

# Maximum standardized uptake value of foot SPECT/CT using Tc-99m HDP in patients with accessory navicular bone as a predictor of surgical treatment

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## Abstract

Quantitative bone SPECT/CT (single-photon emission computed tomography/computed tomography) using Tc-99m hydroxymethylene diphosphonate is emerging as a useful imaging modality for skeletal diseases. Accessory navicular bone (ANB) has been evaluated by bone scintigraphy only qualitatively and semiquantitatively. However, a truly objective quantitative assessment of ANB is lacking. Here, we measured the maximum standardized uptake value (SUVmax) of the ANB and investigated its usefulness as an imaging biomarker for ANB.

Consecutive quantitative bone SPECT/CT studies that had been performed on the foot were retrospectively analyzed. One hundred five patients (male:female = 44:61; median age = 32.0 [range, 11–81] years old; 31 negative controls without ANB and 74 patients with ANB [7 unilateral and 67 bilateral]) and their 210 feet were investigated. The ANBs were classified into types I, II, III (Geist classification), and 0 (contralateral navicular of unilateral ANB). Type II ANBs were subclassified into II-1 (with bony abnormality) or II-0 (without bony abnormality). The treatment modality was observation, conservative treatment, or surgical removal. The associations between the SUVmax and clinical findings, including surgery, were investigated.

Patients with type II-1 ANB had the highest SUVmax among all ANB types ( $P < .001$ ). The SUVmax of symptomatic ANB was greater than that for asymptomatic ANB ( $P < .001$ ), and the SUVmax for the surgically resected ANB group was also significantly higher than that for the observation only or conservative treatment group ( $P < .001$ ). Subtype II-1 had a significantly higher SUVmax compared with subtype II-0 ( $P < .001$ ). Logistic regression analyses in type II ANB showed that young age ( $P = .020$ ) and SUVmax ( $P = .031$ ) were significant predictors for surgery. Receiver operating characteristic curve and survival analyses revealed an optimal SUVmax cutoff of 5.27 g/mL for predicting final surgical treatment.

SUVmax derived from quantitative bone SPECT/CT was strongly associated with symptom, surgical treatment, and a known high-risk type of ANB. Risk stratification for final surgical treatment of ANB can be achieved using the SUVmax from quantitative bone SPECT/CT.

**Abbreviations:** ANB = accessory navicular bone, HDP = hydroxymethylene diphosphonate, IRB = institutional review board, MRI = magnetic resonance imaging, ROC = receiver operating characteristic, SD = standard deviation, SEM = standard error of the mean, SPECT/CT = single-photon emission computed tomography/computed tomography, SUV = standardized uptake value, SUVmax = maximum standardized uptake value, VOI = volume of interest.

**Keywords:** accessory navicular bone, computed tomography, maximum standardized uptake value, single-photon emission computed tomography

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The need for informed consents was waived by the IRB.

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## 1. Introduction

Bone single-photon emission computed tomography/computed tomography (SPECT/CT) using Tc-99m diphosphonates is useful in the localization and evaluation of musculoskeletal pain.<sup>[1,2]</sup> Specifically, pathologies of the foot and ankle have been successfully investigated using SPECT, along with anatomical information on coregistered CT.<sup>[3,4]</sup> The high sensitivity of nuclear imaging and detailed anatomical information from CT seem to be suitable for the complex structure of the foot and ankle, and the results obtained using hybrid SPECT/CT have been reported to be comparable to those obtained using magnetic resonance imaging (MRI) in a variety of foot and ankle diseases.<sup>[5]</sup>

Accessory navicular bone (ANB) is an ossicle that is located in the medial aspect of the navicular. When repetitive injury or stress is inflicted on the ANB, it can induce pain. In some cases, pain can be chronic and may cause deformity in the foot. ANB can be classified into 3 types according to the Geist classification.<sup>[6,7]</sup> Type I ANB is a sesamoid bone within the tibialis posterior tendon which is not directly connected to the navicular. Type II ANB, actually, is a secondary ossification center of the navicular tuberosity which is connected to the navicular by cartilage (synchondrosis). Type II ANB is most likely to be symptomatic. Cortical irregularity and fragmented bones are often observed in CT images, and bone marrow edema on MRI is another common finding of symptomatic type II ANB.<sup>[8,9]</sup> Type III ANB, also called a cornuate navicular, is thought to be a variant of type II ANB unified with navicular tuberosity.

Patients with symptomatic ANB initially undergo conservative treatment such as life style modification, arch support, physical therapy, or medication. However, if the symptom persists, patients can choose to undergo surgery to remove the ANB and repair the tibialis posterior tendon. The most common surgical method is the Kidner or modified Kidner procedure, which involves excision of the ANB.<sup>[10]</sup> There is no clear-cut criterion for the surgical removal of ANB and in most cases the decision is made empirically. Some of the ANB patients experience persistent pain even after the surgery, which reflects the necessity for more accurate risk stratification of ANB.<sup>[11]</sup>

Nuclear medicine imaging of bone scintigraphy has been reported to show increased uptake of bone agent in symptomatic or asymptomatic ANBs.<sup>[12–15]</sup> However, the definition of bone tracer uptake was only qualitative or semiquantitative: bone tracer uptake was either dichotomized (uptake positive vs negative)<sup>[12,13]</sup> or graded (0=no uptake, 1=mild uptake, and 2=intense uptake).<sup>[14,15]</sup> Furthermore, the presence/absence of symptoms of ANB is also highly subjective. Therefore, the comparison of bone tracer uptake with symptom often yielded irrelevant results such as a positive uptake in asymptomatic ANB.

Recently, quantitative SPECT/CT is emerging as a new imaging modality in the field of nuclear medicine.<sup>[16,17]</sup> The standardized uptake value (SUV), a quantitative parameter, has been successfully derived from SPECT/CT, and Tc-99m-labeled radiopharmaceuticals are being tested for their clinical applications using quantitative SPECT/CT.<sup>[18–23]</sup> To the best of our knowledge, however, no study involving bone SPECT/CT has used a truly quantitative parameter to investigate ANB. In this study, we measured the maximum standardized uptake value (SUVmax) of ANB in patients who underwent bone SPECT/CT and attempted to correlate the SUVmax with clinical findings of ANB.

## 2. Materials and methods

### 2.1. Patients

One hundred seventeen patients who underwent bone SPECT/CT of the foot for the evaluation of ankle or foot pain from June 2015 to December 2017 were included in the study. Among the 117 patients, 12 patients were excluded because of tarsal coalition (6 patients), previous history of foot surgery with remnant surgical materials (5 patients), or young age of <10 years old (1 patient). As a result, only 105 patients (male:female=44:61, median age=32.0 years old with a range of 11–81) were included in the current study. This retrospective study was performed at a tertiary referral hospital and approved by the institutional review board (IRB). The need for informed consent was waived by the IRB.

### 2.2. Classification of ANB

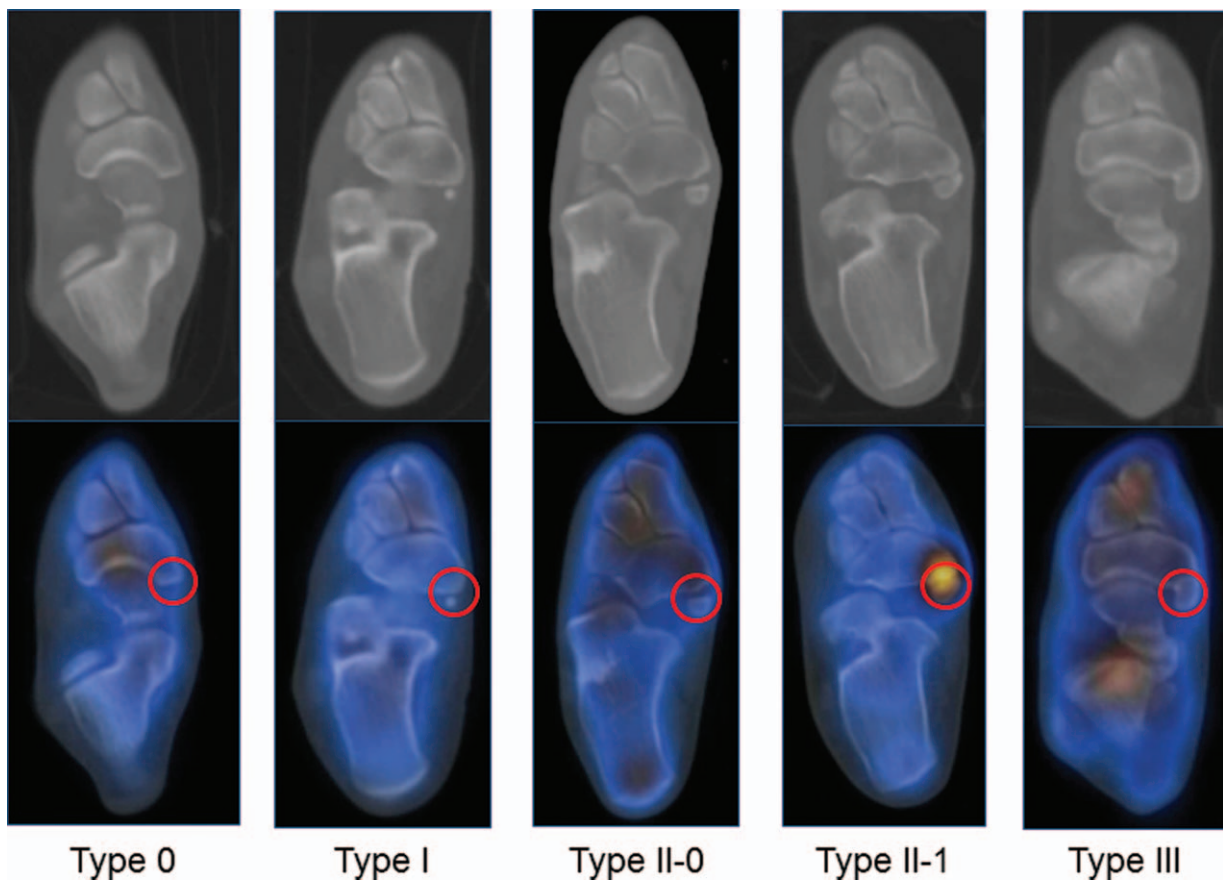
The 105 patients were divided into 2 groups: 31 without ANB (negative control) and 74 with ANB (7 unilateral and 67 bilateral). We classified 141 ANBs in 74 patients according to the Geist classification (type I=22, type II=89, and type III=30) based on CT images of bone SPECT/CT. In addition, type II ANB was subclassified into subtype II-1 (n=31, type II ANB with subchondral irregularity or degenerative change), and subtype II-0 (n=58, type II ANB without such bony abnormality). For convenience, we defined the contralateral navicular of the unilateral ANB as type 0 (n=7). ANB type and subtype classification was performed by a certified radiologist with 10 years of experience in musculoskeletal imaging.

### 2.3. Pain evaluation and surgical treatment

Information regarding gender, age, chief complaint, clinical diagnosis, and final treatment modality were extracted from the institutional electronic medical records. Pain score (numerical rating score) was not well described in majority of cases, so the presence/absence of medial foot pain for each ANB at initial visit was used instead. In patients with vague descriptions of the location of foot pain, we referred to the final diagnosis made by attending physicians. In this study, treatment modalities for symptomatic ANBs were grouped into 3: observation without any intervention, conservative treatment (medication, arch support, or physical therapy), and surgical treatment with ANB excision. These treatment modalities were derived from the documented information of the attending physicians at the last follow-up visit. The endpoint was defined as the last date of visit to the attending physician or the date of the surgery for the removal of the ANB. The follow-up period was defined as the time interval from the date of initial bone SPECT/CT examination to the endpoint.

### 2.4. Bone SPECT/CT

Bone SPECT/CT was implemented using NM/CT670 or NM/CT670 pro scanners (GE Healthcare, Pittsburgh, PA). Tc-99m hydroxymethylene diphosphonate (HDP) was injected at a dose of 740 MBq (20 mCi) and SPECT/CT was performed 2 to 3 hours post injection. SPECT was performed with an energy peak of 140 keV with  $\pm 10\%$  window (126–154 keV), and in the step-and-shoot mode using the body contour option, 120 steps (60 steps/detector) with an angle of 3°, and a 10-second acquisition per step. The scatter window was set at 120 keV with  $\pm 5\%$  window



**Figure 1.** Measurement of the standardized uptake value (SUV). The volume of interest (VOI) was placed over the accessory navicular bone (ANB). Transaxial CT images of ANB types (upper row) and SPECT/CT fusion images with their corresponding VOIs (bottom row) are displayed. Type 0 = contralateral navicular of unilateral ANB patient, Types I, II (II-0 and II-1), III = ANB types according to the Geist classification. CT = computed tomography, SPECT/CT = single-photon emission computed tomography/CT, VOI = volume of interest.<sup>[6,7]</sup>

(115–125 keV). The zoom factor was 1.5. The SPECT image was reconstructed using vendor-provided software (Preparation for Q. Metrix, GE Healthcare). An iterative ordered subset expectation maximization algorithm was used with 2 iterations and 10 subsets. During the SPECT reconstruction, CT attenuation correction, scatter correction, and resolution recovery were applied, and a postreconstruction low-pass filter (Butterworth with frequency 0.48 and order 10) was employed. The matrix size was  $128 \times 128$ . The system sensitivity of the SPECT/CT scanners was  $152.5 \text{ cpm}/\mu\text{Ci}$ . After the acquisition of the SPECT image, a helical CT was performed with a tube voltage of 120 kVp, tube current of 60 to 210 mA with automa function at a noise level of 20, detector collimation of 20 mm ( $16 \times 1.25$ ), helical thickness of 2.5 mm, table speed of 37 mm/s, tube rotation time of 0.5 seconds, and pitch of 0.938:1. CT images were reconstructed using an adaptive statistical iterative reconstruction algorithm (ASiR, GE Healthcare) into a  $512 \times 512$  matrix with Bone Plus filtering. The slice thicknesses were 1.25, 0.98, and 0.98 mm for the transaxial, coronal, and sagittal planes, respectively.

### 2.5. Measurement of SUVmax

SUVmax was measured with dedicated software (Q. Metrix, GE Healthcare). The spherical volume of interest (VOI) was drawn over the ANB based on CT images of the bone SPECT/CT. The VOI was placed over the whole ANB and medial end of the

navicular, including the interspace (Fig. 1). In the case of a non-ANB foot, only the medial end of the navicular was included in the VOI. The VOI volume was  $4.50 \pm 2.57 \text{ cm}^3$  (mean  $\pm$  standard deviation [SD]). Adjacent foot bones (cuneiform, talus) and joints (intertarsal, talo-navicular) were carefully avoided while drawing the VOIs. The SUV was calculated for each VOI with the following formula:

$$\text{SUV} = \frac{\left( \frac{\text{Decay-corrected radioactivity}}{\text{Volume of VOI}} \right)}{\left( \frac{\text{Injected radioactivity}}{\text{Body weight}} \right)} \text{ g/mL}$$

The maximum SUV (SUVmax) was employed to represent the disease activity of the ANB.

### 2.6. Statistical analysis

Statistical analysis was performed using dedicated statistical software (MedCalc, version 14.8.1, bvba). For the evaluation of normal distribution, the D'Agostino–Pearson test was first performed. When assumption of normal distribution was rejected, nonparametric analyses such as Mann–Whitney or Kruskal–Wallis test were implemented. Additionally, chi-squared test, logistic regression, receiver operating characteristic (ROC) curve, and Kaplan–Meier survival analyses were performed. Results with a  $P$  value of  $<.05$  were considered statistically significant.

**Table 1**  
**Patient characteristics.**

	Negative control without ANB (n = 31)	Patients with ANB (n = 74)	P
Gender (male:female)	11:20	33:41	.390
Median age, years old (range)	29.0 (11–78)	34.5 (11–81)	.471
Unilateral: bilateral		7 (right 3 and left 4):67	
Clinical diagnosis	Trauma: 12 Degeneration: 5 Others: 14	ANB: 39 Trauma: 13 Degeneration: 10 Others: 12	

ANB = accessory navicular bone.

### 3. Results

#### 3.1. Patient-based analyses

For the patient-based analyses, 31 negative control patients without ANB were compared with 74 patients with ANB (7 unilateral and 67 bilateral). Gender ( $P = .390$ ) and age ( $P = .471$ ) were not significantly different between the 2 groups. The clinical diagnosis (the reason for bone SPECT/CT referral) of the negative control patients was not related to ANB in any way, whereas ANB evaluation was the main reason for the bone SPECT/CT in 52.7% (39/74) of the ANB patients (Table 1).

#### 3.2. Evaluation of independency of ANB

In order to analyze the SUVmax of individual ANBs as an independent variable, we first compared the contralateral navicular (type 0) of unilateral ANB patients with the negative controls. The SUVmax in patients with type 0 ( $n = 7$ ,  $2.36 \pm 0.47$  g/mL) (mean  $\pm$  standard error of the mean [SEM]) was not significantly different from the mean SUVmax of bilateral navicular in negative controls ( $n = 31$ ,  $1.88 \pm 0.17$  g/mL) (mean  $\pm$  SEM) (Mann–Whitney test,  $P = .283$ ). It implies that the presence of ANB in one foot may not significantly affect the bone tracer uptake in the other foot. Hereafter, the SUVmax of an ANB was considered to be independent of the other foot of the same patient or other feet of different patients.

#### 3.3. SUVmax according to pain, final treatment modalities, and ANB types

For the lesion-based analyses of 74 ANB patients, 7 contralateral naviculars of unilateral ANB (type 0) and 141 ANBs (type I = 22, type II = 89, and type III = 30) were investigated. The presence of medial foot pain ( $P < .001$ ) and final surgical treatment ( $P < .001$ ) were more frequently associated with type II ANB (Table 2). Specifically, the SUVmax was significantly higher in ANB type II-1 compared with ANB types 0, I, II-0, and III ( $P < .001$ ) (Fig. 2).

Regarding the association with medial foot pain, regardless of the ANB type, the SUVmax was significantly higher in 49 symptomatic ANBs (type I = 1, type II = 46, and type III = 2) than 99 asymptomatic ANBs (type 0 = 7, type I = 21, type II = 43, and type III = 28) ( $P < .001$ ) (Fig. 3A). Of the symptomatic ANBs, 24.5% (=12/49) were surgically treated, whereas no asymptomatic ANB was treated with surgery (0/99 = 0%) ( $P < .001$ ).

In addition, the 12 ANBs treated with surgery (all type II) had a significantly higher SUVmax than both the 113 ANBs which were only observed (type 0 = 7, type I = 21, type II = 56, and type III = 29) and the 23 ANBs which were treated with conservative treatment at the endpoint of follow-up (type 0 = 0, type I = 1, type II = 21, and type III = 1) ( $P < .001$ ) (Fig. 3B).

Finally, for the type II subgroup analyses, the SUVmax was compared between subtype II-1 ( $n = 31$ ) and subtype II-0 ( $n = 58$ ). Subtype II-1 ANBs had significantly higher SUVmax compared with subtype II-0 ANBs ( $P < .001$ ) (Fig. 3C) and subtype II-1 ANBs were more frequently symptomatic (24/31 = 77.4%) than subtype II-0 ANBs (22/58 = 37.9%) ( $P < .001$ ).

#### 3.4. Multivariate analysis for association with consequent surgical treatment

The association with surgical treatment was investigated using logistic regression analysis. This analysis was conducted in 141 genuine ANBs excluding type 0 ANBs.

First, 141 ANBs (type I = 22, type II = 89, and type III = 30) were tested using univariate and multivariate logistic regression analyses. In the univariate analyses, young age ( $P = .007$ ) and SUVmax ( $P = .003$ ) were significantly associated with surgical treatment, but gender ( $P = .738$ ) and types of ANB ( $P = .734$ ) were not. In the stepwise multivariate analyses, only age ( $P = .013$ ) and SUVmax ( $P = .007$ ) were associated with surgery (Table 3).

Second, 89 type II ANBs were separately tested because patients with types I and III ANBs are usually not candidates for surgical treatment (Table 2). Type II ANBs were divided into subtypes II-1 ( $n = 31$ ) and II-0 ( $n = 58$ ). In the univariate analysis, young age ( $P = .013$ ) and higher SUVmax ( $P = .018$ ) were significantly associated with surgical treatment, whereas subtype II-1 ANBs, which were more likely to be symptomatic than subtype II-0 ANBs, were not significantly associated with surgery ( $P = .242$ ). Gender ( $P = .705$ ) was not a significant predictor, either. In the stepwise multivariate analysis, age and SUVmax remained significant with  $P$  values of .020 and .031, respectively (Table 4).

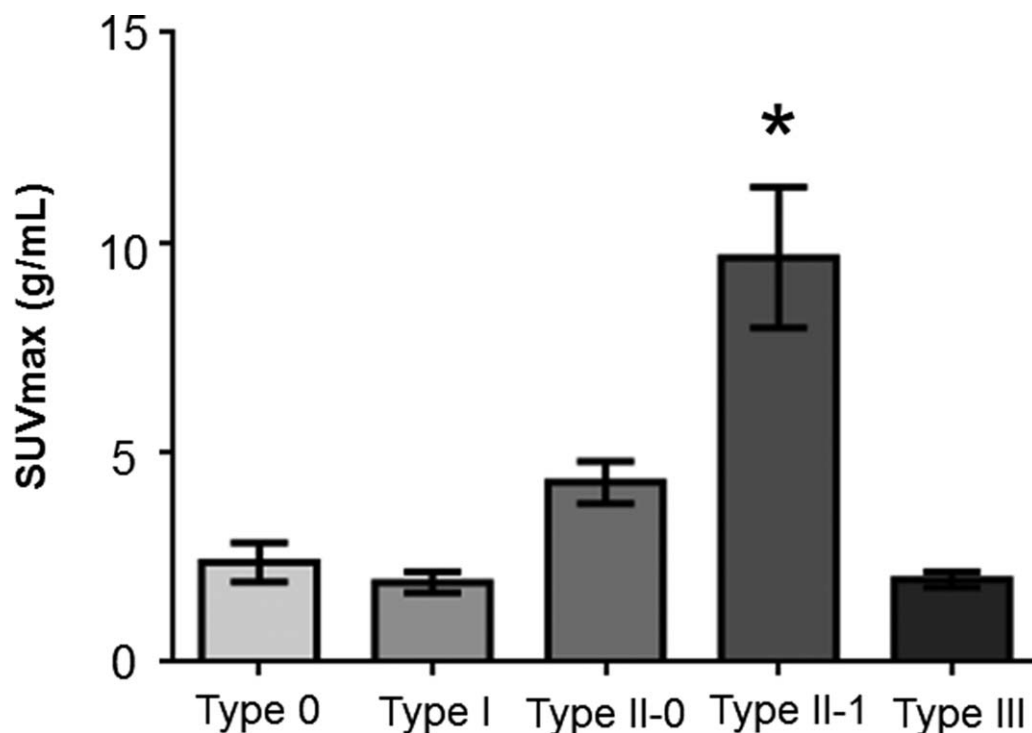
#### 3.5. ROC curve and Kaplan–Meier analyses of the final surgical management

As previously mentioned, 12 ANBs were surgically removed as a definite treatment (Table 2) and the time interval from the bone SPECT/CT to the surgery was  $79.8 \pm 94.8$  days (mean  $\pm$  SD).

**Table 2**  
**Comparison according to ANB types.**

	Type 0 (n = 7)	ANB type I (n = 22)	ANB type II-0 (n = 58)	ANB type II-1 (n = 31)	ANB type III (n = 30)	P
Laterality (right:left)	4:3	12:10	27:31	15:16	16:14	.943
Medial foot pain (yes:no)	0:7	1:21	22:36	24:7	2:28	<.001
Treatment (observation:conservative:surgery)	7:0:0	21:1:0	43:9:6	13:12:6	29:1:0	<.001

ANB = accessory navicular bone.



**Figure 2.** Comparison of the SUVmax according to ANB types. The SUVmax was significantly different among the ANB types ( $P < .001$ ): type II-1 ANBs ( $n=31$ ,  $SUV_{max}=9.63 \pm 1.68$  g/mL) had a significantly higher SUVmax compared with ANB type 0 ( $n=7$ ,  $SUV_{max}=2.36 \pm 0.47$  g/mL) ( $P < .05$ ). However, types I ( $n=22$ ,  $SUV_{max}=1.88 \pm 0.25$  g/mL), II-0 ( $n=58$ ,  $SUV_{max}=4.27 \pm 0.50$  g/mL), and III ( $n=30$ ,  $SUV_{max}=1.95 \pm 0.18$  g/mL) were not significantly different from type 0. Data=mean  $\pm$  standard error of the mean. ANB = accessory navicular bone, SUVmax = maximum standardized uptake value. \* $P < .001$ .

The optimal threshold value of the SUVmax that best predicts surgical resection of ANB at the endpoint of follow-up was determined using the ROC curve and survival analyses.

First, ANB types I, II, and III ( $n=141$ ) were investigated. Twelve ANBs were surgically removed. The remaining 129 ANBs were managed without surgery for  $171.5 \pm 252.9$  days. The area under the ROC curve was 0.88 with a 95% confidence interval of 0.819 to 0.932 ( $P < .001$ ). The optimal cut-off value for the SUVmax was 5.27 with a sensitivity of 91.7% and a specificity of 80.6% for the prediction of the final surgical resection (Fig. 4).

Furthermore, Kaplan–Meier analyses were performed to evaluate how well the SUVmax cutoff of 5.27 differentiates ANBs, which consequently require surgical removal. A total of 141 ANBs (type I, II, and III) were classified into 2 groups: ANBs with  $SUV_{max} > 5.27$  ( $n=36$ ) and ANBs with  $SUV_{max} \leq 5.27$  ( $n=105$ ). The log-rank test showed that among the group with  $SUV_{max} > 5.27$ , surgical treatment was significantly more frequent than the group with  $SUV_{max} \leq 5.27$  ( $P < .001$ ) (Fig. 5).

Second, type II ANB, the main type associated with surgical resection, was analyzed. Apart from the 12 surgically treated ANBs, the remaining 77 ANBs were followed-up for  $121.5 \pm 232.5$  days. The area under the ROC curve was 0.81 with a 95% confidence interval of 0.715 to 0.887 ( $P < .001$ ). The optimal cut-off value for the SUVmax was 5.27 with a sensitivity of 91.7% and a specificity of 68.8%. Kaplan–Meier survival analysis in the type II ANB also revealed similar results. Type II ANBs with  $SUV_{max} > 5.27$  ( $n=35$ ) were significantly different from those with  $SUV_{max} \leq 5.27$  ( $n=54$ ) after performing the log-rank test ( $P < .001$ ). A higher SUVmax was more frequently associated with consequential surgical treatment.

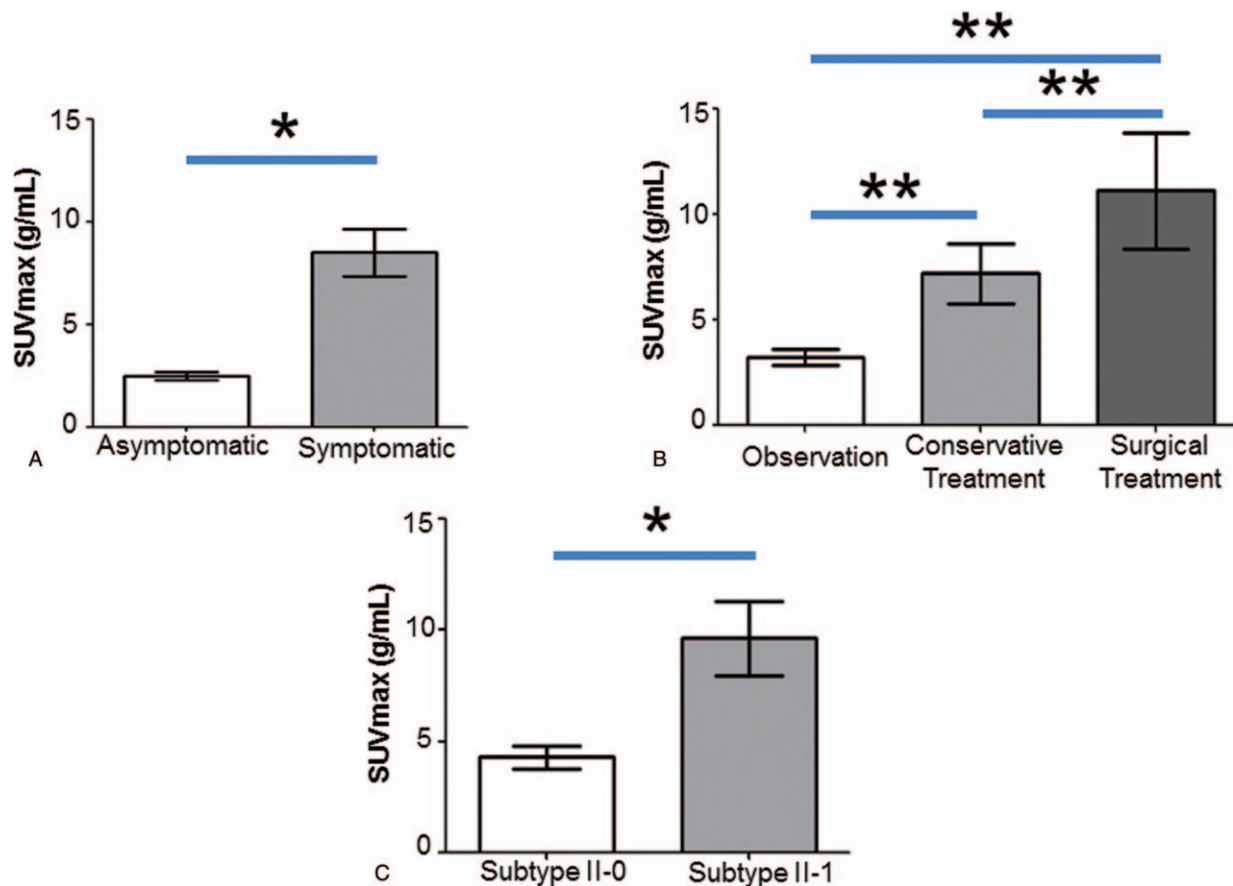
A typical case of ANB type II-1, which was surgically removed, with an SUVmax of 11.57 g/mL, is demonstrated in Fig. 6.

#### 4. Discussion

The current study showed that SUVmax derived from the quantitative bone SPECT/CT was compatible with known clinical risk factors of ANB: the type II-1 ANB, which had been reported to be most likely symptomatic, had the highest SUVmax (Fig. 2); symptomatic ANB, regardless of ANB types, showed greater SUVmax than asymptomatic ANB (Fig. 3A); more aggressive treatment was related with higher SUVmax (Fig. 3B); ANB subtypes with structural abnormality (subtype II-1) had greater SUVmax than those without such bone abnormality (subtype II-0) (Fig. 3C); and logistic regression analyses revealed that SUVmax as well as young age were strongly associated with surgical treatment (Tables 3 and 4). Additionally, the ROC curve (Fig. 4) and survival analyses (Fig. 5) showed that an optimal threshold can be suggested for predicting final surgical treatment (i.e., SUVmax of 5.27 g/mL). All these findings clearly indicate that the SUVmax is a useful biomarker for ANB.

In this study, one foot in a given patient was regarded independent of the other foot in terms of SUVmax measurement. It was based on the statistical result which showed that the mean SUVmax of the bilateral navicular in negative control patients without ANB was not significantly different from that of the contralateral navicular in unilateral ANB patients (type 0). It implies that ANB in a foot does not greatly influence the uptake of Tc-99m HDP in the contralateral navicular. Naturally, this result can be extended to bilateral ANB patients. Thus, either foot of the same patient could be analyzed independently without the concern of a possible influence from the contralateral foot.

High-risk ANB, which requires surgical resection, was mainly related to type II ANB.<sup>[8,9,12,24]</sup> The synchondrosis connection of type II ANB with the navicular is vulnerable to chronic stress or



**Figure 3.** Comparison of SUVmax depending on the presence of medial foot pain, treatment modalities, and subtypes. (A) The SUVmax in symptomatic ANBs (n = 49, SUVmax = 8.51 ± 1.16 g/mL) was significantly higher than that in asymptomatic ANBs (n = 99, SUVmax = 2.48 ± 0.19 g/mL) (*P* < .001). (B) The SUVmax was significantly different according to the treatment modalities (*P* < .001): the SUVmax of surgically resected ANBs (n = 12, SUVmax = 11.11 ± 2.79 g/mL) was significantly higher compared to that of ANBs that were only observed (n = 113, SUVmax = 3.22 ± 0.38 g/mL) and the SUVmax of the conservative treatment group (n = 23, SUVmax = 7.18 ± 1.40 g/mL) (*P* < .05). ANBs with conservative treatment also showed higher SUVmax than those in the observation only group (*P* < .05). (C) Subtype II-1 ANBs had significantly greater SUVmax (n = 31, SUVmax = 9.63 ± 1.68 g/mL) than subtype II-0 ANBs (n = 58, SUVmax = 4.27 ± 0.50 g/mL) (*P* < .001). Data = mean ± standard error of the mean. ANB = accessory navicular bone, SUVmax = maximum standardized uptake value. \**P* < .001 and \*\**P* < .05.

**Table 3**

Logistic regression analyses for association with final surgical treatment in all ANB types (n = 141).

	Univariate analysis			Multivariate analysis		
	Odds ratio	95% CI	<i>P</i>	Odds ratio	95% CI	<i>P</i>
Age, y	0.90	0.84–0.97	.007	0.90	0.82–0.98	.013
Gender (male vs female)	1.22	0.37–4.00	.738	N/A	N/A	N/A
Type (I, II, or III)	0.84	0.32–2.25	.734	N/A	N/A	N/A
SUVmax, g/mL	1.13	1.04–1.22	.003	1.12	1.03–1.22	.007

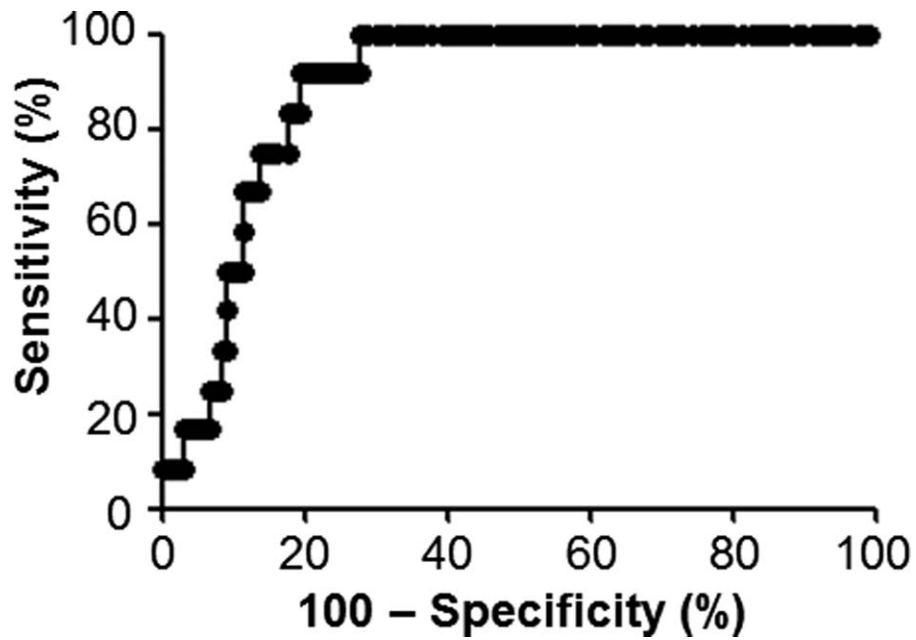
ANB = accessory navicular bone, CI = confidence interval, N/A = not applicable, SUVmax = maximum standardized uptake value.

**Table 4**

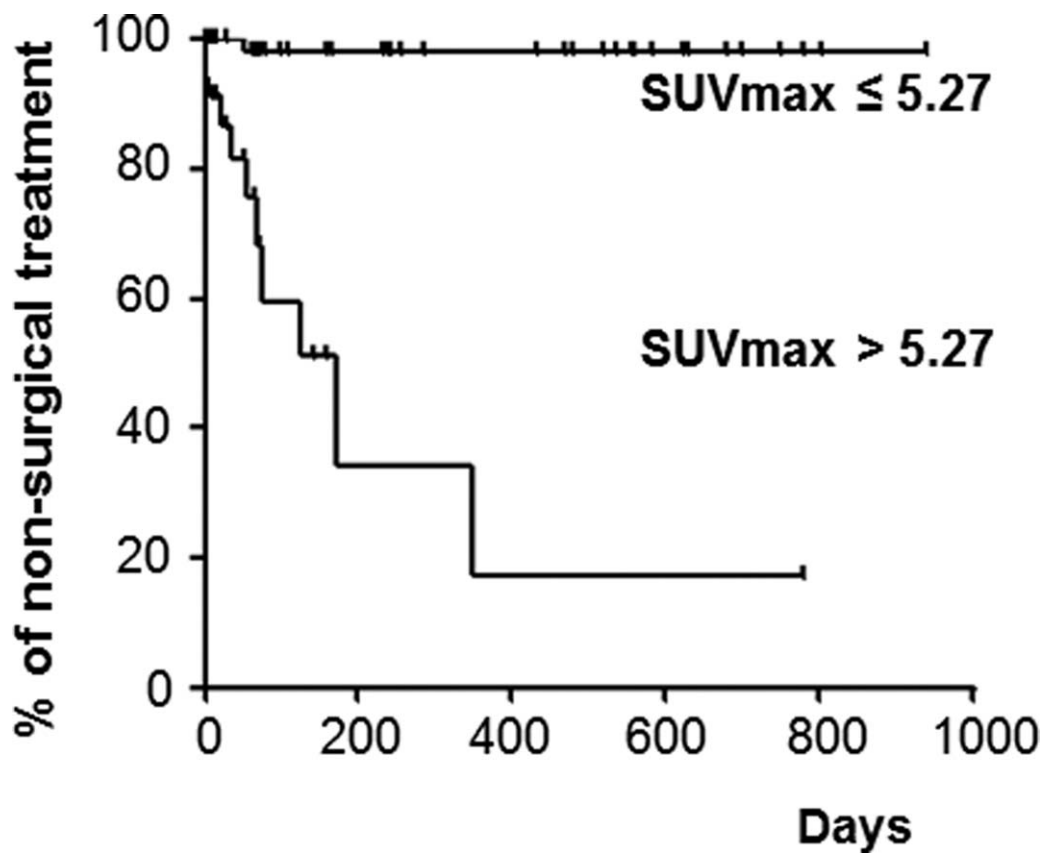
Logistic regression analyses for association with final surgical treatment in ANB type II (n = 89).

	Univariate analysis			Multivariate analysis		
	Odds ratio	95% CI	<i>P</i>	Odds ratio	95% CI	<i>P</i>
Age, y	0.91	0.85–0.98	.013	0.91	0.83–0.98	.020
Gender (male vs female)	0.79	0.23–2.67	.705	N/A	N/A	N/A
Subtype (II-1 vs II-0)	2.08	0.61–7.10	.242	N/A	N/A	N/A
SUVmax, g/mL	1.09	1.01–1.18	.018	1.09	1.01–1.19	.031

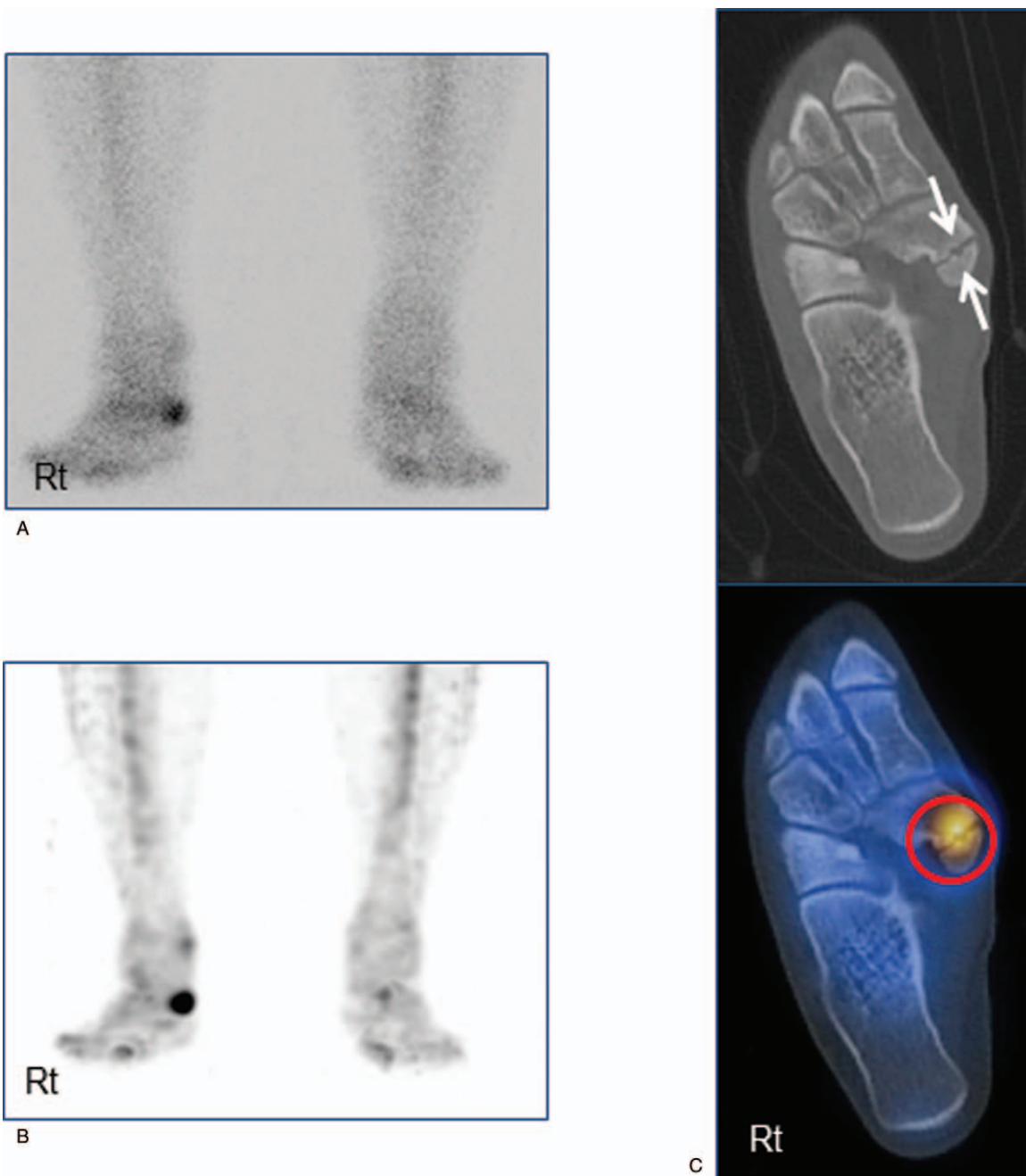
ANB = accessory navicular bone, CI = confidence interval, N/A = not applicable, SUVmax = maximum standardized uptake value.



**Figure 4.** Receiver operating characteristic (ROC) curve analyses to evaluate the diagnostic accuracy of the SUVmax in predicting the decision for final surgical resection. ROC curve analysis in all types of ANB (types I, II, and III; n = 141) with area under the curve of 0.88 and a 95% confidence interval of 0.819 to 0.932 ( $P < .001$ ). ANB = accessory navicular bone, SUVmax = maximum standardized uptake value.



**Figure 5.** Kaplan-Meier analyses for the event defined as surgical resection of an ANB. Survival analysis in all types of ANB (I, II, and III; n = 141) with SUVmax > 5.27 (n = 36) or SUVmax ≤ 5.27 (n = 105). Two groups were significantly different in the frequency of occurrence of the event ( $P < .001$ ). ANB = accessory navicular bone, SUVmax = maximum standardized uptake value.



**Figure 6.** SPECT/CT demonstration of a typical case of subtype II-1 ANB with surgical treatment. A 20-year-old male patient visited the hospital due to right foot medial side pain. The quantitative bone SPECT/CT revealed right ANB (type II-1) with increased uptake (SUVmax: 11.57 g/mL). The symptomatic right ANB was surgically removed. (A) A planar bone scintigraphy image (anterior view). (B) A maximum-intensity-projection (MIP) image from SPECT (anterior view). (C) Transaxial CT (upper) and SPECT/CT fusion (lower) images of the right foot with volume-of-interest overlaid on the SPECT/CT image. White arrows indicate the bony irregularity of the subtype II-1 ANB which is associated with high uptake on SPECT/CT. ANB = accessory navicular bone, CT = computed tomography, SPECT/CT = single-photon emission computed tomography/CT.

injury, leading to cartilaginous structure irritation, bony deformity, or even to osteonecrosis. Bone scintigraphy was shown to be useful for the assessment of high-risk ANB<sup>[12–15]</sup> but the degree of the bone tracer uptake has never been evaluated using unbiased quantitative parameters such as the SUV. From the results of the current study, it is reasonable to think that ANBs with higher SUVmax are more likely to be type II, symptomatic, and structurally disturbed (subtype II-1). Surgical treatment may not be determined solely by SUVmax, but a higher SUVmax may predict the necessity for surgical resection eventually.

The reason why young age was associated with final surgical resection of ANB may be explained by the activity of young people. Although we do not have any supporting data on the daily activities and occupations of patients, we can speculate that younger patients might have more actively participated in exercises which cause repetitive stress to the feet and ANB.

There are several limitations of the study. It is known that severity and duration of medial foot pain are associated with the decision for surgical treatment.<sup>[25]</sup> However, we could not acquire adequate information regarding pain severity due to the



retrospective nature of the study. If the degree of foot pain severity had been more accurately assessed, the significance of SUVmax regarding the association with surgery might have been more relevantly evaluated. Furthermore, the interval from the time when the ANB was triggered and the time when the bone SPECT/CT examination was performed was not thoroughly investigated. Bone tracer uptake may temporarily increase during the acute phase and the decision for surgery may be taken long after conservative treatment. In that case, bone SPECT/CT in chronic phase may be undervalued, while that in the acute phase may be overvalued. Therefore, further prospective studies are required to validate the clinical usefulness of quantitative bone SPECT/CT for surgical resection in symptomatic ANB patients.

## 5. Conclusion

The SUVmax from quantitative bone SPECT/CT was useful for the evaluation of high-risk ANB. Surgical treatment was more frequently associated with the SUVmax as well as young age. Quantitative bone SPECT/CT using Tc-99m HDP is a promising technique, which can be used as an objective imaging modality for ANB patients.

## Author contributions

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