JACC: CARDIOVASCULAR IMAGING
VOL. 3, NO. 5, 2010

ISSN 1936-878X/$36.00
PUBLISHED BY ELSEVIER INC.
DOI:10.1016/j.jcmg.2010.03.003

CVN Interview

EDITORIAL VIEWPOINT

Weighing the Risks and Benefits of Cardiac Imaging With Ionizing Radiation

Thomas C. Gerber, MD, PhD,* Raymond J. Gibbons, MD†
Jacksonville, Florida; and Rochester, Minnesota

The potential risk of fatal malignancy related to cardiac imaging with ionizing radiation is frequently discussed in the medical literature and in the lay press. Clinicians must weigh this risk against the potential benefits of cardiac imaging, which are typically not considered in these reports about radiation risk. This review summarizes the evidence regarding both the radiation risks and clinical benefits of cardiac imaging to provide guidance to the clinician in specific clinical scenarios. Choosing the right test for the right patient, and performing it with the lowest possible radiation dose, remains a challenge. (J Am Coll Cardiol Img 2010;3:528–35) © 2010 by the American College of Cardiology Foundation

The rapid recent growth of medical imaging in clinical practice has heightened concerns about the medical radiation dose received by patients (1). Although it is critical that the health risks of radiation exposure be carefully weighed against the potential benefits of medical imaging with modalities that use ionizing radiation, in most of the existing literature the investigators focus on either the risks or the benefits and only rarely consider both (2). Given the existing uncertainty regarding the carcinogenic potential of ionizing radiation at the doses used in cardiovascular computed tomography (CT) and nuclear cardiology, the "first do no harm" principle argues that responsible clinicians should use these imaging modalities only in situations in which the clinical benefit can be expected to exceed the potential harm. To facilitate an understanding of the elements required for such an appraisal, this viewpoint will summarize current concepts about the potential risks of radiation and relate these risks to the known or expected benefits of cardiac imaging in specific clinical scenarios.

Epidemiology Data on Medical Radiation Exposure

According to a recent report by the National Council on Radiation Protection and Measurements (3), the per-capita effective radiation dose of the U.S. population from all sources increased 72% from the early 1980s to 2006, primarily as the result of a 5.7-fold increase from medical imaging. Background radiation, which accounted for approximately 50% of the per-capita effective dose of the U.S. population in 2006, changed little during this time.

The increase in medical radiation dose is largely related to the increased use of imaging procedures that involve high radiation doses. Overall, all radiographic, and conventional and interventional fluoroscopic procedures together represented 25% of the collective dose from nontherapeutic radiation in 2006. CT repre-

From the *Division of Cardiovascular Diseases and Department of Radiology, Mayo Clinic, Jacksonville, Florida; and the †Division of Cardiovascular Diseases, Mayo Clinic, Rochester, Minnesota. Dr. Gibbons has served as a consultant for Cardiovascular Clinical Studies (WOMEN study); Lantheus Medical Imaging; and Molecular Insight Pharmaceuticals.

Manuscript received March 11, 2010, accepted March 16, 2010.

sented 49%, and nuclear medicine 26%, of the collective dose. Therefore, our discussion will focus on these 2 modalities.

The number of CT studies in general increased by 10% to 11% per year between 1993 and 2006. According to the National Council on Radiation Protection and Measurements report, there were 3.1 million cardiac CT studies in 2006, which represented 4.7% of all CT studies and 12.1% of the collective radiation dose from CT. There were 18.1 million nuclear medicine studies in 2006, a 4.6-fold increase from 1982. Cardiac nuclear medicine studies had the greatest growth. In 2005, cardiac studies represented 57% of all nuclear medicine patient visits and 85% of the collective radiation dose received from nuclear medicine studies.

A large proportion of this diagnostic (nontherapeutic) medical radiation was delivered in specific settings or specific subgroups. For example, 82% of the CT procedures were performed in hospital laboratories. In 2003, 71% of the cardiac nuclear medicine procedures were performed in patients older than 55 years of age (3).

Risk of Cancer From Low-Dose Radiation

Estimates of relative risk of fatal cancer related to ionizing radiation are obtained by comparing the expected number of cancers with the actually observed number in specific populations that were exposed to radiation. In epidemiological human studies, increased risk of cancer has not been observed consistently at "low" effective doses <100 mSv delivered at low dose rates (i.e., over many years, as for most patients undergoing medical imaging). The estimates for cancer risk in the "low-dose" range rely on the assumption that the relationship between the relative risk of cancer and effective dose estimates, observed over decades in Japanese survivors of the atomic bomb explosions (who had whole-body exposures at high dose rates), extends linearly and without any threshold to patient populations of various ethnicities undergoing medical imaging (who receive partial-body irradiation of much lower doses and dose rates). This "linear no-threshold" (LNT) model is considered by many of the organizations that deal with radiation protection as the model best fitting the available data on the relationships between radiation dose and lifetime-attributable risk (LAR) of cancer (4). However, other experts (5) recommend against the quantitative estimation of health risks at low doses (effective dose <50 mSv in 1 year or <100 mSv over a lifetime).

The probability of chromosomal changes that could translate into phenotypic cancer increases with the rate of cell proliferation, number of future divisions, and the degree of differentiation of the cells in question (6). Younger patients are considered to be at greater risk of developing radiation-related cancer because their cells are more sensitive to radiation (as a result of a greater number of future divisions) than those of older patients and because they are more likely to live through the latency period of 10 to 40 years for most radiation-induced solid cancers. In the specific case of cardiac imaging, women are considered at greater risk of radiation-induced cancer than men because of the radiosensitivity of their breasts and lungs (4,7). The effects of age and sex are evident by comparing the LAR estimated based on the LNT model in hypothetical patients undergoing a typical coronary CT angiogram performed without dose-sparing algorithms (effective dose of 21 mSv for women and 15 mSv for men) (8). The LAR of 0.7% (1 in 143) for a 20-year-old woman is nearly 16 times greater than that of 0.044% (1 in 2,273) for an 80-year-old man. The "effective dose" (9) accounts for the body parts exposed to radiation and for the type of radiation being used; LARs derived from specific effective dose values do not therefore differ between the imaging modalities that expose patients to different forms of ionizing radiation.

Given the large number of scans being performed, the potential for increased death rates due to radiation-induced cancer in the population at large is of concern. For example, the investigators of one study (10) based on the LNT model estimated that 29,000 future cancers (two-thirds in women) could potentially occur as a result of CT scans performed in the U.S. in 2007.

There are several important caveats regarding the assessment of relative risk of radiation-induced cancer (9). First, the effective dose typically used to express risk is a generic estimate that pertains to mathematical models of the human body and cannot be applied to individual patients. Effective dose estimates for cardiac imaging tests are available from various sources (1,3,9,11,12). Determining individualized, patient-specific estimates of radiation dose (and risk) is very complex, rarely done, and imperfect (9).

Second, omnipresent background radiation, which averages 3.6 mSv per year in the U.S., may make a contribution to the incidence of cancer in

JACC: CARDIOVASCULAR IMAGING, VOL. 3, NO. 5, 2010
MAY 2010:528–35

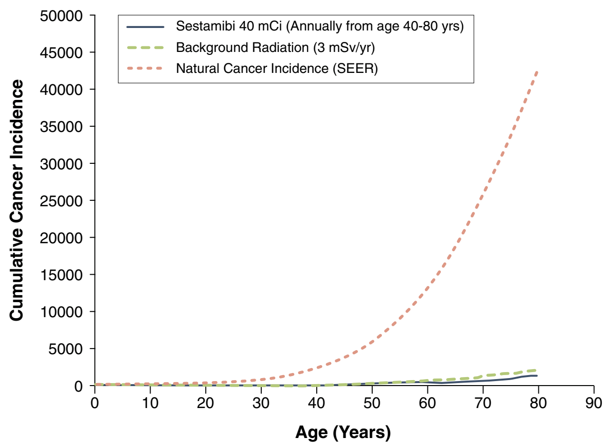

Figure 1. Cumulative Incidence of Cancer in Women

Cumulative cancer incidence (expressed as cases per 100,000 women) that can be attributed to background radiation (3 mSv), an annual dose of 40 mCi of technetium-99m sestamibi from age 40 to 80 years, and naturally occurring cancer. Data are based on the excess absolute risk model from the Biologic Effects of Ionizing Radiation VII report. SEER = Surveillance, Epidemiology and End Results. Figure courtesy of Michael O'Connor, PhD.

the general population because it affects patients at all ages, including children, who are the most vulnerable. Background radiation primarily is due to radon exposure in buildings, radioactive elements in the soil, and cosmic radiation from outer space, all of which vary in different regions of the country.

Third, the intrinsic risk of cancer is much greater than the potential risk of radiation-induced cancer. For example, the intrinsic lifetime risk of dying from malignancy in the U.S. is approximately 21% (13). By comparison, the 10 mSv of ionizing radiation from a typical coronary CT angiogram with dose-sparing algorithms could add 0.05% to that risk in absolute terms (a relative increase of 0.2%). Figure 1 shows an example for the magnitude of the relative contributions of natural cancer incidence, background radiation, and the radiation dose received from an annual 1-day ^{99m}Tc sestamibi myocardial perfusion study (40 mCi corresponding to ~12 mSv; performed every year for 40 years beginning at age 40) to the cumulative cancer incidence in women.

Finally, the statistical power of the available observational studies of populations exposed to low-dose radiation is generally too low to exclude with certainty the possibility of "zero risk" from the error bars of the point estimates for solid cancers and most forms of leukemia (Fig. 2) (14). For example, to quantify the risk of cancer related to an effective dose of 10 mSv, a sample size of 5,000,000 patients with lifetime follow-up might be required (15). In contrast, the Life Span Study of atomic bomb survivors, on which the LNT model is largely based, has to date reported 47 years of follow-up in 86,572 people with a mean dose of 200 mSv (delivered at a very high dose rate) (16).

In studies of radiation workers (14,17,18), standardized mortality rates are less in the workers than those in the general population, which has been attributed to a "healthy worker effect." One cohort of more than 407,000 radiation workers in 15 countries has been extensively studied over many years (17,18). The latest report after 5.2 million person-years of follow-up (18) suggests that all-cause mortality within the cohort (mainly related to an increased risk for cancer) was associated with radiation dose. However, this study cohort is 90% men, and the role of smoking in the unexpectedly high lung cancer mortality is not clear.

Benefits of Cardiac Imaging

These potential risks of low-dose radiation must be weighed against the benefits of cardiac imaging. For this discussion, we will focus on single-photon emission computed tomography (SPECT) because it has the most substantial evidence base (19) among the high-dose, rapid-growth cardiac imaging modalities (3).

Conceivable benefits of cardiac imaging include correct diagnosis, accurate prognostication, and improvement of patient outcomes. Such outcomes could include appropriate refocus on alternative noncardiac diagnoses (e.g., in patients with chest pain and normal SPECT studies), improved quality of life (e.g., attributable to relief of chest pain), and improved survival. Patients with high risk of disability and death from cardiovascular disease have the greatest potential absolute gain from appropriate diagnosis and management. This risk varies with age, cardiovascular risk factors, symptoms, and previous evidence of coronary artery disease (CAD) (i.e., myocardial infarction or revascularization) (20,21).

In symptomatic patients, the ability of stress (either exercise or pharmacologic) SPECT myocardial perfusion imaging (MPI) to diagnose potentially treatable coronary artery disease is well established. For example, in patients who have uninterpretable baseline electrocardiograms as the result of pre-excitation or left bundle branch block, there is a class I recommendation for SPECT MPI (evidence and/or general agreement that the procedure is beneficial, useful and effective) in the American College of Cardiology Foundation (ACCF)/

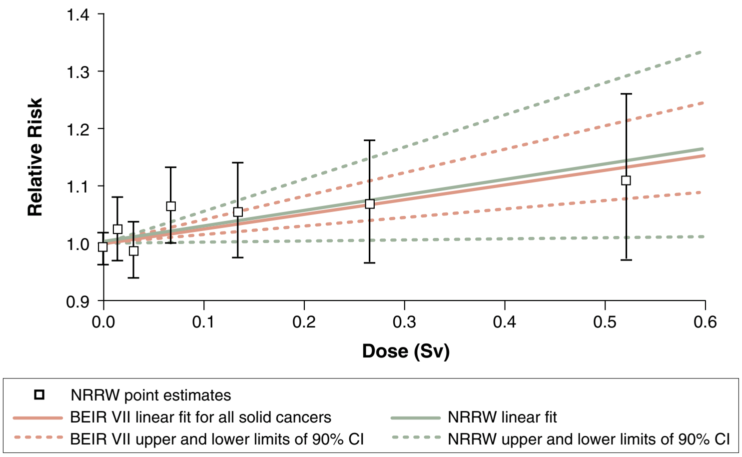

Figure 2. Trends in Relative Risk for Solid Cancers in the National Registry for Radiation Workers

Shown are point estimates and 90% confidence intervals (CI) for relative risk of all malignant neoplasms excluding leukemia in more than 170,000 radiation workers by lifetime radiation dose. The CIs at doses less than 200 mSv include a relative risk of 1, consistent with no increased risk. BEIR VII = Biological Effects of Ionizing Radiation VII; NRRW = National Registry for Radiation Workers. Reprinted, with permission, from Muirhead et al. (14).

American Heart Association (AHA) Guidelines for the management of chronic stable angina (22).

The use of SPECT MPI also can help establish the prognosis of patients with CAD. For example, the risk of cardiac death or myocardial infarction increases as the overall size of myocardial perfusion defects on SPECT MPI increases and left ventricular ejection fraction (which can be determined from gated images) decreases (23). The ACCF/AHA guidelines include several class I indications for the use of SPECT MPI in risk stratification (22).

However, the definition of diagnosis or prognosis does not necessarily imply improved outcomes in terms of patient survival, except in certain subgroups of patients. A potential survival benefit conveyed by cardiac imaging is very relevant to our discussion because it must be balanced against the projected risk of reduced longevity from cancer. Although some radiation-related cancers (leukemia, thyroid cancer, bone cancer) can have short latency periods of 2 to 5 years, most solid cancers have latency periods of 10 to 40 years.

In comparison, approximately one-half of patients with 3-vessel CAD and abnormal left ventricular function will die within 5 years with medical therapy. Because these patients would not otherwise survive the latency period of a radiation-induced cancer, cardiac imaging with ionizing radiation can be used to identify these patients and thereby improve their management and longevity. The probabilities of either adverse outcome will vary greatly for specific clinical scenarios, but in the short-term (e.g., 5 years) the risk from CAD is generally far greater than the risk from radiation-induced cancer.

The use of cardiac imaging in symptomatic patients is largely based on the assumption that it will improve outcomes. This assumption is proven only for small, selected subgroups of patients in whom very severe disease such as left main stenosis is detected. There are no randomized trials to show that patients with chronic stable angina who are

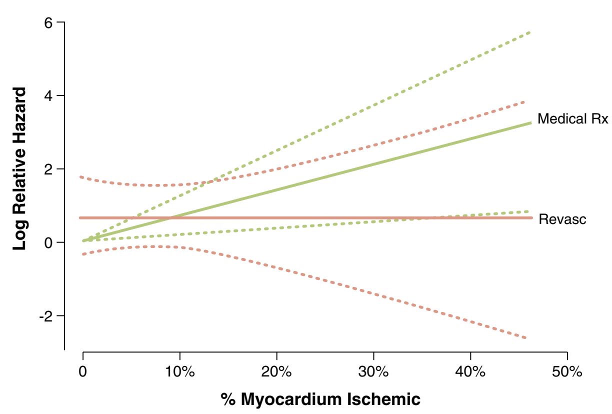

Figure 3. Patient Outcomes With Medical Therapy and Revascularization at Varying Degrees of Myocardial Ischemia

Log relative hazard ratio for revascularization (Revasc) versus medical therapy (Rx) as a function of percent ischemic myocardium based on final Cox proportional hazards model. If more than 10% of the total myocardium is ischemic, the survival benefit for revascularization over medical therapy increases as a function of increasing proportion of ischemic myocardium. Model $p < 0.0001$. Reprinted, with permission, from Hachamovitch et al. (25).

randomized to cardiac stress imaging have better outcomes than similar patients who are managed without "guidance" by noninvasive cardiac imaging. However, the ability of cardiac imaging to improve patient outcomes is supported by observational data. In retrospective analyses, symptomatic patients with no previous history of CAD who have moderate-to-large amounts of inducible ischemia on SPECT MPI have greater absolute and relative short-term survival benefit with revascularization than with medical therapy (Fig. 3). Conversely, patients with no or small amounts of ischemia have better survival with medical therapy (24). The degree of ischemia predicts survival benefit from revascularization compared with medical therapy better than the left ventricular ejection fraction after stress measured on gated SPECT studies (25).

The use of serial stress imaging studies in the follow-up of many patients with chronic, stable, symptomatic coronary artery disease is of less certain benefit. Such studies may lead to cardiac catheterization guided by cine-fluoroscopy, with additional radiation exposure. The incidence and benefit of coronary revascularization prompted by stress imaging studies in such patients requires further study.

The benefit of imaging in asymptomatic patients is far more speculative. Noninvasive cardiac imaging lacks important characteristics of a mature marker of cardiovascular risk in asymptomatic patients (26). The observed versus expected event rates across the range of predicted risk for models with and without imaging, the number of subjects reclassified across risk thresholds with the use of imaging, and the event rates of these subjects are not well established. The ACCF and AHA guidelines generally have not endorsed the use of imaging in asymptomatic individuals to detect CAD. The AHA has given a class IIb recommendation, i.e., "may be considered," to coronary artery calcium scoring with CT in intermediate-risk patients, but recommends against (class III recommendation) calcium scoring in either low-risk or high-risk patients (27,28). Other imaging, such as SPECT and CT coronary angiography, also has not been recommended. A new ACCF/AHA clinical practice guideline regarding the detection of asymptomatic coronary disease is scheduled for publication in 2010.

Table 1. Risks and Benefits of Cardiac Imaging With Ionizing Radiation

Risk of radiation-induced cancer
1. At radiation doses used in medical imaging, cancer risk is projected (but not known with certainty) on the basis of the linear no-threshold model
2. True risk of radiation-related cancer at low (<100 mSv) dose may never be known
A. Individualization of radiation dose and risk is difficult and imperfect
B. Background radiation is omnipresent
C. Radiation-related cancers are biologically indistinguishable from intrinsic cancer
D. Risk of intrinsic cancer is high relative to low projected risk of radiation-induced cancer
E. Appropriately powered observational studies of lifetime-attributable risk of cancer related to low-dose radiation are logistically impossible
3. Latency period for most solid radiation-related cancers is 10–40 years
4. Projected lifetime-attributable risk is greater for younger than for older patients and greater for women than for men
Possible benefits of cardiac Imaging
1. Symptomatic patients
A. Correct diagnosis
a. Choice of disease-specific therapy
b. Improved quality of life by relief of symptoms
B. Prognostication
C. Improved outcomes (survival)—selected subjects
2. Asymptomatic patients
A. Improved survival—unproven
Weighing risks and benefits
1. Missing the right diagnosis in symptomatic patients by avoiding imaging is a risk
2. Improved quality of life due to optimized therapy is difficult to quantify
3. Improved survival due to optimal therapy vs. possible decrease in survival from radiation-induced cancer
4. Benefit/risk ratio greater in symptomatic patients, high-risk patients, older individuals, and men
5. Current evidence does not support imaging with ionizing radiation in asymptomatic individuals
6. Benefit/risk ratio is improving as technical developments facilitate low-dose imaging with high image quality

In asymptomatic patients, there can be no improvement in quality of life or symptoms; therefore, the only conceivable benefit of imaging is improved outcomes such as survival. The hypothesis that targeted, tailored, aggressive risk management based on the "early" recognition of subclinical CAD will improve outcomes is not proven. Several important studies published in 2009 are pertinent to this issue. In the DIAD (Detection of Ischemia in Asymptomatic Diabetics) study, investigators examined the use of adenosine stress SPECT imaging for CAD screening in 1,123 asymptomatic diabetic patients. The cumulative cardiac event rates averaged only 0.6% per year. Although participants with moderate or large perfusion defects had greater event rates than those with small perfusion defects or normal SPECT studies, the use of SPECT for screening did not improve patient outcomes.

In the National Heart, Lung and Blood Institute-sponsored BARI-2D (Bypass and Angioplasty Revascularization in Diabetics) study, investigators randomized mildly symptomatic or asymptomatic diabetic patients to either revascularization or medical management based in part on stress imaging. Revascularization was not associated with improved outcomes. Thus, neither current clinical practice guidelines nor the emerging evidence support the use of any cardiac imaging, with or without radiation, in asymptomatic individuals. This includes asymptomatic diabetic patients, i.e., those who were thought to most likely benefit from screening because they had greater event rates than asymptomatic individuals without diabetes (29).

Practical Considerations

What are the implications for the evidence-based clinician? Our view of the conceivable risks and benefits of cardiac imaging with modalities that use radiation is summarized in Table 1. In the absence of any proven benefit, the small projected LAR of cancer argues against the widespread use of SPECT or CT angiography in asymptomatic individuals but even more so does their cost, which is beyond the scope of this discussion (30).

However, we believe that the situation in symptomatic patients is far different. In these patients, the weight of evidence supports benefits from cardiac imaging which far outweigh the small projected risk of radiation-induced cancer. Patients who undergo imaging for diagnosis and risk stratification of coronary disease are predominantly men who often are older than 60 years of age. These patients are much more likely to die of illnesses, including CAD, rather than radiation-induced cancer during the remainder of their expected life span. Unfortunately, this important concept is often lost in the controversy surrounding asymptomatic individuals among health-care professionals and the media coverage of radiation risk in the lay press.

What are the implications for health-care professionals performing cardiac imaging? Although the risk of radiation-induced cancers at the dose levels used in cardiac imaging is very low, it may not be zero. Considering the endorsement of the LNT model by most consensus committees of radiation safety protection experts, it is rational to perform all

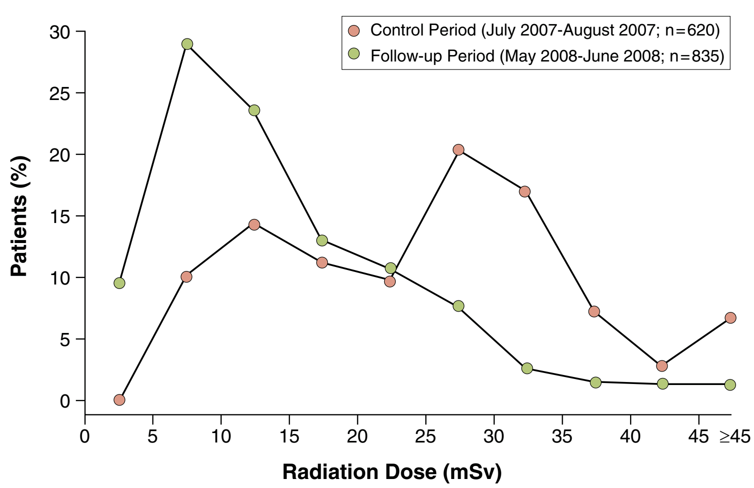

Figure 4. Reduction of Radiation Dose From Cardiac Computed Tomographic Angiography by Education on a Best Practice Model

Distribution of patients by their estimated radiation dose during computed tomography coronary angiography before and after a quality improvement effort in 15 Michigan imaging centers. Reprinted, with permission, from Raff et al. (33).

imaging studies at the lowest possible radiation dose that is consistent with obtaining diagnostic image quality (9). Medical errors that lead to excessive radiation doses (31) must be avoided. The authors of several studies (32–34) have shown that the radiation dose received from cardiac CT varies greatly between different imaging centers, even in the absence of medical error. Appropriate education on best-practice models can decrease the radiation dose by more than 50% (Fig. 4) (33). Such education efforts must become more widespread; they should be supported by professional organizations through education regarding radiation risk and the safety and promotion of standardized, low-dose imaging protocols (35) to guide responsible clinical practice.

New imaging techniques and equipment will allow further substantial reductions in the radiation dose received from both cardiac CT (36) and SPECT (37) without appreciable effect on diagnostic accuracy (38,39). These developments will greatly modify the "risk" aspect of cardiac imaging with ionizing radiation but will not resolve the broader concerns about the appropriateness of the tremendous growth in cardiac imaging, particularly in patient groups who are unlikely to benefit in terms of outcomes and survival. The Center for Medicare and Medicaid Services has started planning a pilot study of imaging appropriateness, which was legislatively mandated by Congress in 2008. Appropriately choosing the right test for the right patient and performing it with the lowest-possible radiation dose to the patient remains a challenge, both to those who order imaging studies and those who perform them.

Reprint requests and correspondence: Dr. Raymond J. Gibbons, Mayo Clinic, 200 First Street, SW, Rochester, Minnesota 55905. *E-mail: gibbons.raymond@mayo.edu.*

REFERENCES

1. Fazel R, Krumholz HM, Wang Y, et al. Exposure to low-dose ionizing radiation from medical imaging procedures. N Engl J Med 2009;361:849–57.
2. McCollough CH, Guimaraes L, Fletcher JG. In defense of body CT. Am J Radiol 2009;193:28–39.
3. NCRP Publications. Report No. 160–Ionizing Radiation Exposure of the Population of the United States (2009). Available at: http://www.ncrppublications.org/Reports/160. Accessed March 26, 2010.
4. Committee to Assess Health Risks from Exposure to Low Levels of Ionizing Radiation. Board on Radiation Effects Research, Division on Earth and Life Studies, National Research Council of the National Academies. Health Risks From Exposure to Low Levels of Ionizing Radiation: BEIR VII-Phase 2. Washington, DC: National Academies Press, 2006.
5. Health Physics Society (HPS) Radiation risk in perspective: position statement of the Health Physics Society. 2004. Available at: http://hps.org/documents/risk_ps010-1.pdf. Accessed March 26, 2010.
6. Preston RJ. Radiation biology: concepts for radiation protection. Health Phys 2005;88:545–56.
7. International Commission on Radiological Protection. 2007 Recommendations of the International Commission on Radiological Protection (ICRP Publication 103). Ann ICRP 2007;37:1–332.
8. Einstein AJ, Henzlova MJ, Rajagopalan S. Estimating risk of cancer associated with radiation exposure from 64-slice computed tomography coronary angiography. JAMA 2007;298:317–23.
9. Gerber T, Carr J, Arai A, et al. Ionizing Radiation in Cardiac Imaging. A Science Advisory From the American Heart Association Committee on Cardiac Imaging of the Council on Clinical Cardiology and Committee on Cardiovascular Imaging and Intervention of the Council on Cardiovascular Radiology and Intervention. Circulation 2009;119:1056–65.
10. Berrington de Gonzalez A, Mahesh M, Kim KP, et al. Projected cancer risks from computed tomographic scans performed in the United States in 2007. Arch Intern Med 2009;169:2071–7.
11. Einstein AJ, Moser KW, Thompson RC, Cerqueira MD, Henzlova MJ. Radiation dose to patients from cardiac diagnostic imaging. Circulation 2007;116:1290–305.
12. Morin RL, Gerber TC, McCollough CH. Radiation dose in computed tomography of the heart. Circulation 2003;116:1290–305.
13. Horner MJ, Ries L, Krapcho M, et al. SEER Cancer Statistics Review, 1975–2006. Based on November 2008 SEER data submission, posted to the SEER web site, 2009. Table 1–17. Available at: http://seer.cancer.gov/csr/1975_2006/. Accessed December 21, 2009.
14. Muirhead CR, O'Hagan JA, Haylock RGE, et al. Mortality and cancer incidence following occupational radiation exposure: third analysis of the National Registry for Radiation Workers. Br J Cancer 2009;100:206–12.
15. Brenner DJ, Doll R, Goodhead DT, et al. Cancer risks attributable to low doses of ionizing radiation: assessing what we really know. Proc Natl Acad Sci U S A 2003;100:13761–6.
16. Preston DL, Shimizu Y, Pierce DA, Suyama A, Mabuchi K. Studies of mortality of atomic bomb survivors. Report 13: solid cancer and noncancer disease mortality: 1950–1997. Radiat Res 2003;160:381–407.
17. Cardis E, Vrijheid M, Blettner M, et al. Risk of cancer after low doses of ionising radiation: retrospective cohort study in 15 countries. BMJ 2005;331:77.
18. Cardis E, Vrijheid M, Blettner M, Gilbert E, Hakama M. The 15-Country Collaborative Study of Cancer Risk among Radiation Workers in the Nuclear Industry: estimates of radiation-related cancer risks. Radiat Res 2007;167:396–416.
19. Gibbons RJ. Noninvasive diagnosis and prognosis assessment in chronic coronary artery disease: stress testing with and without imaging perspective. Circ Cardiovasc Imaging 2008;1:257–69.
20. Hubbard BL, Gibbons RJ, Lapeyre AC, Zinsmeister AR, Clements IP. Identification of severe coronary artery disease using simple clinical parameters. Arch Intern Med 1992;152:309–12.

21. Hachamovitch R, Hayes SW, Friedman JD, et al. Determinants of risk and its temporal variation in patients with normal stress myocardial perfusion scans: what is the warranty period of a normal scan? J Am Coll Cardiol 2003;41:1329–40.
22. Gibbons RJ, Abrams J, Chatterjee K, et al; American College of Cardiology; American Heart Association Task Force on Practice Guidelines. Committee on the Management of Patients With Chronic Stable Angina. ACC/AHA 2002 guideline update for the management of patients with chronic stable angina—summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on the Management of Patients With Chronic Stable Angina). J Am Coll Cardiol 2003;41: 159–68.
23. Hachamovitch R, Berman DS, Kiat H, et al. Exercise myocardial perfusion SPECT in patients without known coronary artery disease: incremental prognostic value and use in risk stratification. Circulation 1996; 93:905–14.
24. Hachamovitch R, Hayes SW, Friedman JD, Cohen I, Berman DS. Comparison of the short-term survival benefit associated with revascularization compared with medical therapy in patients with no prior coronary artery disease undergoing stress myocardial perfusion single photon emission computed tomography. Circulation 2003;107:2900–7.
25. Hachamovitch R, Rozanski A, Hayes SW, et al. Predicting therapeutic benefit from myocardial revascularization procedures: are measurements of both resting left ventricular ejection fraction and stress-induced myocardial ischemia necessary? J Nucl Cardiol 2006;13:768–78.
26. Hlatky HA, Greenland P, Arnett DK, et al; American Heart Association Expert Panel on Subclinical Atherosclerotic Diseases and Emerging Risk Factors and the Stroke Council. Criteria for evaluation of novel markers of cardiovascular risk: a scientific statement from the American Heart Association. Circulation 2009;119:2408–16.
27. Budoff MJ, Achenbach S, Blumenthal RS, et al. Assessment of coronary artery disease by cardiac computed tomography: a scientific statement from the American Heart Association Committee on Cardiovascular Imaging and Intervention, Council on Cardiovascular Radiology and Intervention, and Committee on Cardiac Imaging, Council on Clinical Cardiology. Circulation 2006;114:1761–91.
28. Greenland P, Bonow RO, Brundage BH; American College of Cardiology Foundation Clinical Expert Consensus Task Force (ACCF/AHA Writing Committee to Update the 2000 Expert Consensus Document on Electron Beam Computed Tomography); Society of Atherosclerosis Imaging and Prevention; Society of Cardiovascular Computed Tomography. ACCF/AHA 2007 clinical expert consensus document on coronary artery calcium scoring by computed tomography in global cardiovascular risk assessment and in evaluation of patients with chest pain: a report of the American College of Cardiology Foundation Clinical Expert Consensus Task Force (ACCF/AHA Writing Committee to Update the 2000 Expert Consensus Document on Electron Beam Computed Tomography) developed in collaboration with the Society of Atherosclerosis Imaging and Prevention and the Society of Cardiovascular Computed Tomography. J Am Coll Cardiol 2007;49:378–402.
29. Wackers FJ. Asymptomatic patients with diabetes mellitus should be screened for coronary artery disease. J Nucl Cardiol 2006;13:609–15.
30. Lauer MS. Elements of danger—the case of medical imaging. N Engl J Med 2009;361:841–3.
31. Bogdanich W. Radiation Overdoses Point Up Dangers of CT Scans. New York Times, October 15, 2009. Available at: http://www.nytimes.com/2009/10/16/us/16radiation.html. Accessed March 26, 2010.
32. Hausleiter J, Meyer T, Hermann F. Estimated radiation dose associated with cardiac CT angiography. JAMA 2009;301:500–7.
33. Raff G, Chinnaiyan KM, Share DA. Radiation dose from cardiac computed tomography before and after implementation of radiation dose reduction techniques. JAMA 2009;301: 2340–8.
34. Smith-Bindman R, Lipson J, Marcus R, et al. Radiation dose associated with common computed tomography examinations and the associated lifetime attributable risks of cancer. Arch Intern Med 2009;169:2078–86.
35. Gibbons RJ, Gerber TC. Calcium scoring with computed tomography: what is the radiation risk? Arch Intern Med 2009;169:1185–7.
36. Achenbach S, Ropers U, Kuettner A, et al. Randomized comparison of 64-slice single- and dual-source computed tomography coronary angiography for the detection of coronary artery disease. J Am Coll Cardiol Img 2008;1:177–86.
37. DePuey EG, Bommireddipalli S, Clark JC, Thompson L, Srour Y. Wide beam reconstruction "quarter-time" gated myocardial perfusion SPECT functional imaging: a comparison to "full-time" ordered subset expectation maximum. J Nucl Cardiol 2009;16:736–52.
38. Maruyama T, Takada M, Hasuike T, et al. Radiation dose reduction and coronary accessibility of prospective electrocardiogram-gated computed tomography coronary angiography: comparison with retrospective electrocardiogram-gated helical scan. J Am Coll Cardiol 2008;52:1450–5.
39. Pontone G, Anmdreini D, Bartorelli AL. Diagnostic accuracy of coronary computed tomography angiography: a comparison between prospective and retrospective electrocardiogram triggering. J Am Coll Cardiol 2009;54: 346–55.

Key Words: computed tomography ■ myocardial perfusion imaging ■ coronary artery disease ■ therapy ■ radiation dose and risk.