Hybrid quantitative imaging: Will it enter clinical practice?

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INTRODUCTION

Myocardial perfusion imaging (MPI) with either PET or SPECT is an important imaging modality for the diagnosis of coronary artery disease (CAD). More recently, CT angiography (CTA) has rapidly emerged as a potentially competitive method for evaluating patients with CAD. However, these techniques depict two different aspects of the disease. CTA examines the pathology of the coronary vessels (stenoses, plaques), while MPI allows assessment of blood perfusion in the left ventricle. Both modalities are routinely available for the evaluation of the cardiac patients. Sometimes they can be even available in a hybrid hardware configuration—equipment extensively used in the oncological field. In the last decade, there have been several reports of the synergistic value provided by the hybrid imaging (either by hybrid scanners or by fusion of standalone scans) in cardiology. Nevertheless, cardiac hybrid imaging has not yet entered routine clinical practice.

HYBRID CTA-MPI STUDIES

Several studies to date have demonstrated the improved diagnostic performance of combined MPI–CTA imaging as compared to either modality alone (Table 1). Most of these reports demonstrate explicitly or implicitly the value of fused display as compared to mere ''side-by-side'' use of the two modalities. This benefit has been shown for both the analysis of relative MPI defects and for the quantitative absolute blood flow analysis by PET. The majority of recent studies of hybrid CTA and MPI, including recent large multicenter study,[1] did not utilize automatic fusion process, potentially increasing the review time and introducing additional subjectivity to the final interpretation. Nevertheless, the spatial registration of CTA with PET [2] or SPECT [3] can be fully automated, even if these datasets are obtained on separate scanners, relieving the operator from tedious and subjective alignment process. It has also been demonstrated that fused CTA could be used to guide MPI contour placement (in particular valve plane position), resulting in improved quantitative accuracy of MPI.[3] However, the fused display to date was primarily used only for visual analysis, to assign the perfusion defect to correct vascular territory (improving per-vessel quantitative analysis), or to reject potentially artefactual perfusion defects without corresponding vascular abnormality. Mental integration schemes have been proposed for the observer to combine the CTA and MPI information during image interpretation. Typically, the vessel is considered abnormal only when a significant visual stenosis on coronary CTA is detected in combination with a perfusion or flow abnormality in the region of the corresponding vessel.[4]

QUANTITATIVE HYBRID IMAGING

In this issue of Journal of Nuclear Cardiology Piccinelli et al[11] propose a novel quantification scheme for hybrid MPI and CTA imaging. They extracted CTA image surfaces, reconstructed paths and lumens of main coronary arteries, and automatically fused such surface image with perfusion information from MPI. Subsequently, they defined a quantitative parameter they termed ''myocardium at risk'' (MAR), which can be derived from CTA-alone, MPI-alone, or from both CTA and MPI (fused MAR). The physiological MAR measure was derived using familiar blackout maps with their quantitative MPI software. The anatomic

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Table 1. Studies demonstrating the improved diagnostic performance of hybrid CT angiography (CTA) and myocardial perfusion imaging

	N	Modality	Reference standard
Rispler et al[5]	56	Hybrid SPECT/CTA	ICA
Slomka et al [3]	35	Standalone CTA + SPECT	ICA
Gaemperli et al[6]	38	Standalone CTA + SPECT	ICA
Kajander et al[7]	107	Hybrid PET/CTA	ICA + FFR
Santana et al[8]	50	Standalone CTA + SPECT	ICA
Schaap et al[9]	98	Hybrid SPECT/CTA	ICA + FFR
Danad et al[4]]	120	Hybrid PET/CTA	ICA + FFR
Schaap et al[10]	205	Hybrid SPECT/CTA	ICA + FFR
Liga et al[1]	252	Standalone CTA + SPECT/PET	ICA + FFR

ICA invasive coronary angiography, *FFR* fractional flow reserve

MAR was defined purely from CTA, as a myocardial region potentially affected by a given coronary stenosis (as identified visually on CTA), based on the geometric proximity of the region to the downstream portion of the obstructed vessel. Finally, fused MAR was defined as the surface intersection of the anatomical and physiological regions at risk. The authors evaluated the diagnostic performance of these parameters by comparison to invasive angiography in 47 patients (excluding about 10% of patients due to technical reasons). Despite a relatively small cohort, they showed significant per-vessel diagnostic performance increase for the detection of obstructive stenosis by fused MAR, as compared to either anatomical MAR or physiological MAR. However, the sample was too small to show significant per-patient improvements.

The unique aspect of the study by Piccinelli et al,[11] in comparison to all the previous studies in Table 1 is that the authors derive quantitative rather than qualitative measures from the fused display, by calculating a potentially affected myocardial region and intersecting it with perfusion abnormality. Although in their study, the initial stenosis detection and grading on CTA was interactive, this step could be presumably automated, and thus the proposed quantitative parameter-MAR could conceivably be derived in a fully automated manner.

Some limitations of work by Piccinelli et al[11] should be highlighted. Although the study employed quantitative measure, several manual steps were required. It seems that especially limiting was the need for the physician to manually grade the stenosis and interactively identify its location on the vessel graph. It would have been more practical, if CTA lesions were found and graded automatically. Methods for such analysis have been proposed.[12] Authors utilize invasive coronary angiography as the gold standard for the ''myocardium at risk''; however, the limitations of invasive coronary angiography are well known. Fractional flow reserve measurements (FFR) are potentially better suited as a reference standard. Nevertheless, FFR estimates the functional impact of stenosis in large vessels only, and may not correspond to perfusion defects depicting the final microvascular perfusion. Another limitation is the rather rudimentary CTA information (visual stenosis grade only) utilized in the study by Piccinelli et al.[11] It is likely that inclusion of variables such as plaque volumes [13] and contrast drop through the lesions (to avoid difficulties associated with heavily calcified lesions),[14] derived from coronary CTA could further improve the CTA diagnostic accuracy. It remains to be seen if MPI would still provide sufficient added value in assessing CAD, if such enhanced CTA information is also considered.

HYBRID IMAGING IN ROUTINE CLINICAL PRACTICE?

To date, hybrid cardiac imaging has not been routinely used in most institutions due to additional complexity, time, expense, increased radiation dose, as well as lack of automation in the interpretation of the results. These barriers need to be overcome before hybrid imaging enters routine clinical practice. Objective quantitative analysis of hybrid data will be a key factor, crucial for the clinical acceptance. The study by Piccinelli et al[11] partially addresses this limitation by developing a combined quantitative parameter, capturing information from both scans. Potentially, other methods for integrating the imaging information, for example utilizing machine learning based on features from both modalities [15]—or even considering clinical features—may also be explored for truly quantitative hybrid imaging.

Cost-effective low-radiation hybrid imaging could be accomplished by trading the rest MPI scan for the CTA scan performed before stress MPI. It is likely that all-in-all, the additional CTA will provide more valuable additional information than the rest MPI scan in assessing patients with coronary disease. Such hybrid protocols have been proposed and the overall radiation dose and imaging time were shown to be below those in a typical stress/rest MPI.[16,17] Stress-only MPI-CTA protocols with total doses lower than 5 mSv were reported to predict the need for revascularization with 97.5% accuracy.[18] Very low-dose stress-only MPI may require less radiation than typical CTA scan.[19,20] For PET, it has been demonstrated that stress-only PET analysis of absolute myocardial blood flow is more accurate than the flow reserve derived from stress/rest PET scans.[4] To reduce the cost and dose further, stress-only MPI protocols could be performed in a selective mode, for example, performing CTA-only scan and canceling stress-MPI if there are no anatomical abnormalities.

CONCLUSIONS

Quantitative hybrid imaging has the potential to simplify the interpretation of multimodality cardiac imaging. Such technology should be available on a routine basis in the future. Several manual and subjective steps need to be eliminated before this approach enters wide clinical use.

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