Contrast material was administered in a bolus injection of 100 mL iohexol 300 mg/mL or 1.5 mL/kg body weight in patients with a body weight below 60 kg. Total volume of the tumor and the volume of the tissue with blood-brain barrier damage were measured by the same neuroradiologist in every patient. For tumors with blood-brain barrier disruption, the total volume measured included the area with barrier damage plus areas with necrosis or cysts. For tumors without blood-brain barrier damage, the total area of abnormal attenuation was measured. The presence of blood-brain barrier damage was determined by visual comparison of the precontrast and postcontrast images.

To measure the volume of the tumors and their enhancement, a 5 × 10-cm grid was drawn on a disposed transparent radiograph with a centimeter scale indicated on the image. The grid was placed on the tumor, and areas of enhancement in every section of the tumor were measured along with the area of enhancement or tumor volume. The total volume was then calculated by multiplying the area of each section by the section thickness, and the volumes on each section with disease were added together. In each case the tumor was further categorized according to solid or diffuse tumor growth and to presence of necrotic or cystic tumor components.

Statistical Analysis

The results were expressed as medians and ranges. Thallium-201 indexes and Kernohan groups of histologic

grading were analyzed by means of analysis of variance and illustrated by an interaction plot. The level of significance was set at .05. Between groups, the differences were further assessed by a Games-Howell post hoc test. Associations between thallium indexes and enhancement volumes were assessed by simple linear regression analysis. Computer programs Statview 4.0 and Superanova were used in the analyses.

Results

Thirty-one of 37 patients had histopathologically verified highly malignant gliomas. The other 6 patients had histologically confirmed low-grade malignant gliomas. Three low-grade gliomas had a small or moderate contrast enhancement, and 3 (10%) of the high-grade tumors were nonenhancing on CT scans. A summary of patient data and tumor characteristics is given in Table 1.

CT findings for the high-grade and low-grade gliomas showed a wide range of tumor volumes, enhancement volumes, and thallium-201 indexes, with some overlap in the enhancement volumes and thallium indexes (Table 2). Two of the nonenhancing tumors were Kernohan grade II–III (ie, highly malignant gliomas with areas of low-grade malignancy). In all, there were 6 grade II–III tumors, of which 2 were nonenhancing. Neither of the nonenhancing high-grade gliomas had a high thallium index (Table 3).

Eight high-grade gliomas had a thallium uptake between 1.0 and 1.4, indicating an overlapping range of uptake between high-grade and low-grade gliomas. These eight findings were considered false negative. The distribution in histologic grading of these gliomas is shown in Table 4. Two high-grade gliomas with low thallium uptake were nonenhancing, with diffuse tumor growth and no demarcation of solid tumor on CT scans (Table 1, patients 13 and 30). Six high-grade gliomas with low thallium uptake had a cystic tumor shape with a ring enhancement surrounding a necrotic central tumor portion (Table 1, patients 5, 12, 15, 17, 27, and 31).

Among the high-grade gliomas, we found a significant correlation between thallium indexes and volume of CT contrast enhancement (r = .412, P = .0214) (Fig 1). There was a significant difference in the thallium index between low-grade gliomas and gliomas of grade III and/or grade IV [$F(3, 33) = 3.130$, $P = .0387$], but not between low-grade gliomas and gliomas of grade II–III. There was no significant difference between the thallium indexes among high-grade glioma subpopulations (Fig 2).

The comparative reliability of the CT and thallium-201 SPECT methods for use in identifying high-grade and low-grade gliomas is shown in Table 5 (accuracy = total number of correct estimations/all tumors studied). Because the highest thallium index among the low-grade gliomas was 1.4, an index of more than 1.4 was chosen as the criterion for predicting high-grade malignancy.

Discussion

Malignant gliomas represent almost one half of the primary malignant tumors of the central nervous system. Despite advances in diagnostic and therapeutic techniques, the prognosis for patients with these tumors remains poor. Gliomas are considered a regional disease with growth of a primary tumor mass, but there is a concomitant spread of neoplastic cells within the brain that makes complete surgical resection impossible and recurrence common. Radiation therapy and chemotherapy are the other therapeutic options for these patients. The latter two therapies are frequently combined in treatment of the high-grade malignant gliomas. A centrally located tumor or one in eloquent areas of the brain makes tumor resection impossible; in these cases, a diagnostic biopsy is performed instead. But there is a risk of sampling error in such cases, and alternative assessment methods are of value.

Because treatment approaches differ for low-grade and high-grade gliomas, it is important that assessment methods are reliable. Thallium-201 SPECT studies have shown promise in this regard. In a small study published recently, no overlap was found between the thallium indexes for low-grade and high-grade gliomas (7). Ueda et al (8) found a close relationship between initial thallium uptake and grade of glioma malignancy. Oriuchi et al (9) concluded that thallium-201 SPECT can depict apparently viable, malignant neoplastic tissues and that this noninvasive technique is useful in helping to predict the degree of the gliomas fairly well. In an editorial, Gruber and Hochberg (10) interpreted the findings of Kim et al (6) as indicating that thallium-201 SPECT provides a rational basis for the systematic preoperative examination of patients with nonenhancing lesions on

TABLE 1: Patient data and tumor characteristics for 31 high-grade and 6 low-grade gliomas, for which histologic diagnosis was based on findings from resected tissue or biopsy specimens

Patient	Age, y	Sex	Tumor Grade	Location	Shape	Size, mL	Enhancement, mL	Histologic Diagnosis		Thallium Index
								Resected Tissue	Biopsy Specimen	
1	70	F	III–IV	L parietal	Solid	4	3	+		1.80
2	62	F	III	R temporal	Cystic	88	36	+		2.60
3	55	M	III–IV	R parieto-temporal	Solid	39	36	+		3.00
4	65	M	III	L temporal	Diffuse	10	8	+		1.80
5	11	F	III–IV	Pons	Cystic	11	4	+		1.10*
6	52	M	III	L parietal	Solid	39	27		+	1.90
7	74	M	IV	L fronto-parietal	Cystic	16	7		+	3.40
8	41	M	III–IV	L fronto-parietal	Cystic	28	10	+		1.60
9	71	M	III–IV	R parieto-occipital	Solid	43	40	+		5.10
10	67	M	III–IV	R temporal	Cystic	39	20	+		2.50
11	71	F	III	L temporal	Solid/cystic	32	17	+		2.90
12	44	M	III	L temporal	Cystic	49	14	+		1.30
13	65	M	III	L parietal	Diffuse	8	0		+	1.20
14	10	M	III	L temporal	Solid	5	5	+		2.60
15	64	M	III–IV	R parieto-occipital	Cystic	87	31	+		1.40
16	79	F	III	L parietal	Cystic	25	21		+	1.70
17	63	F	III	L parieto-temporooccipital	Cystic	45	29	+		1.40
18	73	F	III–IV	R fronto-temporoparietal	Diffuse	60	20	+		1.60
19	52	F	III–IV	R parieto-temporal	Solid/cystic	86	67	+		2.10
20	46	M	III–IV	R parieto-temporal	Cystic	99	42	+		3.50
21	58	M	III	L parietal	Cystic	94	47	+		3.40
22	72	F	III–IV	L parietal	Cystic	8	6	+		3.60
23	67	M	III	L fronto-parietal	Cystic	90	32	+		4.20
24	66	F	IV	R frontal	Solid	6	5	+		2.70
25	43	F	III–IV	R temporal	Solid	18	11	+		2.80
26	36	M	II–III	R temporal	Diffuse	8	0	+		1.80
27	40	M	II–III	L frontal	Cystic	30	4	+		1.00
28	67	M	II–III	R parietal	Solid	54	50	+		2.70
29	75	M	II–III	L/R central	Solid	28	15	+		3.10
30	37	M	II–III	R fronto-temporal	Diffuse	10	0	+		1.30
31	42	F	II–III	L frontal	Cystic	22	1	+		1.20
32	26	M	I–II	R temporal	Cystic	87	3	+		1.30
33	35	F	I–II	R fronto-parietal	Diffuse	20	0	+		1.30
34	43	M	I–II	L temporal	Cystic	47	4	+		1.40
35	33	F	I–II	R fronto-parietal	Solid	18	8	+		1.00
36	49	F	I–II	L frontal	Cystic	6	0	+		1.10
37	25	M	I—II	L parietal	Cystic	18	0	+		1.10

* Because this tumor was located in the midline, the thallium index was defined as the uptake in the tumor relative to the uptake in the lateral part of one hemisphere.

TABLE 2: Thallium indexes and CT-based estimates of tumor volume and enhancement volume for high-grade and low-grade gliomas, median (ranges)

	High-Grade Gliomas, n = 31	Low-Grade Gliomas, n = 6
Thallium index	2.1 (1.0–5.1)	1.2 (1.0–1.4)
CT tumor volume, mL	30.0 (4.0–99.0)	19.0 (6.0–87.0)
CT enhancement volume, mL	15.0 (0.0–67.0)	2.0 (0.0–8.0)

TABLE 3: Enhancement volume and thallium index for three nonenhancing high-grade gliomas

Kernohan Grade	Enhancement Volume, mL	Thallium Index
III	0	1.2
II–III	0	1.8
II–III	0	1.3

TABLE 4: Enhancement volume and thallium index for eight high-grade malignant gliomas with low thallium uptake

Kernohan Grade	Enhancement Volume, mL	Thallium Index
III–IV	31	1.4
III–IV	4	1.1
III	0	1.2
III	14	1.3
III	29	1.4
II–III	4	1.0
II–III	0	1.3
II–III	1	1.2

TABLE 5: Sensitivity, specificity, and accuracy between CT and thallium-201 SPECT in the diagnosis of malignancy in high-grade gliomas (malignancy was defined as enhancement on CT scans and as a thallium index of more than 1.4 on thallium-201 SPECT scans)

	Sensitivity, %	Specificity, %	Accuracy, %
CT (n = 37)	90	50	84
SPECT (n = 37)	74	100	78

CT or MR studies; and in another editorial, Tonami and Hisada (11) proffered thallium-201 SPECT as the method of choice for use in grading gliomas.

Our results are in agreement with those of several earlier reports in showing a significantly higher uptake of thallium in high-grade Kernohan grade III and/or grade IV gliomas than in low-grade gliomas (5–9). However, the results did not indicate that it is possible to differentiate low-grade gliomas from Kernohan grade II–III gliomas. Among high-grade gliomas, the degree of blood-brain barrier breakdown, as evidenced on CT scans, correlated significantly with the thallium index. Most probably, breakdown of the blood-brain barrier is a prerequisite for intracerebral penetration of thallium, and in turn for the intracellular uptake of this element into the tumor. This assumption is further confirmed by the fact that none of the nonenhancing high-grade gliomas had a high thallium uptake.

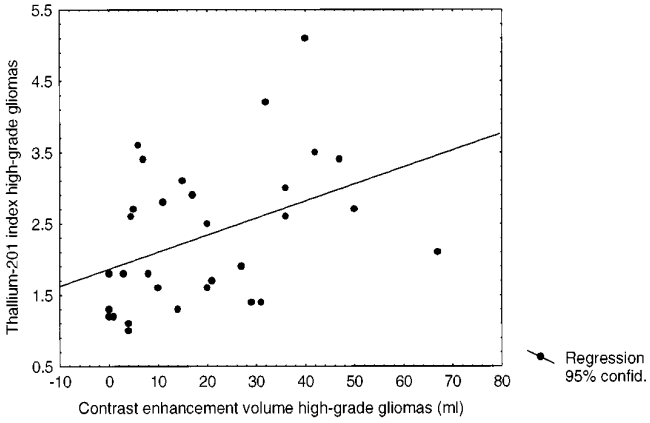

Fig 1. Correlation between thallium indexes and CT enhancement volumes (ie, the tissue with blood-brain barrier damage) in high-grade gliomas (n = 31).

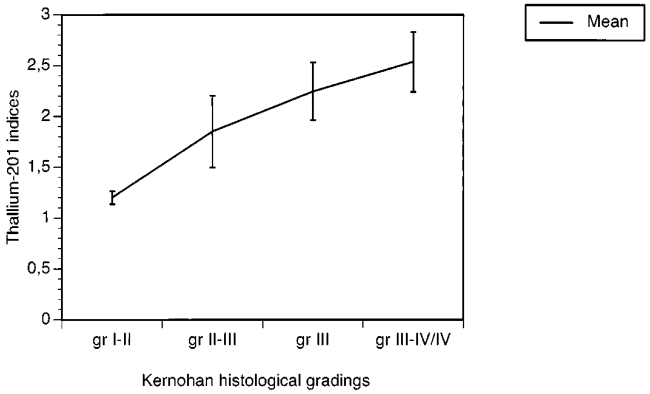

Fig 2. Difference between thallium indexes in Kernohan histologic groups (means and SEM) for tumors of grade I–II, n = 6; grade II–III, n = 6; grade III, n = 11; grade III–IV and/or grade IV, n = 14.

Oriuchi et al (9) found no clear-cut correlation between thallium uptake and the degree of contrast enhancement of the tumor on CT scans. Seven of 14 low-grade gliomas showed contrast enhancement, and only two had significant thallium uptake, whereas all 14 of the high-grade gliomas showed intense accumulation of thallium at the tumor site on contrast-enhanced CT scans. In our study, 3 of 6 low-

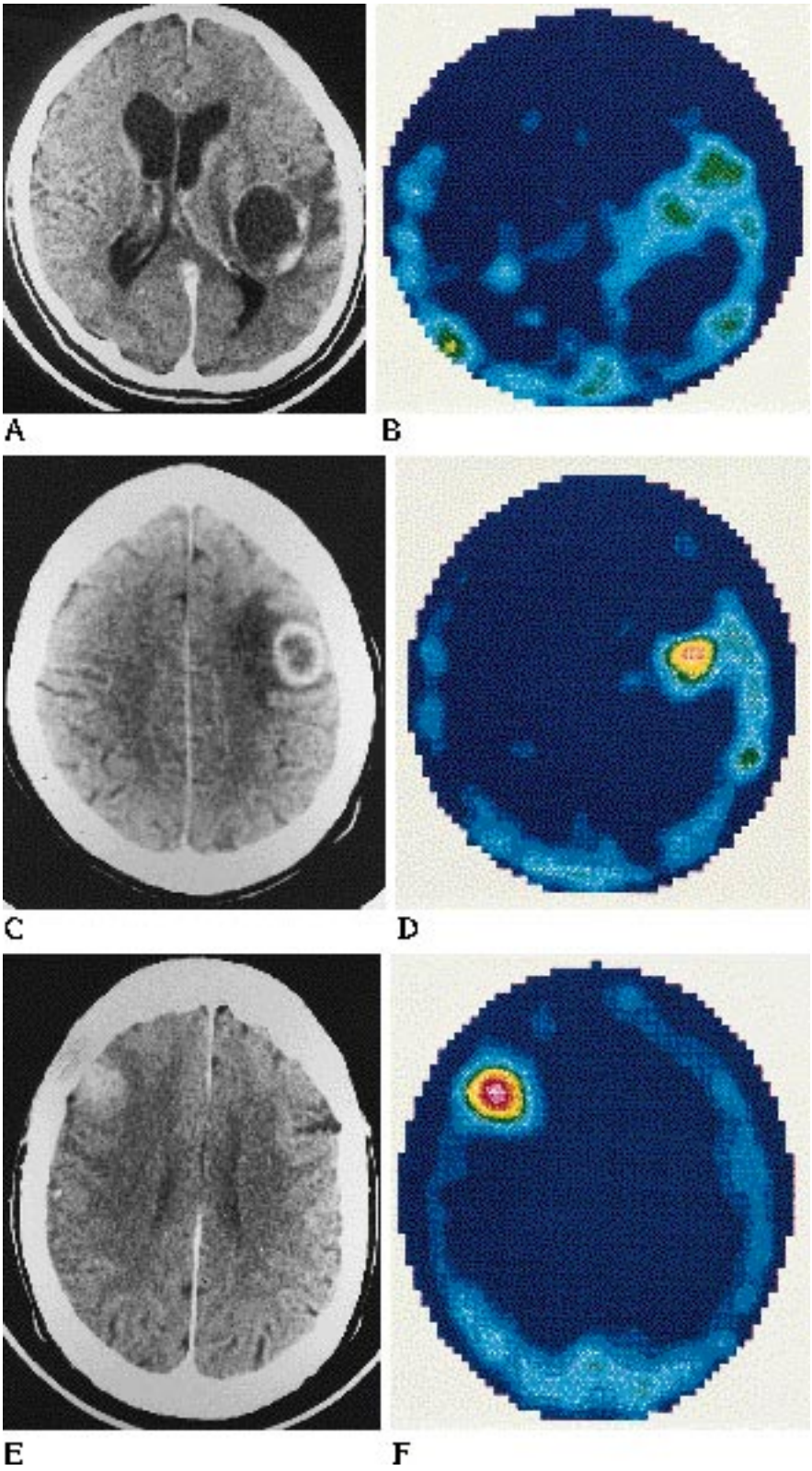

Fig 3. CT and thallium-201 SPECT scans of high-grade gliomas with varying degrees of thallium uptake depending on tumor characteristics and extent of blood-brain barrier breakdown.

A and *B*, A 44-year old man with cystic glioma grade III in the left temporal lobe. The tumor has a large necrotic core and a thin rim of enhancement; the thallium uptake is low (thallium index, 1.3).

C and *D*, A 72-year old woman with cystic glioma grade III to IV in the left parietal lobe with a small central area of necrosis and a relatively thick ring-shaped enhancement. The thallium index is high (3.6).

E and *F*, A 66-year old woman with a solid grade III glioma in the right frontal lobe. The thallium uptake is high (2.7) although total enhancement volume is only 5 mL.

grade gliomas had a small volume of contrast enhancement (3 to 8 mL) and none had a high thallium index. We concluded that the cell biology of the tumor is of crucial importance for thallium uptake.

Six of the high-grade gliomas with a low thallium index showed breakdown of the blood-brain barrier on CT scans. The likely reason for these findings is the cystic/necrotic character of the tumor in all these cases. The resolution of the SPECT scanner used in this study was probably insufficient for detecting thallium-201 uptake in a thin rim of tissue surrounding a larger necrotic core. In contrast, small solid gliomas with tumor volume/enhancement volume close to 1 had a high thallium-201 uptake, although the total volume of the blood-brain barrier breakdown was low (Fig 3). The process of thallium uptake is multifactorial, depending on blood flow in the tumor, extent of pathologic vessel invasion, extent of blood-brain barrier breakdown, cell biology of the tumor influencing cellular uptake, and tumor size. Kim et al (6) reported that lower uptake of thallium than expected in high-grade gliomas could be the result of metabolically inactive areas, such as a necrotic core in the tumor center. These authors concluded that the uptake index could be underestimated in a few selected cases. Yoshii et al (14) noted that thallium-201 SPECT failed to disclose the viability of a tumor that had a thin rim enhancement on MR images. Since 6 of 31 high-grade gliomas with CT enhancement had a low thallium uptake and all 6 showed cystic/necrotic areas on CT scans, those features seem to be a major component in the underestimation of malignancy grade on the basis of SPECT findings.

Thallium-201 SPECT as an examination for early detection of tumor recurrence or malignant transformation of low-grade gliomas has been the subject of a few published articles (14–16). Thallium scintigraphy has also been proposed as a method for evaluating treatment response (17) and for distinguishing tumor recurrence from radiation changes (18). Thallium-201 SPECT may be of value in postoperative treatment of patients with glioma providing that CT changes show enhancement.

In conclusion, this study established a significant correlation between CT enhancement volume and thallium-201 uptake in high-grade gliomas. Thallium uptake in nonenhancing gliomas was very low and was independent of the grade of tumor malignancy. Damage to the blood-brain barrier seems to be a precondition for thallium uptake in gliomas. A number of high-grade gliomas were found to have low thallium uptake indexes. The enhancing, high-grade gliomas with low thallium uptake were all cystic tumors with thin rim enhancement surrounding central necrotic areas of tumor. There is a risk of underestimating the grade of tumor malignancy when using thallium-201 SPECT to study tumors with extensive necrotic areas in combination with moderate surrounding enhancement. Thallium brain scintigrams have to be evaluated with caution and in conjunction with the CT findings.

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References

1. Butler AR, Horii SC, Kricheff II, Shannon MB, Budzilovich GN. Computed tomography in astrocytomas. *Radiology* 1978;129: 433–439
2. Chamberlain MC, Murovic JA, Levin VA. Absence of contrast enhancement on CT brain scans of patients with supratentorial malignant gliomas. *Neurology* 1988;38:1371–1373
3. Brismar T, Collins P, Kesselberg M. Thallium-201 uptake relates to membrane potential and potassium permeability. *Brain Res* 1989;500:30–36
4. Britten JS, Blank M. Thallium activation of the (Na-K-)-activated ATPas of rabbit kidney. *Biochim Biophys Acta* 1968;159:160–166
5. Black KL, Hawkins RA, Kim KT, Becker DP, Lerner C, Marciano D. Use of thallium-201 SPECT to quantitate malignancy grade of gliomas. *J Neurosurg* 1989;71:342–346
6. Kim KT, Black KL, Marciano D, et al. Thallium-201 imaging of brain tumors: methods and results. *J Nucl Med* 1990;31:965–969
7. Sjöholm H, Elmquist D, Rehncrona S, Rosén I, Salford LG. SPECT imaging of gliomas with thallium-201 and technetium-99m-HM-PAO. *Acta Neurol Scand* 1995;91:66–70
8. Ueda T, Kaji Y, Wakisaka S, et al. Time sequential single photon emission computed tomography studies in brain tumor using thallium-201. *Eur J Nucl Med* 1993;20:138–145
9. Oriuchi N, Tamura M, Shibazaki T, et al. Clinical evaluation of thallium-201 SPECT in supratentorial gliomas: relationship to histologic grade, prognosis and proliferative activities. *J Nucl Med* 1993;34:2085–2089
10. Gruber ML, Hochberg FH. Editorial: systematic evaluation of primary brain tumors. *J Nucl Med* 1990;31:969–971
11. Tonami N, Hisada K. Editorial: thallium-201 SPECT in evaluation of gliomas. *J Nucl Med* 1993;34:2089–2090
12. Kernohan JW, Mabon RF, Svein HJ, Adson AW. A simplified classification of gliomas. *Proc Staff Meet Mayo Clinic* 1949;24: 71–75

13. Kleines P, Burger PC, Scheithauser PW, et al. *Histological Typing of Tumors of the CNS. Int Histol Class of Tumors*. 2nd ed. New York: World Health Organization, 1993:10–30
14. Yoshii Y, Sastou M, Yamamoto T, et al. The role of thallium-201 single photon emission tomography in the investigation and characterisation of brain tumors in man and their response to treatment. *Eur J Nucl Med* 1993;20:39–45
15. Carvalho PA, Schwartz RB, Alexander E III, et al. Detection of recurrent gliomas with quantitative thallium-201/technetium-99m HMPAO single-photon emission computerized tomography. *J Neurosurg* 1992;77:565–570
16. Zhang JJ, Park CH, Kim SM, Ayyangar KM, Haghbin M. Dual isotope SPECT in the evaluation of recurrent brain tumor. *Clin Nucl Med* 1992;17:663–664
17. Kaplan WD, Takvorian T, Morris JH, Rumbaugh CL, Connolly BT, Atkins HL. Thallium-201 brain tumor imaging: a comparative study with pathologic correlation. *J Nucl Med* 1987;28:47–52
18. Schwartz RB, Carvalho PA, Alexander E III, Loeffler JS, Folksrth R, Holman BL. Radiation necrosis vs high-grade recurrent glioma: differentiation by using dual-isotope SPECT with thallium-201 and technetium-99m HMPAO. *AJNR Am J Neuroradiol* 1991;12: 1187–1192