The role of standard non-ECG gated chest CT in cardiac assessment: design and rationale of the Cardiac Pathologies in standard chest CT (CaPaCT) study

Nienke G. Eijsvoogel 1,2*, Babs M. F. Hendriks 1,2†, Hugo B. Park 3, Sibel Altintas 2,4, Casper Mihl 1,2, Barbora Horehledova 1,2, Bastiaan L. J. H. Kietselaer 1,2,4, Harry J. G. M. Crijns 2,4, Joachim E. Wildberger 1,2 and Marco Das 1,2,5

Abstract
Modern high-performance computed tomography (CT) scanners with improved scan acquisition times now allow for routine assessment of cardiac pathologies on chest CTs, which can result in numerous incidental cardiac findings. The CaPaCT study, an observer blinded, single-centre study, aims to assess the visibility, management and possible clinical impact of incidental cardiac pathologies that are now becoming visible on standard chest CTs. A total of 217 consecutive patients referred for a chest CT on a high-performance third-generation dual-source CT scanner will be included. Tube voltage settings will be chosen via automated kV selection. Dedicated cardiac reconstructions will be added to the standard post-processing: 0.6-mm slice thickness, 0.4-mm increment and Bv36 kernel (iterative reconstruction/weight 3). Primary endpoints will be the presence and extent of coronary artery disease (CAD) assessed via a 17-segment model. These data will be collected and analysed by two experienced, blinded cardiac radiologists. Furthermore, information on aortic and mitral valve morphology/calcification and pericardial abnormalities will be collected. The CAD Reporting and Data System classification will subsequently be used to assess the management and possible clinical burden of any incidentally detected CAD. Additionally, objective and subjective image quality (attenuation, contrast-to-noise, signal-to-noise and 5-point Likert scale) of the obtained cardiac reconstructions will be assessed.

Keywords: Cardiac diseases, Computed tomography, Coronary artery disease, Incidental findings, Thorax

Key points
- Technical developments facilitate cardiac assessment on chest computed tomography (CT)
- Cardiac assessment on chest CT results in numerous incidental cardiac findings

© The Author(s). 2018 Open Access This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.
examination protocols, these technical improvements enable detailed cardiac assessment on routine standard (not electrocardiographically triggered) chest CTs [1]. Now that it is becoming viable for thoracic radiologists to assess the heart and coronary arteries on a standard chest CT, the result could be an extensive increase of incidental cardiac findings. Herein lies the potential for large-scale reporting of incidental cardiac findings and, consequently, a huge influx of new ‘patients’ for downstream testing and potential overtreatment.

Previous research investigated the prevalence of incidental cardiac findings on chest CTs. In these studies, more than half (52–66%) of all chest CTs showed at least one incidental finding. The most frequent incidental cardiac finding was coronary artery disease (CAD), with a large number of unreported (incidental) CAD (51–80%) [2, 3]. Considering that these numbers were found on scanners equipped with outdated technology (from 4- to 64-slice scanners), the rate of incidental findings on the newest high-end scanners may be even higher. The proportion of assessable coronary arteries on chest CTs will foreseeably follow the same path, since CT techniques and image quality will continue to improve. In a few years, it is likely that current state-of-the-art scanner technology will become available on a broader scale, meaning that more medical centres could report incidental cardiac findings based on standard chest CTs. In 2006, approximately 12 million chest CT examinations were performed in the USA [4, 5]. Since then, the use of CT has continued to increase. The clinical impact of the increased patient inflow into cardiologists’ daily practice would be immense. However, despite the increasing demand, clinical studies reviewing the possible impact of these cardiac findings on patient care and on daily clinical practice are currently lacking.

Recently, a reporting and data system for CAD on CT scans was developed [6]. This new CAD-Reporting And Data System (CAD-RADS) provides a guideline on the management of patients with different CAD severities, added to which, different scoring systems have been developed to help identify patients at risk of cardiovascular events [7–9]. These, together with the CAD-RADS, could be used to assess the severity of incidental cardiac findings and determine how best to manage the care of these patients.

We can no longer overlook the heart and coronary arteries on routine chest CT. Analysis of routine chest CTs should include careful assessment of all depicted thoracic organs. Previously, a comparable imaging issue with specific and unspecific lung nodules on cardiac CT angiography led to the development of guidelines for clinical management in daily routine [10]. The Cardiac Pathologies on standard chest CT (CaPaCT) study has been devised to evaluate the visibility and management of incidental cardiac pathologies on an ultra-high pitch chest CT, with the help of CAD-RADS classification. The role and methods of the CaPaCT study are described here.

Methods

Study design and patient population

The CaPaCT study (NCT02904239) is an observer blinded, single-centre study to assess the visibility, management and possible clinical impact of CAD on standard chest CT scans, using the CAD-RADS classification. The study design was approved by the local ethical committee and institutional review board and complies with the ethical guidelines of the 1975 Declaration of Helsinki. A waiver of written informed consent was obtained from the local ethical committee.

All patients referred for a standard contrast-enhanced not electrocardiographically triggered chest CT are eligible for inclusion. Exclusion criteria consist of the standard exclusion criteria for CT scanning in the radiology department of the Maastricht University Medical Centre (MUCMC), namely pregnancy, renal insufficiency (defined as glomerular filtration rate < 30 ml/min), patients with previous severe adverse reaction to contrast material (CM), i.e. hypointensive shock, respiratory arrest and/or convulsions [11], and age below 18 years (Table 1). Electronic patient dossiers will be checked to see whether patients object to the use of their medical data in medical research.

Sample size calculation

Previous studies have shown that a prevalence of CAD on CT scans in asymptomatic patients increases greatly with age. Prevalence of any calcifications in asymptomatic patients varies from 44% to 54% [12, 13] ; however, no distinction is made between minimal, moderate or severe CAD. Kelkar et al. [12] reported a prevalence of moderate to severe CAD of 17% in a population of 2363 asymptomatic patients with a low-intermediate Framingham risk score. This prevalence of 17% was used for the sample size calculation, as it includes the

Table 1 Inclusion and exclusion criteria for the CaPaCT study

| Inclusion criteria                                      | Exclusion criteria              |
|--------------------------------------------------------|--------------------------------|
| Scheduled for a standard non-ECG gated ultra-high pitch thoracic CT scan | Pregnancy                      |
| ≥ 18 years old                                         | Renal insufficiency (GFR < 30 ml/min) |
| Objection to the use of medical data stated in the EPD | Severe adverse reaction to CM < 18 years old |

CM contrast media, ECG electrocardiogram, GFR glomerular filtration rate, EPD electronic patient dossier
clinically relevant CAD, which requires downstream testing and/or treatment. Given a 95% confidence interval (12–22%), a total of 217 patients and scans are needed to reach a 17% prevalence of moderate to severe CAD in our population.

**Study endpoints**

The primary endpoints of the CaPaCT study are the prevalence and severity of incidental CAD on standard chest CTs. Presence of CAD is defined as the presence of calcified or soft plaques with luminal narrowing in the coronary arteries. Management of patients with CAD will be assessed with help of the CAD-RADS classification (see below evaluation of pathologies). Furthermore, information on other cardiac pathologies will be collected (see below data analysis). Considering that technical advancements are an essential part of the increasing CAD detectability on chest CT scans, secondary endpoints will include the subjective and objective image quality of utilised standard chest CTs, in combination with radiation dose and administered contrast material volume. Thirdly, this study will investigate the magnitude and effect of this newly diagnosed, mostly asymptomatic group of patients on clinical practice.

**CT protocol**

All scans will be performed on a high-end third-generation dual-source CT scanner (Somatom Force, Siemens Healthineers, Forchheim, Germany). The scans will be standard, not electrocardiographically gated, ultra-high pitch chest CT acquisitions. A \( 2 \times 192 \times 0.6 \text{ mm} \) slice collimation and gantry rotation time of 0.25 s will be used. A dynamically adapted pitch value of 2.65 to 3.00 will be used to increase the scan field of view where needed (354–391 mm). The tube voltage will be set by automated tube voltage selection software (automated tube voltage selection, CAREkV, Siemens Healthineers), with a quality reference tube voltage of 110 kV\text{qual.ref} and reference tube current of 40 mA\text{qual.ref} (CareDose 4D\textsuperscript{TM}, Siemens Healthineers). Scan delay will be determined with the bolus tracking technique, wherein a circular region of interest will be placed in the ascending aorta; a threshold of 50 Hounsfield units and an additional delay of 6 s (table movement and breath hold command) will be used to start scanning.

A dedicated cardiac reconstruction will be added to the standard (thoracic) post-processing workflow, namely images will be reconstructed with a 0.6 mm slice thickness, an increment of 0.4 mm and a Bv36 kernel (Advanced Modelled Iterative Reconstruction, ADMIRE, strength 3). Dose monitoring software (Radimetrics Enterprise Platform; Bayer Healthcare, Berlin, Germany) will be used to record all dose-related parameters (e.g. mAs\textsubscript{eff}, CT dose index volume, dose-length product and mSv).

**Contrast injection protocol**

All patients will receive pre-warmed (37 °C, 99 °F) iodinated contrast material (Ultravist; 300 mg I/ml, Bayer Healthcare, Berlin, Germany), administered automatically using a dual-head CT power injector (Stellant, Bayer). The CM injection protocols will be adapted by varying the iodine delivery rate according to the kV setting chosen by ATVS (Table 2). Eighteen, 20 or 22 gauge needles will be inserted in the antecubital vein. CM monitoring software (Certegra\textsuperscript{TM} Informatics Solution, Bayer) will be used to record all relevant CM injection parameters (e.g. volume, flow rate, peak flow rate, peak pressure and total iodine load) for each patient.

**Data analysis**

All CT images will be anonymised before analysis. The images will be assessed using axial slices and multiplanar reconstruction with dedicated software (Syngo.Via\textsuperscript{™}, Siemens). Centrelines will be drawn by an experienced researcher in the coronary arteries, including the right coronary artery, left main, left anterior descending artery and circumflex artery, prior to pathology assessment. Two independent, experienced cardiac radiologists will read the images, blinded to one another’s results as well as patient characteristics. Information about CAD, aortic valve morphology, aortic valve calcifications, mitral valve calcifications and pericardial abnormalities (e.g. effusion or calcifications) will be collected and analysed. The CAD severity will be assessed according to a modified 17-segment model from the American Heart Association [14]. Plaques shall be categorised according to the CAD-RADS classification [6]. Electronic patient dossiers (SAP 7.3, SAP SE, Walldorf, Germany) will be consulted to see whether or not these findings are previously mentioned in the patient’s history or on prior chest CTs.

Objective image quality will be assessed by intravascular attenuation (Hounsfield units), contrast-to-noise ratio and signal-to-noise ratio. Image noise will be defined as the

**Table 2 Contrast injection protocols for different kV settings as chosen by CAREkV**

| Parameter                          | 120 kV | 110 kV | 100 kV | 90 kV | 80 kV | 70 kV |
|------------------------------------|--------|--------|--------|-------|-------|-------|
| Main bolus 100% CM, ml              | 44     | 40     | 36     | 33    | 30    | 27    |
| Mixed bolus (50% CM/50% NaI), ml    | 36     | 33     | 30     | 27    | 25    | 22    |
| Saline flush, ml                   | 20     | 20     | 20     | 20    | 20    | 20    |
| Flowrate, ml/s                     | 5.1    | 4.7    | 4.2    | 3.9   | 3.5   | 3.2   |
| Iodine delivery rate, ml/g/s        | 1.5    | 1.4    | 1.3    | 1.2   | 1.1   | 0.9   |

CM contrast material, kV tube voltage
standard deviation of the vessel attenuation. Contrast-to-noise ratio will be stated as intravascular attenuation minus epicardial fat attenuation, divided by the standard deviation of the epicardial fat attenuation. Signal-to-noise ratio will be stated as intravascular attenuation divided by the standard deviation of the intravascular attenuation [15–17]. Intravascular and epicardial fat attenuation will be measured via circular regions of interests in the vessels and epicardial fat, carefully avoiding vessel walls and atherosclerotic plaques. Subjective image quality in terms of motion artefacts will be evaluated using a 5-point Likert scale (5 = excellent, no motion artefacts; 4 = good, minor motion artefacts; 3 = sufficient, moderate motion artefacts; 2 = moderate, significant motion artefacts but diagnostic; 1 = non-diagnostic due to motion artefacts).

Statistical analysis
Continuous variables will be stated as mean and standard deviation. Categorical variables will be compared by using a \( \chi^2 \) test and stated as percentages. A linearly weighted \( \kappa \) will be calculated for the interobserver agreement on the assessment of CAD and motion artefacts. The image quality of the scans with optimised contrast injection protocols will be assessed. Continuous variables of different kV groups will be compared using one-way analysis of variance. In case the data is not normally distributed, non-parametric tests will be used to compare the means of different kV groups. All \( p \) values will be two-sided and a \( p \) value lower than 0.05 will be considered statistically significant.

Discussion
The importance and clinical impact of assessment of the heart and coronary arteries is becoming clearer with the help of current evidence; cardiovascular disease is the leading cause of death worldwide and CAD accounts for up to 20% of all deaths in Europe annually [18]. The need for detection of CAD in patients with diabetes mellitus or undergoing non-cardiac surgery and in cancer treatment decision-making has been demonstrated [19–25]. The purpose for a contrast-enhanced chest CT is often associated with cancer screening or follow-up. Thus, knowledge of the presence and extent of CAD in these patients is required for optimal treatment.

Other studies that assess patients at risk for future cardiovascular events with help of incidental cardiac findings on chest CT have been conducted. Jairam et al. [8] developed a risk score calculator to evaluate patients at high risk for a cardiovascular event. In contrast to the 64-slice multidetector CT used for that study, the CaPaCT study will use a modern third-generation dual-source CT scanner. Further, these studies did not assess the medical management or clinical impact of these additional patients. Moreover, none of these studies implemented a cardiac reconstruction and coronary centrelines in their scan protocol and no studies used the newly developed CAD-RADS classification. The CaPaCT study will assess the occurrence of incidental CAD in patients undergoing chest CT and how radiologist should report on this. It is hoped that the CaPaCT study will provide insight into the magnitude of this inevitable escalation of possibly asymptomatic cardiovascular patients.

Abbreviations
CAD: coronary artery disease; CAD-RADS: Coronary Artery Disease Reporting and Data System; CaPaCT: Cardiac Pathologies on standard chest CT; CM: Contrast material; CT: computed tomography

Funding
The authors state that this work has not received any funding.

Availability of data and materials
Not applicable.

Guarantor
The scientific guarantor of this publication is Dr Marco Das.

Authors’ contributions
NE and BHE carried out the data inclusion, data analysis, drafting of the manuscript and reviewing. HP participated in reviewing of the manuscript. SA, CM and BHO participated in the data analysis and reviewing of the manuscript. BK and HC also participated in the reviewing of the manuscript. JW participated in the drafting and reviewing of the manuscript. Lastly, MD participated in the data inclusion, data analysis, manuscript drafting and reviewing. All authors read and approved the final manuscript.

Ethics approval and consent to participate
Written informed consent was waived by the local ethical committee (medical ethical committee Academisch ziekenhuis Maastricht/Universiteit Maastricht). Institutional Review Board approval was obtained.

Consent for publication
Not applicable.

Competing interests
The authors of this manuscript declare relationships with the following companies: Siemens, Bayer, Philips, AGFA, Cook, General Electric, Bracco.

Publisher’s Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Author details
1Department of Radiology and Nuclear Medicine, Maastricht University Medical Centre, P. Debyelaan 25, PO Box 5800, 6202, AZ, Maastricht, The Netherlands. 2CARIM School for Cardiovascular Diseases, Maastricht University Medical Centre, Maastricht, The Netherlands. 3Biomedical Sciences, Faculty of Health, Medicine and Life Sciences, Maastricht University, Maastricht, The Netherlands. 4Department of Cardiology, Maastricht University Medical Centre, P. Debyelaan 25, PO Box 5800, 6202, AZ, Maastricht, The Netherlands. 5Department of Interventional and Diagnostic Radiology, Helios Kliniken Duisburg, Duisburg, Germany.

Received: 14 December 2017 Accepted: 1 February 2018
Published online: 27 April 2018

References
1. Sandfort V, Ahlman MA, Jones EC et al (2016) High pitch third generation dual-source CT: Coronary and cardiac visualization on routine chest CT. J Cardiovasc Comput Tomogr 10:282–288
2. Secchi F, Di Leo G, Zanardo M, Ali M, Cannaio PM, Sardanelli F (2017) Detection of incidental cardiac findings in noncardiac chest computed tomography. Medicine (Baltimore) 96:e7531
3. Sverzellati N, Arcadi T, Salvolini L et al (2016) Under-reporting of cardiovascular findings on chest CT. Radiol Med 121:190–199
4. Sarma A, Heilbrun ME, Conner KE, Stevens SM, Woller SC, Elliott CG (2012) Radiation and chest CT scan examinations: what do we know? Chest 142:750–760
5. Smith-Bindman R, Miglioretti DL, Larson EB (2008) Rising use of diagnostic medical imaging in a large integrated health system. Health Aff (Millwood) 27:1491–1502
6. Cury RC, Abbara S, Achenbach S et al (2016) CAD-RADS(TM) Coronary Artery Disease - Reporting and Data System. An expert consensus document of the Society of Cardiovascular Computed Tomography (SCCT), the American College of Radiology (ACR) and the North American Society for Cardiovascular Imaging (NASCI). Endorsed by the American College of Cardiology. J Cardiovasc Comput Tomogr 10:269–281
7. Jairam PM, de Jong PA, Mali WP et al (2014) Age and sex based reference values for incidental coronary artery and thoracic aorta calcifications on routine clinical chest CT: a powerful tool to appreciate available imaging findings. Atherosclerosis 235:546–553
8. Jairam PM, Gondrie MJ, Grobbee DE et al (2014) Incidental imaging findings from routine chest CT used to identify subjects at high risk of future cardiovascular events. Radiology 272:700–708
9. Jacobs PC, Prokop M, Oen AL, van der Graaf Y, Grobbee DE, Mali WP (2010) Semiquantitative assessment of cardiovascular disease markers in multislice computed tomography of the chest: interobserver and intraobserver agreements. J Comput Assist Tomogr 34:279–284
10. Hanell DM, Bankier AA, MacMahon H, McDoulic TC, Müller NL, Remy J (2008) Fleischner Society: glossary of terms for thoracic imaging. Radiology 246:697–722
11. Thomsen HS (2006) European Society of Urogenital Radiology (ESUR) guidelines on the safe use of iodinated contrast media. Eur J Radiol 60:307–313
12. Kok M, de Haan MW, Mihl C et al (2016) Individualized CT angiography protocols for the evaluation of the aorta: a feasibility study. J Vasc Interv Radiol 27:531–538
13. Wong ND, Kouwabunpat D, Vo AN et al (1994) Coronary calcium and atherosclerosis by ultrafast computed tomography in asymptomatic men and women: relation to age and risk factors. Am Heart J 127:422–430
14. Austen WG, Edwards JE, Frye RL et al (1975) A reporting system on patients evaluated for coronary artery disease. Report of the Ad Hoc Committee for Grading of Coronary Artery Disease. Council on Cardiovascular Surgery, American Heart Association. Circulation 51:5–40
15. Leipsic J, Labounty TM, Heilbron B et al (2010) Adaptive statistical iterative reconstruction: assessment of image noise and image quality in coronary CT angiography. AJR Am J Roentgenol 195:649–654
16. Kok M, de Haan MW, Mihl C et al (2016) Optimizing contrast media application in coronary CT angiography at lower tube voltage: Evaluation in a circulation phantom and sixty patients. Eur J Radiol 85:1068–1074
17. Nichols M, Townsend N, Scarborough P, Rayner M (2014) Cardiovascular disease in Europe 2014: epidemiological update. Eur Heart J 35:2950–2959
18. Auerbach A, Goldman L (2006) Assessing and reducing the cardiac risk of noncardiac surgery. Circulation 113:1361–1376
19. Fleisher LA, Beckman JA, Brown KA et al (2008) ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Writing Committee to Revise the 2002 Guidelines on Perioperative Cardiovascular Evaluation for Noncardiac Surgery). Anesth Analg 106:685–712
20. Ivanovic J, Maziak DE, Ramzan S et al (2014) Incidence, severity and perioperative risk factors for atrial fibrillation following pulmonary resection. Interact Cardiovasc Thorac Surg 18:340–346
21. Mansour Z, Kochetkova EA, Santelmo N et al (2009) Risk factors for early mortality and morbidity after pneumonectomy: a reappraisal. Ann Thorac Surg 88:1737–1743
22. Aktas MK, Ozduran V, Pothish CE, Lang R, Lauer MS (2004) Global risk scores and exercise testing for predicting all-cause mortality in a preventive medicine program. JAMA 292:1462–1468
23. Kannel WB, McGee DL (1979) Diabetes and cardiovascular disease. The Framingham Study. JAMA 241:2035–2038
24. Yeh ET (2006) Cardiotoxicity induced by chemotherapy and antibody therapy. Annu Rev Med 57:485–498