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# Radiology

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#### Published online 10.1148/radiol.10100161

#### Radiology 2011; 258:329-339

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Potential conflicts of interest are listed at the end of this article.

See also the article by Sakuma in this issue.

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oronary computed tomographic (CT) angiography and magnetic resonance (MR) angiography are both capable of providing noninvasive images of the coronary arteries (1-4)(Fig 1). Nevertheless, MR angiography has a number of important advantages because it does not involve radiation exposure or the intravenous injection of an iodinated contrast agent. Thus, if MR angiography were shown to have the same diagnostic accuracy in the detection of coronary artery stenoses as does CT angiography in comparison with the reference standard, conventional coronary angiography, it would likely become the preferred diagnostic test in patients who are suspected of having CAD (5). The aim of this Controversies article, which is accompanied by the article by Sakuma (6), is to provide an overview of the comparative effectiveness of CT angiography and highlight the controversial issues in coronary CT and MR angiography.

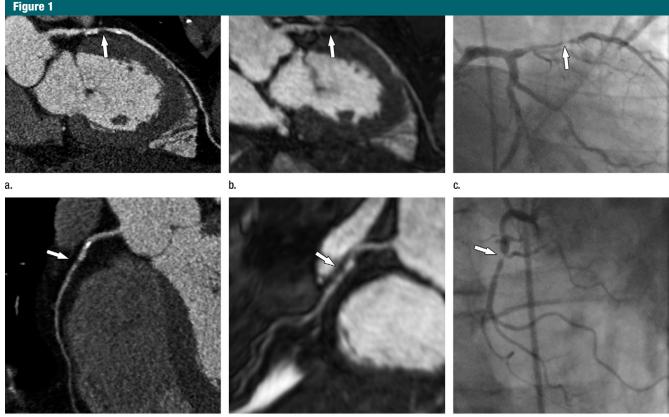
## **Technical Considerations**

Coronary CT and MR angiography each have distinct technical and practical advantages (Table 1). The most important advantages of MR angiography include its greater temporal resolution and the possibility to aid the performance of a comprehensive cardiac evaluation, including function, perfusion, and viability assessment, in the same session (8). Moreover, it is easier to individually set the acquisition window position and length within the R-R interval (9). Because of the lack of radiation exposure, MR angiography would theoretically be a better follow-up test (eg, for plaque imaging) (10) or in patients with intermediate stenoses. However, the spatial resolution of CT angiography is better than that of MR angiography (Table 1), experience with coronary CT angiography is greater, and the modality is more widely available than is cardiac MR imaging. Also, the examination time for coronary CT angiography is significantly shorter (3) and patients greatly prefer CT to MR angiography (11).

# **Patient Preparation**

Absolute contraindications to MR imaging (such as cardiac pacemakers and shrapnel located in biologically sensitive areas) are found in 0.4% of patients referred for MR imaging and may considerably delay work flow (12,13). CT is not contraindicated in those patients, avoiding time-consuming identification of the exact type and location of implants as with MR imaging. Claustrophobia precludes MR imaging in about 2% of patients with a clinical indication (14). These limitations reduce the general applicability of MR imaging.

Selecting the proper diagnostic test for patients who are suspected of having CAD is crucial because not all patients benefit from noninvasive coronary angiography. Patients with a higher pretest probability of disease will very likely have to undergo invasive conventional coronary angiography anyway on the basis of whether they are suspected of having stenoses at noninvasive imaging. The main benefit of percutaneous coronary revascularization is the relief from angina and not the prevention of cardiovascular events (15). Asymptomatic patients will thus not benefit from noninvasive coronary angiography because their outcomes will not be improved by revascularization. Moreover, in patients with a very low likelihood of disease, the probability that a positive result of noninvasive coronary angiography is false-positive is very high. Thus, patients with low-to-intermediate pretest likelihood of CAD (ie, those with atypical angina pectoris and/or equivocal stress test results) are most likely to benefit from noninvasive coronary angiography (16,17) (Fig 3).



d.

Figure 1: (a-f) Comparative performance of (a, d) CT and (b, e) MR imaging for detection of coronary artery disease (CAD) (arrow) in comparison with (c, f) conventional coronary angiography in a 55-year-old man with atypical angina pectoris. Images **a-c** show a significant stenosis in the middle left anterior descending coronary artery, and images d-f show a significant stenosis in the small right coronary artery in the middle segment. Images were obtained by using 320-detector row coronary CT angiography and whole-heart coronary MR angiography with 32-channel technology. Noninvasive coronary images are reconstructed as curved multiplanar reformations. The spatial resolution of CT is greatly superior to that of MR imaging.

f.

e.

Patients with atrial fibrillation or other forms of nonsinus rhythm, such as advanced atrioventricular block (second or third degree), pose a great problem to noninvasive coronary angiography and are currently not considered candidates for the procedure (19). These issues may be overcome in the future by using advanced CT scanning techniques that can collect all required data in a few heartbeats.

For all CT angiography, the risks of and contraindications to iodinated contrast agents must be considered. However, an intravenous contrast agent is also required to assess myocardial perfusion and viability in the setting of comprehensive cardiac MR imaging. Moreover, recently it was suggested that wholeheart coronary MR angiography at 3.0 T should be performed with slow infusion of gadolinium-based contrast medium (20). Thus, the need for an iodinated contrast agent, a major disadvantage of CT, is actually much less of a disadvantage than one might think, especially when the potential risk of nephrogenic systemic fibrosis is considered (21).

Because of the inferior temporal resolution of CT and the benefit that low heart rates have on image quality (22) and diagnostic accuracy (18,23), the use of beta-blockers is one of the cornerstones of patient preparation for this examination (2,24-26). Moreover, in conjunction with the recent dose-reducing prospective scan approaches, which can be used in patients with low and stable heart rates (27) (Fig 2), lowering the heart rate also reduces the effective dose of CT. Sublingual nitroglycerin is beneficial in noninvasive coronary imaging because it dilates the coronary artery diameters by about 10%-20% (28), which in turn facilitates evaluation (29) and comparison with conventional coronary angiography, which is usually performed by using intracoronary nitroglycerin. Thus, more than 80% of cardiac CT centers in both the United States and Europe use nitroglycerin (24,25). Interestingly, despite its positive effect also on coronary MR angiography (30), nitroglycerin has been given only in 25% of all MR imaging research studies (18).

# **Coronary CT Angiographic Scanning**

Prior to the short 20-minute examination in the scanning room, patients should be

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reassured that CT is a noninvasive and convenient test (19). Moreover, there is no relevant confinement in the CT gantry, as is present in MR imaging. Thus, claustrophobic events that prevent CT are rare. Patients are placed in the supine position, as for MR imaging, but with the arms above the head to reduce exposure and beam-hardening effects. As in coronary MR imaging, cardiac CT requires the placement of electrodes for electrocardiographic gating or triggering of the scan. In contrast to whole-heart coronary MR angiography, CT is not performed during free breathing (eg, with diaphragmatic navigator gating) but during a single submaximum inspiration. Moreover, a regular breathing pattern, which is not achieved in all comers (31), is important for the success of free-breathing (32) coronary MR angiography.

Tube current and voltage should be adjusted to the patient's body weight or body mass index to ensure a constant high image quality regardless of body dimensions, while at the same time keeping the effective radiation dose to a minimum (33). A further significant reduction of dose (by 10%-40%) can be achieved with electrocardiographically gated tube current modulation (34) or by using prospectively acquired data ("step-and-shoot," "triggering" dose reduction by approximately 60%-90%) (27,35-38) (Fig 2). Nevertheless, those techniques are limited to patients with slow and stable heart rates to ensure high image quality. In such patients, a fast prospectively acquired spiral scan covering the entire coronary vasculature in a single heartbeat can be obtained by using second-generation dual-source CT, with great reduction of effective dose (39). It was also recently shown that 320-detector row volumetric coronary CT angiography, as the other approach to acquire the entire cardiac volume in a single beat, may result in a significantly less effective dose than with conventional coronary angiography (40).

In patients with low body mass index, reduction of tube voltage to 80 or 100 kV is another useful approach to reduce effective dose without reducing image quality (41). Global and regional left ventricular function, which is important for prognosis (42), cannot be

# Table 1

#### Advantages and Disadvantages of Coronary CT and MR Angiography

Favorability	CT Angiography	MR Angiography
Advantages		
Time, preference, and comprehensive assessment	Shorter total examination time and preferred by patients	Allows combined assessment of function, perfusion, and viability in the same session*
Radiation exposure	Single breath-hold of only 8–10 sec <sup>†</sup>	No radiation exposure or use of iodinated contrast agent <sup>‡</sup>
Resolution	Higher spatial resolution	Better temporal resolution
Disadvantages		
Diagnostic problems and contraindications	Calcifications can lead to overestimation of stenosis	Contraindicated in patients with pacemakers and shrapnel located in biologically sensitive areas
Contrast agent use and cost	Use of iodinated contrast agent (60–100 mL)§	Higher costs and less widely available

\* CT allows functional assessment if retrospectively gated data have been obtained (Fig 2). Assessment of viability and perfusion by using CT requires additional radiation exposure and contrast agent injection.

<sup>†</sup> Performed by using 64–detector row CT. With newer scanners, the scan time is shorter (about 6 seconds by using 128–detector row CT and 3 seconds by using 320–detector row CT, including 2–3-second wait period before the coronary scan to allow the heart rate to normalize after submaximal inspiration).

<sup>+</sup> A gadolinium-based contrast agent (7) is required for MR imaging if myocardial perfusion and/or viability is included in the examination.

 $\ensuremath{\$}$  Depending on the scanner type.



**Figure 2:** Scan modes for coronary CT angiography. **(a)** During a retrospectively electrocardiographically gated helical acquisition shows that the tube current remains constant during subsequent R-R intervals. **(b)** The tube current can also be modulated on the basis of the recorded electrocardiogram to achieve lower doses during systole and constant image quality during the rest phase of coronary artery motion. These two scan modes allow assessment of cardiac function. **(c)** Step-and-shoot acquisition by using a 64–detector row CT scanner in seven heartbeats, with acquisitions being prospectively triggered at the cardiac rest phases. Scanning is performed every other heartbeat because table movement is necessary to acquire the prospective data. **(d)** With wider detectors (eg, 128–detector row CT), such acquisitions can be performed in three heartbeats. **(e)** In contrast, even wider detectors (320–detector row volumetric CT) or dual-source CT with high-pitch acquisition (dual-source CT) allow imaging of the entire heart in a single heartbeat during diastole. **(f)** By using volumetric CT with 320 detector rows, those prospective scans can also be performed with tube current modulation to allow functional assessment.

estimated from prospectively electrocardiographically gated acquisitions (Fig 2). CT has better agreement with MR imaging than do other traditional tests, such as echocardiography and cineventriculography, for global left ventricular function assessment (43). Therefore, retrospectively gated acquisitions should be obtained in patients undergoing the cardiac CT examination with a clinical indication for functional assessment. Unlike MR angiography, coronary CT angiography always requires the use of a contrast agent. With single-beat imaging and the use of either 320-detector row volumetric CT (44) or second-generation

#### Figure 3



Figure 3: Rule-out of significant CAD in a 60-year-old man with mild increase in low-density lipoprotein cholesterol level, treated arterial hypertension, and atypical angina pectoris. (a-c) Curved maximum intensity projections (cardiac catheterization views) obtained by using single-beat 320-detector row coronary CT angiography at a heart rate of 58 beats per minute following oral administration of 50 mg of atenolol (Tenormin; AstraZeneca, Wilmington, Del) show results of test. (a) Right coronary artery without any plaques and stenoses. (b) Left anterior descending coronary artery with noncalcified (arrow) and calcified (arrowhead) plaque components in the proximal and middle segments. (c) Left circumflex coronary artery without any plaques and stenoses. Patients with intermediate pretest likelihood, such as this patient, benefit most from noninvasive coronary CT angiography because a negative test result (for significant stenoses) means that significant lesions (≥50% diameter stenosis) can actually be ruled out with a high degree of confidence, about 97% (Table 2).

# Table 2

#### Diagnostic Accuracy of Coronary CT and MR Angiography

Group	CT Angiography	MR Angiography
All studies*		
Sensitivity (%)	97.2 (96.2, 98.0)	87.1 (83.0, 90.3
Specificity (%)	87.4 (84.5, 89.9)	70.3 (58.8, 79.7
Positive LR	7.7 (6.2, 9.5)	2.9 (2.1, 4.1)
Negative LR	0.03 (0.02, 0.04)	0.18 (0.14, 0.25
Studies with patients suspected of having $CAD^\dagger$		
Positive LR	9.1 (7.0, 11.8)	
Negative LR	0.03 (0.02, 0.04)	
Studies with patients with acute disease at present	ation <sup>‡</sup>	
Positive LR	4.1 (2.0, 8.4)	
Negative LR	0.06 (0.02, 0.19)	

Note.—Results are given on the per-patient level. The nonoverlapping 95% confidence intervals (Cls) are in parentheses and indicate a significantly higher sensitivity and specificity of CT versus MR imaging. Results are based on 89 studies, including 7516 patients, for CT and 20 studies, including 989 patients, for MR imaging. Adapted from reference 18. LR = likelihood ratio.

\* Results are based on 89 studies, including 7516 patients, for CT and 20 studies, including 989 patients, for MR imaging,

<sup>‡</sup> Including seven CT studies.

dual-source CT (39), the volume of contrast agent can be reduced to approximately 40-70 mL.

The use of more detector rows results in higher diagnostic accuracy (18,45,46) and image quality (47) for coronary angiography (Fig 4). Thus, I believe that CT scanners with at least 64 simultaneous

detector rows should be recommended for noninvasive coronary angiography. In clinical practice, more than 70% and 33% of centers use scanners with at least 32 and 64 detector rows, respectively (25). Also, heart rates of less than 60 beats per minute result in significantly better per-patient diagnostic accuracy of coronary CT angiography (18). This further highlights the importance of proper patient preparation for CT, including administration of oral and, if necessary, intravenous beta-blockers. In MR imaging, end-systolic acquisitions are important in patients with higher heart rates to ensure image quality similar to that in patients with low heart rates (48,49).

# **Image Interpretation**

The spatial resolution of CT is greatly superior to that of coronary MR angiography. Even the most sophisticated 3.0-T MR imagers with isotropic resolution yield coronary images with an appearance that was already feasible with 16-detector row coronary CT angiography. With state-of-the-art CT scanners for coronary imaging (at least 64 detector rows,  $\leq 0.35$ -second rotation time), significantly better image quality is achieved than is possible with coronary MR angiography. Before reading the images, selection of a cardiac phase without motion artifacts (eg, at 70%-80% of the R-R interval or with the use of automatic motion mapping approaches [50]) is necessary. This identification of the optimal cardiac phase for

<sup>&</sup>lt;sup>†</sup> Including 45 CT studies, investigating only patients who were suspected of having CAD.



Figure 4: (a-d) Intraindividual comparison of (a, c) 64-detector row CT and (b, d) 320-detector row CT images in a 63-year-old man. Follow-up was performed because of recurrent angina pectoris after stent placement in the large marginal branch of the left circumflex coronary artery (not shown). Curved multiplanar reformations were obtained along the (a, b) right coronary artery and (c, d) the left anterior descending coronary artery. On **b** and **d**, the visible segments tend to be longer (arrow).

reconstruction and the reconstruction and analysis of the CT data sets are still slightly more time consuming (approximately 25 minutes [25]) than they are for MR imaging, but it is expected that the time required will decrease with the development of state-of-the-art automated analysis tools.

With CT, one does not significantly under- or overestimate percent diameter stenosis in comparison with data from quantitative analysis of conventional coronary angiography (40,51-55). Nevertheless, the variability in quantification (95% CIs) of stenoses by using CT in comparison with conventional coronary angiography is wide (about  $\pm 25\% - 30\%$ )

(40.51-55), and thus, CT is not recommended for quantification. Higher spatial resolution may overcome this limitation in the future (56,57). With CT, one tends to overestimate densely calcified plaques because of blooming artifacts (58,59). Accuracy in plaque detection and differentiation into noncalcified and calcified components by using CT is good to very good, compared with intravascular ultrasonography (60); however, the interobserver variability for measurement of plaque dimensions is relatively high, and further improvements are required. For analysis of plaques, vessel or segment involvement may be assigned a score (61), or vulnerability scores that include assessing low-density plaque and positive remodeling (62) have been suggested. Use of MR imaging to identify potential culprit coronary plaques after intravenous gadolinium-based contrast agent administration has been proposed (63), but its accuracy in enabling quantification of plaque dimensions is unknown. Novel molecular probes that are based on iron oxide particles and, in the future, may specifically target coronary artery plaque substructures are under development. With the use of positron emission tomographic/CT scanners, it might also be possible to identify culprit (inflamed) coronary plaques (64).

Whether noncardiac findings should be evaluated has been a subject of some debate (65-67), because it is not absolutely clear whether the additional findings, especially small incidental lung nodules, will lead to therapy at earlier stages, with improved outcomes (68,69), or to unnecessary follow-up scans and interventions (70). Moreover, this discussion is important because noncardiac findings are more commonly observed with coronary CT angiography than with MR angiography (71). Still, a survey study (25) has found that five of six cardiac CT practitioners believe that they are ethically bound to routinely analyze noncardiac findings to not overlook important findings that could explain a patient's symptoms or may even require emergency interventions.

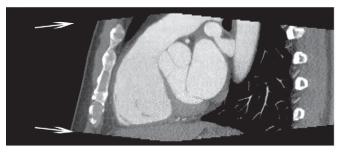
## **Triple–Rule-Out Protocol**

A triple-rule-out protocol for CAD, aortic dissection, and pulmonary embolism is an attractive application of cardiac CT (72). Nevertheless, not all technical issues, such as similar image quality in all vascular beds (coronary arteries, aorta, and pulmonary arteries), have been solved (2), and according to the North American Society for Cardiac Imaging and the European Society of Cardiac Radiology recommendations, in most of the cases, patients are actually suspected of having only two of the three diseases, and these diseases need to be ruled out (73). Thus, dual-rule-out imaging targeted at the specific questions may be more appropriate from a clinical perspective.





b.



**Figure 5:** (**a**–**c**) Coronary CT angiographic images obtained by using single-heartbeat whole-heart imaging with a 320–detector row scanner in a 48-year-old man with atypical angina pectoris who did not have CAD. (**a**, **b**) Three-dimensional reconstructions with semitransparent chest wall overlay demonstrate the shape of the volume obtained, which resembles a cylinder with a cone above and below (arrows). The cone beam of 320–detector row coronary CT has a 15.2° angle. (**c**) Sagittal thin-slab maximum intensity projection also shows this effect (arrows).

#### C.

#### **Comprehensive Cardiac Imaging**

Comprehensive cardiac imaging (including function, viability, and perfusion assessment in addition to coronary artery evaluation) by using MR imaging was proposed a long time ago (74,75), but only viability assessment and perfusion imaging, which allow one to analyze the functional significance of stenoses, has been widely adopted in the clinical setting. In principle, CT is also capable of aiding in the analysis of myocardial viability (76,77) and perfusion (78,79), which would be important to be able to detect reversible myocardial ischemia with CT in patients. However, CT perfusion imaging has not been extensively validated against the current clinical reference standards (80-82). George et al (81), in their study of 64and 256-detector row technology have suggested that the transmural perfusion ratio may be the most relevant parameter for the analysis of myocardial perfusion CT. By using whole-heart scanning such as that with 320-detector row CT (Fig 5), it should eventually become possible to reliably assess myocardial perfusion during rest and stress conditions to evaluate the functional

significance of coronary artery stenoses (Fig 6). With single-beat imaging protocols, contrast gradients along the coronary arteries may also be useful to analyze the functional significance of coronary stenoses (83). The additional radiation exposure and contrast agent necessary for both viability and perfusion assessment nevertheless limit applicability. Large multicenter studies are needed to address the potential of CT for these indications.

# **Training Issues**

At a given institution, the learning curve, during the course of which the radiologists should consider correlating coronary CT with conventional coronary angiography until diagnostic performance of CT is shown to be plateauing, lasts at least 6 months (84). Also, the learning curve of individuals with little prior exposure is considerable, and readers with different experience may also have substantial differences (85). Thus, substantial efforts are necessary to prepare institutions and individuals for the challenges inherent in cardiac CT. The American College of Radiology considers board-approved radiologists with certification for CT (at least 100 general cases in which CT is performed each year) well prepared for cardiac CT if at least 50 contrast-enhanced cardiac CT examinations have been performed in the last 3 years in a supervised environment and 30 hours of cardiac CT continuing medical education have been obtained (86). Correlation of noninvasive findings with conventional coronary angiography is important to understand the comparative effectiveness and the limitations of noninvasive imaging, while hands-on courses have beneficial effects on the skills and knowledge of cardiac CT beginners (87). There is no information in that regard for coronary MR angiography, but because of the greater complexity of the image acquisition, I believe it is more difficult to establish sufficient coronary MR experience than to get a coronary CT center up and running.

# **Diagnostic Accuracy**

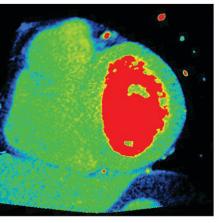
The comparative diagnostic performance of the two tests is summarized in Table 2. A meta-analysis including 89 CT and 20 MR studies has shown that coronary CT angiography is significantly more

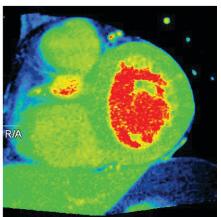
#### **Figure 6**



C.

a.





b.

sensitive and specific than is coronary MR angiography for the detection of CAD (Fig 7a). LRs are used to better understand the clinical usefulness of diagnostic tests. The positive LR is the probability that an individual with the disease has a positive test result versus an individual without the disease. In contrast, the negative LR is the probability that an individual with the disease has a negative test result versus an individual without the disease (88,89). The clinical meaning of LRs lies in the potential to use them to calculate posttest LRs after diagnostic testing (90) to understand the clinical usefulness in populations with different pretest LRs. Positive and negative LRs of greater than 10.0 and less than 0.1, respectively, are considered very good and warrant clinical use of diagnostic tests. The positive and negative LRs of coronary CT in patients who are referred and are suspected of having CAD are 9.1 (95% CI: 7.0, 11.8) and 0.03

(95% CI: 0.02, 0.04), respectively (Fig 7b, Table 2). In other words, a patient with CAD has a more than nine times higher probability of having a positive rather than a negative CT test result. Nevertheless, since the positive LR is below 10.0, CT is not considered to be a very good "rule-in" test. In contrast, the negative LR of 0.03 means that a patient with CAD has an approximately 33 times lower likelihood of a negative CT test result than does a patient without CAD. Thus, coronary CT is considered a good clinical rule-out test and, thus, can function as a gatekeeper prior to other procedures to reduce "layering" of tests. The positive and negative LRs of coronary MR angiography are significantly less favorable than those for CT: 2.9 (95% CI: 2.1, 4.1) and 0.18 (95% CI: 0.14, 0.25), respectively (Table 2). It is of note that the specificity and positive LR of CT are somewhat lower in patients who are suspected of having an acute coronary **Figure 6:** Images obtained in a 67-year-old woman with atypical symptoms 3 years after stent placement in the right coronary artery. **(a)** Curved multiplanar reformation obtained by using a 320-detector row scanner shows mostly noncalcified plaque immediately proximal to the stents (arrowhead). No significant in-stent restenosis can be identified; however, because of the small size of the stents (arrow, 3-mm diameter), significant stenosis cannot be reliably excluded. **(b, c)** Myocardial perfusion images obtained during rest **(b)** and stress **(c)** help exclude significant myocardial defects and demonstrate usefulness of the technique.

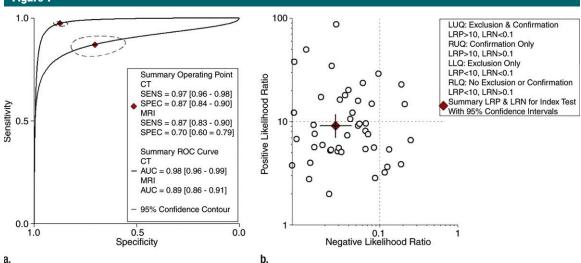
syndrome (Table 2) and that only a few studies correlating CT with conventional coronary angiography have been performed in those patients.

# **Patient Acceptance**

The shorter overall examination time is another decisive advantage of CT over MR imaging (about 20 versus 60 minutes) (3). Widespread clinical use of a diagnostic modality requires not only a high diagnostic accuracy, clinical benefit, and cost-effectiveness (91,92) but also acceptance by the patients. Patients consider noninvasive coronary angiography by using CT more comfortable than they do that by using MR imaging and they consider it less painful than invasive angiography (11). Further, they express concerns about the confinement, the longer image duration, and the noise of MR imaging. Patient acceptance of CT, therefore, appears to be good and, in contrast to that of MR imaging, does not present an obstacle to its widespread use.

# Summary

The moderate specificity and positive predictive value, as well as the few randomized studies available, are important limitations of cardiac CT, while the potential for comprehensive cardiac imaging with CT needs to be further evaluated. Patient preference, examination duration, and spatial resolution are clear advantages of CT over MR imaging. From a clinical perspective, patients with



**Figure 7:** (a) Summary receiver operating characteristic curves (*ROCs*) for CT and MR imaging and (b) LR scattergram for coronary CT angiography on per-patient level. Summary receiver operating characteristic curves for CT (89 studies, including 7516 patients) and MR imaging (20 studies, including 989 patients), with a summary operating point for sensitivity (*SENS*) and specificity (*SPEC*) on the curve and a 95% confidence contour ellipsoid (a). The per-patient receiver operating characteristic curve for CT is significantly superior to that of MR imaging, as indicated by the nonoverlapping confidence interval contours. LR scattergram for CT was based on meta-analysis of 45 studies (one study = one  $\bigcirc$ ), including only patients who were suspected of having CAD (b). The LR profile (positive LR [*LRP*] < 10.0, negative LR [*LRN*] < 0.1) indicates that CT is a potent diagnostic test for ruling out CAD in patients who are suspected of having CAD. *AUC* = area under the curve, *LLQ* = left lower quadrant, *LUQ* = left upper quadrant, *RLQ* = right lower quadrant, *RUQ* = right upper quadrant. (Images a and b, adapted from reference 18.)

low-to-intermediate probability of CAD benefit most from noninvasive testing. Because of its better diagnostic performance, coronary CT angiography is currently preferable to MR angiography for such clinical use, despite its radiation exposure and administration of an iodinated contrast agent.

**Disclosures of Potential Conflicts of Interest:** Financial activities related to the present article: received research grants from European Regional Development Fund, German Heart Foundation /German Foundation of Heart Research, GE Healthcare (Amersham), Bracco, Guerbet, and Toshiba Medical Systems; consultant to Guerbet; and is on the speaker's bureau for Toshiba Medical Systems, Cardiac MR Academy Berlin, and Bayer-Schering. Financial activities not related to the present article: none to disclose. Other relationships: cardiac CT workshops at www. ct-kurs.de, published the books Coronary CT Angiography in 2008 and Cardiac CT in 2010, and participates in institutional research collaboration with Siemens Medical Solutions and Toshiba Medical Systems.

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