

EDITORIAL COMMENT

Dose Optimization in Coronary CTA*

Pat Zanzonico, PhD

New York, New York

The annual number of computed tomography (CT) procedures in the U.S. has increased 20-fold (from 3 to 60 million) between 1985 and 2005 (1), and as a result, the average (i.e., per capita) annual background dose in the U.S. has nearly doubled from 3.0 to 5.6 mSv (2). This has precipitated increasing societal concern over the potential public health impact—an increased risk of cancer—associated with this dramatic growth in radiation exposure. Brenner and Hall (3), for example, have estimated that as much as 2% of all cancers in the U.S. may be

See page 1113

attributable to CT irradiation. For all diagnostic procedures, therefore, the study parameters should always be judiciously selected to deliver the minimum radiation dose consistent with yielding the clinical information being sought. Rigorous validation of diagnostic protocols designed to reduce patient exposure are required, however, before they are recommended for standard practice. The current paper by Hausleiter et al. (4) is an excellent example of this type of validation.

Hausleiter et al. (4) evaluated image quality and radiation dose using a 100-kVp tube voltage protocol compared with the standard 120-kVp protocol for coronary computed tomography angiography (CTA). The rationale of this study is illustrated in Figure 1. For any radiological procedure, the image quality improves progressively with patient dose. In the case of CT, for example, as the tube voltage (kVp) and/or the tube current (mA) are increased, the quantum mottle in the reconstructed images is

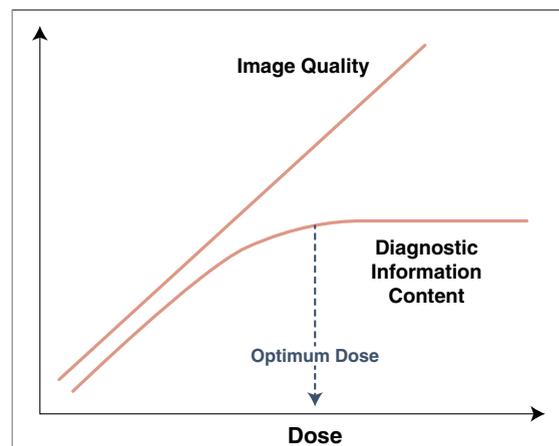


Figure 1. The “Optimum-Dose” Concept

Stylized graph illustrating the relationship among image quality, diagnostic information content, and patient dose for a radiological procedure.

reduced and the resulting images appear “smoother” and more visually aesthetic. Diagnostic information content increases as well with increasing dose, but only to a certain point. The “optimum” patient dose is reached once all of the diagnostic information technically derivable from a particular study has been obtained. Increasing the dose further yields no additional information and thus unnecessarily increases the radiogenic risk (i.e., cancer risk) to the patient (5).

In the study reported by Hausleiter et al. (4), the PROTECTION II (Prospective Randomized Trial on Radiation Dose Estimates of Cardiac CT Angiography in Patients Scanned with a 100 kVp Protocol) study, 400 nonobese patients undergoing clinically indicated 64-slice coronary CTA for suspected coronary artery disease (CAD) at 8 study sites were randomized (200 patients per arm) to either the 100-kVp or a 120-kVp tube voltage scan protocol. Patients with stable sinus rhythm and a body weight of less than 90 kg or body mass index

*Editorials published in *JACC: Cardiovascular Imaging* reflect the views of the authors and do not necessarily represent the views of *JACC: Cardiovascular Imaging* or the American College of Cardiology.

From the Memorial Sloan-Kettering Cancer Center, New York, New York. Dr. Zanzonico has reported that he has no relationships to disclose. H. William Strauss, MD, served as Guest Editor for this article.

(BMI) of less than 30 kg/m² were eligible for this study, whereas those with known or at high risk for CAD were excluded. Other than recommended administration of beta-blockers to maintain heart rates below 70 beats/min and of oral nitrates for coronary vasodilation, site-specific tube current, reconstruction algorithm, and other study parameters and any extant dose-reduction strategies such as electrocardiogram (ECG)-triggered tube current modulation were maintained. The end points were: 1) diagnostic readability, based primarily on an ordinal score (1, nondiagnostic; 2, adequate; 3, good; and 4, excellent) assigned by 2 highly experienced “central” readers, and secondarily on region-of-interest-derived signal intensity, signal-to-noise ratio, and contrast-to-noise ratio measured by 1 of the central readers; 2) radiation-dose parameters, including the volume computed tomography dose index (CTDI_{vol}), dose-length product (DLP), and the DLP-derived effective dose; and 3) the clinically indicated need for subsequent cardiac tests within 30 days of the coronary CTA.

There was no statistically significant difference between the 100-kVp and 120-kVp cohorts in patient characteristics such as age, sex distribution, height, weight, BMI, and heart rate or in study parameters such as scan length, type of cardiac gating (retrospective [~93%] versus prospective [~7%]), and use of ECG-triggered tube current modulation (~70% of studies). There was no statistically significant difference ($p = 0.742$) in the diagnostic readability score between the 100-kVp (3.30 ± 0.67) and 120-kVp (3.28 ± 0.68) cohorts; even when analyzed on an individual coronary artery rather than patient basis, there was no difference between the 2 cohorts. Patient motion was the overwhelmingly predominant reason for a nondiagnostic score (score = 1). The foregoing absence of any difference in diagnostic readability scores was observed despite predictable, statistically significant or nearly significant differences in the image-quality parameters; the signal-to-noise ratio, for example, was 11% lower for the 100-kVp than for the 120-kVp cohort ($p < 0.003$). The need for additional cardiac testing within 30 days of the coronary CTA did not differ significantly ($p = 0.114$) between the 100-kVp (27 patients, 13.4%) and 120-kVp (32 patients, 19.2%) cohorts. Importantly, the radiation dose parameters were significantly (~30%, $p < 0.0001$) lower for the 100-kVp than for the 120-kVp cohort ($p < 0.003$): CTDI_{vol}, 42.6 ± 19.5 versus 62.6 ± 25.1 mGy; and DLP, 599 ± 255 versus 868 ± 317 mGy cm.

The foregoing data make a compelling case that, despite a significant degradation of image aesthetics, diagnostic information content is maintained using a 100-kVp rather than a 120-kVp scan protocol for coronary CTA in nonobese patients while reducing dose by ~30%. The 100-kVp protocol should therefore be considered for coronary CTA in all such patients. One can infer from these findings that the radiation dose corresponding to the 100-kVp protocol is at or above the optimum dose for coronary CTA for the “diagnostic information content” curve in Figure 1. Only further studies with even lower-dose protocols could demonstrate whether further dose reduction is achievable without sacrificing clinical efficacy.

The study by Hausleiter et al. (4) illustrates a number of important considerations for evaluation of a dose-reducing protocol for diagnostic imaging. First, it is a prospective study in which subjects are randomized between the protocols being compared, largely reducing the possibility of biasing of the results. Such randomization presumably controls for variation in patient characteristics, scan parameters, etc., across the study population and study sites. Second, the sample size, based on a clinically realistic power calculation, was sufficiently large to disclose meaningful, even if small, differences between the study groups. Third, the study population (i.e., nonobese patients) were appropriately selected, so as to maximize the likelihood of demonstrating the noninferiority of the low-dose (i.e., the 100-kVp) protocol relative to the standard (i.e., 120-kVp) protocol. Obese patients, of course, attenuate more of the incident X-rays, and the resulting lower X-ray flux through such patients and the greater quantum mottle in the reconstructed images potentially might obscure clinically important features of the CT study. Conceivably, therefore, a study population comprised of obese as well as nonobese subjects may have demonstrated a spurious degradation of diagnostic information content and thus abandonment of a dose-reducing protocol effective in appropriately selected (i.e., nonobese) patients.

Despite the overall strength of this study, there are several opportunities for improvement. First, the critical performance parameter of any diagnostic study is its accuracy (i.e., sensitivity and specificity). Hausleiter et al. (4) used the diagnostic readability score as a surrogate for diagnostic accuracy, since their power analysis indicated that a study population of only 400 subjects would likely demonstrate the noninferiority of the 100-kVp protocol relative to the 120-kVp protocol based on that score. The

authors projected that a study population over 4 times larger (i.e., more than 1,650 subjects)—considered logistically prohibitive—would be required to demonstrate that noninferiority based on diagnostic accuracy. Although considerations of time and cost, and therefore sample size, cannot be ignored, significant changes in standards of practice warrant as definitive a validation as possible, including rigorous comparison of the sensitivity and specificity of the proposed procedure and the standard procedure it may replace. Second, the tube current (mA) was not considered in terms of dose reduction. Since patient dose is proportional to the tube current, it would seem to warrant such consideration. In particular, as indicated in Table 2 in the report by Hausleiter et al. (4), there were significantly ($p < 0.001$) lower tube currents used for the 120-kVp than for the 100-kVp cohorts for those subjects imaged on the GE (~30% of subjects) and on the Toshiba (~35%) CT systems. Likewise, the differences in tube current among the 3 systems used (GE Healthcare, Waukesha, Wisconsin; Siemens Healthcare, Erlangen, Germany; Toshiba Medical Systems, Otawara-shi, Tochigi, Japan) appear to be significant and thus amenable to independent evaluation of the impact of tube current on patient dose. Third, the 2 central readers who assigned the diagnostic readability scores were,

as noted, highly experienced. Evaluation of scans and assignment of scores by less experienced readers might have revealed differences between the 100-kVp and 120-kVp protocols not apparent otherwise, differences that might be meaningful in a clinical setting where the experience of readers varies. Finally, it is worth noting that risk factors for radiogenic cancer induction are far lower in adults than in children and that patients with suspected CAD and undergoing coronary angiography comprise an older (mean patient age in the current study: ~60 years) population at low risk for radiogenic cancer (6). Thus, although significant, the 30% reduction in radiation dose, and thus radiogenic cancer, achievable with a 100-kVp coronary CTA protocol is likely to have only a modest public health impact.

Overall, the strengths of the current study far outweigh its weaknesses, and in many respects, this study represents a model for the validation of dose-reduction strategies in diagnostic radiology. The authors are to be commended for their important contribution.

Reprint requests and correspondence: Dr. Pat Zanzonico, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue New York, New York 10021. *E-mail:* zanzonip@mskcc.org.

REFERENCES

- Amis ES Jr., Butler PF, Applegate KE, et al. American College of Radiology white paper on radiation dose in medicine. *J Am Coll Radiol* 2007;4: 272-84.
- Mettler FA Jr., Bhargavan M, Faulkner K, et al. Radiologic and nuclear medicine studies in the United States and worldwide: frequency, radiation dose, and comparison with other radiation sources—1950-2007. *Radiology* 2009; 253:520-31.
- Brenner DJ, Hall EJ. Computed tomography—an increasing source of radiation exposure. *N Engl J Med* 2007; 357:2277-84.
- Hausleiter J, Martinoff S, Hadamitzky M, et al. Image quality and radiation exposure with a low tube voltage protocol for coronary CT angiography: results of the PROTECTION II trial. *J Am Coll Cardiol Img* 2010;3:1113-23.
- Goske MJ, Applegate KE, Boylan J, et al. Image Gently(SM): a national education and communication campaign in radiology using the science of social marketing. *J Am Coll Radiol* 2008;5: 1200-5.
- NRC. National Research Council, Committee on the Biological Effects of Ionizing Radiation (BEIR VII-Phase 2), Health Risks From Exposure to Low Levels of Ionizing Radiation. Washington, DC: National Academy Press; 2006.

Key Words: computed tomography (CT) ■ coronary computed tomography angiography ■ dose optimization ■ radiation dose.