

## EXECUTIVE SUMMARY

**Objectives:** To briefly review the use of electron beam computed tomography (CT) for determining coronary artery calcification, spiral CT for lung cancer screening, and CT colonography for colon cancer screening in the context of generally accepted criteria that comprise a valid screening test. The use of total body scans for screening purposes was not specifically evaluated.

**Methods:** Literature searches were conducted in the MEDLINE and Nexis databases for English-language articles published between 1990 and March 2003 using the search terms “screening,” “mass screening,” and “tomography, x-ray computed” or “radiography,” as well as the text terms “electron beam computed tomography,” or “virtual colonoscopy,” in combination with “calcium,” “coronary angiography,” “coronary arteriosclerosis,” “coronary disease,” “lung,” “lung neoplasms,” “thoracic,” “adenocarcinoma,” “colon,” “colonoscopy,” “colorectal or colonic neoplasms,” “colonography,” and “colonic polyps.” A total of 812 citations were identified; 272 were retrieved for analysis. Additional references were culled from the bibliographies of these references.

**Results:** The detection and quantification of coronary arterial calcification (CAC) serves as a sensitive surrogate marker of the total plaque burden and carries some positive and negative predictive value for estimating the likelihood of future coronary events. The degree to which CAC independently estimates the risk of coronary heart disease, or adds incremental value to established risk factors is still undetermined. Spiral CT is more sensitive than routine chest x-ray in detecting uncalcified lung nodules, allowing the possibility that more patients may be diagnosed with early stage disease. Spiral CT may prove to be a very important tool for early detection of lung cancer, but at this time, only prevalence-screening data and preliminary survival data in observational cohorts are available. CT colonography is less sensitive than conventional colonoscopy and patients with positive scans ultimately must also undergo a conventional colonoscopy. CT colonography is useful, however, in patients who refuse to undergo colonoscopy for various reasons, and in patients following failed or incomplete colonoscopy. As yet, none of these screening tests have been shown to reduce disease-specific mortality, but trials are under way to answer this question.

**Conclusions:** Large, prospective, multicenter trials are currently under way or in the planning phase to evaluate whether these screening examinations are clinically valid and reduce the rate of mortality. The medical profession should continue to advocate the use of clinically effective and cost-effective procedures and interventions. Relevant specialty societies can assist by continuing to evaluate the validity and clinical use of screening imaging procedures that are advertised directly to the public and make available to the broader physician community unbiased evaluations to help primary care physicians advise their patients on the risks and benefits of these procedures.

## REPORT OF THE COUNCIL ON SCIENTIFIC AFFAIRS

CSA Report 10- A-03

Subject: Commercialized Medical Screening  
(Resolution 508, I-01, Resolution 509, A-02)

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### Background

Resolution 508 (I-01), introduced by the Young Physicians Section and referred to the Board of Trustees (BOT) for decision, asked: (1) that our American Medical Association (AMA) study the marketing and use of commercial medical screening tests for the general public when not recommended by the patient's physician and when performed without physician directives; (2) that our AMA consider developing standards based upon the results of its study; and (3) that our AMA report back to the House of Delegates (HOD) at the 2002 Interim Meeting. At the April 2002 meeting of the BOT, a decision was made to forward a BOT report on this issue to the HOD.

Resolution 509 (A-02), introduced by the Wisconsin Delegation and also referred to the BOT, asked: (1) that our AMA establish as policy that it is inappropriate for physicians to be involved in promoting commercialized screening procedures to the public, unless supported by evidence-based guidelines supporting such screenings; (2) that our AMA undertake a public education campaign using existing publications including the Web site explaining the criteria for effective screening; and (3) that our AMA encourage the public to seek appropriate health screening.

Because the issues raised in these two resolutions are related they were considered together in developing a BOT Report. Subsequently, the BOT reconsidered its decision to provide a report to the HOD and requested instead that both the Council on Scientific Affairs (CSA) and the Council on Ethical and Judicial Affairs address these resolutions. As the first step, the CSA agreed to briefly evaluate the scientific basis of these resolutions in the context of generally accepted criteria for screening. Most of the practices in question involve the use of high-technology, noninvasive imaging scans.

The proliferation and direct marketing of screening tests that lack a credible evidence base, or that misrepresent their true risks and benefits, raise a number of scientific, clinical, and ethical concerns. Although it can be argued that patients (consumers) have the right to purchase these kinds of "health care" scans, the profession of medicine carries certain responsibilities that are relevant to these issues. Our AMA has long-standing policy that any preventive services should be supported by evidence-based data to demonstrate improved outcome or quality of life and the cost-effectiveness of the service (Policy H-425.997, Preventive Services, AMA Policy Database).

A September 2002 statement issued by the American College of Radiology (ACR) stated that "to date, there is no evidence that total body computed tomography (CT) screening is cost-effective or effective in prolonging life. In addition, the ACR is concerned that this procedure will lead to

1 the discovery of numerous findings that will not ultimately affect patient's health but will result  
2 in unnecessary follow-up examinations and treatment and significant wasted expense."<sup>1</sup> The  
3 CSA agrees with this statement and, due to the lack of published sensitivity and specificity data  
4 on this procedure, will not further examine it at this time. This report also does not examine the  
5 emergence of positron emission tomography scans that certain facilities have recently begun to  
6 promote. This report will focus on the use of electron beam computed tomography for  
7 determining coronary calcification and the use of CT for lung and colon cancer screening.  
8 However, a comprehensive review of these technologies is beyond the scope of this report.  
9

## 10 Methods

11  
12 Literature searches were conducted in the MEDLINE and Nexis databases for English-language  
13 articles published between 1990 and March 2003 using the search terms "screening," "mass  
14 screening," and "tomography, x-ray computed" or "radiography," as well as the text terms  
15 "electron beam computed tomography," or "virtual colonoscopy," in combination with  
16 "calcium," "coronary angiography," "coronary arteriosclerosis," "coronary disease," "lung,"  
17 "lung neoplasms," "thoracic," "adenocarcinoma," "colon," "colonoscopy," "colorectal or colonic  
18 neoplasms," "colonography," and "colonic polyps," A total of 812 citations were identified; 272  
19 were retrieved for analysis. Additional references were culled from the bibliographies of these  
20 references.  
21

## 22 Established Screening Criteria

23  
24 *Screening* constitutes the use of laboratory tests, physical examination, or imaging modalities  
25 performed on asymptomatic patients with the intent of identifying subclinical disease. As such,  
26 screening differs from clinical investigation, in which tests are ordered after disease is suspected.  
27 Our AMA defines screening as health care services or products provided to an individual without  
28 apparent signs or symptoms of an illness, injury, or disease for the purpose of identifying or  
29 excluding an undiagnosed illness, disease, or condition (Policy H-320.953).  
30

31 A screening test is the initial action in a screening program, which also includes follow-up tests to  
32 confirm the initial test results (eg, biopsy, angiography) and treatment given for abnormal  
33 findings (eg, surgery, radiation, chemotherapy, pharmacotherapy). *Early detection* represents  
34 discovery of a condition or disease before obvious signs or symptoms have appeared. Screening  
35 can be further subdivided into *mass screening* or *individualized screening*. The former is  
36 conducted with little regard for the risk profile of the individual patient. Most physicians are  
37 involved in the latter, which consists of recommending screening tests in the context of an  
38 ongoing patient-physician relationship. The *sensitivity* and *specificity* of a particular test help  
39 establish its effectiveness. Sensitivity equals the proportion of the disease population who have a  
40 positive test (true-positive rate). The specificity of a test equals the proportion of healthy patients  
41 who have a negative test (true-negative rate). Patients and clinicians are often more interested in  
42 the *positive predictive value* of a test, which equals the proportion of patients with a positive test  
43 result who actually have the disease.  
44

45 For a screening test to be considered effective, certain criteria should be fulfilled, including the  
46 following:  
47

- 48 • The disease must constitute a significant public health problem (common, with  
49 significant morbidity and mortality).
- 50 • The disease or condition should have a readily available and acceptable treatment, and  
51 the potential for cure must be greater among screen-detected patients.

- 1 • The screening test must have appropriate sensitivity, specificity, and positive predictive
- 2 value (capable of detecting a sufficiently high proportion of [disease] in the detectable
- 3 preclinical phase).
- 4 • The screening test should be acceptable (and safe) to the patient and society.
- 5 • There must be demonstrable improved health outcomes related to screening.
- 6 • The screening procedure should have a reasonable cost.
- 7 • Adequate resources and health services should be available to accomplish the screening
- 8 and to provide the necessary intervention triggered by a positive test result.

9  
10 Additionally, when a new screening test becomes available, it should offer significant advantages  
11 in terms of information obtained, cost, or safety over other alternative tests when more than one  
12 test is available to screen for the same disease.

### 13 Variables That Confound Assessment of Screening Tests

14  
15  
16 Several biases are inherent in the conduct of screening tests that can have an impact on apparent  
17 survival measures, thus affecting valid assessment of screening test effectiveness. In particular,  
18 *lead time bias* makes the assessment of mortality improvements difficult. Early detection of  
19 cancer creates a backward shift in the starting point for measuring survival (earlier diagnosis),  
20 which may artificially increase incidence and lengthen survival.

21  
22 Screen-detected incidental cancers represent *length bias*. Individuals with more slowly  
23 progressive disease (eg, prostate cancer) will tend to be detected. Length bias increases the  
24 incidence of early-stage disease and lengthens apparent survival, but has no effect on mortality  
25 rates or advanced-stage disease.

26  
27 People who agree to be screened are a self-selected group who may be more aware of the disease  
28 in question and more health conscious. *Selection bias* can occur whenever the group actually  
29 screened differs from the potential population of individuals to be screened. This bias also can  
30 cause apparent increases in survival of individuals with screen-detected conditions.

31 *Overdiagnosis bias* occurs when a screen-detected abnormality is labeled as the “disease” when  
32 in fact this abnormality would never have been clinically diagnosed in the absence of screen  
33 detection. This may be particularly relevant for lung cancer (or whole body) screening with CT  
34 scans.

35  
36 Because of these biases, case survival cannot be used to assess the effect of screening on  
37 mortality. In fact, 5-year survival figures are unrelated to cancer mortality on a population basis.<sup>2</sup>  
38 Rather, population mortality from the disease over a follow-up period beginning with  
39 randomization should be used. Also, one generally cannot make valid comparisons by comparing  
40 people screened with those who were unscreened in the past. The only way to determine the  
41 degree of benefit without bias is by comparing people offered screening with a group of truly  
42 comparable people who are not offered screening.

43  
44 Some common methodologies used in observational epidemiology, particularly case-control and  
45 cohort studies, are sometimes used to evaluate screening. Valid application of these approaches  
46 requires that screening has been in place in a community for a sufficient length of time for a  
47 benefit to be detectable if it does occur. Case-control studies have limitations because it can be  
48 difficult to differentiate a screening test from a diagnostic test for cancer, and this imprecision in  
49 classification can have a major impact on the results of such studies.

## Commercialized Medical Screening

Community-based screening programs for blood pressure, cholesterol, other serum chemistries, and certain cancer screening tests (eg, mammography, prostate-specific antigen) have been offered for many years. More recently, the development of high-technology imaging tests such as electron-beam computed tomography (EBCT) for the detection of coronary artery calcium, spiral CT scan for lung cancer, CT colonography (“virtual colonoscopy”), and even “whole body scans” have been marketed directly to the public. These new imaging techniques are offered on the premise that they identify the presence of subclinical disease, improve chances of survival, or are more convenient.

Although their relative risks and benefits are not established, ensuing public and professional interest has led to the early adoption and promotion of these scans. Consequently, the emergence of for-profit imaging centers and direct-to-consumer advertising has led to significant numbers of self-referred patients with abnormal test results seeking treatment advice from their physicians.

## Coronary Artery Calcium Screening

The most common commercially available test to evaluate coronary artery calcification is EBCT; multidetector CT protocols and others also are being developed. EBCT uses a stationary source-detector combination and a rotating electron beam to produce serial and contiguous thin-section, 100-millisecond scans at end-diastole in synchrony with the cardiac cycle. Scans can be completed in one or two short breath holds. Calcium is readily apparent as high-density deposits adjacent to lower density soft tissue and fat. Standardized methods for scanning, identification, and quantification of coronary artery calcification (CAC) have been established.<sup>3</sup> EBCT is being directly marketed for the purpose of screening and assessing asymptomatic patients. It is also being used clinically to assess CAC in patients of intermediate to high risk of developing cardiovascular disease; in symptomatic individuals at low to intermediate risk of coronary events to stratify patients for more aggressive primary prevention; and in patients with known coronary artery disease (CAD) to assess progression or regression of the total plaque burden. Most EBCT centers rely on self-referred patients for the majority of their volume of procedures.

Coronary plaque burden has been established as a good predictor of future coronary events.<sup>4,5</sup> Although the amount of CAC detected by EBCT represents a small percentage of the total plaque burden (~20%), the extent of CAC (total calcium score) correlates with the severity of atherosclerosis. EBCT is less sensitive for detecting lipid-laden, vulnerable plaque, the rupture of which is often associated with acute coronary syndromes.<sup>6-12</sup> Additionally, some high-grade stenoses may lack detectable levels of calcium. Nevertheless, because of the above relationships, CAC is believed to have some predictive power for future coronary events.

Currently, clinicians rely on traditional models of risk-factor analysis to predict coronary outcomes, make therapeutic decisions, and attempt to change patients’ behavior. Risk stratification based on the Framingham model has limited sensitivity and specificity for identifying individuals who will suffer an acute catastrophic coronary event. A significant number of events that occur in asymptomatic patients at low to intermediate risk are believed to be caused in part by plaque rupture (or erosion) of mild, nonobstructive arterial stenoses, which may not be calcified.<sup>13,14</sup> Plaque characteristics unrelated to the degree of stenosis, such as lipid content and plaque wall thickness, may be better predictors of rupture than the degree of obstruction. Thus, a question of considerable importance for primary prevention is how the information attained through CAC determinations can be used in risk assessment and in the selection of patients for more intensive risk reduction therapy.

1 Clinical Trials on EBCT. Several prospective studies have been conducted on the use of EBCT  
2 for diagnosis of CAD and/or risk prediction. A meta-analysis of 16 EBCT studies involving  
3 patients without a prior history of coronary disease who presented for diagnostic catheterization  
4 found that the use of EBCT was associated with an 80% sensitivity, 40% specificity, and 59%  
5 positive predictive value for the presence of CAD.<sup>7</sup> The case definition of CAD was variable,  
6 although stenosis  $\geq 50\%$  was used in the majority of these studies. Significant CAD was detected  
7 in 60% of patients, and significant CAC was present in 68%. In this analysis, the sensitivity of  
8 EBCT was similar to that of other noninvasive tests for ischemic heart disease, but had a higher  
9 false-positive rate, particularly in the elderly.<sup>7</sup> Another meta-analysis that included only studies  
10 where CAD was defined as  $\geq 50\%$  stenosis found somewhat higher values of 92% for sensitivity  
11 and 51% for the diagnostic specificity of EBCT (compared with catheterization).<sup>15</sup> Thus, data are  
12 consistent with the “calcium score” being viewed as a surrogate for overall atherosclerotic plaque  
13 burden, and for providing ranges of variable sensitivity and specificity of luminal narrowing for  
14 at least one vessel without identifying specific lesions or sites.<sup>16,17</sup>

15  
16 A more relevant question for the use of EBCT as a commercialized screening test is its ability to  
17 predict the risk of future coronary events, either independently or incrementally in conjunction  
18 with traditional validated risk factors. Several studies attempted to evaluate whether the CAC  
19 score can independently predict risk in asymptomatic patients (who nevertheless have certain risk  
20 factors) (see Table).<sup>18-21</sup>

21  
22 Results of these studies indicate that EBCT calcium scores have some predictive value, although  
23 the studies to date are weakened by selection and treatment biases.<sup>22</sup> A meta-analysis found a  
24 pooled risk ratio for death or nonfatal myocardial infarction of 4.2 (over 42 months) when the  
25 CAC was above the median value, although the validity of this meta-analysis has been  
26 questioned.<sup>23,24</sup> Asymptomatic patients with calcium scores below sex- and age-specific means  
27 are less likely to have obstructive atherosclerosis than patients with greater than average scores,  
28 and the negative predictive value of EBCT is high (92% to 98%). However, the relationship of  
29 EBCT calcium scores to traditional risk factors and whether they offer incremental value is not  
30 established.<sup>8,21</sup> In one recent study involving an age-homogenous male sample (aged 39 to 45  
31 years) with a low predicted risk of coronary events, the prevalence of CAC was 17.6%. Calcium  
32 scores were independently associated with low-density lipoprotein (LDL) concentrations and had  
33 only a weak relationship with the Framingham risk index.<sup>25</sup>

34  
35 Comment. Self-referral for EBCT is based on the premise that conventional cardiovascular risk  
36 factors inadequately quantify risk. Despite promising results, questions remain about the current  
37 value of this technology in asymptomatic patients, because most of the research data come from  
38 symptomatic or high-risk, older, and primarily self-referred populations. Evaluations have  
39 involved mostly comparisons with angiographic disease determination based on variable degrees  
40 of obstruction. It remains to be established how information obtained through EBCT can be used  
41 in risk assessment and in the selection of patients for more intensive primary preventive therapy.  
42 Additionally, the extent to which CAC predicts the development of coronary events independent  
43 of standard risk factors (eg, cigarette smoking, hypertension, elevated LDL, family history of  
44 premature coronary heart disease [CHD], etc) has not been resolved. Furthermore, the use of  
45 EBCT must be evaluated in comparison with alternative noninvasive tests (eg, nuclear stress test;  
46 stress echocardiogram), both of which allow for functional assessment of the coronary arteries (in  
47 contrast to EBCT) and are frequently used to clarify the significance of an abnormal EBCT  
48 before deciding if the patient requires angiography.

49  
50 Several studies are under way in heterogeneous patient sets to confirm the utility of EBCT. A  
51 large registry has been established by the Society for Atherosclerosis Imaging and a large

1 observational epidemiological study sponsored by the National Heart, Lung and Blood Institute is  
2 investigating CAC, detected by EBCT, as a predictor of CHD mortality and morbidity, stroke,  
3 and all-cause mortality. The National Institutes of Health Multiethnic Study of Atherosclerosis  
4 will assess the long-term outcome of 6,500 asymptomatic individuals undergoing EBCT, as well  
5 as other imaging and nonimaging tests.<sup>26</sup> This trial should provide important information on  
6 EBCT and other measurements that may detect subclinical coronary artery disease. The  
7 Prospective Army Coronary Calcium Study includes a study arm to establish the relationship  
8 between CAC and cardiovascular events in a “low risk” military population.<sup>27</sup> As part of the  
9 Dallas Heart Disease Prevention Project, approximately 3,000 randomly selected subjects aged 30  
10 to 60 years will undergo EBCT.

11  
12 The American College of Cardiology/American Heart Association Expert Consensus Document  
13 on Electron-Beam Computed Tomography (EBCT) for the Diagnosis and Prognosis of Coronary  
14 Artery Disease<sup>15</sup> states that the “published literature does not clearly define which asymptomatic  
15 people require or will benefit from EBCT,” and that “EBCT screening should not be made  
16 available to the general public without a physician’s request.” Until clinical trial data become  
17 available, evidence-based guidelines for the prevention of cardiovascular events based on EBCT  
18 results are lacking, particularly in the case of asymptomatic patients. Advice given in regard to  
19 coronary risk stratification or therapy modifications should be based on well-designed  
20 epidemiological studies and prospective randomized clinical trials.

#### 21 22 Spiral Helical (Low-Dose) Computerized Tomography (LDCT) Scanning for Lung Cancer

23  
24 Lung cancer is the number one cause of death in the United States for both adult men and women,  
25 claiming approximately 150,000 lives annually. Most patients who are diagnosed with lung  
26 cancer have advanced stage, symptomatic disease. In the United States, only 20% of diagnosed  
27 lung cancers are in stage 1.<sup>28</sup>

28  
29 Previously, 4 large randomized controlled trials enrolling approximately 37,000 high-risk male  
30 smokers more than 45 years of age evaluated the impact of regular chest X-ray (CXR) on lung  
31 cancer mortality.<sup>29-34</sup> Investigators in each trial found an increased incidence of earlier stage lung  
32 cancers, more resectable cancers, and improved 5-year survival rates in the screened groups, but  
33 no trial found a statistically significant decrease in disease-specific (lung cancer) mortality.<sup>35</sup> The  
34 survival/mortality differential in the Mayo study has been attributed to length and overdiagnosis  
35 bias.<sup>36</sup>

36  
37 Because of contamination of the control group (a large percentage of subjects had CXR) and  
38 other methodological concerns, disagreement persists on the conclusions of the Mayo study, and  
39 whether it truly invalidates the potential benefit of annual CXR screening for lung cancer.<sup>37</sup>  
40 However, based on the results of these trials, the general consensus has been that screening for  
41 lung cancer with chest X-ray ± sputum cytology has no beneficial effect on mortality.  
42 Nevertheless, in another attempt to definitively evaluate the mortality benefit of CXR screening  
43 for lung cancer, its use as a screening tool is currently being studied in the Prostate, Lung,  
44 Colorectal and Ovarian Cancer Screening Trial.<sup>38</sup>

45  
46 LDCT scanning is very sensitive (compared with CXR), and is capable of routinely detecting  
47 nodules 2 to 3 mm in diameter. Three-dimensional reconstruction creates images that can be  
48 assessed sequentially to monitor for growth. The rationale for LDCT as an improved early  
49 detection technology is therefore based on its ability to detect smaller nodules, allowing for  
50 surgical resection of more patients who have stage 1 disease. In Japan, the Anti-Lung Cancer  
51 Association added LDCT screening to CXR screening in 1993. CT screening using mobile units

1 has been offered in certain regions of Japan, and to individuals enrolled in certain insurance  
2 groups.<sup>39-41</sup> A nonrandomized historical comparison of CXR + sputum cytology to CXR ± sputum  
3 cytology + LDCT found that use of CT scans nearly doubled the percentage of stage 1A tumors  
4 represented in the diagnostic cohort, and appeared to markedly improve 5-year survival (48% to  
5 82%).<sup>39</sup> Whether the latter represents a true mortality benefit may be clouded by lead time and  
6 other biases.

7  
8 Clinical Trials of LDCT Screening. LDCT has been studied in several observational screening  
9 studies in high-risk patients.<sup>39,40,42-48</sup> To date, primarily prevalence data from these trials have  
10 been published. Relative to CXR, LDCT enhances the detection of small noncalcified nodules  
11 and of lung cancer at an earlier stage.<sup>49</sup> The rate of lung cancer diagnosis obtained from baseline  
12 screens was 0.4% to 2.7%, much higher than normal baseline rates of lung cancer diagnosis; 77%  
13 to 100% of these malignancies were stage 1 disease. However, all of these studies had a high rate  
14 of false-positive results, with abnormal nodules reported in 12% to 51% of screened patients. The  
15 number of suspicious lesions observed in an asymptomatic general population would be expected  
16 to be much smaller. In one study of subjects who responded to offers of screening (40%  
17 nonsmokers), suspicious nodules were detected in 5.1% of subjects, 8% of whom were confirmed  
18 surgically to have lung cancer (0.4% of original pool).<sup>47</sup>

19  
20 Because LDCT screening advances the stage at which lung cancer is typically diagnosed, and  
21 unresected stage 1 disease has such a dismal 5-year survival rate, screening for lung cancer by  
22 LDCT would seem to be an effective means to prevent deaths from lung cancer.<sup>48</sup> However,  
23 concerns remain that LDCT leads to overdiagnosis and its widespread application may result in  
24 aggregate harm to screened individuals because the rate of benign nodule detection is high. The  
25 apparent false-positive to true-positive ratio in screening studies of high-risk patients has ranged  
26 from 10 to 30.<sup>4,6,49</sup> In one recent study, 50% of patients referred for biopsy had negative results.  
27 Additionally, there are currently no data to show that a 5-mm diameter lung mass is associated  
28 with substantially better prognosis than a 10-mm mass.<sup>50</sup> Various protocols have been used for  
29 following up indeterminate nodules in an effort to reduce unnecessary invasive procedures.<sup>41,46,49-</sup>  
30 <sup>51</sup> Use of serial CT scans and 3-dimensional reconstruction appears to lessen the number of  
31 invasive procedures performed on individuals who have an abnormality.<sup>52</sup>

32  
33 A large New York-based LDCT study enrolling 10,000 current or former smokers and a National  
34 Cancer Institute (NCI) lung screening study will evaluate the risks and benefits of LDCT. The  
35 NCI study is enrolling 50,000 individuals aged 55 to 74 years with a smoking history of at least  
36 30 pack-years. They will be randomized to annual screening with LDCT or CXR for 3 years and  
37 followed up through 2009 (unless an obvious early disease-specific mortality benefit is observed).

38  
39 Comment. The American College of Chest Physicians (ACCP) recently commissioned the  
40 development of evidence-based guidelines for lung cancer prevention, diagnosis, and treatment.  
41 The ACCP recommends “against the use of a single LDCT or serial LDCTs to screen for the  
42 presence of lung cancer.” At-risk individuals who express an interest in undergoing LDCT  
43 screening should be made aware of several ongoing high quality clinical studies of this  
44 technology.”<sup>53</sup> The American College of Radiology statement<sup>54</sup> on LDCT expresses “concern  
45 about the broad dissemination of lung screening outside of experienced, multispecialty settings  
46 and prior to the validation of this new technology and encourages professional organizations to  
47 promote informed decision-making for patients about possible benefits, risks, and limitations of  
48 testing for early lung cancer. Individuals interested in early detection (screening) should be  
49 encouraged to participate in trials.” Similarly, the Society of Thoracic Radiology “does not  
50 recommend mass screening for lung cancer at this time, but strongly encourages appropriate  
51 subjects to participate in trials so that the true effectiveness of lung cancer screening with LDCT

1 can be determined at the earliest possible time.”<sup>55</sup> Until more data are available and the NCI  
2 randomized trial is completed, “physicians, patients, and policy makers should be conservative  
3 about accepting this new, as yet not fully tested, and relatively expensive strategy of using helical  
4 CT scanning for lung cancer.”<sup>56</sup>

5  
6 The appropriate goal of any population-based screening program is to protect the public’s health,  
7 while targeting the test individuals most likely to benefit. The argument over routine use of  
8 LDCT reflects a divide over what evidence is required and how it should be obtained before an  
9 emerging early cancer detection technology is broadly adopted. From a public health perspective,  
10 smoking cessation must remain the first and foremost priority in reducing the burden of lung  
11 cancer in the population. LDCT may prove to be a very important tool for early detection of  
12 lung cancer, but at this time, only prevalence-screening data and preliminary survival data in  
13 observational cohorts are available. It remains to be established whether LDCT screening for lung  
14 cancer will truly reduce mortality in safe, cost-effective manner. Studies like the New York-based  
15 LDCT study and the NCI multicenter trial will likely provide this vital information.

#### 16 17 Computerized Tomography Scanning for Colon Cancer

18  
19 Colorectal cancer is the second most common cause of death due to cancer in the United States.  
20 Most colon cancers arise from pre-existing benign adenomatous polyps. Detection and removal  
21 significantly decreases the subsequent development of colon cancer.<sup>57</sup> Conventional colonoscopy  
22 is considered the most effective modality for the prompt detection of colorectal cancer.  
23 Colonoscopy has a sensitivity of 95% for detection of colorectal cancer in clinical practice, but  
24 complete examination of the colon is not possible in 5% to 15% of all patients, and a missed  
25 lesion rate of 6% has been reported for the detection of polypoid lesions measuring more than 1  
26 cm in diameter and 13% for lesions 6 to 9 mm in diameter.<sup>58,59</sup>

27  
28 CT colonography (CTC), also known by the marketing term “virtual colonoscopy,” was first  
29 introduced in 1994 and has evolved rapidly. Several recent reviews are available.<sup>60-63</sup> CTC  
30 involves thin-section helical computed tomography of a clean, air-distended colon (using a rectal  
31 enema tube), to generate high-resolution, 2-dimensional axial images. Application of advanced  
32 graphical software to the volumetrically acquired helical CT data generates 3-dimensional images  
33 of the colon off-line. Performance over the last decade has improved with the availability of  
34 ultrafast helical CT scanners (multidetector CT) and advances in computer software for image  
35 reconstruction. However, there appears to be a steep learning curve to establish competency in  
36 correct interpretation.<sup>64</sup>

37  
38 Compared with conventional colonoscopy, CTC has lower risk; carries no need for sedation,  
39 analgesia, or recovery time; and can eliminate “blind spots” proximal to colonic folds. CTC  
40 provides a total examination of the colon in more than 90% of patients, including those with  
41 distal occlusive colorectal cancer, the frail and the elderly, and in circumstances of failed or  
42 incomplete colonoscopy. However, patients with abnormal results on CTC will still require  
43 conventional colonoscopy. Additionally, residual solid stool can simulate a true polyp, and  
44 residual liquid also can interfere with test accuracy. A CTC also provides the same information as  
45 a noncontrast CT scan of the abdomen and pelvis outside of the colon.

46  
47 Clinical Trials of CT Colonography. Published data regarding the sensitivity and specificity of  
48 CTC are predominantly based on single detector CT technology and have been performed mostly  
49 in symptomatic or high-risk patients in a small subset of academic medical centers.

1 Some studies comparing CTC with conventional colonoscopy have yielded inadequate results in  
2 that the specificity for polyps less than 1 cm in size, including those in the 5- to 9-mm range, has  
3 been below 70%.<sup>65-69</sup> Results of larger studies have found that the sensitivity of CTC for the  
4 detection of polyps measuring 10 mm or larger generally ranges from 75% to 100%,<sup>70-75</sup> although  
5 it was only 50% in the third largest published study.<sup>65</sup> In the largest series to date, the per polyp  
6 sensitivity was 90.2% for 10 mm or larger, 80.1% for 5 to 9.9 mm, and 59.1% for polyps smaller  
7 than 5 mm.<sup>70</sup> A recent blinded prospective study in 165 patients with suspected colorectal lesions  
8 found CTC to have a diagnostic sensitivity similar to that of conventional colonoscopy for the  
9 detection of colorectal lesions  $\geq 6$  mm in diameter, results that are in agreement with the study of  
10 Fenlon et al<sup>71</sup> in patients at high risk of colorectal neoplasia.<sup>76</sup>

11 The sensitivity of conventional colonoscopy for polyps  $\geq 10$  mm using similar study designs has  
12 been reported at 94% to 100% and at 87% to 88% for polyps in the 6 to 9 mm range.<sup>59,77</sup>

13  
14 Large-scale multicenter trials in patients at average risk are planned and some are currently  
15 underway in the United States and Europe to further clarify the usefulness of CTC as a screening  
16 test. One such trial has been completed.<sup>78</sup> Preliminary results indicated that among 619 subjects  
17  $\geq 50$  years of age presenting for elective conventional colonoscopy, the sensitivity of CTC for  
18 correctly identifying subjects with at least one 6 mm polyp was 36%, with a specificity of 88%.  
19 The corresponding values for 10-mm polyps were 47% sensitivity and 95% specificity. These  
20 results suggest that the performance of virtual colonoscopy may be inadequate for the correct  
21 detection of 6 mm and 1 cm lesions in such patients.

22  
23 Comment. CTC relies on the use of state-of-the-art scanners, software analysis, and trained  
24 radiologists who are familiar with interpreting these studies. CTC requires colon preparation (like  
25 conventional colonoscopy) and the insertion of an enema tube to fill the colon with gas. Three  
26 multidisciplinary groups that create guidelines on colorectal cancer screening, the American  
27 Cancer Society, the United States Multi-Society Task Force on Colorectal Cancer, and the United  
28 States Preventive Services Task Force have recently evaluated the data on CTC and concluded  
29 that its use for colorectal cancer screening is currently inappropriate.<sup>79-81</sup>

30  
31 Routinely, its sensitivity is less than conventional colonoscopy for polyps  $\geq 10$  mm in high-risk  
32 patients and for smaller sized (ie, 6 to 9 mm) polyps. Its value and performance in average-risk  
33 populations in other health care settings is unknown, but preliminary results do not support its  
34 widespread use as a screening test. Nearly all studies to date have been intentionally biased to  
35 create a cohort with a high prevalence of disease. Studying only high-risk patients overestimates  
36 the diagnostic accuracy of a procedure.

37  
38 Sensitivities below 80% to 85% for polyps sized 5 to 9 mm, and substantially less for polyps  $< 5$   
39 mm may be unacceptable for a diagnosis-only screening strategy as expensive as CTC.<sup>82</sup> This  
40 level of performance would probably increase the frequency at which scans would be required,  
41 thereby decreasing cost-effectiveness. Interestingly, in contrast to the lung cancer screening  
42 debate, CTC finds polyps later in the growth process but is being promoted as a useful  
43 intervention. Although CTC is useful in patients who refuse to undergo colonoscopy for various  
44 reasons, and there appears to be sufficient evidence to support its use in patients following failed  
45 or incomplete colonoscopy, further evaluation in the form of multicenter trials is required before  
46 it can compete on a widespread basis as a colonic cancer screening tool. Appropriate targets for  
47 studying the diagnostic accuracy of CTC for colorectal cancer screening are asymptomatic, low-  
48 prevalence populations that represent a cross-section of the US adult population. Pending further  
49 trials, CTC should not be used for routine screening, surveillance, or diagnosis until the numerous  
50 uncertainties about its use are clarified.<sup>82</sup> The possibility that CTC may be able to be performed

1 without prior bowel preparation is a potential development that would clearly have an impact on  
2 its relative utility.

3  
4 Whole Body Scans

5  
6 As briefly discussed in the beginning of this report, there is no evidence to date to support the use  
7 of a “total body scan” as an appropriate or effective tool in the early detection or prevention of  
8 disease. Such services are not evidence-based and are not consistent with accepted guidelines for  
9 screening.

10  
11 Conclusion and Comment

12  
13 Standards for new technology include the development of published evidence where the  
14 estimation of patient outcomes must be established in sufficiently large patient samples, with the  
15 data rigorously collected and analyzed from a diverse array of patient subsets. Ethical and  
16 professional issues are evident in promoting screening techniques with no proven mortality  
17 benefit and in not fully informing patients about the uncertain benefits, risks, and potential harms  
18 of innovative screening techniques. The use of screening tests generally should be based on a  
19 physician’s order to allow for full discussion of these issues, to provide appropriate continuity of  
20 care, and to integrate primary prevention and treatment alternatives.

21  
22 As these tests proliferate, it is appropriate to question the balance among medical science, patient  
23 care, and profits. Widespread use of unproven screening tests (or other therapies) lead to spiraling  
24 costs of health care. Even if patients pay with their own funds for such screenings, there are  
25 financial consequences that affect the rest of the health care system because insurers and health  
26 plans are more likely to bear the costs of subsequent evaluations after an abnormal scan. On the  
27 other hand, an individual’s right to know his or her health status, access to health care in a free  
28 market economy, and other issues based on individual and societal value systems are noteworthy.  
29 In such an environment, the medical profession should continue to advocate the use of clinically  
30 effective and cost-effective procedures and interventions.

31  
32 RECOMMENDATIONS

33  
34 The Council on Scientific Affairs recommends that the following statements be adopted in lieu of  
35 Resolutions 508 (I-0I) and 509 (A-02) and the remainder of the report be filed:

- 36  
37 1. That relevant specialty societies continue to evaluate the validity and clinical use of screening  
38 imaging procedures that are advertised directly to the public and make available to the  
39 broader physician community unbiased evaluations to help primary care physicians advise  
40 their patients of the risks and benefits of these procedures. **(New HOD Policy)**  
41  
42 2. That our AMA urge government funding agencies to continue to fund well-designed, large-  
43 scale clinical trials aimed at determining the safety, value, and cost-effectiveness of screening  
44 imaging procedures. **(Directive to Take Action)**  
45  
46 3. That considering the summary information in this report, the Council on Ethical and Judicial  
47 Affairs further consider the ethical ramifications of commercialized medical screening.  
48 **(Directive to Take Action)**

Table. Characteristics of Follow-up Studies of EBCT<sup>a</sup> and Coronary Event in Asymptomatic Populations

<b>Study</b>	<b>No.</b>	<b>Mean Age/Sex</b>	<b>Follow-up</b>	<b>Calcium Scores</b>	<b>Baseline Risk for Hard Event</b>	<b>Number of Deaths and nonfatal MI<sup>b</sup></b>	<b>RR<sup>c</sup> for MI or Death if &gt;CAC<sup>d</sup> score</b>
Arad <sup>18</sup>	1,173	53 yrs 71% men	43 months	Median 4	Not reported	16	22.2 > 160
Raggi <sup>19</sup>	632	52 yrs 50% men	37 months	Median 3.1; 54% had CAC	10% at 10 yrs	27	7.2, > median for age/sex 3.0, >50 <sup>th</sup> percentile
Detrano <sup>20</sup>	1,196	66 yrs 89% men	41 months	Median 44	3.3% at 3 yrs	50	2.3, >50 <sup>th</sup> percentile
Wong <sup>21</sup>	926	54 yrs 79% men	24-48 months (mean 39)	Median 5	Not reported	28 <sup>c</sup>	4.5, >50 <sup>th</sup> percentile

<sup>a</sup>EBCT = electron beam computed tomography; <sup>b</sup>MI = myocardial infarction; <sup>c</sup>RR = relative risk;

<sup>d</sup>CAC = coronary artery calcification; <sup>e</sup>includes coronary revascularization procedures

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