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Diagnosis of Coronary Stenosis with CT Angiography: Comparison of Automated Computer Diagnosis with Expert Readings

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Abstract:

Purpose: To compare computer generated interpretation of coronary CT angiography (cCTA) by commercially available COR Analyzer software with expert human interpretation.

Materials and Methods: This retrospective HIPAA-compliant study was approved by the institutional review board. Among 225 consecutive cCTA examinations, 207 were of adequate quality for automated evaluation. COR Analyzer interpretation was compared to human expert interpretation for detection of stenosis defined as ≥50% vessel diameter reduction in the left main, LAD, LCX, RCA, or a branch vessel (diagonal, ramus, obtuse marginal or PDA).

Results: Among 207 cases evaluated by COR Analyzer, human expert interpretation identified 48 patients with stenosis. COR Analyzer identified 44/48 patients (sensitivity: 92%) with a specificity of 70%, a negative predictive value of 97% and a positive predictive value of 48%. COR Analyzer agreed with the expert interpretation in 75% of

patients. With respect to individual segments, COR Analyzer detected 9/10 left main lesions, 33/34 LAD lesions, 14/15 LCX lesions, 27/31 RCA lesions and 8/11 branch lesions. False positive interpretations were localized to the left main (n=16), LAD (n=26), LCX (n=21), RCA (n=21), and branch vessels (n=23), and were related predominantly to calcified vessels, blurred vessels, misidentification of vessels and myocardial bridges.

Conclusions: Automated computer interpretation of cCTA with COR Analyzer provides high negative predictive value for the diagnosis of coronary disease in major coronary arteries as well as first order arterial branches. False positive automated interpretations are related to anatomic and image quality considerations.

Introduction:

Although catheter angiography is the accepted "gold standard" for the diagnosis of coronary disease, a negative coronary CT angiography (cCTA) study is sufficient to exclude coronary artery disease because of the high sensitivity and negative predictive value of cCTA.[1,2,3,4] Several recent studies suggest that cCTA is a cost-effective examination for evaluation of low to intermediate risk patients with suspected acute coronary syndrome presenting to the emergency department.[5,6] The diagnostic accuracy and reproducibility of interpretation for cCTA, however, is directly related to the experience of the interpreting physician.[7] A major limitation of cCTA for evaluation of emergency room chest pain patients is the lack of available experienced readers, especially during night time and weekend hours.

The fundamental task required for the interpretation of coronary angiography is identification and quantification of stenosis within the coronary circulation. This task is facilitated by computer-aided vessel tracking and image reconstruction techniques available on CT workstations which improve visualization of the vascular lumen and assist the interpreting physician to quantify the degree of stenosis. The presence and degree of stenosis must be evaluated in the major coronary arteries - including the left main (LM) artery, left anterior descending (LAD) artery, circumflex (LCX) artery, right coronary artery (RCA), posterior descending artery (PDA) – as well as the diagonal branches of the LAD (D1 and D2) and obtuse marginal branches of the LCX (OM1 and OM2). Since this task is well defined and quantitative, and since computer-aided

techniques are currently used to facilitate human observers, it seems reasonable that this task may be amenable to automated computer diagnosis.

The impact of cCTA upon management of acute chest pain could be markedly expanded if an automated computer diagnosis could provide an accurate evaluation of cCTA images for off hours interpretation, especially if this evaluation had sufficient negative predictive value to safely discharge the patient. The latest commercially available version of COR Analyzer software provides automated segmentation and evaluation of stenosis in the major coronary arteries as well as diagonal and obtuse marginal branches. The purpose of this study was to compare computer generated interpretation of cCTA by COR Analyzer with expert human interpretation.

Methods:

Patient selection:

Institutional review board approval was obtained for this HIPPA-compliant, retrospective study. Consecutive cCTA examinations available on our CT Brilliance workstation (Philips Medical Systems; Cleveland, OH) were exported to a COR Analyzer system (version 1.8R.755; Rcadia - Auburndale, MA). Of 225 cCTA examinations downloaded to the COR Analyzer, 18 studies were deemed unevaluable by COR Analyzer due to insufficient image quality. The remaining 207 were processed with automated coronary evaluation for this study. The study population included 118 examinations performed on a 64 slice Brilliance CT scanner and 89 studies performed on a 256 slice iCT scanner (Philips Medical Systems; Cleveland, OH).

Vessel Analysis Software:

All images were evaluated with COR Analyzer version 1.8R.755 (Rcadia - Auburndale, MA). This software has FDA approval for analysis of four major coronary arteries (left main, LAD, LCX and RCA). In addition, this software has a research option for analysis of side branches including the posterior descending artery, diagonal arteries, obtuse marginal arteries and ramus branches. Once the cCTA studies were downloaded to the COR Analyzer, analysis was performed without human interaction. For those cases when multiple phases were downloaded for a single cCTA study, COR Analyzer

performed its analysis based upon automatic selection of the best phase for every major coronary artery as determined by an automated image quality analysis.

The COR Analyzer software splits the coronary tree into disjoint vessel segments; analysis is performed for each segment independently. Blood vessel external boundary and lumen are delineated using an iterative model-based variational approach. Calcified lesions are detected and segmented by hysteresis based adaptive binarization. Non-calcified plaque lesions are detected as hypodense areas without calcium between the external vessel boundary and lumen. Various imaging feature are recorded, including vessel and lumen cross section area, presence and size of calcified and non-calcified plaque lesions, presence and properties of bifurcations, contrast intensity, noise level, presence and strength of various artifacts (e.g. motion blur, phase misregistration, etc.), and distance from the tree ostium. The software was optimized by the vendor with a training set of cCTA studies to provide a best match of decisions based upon imaging features to proven diagnoses.

The output of the COR Analyzer program is presented as a color coded coronary tree. Each major coronary artery and coronary artery branch is coded in a different color, with areas of >50% stenosis marked by a thick red overlay on the stenotic segment. A printout is also presented on the screen documenting the COR Analyzer interpretation of stenosis for each vessel and branch. Finally, three orthogonal sets of CT images are presented with the ability to scroll through the color coded coronary vessels in order to evaluate the stenosis identified on the color coded coronary tree. When image quality is

limited for an individual vessel, COR Analyzer reports a “warning”. Vessels with warnings were considered abnormal for the purpose of our analysis.

cCTA Studies:

All CT scans were performed by one of three experienced cardiac radiologists as dedicated coronary cCTA studies with ECG-gating. Patients with an initial heart rate above 60 were treated with intravenous beta blockers to a target heart rate of 55-60. Metoprolol was administered in boluses of 2.5-5.0mg to a maximum dose of 20mg. Sublingual nitroglycerin spray (800 ug) was administered approximately 2 minutes prior to scanning. Metoprolol and nitroglycerin were not administered if systolic blood pressure was below 100 mm Hg. Prospective tube current modulation or prospective ECG-gating with axial step and shoot mode were utilized at the discretion of the cardiac radiologist. No patient was excluded on the basis of a high or irregular heart rate. Calcium scores are not obtained routinely prior to cCTA at our institution.

A biphasic injection protocol was employed with 70cc of omnipaque-350 (Mallinckrodt Medical; St. Louis, MO) followed by 40cc of saline at 5cc/sec. The upper extent of the scan was programmed to start at the carina, and the caudal extent of the scan continued through the heart. A structured report was created by the responsible cardiac radiologist as part of standard clinical care for each patient. This structured report identified the presence of stenosis individually in the LM, LAD, LCX, RCA, PDA, diagonal, ramus and obtuse marginal arteries, and graded the degree of stenosis as mild

(<50%), moderate (50-70%) or severe (>70%) based upon a subjective estimate of luminal diameter narrowing. This information was extracted from the final radiology report into a database for this study. For the purpose of the study, any stenosis characterized as moderate or severe was classified as abnormal. A vascular segment was classified as normal if the interpretation was normal or mild (< 50%) stenosis. The automated interpretation provided by COR Analyzer was also extracted into the database for comparison with the human expert interpretation.

The sensitivity, specificity, negative predictive value and positive predictive value of COR Analyzer interpretation was computed along with 95% confidence intervals with the human expert interpretation as the gold standard. This tabulation was done on a "by-patient" basis and was repeated as a "by-vessel" analysis for ≥50% vessel diameter reduction in the left main, LAD, LCX, RCA, or a branch vessel (diagonal, ramus, obtuse marginal or PDA). Areas of disagreement between the interpretation of COR Analyzer and the human expert were evaluated by a senior cardiac radiologist in the group to determine the cause of each disagreement. For the purpose of this evaluation, the findings of COR Analyzer were compared with slab maximum intensity projection (MIP) and tracked curved MIP images (figure 1).

Results:

Among 207 cases evaluated by COR Analyzer, the final clinical interpretation by the expert cardiac radiologist identified 48 patients with significant (>50%) stenosis. Although one patient appears to have had a false negative interpretation on the final clinical report (figure 1), the clinical interpretation of the cardiac radiologists in their final report was treated as the gold standard and that case was tabulated as a false positive COR Analyzer interpretation. On a by-patient basis, COR Analyzer demonstrated a sensitivity of 92% (95% CI: 0.80-0.97) with a specificity of 70% (95% CI: 0.63-0.77), a negative predictive value of 97% (95% CI: 0.92-0.99) and a positive predictive value of 48% (95% CI: 0.38-0.58). COR Analyzer agreed with the final clinical interpretation in 75% of patients, and in 89% of major coronary artery segments.

With respect to individual segments, COR Analyzer detected 9/10 left main lesions, 33/34 LAD lesions, 14/15 LCX lesions, 27/31 RCA lesions and 8/11 branch lesions. Each discrepant case was reviewed for associated findings that might explain the false negative interpretation (table 1). One false negative case associated with a branch stenosis had no obvious explanation (figure 2). Five of the 10 stenoses missed by COR Analyzer appeared close to 50% upon re-examination of the discrepant cases (figure 3). With respect to branch vessels, misclassification of a branch artery or failure to include the branch in the coronary tree was responsible for 2 of the 3 missed stenoses. The remaining two false negative diagnoses involved small vessels (< 1.5mm), one a small

RCA in the setting of a left dominant circulation and the other a small LCX in the setting of a right dominant circulation.

COR Analyzer identified the presence of significant (>50%) stenosis in numerous vessels that were interpreted as normal or with <50% stenosis in the final clinical interpretation by the expert cardiac radiologist. The findings associated with these "false positive" interpretations in the left main (n=16), LAD (n=26), LCX (n=21), RCA (n=21), and branch vessels (n=23 stenoses in 20 patients) are summarized in table 2. The branch vessel stenoses included 3 stenoses in D1, 2 stenoses in D2, 2 stenoses in a ramus intermedius, 12 stenoses in OM1, 1 stenosis in OM2 and 3 stenoses in the PDA. Several vessels demonstrated more than one possible explanation for a false positive result, such that the number of associated issues identified in table 2 is larger than the total number of false positive interpretations.

Review of these discrepant cases suggests that at least one of these false positive interpretations in an obtuse marginal branch was related to under-rating of stenosis by the radiologist (figure 1). In addition, several of the vessels demonstrated stenoses that were close to 50% and could easily have been read as positive by another radiologist. The most common association with a false positive interpretation in the left main and LAD arteries was the presence of vascular calcification (figure 4). A large number of the false positive interpretations in the LCX and RCA were related to blurring due to motion artifact. Tracking of the RCA was incomplete in 10 patients, including 6 patients with blurring of the RCA, 2 patients with an anomalous RCA from the left sinus of Valsalva,

and 2 patients with left dominant circulations. The most common reason for a false positive diagnosis in a branch vessel was related to misclassification of a non-vascular structure or an extracardiac vascular structure as a vessel. Coronary stents were always associated with a false positive diagnosis related to blooming of the stent struts that appears to narrow the lumen (figure 5). Myocardial bridging was commonly associated with a false positive result in the LAD (figure 6), and was also associated with a false positive result in a ramus branch (figures 7). Misclassification of small acute marginal branch vessels as the PDA was the reason for a false positive interpretation in two patients (figure 8).

Discussion:

Given the magnitude of coronary disease as a cause of mortality and the increasing use of cCTA to evaluate symptomatic coronary disease, it is surprising how few published reports are available on automated computer diagnosis for cCTA. In this study, we demonstrate that automated computer interpretation of cCTA with COR Analyzer provides a high negative predictive value for the absence of coronary disease in branch vessels as well as the major coronary arteries. One prior study evaluated the performance of an earlier version of COR Analyzer that evaluated only the major coronary arteries. That study of 59 patients demonstrated a negative predictive value of 94% by segment and 100% by patient.[8] The current study evaluated a larger patient population and demonstrated a similar negative predictive value for branch coronary vessels as well as the major coronary arteries.

Previous computer aided tools have been developed for segmentation and display of the coronary tree to facilitate interpretation of cCTA.[9] Although these specialized analysis tools are often more time consuming to use than manual manipulation of slab MIP images, they may result in greater confidence in the final interpretation.[10] Analysis tools have the potential to provide more reproducible measurements and reduce interobserver variability in the interpretation of stenosis. The COR Analyzer program differs from other currently available analysis tools in its completely automated approach. Image data is uploaded to the processor, and human involvement is not required until the algorithm has rendered a diagnosis. The radiologist can review the study independently

and then compare notes with the COR Analyzer. This approach has potential to serve as a preliminary reading for triage of cases, as well as a double check to suggest that the radiologist might wish to take a second look at an area that is marked suspicious by COR Analyzer. Most importantly, the radiologist does not need to spend time interacting with a complicated image processing program. Thus, COR Analyzer has the potential to facilitate a more rapid and accurate interpretation of cCTA studies.

Automated computer based diagnosis depends upon constructing an accurate model of the coronary tree. Our results demonstrate that when image quality is reduced by motion artifact, vessels are improperly identified and the presence of stenosis is overcalled. The presence of coronary calcification is also associated with disagreements between the human expert and COR Analyzer. Our cardiac radiologists classify calcified lesions as <50% whenever a clear vascular lumen is visualized and the calcium does not appear to surround or fill the lumen.[11] COR Analyzer will rate these lesions as >50% whenever the calcium reduces the vascular lumen by more than half, even though the blooming associated with vascular calcification results in overdiagnosis of stenosis (figure 4). Although the specificity of the diagnosis by COR Analyzer is reduced with poor image quality and/or calcified vessels, sensitivity remains high and the negative predictive value remains excellent. This high negative predictive value will be most useful for studies in a population with a low prevalence of coronary disease – such as the emergency room chest pain population - where the COR Analyzer might be used to facilitate the rapid discharge of patients during all hours of the day and night.

Our study suggests that numerous issues may result in overdiagnosis of coronary stenosis by COR Analyzer (table 2), but the list of issues that result in a missed diagnosis is much shorter (table 1). Most of these issues, such as misidentification of vessels, the presence of a left dominant system, or incomplete tracking of coronary arteries, are easily confirmed by evaluating the coronary tree model displayed by COR Analyzer. Given its high sensitivity for coronary stenosis, COR Analyzer should be useful to improve the sensitivity of the less experienced readers in the emergency setting. Alternatively, COR Analyzer might be used to triage cases that require additional or expedited interpretation.

Though our study is limited by a relatively small sample size, it is only the second study to evaluate a completely automated system for analysis of cCTA, and it is the first study to evaluate the automated analysis of first order coronary branches. The high sensitivity and negative predictive value that we found in our evaluation must be substantiated in larger and more diverse patient populations. Our study is also limited by lack of correlation with conventional cardiac catheterization. However, our results are compared with human expert interpretation of cCTA in order to determine whether COR Analyzer successfully automates the function of a human expert for evaluation of cCTA.

An automated system that is able to evaluate first order coronary branches in addition to the major coronary arteries provides a clinically useful tool for evaluation of all AHA coronary arterial segments. Our results suggest that automated computer diagnosis of coronary disease is feasible with currently available technology, and may facilitate more rapid and accurate evaluation of the coronary arteries with cCTA.

Table 1. Associated findings in false negative cases

	Left Main	**LAD**	**LCX**	**RCA**	**Branch vessels**
Stenosis close to 50%	1	1		3	
Vessel misidentification					2
Left dominant coronary system (with small RCA < 1.5mm)				1	
Small vessel (<1.5mm)			1		

Table 2. Associated findings in false positive cases

	Left Main	**LAD**	**LCX**	**RCA**	**Branch vessels**
Stenosis close to 50%	1	1		1	1
Vessel misidentification	1	1	4	1	10
Anomalous coronary artery				2	
Left dominant coronary system (with small RCA < 1.5mm)				2	
Small vessel (<1.5mm)			2		4
Vascular calcification	11	15	7	5	5
Coronary stent		1		2	
Blurred vessel	1		8	10	2
Streak from PM wire		1		1	
Poor contrast opacification	2	1	3		2
Myocardial bridging		6			1

Figure Captions:

Figure 1. Moderate to severe stenosis (~70% narrowing) at the origin of the first marginal branch of the circumflex artery identified by COR Analyzer but overlooked in the final clinical interpretation of the study.

A. Coronary tree created by COR Analyzer demonstrates all of the major coronary arteries. A site of stenosis is identified at the origin of the first obtuse marginal artery. (arrowhead).
B. Slab MIP image demonstrates narrowing at the origin of the first obtuse marginal artery (arrow).
C. Tracked MIP of the first marginal artery again demonstrates the narrowing at the origin of this vessel (arrow).

Figure 2. Moderate lesions in the proximal LAD and at the origin of the first diagonal artery.

A. Coronary tree demonstrates >50% stenosis in the proximal LAD (arrowhead), but the first diagonal artery was not identified in the coronary model created by COR Analyzer, and therefore the stenosis at the origin of D1 was not detected.
B. Tracked, curved MIP confirms areas of stenosis in the proximal LAD (arrowhead) as well as the origin of the first diagonal artery (arrow).
C. Slab MIP demonstrates the LAD (arrowhead) and D1 (arrow) stenoses in a different projection.

Figure 3. RCA stenosis interpretted as >50% narrowing by the human expert reader, but not identified by COR Analyzer.

A. Coronary tree definition by COR Analyzer demonstrates all the major coronary vessels, including the RCA (arrow), but does not define a focal stenosis.
B. Vessel tracking with curved and straightened lumen MIP views demonstrates a focal area of >50% narrowing in the mid-distal (arrows).
C. Slab MIP view demonstrates irregularity with mild narrowing in the mid RCA (arrowheads) as well as a focal narrowing in the mid-distal RCA interpreted by the human expert as >50% (arrow).

Figure 4. Diffusely calcified coronary tree with multi-vessel disease, but no significant narrowing diagnosed by the human expert reader.

A. Coronary tree demonstrates multiple vessels identified with >50% stenosis by COR Analyzer (red overlay). The proximal RCA (arrow) and proximal first diagonal artery (arrowhead) are illustrated in subsequent figure parts.
B. Curved MIP demonstrates a calcified segment of the proximal to mid RCA. (between arrows). The lumen is difficult to visualize under the calcifications.
C. Straightened lumen view suggests that the calcified plaques result in less than 50% diameter narrowing (arrow).
D. Tracked curved MIP of the first diagonal artery also demonstrates calcified plaque (arrowhead) with less than 50% luminal narrowing.

Figure 5. Patent coronary stents in calcified coronary arteries interpreted as areas of stenosis by COR Analyzer.

A. Areas of stenosis are identified by COR Analyzer in the RCA and LAD (red overlays). Stents in the RCA (arrowhead) are illustrated in subsequent figure parts.
B. Slab MIP in the left anterior oblique projection demonstrates patent RCA stents (arrowheads).
C. Orthogonal slab MIP again demonstrates the patent stents with linear beam hardening artifacts extending through the stents (arrowheads).
D. Straightened lumen view more clearly demonstrates that the stents (arrowheads) are patent.

Figure 6. Myocardial bridging of the LAD associated with a false positive interpretation of stenosis by COR Analyzer.

A. Coronary tree model created by COR Analyzer demonstrates a focal stenosis in the mid-LAD (arrowhead). No additional stenosis is identified.
B. Tracked curved MIP of the LAD demonstrates a myocardial bridge (arrowhead) with a very mild narrowing of the mid-LAD.
C. Coronary tree model created by COR Analyzer in another patient with a shorter segment myocardial bridge, suggesting a focal stenosis as the LAD dives into the bridge (arrowhead). MIP imaging demonstrated no stenosis.

Figure 7. Tortuous ramus intermedius branch with subtle myocardial bridge associated with a false positive interpretation of stenosis by COR Analyzer.

A. Coronary tree model created by COR Analyzer demonstrates a trifurcation of the left main coronary artery with a focal stenosis in the ramus intermedius (arrow).
B. Slab MIP again demonstrates the trifurcation of the left main coronary artery with a patent, but tortuous ramus intermedius and a shallow bridged segment (arrow).
C. Tracked, curved MIP of the ramus branch confirms patency of this artery without stenosis. The myocardial bridge is not appreciated in this view.

Figure 8. Coronary tree demonstrates an acute marginal branch of the RCA identified with >50% stenosis by COR Analyzer (red overlay and white arrowhead). This was interpreted as the posterior descending artery (PDA). The true PDA is a more distal branch of the RCA (arrow) with no evidence of stenosis.

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