

## Hybrid cardiac imaging: More than the sum of its parts?

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The constant technological developments in noninvasive cardiac imaging over the past few decades have contributed toward our pathophysiologic understanding of many conditions. Particularly in coronary artery disease (CAD), management is based on the assessment of both the presence of coronary stenoses and their hemodynamic consequences.<sup>1,2</sup> Hence, noninvasive imaging helps guide therapeutic decisions by providing complementary information on coronary morphology and on myocardial perfusion and metabolism, using several imaging tools.<sup>3,4</sup> This imaging includes nuclear techniques such as single-photon emission computed tomography (SPECT) or positron emission tomography (PET), computed tomography (CT) techniques such as electron-beam CT (EBCT) or multislice CT (MSCT), and cardiac magnetic resonance (CMR).

Advances in image-processing software and the advent of hybrid scanners have paved the way for the fusion of image datasets from different modalities, giving rise to multimodality or hybrid imaging. This technology avoids the mental integration of functional and morphologic images, and facilitates a comprehensive interpretation of combined datasets. The interest in hybrid imaging has rapidly spread to cardiac applications, and has changed the landscape of noninvasive cardiac imaging by bringing different clinical specialties (eg, cardiology, radiology, and nuclear medicine) closer together.<sup>5</sup> In addition, this interest has driven the development and production of dedicated hybrid scanners in an effort to simplify image coregistration and improve patient throughput for specialized cardiac imaging centers (ie, hardware-based image coregistration). However, given the high costs associated with such devices, an attractive alternative for hybrid imaging consists of the “offline,” software-based fusion of images obtained from nondedicated standalone scanners (software-based image coregistration). Here, we focus on comparing hardware-based versus software-based image coregistration for car-

diac hybrid imaging and their respective advantages and drawbacks.

### WHAT IS CARDIAC HYBRID IMAGING?

The hallmark of hybrid imaging is the combined or fused imaging of two datasets, where both modalities contribute equally to image information. However, the term “hybrid imaging” has been used in other contexts, raising confusion about its exact meaning.

Some authors have referred to the X-ray-based attenuation correction of myocardial perfusion imaging (MPI) as hybrid imaging.<sup>6</sup> However, in such a setting, CT images do not provide added anatomical or functional information, but are used merely to improve the image quality of the other modality (ie, PET or SPECT). In fact, whereas attenuation correction by <sup>68</sup>Germanium sources, as used in the previous generation of PET scanners, provided the same information, such imaging was not perceived as hybrid, probably because attenuation correction does not contribute to topographic image information. Similarly, the parametric maps obtained from low-dose CT do not provide image information beyond that needed for attenuation correction.<sup>7,8</sup> Others used the term “hybrid imaging” for the mere side-by-side analysis of MPI and CT images.<sup>9</sup> To avoid confusion, we suggest the use of “hybrid imaging” to describe any combination of structural and functional information beyond that offered by attenuation correction or side-by-side analysis, by fusion of the separate data sets into one image (Figure 1). Thus, this definition would not include attenuation-corrected images without integrating anatomical information. Similarly, the separate acquisition of structural information as well as functional data (eg, perfusion) on two separate scanners or on one hybrid device would allow a mental integration of side-by-side evaluation, but only a fusion of both pieces of information would result in a hybrid image.

### INTEGRATED SCANNERS VERSUS SOFTWARE FUSION

The added value of hybrid imaging involves the spatial correlation of structural and functional information on the fused images, which facilitates a comprehensive interpretation of coronary lesions and their pathophysiologic relevance. For cardiac applications, a three-

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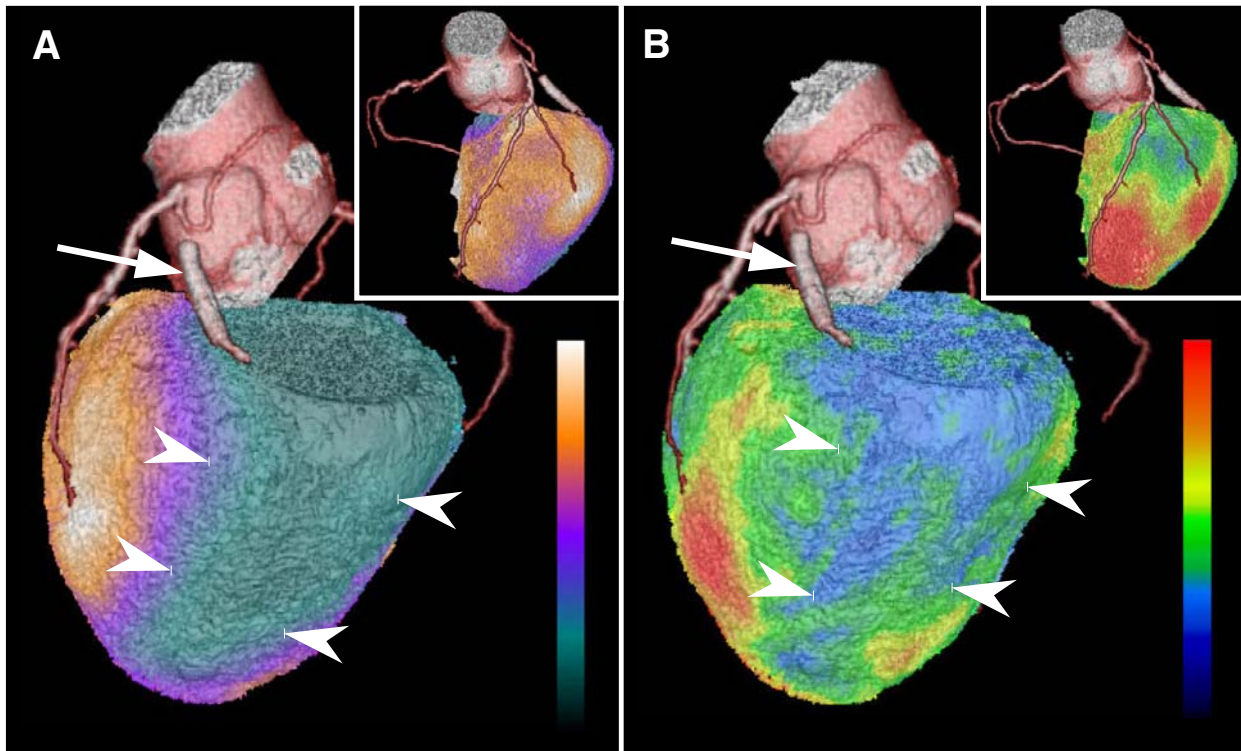
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**Figure 1.** *A*, Three-dimensional (3D) volume-rendered (VR) fusion image generated from computed tomography (CT) angiography and myocardial perfusion SPECT with  $^{99m}\text{Tc}$ -tetrofosmin at rest. Arrow denotes an occluded stent in the proximal left circumflex artery (LCX), and arrowheads demarcate the associated myocardial scar. Inset: Anterior view shows normal perfusion of the anterior wall. *B*, A 3D VR fusion image of the same patient as in *A*, generated from CT angiography and PET with  $^{18}\text{F}$ -fluoro-deoxyglucose. Arrowheads indicate a lack of viability in the posterolateral scar, associated with occlusion of the LCX-stent (arrow). Inset: Anterior view shows normal metabolism of the anterior wall.

dimensional display of fused images (generated by a volume-rendering technique<sup>10</sup>) is of greater value compared with oncologic or neurologic applications, because it allows the best evaluation of myocardial territories and their respective serving coronary-artery branches. Thus, an important prerequisite of hybrid imaging comprises accurate image coregistration, because misalignment may result in erroneous allocations of perfusion defects and coronary-artery territories.

From a computational perspective, image coregistration can be achieved by a software-based or hardware-based approach.<sup>11</sup> Hardware-based image coregistration permits the acquisition of coregistered anatomical and functional images using hybrid scanners (such as PET/CT or SPECT/CT devices), with the capability to perform nuclear and CT image acquisition almost simultaneously with the patient's position fixed. Inherently, image fusion is performed fully or semi-automatically by superposition of image datasets. With software-based coregistration, image datasets can be obtained on standalone scanners, and fused manually through the use of

landmark-based coregistration techniques. Intuitively, the hardware-based approach appears preferable, because manual coregistration may be hampered by issues of accuracy and user interaction. Thus, to date, hybrid PET/CT devices have been widely used for whole-body PET/CT imaging, predominantly in oncology.

However, in contrast to whole-body PET/CT, the routine use of fully automated, hardware-based image coregistration for cardiac hybrid applications is limited by organ-specific characteristics. Despite fixation of the patient's position and orientation, minor beat-to-beat variations in the heart's position may interfere with accurate image coregistration. Furthermore, CT image acquisition and analysis require electrocardiographic gating, and images are generally reconstructed in mid-diastolic phases to obtain optimal image quality.<sup>12</sup> By contrast, to ensure sufficient quality of SPECT images, a nongated dataset is used, resulting in a slight mismatch of ventricular size between CT and SPECT images. Finally, the position of the heart is highly susceptible to respiratory motion. Whereas a CT scan is performed

during a single inspiratory breath hold, SPECT images are acquired during normal breathing, without accounting for respiratory motion unless respiratory gating is conducted. In fact, whole-body PET/CT studies showed significant misalignments of the heart between superimposed PET and CT images acquired during inspiration.<sup>13,14</sup>

These factors contribute to the notion that, despite the integration of high-end CT devices (with the capability to perform state-of-the-art coronary CT angiography) with nuclear scanners to form dedicated cardiac hybrid scanners, manual-image coregistration may remain indispensable. Published reports on X-ray-based attenuation correction indicate that automated coregistration of CT and SPECT images is often unreliable, and manual correction for misalignment is needed in the vast majority of cases.<sup>7,15</sup> Dedicated cardiac fusion software packages are now commercially available, allowing software-based hybrid imaging with excellent interobserver reproducibility and short processing durations.<sup>16</sup> The full integration of these fusion software packages into regular post-processing applications for CT angiography will allow users to further minimize time expenditure and improve workflow for hybrid imaging by avoiding repeated actions, such as coronary-artery tracking from CT angiography images.<sup>16</sup>

### DO WE NEED HYBRID SCANNERS FOR HYBRID IMAGING?

Despite the widespread use of coronary CT angiography and MPI with SPECT or PET, both techniques vary considerably in their image-acquisition times. Whereas CT coronary angiography with the newest generation 64-slice or dual-source CT devices is performed in <12 seconds,<sup>12</sup> emission scans for stress-and-rest gated SPECT with <sup>99m</sup>Technetium-based radiotracers at standard doses take at least 45 minutes.<sup>17</sup> This discrepancy between emission and transmission scan times determines that high-end CT facilities constituting the CT component of hybrid cardiac scanners will be blocked by long emission scan times, and therefore will operate at low capacity. Many advances in nuclear medicine, such as newly developed dedicated cardiac detectors systems<sup>18</sup> and novel image reconstruction algorithms,<sup>19</sup> may contribute to reduce emission scan times considerably. However, to date, in hybrid scanners with high-end CT facilities, the rather long emission scan times preclude operating the high-end CT device at full capacity. In addition, despite the promise of hybrid cardiac imaging, the first clinical experiences with hybrid SPECT/CT imaging showed that in a typical population referred for a noninvasive workup of CAD, only a minority benefited from hybrid imaging, compared with side-by-side interpretation of MPI and CT.<sup>3</sup> Thus, at

present, from the standpoint of patient throughput, a dedicated cardiac hybrid scanner is less profitable than two standalone devices for normal-volume nuclear diagnostic centers. Nonetheless, it will depend on the individual setting of each institution to determine the type of approach (ie, software-based fusion or hybrid scanner) that is best tailored for its particular purpose, and highly specialized cardiac centers may prefer hybrid scanners for integrative cardiac imaging.

### FUTURE PERSPECTIVES

Atherosclerotic disease accounts for the majority of fatalities reported in industrialized countries. Despite major advances in the treatment of CAD patients, a large number of victims of the disease who are apparently healthy die suddenly without prior symptoms. The recognition of the role of vulnerable plaque has opened new avenues of opportunity in the field of cardiovascular medicine.<sup>20</sup> Hybrid technology has the unique potential to enable the detection and quantification of the burden of calcified and noncalcified plaques, the quantification of vascular reactivity and endothelial health, the identification of flow-limiting coronary stenoses, and potentially, the identification of high-risk plaques by using a fusion of morphology and biology with molecularly targeted PET imaging.<sup>21</sup> By such means, in the future, hybrid imaging may allow for the easy and comprehensive noninvasive assessment of coronary plaque burden, its pathophysiologic relevance, and biological plaque activity, thus providing accurate individual risk estimates, on which further management decisions can be based.

At present, however, accurate hybrid imaging to integrate and correlate functional and anatomical data is most efficiently achieved by the software fusion of data acquired on two separate scanners. Thus, integrated scanners are nice to have, but are not a must for hybrid imaging.

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