HHS Public Access

Author manuscript

Clin Imaging. Author manuscript; available in PMC 2017 March 01.

Published in final edited form as:

Clin Imaging. 2016 ; 40(2): 307–310. doi:10.1016/j.clinimag.2015.07.002.

Role of computed tomography screening for detection of coronary artery disease

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INTRODUCTION

Cardiovascular disease (CVD) remains the most prominent cause of morbidity and mortality in western societies, accounting for approximately 17.3 million deaths per year, which is projected to rise substantially to more than 23.6 million by 2030. In the United States, the economic burden of CVD is immense, resulting in an estimated expenditure of 320.1 billion USD in 2011 alone. Of further concern is that the total direct medical costs related to CVD are forecasted to reach around $918 billion by 2030 (1).

The initial manifestation of coronary artery disease (CAD) is generally the presence of myocardial infarction or sudden cardiac death, particularly among asymptomatic individuals, thereby emphasizing the need for improved screening, prediction and treatment approaches for subclinical coronary atherosclerosis (2). To date, a potential pitfall of the classic cardiovascular risk assessment tools is their inability to identify more than 75% of asymptomatic individuals who experience future CAD events (3). Indeed, the availability of an alternative modality capable of detecting significant subclinical atherosclerosis, while additionally targeting prevention of future cardiovascular events would likely augment prognosis in asymptomatic patients at risk for suspected CAD (4).

Screening for coronary artery calcification (CAC) has emerged as a relatively inexpensive non-invasive imaging modality that is widely accessible to asymptomatic adults at risk of CAD. CAC scoring is considered a robust method for early detection of coronary heart disease (CHD), particularly in asymptomatic patients when compared with other risk factor-based paradigms, such as the FRS and the European Society of Cardiology Score (5).

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Disclosures: James K. Min serves as a consultant to HeartFlow, Abbott Vascular, NeoGraft Technologies, MyoKardia, and CardioDx. He is also on the scientific advisory board for Arineta, has a research agreement with GE Healthcare, and has ownership in MDDX and Autoplaq.

Moreover, epidemiological evidence have documented that CAC scoring represents an independent prognostic indicator of adverse cardiovascular events over and above numerous conventional risk factors (6,7).

The following review summarizes the role of CT screening for detection of CAC, by outlining the methods used in the acquisition of CAC, along with its role as an important predictor of adverse events, while also discussing the implications and future directions of CT for determining CAC in the clinical setting.

Image acquisition of CAC

In the field of atherosclerotic imaging, among others, electron beam computed tomography (EBCT) has been used in quantification of CAC; however, multi-detector computed tomography (MDCT) has emerged as the more commonly used imaging modality employed for the quantification of the amount of plaque present in the coronary arteries (8). Indeed, progressive advancements in these imaging tools have allowed researchers and clinicians to expand our understanding of the risk of CAD and its consequences. Some of the major advantages of using EBCT include a lower radiation dose along with less motion artifacts, while notable benefits of using MDCT include a reduction in noise, along with a higher spatial resolution (9), and large volume data acquisition (10).

Typically, CAC is scanned prospectively using an ECG-triggered mode with 2.5–3.0 mm axial slice thickness. EBCT utilizes a sophisticated approach that enables rapid acquisition of 100 msec scanning times in a prospective mode using 3 mm slice thickness that permits reliable measurement of calcium deposits in the coronary arteries (11,12). Some of the most commonly used 64-slice CT scanners use a rotation gantry speed of up to 330 msec (10). More contemporary MDCT scanners are capable of acquiring up to 128–320 slices of the heart, producing a higher temporal resolution. The relative abilities of EBCT and MDCT have been discussed elegantly in a recent review by Nasir and co-workers (11).

Using conventional CT scanners, CAC is defined as a hyper attenuating lesion above a threshold of 130 Hounsfield Units (HU), with an area ≥3 adjacent pixels (8). Several methods have been used to quantify calcium scores based on CT imaging. The Agatston score is the most universal metric used for CAC scoring (8). Although several CAC cut-points have been proposed, the following reference categories have generally been employed when evaluating the relationship between calcium and risk of CAC: 0 (none), 1–99 (mild), 100–400 (moderate), >400 (severe) (13). Inter-reader and intra-reader variabilities of CAC scoring are low, and approximate 3% and <1%, respectively. Inter-scan variability is roughly 15% (8). In light of certain limitations of Agatston CAC scoring (e.g., inconsistent inter-scanner comparability), other scoring approaches have been proposed, and include the calcium volume score and calcium mass score. Prior studies have demonstrated that these methods are comparable with the Agatston approach, especially in terms of reproducibility (14).

Importantly, the radiation dose administered for CAC testing is low, with an effective median radiation dose of 2.3 mSv, which is equivalent to 1.5 screening mammograms performed (15). Though the radiation exposure on the background of a traditional CT

appears low, every effort should be made to attempt to lower the margin in radiation dose even further, without mitigating the ability to assess the burden of CAC in the coronary arteries.

Role of CAC in adverse cardiovascular risk

Prior studies have reported on the robustness of cardiac CT for identifying arterial calcification, indicating a high sensitivity for detecting significant coronary obstructive disease (11). In one study, Rumberger and colleagues revealed an intimate relation between CAC measured by electron beam computed tomography (EBCT) with direct histologic plaque areas in autopsied hearts (16). However, in that investigation, not all plaques were found to be calcified. There can exist individual differences in the coronary arteries with a poor correlation between the degree of plaque calcification and extent of luminal stenosis using invasive coronary angiography (17,18). Despite this, CAC estimates using cardiac CT correlates well with total atherosclerotic burden (17).

Prior studies have indicated some drawbacks when using conventional risk factors (i.e., such as those encompassing FRS) for classifying individuals, especially those belonging to an intermediate risk group. This has led some researchers to consider more novel risk markers for the purpose of screening for cardiovascular disease. For instance, the CAC score, along with carotid intima-media thickness (CIMT), C-reactive protein (CRP), ankle-brachial index (ABI), brachial flow-mediated dilation (FMD), as well as other imaging parameters are beginning to emerge as more informative parameters for risk prediction. Moreover, several studies have assessed the usefulness of these novel risk markers for improving cardiovascular risk assessment. In the Multi-Ethnic Study of Atherosclerosis (MESA) consisting of 6,814 participants, 1,330 individuals were classified as being at intermediate-risk, defined as having a FRS between 5% and 20% (19). In that study, CAC, ABI, CRP, and family history of early CAD were all independently associated with incident CHD. Importantly, CAC provided superior discrimination and risk reclassification compared with the other markers. In the Heinz Nixdorf Recall (HNR) study, Möhlenkamp and colleagues demonstrated a strong relationship of CAC, FRS, and CRP with CAD in 3,966 patients without known CAD or acute inflammation (20). Notably, however, the improvement in risk prediction and discrimination was predominantly driven by CAC. In a recent study from the Rotterdam cohort, Kavousi et al. assessed the predictive ability of CAC along with 11 other novel biomarkers and imaging methods (21). The findings from that study highlighted that the NRI on the background of CAC was 19.3%, whereas the NRI relative to the other markers ranged from 0.4%–7.6%. The improvement in discrimination (defined as the change in C-Statistic) for CAC was 0.05, while for the other markers, the C-statistic ranged between 0.00–0.02. Notably, most of the extant literature has proposed that CAC scoring reflects a robust, independent and incremental predictor of future adverse cardiovascular events over and above other available risk markers.

CAC is a well-established surrogate of cardiovascular risk and has shown to provide incremental benefit over traditional risk tools. In a meta-analysis comprising 6 CAC studies, a higher CAC score was associated with a higher event rate and higher relative risk ratio (22). In the latter analysis, the adjusted relative risks according to CAC categories 11–100,

101–400, 401–1,000, and >1,000 were 1.9, 4.3, 7.2, and 10.8, respectively. Additionally, CAC displays a meaningful improvement in the prediction of CVD beyond traditional risk algorithms, such as FRS (23,24). In MESA, the CAC score provided improved prediction beyond that conveyed by traditional risk factors, a finding that extended to different racial and ethnic groups (25).

Given that the addition of CAC to traditional risk factors led to a significant improvement in the classification of risk, (21,26,27) further stratification by use of the CAC score may help guide treatment decision-making in clinical practice. Foremost, in a sub-study of participants enrolled in MESA who presented with similar inclusion criteria as reported in the JUPITER Trial (28), nearly half had a zero CAC score, and these individuals had a very low event rate (29). In the same study, one quarter of patients were identified as having a CAC score greater than 100, in which, most coronary heart disease events (74%) had occurred in this subset of individuals. Moreover, the number needed to treat (NNT) with statin medication in order to prevent one CHD outcome over the course of a 5-year study period was favorable at 24 (29). Similarly, of those eligible to receive aspirin treatment for the primary prevention of CVD in a sub-study from MESA, patients with ≥100 had favorable risk/benefit estimation on the background of aspirin use, while subjects with a zero CAC were more likely to experience harm from using aspirin (30). These observations underline the importance of CAC and how it may be used to stratify subgroups of patients who are expected to derive the most and least optimal benefits from receiving medical treatment. Forthcoming randomized controlled trials are needed to examine whether treatments guided by a patient's CAC status may lead to improved health and wellbeing (31).

Clinical implications

Zero CAC score

Understanding the broad spectrum of CAC scoring for the identification of patients at risk of developing CAD, while advocating clinically relevant cut-off points and their use in forthcoming studies, is of important concern. Several studies have documented the utility of a zero CAC score for the purpose of risk stratification in clinical practice. In a meta-analysis of CAC screening comprising a study sample of 71,595 asymptomatic patients, the pooled risk of experiencing a cardiovascular event in the absence of CAC relative to the presence of any CAC was 0.15 (95% CI: 0.10–0.21; $p < 0.001$) (32). Notably, the presence of minimal CAC (i.e., CAC score 1–10) has been shown to exacerbate the risk of experiencing a CHD event by 3-fold as compared with the absence of CAC (33). Likewise, the hazard ratio for all-cause mortality on the background of a CAC score 1–10 was 1.99 versus CAC = 0 even after adjustment for traditional risk factor of CVD (34). On the background of these findings, the absence of CAC likely predicts very low risk of CAD in asymptomatic adults, and may serve as a useful tool for guiding preventative treatment decision-making in clinical practice.

Usefulness of CAC in symptomatic adults

Current guidelines advocate performing CAC screening primarily in asymptomatic populations. Others have speculated that CAC may also provide incremental diagnostic and

prognostic value in symptomatic persons. Similar to asymptomatic persons, the absence of calcium in the coronary arteries was found to be associated with lower cardiovascular risk in patients presenting with chest pain. In a meta-analysis consisting of 3,924 symptomatic adults, 921 persons presented with no CAC, and of these, only 17 (1.8%) experienced an adverse cardiovascular event (32). In a separate study examining the severity of coronary stenosis among 10,037 symptomatic patients, a zero CAC score displayed a negative predictive value of 96% and 99% according to 50% and 70% coronary stenosis, respectively (35). It is therefore plausible to consider the utility of CAC screening as a potential gatekeeper for initiating more advanced and in some cases more aggressive assessment of CAD in patients deemed at-risk. At present, additional studies are needed to determine the importance of a zero CAC score as a possible gatekeeper, especially as the absence of CAC alone does not fully dismiss certain adverse outcomes such as occlusive CAD or acute coronary syndromes, which frequently occur in individuals with less than 50% coronary stenosis (36).

CT screening for simultaneous detection of CAD and lung cancer

Thoracic non-gated CT is extensively used for lung cancer screening. In 2007, approximately 13.6 million non-gated thoracic CT examinations were performed in the United States alone (37), with the number of patients fulfilling the criteria for screening by the US cancer prevention task force almost 7 million (38). Current National Comprehensive Cancer Network (NCCN) guidelines recommend annual thoracic CT scanning among older at-risk individuals, as well as those who smoke (39). Importantly, plaque in the coronary arteries is a common finding in patients undergoing screening for lung cancer by CT (40). The latter findings are somewhat unsurprising, as those recommended for lung cancer screening (i.e., generally older and/or those who smoke), are often considered to be at least intermediate risk for future cardiac events. Despite this, CT screening for CAC most often does not occur in combination with thoracic CT screening for lung cancer, and some patients may be overlooked as having CAC in the coronary arteries as these patients were referred to undergo lung cancer assessment only (41). Notably, the benefits of utilizing a one-time CT scan for determining both CAC and lung cancer include a lower overall cost while additionally reducing the radiation dose that patients will be exposed to.

If performed together, it is important to note that there are differences in the methods employed to determine CAC versus detection of lung cancer by CT. Screening for lung cancer by CT is routinely performed using a non-gated approach, administering a radiation dose typically between 0.8–0.9 mSv (42), with the heart constantly visualized. In comparison, CAC screening is performed using ECG-gated CT with a mean radiation dose between 1.0–2.9 mSv, depending on type of scanner and protocol (43,44). The latter gated CT method provides a more accurate measurement of calcium, while conceding that the lung region is not fully covered in an effort to lower the overall radiation dose required for screening. It is important to note that the estimation of CAC is influenced by motion artifact (45), and this may contribute to substantial variability between non-gated and ECG-gated CT. Despite this potential variability, CAC scores detected by non-gated CT have been shown to be well correlated with CAC scoring as determined by ECG-gated scans (46). It bears mentioning, however, that non-gated CT has previously yielded a false negative for

CAC among 8.8% of individuals, while underestimating the presence of CAC in 19.1% (46). Although additional studies are clearly needed to explore the possibility of a single CT scan to simultaneously screen for lung cancer and CAC, if confirmed, this approach would likely provide a major benefit by lowering the cost attributable to multiple CT scans while also attenuating the radiation dose administered from two separate scans.

Conclusion

CT scanning for the detection of CAC has proven to reflect a robust predictor of cardiovascular outcomes. For CAD risk estimation, CAC as detected by CT has demonstrated incremental benefit over and above traditional risk factors. In asymptomatic adults undergoing screening for CAD, the majority of these patients tend to present with a zero CAC, and the findings from these investigations propose that the absence of CAC should perhaps be considered a ‘ marker of protection’ from CAD. The role of CAC has received some attention in symptomatic patients, particularly in a low-to-intermediate risk setting, whereby CAC may act as a ‘gate keeper’ to guide further treatment decision-making. Studies have also underlined the value of CAC for the purpose of reclassifying as well as stratifying patients who are most likely to benefit from additional medical treatment, while the possibility of simultaneously screening for lung cancer and CAC may substantially lower the cost associated with multiple CT scans and diminish the radiation dose administered from two separate scans. Although the evident data suggest promise for CAC for routine clinical use for prediction of CAD, additional studies are needed to determine its cost effectiveness and ability to properly stratify treatment options for patients with suspected CAD.

Acknowledgments

Research funding: This manuscript was funded, in part, by grants from the National Heart Lung and Blood Institute (R01 HL111141, R01 HL115150 and R01 HL118019), as well as from a generous gift from the Dalio Foundation and the Michael Wolk Foundation.

REFERENCES

1. Mozaffarian D, Benjamin EJ, Go AS, et al. Heart disease and stroke statistics--2015 update: a report from the American Heart Association. Circulation. 2015; 131:e29–e322. [PubMed: 25520374]
2. Choi EK, Choi SI, Rivera JJ, et al. Coronary computed tomography angiography as a screening tool for the detection of occult coronary artery disease in asymptomatic individuals. Journal of the American College of Cardiology. 2008; 52:357–365. [PubMed: 18652943]
3. Rosamond W, Flegal K, Furie K, et al. Heart disease and stroke statistics--2008 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation. 2008; 117:e25–e146. [PubMed: 18086926]
4. Shaw LJ, Blumenthal RS, Raggi P. Screening asymptomatic low-risk individuals for coronary heart disease: issues and controversies. Journal of nuclear cardiology : official publication of the American Society of Nuclear Cardiology. 2004; 11:382–387. [PubMed: 15295406]
5. Hecht HS. Coronary artery calcium: utilization for primary prevention of CHD. Current cardiology reports. 2011; 13:465–474. [PubMed: 21892753]
6. Park R, Detrano R, Xiang M, et al. Combined use of computed tomography coronary calcium scores and C-reactive protein levels in predicting cardiovascular events in nondiabetic individuals. Circulation. 2002; 106:2073–2077. [PubMed: 12379576]

7. Roberts WC, Jones AA. Quantitation of coronary arterial narrowing at necropsy in sudden coronary death: analysis of 31 patients and comparison with 25 control subjects. The American journal of cardiology. 1979; 44:39–45. [PubMed: 88171]
8. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M Jr, Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. Journal of the American College of Cardiology. 1990; 15:827–832. [PubMed: 2407762]
9. Tseng PH, Mao S, Chow DZ, et al. Accuracy in quantification of coronary calcification with CT: a cork-dog heart phantom study. Academic radiology. 2010; 17:1249–1253. [PubMed: 20621526]
10. Nasir K, Budoff MJ, Post WS, et al. Electron beam CT versus helical CT scans for assessing coronary calcification: current utility and future directions. American heart journal. 2003; 146:969–977. [PubMed: 14660987]
11. Nasir K, Clouse M. Role of nonenhanced multidetector CT coronary artery calcium testing in asymptomatic and symptomatic individuals. Radiology. 2012; 264:637–649. [PubMed: 22919038]
12. Budoff MJ, Georgiou D, Brody A, et al. Ultrafast computed tomography as a diagnostic modality in the detection of coronary artery disease: a multicenter study. Circulation. 1996; 93:898–904. [PubMed: 8598080]
13. Rumberger JA, Brundage BH, Rader DJ, Kondos G. Electron beam computed tomographic coronary calcium scanning: a review and guidelines for use in asymptomatic persons. Mayo Clinic proceedings. 1999; 74:243–252. [PubMed: 10089993]
14. Rumberger JA, Kaufman L. A rosetta stone for coronary calcium risk stratification: agatston, volume, and mass scores in 11,490 individuals. AJR American journal of roentgenology. 2003; 181:743–748. [PubMed: 12933474]
15. Kim KP, Einstein AJ, Berrington de Gonzalez A. Coronary artery calcification screening: estimated radiation dose and cancer risk. Archives of internal medicine. 2009; 169:1188–1194. [PubMed: 19597067]
16. Rumberger JA, Simons DB, Fitzpatrick LA, Sheedy PF, Schwartz RS. Coronary artery calcium area by electron-beam computed tomography and coronary atherosclerotic plaque area. A histopathologic correlative study. Circulation. 1995; 92:2157–2162. [PubMed: 7554196]
17. Sangiorgi G, Rumberger JA, Severson A, et al. Arterial calcification and not lumen stenosis is highly correlated with atherosclerotic plaque burden in humans: a histologic study of 723 coronary artery segments using nondecalcifying methodology. Journal of the American College of Cardiology. 1998; 31:126–133. [PubMed: 9426030]
18. Rumberger JA, Sheedy PF, Breen JF, Schwartz RS. Electron beam computed tomographic coronary calcium score cutpoints and severity of associated angiographic lumen stenosis. Journal of the American College of Cardiology. 1997; 29:1542–1548. [PubMed: 9180117]
19. Yeboah J, McClelland RL, Polonsky TS, et al. Comparison of novel risk markers for improvement in cardiovascular risk assessment in intermediate-risk individuals. Jama. 2012; 308:788–795. [PubMed: 22910756]
20. Mohlenkamp S, Lehmann N, Moebus S, et al. Quantification of coronary atherosclerosis and inflammation to predict coronary events and all-cause mortality. Journal of the American College of Cardiology. 2011; 57:1455–1464. [PubMed: 21435514]
21. Kavousi M, Elias-Smale S, Rutten JH, et al. Evaluation of newer risk markers for coronary heart disease risk classification: a cohort study. Annals of internal medicine. 2012; 156:438–444. [PubMed: 22431676]
22. Greenland P, Smith SC Jr, Grundy SM. Improving coronary heart disease risk assessment in asymptomatic people: role of traditional risk factors and noninvasive cardiovascular tests. Circulation. 2001; 104:1863–1867. [PubMed: 11591627]
23. Greenland P, LaBree L, Azen SP, Doherty TM, Detrano RC. Coronary artery calcium score combined with Framingham score for risk prediction in asymptomatic individuals. Jama. 2004; 291:210–215. [PubMed: 14722147]
24. Taylor AJ, Bindeman J, Feuerstein I, Cao F, Brazaitis M, O'Malley PG. Coronary calcium independently predicts incident premature coronary heart disease over measured cardiovascular risk factors: mean three-year outcomes in the Prospective Army Coronary Calcium (PACC) project. Journal of the American College of Cardiology. 2005; 46:807–814. [PubMed: 16139129]

25. Detrano R, Guerci AD, Carr JJ, et al. Coronary calcium as a predictor of coronary events in four racial or ethnic groups. The New England journal of medicine. 2008; 358:1336–1345. [PubMed: 18367736]
26. Polonsky TS, McClelland RL, Jorgensen NW, et al. Coronary artery calcium score and risk classification for coronary heart disease prediction. Jama. 2010; 303:1610–1616. [PubMed: 20424251]
27. Rana JS, Gransar H, Wong ND, et al. Comparative value of coronary artery calcium and multiple blood biomarkers for prognostication of cardiovascular events. The American journal of cardiology. 2012; 109:1449–1453. [PubMed: 22425333]
28. Ridker PM, Danielson E, Fonseca FA, et al. Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein. The New England journal of medicine. 2008; 359:2195–2207. [PubMed: 18997196]
29. Blaha MJ, Budoff MJ, DeFilippis AP, et al. Associations between C-reactive protein, coronary artery calcium, and cardiovascular events: implications for the JUPITER population from MESA, a population-based cohort study. Lancet. 2011; 378:684–692. [PubMed: 21856482]
30. Miedema MD, Duprez DA, Misialek JR, et al. Use of coronary artery calcium testing to guide aspirin utilization for primary prevention: estimates from the multi-ethnic study of atherosclerosis. Circulation Cardiovascular quality and outcomes. 2014; 7:453–460. [PubMed: 24803472]
31. Ambrosius WT, Polonsky TS, Greenland P, et al. Design of the value of imaging in enhancing the wellness of your heart (VIEW) trial and the impact of uncertainty on power. Clinical trials (London, England). 2012; 9:232–246.
32. Sarwar A, Shaw LJ, Shapiro MD, et al. Diagnostic and prognostic value of absence of coronary artery calcification. JACC Cardiovascular imaging. 2009; 2:675–688. [PubMed: 19520336]
33. Budoff MJ, McClelland RL, Nasir K, et al. Cardiovascular events with absent or minimal coronary calcification: the Multi-Ethnic Study of Atherosclerosis (MESA). American heart journal. 2009; 158:554–561. [PubMed: 19781414]
34. Blaha M, Budoff MJ, Shaw LJ, et al. Absence of coronary artery calcification and all-cause mortality. JACC Cardiovascular imaging. 2009; 2:692–700. [PubMed: 19520338]
35. Villines TC, Hulten EA, Shaw LJ, et al. Prevalence and severity of coronary artery disease and adverse events among symptomatic patients with coronary artery calcification scores of zero undergoing coronary computed tomography angiography: results from the CONFIRM (Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter) registry. Journal of the American College of Cardiology. 2011; 58:2533–2540. [PubMed: 22079127]
36. Stone GW, Maehara A, Lansky AJ, et al. A prospective natural-history study of coronary atherosclerosis. The New England journal of medicine. 2011; 364:226–235. [PubMed: 21247313]
37. Berrington de Gonzalez A, Mahesh M, Kim KP, et al. Projected cancer risks from computed tomographic scans performed in the United States in 2007. Archives of internal medicine. 2009; 169:2071–2077. [PubMed: 20008689]
38. Polonsky TS, Greenland P. Coronary artery calcium scores using nongated computed tomography: what to do with incidental results? Circulation Cardiovascular imaging. 2013; 6:494–495. [PubMed: 23861448]
39. Network NCC. NCCN clinical practice guidelines in oncology. lung cancer screening. 2013 Version 1.
40. Jacobs PC, Gondrie MJ, van der Graaf Y, et al. Coronary artery calcium can predict all-cause mortality and cardiovascular events on low-dose CT screening for lung cancer. AJR American journal of roentgenology. 2012; 198:505–511. [PubMed: 22357989]
41. Hecht HS, Henschke C, Yankelevitz D, Fuster V, Narula J. Combined detection of coronary artery disease and lung cancer. European heart journal. 2014; 35:2792–2796. [PubMed: 25112665]
42. van Klaveren RJ, Oudkerk M, Prokop M, et al. Management of lung nodules detected by volume CT scanning. The New England journal of medicine. 2009; 361:2221–2229. [PubMed: 19955524]
43. Dey D, Nakazato R, Pimentel R, et al. Low radiation coronary calcium scoring by dual-source CT with tube current optimization based on patient body size. Journal of cardiovascular computed tomography. 2012; 6:113–120. [PubMed: 22381663]

44. Wu MT, Yang P, Huang YL, et al. Coronary arterial calcification on low-dose ungated MDCT for lung cancer screening: concordance study with dedicated cardiac CT. AJR American journal of roentgenology. 2008; 190:923–928. [PubMed: 18356438]

45. Greuter MJ, Groen JM, Nicolai LJ, Dijkstra H, Oudkerk M. A model for quantitative correction of coronary calcium scores on multidetector, dual source, and electron beam computed tomography for influences of linear motion, calcification density, and temporal resolution: a cardiac phantom study. Medical physics. 2009; 36:5079–5088. [PubMed: 19994518]

46. Xie X, Zhao Y, de Bock GH, et al. Validation and prognosis of coronary artery calcium scoring in nontriggered thoracic computed tomography: systematic review and meta-analysis. Circulation Cardiovascular imaging. 2013; 6:514–521. [PubMed: 23756678]