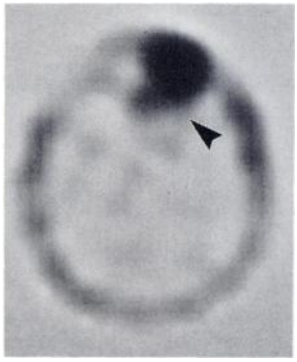

**FIGURE 3**
Anatomic resolution of $^{201}$Tl SPECT. SPECT $^{201}$Tl image demonstrating an area of high uptake at the left frontal pole, with a $^{201}$Tl index of 3.27 and a second area of moderate uptake caudal to the first (arrow). Pathologic examination of the surgical specimen revealed an anaplastic astrocytoma in the frontal pole, but a more benign low-grade oligodendroma in the rest of the tumor.

useful clinical information on the biology of primary brain tumors. Our work is consistent with the findings of other investigators who noted thallium uptake in brain tumors with planar imaging. We developed a method that has been easily integrated into the routine processing of $^{201}$Tl SPECT scans in our clinical nuclear medicine department. Thallium uptake indices using a ratio of average counts (Method 3) of suspected brain lesions are being routinely reported to the neurosurgeons. We recommend the routine use of attenuation correction. As expected, this correction has the most effect on low-grade lesions in the deep parenchyma and can result in better lesion discrimination on qualitative inspection. Although partial volume effects can cause an underestimation in the uptake index in a few selected cases, the resolution of SPECT is sufficient for utilizing this quantitative method clinically as reported recently (*3*).

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# Editorial: Systematic Evaluation of Primary Brain Tumors

In the United States, 8,000 patients die each year of primary intracranial malignant tumors. Glioblastoma multiforme, the most common primary malignant brain tumors, accounts for 75% of gliomas in adults. For afflicted patients, the prognosis remains grim. Following operation and irradiation, the median survival is less than one year. Fewer than 10% of patients survive two years.

Neurooncologists are confronted with difficult diagnostic and therapeutic issues when providing care for patients suspected of harboring a primary brain tumor. Of major concern is the need to correctly diagnose a tumor of glial origin and to determine the grade of the tumor. The WHO grading classification separates glial tumors into three grades reflecting increasing degrees of malignant potential: Grade 1 (low-grade with median

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survivals of 3–5 yr), Grade 2 (anaplastic tumors with median survivals of 2–3 yr) and Grade 3 (glioblastoma with median survivals of 1 yr).

The evaluation begins with a detailed history and examination. This is followed by diagnostic imaging (computed tomography/magnetic resonance imaging), the interpretation of which frequently determines the future management of the patient. The purpose of the "scan" is to identify the lesion, determine its location, and if possible access the grade of the tumor. Previously, the grade of tumor was thought to directly correlate with the degree of enhancement on CT. However, recent studies indicate that 40% of nonenhancing lesions on CT are histologic high-grade tumors (*1,2*) Gadolinium MRI studies have not yet provided histologic insights although it appears that lack of enhancement may correlate with lower histologic grades. Phosphorus and pyruvate/lactate MRI studies remain experimental. Positron emission tomographic (PET) studies using fluorine-18-fluorodeoxyglucose have been shown to correlate with the grade of the tumor. The higher grade gliomas are hypermetabolic (*3,4*). However, the limited availability and the high cost of PET creates a mandate for an alternative procedure. Anecdotal reports exist of single-photon brain images following the intravenous or intra-carotid administration of radiolabeled glioma-specific monoclonal antibodies of murine;human or human:human origin. These approaches suffer from inconsistencies reflecting the variability of the blood brain barrier as well as the nonspecificities of the antibody.

The report in this issue of the *Journal* by Kim et al. (*5*) confirms earlier studies by Kaplan (*6*), Mountz (*7*), and Black (*8*), and provides a new technique which measures thallium-201 ($^{201}$Tl) uptake in primary brain tumors by single-photon emission computed tomography (SPECT) imaging.

It has been shown that $^{201}$Tl is preferentially taken up by active tumor cells and not by normal cells, edematous tissue, nor necrotic areas. Using an index comparing tumor uptake normalized to the homologous contralateral hemisphere and corrected for tissue attenuation, Kim has been able to differentiate low- from high-grade gliomas. A prospective study will be required to quantitate the accuracy and sensitivity of the technique for preoperative assessment of tumor grade as well as the response to postoperative therapy. (Chemotherapy and radiation are provided with the hope of reducing the population of malignant cells and, if successful should reduce the metabolic rate of the tumor.)

Fully 80% of malignant glial tumors either contain benign glial precursors or develop in the setting of a previously nonenhancing "benign" glioma (*9*). The care of patients, whose seizure or personality change heralds the appearance of a nonenhancing CT or MRI benign glioma, has divided physicians into two camps. The more aggressive neurooncologist argues for early biopsy of "apparently low-grade astrocytoma" and emphasizes data supporting the role of early irradiation. More conservative therapists, aware of the uncertain efficacy and toxicity of cranial irradiation, reserve operative intervention until either the mass enlarges or enhances on scan (CT or MRI). Two national cooperative cancer study groups The Brain Tumor Collaborative Group and the Radiation Therapy Oncology Group are in the process of evaluating the efficacy of biopsy of presumed low-grade gliomas followed by immediate, in comparison to delayed irradiation (BTCG Protocol 87-30).

Radiation therapy and chemotherapy are provided for patients with anaplastic astrocytoma or glioblastoma multiforme. Because of tumor heterogeneity, histologic diagnosis may not always be accurate. This is especially true with stereotactic biopsies where sampling errors are more likely and the grade of the tumor incorrectly stated. The natural history of a tumor is dictated by its most malignant part. It is expected that two approaches will solve these sampling concerns: Investigators have begun to perform CT or MRI in registration with both radionuclide and PET imaging while others have used radionuclide scans to plot coordinates for stereotactic brain biopsy (*10*).

The evaluation of the response of malignant glioma to treatment poses an additional burden to clinicians. Necrosis of tumor and surrounding brain tissue is associated with conventional radiation therapy and occurs in fully three-quarters of patients treated with CT-guided stereotactic brain implants of iodine-125, high-dose focused proton beam boosts, or computer-oriented stereotactic radiosurgery (gamma knife).These necrotic masses appear as edematous-enhancing CT or MRI lesions 6–18 mo after therapy (*11*). Similar necrotic changes follow intraarterial infusions of drugs such as BCNU and Cis-Platin or high doses of Methotrexate given by vein after cranial irradiation. CT and MRI studies are unable to distinguish residual tumor from tumor necrosis and tumor recurrence. PET imaging has been reported to be very helpful in separating tumor from necrosis.

By demonstrating "strong statistical differences" between the $^{201}$Tl index in low-grade versus high-grade tumors, Kim et al. provide a rational basis for the systematic evaluation of preoperative patients with nonenhancing CT or MRI lesions as well as those patients whose enhancing lesions have emerged in the setting of an experimental therapy.

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