Primary aldosteronism (PA) is currently considered the most frequent cause of secondary hypertension, with an estimated prevalence of ≥11% in hypertensive patients. Because guidelines recommend multidetector computed tomography (CT) to evaluate the adrenal gland, some past reports used multidetector CT as a guide for adrenal venous sampling. However, the detailed anatomy of the right adrenal vein and its relationship with an accessory hepatic vein remains uncertain. The purpose of this study was to describe detailed anatomical variations of the right adrenal vein and to determine the concordance between CT and catheter venography in patients with primary aldosteronism. In total, 440 consecutive patients who underwent adrenal venous sampling were included. Four-phase dynamic CT was performed. Anatomical locations and variations of the right adrenal vein and its relationship with the accessory hepatic vein were compared with catheter venographic findings. Successful catheterization was achieved in 437 patients (99%). The right adrenal vein was visualized in the late arterial phase with CT in 420 patients (95%). The right adrenal vein formed a common trunk with the accessory hepatic vein in 87 patients (20%). CT identified the correct craniocaudal level of the orifice in 354 patients (84%). Anatomical variations, location, and angle of inflow of the right adrenal vein based on CT demonstrated high concordance with catheter venography. CT may provide useful information for preparation before adrenal venous sampling. (Hypertension. 2017;69:428-434. DOI: 10.1161/HYPERTENSIONAHA.116.08375.) • Online Data Supplement

Key Words: adenoma ■ adrenal gland ■ hyperaldosteronism ■ multidetector computed tomography ■ prevalence
Methods

This retrospective study was approved by the institutional review board, and informed consent was waived.

Patient Population

Between January 2008 and February 2014, both MDCT and AVS were performed in 474 consecutive patients with suspected or confirmed PA. Diagnosis of PA was confirmed when the aldosterone-to-renin ratio exceeded 20 after loading 50 mg of captopril in 334 patients. The remaining 140 patients did not meet this criterion; however, AVS indications were determined from other clinical findings by endocrinologists at our institution. Among 474 patients, 27 patients who underwent MDCT with different protocols were excluded. These 27 patients had undergone non–contrast-enhanced CT because of a high risk of iodine-contrast-induced nephropathy or had a history of allergic reactions to iodine-contrast materials. Four patients were excluded because of missing selectivity index data after adrenocorticotropic hormone stimulation in the left adrenal vein. One patient was also excluded because a blood sample was only obtained from a collateral circulation because of an occlusion in the right adrenal vein. Two other patients who had previously undergone right unilateral adrenalectomy were also excluded. Therefore, the study group comprised 440 patients. The patients’ demographic and endocrine data are shown in Table. The median interval between MDCT and AVS was 69 days (range, 1–1573 days).

CT Image Interpretation

The extraglandular part of the RA V was identified by MDCT according to the criteria previously reported: an enhanced tubular or linear structure from the right adrenal gland that eventually entered the inferior vena cava (IVC) either directly or indirectly. The degree of visualization was recorded using a 5-point scale. A score of 5 was considered excellent and indicated that the RA V runs between the IVC and right adrenal gland ≥2 mm in length and shows strong contrast; 4, good—the RA V runs between the IVC and right adrenal gland <2 mm in length but shows strong contrast; 3, fair—although the RA V did not contrast strongly, it is unequivocally detectable; 2, poor—equivocal detection of the RA V with minimal contrast; and 1, none—the RA V is not visualized. Scores ≥3 were defined the RA V as detectable. The RA V was evaluated in the best visualized phase.

Two radiologists (readers A and B) reviewed all the images independently. If RA V visualization was uncertain, reader C, who was board certified by the Japan Radiological Society, evaluated the images with readers A and B to achieve a consensus.

Anatomical Variation

We determined whether the RA V and an AHV formed a common trunk (common-trunk type or independent type). The independent type was subdivided into the following 3 groups: near type, wherein the distance between the orifices of the RA V and the AHV was <3 mm; distant type, ≥3 mm; absent type, no AHV was detected. If multiple AHVs were detected, the one nearest to the RA V was recorded.

The location of the RA V orifice and its angles of the inflow with respect to the IVC were also measured. The cranio-caudal level of the RA V orifice was determined from the cranial to caudal ends relative to vertebral bodies. Each vertebral body was subdivided into 3 equal levels from the cranial to the caudal ends and one additional section representing the vertebral disc. The location of the orifice was evaluated along the circumference of the IVC as an angle (A1) in the x–y plane (Figure 1A). To evaluate the direction of the RA V, 2 angles were measured: angle B1, between the RA V and x axis when the RA V was projected onto the x–y plane (Figure 1B) and the cranio-caudal angle (B2), between the RA V and x–y plane when the RA V was projected onto the vertical plane that was parallel to the RA V at the branching portion (Figure 1C).

For the common-trunk type, an angle (C1) that represents the orifice location of the common trunk was recorded (Figure 1D). The 2 angles were measured from each point of the IVC-to-AHV (D1 and D2), and the AHV-to-RAV (E1 and E2) (Figure 1E and 1F, respectively).

The RA V length was measured. The length and width of the common trunk were also measured (Figure 1D). For near and distant types, the distance between the RA V orifices and the AHV was also measured.

Table. Demographic and Endocrine Data of 440 Patients With Primary Aldosteronism

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Unless otherwise indicated, data are either mean±SD or number of patients with the percentage in parentheses. Blood pressure was measured at the first visit while on continuing treatment with antihypertensive drugs. To convert the plasma aldosterone value to International System of Units (nanomoles per liter), multiply by 0.0277. To convert the serum creatinine level to SI units (micromoles per liter), multiply by 88.4. ARR indicates aldosterone per renin activity ratio; and eGFR, estimated glomerular filtration rate.

*Data are geometric means±geometric SD because the data distribution was highly skewed.

MDCT Protocol

Images were obtained using 1 of the following 3 CT scanners: a 16-detector row CT (SOMATOM Sensation Cardiac; Siemens Healthcare, Forchheim, Germany), a 64-detector row CT (SOMATOM Definition; Siemens Healthcare), and a 64-detector row CT (Aquilion 64; Toshiba Medical Systems, Otawara, Japan). CT parameters and patient characteristics for each scanner are shown in Table S1 in the online-only Data Supplement.

Four-phase dynamic scans were performed. Before scanning was started, 600 mg iodine per kg body weight (maximum dose: 45 g) of a nonionic contrast material was injected into an antecubital vein. The injection time was fixed at 25 seconds. The scan delay was set using an automatic triggering system. When the attenuation value reached a preset threshold (CT value on plain CT plus 50 Hounsfield Unit) at the level of the abdominal aorta, early arterial-phase scanning automatically started. Late arterial-phase scanning began 13 seconds after completion of the first scan. Venous-phase and delayed-phase scanning began 70 seconds and 3 minutes, respectively, after the start of contrast injection. Transverse sections were reconstructed with <1-mm-thick (0.5–0.75 mm) sections at the same interval. Effective radiation dose was estimated by multiplying the dose-length product by a conversion factor of 0.015 mSv/mGy/cm. The total dose-length product of each phase including a noncontrast scan was used.

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Figure 1. Locations and directions of the right adrenal vein (RAV; the independent type, A–C and the common-trunk type, D–F). A, Horizontal (x–y) plane demonstrates a location of the RAV orifice along the circumference of the inferior vena cava (IVC). A1 indicates an angle between the radius through the RAV orifice and the x axis on the x–y plane when the origin of the coordinate axes is set at the IVC center. B, Horizontal (x–y) plane demonstrates a direction of the RAV to the IVC. B1 indicates an angle between the direction of the RAV projected onto the x–y plane and the x axis when the origin of the coordinate axes is set at the RAV orifice. C, Vertical plane parallel to the RAV demonstrates a craniocaudal direction of the RAV to the IVC. B2 indicates an angle between the direction of the RAV and the x–y plane when the origin of the coordinate axes is set at the RAV orifice. D, Horizontal (x–y) plane demonstrates a location of the common trunk orifice along the circumference of the IVC. C1 indicates an angle between the radius through the common trunk and the x axis on the x–y plane when the origin of the coordinate axes is set at the IVC center. The length of the common trunk was measured from the orifice to the confluent portion of the RAV. The width of the common trunk was measured at the orifice. E, Horizontal (x–y) plane demonstrates directions of the accessory hepatic vein (AHV) and the RAV. D1 indicates an angle between the direction of the common trunk projected onto the x–y plane and the x axis when the origin of the coordinate axes is set at the orifice of the common trunk. E1 indicates an angle between the direction of the RAV projected onto the x–y plane and the x axis when the origin of the coordinate axes is set at the RAV orifice. F, Vertical plane demonstrates craniocaudal directions of the AHV and the RAV. D2 indicates an angle between the direction of the common trunk and the x–y plane when the origin of the coordinate axes is set at the orifice of the common trunk. E2 indicates an angle between the direction of the RAV and the x–y plane when the origin of the coordinate axes is set at the RAV orifice.

AVS Procedure

Seven-F sized introducer sheaths were inserted into the bilateral femoral vein to perform simultaneous bilateral AVS. A 6.5-F N-shaped catheter was inserted from the left side to target the left adrenal vein. A high-flow-type microcatheter was inserted into the left adrenal vein above the inferior phrenic vein confluence. A 6.5-F catheter designed for the RAV was inserted from the right femoral sheath. CT information was used as reference for catheter manipulations. The correct position of the catheter was confirmed by injecting a small volume of diluted iodine-contrast material. Adrenal venous samples were simultaneously obtained from the catheters, and an external iliac venous sample was obtained from the sheath 15 minutes after an intravenous 1-shot injection of 0.25 mg adrenocorticotropic hormone.14

The location of the orifice and the direction of inflow of the RAV visualized by catheter venography were documented. The craniocaudal level of the RAV orifice was specified relative to vertebral bodies. The location of the orifice was classified on the basis of its location as lateral (+) or medial (−) to the center (Figure 2A). Whether the direction of inflow was horizontal to the right (+) or left (−) and vertically upward (+) or downward (−) was also recorded (Figure 2B). If the location seemed to be midmost, or the direction of inflow seemed to be straight backward, it was recorded as 0.

Catheterization of the RAV was considered successful when the selectivity index (ratio of the RAV and the external iliac vein plasma cortisol concentrations) after adrenocorticotropic hormone stimulation was at least 5.14,15

Concordance Between MDCT and Catheter Venography

We evaluated the concordance between MDCT and catheter venography in patients who had a detectable RAV using MDCT and had undergone successful AVS. CT-based cranio-caudal level was assumed correct, when it did not vary by ≥2 levels in comparison with catheter venography; almost correct, a difference of 22 levels; unconfident, ≥3 levels of difference; and false, >3 levels of difference. When the plus (+) or minus (−) sign of the orifice location or the angle of inflow that projected onto each horizontal or vertical plane was in agreement with catheter venography, CT-based location or direction was assumed correct. When the location or direction obtained by catheter venography was 0, CT angles of between ±15° were considered correct.

Statistical Analysis

Data are expressed as either mean± SD or number of patients with the percentage. A Fisher exact test was used for binary variables, and ANOVA with Tukey test for post hoc comparisons was used for continuous variables. A weighted κ statistic was used to evaluate inter-reader agreement of visualization scores. Statistical analyses were performed with EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan).16 P value of <0.05 indicates a significant difference.
Results

Success Rate of AVS

Successful bilateral AVS was obtained in 433 of 440 patients (98%). The technical success rate of AVS was 99% (437/440 patients) and 99% (436/440 patients) from the right and left sides, respectively.

Visualization of the RAV

The RAV was detected on MDCT in 425 patients (97%). The RAV detection rates of each CT scanner were as follows: 95% (153/161 patients) by SOMATOM Sensation Cardiac, 97% (148/152 patients) by SOMATOM Definition, and 98% (124/127 patients) by Aquilion 64. There were no significant differences among the 3 scanners (P=0.48). The mean overall effective radiation dose was 29.9±14.6 mSv. The radiation doses of each CT scanner were given in the online-only Data Supplement. The degree of visualization was rated as excellent in 332 patients (75%), good in 62 patients (14%), fair in 31 patients (7.0%), poor in 12 patients (2.7%), and none in 3 patients (0.7%) out of 440 patients. Inter-reader agreements between the 2 reviewers for visualization scores were excellent; the weighted κ=0.90 (95% confidence interval, 0.87–0.94).

The RAV was best visualized in the early arterial phase in 3 patients (0.7%), the late arterial phase in 410 patients (96%), and the venous phase in 12 patients (2.8%) out of 425 patients. The RAV was detectable in 420 of 440 patients (95%) when only the late arterial phase images were reviewed.

Relationship With the AHV

One or more AHV was detected on MDCT in 290 of 425 patients (68%). The AHV was best visualized in the late arterial phase in 5 patients (1.7%), the venous phase in 284 patients (98%), and the delayed phase in 1 patient (0.3%) out of 296 patients. All detectable AHVs were visualized in the venous phase, except one that was only visualized in the delayed phase.

The RAV and the AHV formed a common trunk in 87 patients (common-trunk type, 20%; 95% confidence interval, 17%–25%). The AHV orifice was located near the RAV in 54 patients (near type, 13%). The AHV was located >3 mm from the RAV in 149 patients (distant type, 35%). No AHV was detected on MDCT in 135 patients (absent type, 32%). The mean distance between the orifices of the RAV and the AHV was 10.1±8.1 mm.

Location and Direction of the RAV

The orifice was craniocaudally located between the T10 and L1 vertebrae (Figure 3).

Independent Type (n=338)

The angle A1 ranged from −9° to 72° (mean, 36°±13°; Figure 4A). The RAV orifice was located in the right posterior quadrant in 338 patients (99%). The angle B1 ranged from −63° to 70° (mean, 9°±21°; Figure 4B), and the angle B2 ranged from −82° to 49° (mean, −23°±28°; Figure 4C). The most frequent angle of inflow of the RAV was a posterior, rightward, and caudal course found in 172 patients (51%). A posterior, leftward, and caudal direction was found in 92 patients (27%); a posterior, rightward, cranial direction in 58 patients (17%); and a posterior, leftward, cranial direction in 16 patients (4.7%). The mean length of the RAV was 3.3±1.6 mm.

Common-Trunk Type (n=87)

The angle C1 ranged from 11° to 65° (mean, 41°±11°; Figure 5A). The orifices of the common trunk were located in the right posterior quadrant in all patients. The angle D1 ranged from −2° to 79° (mean, 37°±17°; Figure 5B), and the angle D2 ranged from −26° to 58° (mean, 1°±16°; Figure 5C). The most frequent angle of inflow of the common trunk was a posterior, rightward, and nearly horizontal (−20° to 20°) course found in 71 patients (82%). The angle E1 ranged from −76° to 29° (mean, −22°±24°; Figure 5D) and the angle E2 ranged from −88° to 39° (mean, −29°±30°; Figure 5E). The most frequent angle of inflow of the RAV was a posterior, leftward, and caudal course found in 57 patients (66%). The mean length of the common trunk was 2.7±1.7 mm, and the mean...
width of the common trunk was 5.1±1.5 mm. The mean length of the RAV was 3.3±1.2 mm.

Concordance Between MDCT and Catheter Venography

The RAV was detected by MDCT, and successful AVS was performed in 422 patients. MDCT identified the correct cranio-caudal level of the orifice in 354 patients (84%). Almost correct locations were found in 57 patients (14%), unconfident locations were found in 11 patients (2.6%), and no false localization was found. Lateral, medial, or midmost locations of the orifice were considered correct in all 422 patients. For the independent type, the horizontal directions (rightward, leftward, or straight backward) were considered correct in 327 of 335 patients (98%), and the vertical directions (upward, downward, or straight backward) were considered correct in 317 of 335 patients (95%). The common trunk was identified using both MDCT and catheter venography in 75 patients, only by MDCT in 12 patients, and only by AVS in 1 patient. All 12 patients whose common trunks were detected only by MDCT underwent AVS in an early period (2008–2010).

Discussion

The present study examined the detailed anatomical variations of the RAV and the concordance between MDCT and catheter venography in a large population of PA patients.

Bilateral AVS is required to distinguish between unilateral and bilateral excessive aldosterone secretion in patients with PA. However, AVS is a difficult procedure because of a small RAV that is difficult to identify, cannulate, and draw blood from. Therefore, anatomical variations should be carefully assessed to avoid sampling failure. Our success rate of bilateral AVS (98%) was higher than that previously reported in a multicenter study (31% to 61%). In addition, our success rate for AVS from the right side (99%) was higher than that reported in single-center studies (93% to 98%). Angiographers at our institution usually apply RAV mapping before AVS to determine appropriate catheter types, catheter manipulation, and occasional steam shaping of the catheter. Meanwhile, left-sided failures were observed in 4 procedures in our study. Because the catheter position was correctly confirmed by venography, these failures were presumed to be attributable to dilution.

The RAV was visualized in the late arterial phase in 95% of patients with PA. Two previous studies reported RAV visualization rates of 76% in the arterial phase on an 8-detector row CT, and 78% in 90 seconds after contrast injection on a 64-detector row CT. A 64-detector row CT during the dual adrenal venous phase (45 and 55 seconds after contrast injection) provided higher detectability (91% and 92%, respectively). On the contrary, 88% detectability was reported using a 320-detector row CT with 4-phase dynamic protocols (30, 45, 60 and 90 seconds after contrast injection). Although 320-detector row CT has significantly higher temporal resolution, the RAV detectability was not improved. Moreover, our study showed no significant differences in the RAV detectability among the 3 CT scanners comprising one 16-detector row CT scanner and two 64-detector row CT scanners. These results suggest that appropriate scan delay is important for successful visualization.

The RAV formed a common trunk with the AHV on MDCT in 20% of patients. The prevalence in our population was in agreement with that of previous studies reporting 22% in autopsies. These results indicated that a common trunk was observed in more than the generally considered 10% of cases. The AHV orifice was located near the RAV in 13% of patients. Even without the common trunk, there is the potential risk that the nearby AHV may be misidentified as the RAV. Sampling failures may be avoided by precisely identifying relationships between the RAV and AHV before AVS.

Our study demonstrated that CT-based location and angle of inflow corresponded well with catheter venographic findings. Evaluations of the orifice location on the horizontal plane and the angle of inflow of the RAV almost completely corresponded to catheter venographic findings. All CT-based cranio-caudal levels did not vary by >1 vertebral body height compared with the venographic findings. The mean cranio-caudal movement of the IVC during the respiratory cycle was...
reported as 21.7 mm, and the mean vertebral body and disc heights of lower thoracic spines were described as 19.6 mm (T11), 6.0 mm (T11/12), and 20.8 mm (T12). These results indicate that the differences within 1 vertebral body height should be accepted as a potential respiratory movement.

Our study had several limitations. First, our 4-phase dynamic CT protocol requires high radiation exposure. We usually perform the early arterial phase to rule out renal arterial stenosis causing renovascular hypertension and the delayed phase to differentiate adrenal tumors. If only the anatomical information of the RA V and the AHV is needed, the other 2 phases may be omitted.

Second, not all AHVs were identified by AVS. According to our results, the common trunks of 12 patients were detected only by MDCT and not by catheter venography. The presence of the common trunk may have been overlooked in these 12 patients because we assessed catheter venograms prospectively. Recently, however, in the cases with previous identification of the common-trunk type on MDCT, we identified the common trunk carefully during AVS to achieve selective cannulation instead of sampling from the common trunk.

Third, we did not consider the concordance of the angle of inflow in common-trunk types. It is difficult to determine the direction of inflow of the RA V and AHV by catheter venography because of the complexity of the 3-dimensional structure of the common-trunk type.

In conclusion, anatomical locations and variations of the RA V identified by MDCT demonstrated high concordance with catheter venographic findings. RA V mapping obtained by an appropriate CT scan protocol may help prepare for an AVS procedure.

**Perspectives**

We found that the late arterial phase allowed visualization of the RA V in 95% of PA patients, and CT-based anatomical information showed high concordance with catheter venographic findings. The prevalence of having a common trunk with an AHV was 20%, 2x higher than that reported by previous studies. By using CT mapping as the reference for catheter manipulations, AVS may be performed successfully. However, these findings were retrospectively obtained from only Japanese patients with PA; therefore, a multicenter cohort study, including various ethnic populations, should be considered for future study.


Anatomical Variations of the Right Adrenal Vein: Concordance Between Multidetector Computed Tomography and Catheter Venography
Kensuke Omura, Hideki Ota, Yuuki Takahashi, Tomonori Matsuura, Kazumasa Seiji, Yoichi Arai, Ryo Morimoto, Fumitoshi Satoh and Kei Takase

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Anatomical variations of the right adrenal vein: concordance between multidetector computed tomography and catheter venography

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Supplemental Methods

Evaluating Curative Effect after Unilateral Adrenalectomy

Patients who were diagnosed with primary aldosteronism (PA) with unilateral aldosterone excess underwent unilateral adrenalectomy. Plasma aldosterone levels obtained on postoperative day 7 were compared with those obtained before surgery. Aldosterone excess was considered remitted when the aldosterone level on postoperative day 7 was less than 15 ng/dL, or the aldosterone-to-renin ratio (ARR) on postoperative day 7 was less than 30 ng/dL per ng/mL/h. Patients who underwent medical treatment or bilateral operation (ipsilateral total adrenalectomy with contralateral partial adrenalectomy) were excluded from this analysis because no established criterion to evaluate curative effect of medical treatment has been developed and bilateral operations were performed based on the result of segmental adrenal venous sampling (S-AVS).1,2

Statistical Analysis

A paired t-test was used to compare preoperative and post-operative plasma aldosterone levels after logarithmic transformation since the data distribution was highly skewed. Analysis of variance with Tukey’s test for post hoc comparisons was used for continuous variables.

Supplemental Results

Curative Effect after Unilateral Adrenalectomy

Unilateral aldosterone excess was confirmed by AVS in 148 of 440 patients, and 292 patients were diagnosed with bilateral disease. Among the 148 patients with unilateral hypersecretion, 132 patients underwent unilateral adrenalectomy. In these cases, the geometric mean plasma aldosterone level decreased significantly at one week after surgery (from 32.5 ± 1.9 to 7.1 ± 1.5; \( P < 0.001 \)). The aldosterone excess was remitted in 129 of 132 patients (98%).

Effective Radiation Dose

The mean overall effective radiation dose was 29.9 ± 14.6 mSv. The radiation doses of the 3 CT scanners were as follows: 23.1 ± 6.3 mSv for the SOMATOM Sensation Cardiac, 29.5 ± 8.6 mSv for the SOMATOM Definition, and 38.2 ±22.1 mSv for the Aquilion 64 (Table S1). The radiation dose of the SOMATOM Sensation Cardiac was significantly lower than those of the other 2 scanners \( (P < 0.001) \). The radiation dose of the SOMATOM Definition was significantly lower than that of the Aquilion 64 \( (P < 0.001) \).
References


## Supplemental Table

### Table S1. CT Scan Parameters and Patient Characteristics

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**Patient characteristic**

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<td>Age (y)</td>
<td>51.9 ± 11.5</td>
<td>52.1 ± 11.2</td>
<td>54.1 ± 12.1</td>
<td>0.23</td>
</tr>
<tr>
<td>Male sex</td>
<td>75 (47)</td>
<td>74 (49)</td>
<td>67 (53)</td>
<td>0.58</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>162.2 ± 9.4</td>
<td>163.7 ± 8.4</td>
<td>161.9 ± 9.3</td>
<td>0.74</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>66.1 ± 13.5</td>
<td>68.6 ± 15.6</td>
<td>67.5 ± 13.4</td>
<td>0.30</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>24.9 ± 3.9</td>
<td>25.7 ± 4.6</td>
<td>25.6 ± 4.0</td>
<td>0.18</td>
</tr>
</tbody>
</table>

Data are either means ± standard deviation or number of patients with the percentage in parentheses. Siemens 16 indicates SOMATOM Sensation Cardiac (Siemens Healthcare, Forchheim, Germany); Siemens 64, SOMATOM Definition (Siemens Healthcare); Toshiba 64, Aquilion 64 (Toshiba Medical Systems, Otawara, Japan)

* Value was significantly lower (P < 0.001) than those at Siemens 64 and Toshiba 64.

† Value was significantly lower (P < 0.001) than that at Toshiba 64.