Non-Invasive Coronary Angiography With 16 Multidetector-Row Spiral Computed Tomography: a Comparative Study With Invasive Coronary Angiography

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Introduction and objectives. Non-invasive coronary artery angiography by 16 multidetector-row spiral computed tomography is a novel diagnostic tool whose reliability is still unclear. The aim of our study was to compare this technique with invasive coronary angiography.

Patients and method. A total of 31 selected patients were examined with both angiographic methods. Non-invasive studies were performed with a helical computed tomography system (Toshiba Aquilion 16). A contrast agent was injected into a peripheral vein, and cross-sectional images were reconstructed with a slice thickness of 0.5 mm or 1.0 mm. Findings from both techniques were analyzed according to a predetermined segmented anatomical model of the coronary artery. The detection and relevance of coronary artery lesions were evaluated, and lesions with a reduction in diameter of more than 50% were considered significant.

Results. Non-invasive coronary angiography yielded an appropriate assessment in 88.4% of the coronary artery segments. The reasons that prevented correct segment evaluation were extensive coronary calcifications, inappropriate breath-hold, motion artifacts and small vessel size. Sensitivity and specificity for the detection of significant coronary lesions with the non-invasive method were 75% and 91%, respectively. Sensitivity and specificity for individual coronary artery segments were as follows: proximal, 89% and 93%; medial, 87% and 90%; distal, 50% and 90%; and main branches, 62% and 92%.

Conclusions. Non-invasive coronary artery angiography with 16 multidetector-row computed tomography is a powerful diagnostic tool, especially for the evaluation of the proximal and medial segments of the major coronary arteries.

Key words: Coronary disease. Coronary artery angiography. Computed tomography. Multidetector.

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Coronariografía no invasiva mediante tomografía computarizada con 16 detectores: estudio comparativo con la angiografía coronaria invasiva

Introducción y objetivos. La coronariografía no invasiva mediante tomografía computarizada con 16 detectores es una herramienta diagnóstica de reciente aparición cuya fiabilidad está por determinar. El objetivo del presente estudio es la comparación entre esta técnica y la coronariografía invasiva.

Pacientes y método. Se estudió a 31 pacientes por ambas técnicas. El estudio no invasivo se realizó con un equipo Toshiba Aquilion 16. Se realizó una toma helicoidal del volumen cardiaco durante una apnea, inyectándose contraste en una vena periférica y reconstruyendo posteriormente las imágenes con cortes de 0.5 o 1 mm. Ambas coronariografías fueron evaluadas según un modelo anatómico predefinido de segmentación del árbol coronario. Se analizaron la presencia y la magnitud de las lesiones coronarias, considerando significativas las estenosis > 50%.

Resultados. La coronariografía no invasiva permitió evaluar el 88,4% de los segmentos analizados por coronariografía convencional. Las causas de no evaluación de un segmento fueron: presencia extensa de calcio parietal coronario, apnea incorrecta, artefacto de movimiento y reducido calibre del segmento estudiado. La sensibilidad y la especificidad global de la coronariografía no invasiva para la detección de lesiones coronarias significativas fueron del 75 y del 91%, respectivamente. Los valores de sensibilidad y especificidad para los distintos segmentos coronarios considerados independientemente fueron: proximales, 89 y 93%; medios, 87 y 90%; distales, 50 y 90%, y ramas secundarias, 62 y 92%.

Conclusiones. La coronariografía no invasiva mediante tomografía computarizada con 16 detectores muestra un elevado poder diagnóstico, en especial en las lesiones proximales y medias de los principales troncos coronarios.

INTRODUCTION

Multidetector computed tomography (MDCT) applied to the study of the coronary arterial tree is a new diagnostic tool whose potential in the cardiologic setting is not widely known. The technique, which is based on helical computed tomography technology, basically consists of a series of x-ray detectors installed on an axial rotational system that allows simultaneous acquisition of multiple axial slices of an anatomic region as the examination table advances. This set of slices forms an anatomic volume that can be reconstructed, treated and analyzed in any axis by postprocessing on a digital work station.\textsuperscript{1,2}

Multidetector computed tomography currently has two relevant applications in the field of cardiology: determination and measurement of calcium deposit in the coronary arteries (study performed without contrast enhancement), which has proven to be a potent tool in cardiovascular risk stratification,\textsuperscript{3,5} and non-invasive coronary angiography,\textsuperscript{4} performed after injection of iodinated contrast material in a peripheral vein.

In the span of a few years, MDCT has experienced considerable technological advances, with the introduction of 2, 4 and, recently, 16 detectors. This last system has provided an appropriate degree of image resolution for analysis of the coronary arteries.\textsuperscript{7} The aim of this study was to determine the diagnostic usefulness of 16-detector MDCT for the detection and quantification of coronary artery lesions by comparison with conventional invasive coronary angiography.

PATIENTS AND METHODS

A total of 31 patients (28 men) with a mean age of 66 years (range, 37-79 years) were studied with MDCT. Previously, all patients had undergone clinically indicated invasive coronary angiography. Patients were consecutively selected for MDCT study, with no previous knowledge of coronary angiography findings. The interval between the 2 studies was short in the majority of cases, with a median of 16±52.6 days (range, 2-193 days).

All studies were performed on an outpatient basis. The exclusion criteria were as follows: atrial fibrillation, kidney failure, allergy to iodinated contrast agents, claustrophobia and inability to maintain an inspiratory breath-hold for at least 15 seconds. Among the group studied, the prevalence of hypertension was 58%, dyslipidemia 35%, smoking 56% and diabetes 23%. A history of myocardial infarction was present in 45%; 13% had undergone surgical coronary revascularization, and 38% had undergone angioplasty with stent implantation. The study was approved by the Ethics Committee of Hospital de la Santa Creu i Sant Pau.

Study Protocol

The scanner used was a Toshiba Aquilion\textsuperscript{®} 16, (Toshiba Corporation, Medical Systems Company), equipped with 16 detectors, completing a 360° rotation in 0.5 seconds, and able to acquire up to 32 0.5-mm thick axial slices in 1 second, thereby covering the entire cardiac volume within a breath-hold of less than 30 seconds.

The imaging protocol started with a scout view (image similar to a plain chest x-ray) to determine the limits of cardiac volume to be acquired, generally within the boundaries of the tracheal carina and the diaphragmatic domes. The settings for the irradiation used were adjusted by conventional methods according to the morphological characteristics of each patient: 120 kV x-rays with a tube current of 250 to 350 mAs. Slice thickness was adjusted to the duration of the inspiratory breath-hold each patient was able to maintain as determined by a prior test, and was set at 0.5 mm with a breath-hold greater than 20 seconds and 1 mm with a breath-hold less than 20 seconds.

The patients’ heart rates were between 47 and 105 bpm, with a mean of 60 bpm. No cardiovascular drugs were administered before the MDCT study, since the scanner’s segmentation system optimizes image reconstruction according to the spontaneous heart rate.

Contrast was administered by infusion pump through an antecubital vein to enhance the coronary arterial tree. Contrast volume was 120-150 mL of iobitridol (Xenetix\textsuperscript{®}) at a concentration of 300 mg/mL and infusion rate of 4-5 mL/s. Coordination between contrast administration and image acquisition was adjusted automatically by the scanner when arrival of contrast was detected at a region of interest located in the left atrium.

Acquisition of the cardiac volume images was continuous (helical) in all phases of the heart cycle, with simultaneous recording of an electrocardiogram (ECG). Reconstruction of the cardiac volume images was started at the end of acquisition, with the patient outside the scanner. The diastolic phase of the cardiac cycle, in which there is least motion artifact and best visualization of the cardiac arteries, was selected for the reconstruction. Retrospective segmented reconstruction, using an interval of 0.3 mm in studies with 0.5-mm slice thickness and a temporal resolution

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<th>ABBREVIATIONS</th>
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<td>MDCT: multidetector computed tomography.</td>
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of 80 ms, gave a cardiac volume comprised of 350-400 anatomical slices.

Analysis of the images was done on a workstation with dedicated software (Vitrea2®, Vital Images, Plymouth, MN), using the available tools: axial images (Figure 1A), oblique and curved multiplanar reformatted (MPR) reconstructions (Figure 1B), maximum intensity projections (MIP), and volume-rendered three-dimensional reconstructions (Figure 1C).

Each study was analyzed by 4 observers, 3 cardiologists from the Cardiac Imaging Section with experience in the interpretation of coronary anatomy by cardiac magnetic resonance (RL, FC, and GPL), and 1 radiologist with experience in non-invasive angiography and axial computed tomography (XA). Systematic coronary artery study was done with a 15-segment model that included all the large coronary arteries and their main branches. Coronary grafts were analyzed separately, with each one considered an independent segment. The following were determined by consensus among the observers: a) adequate or inadequate visualization of each coronary segment, as well as the reason for inadequate visualization, and b) presence and magnitude of stenotic coronary lesions, with those visually estimated to be more than 50% of the vessel lumen considered significant, using as reference the lumen area of the vessel segments adjacent to the stenosis. Quantitative estimates were not made because there is no method for comparison of MDCT measurements. Average duration of the interpretation of each study was 45 minutes.

In a separate analysis, coronary angiography was interpreted by 2 expert angiographers (JGP and JMA) who were blinded to the MDCT findings. Invasive coronary angiography was performed with a Philips Integris HM 3000® system (Philips Medical Systems, Netherlands) by conventional femoral artery puncture, coronary catheterization and injection of approximately 60 mL of iodinated contrast in the coronary ostia. Standard anteroposterior oblique and lateral angiographic projections were obtained and the presence of coronary lesions was determined and quantified by quantitative coronary angiography; lesions producing more than 50% stenosis were considered significant.

Statistical Analysis

The statistical analysis was based on determination of the sensitivity, specificity, and positive and negative predictive values for the detection of stenotic lesions. Overall sensitivity was calculated from the sum of all the segments with significant lesions on MDCT (of the 15 territories analyzed) as related to the sum of all the segments with significant lesions on invasive coronary angiography. Overall specificity was calculated from the sum of all the segments without significant lesions on MDCT as related to the sum of all the segments without significant lesions on invasive coronary angiography. The mean, standard deviation, standard error of the mean and 95% confidence interval (CI) were determined for all the parameters mentioned.

RESULTS

None of the patients studied experienced complications due to either invasive angiography or MDCT.

Invasive Angiography

All the coronary segments, including native vessels and coronary grafts (a total of 474 segments), were assessable by invasive coronary angiography. Angiography showed significant stenotic lesions in 83 segments (17.5%), and among these, 28 (5.9%) were occlusive lesions; 7 segments (1.5%) corresponding to a single patient were affected with a coronary anomaly (congenital fistula). Stents had been implanted in 12
TABLE 1. Prevalence of the Various Factors Preventing Evaluation of an Arterial Segment by Multidetector Computed Tomography*

<table>
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<th>Percentage</th>
<th>Coronary Segments Implicated</th>
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<tr>
<td>Extensive parietal calcification</td>
<td>3.8 (18/474) pLAD (1), mLAD (2), dLAD (3), D1 (2), pCx (1), mCx (2), OM1 (1), OM2 (1), pRCA (1), dRCA (1), PD (2), PLA (1)</td>
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<tr>
<td>Motion artifacts (respiratory, cardiac)</td>
<td>2.3 (11/474) mRCA (3), dRCA (1), PD (1), PLA (2), mCx (1), dCx (1), OM1 (2)</td>
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<tr>
<td>Reduced size of the vessel</td>
<td>2.9 (14/474) dLAD (2), dRCA (1), PD (1), PLA (2), dCx (4), OM1 (1), OM2 (2), D1 (1)</td>
</tr>
<tr>
<td>Artifact caused by stent</td>
<td>2.5 (12/474) LMC (1), pLAD (2), mLAD (2), pCx (2), dCx (1), OM1 (1), pRCA (2), mRCA (1)</td>
</tr>
<tr>
<td>Total of non-assessable segments</td>
<td>11.6 (55/474)</td>
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*RCA indicates right coronary; Cx, circumflex; LAD, left anterior descending; D1, first diagonal; PD, posterior descending; OM1, first obtuse marginal; OM2, second obtuse marginal; LMC, left main coronary; PLA, posterolateral artery; p, proximal segment; m, middle segment; d, distal segment.

segments (2.5%). The coronary grafts included 4 internal mammary artery to left anterior descending artery, all without lesions on invasive angiography, and 5 internal saphenous vein, 4 of which were occluded (3 to the first obtuse marginal and 1 to the right coronary artery) and 1 without lesions (to the first obtuse marginal).

Non-Invasive Multidetector Computed Tomography

Breath-hold time and image acquisition in the MDCT study lasted an average of 23 seconds (range, 15-34 s). Mean irradiation dose received by the patients during MDCT study was 24.2 mSv. Among the 31 MDCT studies, 23 (74%) were performed with 0.5-mm slice thickness and the remaining with 1-mm thickness, in keeping with the patients’ breath-holding capacity.

A total of 419 coronary segments were assessable by MDCT (88.4%). The reasons for classifying a segment as non-assessable are shown in Table 1. Among the 55 segments considered to be non-assessable by MDCT, coronary angiography had detected significant lesions in only seven (12.7%).

To evaluate the diagnostic performance of MDCT in the study of significant coronary lesions, defined as those producing >50% stenosis, the comparative analysis included 458 of the 474 segments assessed by invasive coronary angiography. Sixteen segments were excluded, 7 from the patient with coronary fistulas and 9 corresponding to coronary grafts, which were assessed separately. A total of 403 of the 474 initial segments evaluated by MDCT were considered valid for the analysis. In addition to the 55 segments with limited assessment (Table 1), we excluded the 7 corresponding to coronary anomalies and the 9 corresponding to coronary grafts, as was done for the invasive angiography studies.

The overall sensitivity and specificity of MDCT for the detection of significant stenotic coronary artery lesions was 75% (69.33±28.87; 95% CI, 54.21-84.46) and 91% (90.73±3.84; 95% CI, 88.72-92.75), respectively. Positive and negative predictive values were 65% (57.07±22.94; 95% CI, 45.04-69.09) and 94% (94.13±3.87; 95% CI 92.10-96.16), respectively. Table 2 summarizes the sensitivity and specificity analysis for each coronary artery and coronary artery segment, and the evaluation of these parameters in the groups of proximal, middle and distal segments, and main branches. Among the significant stenotic lesions, the subgroup of occlusive lesions (100% stenosis) was analyzed separately. The sensitivity and specificity of MDCT for the detection of occlusive coronary artery lesions was 64% (18/28 occluded segments; 46.4±43.98; 95% CI, 24.14-68.65) and 80% (44/55 non-occluded segments; 65.2±38.48; 95% CI, 45.72-84.67), respectively. In this subgroup, MDCT showed positive and negative predictive values of 62% and 81%, respectively.

Finally, in the small number of segments with coronary grafts analyzed (9 segments assessable with coronary angiography and 9 segments with MDCT), sensitivity and specificity were both 100% (Figures 2A-D).

DISCUSSION

Coronary angiography is the reference method for the assessment of coronary anatomy. Even though it is a safe procedure when performed by experts, coronary angiography is invasive by nature and is not without associated risks. This fact, together with its high cost, restricts the indications for its use.\(^8\) Considerable effort is now devoted to finding non-invasive alternatives for the study of coronary artery anatomy,\(^9,10\) particularly for application in preventive medicine, where invasive angiography is not used.

Multidetector-row computed tomography seems to have the appropriate characteristics to meet this function. The technique has already demonstrated a capacity for the detection and quantification of calcium deposit in the coronary arteries, providing prognostic value that goes beyond simple clinical
TABLE 2. Diagnostic Performance of Multidetector Computed Tomography for the Detection of >50% Stenotic Coronary Artery Lesions*

<table>
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<tr>
<th>LMC</th>
<th>Left Anterior Descending</th>
<th>Circumflex</th>
<th>Right Coronary</th>
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<tr>
<td>P</td>
<td>m</td>
<td>d</td>
<td>D1</td>
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| Sensitivity, % | 4/4 100 | 9/10 (90) | 5/6 (83) | 2/2 (100) | 6/7 (86) | 5/6 (83) | 3/6 (50) | 6/8 (75) | 0/2 (0) | 5/6 (83) | 10/11 (91) | 2/3 (67) | 2/5 (40) | 1/4 (25) |
| Specificity, % | 25/26 (96) | 19/21 (90) | 22/24 (92) | 24/29 (83) | 21/23 (93) | 22/24 (92) | 21/24 (91) | 19/22 (86) | 27/28 (96) | 23/25 (92) | 17/20 (85) | 26/28 (93) | 24/26 (93) | 25/27 |
| Overall sensitivity | 75% (82/108) | PPV 65% | NPV 94% |
| Overall specificity | 91% (341/375) |

*OX indicates circumflex; LAD, left anterior descending; RCA, right coronary artery; D1, first diagonal; PD, posterior descending; OM1, first obtuse marginal; OM2, second obtuse marginal; LMC, left main coronary; PLA, posterolateral artery; PPV, positive predictive value; NPV, negative predictive value; p, proximal segment; m, middle segment; d, distal segment. Results are expressed per coronary artery and per coronary artery segment assessed.

stratification by conventional risk factors. Moreover, because of recent technological advances in this field, it is now possible to obtain images that provide a close approximation to coronary angiography. There is relatively little experience with this technique and few comparative studies with invasive angiography are currently available. As in the study by Ropers et al., our experience has shown that 16-multidetector-row MDCT has a high diagnostic capacity when compared with conventional coronary angiography, showing a sensitivity of 75% and a specificity of 91% for the detection of coronary lesions producing more than 50% stenosis. In contrast to other studies, our analysis did not exclude assessment of distal coronary segments with a lumen diameter smaller than 1.5 mm and despite this fact, MDCT showed an acceptable positive predictive value of 65% and a high negative predictive value of 94% for the detection of significant coronary lesions. Detailed analysis of our results showed that MDCT provides high diagnostic yield in proximal and middle segments, portions of the vessels that are potentially accessible by interventional procedures, with a sensitivity higher than 87% and a specificity higher than 90% for the detection of significant lesions.

In contrast to what occurs with coronary angiography, the information provided by MDCT is not limited to a luminogram. The capability of MDCT to differentiate elements with a high calcium content from those with a high lipid or fibrous component allows a more precise analysis of the arterial wall and its lesions than that achieved with invasive angiography. These data, together with the non-invasive character of MDCT, make it an attractive option for anatomic study of coronary lesions. Because of its recent introduction in this clinical setting, the role of non-invasive coronary imaging in the diagnostic algorithms used in current cardiological practice has still not been defined. Nevertheless, on the basis of the favorable results from the present study and previous ones, it is possible to outline the clinical applications this technique will have in the near future. However, the precise limitations of coronary artery study by MDCT must first be considered.

The limitations of MDCT are imposed by factors that decrease the quality of the image to be analyzed, such as motion artifacts related to incorrect breath-holding, reconstruction in an inadequate phase of the cardiac cycle or frequent premature beats, image artifacts caused by the presence of highly calcified lesions or implanted vascular devices, or very small diameter of the vessel under study (Figures 3A-D). Another aspect encountered in our experience is the limited capacity of MDCT for the diagnosis of occlusive coronary lesions. In contrast to conventional coronary angiography, MDCT does not provide a dynamic analysis; that is, gradual filling of the coronary tree with contrast is not visualized during image acquisition. Instead, MDCT offers the “final image” of contrast distribution along the coronary system. This fact explains the lower sensitivity of MDCT in occlusive lesions. MDCT might underestimate the severity of an occlusive lesion in which the distal vessel is filled by retrograde collateral circulation. In our experience, the ten cases of occlusive lesions incorrectly diagnosed by MDCT were...
were diagnosed as significant lesions. This aspect limits the technique if a percutaneous coronary procedure is contemplated. Underestimation of an occlusive lesion might result in a decision to perform coronary angioplasty under conditions that make the procedure technically difficult or even unfeasible, particularly in cases of chronic occlusions. On the other hand, from the viewpoint of surgical coronary revascularization, the capacity of MDCT to visualize the vessel distal to the occlusion is advantageous, since patency of the distal vessel is a relevant condition in the decision to revascularize an occluded coronary territory.

In addition, the use of MDCT is limited in critical patients because of the difficulty involved in breath holding and the relatively lengthy time required for complete analysis of the study. Thus, it may not be a suitable technique for basing therapeutic decisions in these patients.

In the specific case of stents, patency of the stent can be determined by visualization of distal vessel opacification (Figures 3 C). However, the presence or absence of in-stent stenosis still cannot be determined, and there are few studies that clarify this aspect. Thus, in the present study, segments with implanted stents were considered non-assessable (Table 1).

Finally, the irradiation dose should be considered. Irradiation in the MDCT examination is higher than that of conventional coronary angiography, although strategies have been devised to optimize the degree of irradiation according to the requirements of the study.

Considering these limitations, the diagnostic capability of non-invasive coronary angiography by MDCT is generally good, but still lower than the invasive gold standard, as evidenced by our experience and that of other groups. Therefore, at the present, this diagnostic method still cannot replace invasive diagnostic coronary angiography in the cases in which this method is clinically justified. Detailed analysis of our results shows that this diagnostic limitation is more evident in the evaluation of distal coronary segments (Table 2), although the number of angiographic lesions in these segments was small in our series. It can be suggested, however, that a potential diagnostic error in the case of these coronary segments could have smaller clinical and therapeutic repercussions.

Our experience seems to indicate that MDCT has a prominent role in the study of coronary grafts. The larger diameter of these vessels, the fact that their movement in the cardiac cycle is smaller and the good quality of the images obtained (Figures 2C and D) are all factors that could contribute to the high diagnostic performance of the technique in these patients, both in our study, with a limited number of cases, and in others. The non-invasive nature of MDCT and the possibility to perform follow-up
studies confers an added value to the technique. Nevertheless, there is a potential limitation to MDCT in the study of coronary grafts. The proximal portion of internal mammary artery grafts was not included in the volume obtained with the protocol we used because of the duration of the breath-hold required, and therefore this segment could not be assessed. Nevertheless, clinical practice has shown that the percentage of obstructive lesions developing in the segments proximal to the internal mammary artery is very small.

This comparative study should be considered an initial experience. There is no doubt that the findings with respect to MDCT are promising, but the results of this technique may improve when the learning curve inherent to any newly incorporated diagnostic method is included in the analysis.

Despite these considerations, we believe that noninvasive coronary angiography by MDCT will occupy a major diagnostic role in several situations: screening for significant coronary artery disease in patients with cardiovascular risk who are not considered candidates for invasive coronary angiography; in patients requiring routine coronary study, as in preoperative workup for valvular cardiac surgery; and in studies to determine the patency of coronary grafts.

Our experience contributes to the knowledge of the diagnostic performance of MDCT applied to non-invasive coronary angiography with the presently available technology (16 detectors). It is to be expected that the rapid technological advances in this field will be accompanied by diagnostic improvements, as can be seen by comparing the present results with those described less than two years ago in studies using 4-detector scanners. The true diagnostic performance of the technique probably still remains to be defined, given the dynamic nature of the technology.

**CONCLUSIONS**

Anatomic study of coronary lesions by MDCT is feasible and allows assessment of 88% of the coronary segments. As compared to conventional angiography, the technique demonstrated a high diagnostic performance for the detection of angiographically significant coronary lesions, particularly in the proximal and middle segments of the large coronary arteries. Furthermore, MDCT seemed to demonstrate high diagnostic yield in the evaluation of coronary grafts.

The limitations of the technique are manifested when attempting to acquire adequate images during incorrect breath holding, when evaluating lesions with a high calcium content or in the presence of implanted coronary devices, and particularly when assessing distal coronary segments and occlusive lesions.

Altogether, the findings from this study indicate that a reliable non-invasive diagnostic technique for the study of coronary artery anatomy is now available.
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