

IMP SPECT in choroidal melanoma

**Assessment of SPECT-CT fusion images and semi-quantitative evaluation using SUV in  $^{123}\text{I}$ -IMP SPECT in patients with choroidal melanoma**

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1 [Abstract]

2 **Objectives**

3 The aim of this study was to assess the diagnostic ability of *N*-isopropyl-*p*-[I-123]  
4 iodoamphetamine (IMP) SPECT semi-quantitative evaluation based on the standardized  
5 uptake value (SUV) in patients with choroidal melanoma. The secondary aim was to  
6 investigate the 6-h IMP SPECT imaging in comparison with 24-h imaging.

7 **Methods**

8 Twenty-five patients (14 males and 11 females, mean age of 59.2-year-old) were analyzed in  
9 this retrospective study. Patients underwent 24-h IMP SPECT imaging with a gamma camera  
10 after intravenous injection of IMP. Twelve of 25 patients underwent 6-h SPECT imaging in  
11 addition to the 24-h imaging. All acquired SPECT images were fused with CT images using  
12 an image-analysis software. To assess the utility of semi-quantitative evaluation method, we  
13 introduced an image evaluation method using SUV<sub>max</sub> comparing with conventional count-  
14 based uptake index (UI) evaluation of the lesion. Volumes-of-interest (VOIs) for SUV<sub>max</sub>  
15 and regions-of-interest (ROIs) for UI were drawn referring to the SPECT-CT fusion image.  
16 Then the relationship between the 6- and 24-h images was examined both in SUV and UI  
17 evaluation. Furthermore, the relationship between the size category classification (SCC) by

1 UICC/AJCC: 1-4 scales and each semi-quantitative value using SUVmax and UI was also  
2 assessed.

### 3 **Results**

4 SUVmax of the tumor was significantly higher than that of the normal side;  $2.37 \pm 0.88$  and  
5  $1.77 \pm 0.39$  ( $P < 0.05$ ) on 6-h image,  $4.17 \pm 1.73$  and  $2.04 \pm 0.45$  ( $P < 0.001$ ) on 24-h image,  
6 respectively. UI of the tumor was also significantly higher than that of the normal side;  $2.24 \pm$   
7  $0.67$  and  $1.53 \pm 0.35$  ( $P < 0.01$ ) on 6-h image,  $3.79 \pm 1.24$  and  $1.67 \pm 0.44$  ( $P < 0.001$ ) on 24-  
8 h image, respectively. There was a strong significant linear relationship in the evaluation with  
9 SUVmax between 6- and 24-h on the tumor side ( $R^2 = 0.88$ ,  $P < 0.0001$ ), compared to that  
10 with Tumor-UI ( $R^2 = 0.35$ ,  $P < 0.05$ ). In addition, SUVmax of the tumor clearly differentiated  
11 the SCC of the tumor category 4 from that of category 1, where SUVmax of the tumor for  
12 categories 1–4 were  $2.56 \pm 0.59$ ,  $4.33 \pm 1.92$ ,  $4.63 \pm 1.45$ , and  $5.73 \pm 1.69$ , respectively ( $P <$   
13  $0.05$ , for categories 1 and 4).

### 14 **Conclusions**

15 The semi-quantitative evaluation by SUV of  $^{123}\text{I}$ -IMP SPECT images fused with CT images  
16 is useful for detecting choroidal melanoma. Moreover, 6-h imaging with SUV-based  
17 evaluation of  $^{123}\text{I}$ -IMP SPECT is promising compared to the conventional count-based UI  
18 evaluation method.

## 1 **Introduction**

2 Choroidal melanoma is the most common primary ocular malignant tumor in adults  
3 (1, 2). The incidence has been reported in 6-7 cases per million in Caucasians who are the  
4 most affected population, and about 4-6 cases per million in the United States (1-3), while the  
5 annual incidence in Japanese is 0.25 per million (1, 3). Usually, the diagnosis of typical  
6 choroidal melanoma is not difficult (3, 4); however, it may be difficult in some cases with  
7 atypical ocular manifestations or ocular complications, in which invasive procedures such as  
8 histopathological examination are required (3, 5).

9 *N*-isopropyl-*p*-[I-123] iodoamphetamine (<sup>123</sup>I-IMP) was initially developed for  
10 evaluation of cerebral blood flow (6), but <sup>123</sup>I-IMP also accumulates in melanocytes that are  
11 actively producing melanin (7). <sup>123</sup>I-IMP SPECT (IMP SPECT) imaging was reported to be  
12 useful for noninvasive diagnosis of choroidal melanoma (8, 9), especially with late-phase  
13 imaging obtained at 24- or 48-h after intravenous injection of <sup>123</sup>I-IMP(1, 5). However, the  
14 physical burden for patients is significant because the examination takes few days to  
15 diagnose. It is, therefore, essential to develop diagnostic techniques that can be performed in  
16 a shorter period. Although IMP SPECT was also reported to be useful as a diagnostic tool, its  
17 diagnosis was based on visual, qualitative assessment, lacking accuracy and reproducibility.  
18 Therefore, semi-quantitative evaluation has been performed using the tumor-to-normal ratio  
19 (T/N) derived from radioisotope counts of the tumor and normal tissue(5, 10). However,

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1 SPECT alone lacks sufficient anatomical information and needs greater accuracy for  
2 evaluation. Recently a new method has been developed to evaluate semi-quantitative indices  
3 using the standardized uptake value (SUV) in the evaluation of bone SPECT with  $^{99m}\text{Tc}$ -MDP  
4 or  $^{99m}\text{Tc}$ -HMDP (11-13). Therefore, we have attempted semi-quantitative evaluation of  
5 choroidal melanoma by the SUV calculated by recently developed software “GI-BONE” in  
6 SPECT and CT fusion images(11, 12), which has not been reported in the evaluation of  
7 choroidal melanoma previously.

8           The purpose of this study was to assess the diagnostic ability of IMP SPECT using  
9 fused IMP SPECT and CT images in patients with choroidal melanoma. Besides, our aim was  
10 to assess the utility of SUV-based semi-quantitative evaluation, especially for 6-h images  
11 after intravenous injection of  $^{123}\text{I}$ -IMP as an early-phase imaging.

12

1 **Methods**

2 *Patients*

3           This study was approved by the Institutional Review Board (#19-021). Written  
4 informed consent was obtained from each patient. This retrospective study included 27  
5 patients diagnosed having choroidal melanoma, who underwent IMP SPECT imaging  
6 between November 2017 and October 2019. Inclusion criteria for the study were as follows;  
7 1) clinically diagnosed with choroidal melanoma and were planned for carbon-ion  
8 radiotherapy (CIRT), 2) who underwent IMP SPECT imaging and CT before the CIRT. Two  
9 of 27 patients were excluded; one patient had undergone enucleation of an affected eye at  
10 another hospital after IMP SPECT, and 1 patient visited our institution for recurrence after  
11 treatment. Therefore, we examined 25 patients (male: 14, female: 11), mean age:  $59.2 \pm 11.1$ ,  
12 range: 33-76 years. In all cases, the lesion was limited to the choroid, and there were neither  
13 lymph node metastasis nor distant metastasis in any of the patients.

14

15 *IMP SPECT procedure*

16           All patients underwent IMP SPECT imaging with a gamma camera (E.CAM, Canon  
17 Medical, Tokyo, Japan) at 15 min as well as 24 h after intravenous injection of  $209.7 \pm 12.7$   
18 MBq (range: 172.0–223.8 MBq) of IMP (Nihon Medi-Physics, Tokyo, Japan). From February

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1 2019 to October 2019, 12 of 25 patients underwent 6-h SPECT imaging in addition to the 15-  
2 min and 24-h imaging to assess the utility of early phase SPECT imaging using semi-  
3 quantitative evaluation method. SPECT images were acquired for 30 min. The matrix size  
4 was  $128 \times 128$  pixels. The images were reconstructed by filtered back projection using a  
5 Butterworth filter and a ramp filter; no attenuation correction was performed.

6

### 7 *Becquerel calibration factor (BCF) measurement and evaluation of linearity between* 8 *radioactivity density and pixel values*

9 For the measurement of SUVmax, we performed preclinical phantom studies using a  
10 cylindrical phantom (Molecular Imaging Labo, Suita, Japan) with an inner diameter of 160  
11 mm  $\times$  150 mm and a volume of 3.016 mL referring to the modified method reported by  
12 previously(14). The radioactivity at the time of measurement of  $^{123}\text{I}$  enclosed in the phantom  
13 was 100 MBq. After inspection once every 3 months, phantom images were collected under  
14 the same imaging conditions as used for clinical settings. GI-BONE image-analyze software  
15 (AZE, Kawasaki, Japan) was used for BCF calculation.

16 To confirm the reliability of our semi-quantitative analysis under clinical conditions,  
17 pixel values were evaluated at a time when the radioactivity was sufficiently attenuated, after  
18 the measurement of BCF. SPECT imaging was performed using the same phantom and  
19 method as used for BCF measurement. Images were collected within one half-life, and a total



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1 of 9 measurements were made. The range of the measured radioactivity density was 0.3-30  
2 kBq/mL.

3 In the phantom, it was confirmed that there was a highly positive correlation  
4 between the radioactivity concentration and the radioisotope count of SPECT images in the  
5 linear regression analysis ( $R^2 = 1.00$ ,  $p < 0.0001$ ). Since the location of the choroidal  
6 melanoma in the eye is near the head surface, the value was considered to be obtained from  
7 the surface layer of the phantom. SUV was defined as below(14):

$$8 \quad \text{SUV} = \text{BCF} [\text{Bq/count/s}] \times (\text{measured SPECT count density per scan duration} \\ 9 \quad \quad \quad [(\text{count/mL}) \times (1/\text{s})] \times \{\text{body weight}[\text{g}] / \text{injected activity} [\text{Bq}]\})$$

10

### 11 *CT procedure*

12 CT scan had been performed as routine clinical studies within a few days before or  
13 after SPECT for all patients. We used a  $128 \times 2$ -detector-row CT scanner (SOMATOM  
14 Definition Flash, SIEMENS, Erlangen, Germany), in dual-energy mode. The scanning  
15 procedures were 80 and 140 kVp with Sn filter, 460mA, and automatic exposure control.  
16 Contrast-enhanced CT images were obtained starting at 70 seconds after administration of  
17 100 ml of 370 mgI/ml contrast material (OYPALOMIN, FujiPharma, Toyama, Japan) for 60  
18 s. The images were reconstructed at 3-mm slice thickness.

19

1 ***Data analysis***

2           For data analysis using SUV, 6- and 24-h SPECT images were selected. All acquired  
3 SPECT images were fused with CT images using an image-analysis software, GI-BONE.  
4 For the evaluation of IMP uptake of the lesion, we employ following two methods for  
5 SUVmax and UI, as follows; 1) for assessing semi-quantitative evaluations with SUVmax,  
6 volumes-of-interest (VOIs) were drawn to accommodate the whole affected eye and the  
7 whole normal contralateral eye, after which semi-quantitative evaluations based on SUVmax  
8 was assessed referring to the modified method by Yoshimura et al(10, 15, 16). For this  
9 evaluation, the other factors, including body weight, injection dose, injection time, and data  
10 acquisition time for 6- or 24-h after intravenous injection were also examined (Fig. 1a). Since  
11 the tumor itself is sometimes small with a lack of high accumulation of IMP, for reproducible  
12 quantitative assessment, the VOI was set to the entire eye. 2) To compare the usefulness of  
13 SUV, the count-based uptake index (UI) was also examined using counts per second (CPS) in  
14 SPECT images. Regions-of-interest (ROIs) were drawn along the margin of uptake with  
15 reference to the SPECT-CT fusion image created with Fusion Viewer Software (AZE,  
16 Kawasaki, Japan) (Fig. 1b)(10, 15, 16). Then ROI was placed over the contralateral normal  
17 eyeball as the normal tissue. The ROI of normal soft tissue was also placed at the temporal  
18 muscle to obtain a background count for standardizing the uptake of the affected and normal  
19 eyeballs.

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1           The UI were defined as follows:

2    UI in the tumor (Tumor-UI): (tumor lesion count) / (background count)

3    UI in the contralateral normal eyeball (Normal-UI): (contralateral normal eyeball count) /  
4    (background count)

5           We measured both 6- and 24-h SUVmax and UI, for patients who underwent  
6    imaging at both time points. In order to evaluate the association between IMP uptake and the  
7    Union for International Cancer Control (UICC)/American Joint Committee on Cancer  
8    (AJCC) size category, we classified the 25 patients into categories 1–4 (Fig. 2). Tumors are  
9    classified into 4 size categories based on the tumor’s largest basal diameter and thickness(17,  
10   18). Then the relationship between the size category classification (SCC) by UICC/AJCC: 1-  
11   4 scales and each semi-quantitative value using SUVmax and UI was also assessed.

### 12    *Statistical analysis*

13           All values are expressed as mean  $\pm$  standard deviation (SD). Statistical analyses were  
14    performed using JMP statistical software (SAS Institute, Cary NC, USA). The tumor and  
15    normal side were compared with the non-parametric Wilcoxon rank-sum test, the comparison  
16    among categories (category 1–4) was performed with the Tukey–Kramer HSD test,    Linear  
17    regression between SUVmax at 6- and 24-h, those of UI at 6- and 24-h on tumor side were

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- 1 calculated, and the correlation between the two groups was analyzed by Spearman's analysis.
- 2 P values less than 0.05 were considered statistically significant.

1 **Results**

2 *Semi-quantitative analysis*

3           Semi-quantitative evaluations were as follows in 12 patients who underwent both 6-  
4 and 24-h imaging. Table. 1 summarizes the SUVmax and UI of IMP SPECT-CT fusion image  
5 in patients with choroidal melanoma.

6 *Evaluation by SUVmax*

7           SUVmax of 6-h images on the tumor side was  $2.37 \pm 0.88$ , which was significantly  
8 higher than that on the normal side was  $1.77 \pm 0.39$  ( $P < 0.05$ ). The SUVmax of 24-h images  
9 on the tumor side was  $4.17 \pm 1.73$ , which was also significantly higher than that on the  
10 normal side ( $2.04 \pm 0.45$ ;  $P < 0.001$ ) (Fig. 3a, b).

11 *Evaluation by radioisotope uptake index*

12           Tumor-UI of 6-h images was  $2.24 \pm 0.67$  and Normal-UI was  $1.53 \pm 0.35$ ; thus, the  
13 radioisotope count was significantly higher on the tumor side ( $P < 0.01$ ). Tumor-UI of 24-  
14 hours images ( $3.79 \pm 1.24$ ) showed higher value than Normal-UI ( $1.67 \pm 0.44$ ,  $P < 0.001$ )  
15 (Fig. 3c, d).

16

17 *Correlation between SUVmax and radioisotope count*

1 Correlation between SUVmax and the conventional count-based method was also  
2 examined for 12 individuals who underwent imaging at both time points. On the tumor side,  
3 correlation between SUVmax and UI at 6 h after injection was not significant ( $\rho = 0.47$ ,  $P =$   
4  $0.124$ ) (Fig. 4a), but there was positive correlation between the values at 24 h ( $\rho = 0.52$ ,  $P <$   
5  $0.05$ ) (Fig. 4b).

6 In the relationship of semi-quantitative values between 6-h image and 24-h image,  
7 there was a strong linear relationship between SUVmax at 6- and 24-h on the tumor side  
8 ( $y = -0.74 + 1.68x$ ,  $R^2 = 0.88$ ,  $P < 0.0001$ ) (Fig. 5a), while there was a weak relationship  
9 between Tumor-UI at 6- and 24-h compared to those of SUVmax ( $y = 1.46 + 1.15x$ ,  $R^2 = 0.35$ ,  
10  $P < 0.05$ ) (Fig. 5b).

11

12 ***Relationship between size category classification by UICC/AJCC and each semi-***  
13 ***quantitative value***

14 In the assessment of the relationship between SCC by UICC/AJCC and each semi-  
15 quantitative value, SUVmax of the tumor for categories 1–4 were  $2.56 \pm 0.59$ ,  $4.33 \pm 1.92$ ,  
16  $4.63 \pm 1.45$ , and  $5.73 \pm 1.69$ , respectively ( $P < 0.05$ , for categories 1 and 4; the correlations  
17 with the other categories were not statistically significant) (Fig. 6a). Tumor-UI for each

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- 1 category was  $2.83 \pm 0.99$ ,  $4.45 \pm 1.48$ ,  $3.54 \pm 0.86$ , and  $4.63 \pm 0.45$ , respectively (not
- 2 significant) (Fig. 6b). Two representative cases are shown in Fig. 7.
- 3

1 **Discussion**

2           This study assessed the diagnostic ability of IMP SPECT using fused image with CT,  
3 and evaluated the utility of semi-quantitative evaluation based on the SUV in IMP SPECT  
4 images in patients with choroidal melanoma. We found that evaluation by SUVmax was  
5 equivalent to the conventional radioisotope count-based evaluation with UI. Moreover, there  
6 was a correlation between the degree of IMP uptake and size category, which is important for  
7 prognosis. As the incidence of primary choroidal melanoma per 1 million population is 0.25  
8 cases in Japan and about 4-6 in the USA (1-3), there have been few published reports  
9 examining more than 25 cases as in this study except for the report by Yoshimura et al (10).  
10 that assessed the tumor-to-nontumor ratio of IMP uptake using the 24-h image in 29 patients.  
11 Therefore, the current study about IMP semi-quantitative SUV evaluation using 6-h and 24-h  
12 images in patients with choroidal melanoma with a number of cases would be of great  
13 clinical significance.

14           From its development in the 1980s, <sup>123</sup>I-IMP has been reported to be well  
15 accumulated in melanoma (8, 9). Several reports have assessed the usefulness of semi-  
16 quantitative values, such as T/N of ocular tumors other than choroidal melanoma(5, 10).  
17 However, no studies have investigated the usefulness of this semi-quantitative approach such  
18 as SUV method in patients who were all clinically diagnosed with choroidal melanoma.



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1           Recently a new method has been developed for the evaluation of semi-quantitative  
2 indices using SUV in the evaluation of bone SPECT with  $^{99m}\text{Tc}$ -MDP or  $^{99m}\text{Tc}$ -HMDP (11-  
3 13). In the current study, we applied this method to SPECT with  $^{123}\text{I}$ -IMP, and evaluated the  
4 utility of SUV as a semi-quantitative value for the diagnosis and evaluation of choroidal  
5 melanoma. This study is the first report applying the semi-quantitative SUV method to  
6 diagnose choroidal melanoma in IMP SPECT imaging.

7           For assessing the count-based UI evaluation, the ROI method was considered to be  
8 inadequate, resulting in intra- and inter-observer variation was inevitable. Abe et al. has also  
9 pointed out that the slice-level ROI was not placed at exactly the same level as the lesion,  
10 especially when the uptake of lesions was low, and stated the necessity of analysis using  
11 SPECT-CT or MRI fusion images, or hybrid SPECT/CT for these evaluations(5).

12           Our method in the current study, the VOI was placed over the whole affected eye  
13 followed by SUVmax was determined as a maximum value of SUV in the VOI. Since the  
14 SUV evaluation method using software is performed by drawing a three-dimensional  
15 spherical VOI, instead of a planar ROI, it is also ideal for the assessment of the entire tumor.  
16 Thus, this semi-quantitative SUVmax approach is considered more stable and suitable than  
17 the UI method for the IMP semi-quantitative evaluation of the choroidal melanoma with an  
18 advantage in daily clinical practice.

1           Regarding of the relationship of the semi-quantitative values between SUV  
2   evaluation and UI evaluation, the SUVmax evaluation method provided results similar to  
3   those of conventional count-based UI evaluation. SUVmax on the tumor side in 6- and 24-h  
4   images were significantly higher than those of the normal side, with similar results for UI.  
5   There was a strong correlation between SUVmax and UI at 24 h imaging. Considering the  
6   ease and the reproducibility of the measurement procedure, as described above, this semi-  
7   quantitative SUVmax evaluation method is expected to be a high clinical utility compared to  
8   the UI method.

9           In terms of the evaluation of 6- and 24-h image, the linear relationship between  
10   SUVmax at 6 h and at 24 h was high. On the other hand, there was less relationship between  
11   the Tumor-UI at 6 h and at 24 h. Therefore, 6-h images with SUV-based evaluation may be  
12   sufficient to predict the degree of uptake on 24-h images of patients clinically diagnosed with  
13   choroidal melanoma. From these results, we considered that the SUV-based evaluation is  
14   more feasible in the reproducibility, compared to the count-based UI evaluation. Thus, 6-h  
15   images with SUV-based evaluation is expected to reduce the burden on patients and provide  
16   an easy-to-use method for the diagnosis choroidal melanoma.

17           Prognostic value of our IMP semi-quantitative evaluation with SUVmax should be  
18   discussed. There was a significant difference in SUVmax between category 1 and 4 on the  
19   tumor, while there was no significant correlation among the other categories. As described in

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1 previous reports, size of the tumor is one of the prognostic indicators of choroidal  
2 melanoma(17, 19, 20). In the present study, some category 2 tumors showed relatively high  
3 SUV, whereas some category 3 tumors, which were relatively large, showed low SUV.  
4 Consequently, there was an overlap between the SUV of category 2 and category 3 tumors.  
5 This indicated that other factors may be important for prognosis. If not only the size but also  
6 the other factor such as the degree of IMP uptake is a prognostic factor, semi-quantitative  
7 evaluation with SUV would allow prediction of the prognosis more easily and more  
8 precisely, which is considered useful for evaluation of choroidal melanoma. It has been  
9 reported that the degree of IMP uptake is low in amelanotic melanoma(7, 8). Some features  
10 have been shown to be poor prognostic factors, such as cytological types, chromosomal  
11 alterations, histopathological features, such as higher mitotic counts, higher mean diameter at  
12 the 10 largest nucleoli, presence of extravascular matrix patterns, higher counts of  
13 microvascular density, etc.(18). Further investigation is needed to examine the relationship  
14 between the degree of IMP uptake and prognosis, such as recurrence and metastasis in the  
15 future.

16 As for the limitation of this study, there are several issues to be discussed. First, all  
17 participated patient was clinically diagnosed with choroidal melanoma for CIRT. The  
18 histopathologic evaluation was not performed in our current study because of its invasive  
19 procedure. Therefore, the development of non-invasive semiquantitative imaging is of

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1 paramount importance for the accurate diagnosis of choroidal melanoma. Although the  
2 current 6-hour imaging with the SUV method was as a preliminary study, there was a  
3 relatively small number in the study population for the evaluation. Further examination with a  
4 large number of subjects was considered to be needed. And the method of calculating SUV  
5 with SPECT has not been established in terms of technical aspects given the low spatial  
6 resolution of SPECT and the standardization and is controversial(10). Technical verification  
7 using a scanner with high spatial image resolution such as a digital SPECT/CT is needed.

8 The proposed SUV and the conventional UI methods were originally based on the amount of  
9 radioactivity in the image. The SUV method is expected to be simpler than the UI method  
10 and to have less variability among operators in clinical practice. However, it may not be  
11 feasible to compare the two methods directly. Besides, the proposed SUV method may be  
12 affected by the sensitivity of the SPECT-CT system and the process of image reconstruction  
13 among facilities. Further validation study about these issues is also needed. Additionally, no  
14 patients underwent IMP SPECT assessment after CIRT; therefore, we have not assessed the  
15 efficacy of treatment or prognosis prediction. If several factors affect prognosis, such as local  
16 recurrence or metastasis in follow-up after CIRT, it will be necessary to examine the  
17 correlation of these with the degree of IMP uptake before and after CIRT. For these purposes,  
18 further studies, including long-term follow-up data, are needed to confirm these preliminary  
19 findings.

1 **Conclusions**

2           The semi-quantitative evaluation by SUV is useful for detecting choroidal melanoma  
3 of  $^{123}\text{I}$ -IMP SPECT images fused with CT images. Moreover, 6-h imaging with SUV-based  
4 evaluation of  $^{123}\text{I}$ -IMP SPECT is promising compared to the conventional count-based UI  
5 evaluation method.

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6  
7 **Author contributions**

8           Kana Yamazaki was responsible for the research and wrote the main manuscript text  
9 as the first author. Ryuichi Nishii was responsible for this study as a corresponding author,  
10 and coordinated and served the entire study. Takamasa Maeda was a radiological technologist  
11 and contributed to confirm the reliability of the SPECT imaging and provided technical  
12 advice. Hirokazu Makishima, Goro Kasuya, Tachen Chang, and Hiroshi Tsuji were radiation  
13 oncologists who were responsible for the planning patient examination, carbon-ion  
14 radiotherapy, and subsequent management. Kentaro Tamura, Koji Murakami, and Tatsuya  
15 Higashi contributed to writing the final manuscript. All members administrated this study. All  
16 authors also read and approved the final version of the manuscript.

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## IMP SPECT in choroidal melanoma

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10

1 **Table and Figure Legends**

2 Table 1.

3 Summary of SUVmax and UI of IMP SPECT-CT fusion image in patients with choroidal  
4 melanoma

5

6

7 **Figure 1. Methods of IMP SPECT-CT fusion and semi-quantitative evaluation.**

8 IMP SPECT images were fused with CT images using an image-analysis software, GI-  
9 BONE. VOIs were drawn to accommodate the whole affected eye and the contralateral  
10 normal eyeball, followed by semi-quantitative evaluations based on SUVmax (a). Then  
11 SPECT-CT fusion image created with Fusion Viewer software. The ROIs of tumor lesion,  
12 contralateral whole eyeball, and background were placed with reference to the SPECT-CT  
13 fusion image (b).

14

15 **Figure 2. Profile of number of patients according to UICC / AJCC size category criteria.**

16

1 **Figure 3. Semi-quantitative analysis by SUVmax, radioisotope uptake index (UI).**

2 SUVmax of tumor sides were significantly higher both 6- ( $p < 0.05$ ) (a) and 24-h image ( $p <$   
3  $0.001$ ) (b). UI of tumor sides were significantly higher both 6- ( $p < 0.01$ ) (c) and 24-h image  
4 ( $p < 0.001$ ) (d). Wilcoxon rank sum test was used for the statistical analysis.

5

6 **Figure 4. Relationship between SUVmax and radioisotope count.**

7 On the tumor side, correlation between SUVmax and UI of at 6 -hours after injection was not  
8 significant(a), but there was positive correlation between those the values of at 24- hours(b).  
9 The dot-lined area represents the 95 % confidence ellipse. Spearman's test was used for the  
10 statistical analysis.

11

12 **Figure 5. Relationship of semi-quantitative values between 6-h image and 24-h image.**

13 There was an excellent linear relationship between SUVmax at 6- and 24-h on the tumor  
14 side(a), on the other hand, there was less relationship between the Tumor-UI at 6- and 24-h  
15 compared to those of SUVmax(b). The dot-lined area represents the 95 % confidence  
16 interval.

17

1 **Figure 6. Relationship between size category classification by UICC/AJCC and each**  
2 **semi-quantitative value.**

3 There was a significant difference in SUVmax between categories 1 and 4 on the tumor side,  
4 while there was an overlap in patients with tumors of category categories 2 and 3. Also, it  
5 could not be determined whether there was a correlation between SUVmax and size  
6 category(a). There was no significant difference in Tumor-UI between each category(b).  
7 Tukey-Kramer HSD test was used for the statistical analysis.

8

9 **Figure 7. Representative cases.**

10 (a); A case of a 69-year-old male with choroidal melanoma on his left eye, tumor size was  
11  $12.5 \times 6.0$  mm (size category 2, case #19). SUVmax at 6-h on the tumor side was 1.69, that  
12 of at 24-h was 2.46. (b); A case of a 60-year-old male with choroidal melanoma on his right  
13 eye, tumor size was  $18.1 \times 7.5$  mm (size category 4, case #18). SUVmax at 6-h on the tumor  
14 side was 2.25, that of at 24-h was 4.06.