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ORIGINAL ARTICLE

# Computer-aided simple triage (CAST) for coronary CT angiography (CCTA)

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**Abstract** *Purpose* Following a recent introduction of computer-aided simple triage (CAST) as a new subclass of computer-aided detection/diagnosis (CAD), we present a CAST software system for a fully automatic initial interpretation of coronary CT angiography (CCTA). We show how the system design and diagnostic performance make it CAST-compliant and suitable for chest pain patient triage in emergency room (ER).
*Methods* The processing performed by the system consists of three major steps: segmentation of coronary artery tree, labeling of major coronary arteries, and detection of significant stenotic lesions (causing $>$ 50 % stenosis). In addition, the system performs an automatic image quality assessment to discards low-quality studies. For multiphase studies, the system automatically chooses the best phase for each coronary artery. Clinical evaluation results were collected in 14 independent trials that included more than 2000 CCTA studies. Automatic diagnosis results were compared with human interpretation of the CCTA and to cath lab results.
*Results* The presented system performs a fully automatic initial interpretation of CCTA without any human interaction and detects studies with significant coronary artery disease. The system demonstrated higher than 90 % per patient sensitivity and 40–70 % per patient specificity. For the chest pain, ER population, the specificity was 60–70 %, yielding higher than 98 % NPV.
*Conclusions* The diagnostic performance of the presented CCTA CAD system meets the CAST requirements, thus enabling efficient, 24/7 utilization of CCTA for chest pain patient triage in ER. This is the first fully operational, clinically validated, CAST-compliant CAD system for a fully automatic analysis of CCTA and detection of significant stenosis.

**Keywords** Computer-aided detection/diagnosis · Computer-aided simple triage · Emergency diagnostic imaging · Coronary CTA

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## Introduction

Recently, a new class of computer-aided diagnosis (CAD) has been introduced—computer-aided simple triage (CAST) [1]. In this study, we discuss how the CAST paradigm can be applied to the computer-aided analysis of coronary CT angiography (CCTA). We start from a brief review of the CAST concept. We then discuss how the CCTA can be used for the triage of chest pain patients in emergency room (ER) and point at obstacles preventing its wider utilization. Then, we present a CAST system for a fully automatic analysis of CCTA and detection of significant coronary artery disease. A brief description of major system components is provided. Finally, we present a summary of clinical evaluation trials performed on the system. We show how the system characteristics make it CAST-compliant and discuss typical use case scenarios

The main contribution of this work is a report about the first fully operational and clinically validated CAST-compliant medical CAD system. To the best of our knowledge, it

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is the first radiology CAD system able to perform a fully automatic initial classification of studies into positive and negative categories, with the diagnostic performance good enough to be used for patient triage in ER.

## Computer-aided simple triage (CAST)

CAST is a subclass of CAD aimed to provide a fully automatic initial interpretation of a study—a "wet read." For an in-depth discussion of CAST properties, use case scenarios, clinical benefits, as well as comparison with traditional CAD, we refer the reader to [1]. Here, we only briefly summarize the most important CAST features.

Unlike most existing CAD systems designed to detect malignant lesions, CAST systems deal primarily with acute, life-threatening conditions, when a prompt diagnosis is time critical. Large portion of the diagnostic imaging tests analyzed by CAST are performed while the patient is still in the ER. Those examinations are usually performed on low to mid risk patients to rule out the disease, rather than detect it. Therefore, the expected prevalence of the disease is low. In addition to, and beyond the traditional "second reader" role, CAST should perform an automatic study triage indicating the presence or absence of the disease.

Since most of the CAST-targeted studies are expected to be negative and disease rule out is one of the major goals, the specificity of CAST is much more important than in the "second reader" scenario. The average of one or more false alarms per study, tolerable for a traditional CAD, is not acceptable here, as almost every study would be reported as positive.

As CAST operates in a fully autonomous mode, it should be able to deal with any kind of input including poor quality studies, anatomical anomalies, artifacts, and other phenomena inhibiting a reliable diagnosis. If no confident result can be achieved, the system should gracefully fail, preferably by reporting the reason.

## Coronary CTA (CCTA) for chest pain patients

The use of CCTA for chest pain patients triage in ER has been advocated by numerous research groups. A large body of work has been published showing high CCTA diagnostic accuracy [2], proving its prognostic value in chest pain patients [3] and demonstrating its cost-effectiveness [4]. Current ACC/AHA guidelines [5,6] recommend using CCTA for patients with acute chest pain and low to intermediate risk profile for acute coronary syndrome (ACS), to exclude significant coronary artery stenosis. CCTA is especially good for this task due its very high negative predictive value (NPV). Therefore, the expected prevalence of the disease in the target population is low, which fits well with the CAST requirements.

Despite CCTA's proven potential as an effective diagnostic modality, there are several challenges associated with its use which have slowed its adoption and led to under-utilization.

Image quality of CCTA study is influenced both by patient's condition—heart rate, arrhythmia, breath hold, body mass, and by preparation and scanning protocols—beta-blockers, blood vessel dilators, contrast media injection, etc. It becomes even more complicated since more than one data set is usually available for a given study, as the heart can be reconstructed in different cardiac phases.

The interpretation time can vary accordingly from 1–2 min for a simple study to 40–60 min for complex studies. In the latter case, special reformatting and visualization techniques are usually applied to extract and present the data, and the information is combined from different cardiac phases. The required skills and experience level may also depend on image complexity. Beginners can cope well with good quality studies, while low SNR, artifact rich images of heavily calcified coronaries could be a tough riddle even for an expert.

As a result, an average hospital has only a few people certified to read CCTA, and even less experts. Those are radiologists or cardiologists overwhelmed with other daily tasks, who, in general, may not be immediately available to read an emergent CCTA study. The situation is even worse during off hours, nights, and weekends, when there might be no CCTA readers at the facility. This may result in a significant delay in diagnosis in some facilities, while in others the CCTA is not performed during those hours and patients are treated differently.

## CAST for CCTA

The system we present here analyzes CCTA study data and detects significant (causing more than 50 % stenosis) lesions in coronary arteries. Unlike many other cardiac software packages assisting physician in interpretation by reformatting and visualizing the imaging data and providing sophisticated measurement tools, our system performs a fully automatic analysis and yields a preliminary report indicating the presence or absence of significant coronary artery disease.

The system we present here is very large and complex. Some of the used methods are quite simple and straightforward (yet providing the required performance), while others are novel and sophisticated and exhibit excellent performance as stand-alone units. Due to the format limitations of this publication, we cannot provide detailed description of used algorithms, discuss the performance of every component, and get into the comparative analysis with prior art. Therefore, we do not claim superiority of individual system components over published "state of the art" methods and algorithms. Only the overall system performance is compared with a competing solution. In what follows, we briefly

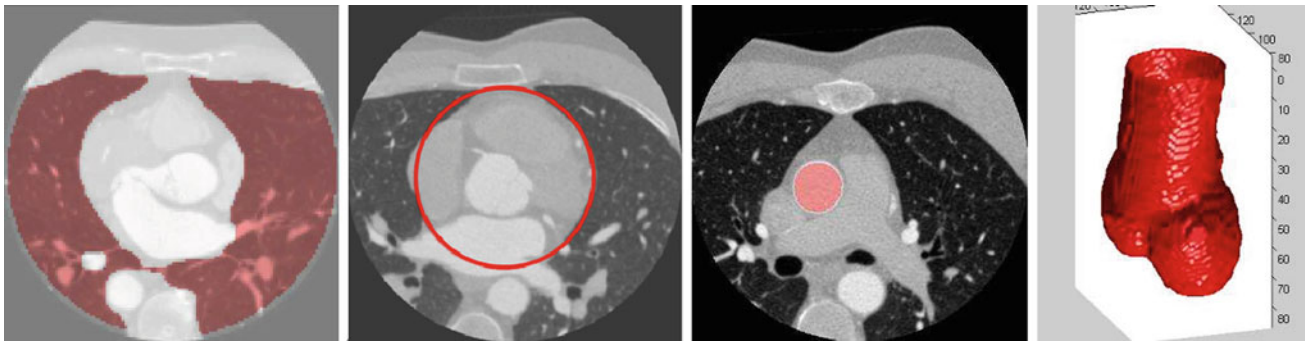

**Fig. 1** Lungs, mediastinum and aorta detection and segmentation

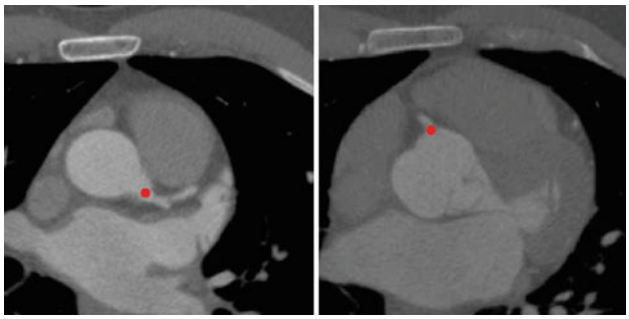

**Fig. 2** Coronary tree ostia localization (*left* and *right* ostia are marked with *red dot*)

overview major system components and mention the prior art wherever applicable.

## Fully automatic CCTA interpretation

The processing performed by the system can be coarsely divided into three major steps: segmentation of coronary artery tree, labeling of major coronary arteries, and detection of stenotic lesions.

### Coronary artery tree segmentation

The processing starts with the identification of major chest anatomical structures—lungs, mediastinum, and aorta (see Fig. 1). Lungs are detected as large air-filled areas and segmented using thresholding followed by a series of morphological filters. A set of heuristics is applied to distinguish between the connected air components inside the patient body and outside. Mediastinum is detected as the area surrounded by lungs and the ascending aorta is identified by looking for typical circular cross-sections in axial slices using circular Hough transform [7,8]. The aorta is then segmented using a 3D active surface minimization [9].

The system proceeds with the localization of coronary tree ostia (see Fig. 2) by following contrast filled areas connected to the aorta. A similar approach using front propagation from the aorta surface is reported in [10].

Vessel enhancing filter is applied to the mediastinum volume image [11]. Voxels with high filter response are combined into connected tubular components. The whole coronary tree is built by tracking tubular components using the depth-first-search (DFS) approach [12] while joining geometrically compatible segments. The resulting coronary tree is pruned to get rid of various erroneously connected structures, for example, coronary veins, pulmonary vessels, and other debris (see Fig. 3).

Our coronary tree segmentation method is described in detail in [13]. For an extensive review of other blood vessel extraction techniques, we refer the reader to [14,15]. A 2-D variant of coronary artery tree pruning based on information about branch lengths, gray level profile information, and information about the structure of the identified tree is presented [16] in and a 3D learning-based approach for tree filtering using random forest classifier is presented in [17].

### Coronary artery tree labeling

Four major coronary arteries (LM, LAD, LCX, and RCA) are labeled in order to validate the correctness of the segmentation, perform additional anatomy-based tree filtering, and report lesions by specific artery.

A probabilistic anatomical model of left and right coronary trees is created based on manual labeling of CCTA training data sets. This model allows computing the likelihood of a given path to be RCA, LM-LAD or LCX. Labeling is then performed following the maximal likelihood approach and a series of tests which check expected spatial relationships between major arteries (see Fig. 4). For example, the pair of RCA and LCX arteries, both located in the atrioventricular groove, is tested for quasi-planarity. LAD artery, which travels in the inter-ventricular groove, is tested for being roughly perpendicular to the RCA-LCX plane. A similar probabilistic approach for coronary tree labeling is reported in [18].

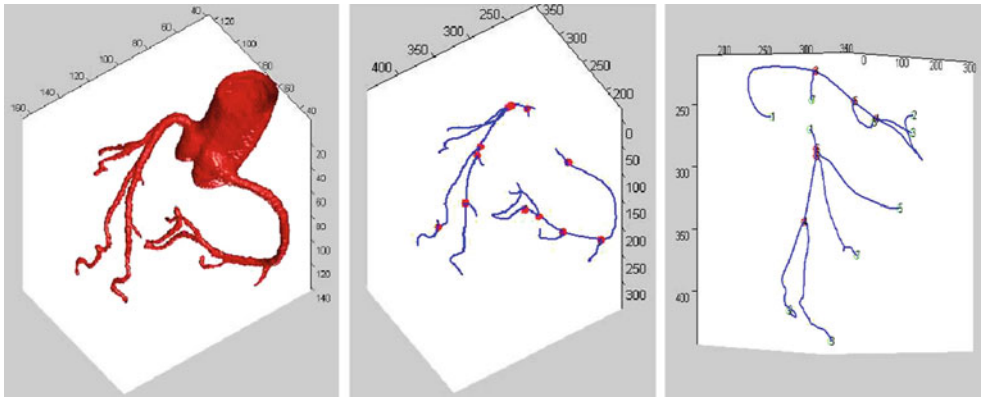

**Fig. 3** Reconstructed coronary tree, center-line graph, and filtered tree. Graph nodes are marked with *red dots*. Some of the nodes are filtered out by branch pruning

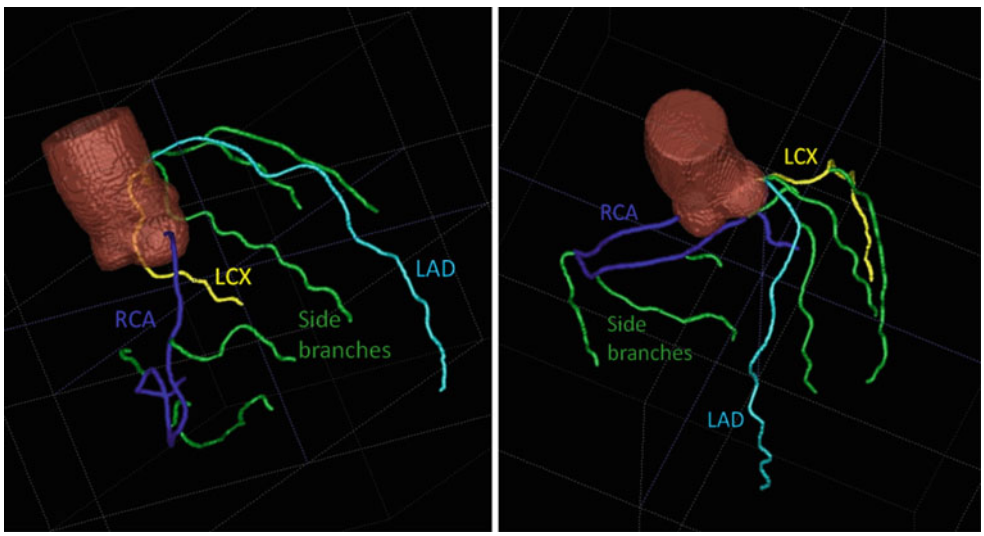


**Fig. 4** Labeled coronary artery tree. RAO (*left*) and LAO (*right*) views

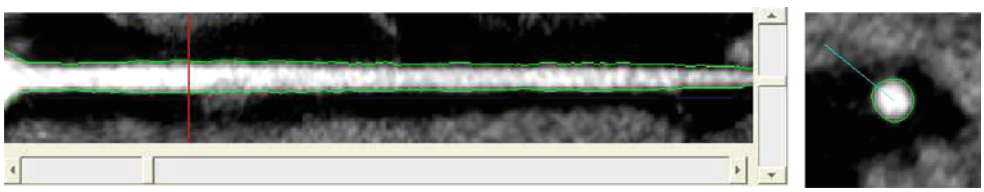

**Fig. 5** Straightened CPR vessel representation. Longitudinal (*left*) and cross-section (*right*) views. External vessel boundary is shown in *green*

Knowing the location of major coronary arteries allows performing additional coronary tree cleanup. For example, any branches going from LCX toward atrium are removed, as most of them are not arteries, or too small to be analyzed. The same is applicable for septal perforators or septal-alike branches.

In addition, coronary tree dominance (left, right, or balanced) is detected. If the dominant artery is short, a tracking/labeling failure is declared.

Detecting stenotic lesions

The reconstructed coronary tree is split into disjoint vessel segments using a greedy tree traversing algorithm by choosing the largest and the less convoluted branch at every bifurcation. Each segment is re-projected into a straightened CPR [19] on which the further analysis is performed (see Fig. 5). Blood vessel external boundary and lumen are delineated using iterative model-based active contour approach.

Given the first approximation of the center-line, anchor points are detected in every vessel cross-section by fitting elliptical model to the high gradient points. Then, the boundary is segmented using tubular active surface model with forces controlling attraction to the anchors [20], tubular geometry fitting, and intensity uniformity inside the surface [21]. Once the boundary surface is reconstructed, the center-line is re-computed and the vessel is re-sampled. Several iterations of boundary segmentation and center-line adjustment are performed. Lumen segmentation is achieved by applying the same approach within the limits defined by the vessel boundary.

Calcified lesions are detected and segmented by hysteresis based adaptive binarization. Non-calcified plaque lesions are detected as hypodense areas between the external vessel boundary and lumen. The detailed description of our plaque detection and segmentation algorithm is available in [22]. For a comprehensive review on various vessel segmentation and lesion modeling methods, we refer the reader to [15].

A large set of parameters is extracted for every cross-section of the stretched vessel including vessel and lumen cross-section area, presence and size of calcified and non-calcified plaque lesions, presence and properties of bifurcations, contrast material intensity, noise level, presence and strength of various artifacts (e.g., motion blur, phase misregistration, etc.), distance from the tree ostium, surrounding tissue (e.g., fat or myocardium) and others. On a training set of CCTAs comprising hundreds of studies, pathology ground truth was formed by consensus reading of several physicians requested to mark significant lesions. The system is then trained using a fuzzy logic approach [23] to yield the best match for the lesions marked in the ground truth, based on the extracted features and associated confidence levels.

While a large body of work exists for coronary plaque segmentation, quantification and stenosis assessment, most developed methods are either not fully automatic or not aimed at automatic detection of significant stenosis [24–28]. Recently, a fully automatic method was reported for the detection of significant stenotic lesions in coronary arteries [17].

## Image quality assessment and results quality control

Image quality assessment is important for a number of reasons. First, the system discards low-quality studies for which no reliable diagnosis can be achieved. Second, local image quality parameters and artifact indications are used for adaptive tuning of various segmentation and analysis algorithms. Third, image quality is one of the parameters used for choosing between different cardiac phases. If more than one cardiac phase is available, the system builds the final report by choosing for each coronary artery the phase on which the analysis is based. Phase selection is based both on the image quality along the analyzed blood vessel (SNR, the presence and severity of artifacts) and the success of the vessel tracking and segmentation.

The system automatically computes global and local SNR based on image values inside the descending aorta or large blood areas in heart chambers. In addition, the system assesses the contrast material intensity and searches for misregistration artifacts. Studies with unacceptable SNR or insufficient contrast intensity are reported as "invalid" by the system. The image quality assessment method used by the system was previously described in detail in [29].

At every processing step, the system runs a number of validation tests to verify the correctness of the result. If the confidence level of the result is low the system reports either a "failure", or, if the problem relates not to the whole study, but only to a part of it, issues a "warning". For example, if the system determines that the vessel tracking might have missed part of the artery due to an artifact, it warns the user and suggests analyzing the vessel manually. Other examples of self-validation include detection of abrupt vessel disappearance, especially in the proximal or mid part, or in the presence of an imaging artifact; low likelihood of a named vessel to be a specific coronary artery; insufficient coverage of the atrioventricular groove by the tracked vessels, etc.

## Reporting

The automatic processing takes 5–7 min and, after completion, the result appears as an icon on the studies list (see Fig. 6). Every study is classified into two major categories—those who have significant coronary stenosis, and those who do not. Other possibilities include warning, failure or invalid study.

The user can then verify the findings using a number of visualization tools including curved MPR, schematic 3D view of the coronary artery tree and color overlay on original images. If multiple phases are available, the system automatically chooses and reports the best phase for each one of the analyzed arteries.

## Clinical evaluation

The system underwent extensive testing in a number of academic centers, hospitals, and imaging centers. Table 1 summarizes published results from 14 independent clinical trials that tested system's diagnostic performance in the detection of significant coronary artery disease. In most trials, automatic diagnosis results were compared with human interpretation of the CCTA (either by a single expert or by consensus). In a small number of trials, when both CCTA and catheterization were performed, cath lab results were used

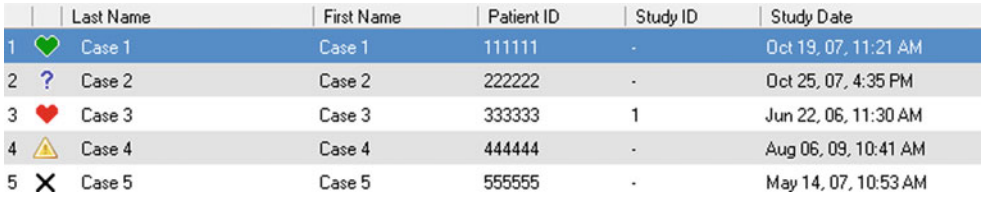


**Fig. 6** An example of "per study" reporting: CAST system for coronary CT angiography analysis encodes results by colored icons: —no significant disease, —inconclusive result, —significant coronary artery lesion detected, —invalid/poor quality study, —other automatic processing failure

**Table 1** Diagnostic performance evaluation statistics

| Trial/site | Cases | Population | Prevalence (%) | Sens. (%) | Spec. (%) | NPV (%) | PPV (%) | Ground truth |
|---|---|---|---|---|---|---|---|---|
| Cardiac CT Institute, Philadelphia, PA [30] | 138 | Cardiology, outpatient | 45.7 | 95.2 | 68 | 94.4 | 71.4 | CCTA consensus reading |
| Washington Hospital Center [31] | 88 | Cardiology, outpatient | 24 | 89.7 | 56.5 | 92.9 | 56.5 | CCTA consensus reading |
| Stony Brook Univ. MC [32] | 96 | ED, chest pain | 8.3 | 100 | 64.2 | 100 | 21.6 | CCTA consensus reading |
| Dr. Poon Cardiac Ctr., NY [32] | 49 | Cardiology, outpatient | 26.5 | 100 | 38.2 | 100 | 38.2 | CCTA consensus reading |
| Cardiac Study Ctr., Tacoma [33] | 196 | Cardiology, outpatient | 13.3 | 100 | 41.1 | 100 | 21.3 | Cath Lab |
| Beth Israel Deaconess MC, Boston [34] | 100 | ED, chest pain | 6 | 83 | 82 | 98 | 23 | CCTA consensus reading |
| Medical Univ. of SC [35] | 59 | Cardiology, outpatient | 32.2 | 100 | 65 | 100 | 58 | Cath Lab, QCA |
| Stony Brook Univ. MC [36] | 341 | Low/mid/high risk | 8/13/27 | 100 | 64/41/38 | 100 | 22/21/38 | CCTA consensus reading |
| Cardiac Study Ctr., Tacoma [37] | 208/75 | Low/mid risk | | 100/98 | 41/33 | 100/90 | 21/71 | Cath Lab |
| Univ. of Chicago MC [38] | 80 | Mixed | 15 | 91.7 | 61.7 | 97.4 | 32.4 | CCTA expert reader |
| Erlangen University [39] | 50 | Mixed | 42 | 100 | 59 | | | CCTA expert reader |
| Thomas Jefferson Univ. [40] | 207 | Mixed | 23 | 92 | 70 | 97 | 48 | CCTA consensus reading |
| Mannheim/Heidelberg Univ. [41] | 93 | ED, chest pain | 50 | 100 | 78 | 100 | 82 | CCTA consensus reading |
| Eulji Univ. Hospital, Republic of Korea [42] | 398 | ED, chest pain | 52.8 | 95 | 63 | 97 | 72 | CCTA consensus reading, Cath lab, QCA |

as the ground truth. Sensitivity, specificity, NPV and PPV were computed at per study level, that is, the ability of the system to identify studies/patients with or without significant coronary artery disease was tested.

The system demonstrated stable high sensitivity and NPV (usually above 90 and 95 % respectively), while the specificity range is much wider (from 40 to 70 %). One can see that the specificity of the system is lower when the significant coronary artery disease prevalence is higher, for example, for cardiology department patients. In those groups of population, most negative patients (with no significant disease) still have a mild disease. In some of those cases, the system does not agree with human reader on the severity of mild lesions (the system is usually more conservative), which results in increased number of false alarms and, hence, reduced specificity. It is easier for the system to classify a study as negative if no disease is present at all. For ED and low-risk patients, when the prevalence is below 20 %, the specificity is in the range of 60–70 %.

The trials in Table 1 included CCTA studies acquired on all types of CT scanners (64 or more slices) available today. No significant variations in system's diagnostic performance

were observed between different CT machines. The only CT scanner specific adaptation we had to implement was for the Toshiba 320-slice scanner to support its non-standard conic field of view reconstruction. The participating sites used different CCTA acquisition and reconstruction protocols including both prospective and retrospective gating, low-dose scans, use of beta-blockers, vessel dilators, etc.

As one could expect, the system performed better for better quality studies and vise a versa. For example, there are more false alarms in prospective gating studies due to severe misregistration artifacts, or, the system makes more mistakes and reports more invalid studies for noisy low-dose scans, or for patients with high heart rate. Overall, we have seen that with the same equipment the quality of studies and, hence, the CAST system diagnostic performance may vary significantly as a function of staff experience, selection of adequate protocol parameters, patient selection and preparation.

To the best of our knowledge, the only other system that performs a fully automatic detection of significant coronary lesions is the one recently reported by Kelm et al. in [17]. Unfortunately, the system performance per study is not reported there, and hence, we can only roughly assess it from the statistics per lesion and per vessel that are provided. The Kelm et al. system produces on average 2.97 false-positives per study while analyzing three major coronaries only and looking for non-calcified lesions only. For comparison, our system produces on average 0.72 false-positives per study, while analyzing all coronaries (8 vessels on average per study) and looking for all types of plaque (calcified, non-calcified and mixed).

Assuming

- the same ratio between the prevalence of the disease per vessel and per study in both data sets, and
- the same ratio between the average number of false-positives per negative study and per positive study for both systems,

one can deduce that the expected average number of false-positives per negative study in Kelm et al. system is 2.18. This means that the expected per study specificity is close to zero, and almost every study would be reported as positive. Therefore, such system cannot be used for study triage and is not CAST-compliant.

For comparison, the average number of false alarms per negative study in our system is 0.48, which well explains the per study specificity of 65 %.

The vessel tracking part of our system was tested in Rotterdam Coronary Artery Algorithm Evaluation Framework [43] and demonstrated some of the best results. In the fully automatic extraction group, based on the combined tracking coverage and centerline accuracy index, the system was ranked 1st on the combined training and test sets and 2nd on the test set [44].

To evaluate the prognostic value of the system a follow-up study was conducted on 209 patients [45]. During the follow-up period of $12.8 \pm 7$ months, no major adverse cardiac events (MACE) occurred to any of the 78 patients reported as negative by the system, yielding a 100 % NPV. In the 131 patients reported as positive by the system, 40 MACE in 28 patients had occurred.

## Use case scenario

A typical use case scenario involves a low-risk chest pain patient admitted to ER in the middle of the night, showing equivocal ECG and enzymes. The patient is referred to CCTA, and right after the image acquisition is completed, the study is sent to the CAST system. Five minutes later an initial interpretation of the study is completed. There are no expert CCTA readers in the hospital at that time of the day. An ER physician, trained to work with the CCTA CAST, performs visual validation of the findings.

If the result is negative, the patient can be either released or transferred to the observation ward. A thorough, final interpretation of the CCTA study by expert reader can be postponed till the next morning. Assuming reasonable specificity (60 %) and low prevalence of the disease in this population (15 %), at least $(1 - \text{prevalence}) \times \text{specificity} = 51\,\%$ of studies will be reported as negative, which means half of the patients referred to CCTA can be handled this way. Assuming CAST sensitivity of 95 %, the NPV would be 98.5 % and the expected miss rate will be less than $(100\,\% - \text{NPV}) = 1.5\,\%$.

If the result is positive (or inconclusive, i.e., failure, warning or invalid), the study can be immediately interpreted by a remote expert reader on call, or by remote reading "nighthawk" service. Alternatively, a conservative, "standard of care" treatment can be taken with later CCTA analysis by an expert.

## Conclusions

The CAD system presented here is able to automatically detect significant coronary artery disease in CCTA studies. The system's design and exhibited performance allow it to be used in CAST scenarios, thus enabling efficient, 24/7 utilization of CCTA for chest pain patient triage in ER. To the best of our knowledge, it is the only CAST-compliant CAD system existing today. Moreover, it is the only fully operational, clinically validated CAD system for a fully automatic analysis of CCTA and detection of significant stenosis.

The system does not replace humans in making the final decision. It only alerts about the possibility of acute, critical condition, or suggests that the study is free of severe disease. In both cases, the diagnosis should be verified by a trained physician. The benefit is achieved by bringing

expert's attention to critical cases faster than it would happen without CAST (for positive cases) and letting less experienced staff be the first to deal with simple negative cases, thus releasing pressure from less available and more expensive experts (for negative cases).

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