Semi-quantitative evaluation of uveal malignant melanoma with N-isopropyl-p-^{123}I-iodoamphetamine (I-123 IMP)

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Abstract

N-isopropyl-p-^{123}I-iodoamphetamine (I-123 IMP), which was originally designed for brain scanning, has been used in the assessment of malignant melanoma. Sometimes I-123 IMP is the only or the best tool to evaluate malignant melanoma, for example, when the ocular manifestations are not clear or not characteristic and when the viability needs to be assessed after therapy. It is thought very important to establish the objective and quantitative evaluation of I-123 IMP.

Thirty patients who underwent 35 examinations were evaluated. Fourteen patients (19 examinations) were histologically proved to have uveal malignant melanoma (group A), and 2 patients were clinically diagnosed as metastatic choroidal tumor from lung and breast (group B), and 14 patients were given clinical or histological diagnoses of benign pigmented lesion or tumor (group C). We employed two parameters, i.e. the retention index and the tumor to non-tumor (T/N) ratio. Accuracy was 80.0% by the retention index and 88.6% by the T/N ratio. Malignant melanoma could usually be distinguished from other lesions. However, more accurate semi-quantification is needed to borderline disease or for follow up study. Further studies are needed.

Introduction

Uveal malignant melanoma, which arises in the iris, the ciliary body, or the choroids, is a rare disease. As most of the cases show a characteristic ocular manifestation on slit-lamp biomicroscopy, binocular fundus examination, ultrasonography, and MRI, the diagnosis is not difficult. But on account of the complications such as cataract, retinal detachment, and vitreous hemorrhage, sometimes the ocular manifestation becomes unclear[1]. After treatment such as brachytherapy (episcleral plaque radiotherapy) and transpupillary thermotherapy (TTT), tumor size and/or contour seldom changes, so it is very difficult to evaluate the effectiveness of the therapy. After local resection of the tumor, some iatrogenic substance or the complications makes the ocular manifestation more intricate.

We tried semi-quantitative evaluation of I-123 IMP SPECT in orbital tumors to evaluate its usefulness for the diagnosis of malignant melanoma.

Materials and methods

Patient Characteristics

Thirty patients (17 women, 13 men, mean age = 54.7 yrs) were evaluated in 35 examinations. Fourteen patients (19 examinations) were histologically proved to have uveal malignant melanoma (group A), and 2 patients were given clinical diagnoses of metastatic choroidal tumor from lung and breast (group B), and 14 patients were clinically or histologically founded to have benign pigmented lesion or tumor (group C). They included hemangioma, adenoma (operated), melanocytoma, nevocellular nevus (operated) and choroidal nevus, age-related macular degeneration. In those

non-operated cases, the ocular manifestations are stable more than one year.

Semi-quantitative I-123 IMP SPECT

Early images were obtained 20 minutes after intravenous injection of 111MBq I-123 IMP, supplied by Nihon Medi-Physics Co. Ltd. (Tokyo, Japan). Delayed images were obtained after 24 hours. In each phase, the whole body and SPECT images were obtained during a period of 30 minutes using a IRIX triple head gamma-camera (Picker International, Inc., Cleveland, OH, USA) equipped with a high-resolution parallel collimator. The acquisition parameters included a 20% energy window centered on 159 KeV, 120 projection angles over 360°, and a 128×128 matrix with a pixel width of 2.3 mm in the projection domain. The projection data were profiltered through a Butterworth. For uniform attenuation correction, Chang's first-order method was used. The final image slices were set up parallel to the orbitomeatal line (OM line) and were obtained at intervals of 4.6 mm through the entire brain.

Data analysis

On the cross section, which shows the largest area of the orbit, circular regions of interest (ROI) with a diameter of about 1.7 cm corresponded to the eyeball of the affected side as the specific uptake, and the contralateral eyeball as the non-specific uptake (Fig. 1) were drawn on both early and delayed images. The retention index was calculated as follows: retention index=(delayed ratio-early ratio)/early ratio×100 (%). The tumor-to-non tumor ratio (T/N ratio) was also calculated. These values were compared among the three groups, i.e. malignant melanoma (group A), malignant tumor except for malignant melanoma (group

Fig. 1 ROIs on the I-123 IMP: No. 1 was drown on the affected eyeball as the specific uptake, and No. 2 was on the contralateral eyeball as the non-specific uptake.

B), and benign pigmented lesion or tumor (group C).

Results

1) Retention Index

The mean retention index of all cases was 86.3±119.6 (minimum value: −72.2, maximal value: 450.5), and 155.9±120.1 in group A, 0.3±41.4 in group B, 4.0±42.0 in group C, and 3.5±40.6 in group (B+C) (Fig. 2). When the cutoff level of the retention index was set at 30, 17 of 19 melanomas were identified correctly. As for the other 16 lesions, 5 cases showed a high retention index. One was operated and proved out to be nevocellular nevus with atypical cells, and one was an atypical shaped choroidal nevus, and there were 3 cases of melanocytoma. There was a significant difference in retention index between group A and (B+C) ($P<$0.005). The sensitivity when the retention index cutoff was set at 30 was 89.5%, specificity was 68.8% and accuracy was 80.0%.

2) T/N ratio

The T/N ratio of all the melanomas increased on the delayed image and the ratio distributed from 1.4 to 8. On the other hand, in cases of metastases and benign lesions, the T/N ratio increased in six cases and decreased in 10 cases. They were all below 1.7 on the delayed image (Fig. 3). There was a significant difference in the T/N ratio on the delayed image between group A and (B+C) ($P<$0.001). The sensitivity when the T/N ratio cutoff was set at 1.5 was 94.7%, specificity was 81.2% and accuracy was 88.6%. This fact corresponds to the visual evaluation indicating that delayed images are more useful.

(Case 1)

A 47-year-old woman with a choroidal pigmented tumor was evaluated on the MRI T1-weighted image (Fig. 4a) and T2-weighted image (Fig. 4b). The tumor showed the typical signal intensity of malignant melanoma. The I-123 IMP early image (Fig. 4c) showed good accumulation on the whole brain cortex, but the orbital uptake was not clear on both sides. In the delayed image (Fig. 4d), the left orbital uptake increased compared with the opposite side. Moreover decrease in brain accumulation made it clearer. The retention index was 172.0. The T/N ratio increased from 1.7 to 4.7. Choroidal malignant melanoma was conformed by tumorectomy.

(Case 2)

A 32-year-old woman was followed by I-123 IMP after local resection of choroidal malignant melanoma (Fig.5a). As the eyeball was filled with silicon oil, ocular manifestations, including MRI, were not clear (Fig. 5b). I-123 IMP was performed at 6 (Fig. 5c) and 15 months (Fig. 5d) after local resection of the tumor. The accumulation in the left eyeball in the delayed
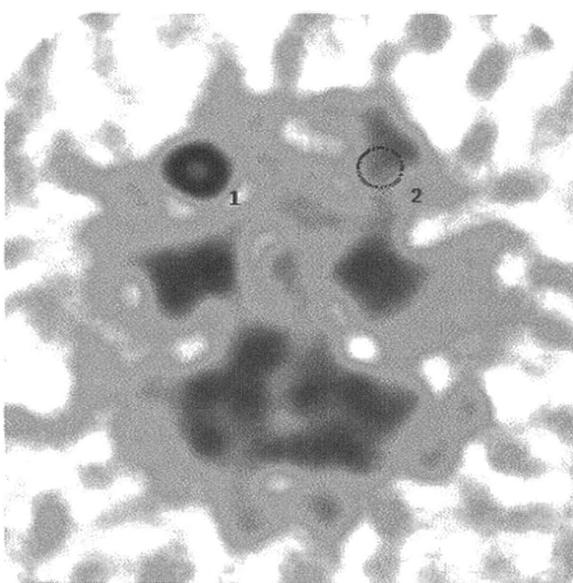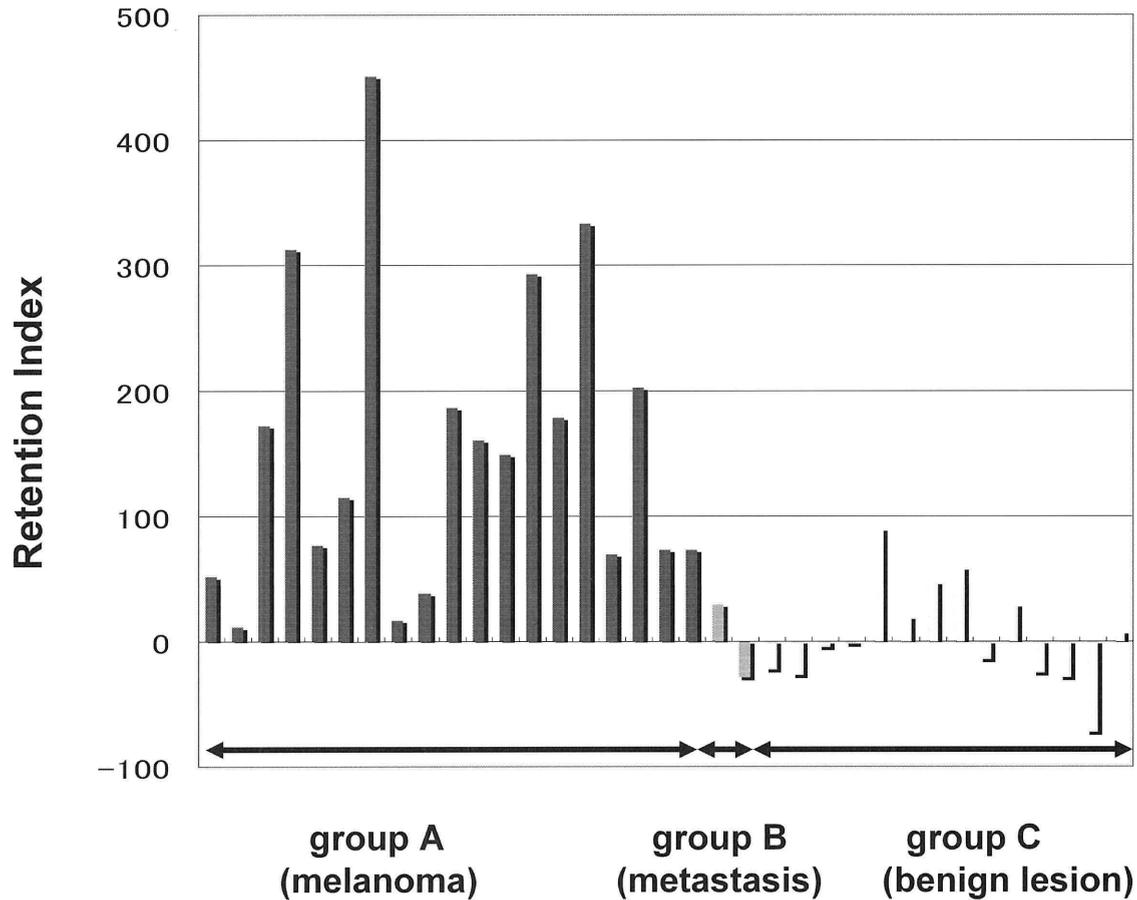
Fig. 2　Retention index was calculated based on the early and delayed ratio of the affected eyeball.　[retention index=(delayed ratio-early ratio)/early ratio ×100 (%)]
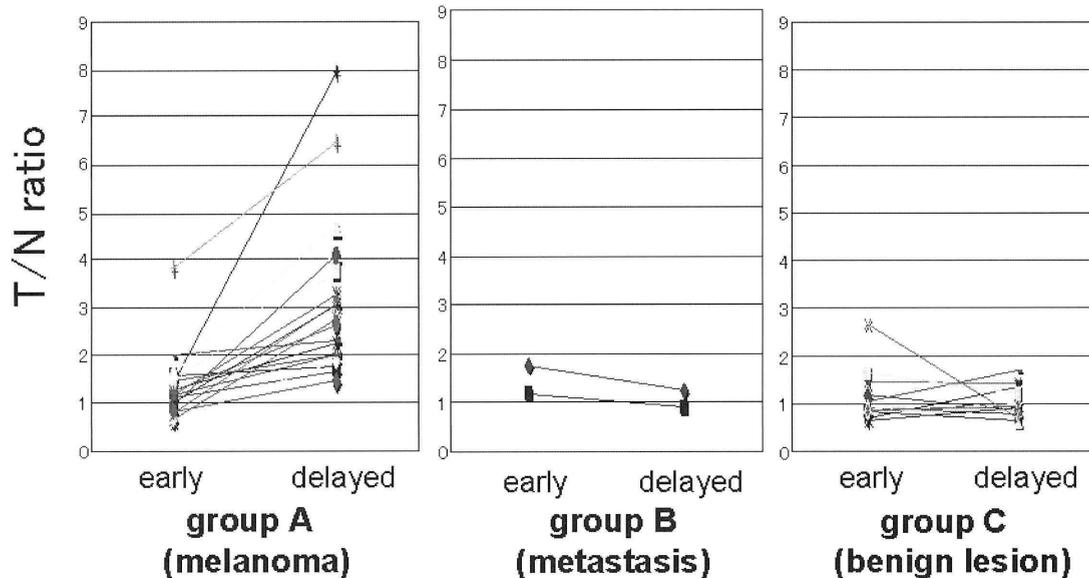

Fig. 3　T/N ratio was calculated based on the affected and non-affected uptake on the same phase image.　[T/N ratio= tumor counts/non-tumor counts]

image became clearer on the latter examination and the retention index increased from 17.1 to 37.9. The T/N ratio on the delayed image decreased from 2.3 to 2.0, but both are above 1.5. Enucletion of the recurrent 3×4 mm tumor was performed.
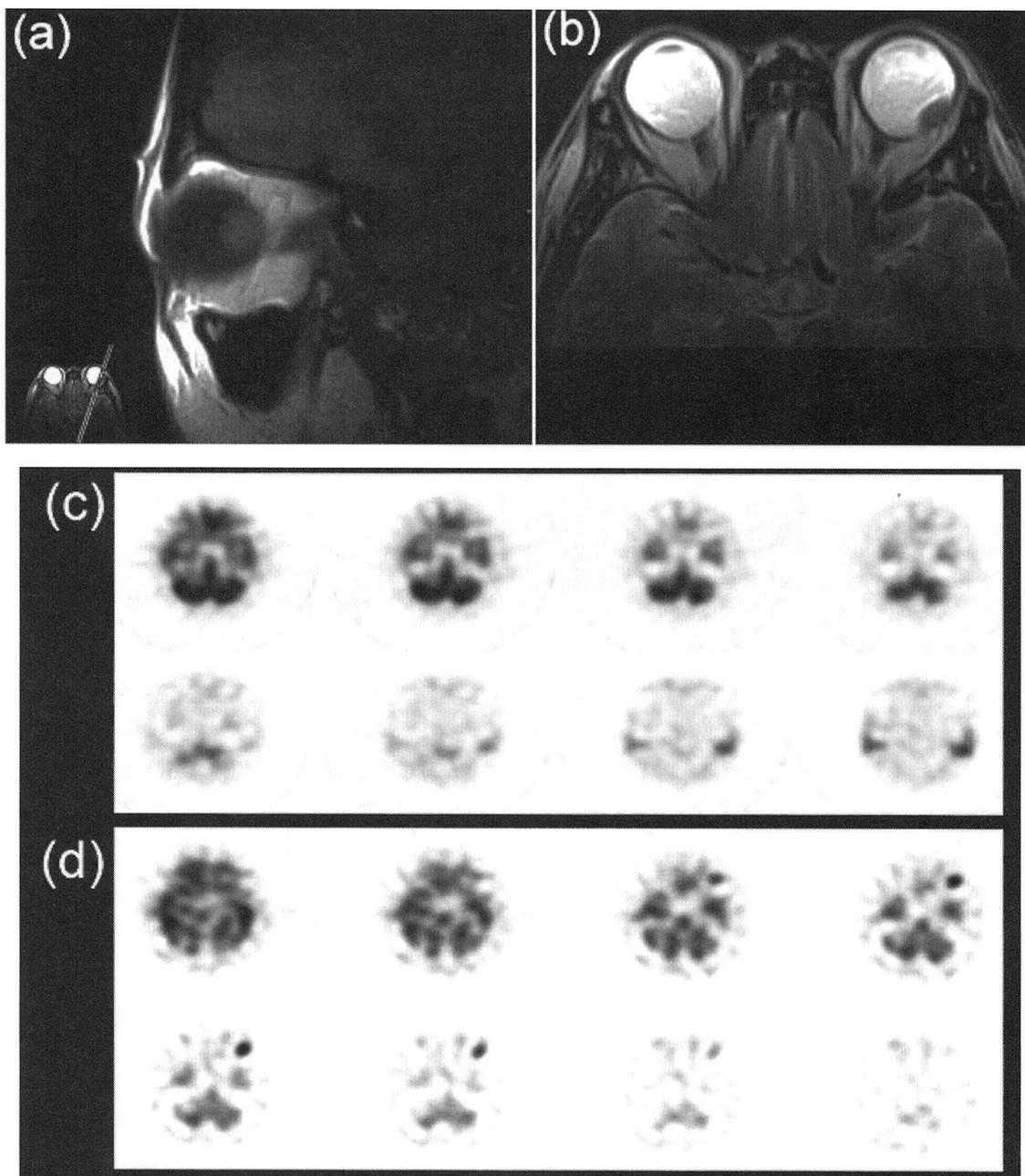
Fig. 4 A case of choroidal malignant melanoma : (a) MRI T1-weighted oblique image (b) MRI T2-weighted axial image (C) I-123 IMP early image (d) I-123 IMP delayed image

Discussion

I-123 IMP, which was originally designed for brain scanning, has been used in the assessment of malignant melanoma[2-5]. A recognized feature of this agent is that it accumulates in melanin- producting tissue[6)7]. Though the mechanism is unclear, this tracer is hypothesized to be taken up by melanin-producting tissue through the melanin synthesizing process from the precursor thyosine[8]. Moreover the accumulation depends on the tumor size and the quantity of melanin produced[9)10].

F-18 FDG PET is now used for the evaluation of malignant melanoma. However, the accumulation is not specific and the sensitivity is not so good[11)12]. Sometimes I-123 IMP is the only or the best tool to estimate the malignant melanoma, for example, when the ocular manifestations are unclear or not characteristic, and when the viability is to be assessed after therapy[13]. So it is very important to establish the objective and quantitative evaluation of I-123 IMP.

We employed two parameters, i.e. the retention index and T/N ratio. Accuracy was 80.0% by the retention index and 88.6% by the T/N ratio. The sensitivity was better than the specificity for each parameter. However there were two problems. First of all,
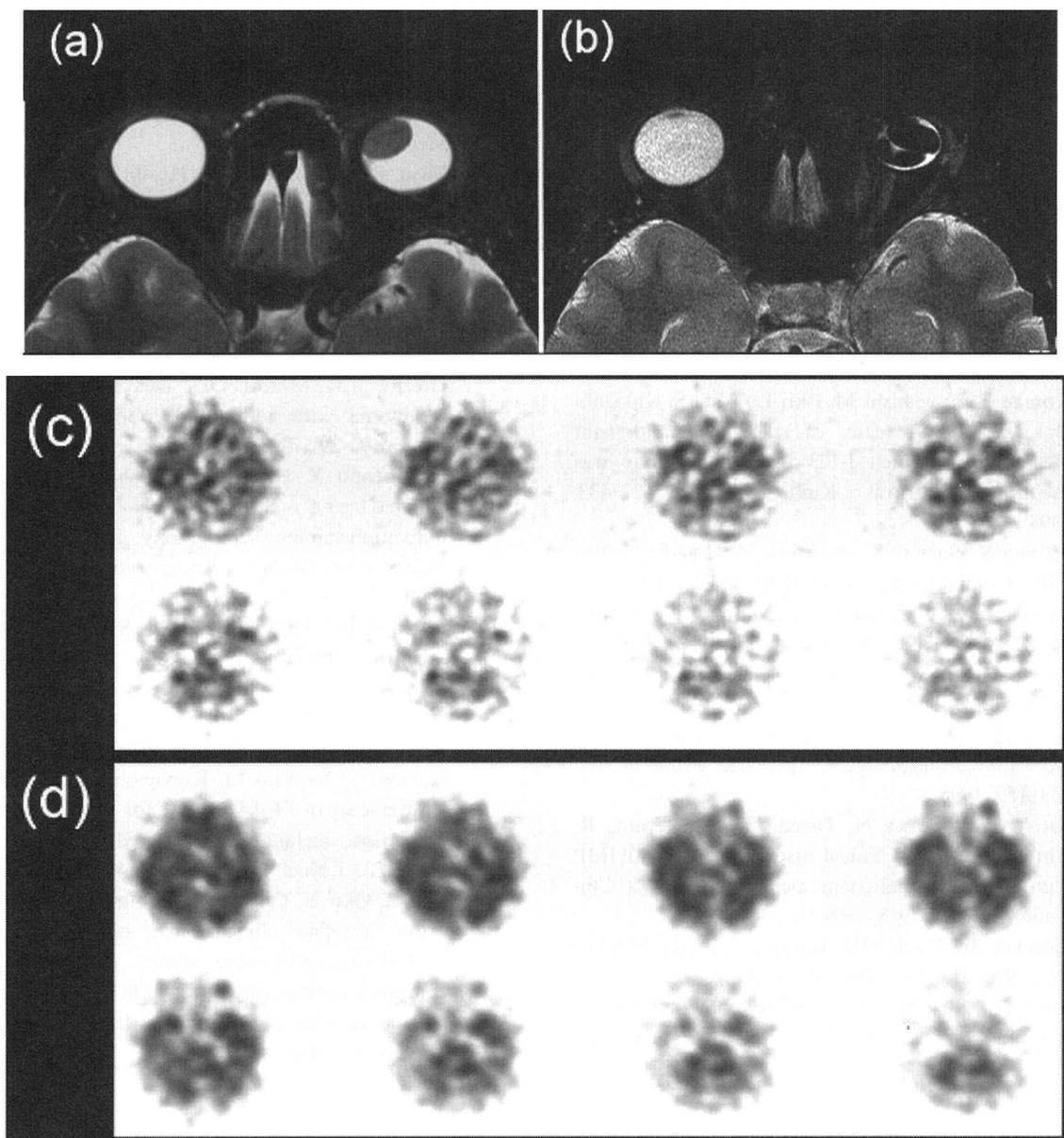
Fig. 5　A case of recurrence of choroidal malignant melanoma : (a) Preoperative MRI T1-weighted axial image (b) Postoperative MRI T1-weighted axial image (c) I-123 IMP delayed image 6 months after operation (d) I-123 IMP delayed image 12 months after operation

sometimes establishing the ROI might be arbitrary especially when the regional accumulation is faint. That is, in the delayed image accumulation of the whole brain the landmark image of the orbit is already decreased, in addition to the difficulty of distinguishing the faint accumulation from noise. That is the reason why specificity is lower than sensitivity. To use this method effectively for follow-up studies to estimate the effectiveness of therapy, or to predict the malignant transformation in the future, it is essential to quantitate the accumulation reproducibly and objectively. Fusion imaging with CT or MRI might be helpful. The second problem was what to select as the background. The retention index means the early uptake of the same

place is selected as the reference value, and the T/N ratio is calculated using the contralateral side of the same phase for the reference value. Lower accuracy obtained by the retention index might be related to the variation of the noise from early cerebral blood flow. Therefore a stable reference value should be selected. For more correct quantification, further studies are needed.

Conclusion

To semi-quantificate I-123 IMP, two parameters, i.e. retention index and T/N ratio were assessed. Malignant melanoma could usually be distinguished from other lesions. However, more accurate semi-quantification is needed to borderline disease or for

follow up study. Further studies are needed.

Acknowledgement

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ブドウ膜悪性黒色腫診断における N-isopropyl-p-^{123}I-iodoamphetamine (I-123 IMP) 半定量評価の有用性

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【要旨】　I-123 IMP は脳血流シンチグラフィ用トレーサーとして開発されたが、メラニン産生組織に強い親和性を示す事が知られており、悪性黒色腫の診断に用いられている。特に臨床所見または各種の画像診断が特異的でない場合には I-123 IMP 所見が診断根拠となる場合がある。また、治療効果を判定する上では集積の変化の検討が有用である。今回我々は、I-123 IMP による半定量評価を試み、その有用性を検討した。

　対象は 30 症例、延べ 35 回の I-123 IMP 検査で、症例の内訳は悪性黒色腫 14 例 (group A)、転移性悪性腫瘍 2 例 (group B) および良性腫瘍または色素沈着病変 14 例 (group C) である。I-123 IMP・111MBq を投与後 20 分と 24 時間後に頭部 SPECT を撮像し、各々早期相・遅延相とした。両側眼球に ROI を設定し、病変側および非病変側の集積カウントから retention index および T/N ratio の 2 つのパラメーターを算出した。

　悪性黒色腫の正診率は retention index を 30 以上とした場合は 80.0% であり，また T/N ratio を 1.5 以上とした場合は 88.6% であった。上記パラメーターによる半定量判定は有用であると考えられた。ただし ROI の設定は，遅延相の特に集積の弱い腫瘍では恣意的になりやすく、再現性が低い可能性があった。また retention index と T/N ratio の間には軽度の解離があった。半定量判定をより正確に行うには更なる工夫が必要であると考えられた。