Radiology: Cardiothoracic Imaging COMMENTARY

Ultra-High-Resolution Coronary CT Angiography: The "Final Frontier"—Are We There Yet?

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Coronary CT angiography (CTA) has emerged as a cornerstone for the noninvasive detection of coronary artery disease (CAD). Multiple recent clinical trials such as ISCHEMIA, SCOT-HEART, and PROMISE have paved the way for coronary CTA to be incorporated into the European Heart Guidelines (1). The strengths in diagnostic accuracy of coronary CTA have largely been driven by its high negative predictive value (NPV) and its ability to exclude obstructive CAD. However, its performance in the settings of coronary calcification, stent evaluation, and small (< 3 mm) vessel luminal assessment has been hampered largely due to limitations in spatial resolution of conventional energy-integrating detector (EID) technology. Blooming artifacts, beam hardening, and partial volume effects from dense calcification and stent struts have impaired visualization of the vessel lumen, especially for vessels measuring less than 2 mm in diameter. These limitations have restricted the application of coronary CTA in populations with known or advanced cardiovascular disease (2,3). As percutaneous intervention of small (< 3 mm) coronary vessels becomes feasible, there is growing impetus to overcome these limitations to translate the application of coronary CTA to populations with high pretest probability for disease, with the goal of providing a noninvasive alternative to invasive diagnostic angiography (4).

Since the introduction of CT in the 1970s, technological advancements in CT scanners have used multidetector arrays of EIDs to attain isotropic spatial resolution on the order of 400–450 µm. CT technical development from 2004 to 2012 increased the number of detector rows to 64, 192, or up to 320 and introduced dual-source technology, faster gantry rotation times up to 0.25 second, and new cardiac scan modes. No new CT hardware development has occurred over the past 9 years, until now.

Multiple factors, including x-ray tube focal spot size, matrix size, or reconstruction kernel algorithms, impact spatial resolution. However, one of the most effective methods to improve spatial resolution is by decreasing the size of the detector element. Ultra-high-resolution coronary CT (UHR-CT) by this method quadruples resolution, achieving a spatial resolution of 150–200 µm by reducing the detector element size to 0.25 × 0.25 mm compared with conventional models, which range from 0.4 mm to 0.625 mm. Since coronary luminal size is on the order of 1–5 mm in diameter, the amplification of spatial resolution can theoretically have a powerful effect on luminal evaluation. The only clinically and commercially available scanner to achieve this hardware advancement to date is the Aquilion Precision CT platform (Canon Medical Systems). Higher matrix reconstruction (1024 × 1024 and 2048 × 2048) combined with a substantial reduction in focal spot size (0.4 × 0.5 mm), thinner septae between detectors to improve dose efficiency, and model-based iterative reconstruction techniques to offset the expected effects on image noise and radiation dose, are all advantages of this design (5).

In this issue of *Radiology: Cardiothoracic Imaging*, Latina et al take an important step in actualizing the potential impact of advanced spatial resolution and its application to a patient population with advanced CAD. This prospective, single-center assessment of diagnostic accuracy enrolled 15 predominantly male patients with a mean age of 67 years ± 7 (standard deviation), with an average body mass index (BMI) of 29.2 kg/m^2 ± 4.9, including seven patients

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See also article by Latina et al in this issue. Conflicts of interest are listed at the end of this article.

with obesity (BMI ≥ 30 kg/m^2) and eight with prior stent placement (20 stents), who underwent both UHR-CT angiography as well as invasive coronary angiography (ICA) for suspicion of obstructive CAD between November 2019 and May 2021, with an 8-month interruption in enrollment due to the COVID-19 pandemic. To be eligible, participants had to have severe (> 50%) stenosis at prior coronary CTA or ICA, prior coronary stent placement, or a coronary calcium score higher than 400. UHR-CT angiography was performed between 48 hours and 30 days of ICA. Conventional CTA images within 30 days of enrollment were also incorporated into the analysis (6).

Despite the relatively small sample size and higher levels of image noise and subsequent impact on lower signal-to-noise and contrast-to-noise ratios, all studies were determined to be interpretable in a range in which diagnostic quality was maintained despite mild image artifact, with a mean image quality score of 4.3 ± 0.9 (range, 3–5 on a five-point scale). All UHR-CT studies were interpretable. Interreader agreement for UHR-CT was 83.8% for the ability to detect 70% or greater stenosis on a per-vessel analysis. Moreover, the results demonstrated a remarkably high sensitivity (86%; 95% CI: 65%, 97%) and specificity (88%; 95% CI: 77%, 95%) for UHR-CT versus ICA. The analysis included 86 analyzable vessel segments, including approximately 25% with 70% or greater stenosis, either with UHR-CT (*n* = 27 of 86) or ICA (*n* = 22 of 86). The examples provided illustrate how these gains in higher spatial resolution of UHR-CT can potentially help resolve luminal interpretation even in heavily calcified or stented vessels, with prospective value for small vessel assessment.

There are, to our knowledge, only two prior publications describing the application of this ultra-high-resolution EID scanner technology in patient populations. Motoyama et al evaluated 79 consecutive patients using UHR-CT and conventional CT with 102 calcified lesions and 79 stents (7) and demonstrated improved median stenosis grading and reduction in stent strut thickness and luminal diameter of UHR-CT compared with conventional CT. They included 59 participants who underwent ICA within 3 months of their UHR-CT evaluation and who had a median coronary artery calcium score (CACS) of 171 (interquartile range, 49–503), 17 of whom (29%) had a CACS of 400 or higher. On a per-patient basis, UHR-CT performed with a high diagnostic accuracy to detect severe (≥ 70%) stenosis at ICA (sensitivity 100%, specificity 80%) and had a positive predictive value (PPV) of 93.6% and NPV of 100%. The per-segment analysis showed similarly high sensitivity (100%), specificity (95.8%), and NPV (100%), with a slight reduction in PPV (79.5%). They were also able to demonstrate that 80% of stents with a diameter of 2.5 mm were evaluable with UHR-CT (7).

Takagi et al analyzed 38 patients suspected of having CAD who underwent ICA within 3 months of their UHR-CT examination. Thirty-two patients (84%) with 51 (45%) vessels and 65 (12%) segments had obstructive CAD as defined as coronary stenosis greater than or equal to 50% as demonstrated with ICA. Sensitivity of UHR-CT for the detection of obstructive disease per patient, vessel, and segment demonstrated similarly high sensitivity of 100%, 96%, and 95%, respectively. However, specificity was reduced at 67%, 81%, and 96%, respectively (8).

In spite of the prolonged interruption in enrollment caused by the COVID-19 pandemic and the resulting small sample size, the authors of the current study were still able to translate some of the technical advantages seen in UHR-CT from in vitro and phantom studies to the clinical cardiac sphere. These preliminary findings highlight the added precision and diagnostic accuracy of ultra-high-resolution technology in a group of patients with known obstructive CAD, elevated calcium score, and coronary stents. Additionally, the authors were able to achieve these results and demonstrate feasibility in patients with a substantially higher BMI compared with prior studies where the average BMI was substantially lower (22.9 ± 3.3 [7]; 25 ± 3 [8]). This was notwithstanding higher penalties in image noise and the absence of deep learning iterative reconstruction (DLIR) algorithms, which may have further improved image quality and reduced radiation dose.

Within the context of prior studies, this manuscript carries with it preliminary evidence that ultra-high-resolution techniques may fulfill current unmet needs in diagnostic accuracy facing conventional CT technology (9). Future studies will be needed to address whether these results can be reproduced in large multicenter populations. There remain notable challenges to routine adoption of UHR-CT technology, including limitations in temporal resolution, increased image noise, and limited coverage in z-direction that will need to be addressed. However, it is immediately, commercially available and directly translatable to patient care. Successive applications in DLIR will have the potential to further improve image quality by offsetting image noise and help mitigate the impact on radiation dose. With future refinements in UHR-CT technology, there is promise for improved patient risk stratification, plaque characterization, function flow reserve assessment, and microvascular disease assessment. Technological advancements may not only lead to improvements in the use of coronary CTA for disease detection but may also play a role in tracking progression or regression of disease as a useful surrogate target for treatment response. As the demand for improved diagnostic performance of coronary CTA in populations with high pretest probability of coronary disease increases, so will the demands on spatial resolution to approach that of invasive angiography. It still remains a part of the future and final frontier.

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References

1. Knuuti J, Wijns W, Saraste A, et al. 2019 ESC Guidelines for the diagnosis and management of chronic coronary syndromes. Eur Heart J 2020;41(3):407–477 [Published correction appears in Eur Heart J 2020;41(44):4242.].
2. Kruk M, Noll D, Achenbach S, et al. Impact of coronary artery calcium characteristics on accuracy of CT angiography. JACC Cardiovasc Imaging 2014;7(1):49–58.
3. Dai T, Wang JR, Hu PF. Diagnostic performance of computed tomography angiography in the detection of coronary artery in-stent restenosis: evidence from an updated meta-analysis. Eur Radiol 2018;28(4):1373–1382.
4. Silverio A, Buccheri S, Venetsanos D, et al. Percutaneous treatment and outcomes of small coronary vessels: A SCAAR report. JACC Cardiovasc Interv 2020;13(7):793–804.

5. Kwan AC, Pourmorteza A, Stutman D, Bluemke DA, Lima JAC. Next-generation hardware advances in CT: Cardiac applications. Radiology 2021;298(1):3–17.
6. Latina J, Shabani M, Kapoor K, et al. Ultra-high-resolution coronary CT angiography for assessment of patients with severe coronary artery calcification: initial experience. Radiol Cardiothorac Imaging 2021;3(4):e210053.
7. Motoyama S, Ito H, Sarai M, et al. Ultra-high-resolution computed tomography angiography for assessment of coronary artery stenosis. Circ J 2018;82(7):1844–1851.
8. Takagi H, Tanaka R, Nagata K, et al. Diagnostic performance of coronary CT angiography with ultra-high-resolution CT: Comparison with invasive coronary angiography. Eur J Radiol 2018;101:30–37.
9. Miller JM, Rochitte CE, Dewey M, et al. Diagnostic performance of coronary angiography by 64-row CT. N Engl J Med 2008;359(22):2324–2336.