Preoperative assessment of meningioma aggressiveness by Thallium-201 brain SPECT

Reza Mirfallah[1], Masoud Mehrazin[1], Fereydoun Rastgou[2], Ahmad Bitarafan-Rajabi[2], Abdoulreza Shojaei[1], Hasan Firoozabadi[2], Nahid Yaghoobi[2], Hadi Malek[2], Mahsa Kargar[3]

[1]Department of Neurological Surgery, Dr Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran
[2]Department of Nuclear Medicine, Rajaei Cardiovasular, Medical & Research Center, Iran University of Medical Sciences, Tehran, Iran
[3]Department of Pathology, Emam Hosein Hospital, Semnan University of Medical Sciences, Semnan, Iran

ABSTRACT

Introduction: Meningioma is usually a benign brain tumor, but sometimes with aggressive course. The aim of this study was to assess the ability of ^{201}Tl Brain SPECT to differentiate the pathologic grade of meningioma preoperatively.

Methods: Thirty lesions in 28 patients were evaluated in this study. Early (20 minutes) and late (3 hours) brain SPECT images were performed and early uptake ratio (EUR), late uptake ratio (LUR) and retention index (RI) were calculated. All patients were operated and pathologic grade of tumors were defined according to World Health Organization grading system.

Results: SPECT results were compared in different pathologic groups. Data analysis clarified no significant difference of EUR in benign and aggressive meningioma (P=0.2). However LUR and RI were significantly higher in aggressive tumors (P=0.001 and P=0.02, respectively).

Conclusion: According to our data Tl-201 Brain SPECT with early and late imaging has 80% sensitivity and specificity to differentiate malignant from benign meningioma.

Key words: Thallium-201; Brain SPECT; Meningioma; Aggressiveness

Corresponding author: **Dr** Reza Mirfallah, Arad Hospital, Somaye Streert, Tehran, Iran. E-mail: rmflialestani@yahoo.com

INTRODUCTION

Meningiomas are the second most common primary brain tumors which their incidence increases with age [1, 2]. They are typically considered as benign lesions with slow growth, but some of them (1-10%) have aggressive course [3]. Routinely, surgery is the modality of choice for treatment. Ten to thirty percent of meningioma reoccurs following complete surgical resection. Although, degree of tumor resection is the most important factor that affect tumor recurrence, there are some other factors including brain invasion, bone and soft tissue involvement and tumor higher pathologic grade that have strong prognostic effects [4, 5]. Total tumor removal may be difficult to achieve in some circumstances such as involvement of venous sinuses or major vessel encasement [3].

The prediction of the outcome and prognosis of the tumors is outmost importance to the surgeon as well as the patients. Although routine imaging studies such as computed tomography (CT), magnetic resonance imaging (MRI) and angiography provide some important information about tumor size, location and invasion to surrounding tissues, they cannot predict aggressiveness and malignant behavior of high grade tumors [6]. Therefore a new less invasive functional method to evaluate tumor behavior is needed. In recent years quite a number of different methods like karyotyping, genetic survey, hormonal receptor studies, detection of MIB1 labeling index and Ki67 are introduced to predict the course of meningioma and their outcome. All of these modalities however, need tumor tissue sampeling [7-9].

Thallium-201 chloride (^{201}Tl) is a potassium analogue which has an affinity for the sodium-potassium-adenosine triphosphate pump [3, 10]. It has good imaging characteristics without excessive patient radiation dose and can substitutes for potassium ions and be taken up by cells through activation of sodium-potassium-adenosine triphosphate pump [11]. [201]Tl uptake correlates to regional blood flow, blood brain barrier (BBB) function, cellular activity and cell number of the tumor [3, 10].

There are strong evidences that tumor imaging with ^{201}Tl definitely reflects more advantages cellular characteristics than other radionuclide traces [12, 13]. Recently some investigations have been done on gliomas and ring enhancing lesions to predict their pathology or to differentiate tumor recurrence from radionecrosis [14-18]. However the roll of ^{201}Tl brain single photon emission tomography (SPECT) in differentiation of histopathology and invasiveness of meningioma is not fully defined. The purpose of this study was to evaluate the usefulness of [201]Tl Brain SPECT for possible differentiation of the pathologic grade of meningioma, preoperatively.

METHODS

Patient population

During 3 years period, all patients with brain tumor who were labeled according to physical exam and imaging as meningioma and were candidate for surgery, were referred to nuclear medicine ward to perform TL- 201 brain SPECT.

Due to paranasal region uptake and posterior fossa venous sinus flow and probable technical error, skull base and posterior fossa meningioma were excluded. All the patients provided written, informed consent for participation in the study, and the study protocol was approved by the institutional Review Board and the Ethics Committee of Tehran University of Medical Sciences.

Data gathering

Early, at 20 minutes post-injection and late, at 3 hours, brain SPECT images were acquired using 3 mCi of [201]Tl. All acquisitions were performed in SPECT mode by a GE DST-Xli (USA) dual-head gamma camera, equipped with low energy-high resolution (LEHR) collimators. Data were collected from 64 projections of 30 sec, each were acquired with 64x64 matrix size and a zoom factor of 1.14 in a circular 360-degree arc around the patient. Energy windows were set at photo peak of ^{201}Tl with 10% width (70 ±10%, 135±10%, 167±10%, Kev).

All images were reconstructed using Brain SPECT application of VISION®POWER station (Version 6.0.0) GE Medical system.

Data were reconstructed using the ordered subset exceptional maximization (OSEM) with iteration=5 and subset=8. Transverse, coronal and sagittal sections were reconstructed without attenuation and scatter correction. Slice thickness was 3.8 mm.

Our system could not reconstruct images as a composite, so we decided to analyze only transverse images. Region of interest (ROI) were manually drawn around the lesion on the transverse image with maximum diameter of tumor in both early and late image.

Tumor margin was precisely determined by MRI images. For comparison, ROI were also drawn in the same size on contralateral normal brain in the same slice.

Average counts in each ROI were obtained and used for analysis. SPECT images analysis were performed by a single operator which was blinded about patient's clinical and pathologic data.

Three parameters were calculated according to following formula:

1: Early uptake ratio (EUR) = Average count of lesion/Average count of contralateral brain in early image

2: Late uptake ratio (LUR) = Average count of lesion/Average count of contralateral brain in late image

3: Retention index (RI) = LUR/EUR

Following the scanning, the patients were admitted in neurosurgery ward and underwent operation according to standard procedure. All patients were medicated by dexamethasone and loaded by IV dilantin for seizure prophylaxis. During operation, invasion of tumor to pia arachnoid, venous sinuses, Dura, bone, soft tissue and skin were recorded.

Tumoral tissues were sent for pathologic examination and an experienced pathologist who was blinded about SPECT data reported the grade of tumors according to the World Health Organization (WHO) classification, which have been updated in 2007 on the basis of number of mitosis, existence of macronucleoli, tumor cellularity, existence of cell components with high nuclear to cytoplasmic ratio, growth pattern, loss of differentiated features, zones of necrosis and invasion to surrounding tissue [19].

Due to variable range of tumor invasion to surrounding tissues in both low-grade and high-grade tumors, we divided the tumors into two groups of benign and invasive types. Therefore, grade I tumors were classified as benign whereas grade II and III tumors were categorized as invasive lesions. SPECT images analysis were performed by a single operator which was blinded about patient's clinical and pathologic data. This study was a prospective semi-quantitative research. The statistical analyses were performed with SPSS software (SPSS 16.0 for Windows, SPSS Inc., Chicago, Illinois) with Mann-Whitney Test and for detection of cut off point, ROC curve was drawn. Also sensitivity and specificity were calculated.

RESULTS

Twenty eight patients (19 females, 9 men) diagnosed for brain tumor, were included in this study. Of these patients, one had two lesions, and one patient was scanned two times due to tumor recurrence after 2 years follow up so 30 tumor lessions in histopathologic evaluation were recorded.

Mean age of patients was 51.8 years in range of 19-78 years. In pathologic analysis, twenty (63.7%) tumors were reported as grade I, including 16 meningothelial, 3 transitional and 1 angiomatous subtypes (Figure 1).
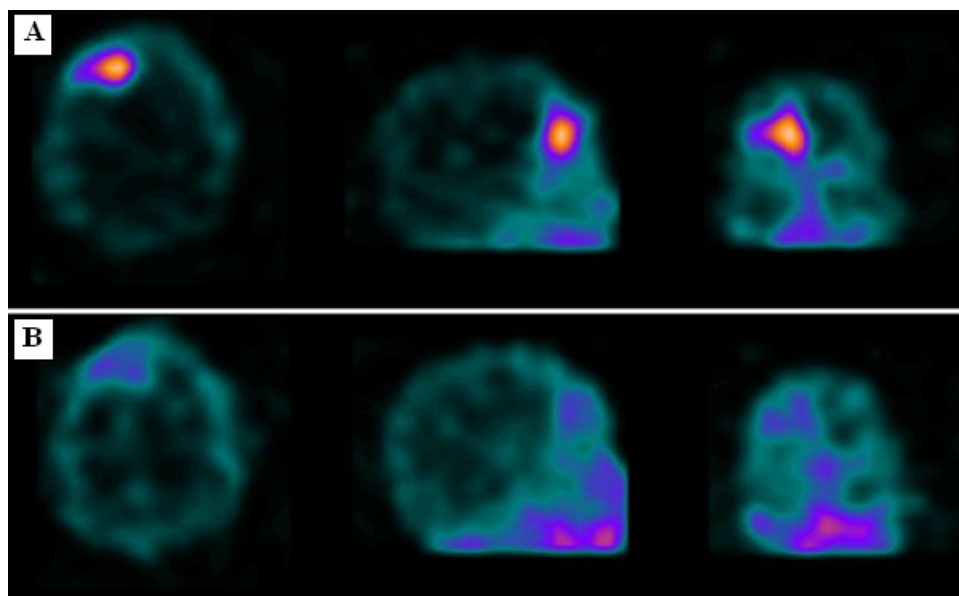

Fig 1. Early (A) and late (B) Tl-201 brain SPECT in a 48-year-old male with meningothelial grade I; EUR, LUR and RI were 9.11, 3.06 and 0.336, respectively.
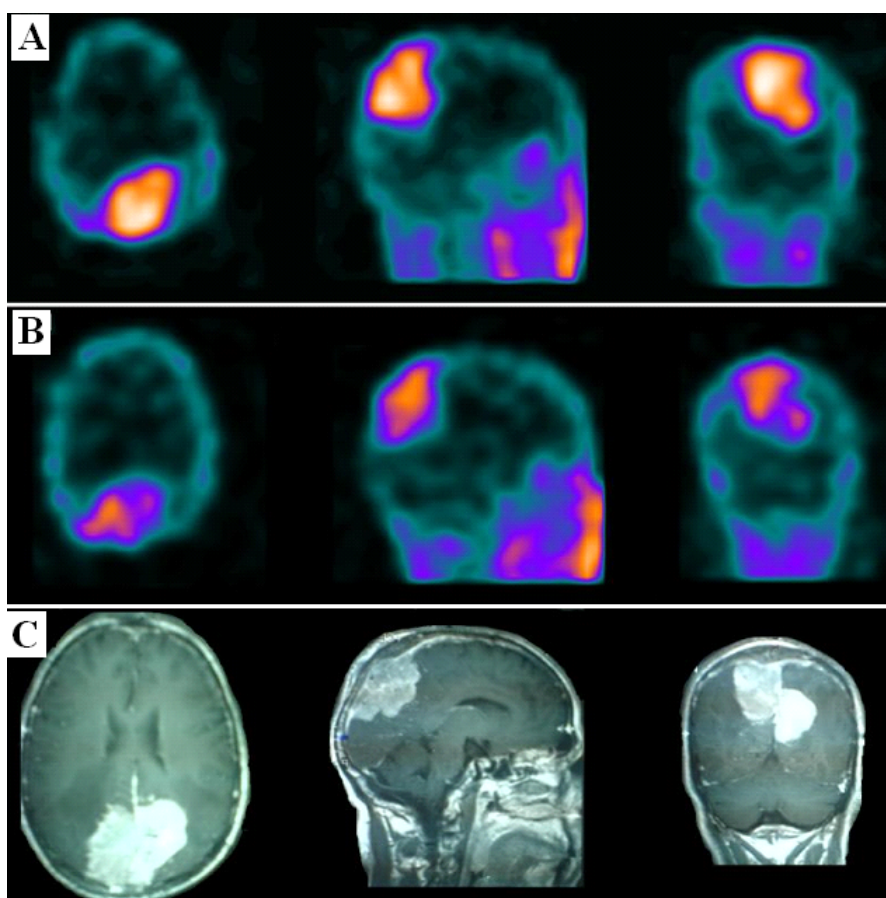
Fig 2. Early (A) and late (B) Tl-201 brain SPECT and comparable brain MRI (C) in a 57-year-old male with pathology finding atypical grade II; EUR = 18.01, LUR = 8.54 and RI = 0.474.

Eight (26.7%) tumors were reported as grade II, all of which were atypical meningioma (Figure 2). The remaining two (6.7%) were reported as grade III. One was anaplastic (Figure 3) and the other was papillary meningioma (Figure 4). The pathologic examination of the recurrent tumor re-confirmed the diagnosis of atypical meningioma (grade II) twice. In a patient with two simultaneous lesions, both of them demonstrated a benign appearance (grade I) in pathologic examination.

Results of SPECT are shown in Table 1. All tumors clearly demonstrated uptake in both early and late images. EUR values were slightly higher in malignant tumors relative to benign lesions but there was no significant difference between two groups (P= 0.08). LUR & RI values were significantly higher in malignant tumors relative to benign lesions (P = 0.001 and P =0.02, respectively).

For detection of cut off point, we draw ROC curve for two parameters which had significant differences between two groups. Area under surface of LUR and RI were 0.92 (P < 0.001) and 0.76 (P < 0.022) respectively. According to coordinates of curves, in RI >0.75 and LUR >4, the sensitivity and specificity of ^{201}Tl Brain SPECT were 80% to predict aggressiveness of meningioma (Figure 5).

DISCUSSION

The current study revealed that ^{201}Tl Brain SPECT can be considered as feasible modality to predict aggressiveness of meningioma preoperatively with 80% sensitivity and specificity. Although Nadel have reported the sensitivity and specificity as 77% and 93% for detection of pediatric brain tumors with ^{201}Tl, Datta and co-authors have demonstrated that sensitivity and specificity of ^{201}Tl were 82.7%, and 83.3% in evaluation of morphological alterations of brain tumors post radiation therapy with and without evidence of recurrent tumor based on imaging studies [13, 20]. In our study, although EUR showed no significant differences between malignant and benign lesions in agreement with Sun et al, it was a good indicator of vascularity and blood flow of tumors [12]. Review of our cases showed that EUR in angiomatous meningioma, was 10.3.
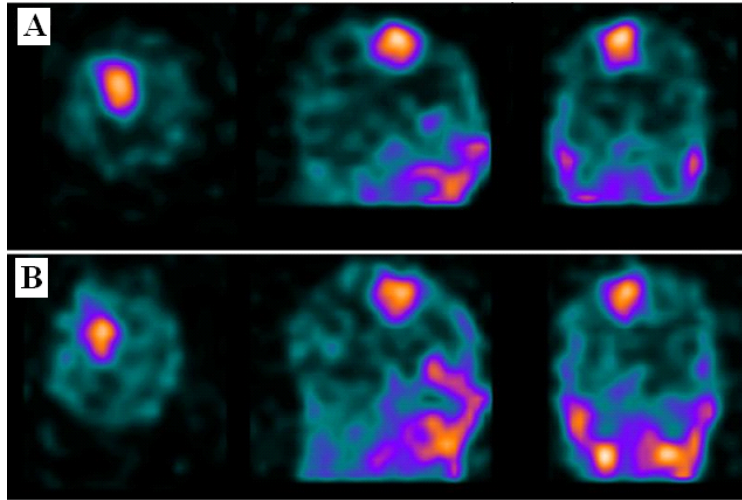
Fig 3. Early (A) and late (B) Tl-201 brain SPECT in a 69-year-old male representing anaplastic grade III ; EUR = 5.57, LUR = 4.49 and RI = 0.815.
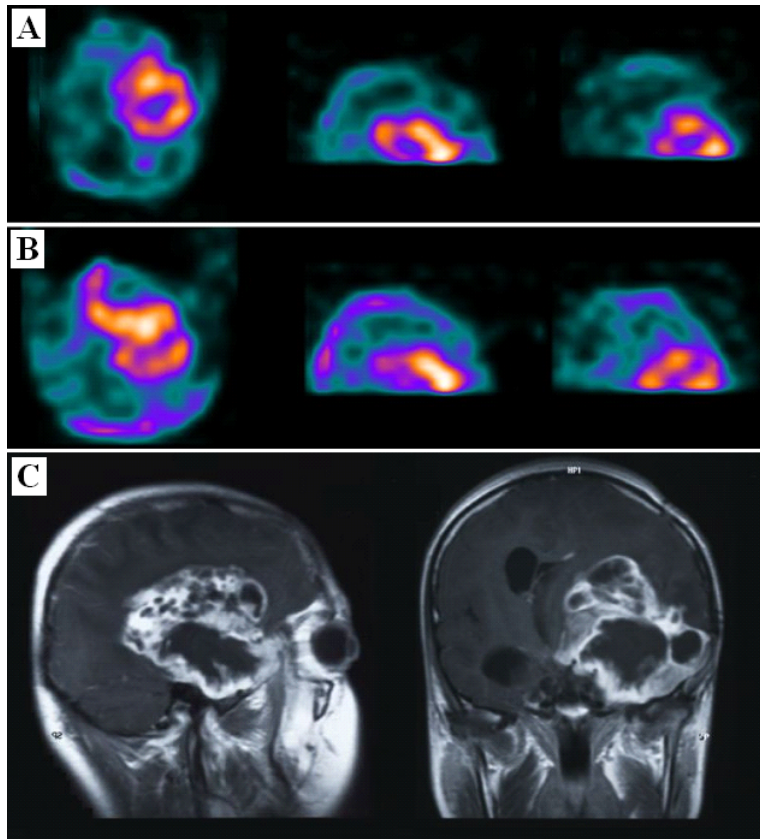

Fig 4. Early (A) and late (B) Tl-201 brain SPECT and comparable brain MRI (C) in a 20-year-old male with pathology finding clear cell papillary grade III; EUR = 6.11, LUR = 6.00 and RI = 0.982. This patient expired 5 month after surgery.

	Area	SE	P Value	95% Confidence Interval	
				Lower Bound	Upper Bound
Late uptake	0.92	0.048	0.000	0.775	1.000
Retention index	0.76	0.107	0.022	0.551	0.969

P<0.05 is significant
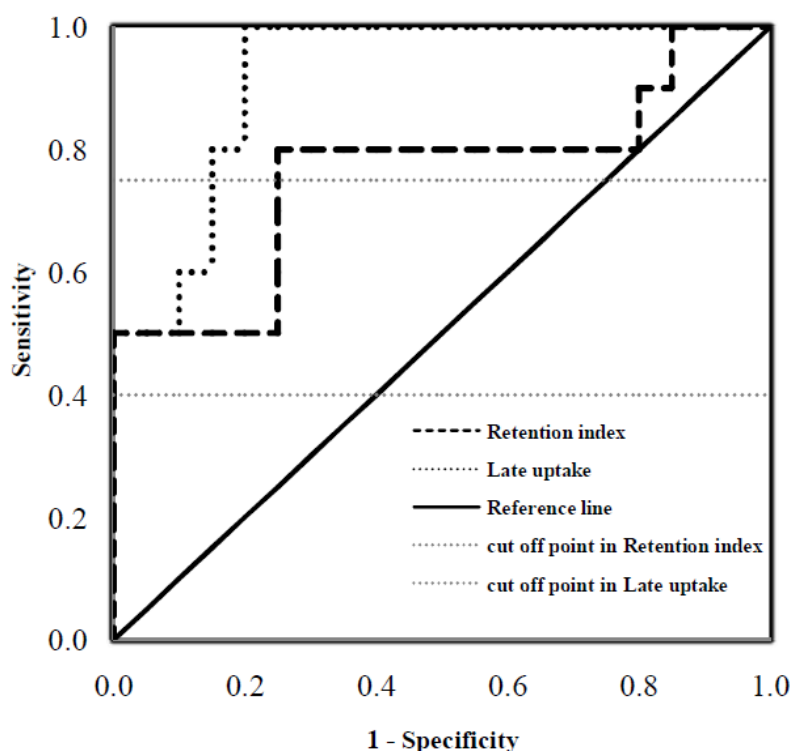SE (Standard Error)

Fig 5. The ROC curve analysis.

It was more than mean early ²⁰¹Tl uptake for malignant and nearly 2 times more than early uptake for benign group. Conversely in transitional type tumors which had less vascularity and low blood flow, mean EUR was less than benign group. In fact vascularity of lesion may be determined by high EUR and ²⁰¹Tl accumulation. These findings are congruent with other investigations that showed positive correlation between thallium early uptake and tumor vascularity [21, 22]. Perhaps high EUR can be considered as a good index for preoperative embolization. On the contrary, LUR and RI were significantly higher in malignant group. This may be due to higher mitotic activity, rapid growth rate and higher sodium potassium pump activity in malignant lesions [5]. Surprisingly, we noticed that both benign and low vascular meningioma or two of three

invasive tumors which had been located in posterior parasagittal region, had very low RI values. Review of Magnetic resonance venography (MRV) of these 3 patients revealed that in 2 patients with low RI values, venous sinus flow was high and in third with high RI values, lumen of the sinus had been completely occluded. We propose that RI could be influenced by tumor vascularity and blood flow. In fact transitional type tumors with low LUR amounts had definitely high retention indexes irrespective of their benign course and low mitotic activity because of low blood flow of the lesions. Regarding different retention rate in various subtypes of meningioma, it indicates that, factors like proliferation rates (other than vascularity) are associated with malignant course [3]. Long–lasting retention of thallium provides some information about malignant potential

of meningioma. We observed that in some malignant tumors due to a high venous flow around the tumors, thallium was washed out rapidly and consequently decreased RI values were obsereved. Sun and colleagues suggest that thallium uptake and retention in brain tumors are associated with histologic grade of the tumor [12]. According to Ooigawa et al rapid and high thallium uptake with low washout is an indicator for brain tumor malignancy [23]. So tumors with high EUR and rapid thallium washout may not be malignant.

We suggest that a benign and highly vascular meningioma could be considered if ^{201}TI retained index <0.75 and EUR is high, but a benign and low vascular meningioma could be considered if ^{201}TI retained index >0.75 but EUR and LUR are low and a malignant meningioma could be considered If RI >0.75 and LUR > 4. According to these findings, sensitivity and specificity of ^{201}Tl Brain SPECT were 80% to differentiate malignant from benign meningioma.

CONCLUSION

^{201}Tl Brain SPECT is a feasible preoperative method to differentiate benign and aggressive meningioma with 80% sensitivity and specificity. Repeating the study with more number of patients may be helpful to confirm these results.

REFERENCES

1. van Alkemade H, de Leau M, Dieleman EM, Kardaun JW, van Os R, Vandertop WP, van Furth WR, Stalpers LJ. Impaired survival and long-term neurological problems in benign meningioma. Neuro Oncol. 2012 May;14(5):658-66.

2. Larjavaara S, Haapasalo H, Sankila R, Helén P, Auvinen A. Is the incidence of meningiomas underestimated? A regional survey. Br J Cancer. 2008 Jul 8;99(1):182-4.

3. Kinuya K, Ohashi M, Itoh S, Sakai S, Yamamoto K, Kakuda K, Nobata K, Terahata S, Taki S, Kinuya S. Thallium-201 brain SPECT to diagnose aggressiveness of meningiomas. Ann Nucl Med. 2003 Sep;17(6):463-7.

4. Marosi C, Hassler M, Roessler K, Reni M, Sant M, Mazza E, Vecht C. Meningioma. Crit Rev Oncol Hematol. 2008 Aug;67(2):153-71.

5. Valotassiou V, Leondi A, Angelidis G, Psimadas D, Georgoulias P. SPECT and PET imaging of meningiomas. ScientificWorldJournal. 2012;2012:412580.

6. Jaeckle KA. Neuroimaging for central nervous system tumors. Semin Oncol. 1991 Apr;18(2):150-7.

7. Monleón D, Morales JM, Gonzalez-Segura A, Gonzalez-Darder JM, Gil-Benso R, Cerdá-Nicolás M, López-Ginés C. Metabolic aggressiveness in benign meningiomas with chromosomal instabilities. Cancer Res. 2010 Nov 1;70(21):8426-34.

8. Hilbig A, Barbosa-Coutinho LM. Meningiomas and hormonal receptors. Immunohistochemical study in typical and non-typical tumors. Arq Neuropsiquiatr. 1998 Jun;56(2):193-9.

9. Quiñones-Hinojosa A1, Sanai N, Smith JS, McDermott MW. Techniques to assess the proliferative potential of brain tumors. J Neurooncol. 2005 Aug;74(1):19-30.

10. Tonami N. Thallium-201 SPECT in the evaluation of gliomas. J Nucl Med. 1993 Dec;34(12):2089-90.

11. Maddahi J, Berman D. Detection, Evaluation, and Risk Stratification of Coronary Artery Disease by Thallium-201 Myocardial Perfusion Scintigraphy. In: DePuey EG, Berman DS, Garcia EV. Cardiac SPECT imaging. 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 2001. p. 155-78.

12. Sun D, Liu Q, Liu W, Hu W. Clinical Application of 201Tl SPECT Imaging of Brain Tumors. J Nucl Med 2000; 41(1):5-10.

13. Nadel HR. Thallium-201 for oncological imaging in children. Semin Nucl Med. 1993 Jul;23(3):243-54.

14. Ancri D, Basset JY, Lonchampt MF, Etavard C. Diagnosis of cerebral lesions by Thallium 201. Radiology. 1978 Aug;128(2):417-22.

15. 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 Jan;28(1):47-52.

16. 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 Sep;71(3):342-6.

17. Kim KT, Black KL, Marciano D, Mazziotta JC, Guze BH, Grafton S, Hawkins RA, Becker DP. Thallium-201 SPECT imaging of brain tumors: methods and results. J Nucl Med. 1990 Jun;31(6):965-9.

18. Kosuda S, Fujii H, Aoki S, Suzuki K, Tanaka Y, Nakamura O, Shidara N. Reassessment of quantitative thallium-201 brain SPECT for miscellaneous brain tumors. Ann Nucl Med. 1993 Nov;7(4):257-63.

19. Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, Burger PC, Jouvet A, Scheithauer BW, Kleihues P. The 2007 WHO classification of tumours of the central nervous system. Acta Neuropathol. 2007 Aug;114(2):97-109.

20. Datta NR, Pasricha R, Gambhir S, Prasad SN, Phadke RV. Comparative evaluation of 201Tl SPECT and CT in the follow-up of irradiated brain tumors. Int J Clin Oncol. 2004 Feb;9(1):51-8.

21. Sugo N, Kuroki T, Nemoto M, Mito T, Seiki Y, Shibata I. Difference in 201TlCl accumulation mechanism in brain tumors: a comparison of their Na(+)-K+ ATPase activities. Kaku Igaku. 2000 Jul;37(4):311-8.

22. Taki S, Kakuda K, Kakuma K, Kobayashi K, Ohashi M, Ito S, Yokoyama M, Annen Y, Tonami N. 201Tl SPET in the differential diagnosis of brain tumours. Nucl Med Commun. 1999 Jul;20(7):637-45.

23. Ooigawa H, Miyazawa T, Otani N, Fukui S, Nawashiro H, Shima K. Usefulness of thallium-201 chloride single photon emission computed tomography for the preoperative diagnosis of fourth ventricle meningioma--case report. Neurol Med Chir (Tokyo). 2004 Dec;44(12):660-4.