Coronary Artery Disease Imaging

Summaries of Ten Seminal Papers

Inês Z. Cabrita, PhD¹; Francisca P. Figueiras, PhD¹; Fausto J. Pinto, MD, PhD²

¹CETERA - Academic Consulting Research Organization - Association for Research and Development of the Faculty of Medicine (AIDFM) - Lisbon - PORTUGAL
²University Hospital Santa Maria - Department of Cardiology - Lisbon Academic Medical Centre CCUL - Lisbon - PORTUGAL (e-mail: faustopinto@medicina.ulisboa.pt)


1. Multimodality cardiovascular molecular imaging, part II
   M. Nahrendorf and others.
   Circ Cardiovasc Imaging. 2009

2. Appropriateness criteria for cardiovascular imaging use in clinical practice: a position statement of the ESC/EACVI taskforce
   M. Garbi and others.
   Eur Heart J Cardiovasc Imaging. 2014

3. Outcomes of anatomical versus functional testing for coronary artery disease
   P. S. Douglas and others.
   N Engl J Med. 2015

4. Cardiovascular imaging practice in Europe: a report from the European Association of Cardiovascular Imaging
   P. Lancellotti and others.
   Eur Heart J. 2015

5. Echocardiographic chamber quantification in the era of multimodality imaging: beware of unintended consequences
   H. Feigenbaum.
   J Am Soc Echocardiogr. 2015

6. Low-dose CT coronary angiography with a novel IntraCycle motion-correction algorithm
   D. Andreini and others.
   Eur Heart J Cardiovasc Imaging. 2015

7. Prognostic value of coronary artery calcium scoring in addition to single-photon emission computed tomographic myocardial perfusion
   E. M. Engbers and others.

8. Workstation-based calculation of CTA-based FFR for intermediate stenosis
   M. Kruh and others.

9. Echocardiographic and fluoroscopic fusion imaging for procedural guidance: an overview and early clinical experience
   J. J. Thaden and others.

10. Diagnostic performance of the 3D bull’s eye display of SPECT and coronary CTA fusion
    T. Nakahara and others.

Selection of seminal papers by Fausto J. Pinto, MD, PhD
University Hospital Santa Maria - Department of Cardiology - Lisbon Academic Medical Centre - CCUL - Lisbon - Portugal

Highlights of the years by Sherri Smith, PhD
Publications office
Multimodality cardiovascular molecular imaging, part II


*Circ Cardiovasc Imaging*. 2009;2:56-70

Molecular imaging has the potential to impact cardiovascular medicine in several ways, including risk assessment, early disease detection, development of personalized and targeted therapeutic regimens, and monitoring of therapeutic efficacy and outcome. In addition to these direct implications, molecular imaging will affect clinical care indirectly by facilitating a more rapid development of novel pharmaceutics and improving the basic understanding of cardiovascular pathophysiology.

Nahrendorf et al summarized the available targeted imaging probes and the specific future applications of molecular imaging for the identification and evaluation of critical pathophysiological processes of the cardiovascular system. Novel imaging strategies for the evaluation of inflammation, thrombosis, apoptosis, necrosis, vascular remodeling, and angiogenesis were also included in the review. Nahrendorf et al also examined the role of targeted imaging for some cardiovascular diseases, such as atherosclerosis, ischemic injury, postinfarction remodeling, and heart failure, and the emerging fields of regenerative, genetic, and cell-based therapies.

Particular emphasis is placed on multimodal imaging, as these hybrid techniques promise to advance the field by combining approaches with complementary strengths and offsetting limitations. The routine application of molecular imaging in the management of patients with cardiovascular disease is likely very close to being achieved. Molecular imaging should develop further with appropriate education of the cardiovascular community and the increased availability of various hybrid-imaging systems (i.e., single-photon emission computed tomography [SPECT]/computed tomography [CT], positron emission tomography [PET]-CT, PET-magnetic resonance imaging [MRI]) that will facilitate quantification of molecular imaging agents. A number of challenges, however, stand in the way of realizing these promises. Current imaging systems have not been optimized for cardiac applications due to the inadequate correction for cardiac and respiratory motion and a lack of quantitative software for targeted agents. The full realization of the promise of cardiovascular molecular imaging will thus require an ongoing and concerted collaboration between industry and both the basic science and imaging communities.

“Smart” amplification strategies, comparative head-to-head analysis of markers, improved reporter performance, and improved hardware will enable the detection of minuscule or trace amounts of novel targets. These noninvasive and targeted approaches will need to be tested for their prognostic value, cost effectiveness, and potential long-term toxicity to translate these technological advances into improved patient care.
Interest from the scientific community is growing regarding the appropriate use of cardiovascular imaging techniques for diagnosis and decision making in Europe. A dedicated taskforce has been appointed by the European Society of Cardiology (ESC) and the European Association of Cardiovascular Imaging (EACVI) to develop appropriateness criteria for cardiovascular imaging use in clinical practice in Europe. Cardiovascular imaging is characterized by continuously evolving technology developments in all modalities. Therefore, assistance with the decision-making process regarding both the choice of imaging modality in a certain clinical scenario and the future development of availability at local, national, and European levels becomes crucial.

The appropriateness criteria involve the evidence, guideline-based criteria, and best practice–based criteria for the appropriate use of cardiovascular imaging modalities in clinical practice, which are meant to assist in the decision-making process. These appropriateness criteria will be developed to ensure the best use of diagnostic cardiovascular imaging resources for a given individual, the rational use of cardiovascular imaging resources for all individuals in need of diagnosis, the most efficient use of available funds for society, and the judicious implementation of evolving technology and evidence in clinical practice.

The determination of appropriateness criteria, updated at regular 3-year intervals, will start with the appointment of a panel of reviewers consisting of experts in each cardiovascular imaging modality and a voting panel. The panel will make a selection of clinical scenarios; review the evidence, guidelines, position papers, etc.; define indications; and assign an appropriateness score. For more information on the development process, please see Figure 1 from the paper by Garbi et al.

The appropriateness criteria, statement papers, educational material, supporting clinical implementation, and all related documents will be made available online and distributed actively to different entities (eg, European Commission, the European National Societies, Working Groups, and Associations). Additionally, web-based tools and applications will be developed to assist with the clinical decision-making process and the selection of an appropriate imaging test for a particular indication.

The appropriateness criteria will be patient-centered, facilitating the best use of cardiovascular imaging resources for an individual who needs a test, while encouraging the best use of material resources for the entire society, structured development of resources, efficient financial expenditure, and homogenization of care across Europe.

Eyesight has been restored in six patients using a new gene therapy technique; the tsetse fly genome sequencing project is complete after a 10-year multimillion dollar effort; and the length of a day for an exoplanet is measured for the first time
Outcomes of anatomical versus functional testing for coronary artery disease


Patients who have symptoms suggestive of coronary artery disease are often evaluated with the use of diagnostic testing, although limited data are available from randomized trials to guide care. The coronary computed tomography angiography (CCTA) technique is one possible tool that may reduce unnecessary invasive testing and improve patient outcomes. However, the impact of data from noninvasive vs invasive testing on the management of the disease and clinical outcomes is unknown. The PROMISE trial (PROspec-tive Multicenter Imaging Study for Evaluation of chest pain) was designed to compare health-related outcomes between CCTA and functional testing in patients presenting with symptoms of coronary artery disease that required further evaluation.

Douglas et al randomly assigned 10,003 symptomatic patients to a strategy of initial anatomical testing with the use of either CCTA or functional testing (exercise electrocardiography, nuclear stress testing, or stress echocardiography). The composite primary end point was death, myocardial infarction, hospitalization for unstable angina, or major procedural complications. Secondary end points included radiation exposure and invasive cardiac catheterization that did not show obstructive coronary artery disease.

The mean age of the patients was 60.8±8.3 years, 52.7% were women, and 87.7% had chest pain or dyspnea on exertion. The mean pretest likelihood of obstructive coronary artery disease was 53.3±21.4%. Over a median follow-up period of 25 months, a primary end point event occurred in 164 of 4996 patients in the CCTA group (3.3%) and in 151 of 5007 (3.0%) in the functional testing group (adjusted hazard ratio, 1.04; 95% confidence interval, 0.83 to 1.29, P=0.75). CCTA was associated with fewer catheterizations showing no obstructive coronary artery disease than functional testing (3.4% vs 4.3%, P=0.02), although more patients in the CCTA group underwent catheterization within 90 days after randomization (12.2% vs 8.1%). The median cumulative radiation exposure per patient was lower in the CCTA group than in the functional testing group (10.0 mSv vs 11.3 mSv), but 52.6% of the patients in the functional testing group had no exposure, so the overall exposure was higher in the CCTA group (mean, 12.0 mSv vs 10.1 mSv, P<0.001).

In conclusion, in symptomatic patients with suspected coronary artery disease who required noninvasive testing, an initial strategy of CCTA was not associated with better clinical outcomes than functional testing over a median follow-up of 2 years.
Epidemiology changes in cardiovascular disease and an aging population are expected to result in an increased need for cardiovascular imaging (CVI). However, reliable statistics on the use of CVI in Europe are lacking. The European Association of Cardiovascular Imaging (EACVI) and the European Society of Cardiology (ESC) Taskforce on CVI established the status of CVI use across Europe. In 2013, a survey with relevant information regarding CVI was sent to every national imaging/echocardiography society and working group. The survey was designed to assess existing education, training, certification and national accreditation programs, health care organizations, and reimbursement systems.

The percentage of countries with a national certification in CVI for cardiologists was different between imaging modalities. Transthoracic and transesophageal echocardiography were commonly certified techniques, and about one-third of the countries had a certification program for the other imaging modalities. The majority of national societies recommended the Imaging Taskforce of the EACVI (EACVI) certification, but one-fifth of the societies had their national certification system. Irrespective of the CVI modality, a national accreditation for centers/laboratories was not required for practice in most countries.

Overall, there were diverse country-specific regulations for performing CVI and a widespread lack of national certification/accreditation. However, the majority of countries recommended the EACVI certification and one-fifth of the countries applied it as a national certification. Cardiologists commonly performed echocardiography, but not computed tomography (CT), cardiovascular magnetic resonance imaging (CMR), or nuclear imaging. However, in most countries, medical imaging performance requires a specialist license (eg, cardiologist, radiologist, and a nuclear imaging specialist). Unexpectedly, a predefined period of training in CVI during specialization was absent in one-third of the countries. In addition, only a few countries offered official national certification guidelines to perform CVI examinations. Interestingly, the adherence to ESC/EACVI guidelines in CVI was reported in a high number of European countries.

Finally, the access to CVI examinations in the public health care system was marked by a long waiting period in some countries.

The current mapping of the practice of CVI techniques across Europe represents the first comprehensive project of the ESC/EACVI Taskforce on CVI. The report symbolizes a preliminary step for further data collection and networking with national imaging societies and working groups. In the future, direct comparisons among the different ESC countries should help standardize health care resources by promoting knowledge of their status and by bringing this information to the attention of all public authorities. It is the hope that such data collection will contribute to improved quality of care through a better use of resources (avoid unnecessary procedures and expenses) and a consequent reduction in the waiting time, thus increasing the availability of CVI.

The Japanese L0 Series maglev becomes the first train to operate at a speed of 600 km/hour; NASA’s MESSENGER spacecraft concludes its 4-year orbital mission over Mercury; and the opah is confirmed as the first warm-blooded fish.
Echocardiographic chamber quantification in the era of multimodality imaging: beware of unintended consequences

H. Feigenbaum

J Am Soc Echocardiogr. 2015;28:847-850

The primary purpose of the recently published upgrade to the guideline document for echocardiographic chamber quantification is to set standard measurements, labels, and orientations to improve the communication and standardization among all echocardiography laboratories both in the United States and in Europe. Another aim of upgrading the document was to integrate echocardiographic chamber quantification with other cardiovascular imaging modality categories, with a notorious effort to recognize echocardiography as part of the noninvasive cardiovascular imaging modalities. In this paper, Feigenbaum clearly emphasizes that as with all changes or “advances,” there are likely to be unexpected or unintended consequences, which has been the case for this modality.

An early effort to improve the communication and coherence between echocardiography and nuclear cardiology was to change echocardiography’s standard 16-segment wall motion scoring system by adding a 17th segment at the apex. Echocardiography representatives agreed to make the change so that the scoring would be compatible with the nuclear apical perfusion and multiple-gated acquisition scan for apical motion. However, it was later decided that due to recording specifications in echocardiography when using the 17-segment model to assess wall motion or regional strain, the 17th segment (the apical cap) should not be included.

Another effort was made to obtain standard echocardiographic segmentation labels and orientation so that they would be similar to those used in nuclear perfusion. Unfortunately, this was not possible, for example, it was not possible to standardize the labels for the right ventricle and the papillary muscle. Importantly, the back wall of the left ventricle, which had been labeled “posterior,” is now being labeled “inferior lateral” to make it compatible with nuclear cardiology. This change has caused some comprehensible controversy. Besides the desire to set standard measurements, labels, and orientation, there are likely to be significant differences between echocardiography and cardiac computed tomography and magnetic resonance.

Care must be taken with the concept of integrated and “consensus” multimodality imaging applications in the clinical setting.

Lokiarchaeota, a transitional form between Archaea and Eukaryotes, is discovered; the US Fish and Wildlife Service declares that the eastern cougar is extinct; and the first artificial ribosome is created.
Low-dose CT coronary angiography with a novel IntraCycle motion-correction algorithm in patients with high heart rate or heart rate variability


*Eur Heart J Cardiovasc Imaging.* 2015;16:1093-1100

While coronary computed tomography angiography (CCTA) has achieved good diagnostic performance, motion artifacts due to a high heart rate or high heart rate variability significantly affect the image quality of CCTA. As a result, a motion-correction algorithm has been developed. In this study by Andreini et al, the impact of this algorithm when used in conjunction with low-dose prospective ECG-triggering CCTA on motion artifacts, image quality, and coronary assessability was evaluated. Only one previous study assessed the diagnostic performance of the motion-correction algorithm in conjunction with retrospective ECG-triggering CCTA in a small patient population referred for transcatheter aortic valve implantation. A secondary aim of the study was to evaluate the diagnostic accuracy of CCTA performed with the motion-correction algorithm and standard reconstruction in comparison with invasive coronary angiography—the gold-standard imaging technique.

Of the 410 consecutive patients undergoing CCTA for suspected coronary artery disease who were considered for inclusion in this study, 120 patients with a prescanning heart rate >70 bpm or a heart rate variability >10 bpm during scanning irrespective of prescanning heart rate or both were selected. Mean prescanning heart rate and heart rate variability were 70±7 bpm and 10.9±4 bpm, respectively. Overall, the mean effective dose of radiation was 3.4±1.3 mSv, while a lower dose (2.4±0.9 mSv) was measured for padding of 80 ms. In a segment-based analysis, coronary assessability was significantly higher (P<0.0001) with motion correction (97%) when compared with standard reconstruction (81%) due to a significant reduction (P<0.0001) in severe artifacts (54 vs 356 cases, respectively). An artifact subanalysis showed a significantly lower number of motion artifacts and artifacts related to chest movement with motion correction (16 and 4 cases) than with standard reconstruction (286 and 24 cases, P<0.0001 and P<0.05, respectively).

In conclusion, this study showed that in a subset of patients with high prescanning heart rate, increased heart rate variability, and high mean maximum heart rate during scanning, CCTA with motion-correction reconstruction achieved good image quality, very high coronary assessability, and a lower radiation exposure.

The genes responsible for the 200-year lifespan of the bowhead whale are mapped; astronomers identify a method to determine a star’s age from how fast it spins; and an exoplanet with a gigantic ring system that is 200 times larger than that around Saturn is discovered
Prognostic value of coronary artery calcium scoring in addition to single-photon emission computed tomographic myocardial perfusion imaging in symptomatic patients


Single-photon emission computed tomography (SPECT) myocardial perfusion imaging is well established for the prognostic evaluation of patients with suspected coronary artery disease. However, this functional imaging modality is not able to detect nonflow-limiting coronary artery disease. The increased interest in using coronary artery calcium (CAC) to identify subclinical atherosclerosis has demonstrated a close correlation with atherosclerotic plaque burden. With the advent of combined SPECT and computed tomography cameras, it is possible to acquire both SPECT images and CAC scores in a single session.

Engbers et al investigated the prognostic value of CAC scoring as an adjunct to SPECT in a population who are at a low-to-intermediate-risk for stable coronary artery disease. A total of 4897 symptomatic patients with no history of coronary artery disease who were referred for SPECT and CAC scoring were included. Major adverse cardiac events were defined as late revascularization (>90 days after scanning), nonfatal myocardial infarction, and all-cause mortality.

The frequency of abnormal SPECT increased with higher CAC scores, from 12% in patients with CAC scores of 0% to 19%, 32%, 37%, and 50% among those with CAC scores 1 to 99, 100 to 399, 400 to 999, and ≥1000, respectively (P<0.001). During a median follow-up of 940 days (25th to 75th percentile, 581-1377), 278 major adverse cardiac events were observed, and the overall incidence of major adverse cardiac events was 2.3% per year. A stepwise increase in major adverse cardiac events was present with increasing CAC scores, both in patients with a normal SPECT result (annual event rate CAC score 0, 0.6%; CAC score ≥1000, 5.5%) and an abnormal SPECT result (annual event rate CAC score 0, 0.4%; CAC score ≥1000, 7.6%). After multivariate analysis, both SPECT results and CAC scores were independent predictors of major adverse cardiac events (CAC score ≥1000: hazard ratio, 7.7; P<0.001 and large perfusion defect on SPECT: hazard ratio, 3.7; P<0.001).

CAC score and SPECT are independent predictors of major adverse cardiac events in patients suspected of coronary artery disease. Our findings strongly support acquiring a CAC score in addition to SPECT in symptomatic patients to define the risk of events during follow-up better.
Workstation-based calculation of CTA-based FFR for intermediate stenosis


Coronary computed tomography angiography (CCTA) is a common diagnostic test indicated in patients with an intermediate probability of coronary artery disease. However, it often ends up in a diagnosis of intermediate coronary stenosis that leads to further functional testing. CCTA-based fractional flow reserve (CCTA-FFR) is an emerging method for the noninvasive functional diagnosis of coronary artery disease. This imaging technique is the result of the fusion of both an anatomical test and a computationally simulated surrogate of FFR, providing a “one-stop shop” diagnostic tool. Both method developers and clinicians pursue a better understanding of the technique and aim to compare the clinical value across different CCTA-FFR results.

Kruk et al conducted a study to evaluate the proportion of patients with intermediate coronary stenosis diagnosed on CCTA, who may be saved from any further testing due to the use of CCTA-FFR. The study involved determining the upper and lower CCTA-FFR thresholds that predict nonischemic and ischemic stenosis, respectively, (based on an invasive FFR cutpoint ≤0.80) with ≥90% accuracy, and subsequently determining the proportion of patients who fall between these thresholds.

A total of 90 patients were included in this prospective, single-center, cohort study, and 96 lesions were analyzed. The patients who underwent routine CCTA due to an intermediate probability of having a significant coronary artery stenosis and who had a CCTA diagnosis of at least one intermediate coronary stenosis (50% to 90% by visual estimation) in an artery ≥2 mm in diameter were scheduled to undergo invasive FFR within 6 months of the CCTA examination.

The study demonstrated that an invasive FFR ≤0.8 was observed in 41 of 96 lesions (42.7%). According to a Bland-Altman analysis, CCTA-FFR underestimated FFR by 0.01 and the 95% limit of agreement was ±0.19. The CCTA-FFR thresholds for which the positive and negative predictive values were each ≥90% (corresponding to an FFR ≤0.80) were >0.87 or <0.74, respectively, and they involved 49 lesions (51%) and 45 of the 90 patients. The authors concluded that this hybrid diagnostic approach (the prototype CCTA-FFR based on CCTA) may discriminate between ischemic vs nonischemic stenoses in around 50% of patients with an intermediate coronary stenosis, potentially saving them from further functional testing. Further studies are needed for the validation of the methodology in an independent multicenter cohort.
Echocardiographic and fluoroscopic fusion imaging for procedural guidance: an overview and early clinical experience


During the last few years, there has been an exponential growth in the novel percutaneous structural heart interventions developed to treat valvular and structural heart conditions through a transcatheter approach. Investigational device-based therapies, such as transcatheter aortic valve replacement, transcatheter mitral valve repair, left atrial appendage occlusion, and percutaneous paravalvular leak closure, have necessitated increased sophisticated imaging guidance that is not supported solely by fluoroscopy.

There has been increased interest in the multimodality imaging that has fueled the development of fusion imaging to facilitate procedural guidance. Echocardiographic and fluoroscopic fusion imaging combines the precise catheter and device visualization of fluoroscopy with the soft tissue anatomy and color flow Doppler information afforded by echocardiography in a single image. This type of fusion imaging allows for precise catheter manipulations under fluoroscopic guidance while visualizing critical tissue anatomy provided by echocardiography. Thaden et al elegantly review this emerging technology’s strengths, limitations, and potential clinical applications.

Image registration is the first step of fusion imaging, and it involves reorientation of one image (echocardiography image) to match the orientation of a second image (fluoroscopy). These fusion images are compatible with 2D echocardiographic imaging with or without color Doppler, simultaneous multiplane echocardiographic imaging, and 3D echocardiographic imaging.

Three-dimensional volume data sets can also be displayed as the complete volume of data, which can be cropped in the plane of the fluoroscopic image to display soft tissue anatomy relevant to the procedure or as a partial-thickness slice that can be moved from near to far and in the direction of the fluoroscopic beam. Procedure-specific considerations have been made concerning transseptal puncture, left atrial appendage occlusion, paravalvular leak closure, and transcatheter mitral valve repair.

In conclusion, echocardiographic guidance for transcatheter mitral valve repair is essential for procedural success and remains challenging in current clinical practice. As with many new devices and technologies, a learning curve is involved. In some cases, performing the imaging study while also manipulating the fusion imaging system can be a challenge. Furthermore, it would be interesting to know whether this technology and its accuracy will be important to improve the outcomes of patients undergoing structural procedures.

Oxygen is detected in the Martian atmosphere; a successful monkey head transplant is conducted; and a pregnant *Tyrannosaurus rex* is discovered
Myocardial perfusion single-photon emission computed tomography (SPECT) and coronary computed tomography angiography are distinct diagnostic imaging modalities that provide functional and anatomical information, respectively. SPECT/coronary computed tomography angiography hybrid imaging might be one of the forms that routine myocardial perfusion imaging will take because image fusion significantly improves detection of hemodynamically significant coronary lesions.

Nakahara et al developed a display method to present the fusion data of myocardial perfusion SPECT and coronary computed tomography angiography into a single image that they call the fusion-based bull's eye. A 3D display is mostly used when reviewing SPECT/coronary computed tomography angiography fusion images, although multidirectional interpretation is required to sweep the entire heart. Fusion-based bull's eye images are generated from 3D fusion data by determining a cardiac axis, adding a cylindrical object around the aortic root, obtaining a panoramic image from circumferential data of the 3D images, and converting it into a polar coordinate display image. The diagnostic performances between SPECT, conventional 3D fusion, and the fusion-based bull's eye as regards the presence of hemodynamically relevant coronary vessels were compared in 39 patients with abnormal SPECT findings.

Of an evaluated 105 coronary segments in 35 patients without coronary artery bypass grafting, SPECT showed 17 segments (16%) equivocal to determine hemodynamically relevant coronary vessels. The fusion-based bull's eye corrected the diagnoses of 5 segments, where SPECT provided a false-negative in 2 segments and a false-positive in 3 segments, with only 2 equivocal segments ($P=0.0017$).

The fusion-based bull's eye also revealed 4 culprit lesions in all 4 patients with coronary artery bypass grafting. There was no discordance between the fusion-based bull's eye and conventional 3D fusion.

DNA is sequenced in outer space for the first time; the second largest meteorite ever found is exhumed near Gancedo, Argentina; and Jemma Redmond, Irish biochemist and a pioneer of 3D bioprinting, dies at age 38.