Background—Available data on the radiation burden from coronary computed tomography (CT) angiography (CCTA) are mostly limited to effective dose estimates. This study provides individualized estimates of doses and associated life attributable risks of radiation-induced cancer in a clinical patient population undergoing 256-slice CCTA.

Methods and Results—Typical retrospectively and prospectively ECG-gated CCTA exposures in a 256-slice CT scanner were simulated on 52 patient-specific voxelized phantoms. Dose images depicting the dose deposition on the exposed region were generated, and normalized organ doses for all primarily irradiated radiosensitive organs were derived and correlated to patient body habitus. Lung, breast, and esophagus absorbed doses were then determined in 136 consecutive patients subjected to CCTA. Projected life attributable risks of radiation-induced cancer were estimated through the use of appropriate sex-, age- and organ-specific cancer risk factors and compared with corresponding nominal cancer risks. The total projected life attributable risk of radiogenic cancer after CCTA decreases steeply with age at exposure, and lung cancer constitutes the most probable detriment for both sexes. The relative risks of lung cancer associated with prospectively ECG-gated CCTA were 1.0032 and 1.0008 for women and men, respectively. The mean total projected life attributable risks were estimated to be $24.9 \pm 7.4$ and $71.5 \pm 30.0$ per 100,000 women undergoing prospectively and retrospectively ECG-gated CCTA, respectively. The corresponding values for men were $7.3 \pm 1.3$ and $31.4 \pm 5.0$ per 100,000 patients.

Conclusions—The mean projected life attributable risks of radiation-induced cancer in a typical clinical patient cohort undergoing standard prospectively ECG-gated CCTA with a 256-slice scanner were found to inconsequentially increase the natural cancer incidence rates. (Circulation. 2010;122:2394-2402.)

Key Words: cancer risk • coronary angiography • diagnostic imaging • radiation dosage • tomography, x-ray computed
The present study was motivated by the limited dosimetric data on patients undergoing CCTA on wide-area detector CT scanners and the absence of data for the assessment of individualized radiation burden and lifetime attributable risk (LAR) of radiation-induced cancer associated with CCTA performed on modern CT scanners. The aims of the present study were to simulate standard CCTA exposures of a 256-slice CT scanner on patient-specific anthropomorphic voxelized phantoms, to assess individualized absorbed doses to the primarily irradiated radiosensitive organs for men and women subjected to typical CCTA with 256-slice CT scanners, and to estimate projected LAR of cancer induction for a typical patient cohort referred for CCTA.

Methods
Monte Carlo Simulation of CCTA and Determination of Normalized Organ Doses
A recently developed and validated\textsuperscript{12,13} Monte Carlo simulation software package for CT dosimetry (ImpactMC, Vamp GmbH, Erlangen, Germany) was used. This software is capable of generating patient-specific voxelized phantoms using the CT images derived from patients’ scans. Any CT exposure may then be simulated on the voxelized phantom, taking into account scanner-specific exposure characteristics. The output is a series of transverse dose images in 1-to-1 correspondence to input CT images. A representative input CT image and the corresponding output dose image are shown in Figure 1. Output dose images depict the dose absorbed by each voxel normalized to the free-in-air measurement of CTDI (CTDI\textsubscript{vol}) for the tube voltage, tube load, and beam collimation used during the exposure.

Raw CT data obtained from 26 consecutive men (mean age, 59.4 years; weight range, 69 to 130 kg) and 26 consecutive women (mean age, 60.6 years; weight range, 53 to 120 kg) subjected to chest CT were used to reconstruct series of consecutive, 2-mm-thick, transverse images. These image series were imported to ImpactMC, and 52 patient-specific voxelized phantoms were produced, with a voxel size of 0.98×0.98×2 mm. The scanner modeled was a 256-slice CT scanner (Brilliance iCT, Philips Healthcare, Best, the Netherlands). Data on the geometry, x-ray spectrum, and composition and dimensions of the filters of the scanners were included in the input data. For each voxelized phantom, standard retrospectively and prospectively ECG-gated CCTA exposures were simulated (120-kVP tube voltage, 128×0.625 mm beam collimation). The prospectively ECG-gated exposure was simulated by 2 rotations in sequential mode with a table feed of 44.8 mm. The scanned length along the z axis was 124.8 mm. The retrospectively ECG-gated exposure was simulated by a spiral acquisition with a pitch of 0.18 and a nominal scan length of 125.1 mm along the z axis. Experimental details on the use of ImpactMC in the present study are provided in Appendix I in the online-only Data Supplement.

Output dose images, along with input CT images, were exported to Image J software package (Image J, version 1.38x Java, National Institutes of Health, Bethesda, Md). Normalized (to CTDI\textsubscript{vol}) organ doses (NODs) from a CCTA scan were determined by appropriately delineating organ contours. NODs were derived for all radiosensitive organs located in the primarily exposed body region during a CCTA scan (ie, lung, breast, and esophagus). Details are provided in Appendix I in the online-only Data Supplement. For each modeled patient, the chest circumference at the transverse CT image containing the central heart plane was measured. To investigate the effect of patient body size on NOD values, correlations between NOD and chest circumference were calculated with linear regression analysis.

Estimation of Organ Doses and Associated Radiation Risks in a Typical CCTA
Patient Cohort
The absorbed doses to the primarily exposed radiosensitive organs were estimated for 136 consecutive patients (41 women and 95 men) who underwent CCTA in the Philips 256-slice CT scanner. Retrospectively ECG-gated spiral acquisition was used for only 6 women and 6 men presenting with heart rate >75 bpm and/or arrhythmia. Informed consent was obtained from all patients participating in the present study, and the study was approved by the institutional research review committee. For each patient, the absorbed organ

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Figure 1. A representative input CT image (A) used together with all other images in the same patient series to create a voxelized phantom and the corresponding output dose image (B) generated from Monte Carlo simulation of a standard prospectively ECG-gated CCTA exposure.
doses were obtained by multiplying the patient-specific NOD values by the CTDI_{LP} for the specific patient’s exposure settings. The NOD values were derived from regression equations for the specific patient’s sex, body size, and acquisition mode used. The CTDI_{LP} for 120 kVp and 100 mA was measured with a pencil probe positioned free in air at the gantry isocenter and was then adjusted for the milliampere used to scan that particular patient. The CTDI_{LP} and the DLP values for each patient exposure were obtained from the operator’s console for the specific exposure settings.

LARs of site-specific solid cancer incidence associated with a typical CCTA study were estimated with sex- and age-specific risk factors provided by the National Academies’ committee on Biological Effects of Ionizing Radiation (BEIR) report VII14 and ICRP publication No. 103.15 These reports provide the framework for estimating projected LAR of radiation-induced cancer resulting from low-level exposures to ionizing radiation. The projected LAR for a particular individual refers to the risk of developing a radiation-induced cancer at any time subsequent to the age at exposure. For each patient in the CCTA cohort, the projected LARs for radiogenic cancer to the lung and female breast were determined by multiplying organ doses by corresponding age- and sex-specific risk factors obtained from Table 12 D-1 of the BEIR-VII report. The LAR for the esophagus was estimated with the sex-specific risk factors provided in Table A.4-19 of ICRP publication No. 103.15 Site-specific LARs were summed to provide a total cancer risk estimation for each patient subjected to CCTA.

The risk of cancer induction was also calculated from the DLP-derived effective dose values and total risk factors for cancer induction obtained from the BEIR-VII report.14 The effective dose for each patient was calculated as the product of DLP, obtained from the operator’s console for the specific exposure settings, and the most widely used DLP-to-effective-dose conversion factor for the adult thorax (ie, 0.014 mSv · mGy⁻¹·cm⁻¹).16

For the patients subjected to prospectively ECG-gated CCTA, the projected LARs of cancer associated with other relevant medical exposures such as diagnostic cardiac angiography and coronary artery calcification screening were also estimated. These LARs were estimated for each patient separately using BEIR-VII sex- and age-specific factors for all solid cancers, along with recently published estimates of effective dose. Following the same methodology and assuming typical organ doses, we estimated LARs of lung and breast cancer associated with lung and breast screening, respectively, per patient. Recently published data17 were used to estimate lifetime intrinsic risks of breast and lung/bronchus cancer for each patient subjected to CCTA, given alive and not diagnosed with cancer at the time of exposure. These lifetime intrinsic risks were used to derive CCTA-related relative risks (RRs) of lung or breast cancer for the examined patient cohort, which were subsequently compared with miscellaneous RRs of lung or breast cancer. The CCTA-related RR denotes the projected increase, inflicted by CCTA exposure, in the lifetime risk of developing malignancies (ie, a RR of 1 indicates no additional risk).

**Statistical Analysis**

Continuous data are presented as mean±SD (range). Association between 2 variables was determined by linear regression analysis. Tests for normality were performed with the Shapiro-Wilk test. The statistical software package OriginPro 7.0 (OriginLab Corp, Northampton, Mass) was used. The correlation coefficient (r) and the P value were used to evaluate goodness of fit. A value of P<0.05 was required to consider a test significant.

**Results**

Results of regression analysis between the NODs and chest circumference for all primarily exposed radiosensitive organs are shown in Table 1. The absorbed doses to female breast, lung, and esophagus were found to have a negative correlation with patient body size (P<0.01). Mean organ doses and projected LARs of radiation-induced cancer from typical CCTA scans are presented in Table 2. In women, the main contribution to total cancer LAR was found to come from lung exposure despite the breast absorbing a higher dose than the lung. Compared with breast cancer, the LAR of esophageus cancer was much lower (ie, about 3 times lower). In men, the main contribution to total cancer LAR was also found to result from lung exposure, whereas the LAR of esophageus cancer was much lower. The total cancer LAR estimated as the sum of site-specific LARs versus patient age is shown in Figure 2.

Compared with prospective CCTA scans, retrospective acquisitions were associated with 3- and 4-times higher radiation risk for women and men, respectively. For the same acquisition protocol, the projected LAR of radiation-induced cancer was much higher for women compared with men.

The majority of the referred patients (ie, >90%) were scanned with the prospectively ECG-gated protocol (Table 2). In men subjected to prospectively ECG-gated CCTA, the use of the DLP method results in an effective dose and a radiogenic risk 2.4 and 2.1 times higher, respectively, than the corresponding values derived from organ dose data. The use of the DLP method in women scanned with the prospective protocol resulted in a similar effective dose and a 30% lower radiogenic risk compared with the organ dose–based estimations.

Table 1. Results* of Linear Regression Analysis Between NODs† and Chest Circumference

<table>
<thead>
<tr>
<th>Patient Sex, Organ, and Mode</th>
<th>r</th>
<th>P</th>
<th>α</th>
<th>β</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retrospective</td>
<td>-0.55</td>
<td>&lt;0.01</td>
<td>3.16</td>
<td>-0.017</td>
</tr>
<tr>
<td>Prospective</td>
<td>-0.53</td>
<td>&lt;0.01</td>
<td>0.72</td>
<td>-0.0037</td>
</tr>
<tr>
<td>Breast</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retrospective</td>
<td>-0.74</td>
<td>&lt;0.0001</td>
<td>3.88</td>
<td>-0.018</td>
</tr>
<tr>
<td>Prospective</td>
<td>-0.76</td>
<td>&lt;0.0001</td>
<td>0.89</td>
<td>-0.0037</td>
</tr>
<tr>
<td>Esophagus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retrospective</td>
<td>-0.75</td>
<td>&lt;0.0001</td>
<td>4.28</td>
<td>-0.024</td>
</tr>
<tr>
<td>Prospective</td>
<td>-0.80</td>
<td>&lt;0.0001</td>
<td>1.12</td>
<td>-0.0066</td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retrospective</td>
<td>-0.64</td>
<td>&lt;0.0001</td>
<td>2.80</td>
<td>-0.017</td>
</tr>
<tr>
<td>Prospective</td>
<td>-0.64</td>
<td>&lt;0.0001</td>
<td>0.72</td>
<td>-0.0046</td>
</tr>
<tr>
<td>Esophagus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retrospective</td>
<td>-0.74</td>
<td>&lt;0.0001</td>
<td>4.01</td>
<td>-0.024</td>
</tr>
<tr>
<td>Prospective</td>
<td>-0.73</td>
<td>&lt;0.0001</td>
<td>0.95</td>
<td>-0.0058</td>
</tr>
</tbody>
</table>

r, P, and the coefficients α and β of regression equations, α+β×CC, where CC is chest circumference, for each organ and mode of operation are presented for female and male patients.

*Data are applicable for CCTA studies performed at 120 kVp.

†Descriptive statistics of the 2 variables are presented in Table 2. A normal distribution adequately describes all data sets tested.

**Table 1. Results* of Linear Regression Analysis Between NODs† and Chest Circumference**

**Table 2.** Risk of Lung and Breast Cancer from CCTA

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean (range)</th>
<th>SD (range)</th>
<th>r</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>0.74 (0.55–1.00)</td>
<td>0.22 (0.01–0.43)</td>
<td>-0.55</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Breast</td>
<td>0.90 (0.72–1.00)</td>
<td>0.18 (0.01–0.32)</td>
<td>-0.53</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Esophagus</td>
<td>0.88 (0.74–1.00)</td>
<td>0.20 (0.01–0.36)</td>
<td>-0.74</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

r, P, and the coefficients α and β of regression equations, α+β×CC, where CC is chest circumference, for each organ and mode of operation are presented for female and male patients.

*Data are applicable for CCTA studies performed at 120 kVp.

†Descriptive statistics of the 2 variables are presented in Table 2. A normal distribution adequately describes all data sets tested.
LARs of solid cancer associated with a single prospective CCTA scan compare favorably with projected LARs at the age of the CCTA exposure related to either diagnostic cardiac angiography or coronary artery calcification screening repeated every 5 years between 50 and 74 years of age. LAR at the CCTA exposure age from repeated annual low-dose CT screenings for lung cancer is at least 3 times higher than the CCTA-related LAR of lung cancer. For women between 50 and 65 years of age, biennial mammographic screening leads to almost double the LAR of breast cancer compared with CCTA, whereas for women >65 years of age, the breast-screening LAR is 7 times higher than the CCTA LAR. The RRs of lung cancer caused by CCTA exposure are 1.0032 and 1.0008 for women and men, respectively; corresponding values resulting from smoking are 12.8 and 23.2.23 A CCTA scan may add 1.3 and 0.3 new cases to every 1000 natural breast cancer cases for women ≤50 and >65 years of age, respectively. Comparatively, the RRs if a first- or second-degree relative is diagnosed with breast cancer are 2.1 and 1.5, respectively.20

**Discussion**

Evaluating referring clinicians about CCTA-related radiation burden is imperative because the concerns about associated risks may often be exaggerated.27 Besides, the rapid and continuous technological advances in CT, the differences in CCTA-performing practices, and recent changes relative to continuous technological advances in CT, the differences in radiogenic factors applicable for doses risk models described in BEIR VII and ICRP 103 reports.14,15 Radiogenic factors applicable for doses risk models described in BEIR VII and ICRP 103 reports have been derived from the so-called linear, no-threshold (LNT) hypothesis, combined with an uncertain dose and dose-rate effectiveness factor for extrapolation from high to low absorbed radiation doses. The BEIR VII methodology thus provides projected LARs of radiation-induced cancer for exposed individuals of any age and gender. Although the existence of a low-dose threshold for cancer induction is not implausible and the longstanding question of the true validity of the LNT hypothesis may well prove to be beyond definitive scientific resolution, the LNT model remains a prudent basis for the practical purposes of radiological protection at low doses and low dose rates.14,15,30 Effective dose and radiogenic cancer risk estimates recently reported in literature for 256- and 64-slice CCTA are presented in Table 4. Current DLP-derived effective dose and radiogenic risk estimates are in good agreement with corresponding results obtained with similar 256-slice scanners.3,5,7 The effective dose from CCTA performed on 256-slice scanners in the prospective mode is ~4 times lower than corresponding values for studies performed on 64-slice CT scanners in the retrospective mode. Consistent with published data,31 CCTA-related cancer LAR is markedly higher for women and decreases with patient age, as shown in Figure 2, with the decrease being much steeper for women. This is attributed to the inclusion of the female breast in the primarily exposed body region. Female breast is highly radiosensitive15 in young adults; its radiosensitivity drops abruptly with age.14 Several methods have been proposed to reduce the dose to the female breast from thoracic CT exposures such as the use of bismuth shields and, more recently, switching off the CT beam when the tube is rotating anteriorly.23 However, the applicability of these tools in CCTA examinations has not been tested. Despite the low LARs of cancer associated with a typical CCTA patient cohort, which is skewed in age to older individuals (>50 years of age), young adult women (<30 years of age) undergoing CCTA face 2 to 4 times higher LAR of radiogenic cancer.

The RRs of lung cancer estimated for the women and men studied (1.0032 and 1.0008, respectively) and the estimated RR of breast cancer (1.0005 for women 50 to 65 years of age) indicate that CCTA exposure results in an inconsequential increase in the natural breast and lung cancer incidence rates. Estimates also suggest that the CCTA LAR compares favorably with similar risks such as those involved in diagnostic coronary angiography and in screening procedures that expose asymptomatic populations to ionizing radiation. Caution should be used, however, when comparing radiation burden from alternative imaging tests that refer to disparate groups. Although there are no solid data available that support that CCTA conveys a clear clinical benefit, the small projected LAR of cancer induction resulting from CCTA can be charitably

### Table 2. Risk of Developing Radiation-Induced Cancer at the Primarily Exposed Radiosensitive Organs at Any Time Subsequent to the Age at Exposure

<table>
<thead>
<tr>
<th>Acquisition Mode</th>
<th>CC, cm</th>
<th>Age, y</th>
<th>mA</th>
<th>CTDI&lt;sub&gt;vol&lt;/sub&gt;, mGy</th>
<th>Breast Dose, mGy</th>
<th>Lung Dose, mGy</th>
<th>Esophagus Dose, mGy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Women (n=41)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retrospective (6)</td>
<td>111 ± 8 (87.5–119.5)</td>
<td>59.2 ± 11.9 (43–74)</td>
<td>804 ± 20 (781–841)</td>
<td>50.5 ± 1.3 (49–53)</td>
<td>37.4 ± 3.0 (34–42)</td>
<td>25.4 ± 2.8 (22–30)</td>
<td>32.2 ± 3.8 (28–38)</td>
</tr>
<tr>
<td>Prospective (35)</td>
<td>106 ± 13 (81.8–132.7)</td>
<td>59 ± 6 ± 8.6 (39–78)</td>
<td>204 ± 24 (170–300)</td>
<td>16.4 ± 2.4 (10–24)</td>
<td>13.9 ± 1.8 (11–21)</td>
<td>9.1 ± 1.5 (6.6–14)</td>
<td>11.7 ± 2.4 (7.0–18)</td>
</tr>
<tr>
<td><strong>Male patients (n=95)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Retrospective (6)</td>
<td>110 ± 6 (106–120)</td>
<td>54.0 ± 6.4 (46–63)</td>
<td>897 ± 167 (752–1200)</td>
<td>56.3 ± 10.5 (47–75)</td>
<td>NA</td>
<td>28.3 ± 3.6 (25–33)</td>
<td>30.0 ± 3.4 (26–33)</td>
</tr>
<tr>
<td>Prospective (89)</td>
<td>106 ± 7 (89.6–128)</td>
<td>53.8 ± 10.1 (32–75)</td>
<td>205 ± 21 (150–300)</td>
<td>16.6 ± 1.7 (12–24)</td>
<td>NA</td>
<td>6.5 ± 0.9 (3.5–8.9)</td>
<td>9.4 ± 1.2 (5.5–13.0)</td>
</tr>
</tbody>
</table>

Table 2 is continued on the following page.

CC indicates chest circumference. Data refer to patients undergoing CCTA and are presented as mean ± SD (range).

*CTDI<sub>vol</sub> and DLP were obtained from operator’s console for the selected exposure settings.
weighed against the risks of not performing the study. For example, the lifetime risk of developing coronary artery disease after 40 years of age is 52% for asymptomatic men. If the entire US male population between the ages of 50 and 65 years (21 million people) were subjected to a prospectively ECG-gated 256-slice CCTA, the estimated total increase in cancer incidence would be just 1470 cases (This number would be much smaller if only symptomatic men with an intermediate likelihood of having coronary artery disease underwent CCTA). However, if the CCTA is not performed, the result may be failure to administer to those in need the appropriate treatments that could improve medical outcomes. Approximately 98 942 male US citizens 35 to 74 years of age died in 2006 of coronary artery disease, which means that they did not live long enough for hypothetical malignancies caused by earlier radiation exposure to develop. Nevertheless, it has to be stressed that a decision for performing CCTA on an individual should be always grounded on a careful clinical judgment according to relevant appropriateness criteria and guidelines.

DLP-based estimates of effective dose have been used extensively to quantify and report radiation burden to patients undergoing CCTA. However, reported doses exhibit great variation, thus enhancing confusion. Apart from differences in CCTA-performing practices and technological characteristics, variations may also be attributed to the use of different DLP-to-effective-dose conversion factors. As recently reported, conversion coefficients ranging from 0.014 to 0.018 mSv/mGy have been proposed and used, resulting in variations of effective dose estimates up to 29%. Moreover, the use of effective dose to determine LARs for radiation-induced cancer from CT exposures has been reported to be problematic. In the present study, the CCTA LARs of radiogenic cancer for women estimated from the DLP-derived effective dose data were found to approximate the total LAR of cancer induction estimated from calculated organ dose data. For men, however, the DLP method overestimated radiation LARs by a factor of 2. Given that the majority of individuals, up to 70%, undergoing CCTA are men, the latter method significantly overestimates radiogenic cancer LARs for the patient cohort commonly referred for CCTA. Observed differences also highlight the need for adopting sex-specific DLP-to-effective-dose conversion coefficients.

The small number of patients scanned with the retrospective protocol constitutes a study limitation. Despite, however, the small sample size, the observed relative variations in doses reported are minor and consistently smaller than those
Table 3. Estimates of Absolute Risk and RR of Breast, Lung, and Total Cancer for the CCTA Patient Cohort Examined With the Prospective Protocol, Along With Lifetime Risk of Coronary Artery Disease

<table>
<thead>
<tr>
<th>Absolute Risks</th>
<th>RRAs</th>
<th>≤49</th>
<th>50–65</th>
<th>≥66</th>
<th>≤49</th>
<th>50–65</th>
<th>≥66</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Breast cancer</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><a href="#">LAR-breast: LAR of breast cancer from prospective CCTA</a></td>
<td>0.014%</td>
<td>0.005%</td>
<td>0.002%</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td><a href="#">LIR-breast: LIR of invasive breast cancer given alive and cancer free at the CCTA age</a></td>
<td>11.19%</td>
<td>9.23%</td>
<td>6.06%</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>[LAR-breast screening: LAR at the CCTA age from repeated biennial screening mammography (50–74 y, 2 views/breast, 1.8 mGy mean glandular dose/view)]</td>
<td>NA</td>
<td>0.009%</td>
<td>0.014%</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>RR-breast: RR of breast cancer from CTCA, defined as [LIR-breast + LAR-breast] / LIR-breast</td>
<td>1.0013</td>
<td>1.0005</td>
<td>1.0003</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>RRfamily: RR* of breast cancer if first-degree relative diagnosed with breast cancer</td>
<td>2.1</td>
<td>2.1</td>
<td>2.1</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td><strong>Lung cancer</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><a href="#">LAR-lung: LAR of lung cancer from prospective CTCA</a></td>
<td>0.021%</td>
<td>0.019%</td>
<td>0.014%</td>
<td>0.007%</td>
<td>0.006%</td>
<td>0.004%</td>
<td></td>
</tr>
<tr>
<td><a href="#">LIR-lung: LIR of lung/bronchus cancer given alive and cancer free at the CCTA age</a></td>
<td>6.50%</td>
<td>5.92%</td>
<td>4.40%</td>
<td>7.87%</td>
<td>7.37%</td>
<td>5.44%</td>
<td></td>
</tr>
<tr>
<td>[LAR-lung screening: LAR at the CCTA age from repeated annual low-dose CT screening (55–74 y, 5.2 mGy lung dose per scan)]</td>
<td>NA</td>
<td>0.045%</td>
<td>0.151%</td>
<td>NA</td>
<td>0.019%</td>
<td>0.070%</td>
<td></td>
</tr>
<tr>
<td>RRsmoking: RR* of lung cancer resulting from smoking [23]</td>
<td>12.8</td>
<td>12.8</td>
<td>12.8</td>
<td>23.2</td>
<td>23.2</td>
<td>23.2</td>
<td></td>
</tr>
<tr>
<td><strong>Total cancer</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>[LAR-CCTA: total LAR of cancer from prospective CCTA (only primarily irradiated organs)]</td>
<td>0.037%</td>
<td>0.026%</td>
<td>0.017%</td>
<td>0.008%</td>
<td>0.007%</td>
<td>0.006%</td>
<td></td>
</tr>
<tr>
<td>[LAR-calciification screening: total LAR of cancer at the CCTA age from coronary artery calcification screening repeated every 5 y (50–75 y, 2.3 mSV per scan)]</td>
<td>NA</td>
<td>0.036%</td>
<td>0.063%</td>
<td>NA</td>
<td>0.027%</td>
<td>0.053%</td>
<td></td>
</tr>
<tr>
<td>[LAR-CC: total LAR of cancer at the CCTA age from diagnostic cardiac angiography (7 mSV per exam)]</td>
<td>0.058%</td>
<td>0.044%</td>
<td>0.027%</td>
<td>0.043%</td>
<td>0.036%</td>
<td>0.023%</td>
<td></td>
</tr>
</tbody>
</table>

*(Continued)*
obtained with the prospective protocol (eg, 8% versus 13% relative to breast dose, as shown in Table 2). This work focused on the angiographic acquisition solely, not on a comprehensive cardiac study. In our protocol, calcium scoring is accomplished only if explicitly requested, whereas low-dose topogram, bolus tracking localizer, and contrast monitoring acquisition increase the reported DLP-derived effective dose by 10%. Reported organ dose data are applicable to patients undergoing 256-slice CCTA with a scanning length of 125 mm and a tube voltage setting of 120 kVp. Although these settings were proven to be adequate for all 136 patients participating in this study, obese or large patients may require a greater scanning length or a higher operating tube voltage. In the present study, however, adjustment of exposure parameters to account for different patient body sizes was limited to the milliampere value. Only 3 organs were used for radiogenic cancer LAR assessment, leading to a slight underestimation of the total LAR. According to LAR estimates in 16-slice CCTA, lung and breast cancer account for 84% of all solid cancers in women; for men, lung cancer contributes 79% to solid cancer risk. Uncertainties related to organ dose estimation such as the potential variability of the manual tracing of the organ contours on the original CT images and assumptions inherent in the cancer risk model used inevitably limit the accuracy of the reported results. Nevertheless, the proposed methodology negates the main limitation of dose estimation methods based on standardized phantoms allowing individualized dosimetry and risk assessment.

Conclusions

The total projected LAR of radiation-induced cancer in a typical clinical patient cohort undergoing routine prospectively ECG-gated CCTA with a 256-slice scanner was estimated to be 24.9 per 100 000 women (ie, 1 in 4000) and 7.3 per 100 000 men (ie, <1 in 13 500). Given that CCTA-

![Table 3. Continued](image)

<table>
<thead>
<tr>
<th>Age Group, y</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤49</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50–65</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥66</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Life-Risk</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

LIR indicates lifetime intrinsic risk; or, SE; NA, not applicable; CAD, coronary artery disease; and ellipses, not available. Decimal places provided signify numerical variation and not precision. Estimate provided does not account for changes as a function of age.

Table 4. Reported Effective Doses and Radiogenic Cancer Risks From CCTA

<table>
<thead>
<tr>
<th>Study (Year)</th>
<th>CT Technology (Slices), n</th>
<th>Vendor</th>
<th>Method</th>
<th>Effective Dose, mSv</th>
<th>Cancer Risk, ×10⁻¹⁵</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current study</td>
<td>256</td>
<td>Philips</td>
<td>Organ doses</td>
<td>8.9 (F)</td>
<td>4.6 (M)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>DLP</td>
<td>12.3 (F)</td>
<td>13.7 (M)</td>
</tr>
<tr>
<td>Weigold et al (2009)</td>
<td>256</td>
<td>Philips</td>
<td>DLP</td>
<td>3.2</td>
<td>0.0</td>
</tr>
<tr>
<td>Einstein et al (2007)</td>
<td>64</td>
<td>Siemens</td>
<td>Organ doses</td>
<td>14 (F)</td>
<td>9 (M)</td>
</tr>
<tr>
<td>Hausleiter et al (2009)</td>
<td>64</td>
<td>GE</td>
<td>DLP</td>
<td>19</td>
<td>18.1</td>
</tr>
<tr>
<td></td>
<td>64</td>
<td>Philips</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>64 ss</td>
<td>Siemens</td>
<td>9</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>64 ds</td>
<td>Siemens</td>
<td>11</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>64</td>
<td>Toshiba</td>
<td>15</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shuman et al (2008)</td>
<td>64</td>
<td>GE</td>
<td>DLP</td>
<td>4.2</td>
<td>3.36</td>
</tr>
<tr>
<td>Klass et al (2010)</td>
<td>64</td>
<td>Philips</td>
<td>DLP</td>
<td>3.42</td>
<td>1.5</td>
</tr>
</tbody>
</table>

Retro indicates retrospective; pro, prospective; F, female patients; M, male patients; NR, not reported; ss, single source; and ds, dual source.

*Values corresponding to 60-year-old patients.
related LARs of radiogenic cancer depend significantly on patient age, sex, and body habitus, individualized risk assessment based on organ dose calculations should be preferred against risk evaluation based on DLP-derived patient effective dose.

Acknowledgment
We thank Dr J. Grebac for his invaluable contribution to the performance of the CCTA studies.

Disclosures
Dr Seimenis was a Philips Healthcare employee up to February 2006. The other authors report no conflicts.

References
CLINICAL PERSPECTIVE

The dramatic advances in computed tomography (CT) technology over the past decade have facilitated the rapid evolution of coronary CT angiography (CCTA) and have enhanced its diagnostic value in the noninvasive assessment of coronary artery disease. However, concomitant with the rapidly advancing knowledge pertaining to CCTA and the booming availability of the technique have been the ever-increasing concerns for the patient doses and cancer risks associated with CCTA. Unfortunately, incomplete and contradicting data, attributed partly to the unceasing technology changes, have served to heighten confusion. This study provides estimates of organ doses (based on a novel methodology using patient-specific phantoms) and projected life attributable risks of radiogenic cancer (based on the BEIR-VII approach) in a clinical patient population undergoing CCTA with a 256-slice system. The cancer life attributable risks from CCTA exposure were found to depend significantly on body habitus and to decrease steeply with age at exposure, whereas lung cancer constitutes the most probable detriment for both genders. The recent introduction of wide-detector CT systems in clinical practice has facilitated the routine use of prospectively ECG-gated CCTA. With this technique, the life attributable risks of cancer incidence associated with CCTA exposure were estimated to be as low as 1 in 4000 women and 1 in 13 500 men. These estimated life attributable risks of malignancy may inconsequentially increase lifetime intrinsic cancer risks and compare favorably with hypothetical cancer risks resulting from exposures from alternative imaging tests or screening procedures estimated for the identical patient cohort. Regardless, however, of the scant associated life attributable risks, CCTA exposure should be always carefully considered and clinically justified.
Individualized Assessment of Radiation Dose in Patients Undergoing Coronary Computed Tomographic Angiography With 256-Slice Scanning
Kostas Perisinakis, Ioannis Seimenis, Antonis Tzedakis, Antonios E. Papadakis and John Damilakis

_Circulation_. 2010;122:2394-2402; originally published online November 22, 2010;
doi: 10.1161/CIRCULATIONAHA.109.935346

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Appendix A
The ImpactMC software package (Vamp GmbH, Germany)\(^1\) used in the current study is a PC-driven Monte Carlo CT dosimetry software, which simulates CT exposures on patient-specific voxelized phantoms and generates dose-images depicting the dose deposition on the exposed body region. This is accomplished via a graphical user’s interface in three steps: a) generation of a voxelized patient specific phantom, b) input of scanner characteristics and scan parameters, c) Monte Carlo simulation of CT exposure and presentation of results.

Patient-specific voxelized phantoms were generated from 52 CT image series from consecutive patients undergoing thoracic CT examinations. Input scanner characteristics include the x-ray spectrum for the operating tube voltage, and geometric and composition characteristics of all filters involved. Scan parameters include scan mode, beam collimation, fan angle, distance between focal spot and center of rotation, number of rotations, table increment and start position of the x-ray tube. In the current study all above parameters and settings were specified in consistence to the standard protocols of the Philips iCT 256-slice CT scanner for prospectively and retrospectively ECG-gated CCTA studies. Voxel values of resulting output dose images correspond to the dose accumulated in the corresponding voxel of the patient-specific phantom, normalized to the free-in-air measurement of computed tomography dose index (CTDIF). Voxel values are given in mGy per 1 mGy CTDIF. CTDIF is commonly measured with standard 100 mm long pencil ionization chamber appropriately placed at the isocenter. Output dose-images were exported to Image J software package (Image J, version 1.38x Java, NIH, USA) together with input CT image series. The absorbed dose to any organ included in the body region scanned was determined as follows: A region of interest (ROI) representing the imaged organ of interest was delineated on the original CT image and then copied to the output dose-image. The mean pixel value of the latter ROI was the mean normalized dose for the fraction of the organ depicted in that particular image. However, an organ may
extend to several consecutive images. Therefore, the total NOD for a specific organ of interest was estimated as the area-weighted average of mean ROI values derived from all dose-images where this organ was extended.

ImpactMC software package was validated through CT Dose Index (CTDI) measurements on standard cylindrical CTDI phantoms and through dose measurements in anthropomorphic thorax phantoms of various sizes. ImpactMC software has been used for CT dosimetry in several recent studies.

References: