Since the development of multidetector row computed tomography (MDCT), coronary computed tomography angiography (CTA) has been widely used as a non-invasive imaging tool for the assessment of coronary artery disease (CAD). Coronary CTA has high diagnostic accuracy for the identification of coronary artery stenosis on invasive coronary angiography (ICA). Moreover, a randomized controlled trial showed that coronary CTA allowed for significant reduction of cardiac death or non-fatal myocardial infarction. However, the clinical usefulness of coronary CTA should exceed the risk of the radiation dose, including the carcinogenic risk. Patients with arteriosclerosis tend to undergo additional tests including ICA or follow-up CTA, thereby increasing their cancer risk, and the proper management of the radiation dose is an important issue. The radiation dose of coronary CTA varies depending on the institution despite the published guidelines, and standardization of the radiation dose associated with coronary CTA is necessary. In Japan, the actual status of radiation exposure in daily clinical practice and the independent factors associated with radiation dose have not been clarified. The purpose of this study was to investigate (1) the actual status of the radiation dose associated with coronary CTA in daily clinical practice; (2) the independent factors contributing to radiation dose; and (3) the currently available strategies for radiation dose reduction.

Key Words: Computed tomography angiography; Coronary artery; Dose-length product; Radiation dose; Tube voltage

Background: Although coronary computed tomography angiography (CTA) is frequently used for identifying coronary artery disease, no studies have investigated the radiation dose in detail in Japan. The aim of this study was to estimate the radiation dose of coronary CTA in Japanese clinical practice and to identify the independent predictors associated with radiation dose.

Methods and Results: A multicenter, retrospective, observational study (54 institutions) was conducted for estimating the radiation dose of coronary CTA in 2,469 patients between January and December 2013. Independent predictors associated with radiation dose were investigated on linear regression analysis. Median dose-length product (DLP) was 809.0 mGy·cm (IQR, 350.0–1,368.8 mGy·cm), corresponding to an estimated radiation dose of 11 mSv. The DLP per site significantly differed between institutions (median DLP per site, 92–2,131 mGy·cm; P<0.05). Independent predictors associated with radiation dose on multivariable linear regression were body weight, heart rate, non-stable sinus rhythm, scan length, tube voltage setting, electrocardiogram (ECG)-gated scanning protocol, and the image reconstruction technique (P<0.05 each).

Conclusions: The coronary CTA radiation dose was relatively high in 2013, and it varied significantly between institutions. Effective strategies for radiation dose reduction were low tube voltage ≤100 kVp, retrospective ECG-gated scanning with dose modulation technique, prospective ECG-gated scanning, and the iterative reconstruction technique.
Methods

Subjects
This study was approved as a retrospective multicenter study by the institutional review board at the individual study sites. The dose survey was an industry-independent, multivendor, multicenter, retrospective, observational study. The need for informed consent was waived in view of the retrospective nature of the analysis and the anonymity of the data. Fifty-four institutions in Japan participated in the present study, and the local investigators enrolled consecutive patients who underwent coronary CTA in clinical practice between January 2013 and December 2013 in the range of 20–150 patients. Coronary CTA was performed based on local clinical decision making in each institution. The inclusion criteria were coronary CTA using ≥64-row MDCT; and age ≥20 years. The exclusion criteria were as follows: non-diagnostic image quality for clinical use (e.g., insufficient breathholding; body movement); incomplete CT study because of adverse events during scanning; registration to other studies; and incomplete datasets.

All observational data were analyzed at a core laboratory. The following patient characteristics were collected: height; body weight; indication for coronary CTA (coronary artery evaluation or others); heart rate; heart rhythm (stable sinus rhythm, or non-stable sinus rhythm); and β-blocker preparation. The following imaging parameters were recorded: scan length; CT system (64-row CT or >64-row CT); tube voltage (≤100 kVp, ≤120 kVp, ≤100 kVp, or dual energy); electrocardiogram (ECG)-gated technique (retrospective, retrospective + dose modulation, or prospective); and image reconstruction technique (filtered back projection [FBP] or iterative reconstruction [IR]).

Radiation Dose Estimation
The local investigators assessed the volume CT dose index (CTDVol) and dose-length product (DLP) associated with coronary CTA from the dose report. The CTDVol is calculated as the integral of the radiation dose profile of a single rotation scan. The DLP is calculated by multiplying the CTDVol with the respective scan length and represents the radiation dose received during the entire CT scan. The effective coronary CTA dose is calculated by multiplying the DLP with an organ weighting factor for the chest as the investigated anatomic region. The organ weighting factor for the chest is 0.014 or 0.026 mSv/(mGy·cm)\(^{-1}\).

Image Quality Assessment and Strategies for Radiation Dose Reduction
Radiation dose reduction strategies in the present study were low-tube voltage ≤100 kVp, retrospective ECG-gated scanning with dose modulation technique, prospective ECG-gated scanning, and the IR technique. The local study investigators determined the indications for the radiation dose reduction strategies according to patient condition, institution facilities, and other factors. A lower tube voltage ≤100 kVp has become available for coronary CTA (except for obese patients) thanks to developments in CT technology (e.g., in the X-ray tube or detector). The retrospective ECG-gated scanning protocol is a stable scanning technique, but it requires higher radiation dose than for other scanning protocols. The dose modulation technique can effectively reduce radiation dose during retrospective ECG-gated scanning by reducing the tube current during the phases of the cardiac cycle with large cardiac motion, which causes motion artifacts in coronary CTA. The prospective ECG-gated scanning technique is also a useful scanning protocol for radiation dose reduction by data acquisition only during the phase of the cardiac cycle with minimum cardiac motion and it is used in patients with heart rate ≤65 beats/min and stable sinus rhythm. IR is an advanced image reconstruction technique for CT. IR allows for reconstruction of CT images with less image noise than FBP and reduced radiation dose without reducing diagnostic image quality by integrating low tube voltage or low tube current.

A representative local investigator at each institution, who was blinded to the clinical data and CT acquisition details, measured image noise using a round region of interest (ROI) with a size of 100 mm\(^2\) in the ascending aorta. Image noise (Hounsfield unit; HU) was defined as the standard deviation of the ROI located in the ascending aorta.

Statistical Analysis
Continuous data are expressed as mean±SD or as median (IQR). A generalized estimation equation model was used to account for the clustering effect of this multicenter trial. The independent predictors associated with radiation dose in coronary CTA were assessed on multivariable linear regression analysis of patient and imaging characteristics. Only variables with P<0.10 on univariate analysis were used in multivariable linear regression analysis, to avoid overfitting the multivariable model. The differences in DLP per site were compared among the sites using the Kruskal-Wallis test. Differences in DLP and image noise were assessed the Mann-Whitney U-test, for tube voltage (≤120 kVp and ≤100 kVp), ECG-gated scanning technique (retrospective, retrospective + dose modulation, or prospective), and the image reconstruction technique (FBP or IR). In all tests, statistical significance was determined at P<0.05. The familywise error rate was adjusted in multiple comparisons using the Bonferroni correction. Statistical analysis was performed using IBM SPSS Statistics 25.0 (IBM, Armonk, New York, USA) and R version 3.4.1 (R Core Team 2017, R Foundation for Statistical Computing, Vienna, Austria).

Results

Subjects
Investigators from 54 study sites agreed to participate in the study. These institutions enrolled 3,635 participants who underwent coronary CTA in daily practice (median, 60 patients per site; IQR, 40–100 patients). Of the 3,635 patients, 1,166 were excluded due to incomplete data (height, 12%; weight, 5%; indication for CTA, 6%; heart rate during scanning, 2%; heart rhythm, 1%; β-blocker medication, 6%; tube voltage, 6%; scanning protocol, 6%; image reconstruction technique, 6%; scan length, 9%; CTDVol and DLP, 13%; Figure 1). Finally, 2,469 eligible patients were enrolled in the present study. Patient characteristics are listed in Table 1. Mean patient age was 66.5±11.9 years, the proportion of male patients was 65%, and mean body mass index (BMI) was 23.5±3.7 kg/m\(^2\). Eighty-one percent of patients underwent coronary CTA with stable sinus rhythm and a mean heart rate of 64.1±12.5 beats/min. Beta-blockers were used in 50% of patients to reduce heart rate during scanning. Seventy-nine
percent of patients underwent coronary CTA for the assessment of coronary arteries, which was the main indication for coronary CTA. Other indications for coronary CTA included visualization of bypass grafts (8%), valve assessment (1%), planning of electrophysiological procedures (0.3%), and others.

The imaging characteristics of coronary CTA are given in Table 2. Sixty-four-row CT was used in 42% of patients, and >64-row CT was used in 58% of patients. Retrospective ECG-gated scanning was used in 26% of patients, retrospective ECG-gated scanning with dose modulation was used in 38% of patients, and prospective ECG-gated scanning was used in 58% of patients. In 35% of patients, the tube-voltage was 120 kVp, FBP was used in 41% of patients, and IR was used in 59% of patients. The median scan length was 14.0 cm (IQR, 12.3–16.0 cm).

Radiation Dose and Independent Predictors
Median CTDIvol was 53.8 mGy (IQR, 23.4–84.6 mGy), median DLP was 809.0 mGy·cm (IQR, 350.0–1,368.8 mGy·cm), and the median estimated effective radiation dose was 11.3 mSv (IQR, 4.9–19.2 mSv) for 0.014 mSv·(mGy·cm)−1, and 21.0 mSv (IQR, 9.1–35.6 mSv) for 0.026 mSv·(mGy·cm)−1. Median DLP per site (range, 92.0–2,131.0 mGy·cm) differed significantly among the institutions. In coronary CTA indicated for only coronary artery assessment, the median CTDIvol was 51.1 mGy (IQR, 21.5–83.3 mGy), median DLP was 712.1 mGy·cm (IQR, 303.7–1,259.5 mGy·cm), and the median estimated effective radiation dose was 10.0 mSv (IQR, 4.3–17.6 mSv) for 0.014 mSv·(mGy·cm)−1, and 18.5 mSv (IQR, 7.9–32.7 mSv) for 0.026 mSv·(mGy·cm)−1. In coronary CTA indicated for coronary artery bypass graft (CABG), median CTDIvol was 72.2 mGy (IQR, 41.6–117.9 mGy), median DLP was 1,528.3 mGy·cm (IQR, 1,022.0–2,314.7 mGy·cm), and the median estimated effective radiation dose was 23.5 mSv (IQR, 14.3–32.4 mSv) for 0.014 mSv·(mGy·cm)−1, and 43.6 mSv (IQR, 26.6–60.2 mSv) for 0.026 mSv·(mGy·cm)−1.

Results of univariable and multivariable linear regression analysis are listed in Table 3. Eleven of 13 variables had a significant association with DLP on univariate linear regression analysis and were used in the multivariable linear regression analysis. Finally, increase in body weight and heart rate during scanning, non-stable sinus rhythm, and scan length were independent predictors associated with DLP increase on multivariable linear regression analysis. A 10-kg increase in body weight was associated with a 16.3 mGy·cm increase in DLP (95% CI: 14.3–19.2 mSv, 0.014 mSv·(mGy·cm)−1, and 43.6 mSv (IQR, 26.6–60.2 mSv) for 0.026 mSv·(mGy·cm)−1).
Table 3. Predictors of Radiation Dose Associated With Coronary CTA

| Predictors                              | Univariable linear regression analysis | Multivariable linear regression analysis |
|-----------------------------------------|----------------------------------------|----------------------------------------|
|                                         | Change in DLP (95% CI) (mGy·cm)         | P-value                                |
|                                         |                                         | Change in DLP (95% CI) (mGy·cm)         | P-value |
| Patient height (per 1 cm)               | 8.4 (5.9–10.9)                         | <0.001                                 | −1.3 (−4.9–2.2) | 0.463 |
| Patient weight (per 1 kg)               | 6.2 (4.2–8.1)                          | <0.001                                 | 6.6 (4.1–9.1)   | <0.001 |
| Heart rate (per 1 beat/min)             | 9.5 (5.6–13.4)                         | <0.001                                 | 2.6 (0.2–5.1)   | 0.035 |
| Heart rhythm, sinus vs. non-stable sinus rhythm | 314.0 (205.2–422.7)                   | <0.001                                 | 127.3 (61.0–193.7) | <0.001 |
| β-blocker preparation                    | −44.0 (−164.9–77.0)                    | 0.476                                  | NA              | NA    |
| CT system, 64-row CT vs. >64-row CT      | 41.1 (−221.9–304.1)                    | 0.759                                  | NA              | NA    |
| CTA indication, coronary vs. others      | 605.5 (393.1–818.0)                    | <0.001                                 | 81.6 (−31.2–194.5) | 0.156 |
| Tube voltage, ≥120kVp vs. ≤100kVp        | −289.4 (−390.9–187.8)                  | <0.001                                 | −193.3 (−297.1–−89.4) | <0.001 |
| Tube voltage, ≥120kVp vs. dual energy scanning | −890.1 (−1,580.1–−200.1)            | 0.011                                  | −193.3 (−388.2–1.6) | 0.052 |
| Retrospective scanning vs. retrospective scanning with DM | −390.3 (−542.2–−238.2)       | <0.001                                 | −335.6 (−460.1–−210.7) | <0.001 |
| Retrospective scanning vs. prospective scanning | −1,168.2 (−1,354.8–−981.6)   | <0.001                                 | −919.7 (−1,082.7–−756.6) | <0.001 |
| Image reconstruction, FBP vs. IR         | −1,412.5 (−2,710.0–−115.1)             | 0.033                                  | −373.6 (−731.5–−15.7) | 0.041 |
| Scan length (per 1 cm)                   | 56.7 (38.0–75.5)                       | <0.001                                 | 44.5 (26.3–62.7) | <0.001 |

CT, computed tomography; CTA, computed tomography angiography; DLP, dose-length product; DM, dose modulation; FBP, filtered back projection; IR, iterative reconstruction; HU, Hounsfield unit; NA, not applicable.

Table 4. Strategies for Dose Reduction

| DLP (mGy·cm) | P-value |
|--------------|---------|
| Tube voltage ≥120kVp | 900.0 (436.5–1,440.0) | Ref. |
| Tube voltage ≤100kVp | 467.0 (168.2–747.2) | <0.05 |
| Retrospective ECG-gated scanning | 1,427.5 (834.4–1,863.0) | Ref. |
| Retrospective ECG-gated scanning + DM | 991.6 (659.6–1,398.2) | <0.05 |
| Prospective ECG-gated scanning | 274.0 (137.3–451.0) | <0.05 |
| FBP | 992.5 (661.2–1,460.4) | Ref. |
| IR | 561.4 (243.2–1,234.6) | <0.05 |

% DLP reduction†

| Tube voltage ≤100kVp | 41% decrease |
| Tube voltage ≤100kVp + IR | 47% decrease |
| Tube voltage ≤100kVp + IR + prospective ECG-gated scanning | 67% decrease |

Data given as median (IQR). †Relative to tube voltage ≥120kVp, retrospective ECG-gated scanning, and FBP. DLP, dose-length product; DM, dose modulation; ECG, electrocardiogram; FBP, filtered back projection; IR, iterative reconstruction.

Image Quality and Strategies for Dose Reduction

The radiation dose reduction strategies used in the present study are given in Table 4. A low tube voltage ≤100kVp was used in only 303 patients (12%) and allowed for a 48% significant reduction in DLP compared with a tube voltage ≥120kVp (Figure 2A, P<0.05). The retrospective ECG-gated scanning with dose modulation technique was applied in 929 patients (38%) and allowed for a 30% significant reduction in DLP compared with retrospective ECG-gated scanning alone (Figure 2B, P<0.05). Prospective ECG-gated scanning was used in 884 patients (36%) and allowed for an 81% significant reduction in DLP compared with retrospective ECG-gated scanning alone (Figure 2B, P<0.05). IR was used in 1,467 patients (59%), and allowed for a 43% significant reduction in DLP compared with FBP (Figure 2C, P<0.05).

Regarding image quality, median image noise was 22.0 HU (IQR, 17.8–25.9 HU) for tube voltage ≥120kVp and 26.5 HU (IQR, 21.5–32.9 HU) for tube voltage ≤100kVp; median image noise was 21.9 HU (IQR, 17.3–26.9 HU) for retrospective ECG-gated scanning, 20.4 HU (IQR, 16.6–24.7 HU) for retrospective ECG-gated scanning with dose modulation, and 24.1 HU (IQR, 20.8–29.9 HU) for prospective ECG-gated scanning; median image noise was 21.1 HU (IQR, 16.6–25.6 HU) for FBP, and 23.0 HU (IQR, 19.0–27.6 HU) for IR. There were significant differences in image noise for tube voltage (≥120kVp and ≤100kVp), ECG-gated scanning technique (retrospective, prospective + dose modulation, or prospective), and the image reconstruction technique (FBP or IR; P<0.05 in each).

Discussion

The present study has shown that (1) median radiation dose (DLP) in coronary CTA was 809.0 mGy·cm (IQR, 350.0–1,368.8 mGy·cm) with significant variation between institutions; (2) the independent predictors associated with radiation dose in coronary CTA were body weight, heart rate during scanning, non-stable sinus rhythm, scan length,
not to underestimate the risk of radiation exposure. In the present study, using the data from the multicenter registry in 2013, the median DLP in coronary CTA was 809.0 mGy·cm (IQR, 350.0–1,368.8 mGy·cm), which was similar to that in the Japanese radiation dose survey in 2015. Additionally, the median DLP for only coronary artery assessment was extremely higher than that in a recent worldwide dose survey in 2017 (712.1 mGy·cm; IQR, 303.7–1,259.5 mGy·cm vs. 195 mGy·cm, IQR, 110–338 mGy·cm) even though the patients with CABG were excluded. The higher radiation dose for CABG was reasonable to some extent due to the longer scan length, but it was too high compared with thoracoabdominal CT or dynamic hepatic CT.

The risk of carcinogenesis due to radiation exposure was reported to be the highest in Japan among the developed countries, and the physicians in Japan should be more familiar with the magnitude of radiation exposure associated with coronary CTA in daily practice. Indeed, the rate of incomplete datasets (32%) was very high in the present study, which might indicate the low awareness of radiation dose control causing the high radiation dose associated with coronary CTA. Moreover,
there was a large difference in radiation dose per site, indicated that standardizing of the scanning protocol of coronary CTA and further education and practice on dose reduction strategies are necessary.

In the present study, increase in body weight and heart rate during scanning, non-stable sinus rhythm, and scan length were independent predictors of higher radiation dose. Although there are limits to how much control can be exercised with regard to the patient characteristics that are independent predictors, we should strive to strictly reduce the heart rate during scanning and the scan length.\textsuperscript{22,23} Conversely, low tube voltage ≤100 kVp, retrospective ECG-gated scanning with dose modulation technique, prospective ECG-gated scanning, and IR were independently associated with lower radiation dose in coronary CTA. A low tube voltage ≤100 kVp has been available in clinical practice along with the recently improved detector, image reconstruction technique, and tube designs with the capacity to generate high tube current at low tube voltage, resulting in radiation dose reduction with acceptable image quality.\textsuperscript{24} The Society of Cardiovascular CT (SCCT) guidelines also recommend low tube voltage scanning, especially in non-obese patients (e.g., body weight ≤100 kg, BMI ≤30 kg/m\textsuperscript{2}) and in children.\textsuperscript{7} In the present study, a low tube voltage ≤100 kVp was used in only 13\% of eligible patients with BMI ≤30 kg/m\textsuperscript{2}. Moreover, the IR technique allows for a scanning protocol with a lower tube voltage ≤80 kVp or lower tube current, which leads to greater radiation dose reduction without reducing image quality.\textsuperscript{25,26} Recently, the most advanced IR technique was found to enable coronary CTA with a submillisievert radiation dose.\textsuperscript{27,28} The respective utilization rates, however, of low tube voltage ≤100 kVp and IR were 12\% and 59\% in the present study, which were lower than those reported (56\% and 83\%) in a recent worldwide dose survey in 2017.\textsuperscript{29} Therefore, low tube voltage ≤100 kVp and IR should be used, especially in patients with small physique. The dose modulation techniques associated with retrospective ECG-gated scanning and prospective ECG-gated scanning are also useful for the reduction of radiation dose.\textsuperscript{11,12} Basically, prospective ECG-gated scanning should be considered as the default scan mode in patients with adequate heart rate control when the main indication for coronary CTA is the evaluation of the coronary arteries.\textsuperscript{7} However, it was selected in only 36\% of patients in this study, which was lower than that reported (89\%) in a recent worldwide dose survey in 2017.\textsuperscript{28} Although the optimal scanning protocol is decided according to patient condition, CT scanner, indication for coronary CTA, and radiation dose, more effort should be made to use the prospective ECG-gated scanning protocol. In terms of image quality, these strategies for radiation dose reduction have little influence on diagnostic image quality.\textsuperscript{8,20} In the present study, the image noise was approximately 25 HU regardless of the presence or absence of strategies for radiation dose reduction, as also reported in a previous study published in 2013.\textsuperscript{19} Although significant differences in image noise were observed between CT with and without dose reduction strategies, the actual (absolute) difference in image quality was small, which resulted in small clinical significance. Indeed, the study dataset did not include CT with non-diagnostic image quality.

These results were from the clinical data in 2013, and the actual status of radiation exposure and the image quality of coronary CTA have changed since 2013. The management of medical radiation dose will be required by law in Japan starting in 2020, which has the potential to facilitate the raised awareness of radiation dose control. A new survey should be performed in the near future, for which the present results could serve as an important reference comparison.

Study Limitations
There were some limitations in this study. First, it was retrospective, and there was selection bias pertaining to the local investigators. Moreover, the institutions were limited to university hospitals in this first survey, which resulted in institution characteristic bias, and multicenter prospective studies should be conducted at both university hospitals and general city hospitals in the future. Second, the effect of the tube current setting could not be evaluated in the present study because the tube current was not universally determined depending on the CT system and software, although CTDIvol and DLP used for analysis included the effect of tube current. Third, the institution experience for coronary CTA was not evaluated here, and it has the potential to be an independent predictor of the radiation dose associated with coronary CTA.\textsuperscript{20} Additionally, the characteristics of the managers of radiation dose control (e.g., cardiologists, radiologists, and technologists) and the implementation rate of dose reduction methods in the CT scanner are important predictors associated with the radiation dose. These factors will be evaluated in further studies. Finally, the influence of radiation dose reduction strategies on the diagnostic performance of coronary CTA was not evaluated in this study. However, prospective multicenter trials have shown that these strategies are feasible for radiation dose reduction without reducing diagnostic image quality.\textsuperscript{30–32}  

Conclusions
The radiation dose for coronary CTA was 11 mSv in 2013, and it could be reduced substantially using strategies for radiation dose reduction including low-tube voltage scanning, retrospective ECG-gated scanning with dose modulation, prospective ECG-gated scanning, and IR. However, these strategies were used infrequently in 2013, and education of physicians and technicians performing coronary CTA with regard to the magnitude and the independent predictors of radiation dose should have been continued, to maintain a radiation dose “as low as reasonably achievable” in all patients undergoing coronary CTA. A future survey is necessary to elucidate the current status of the radiation dose associated with coronary CTA in Japan.

Acknowledgments
Participants in this multicenter trial were drawn from radiology departments of the following institutions: Ehime Prefectural Central Hospital, Ehime University Hospital, Kyorin University Hospital, Yokohama City University Hospital, Iwate Medical University Hospital, Kyoto University Hospital, Kanazawa Medical University Hospital, Kanazawa University Hospital, Kumamoto University Hospital, Gunma University Hospital, Hiroshima University Hospital, Saitama Medical University International Medical Center, Saitama Medical University Hospital, Mie University Hospital, Yamaguchi University Hospital, University of Occupational and Environmental Health, Jichi Medical University Hospital, Jichi Medical University Saitama Medical Center, Shinsyu University Hospital, Niigata University Medical and Dental Hospital, St. Marianna University School of Medicine Hospital, St. Marianna University School of Medicine.
Disclosures

This study was funded by Bayer Yakuhin.

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