

## SPECT/CT Fusion Imaging Integrating Anatomy and Perfusion of the Heart

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In the clinical setting, contrast coronary angiography (CA) is a widely accepted invasive imaging technique for the visualization of coronary anatomy. Pooled data in the subset of patients with suspected coronary artery disease undergoing diagnostic CA demonstrate that 20-40% of them are inconclusive for the documentation of hemodynamically severe atherosclerotic disease.<sup>1</sup> Another important issue is that, despite many technical advances in invasive CA, the definition of functionally relevant coronary stenoses by purely morpho-anatomical criteria remains controversial. Finally, CA is limited by its invasive nature and bears low, but nevertheless not negligible, rates of procedure-related mortality (0.15%) and morbidity (1.5%), as well as having a relatively high cost.<sup>2,3</sup>

With the availability of noninvasive computed tomography angiography (CTA), more patients –or even asymptomatic subjects– will undergo CTA, often in the absence of prior functional testing, thus increasing the potential for inappropriate use of percutaneous coronary intervention (PCI). It is likely that the simple documentation of the presence of plaque, also visible to the patient, will be deemed sufficient to trigger coronary stenting, irrespective of symptomatic status, functional significance of the stenosis, or any form of prognostic evaluation.

Currently applied workup strategies

recommend that patients with suspected or probable coronary artery disease (CAD) should undergo noninvasive evaluation for diagnostic and prognostic stratification purposes. In patients with known CAD, extensive data support the use of ischemia testing or viability testing (or both) regarding the need to consider revascularization. Stress rest single-photon emission computed tomography (SPECT) is a well-established imaging method for evaluating the presence and extent of hemodynamically significant coronary artery disease, further improved by the introduction of gated studies.<sup>4</sup> Although the diagnostic performance of SPECT is excellent for the detection of any significant CAD on a “per-patient” basis, it appears that knowledge of flow reserve would greatly augment its value.

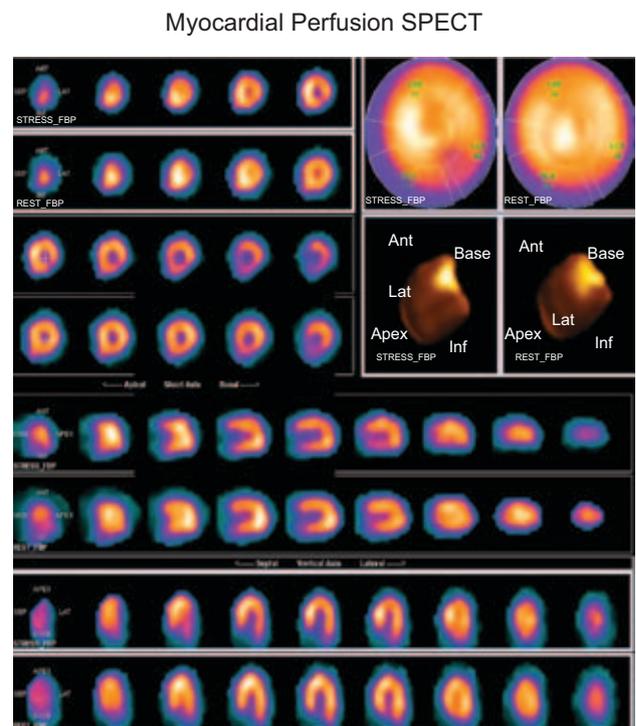
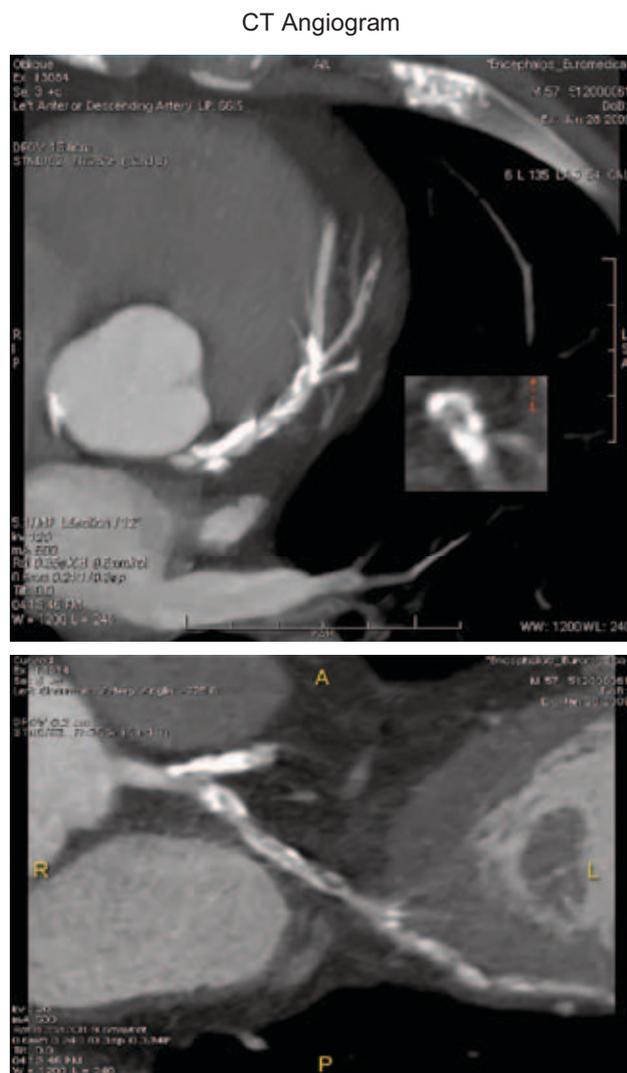
In this context, the potential superiority of stress positron emission tomography (PET) over SPECT may lie in its ability to routinely acquire flow reserve data in all patients. Accordingly, although myocardial perfusion imaging (MPI) may be superior to CTA as a gatekeeper to the catheterization laboratory, this superiority may necessitate the use of PET as the MPI approach.

In response to the need for accurate identification of the extent and severity of inducible ischemia in patients with multi-vessel disease, a hybrid approach that combines SPECT or PET with CTA is being developed.<sup>5,6</sup>

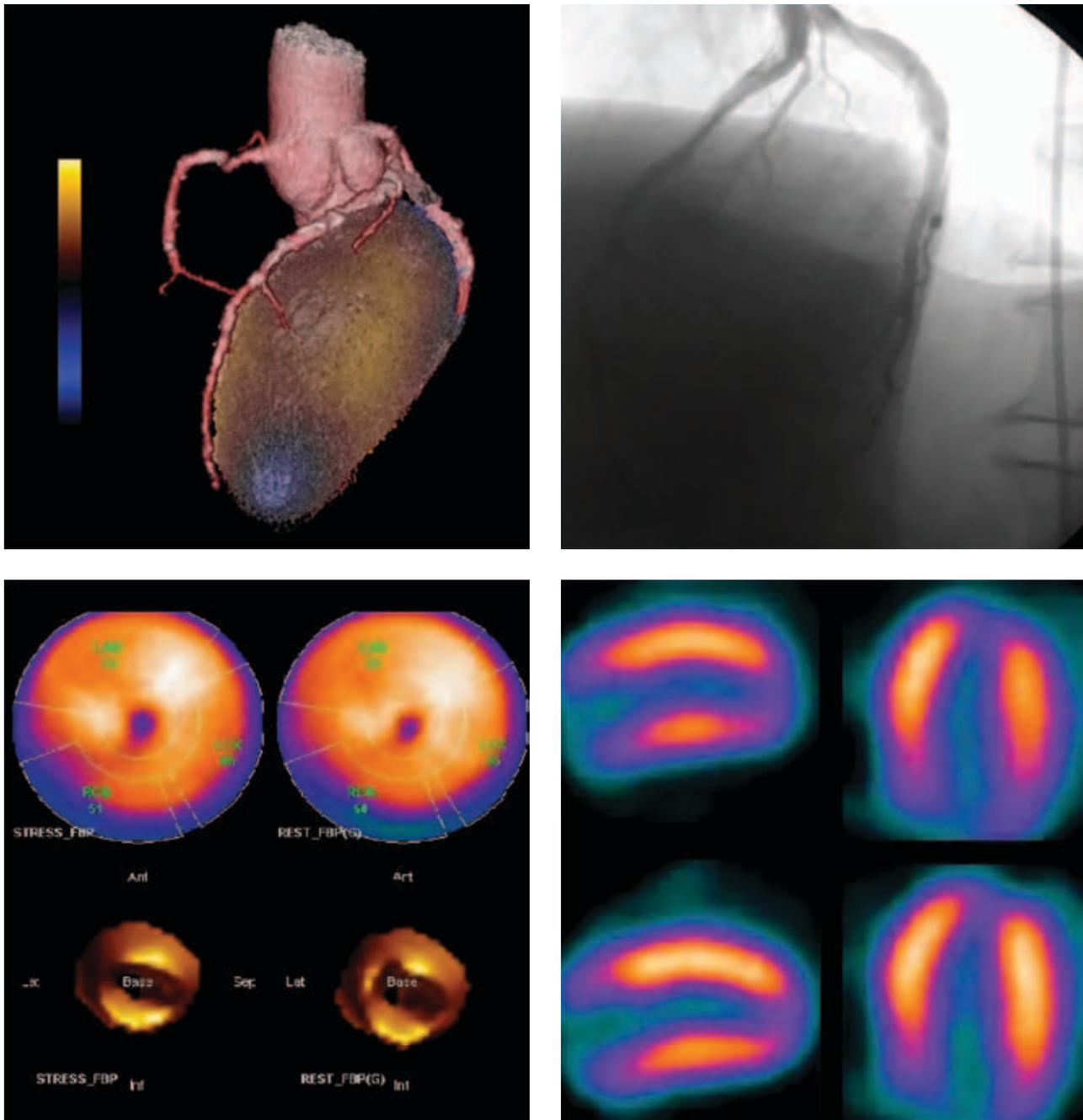
Fused and hybrid imaging of SPECT or PET myocardial perfusion imaging and CTA datasets, either as a single unit or as a software-based integration from non-dedicated standalone scanners, can provide a simultaneous noninvasive assessment of coronary anatomy and myocardial perfusion that can overcome the drawbacks of each technique performed separately. Hardware-based image co-registration permits the acquisition of co-registered anatomical and functional images, using hybrid scanners with the capability to perform nuclear and CT image acquisition simultaneously while the patient remains immobile. Image fusion is performed fully or semi-automatically. With software-based co-registration, image datasets can be obtained separately, from non-dedicated, commonly used scanners, potentially on different dates, and can be fused manually using novel software. The ratio-

nale for the development of the fusion technique is based on the assumption that not all coronary artery stenoses are flow-limiting, while perfusion imaging often falls short in patients with multiple stenoses, with a proportion of cases showing normal MPI results and other studies failing to identify less critical but significant stenoses (Figure 1).<sup>7</sup>

This combined approach offers several advantages compared to a single modality approach: more appropriate selection of patients who may benefit from revascularization procedures; calcium scoring, which has incremental prognostic value; and attenuation correction, which limits false positive perfusion results. Furthermore, with the integration of PET and CT into hybrid PET/CT scanners, the diagnostic potential is expanded in that balanced reduction can be identified by deficits of flow, despite normal perfu-



**Figure 1.** SPECT<sup>99m</sup>Tc-tetrofosmin myocardial perfusion and CT coronary angiography images in a patient with suspected coronary artery disease. Rest and stress myocardial perfusion SPECT images are essentially normal. The coronary anatomy was left-dominant (images not shown). The CT angiogram demonstrates extensive calcification of the dominant left coronary artery, with a short segment of heavily calcified plaque in the distal left main coronary artery. The inset shown in the panel on the upper left is a cross section through the left main coronary artery, suggesting moderate calcified luminal stenosis.



**Figure 2.** Example of a 59-year-old man with a history of a “cardiac event” in the past. Upper left panel: fusion imaging with atherosclerotic lesions in all 3 vessels and occlusion of the second diagonal artery, whose distribution shows an apical perfusion defect. Upper right panel: conventional coronary angiography confirms the finding. Lower panel: quantitative and qualitative results of the SPECT study are consistent with the above.

sion. Newer techniques can extend this approach by demonstrating the extent of reductions of flow reserve on a segmental basis, using a conventional polar map approach. A hybrid imaging approach may help to identify those patients with abnormal endothelial function, microvascular disease, and other vascular

pathologies that in the past could not be identified by SPECT techniques alone.<sup>8</sup>

At present, PET/CT hybrid scanners have been used for whole-body imaging, predominantly in oncology. Their use for cardiac hybrid imaging is limited by organ-specific characteristics and the high cost

associated with their installation and maintenance.

Similarly, SPECT/CT hybrid scanners reveal several drawbacks that may influence optimal image quality. The non-gated dataset used for SPECT acquisition may cause a slight mismatch of ventricular size between CT and SPECT images. The position of the heart is highly susceptible to respiratory motion; whereas CT acquisition is obtained during single respiratory breath hold, SPECT images are acquired during normal breathing.

Given all the above, accurate hybrid imaging to integrate and correlate functional and anatomical data with SPECT/CT is most efficiently achieved by dedicated cardiac fusion software acting on data acquired from separate devices. Until now, published data have demonstrated an excellent interobserver reproducibility, short processing duration and a marked increase in specificity and positive predictive value.<sup>9,10</sup> Preliminary data from our laboratory suggest that three-dimensional fused SPECT/CT images from standalone devices in as many as 75% of the studied population show a match of coronary anatomy and myocardial perfusion, with 37% showing perfusion defects corresponding to non-obstructive coronary atherosclerosis (both calcified and non-calcified plaques) (Figure 2).<sup>11</sup>

Our results also lend credence to the relevant literature, advocating the low radiation exposure achieved by the ECG-retrospective gating program (Snapshot technique) of the CT. The mean effective radiation dose was 3.5-6 mSv (mean dose 5.5 mSv) for CTA (including calcium scoring) and  $6 \pm 0.2$  mSv for SPECT, favoring a low heart rate  $62 \pm 3$  bpm and body mass index ( $29 \pm 4$  kg/m<sup>2</sup>).<sup>12</sup>

### Limitations to be resolved

The application of the novel software is at present feasible only for data acquired from specific scanners, the length of time required to process the image is quite long, and the superimposition of SPECT segments onto cardiac CT anatomy needs experience to avoid erroneous allocations of perfusion defects and coronary artery territories. Furthermore, there are important shortcomings in the quantitative assessment of coronary stenoses on CTA. Finally, to reduce radiation exposure, prospective tube current modulation is used, which allows a reduction in radiation exposure of approximately 50% but precludes the use of end-systolic phases for ventricular functional information.

### Conclusion

The integration of SPECT/CT and PET/CT technology allows the acquisition of anatomical and function information, detection and quantification of the burden of the extent of calcified and non-calcified plaques, and immediately obtains CT information for attenuation correction. Software-based integration of images acquired from standalone devices is a promising alternative to hybrid devices, offering high accuracy, low cost and low radiation exposure for patients.

The major challenge for future developments will be to identify which patients will benefit from a combined hybrid approach, as opposed to a single modality approach with stepped testing. It will also provide clinicians with a new tool for the exploration of the very early and late phases of cardiac diseases and will continue to play a major role in research, particularly in molecular imaging and the detection of vulnerable plaque.

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