The future of positron emission tomography/computed tomography imaging of the heart

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Abstract

Metabolic cardiac imaging with [18F]-fluorodeoxyglucose (FDG) and positron emission tomography (PET) has been established as the diagnostic and prognostic gold standard. This is usually combined with a perfusion scan, as the classical diagnostic finding is the so-called flow–metabolism mismatch (low flow, preserved FDG uptake). Hybrid PET/computed tomography (CT) and single photon emission computed tomography (SPECT)/CT scanners add a new dimension to non invasive diagnostic procedures, as they allow simultaneous assessment of function (metabolism or perfusion) and coronary anatomy. Hybrid imaging can integrate metabolic FDG information with CT-visualized anatomy, thus providing a new approach for diagnosing dysfunctional but viable myocardium by directly visualizing information on viability in segments subtended by severely stenosed/occluded coronary vessels.
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Introduction

Positron emission tomography (PET) represents the most advanced technique in nuclear medicine and is widely used, not only for research, but also in the clinical setting for patients with a large diversity of cardiac diseases. PET allows non invasive functional assessment of myocardial perfusion, metabolism, innervation, and receptor density and can provide quantitative data. At present, PET is the most accurate method for the quantitative measurement of myocardial perfusion in cardiology. In addition, it is the 'gold standard' for the assessment of dysfunctional but viable (hibernating) myocardium. Despite this impressive proof of excellence for clinical use, PET has not been in wide use for long. Only recently has the widespread use of PET and PET/computed tomography (CT) in oncology helped to overcome one of the most important limitations of PET technologies – its limited availability.

Diagnostic conventional coronary angiography – the past

Conventional coronary angiography has been the only accepted 'gold standard' method for clinical imaging of coronary artery disease (CAD) over past decades. Despite its cost, inconvenience to patients, and small but distinct procedure-related morbidity (1.5%) and mortality (0.15%), in 2002, for example, about 2 million conventional coronary angiography procedures were performed in Europe [1]. As a percutaneous coronary intervention was performed only in one-third of these procedures, coronary angiography is mostly used as purely diagnostic tool. The associated economic burden and the inconvenience to patients

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have prompted an intensive search for alternative, non invasive means of coronary artery imaging [2].

Coronary angiography by computed tomography – the present challenge

Recent advances in CT using multislice CT (MSCT) with 64 slices [3] and dual-source CT (DSCT) [4] now make it possible to obtain, non invasively, excellent quality images of coronary arteries. The negative predictive value to exclude CAD approaches 100%, severely challenging the role of coronary angiography as a purely diagnostic tool. The accuracy of coronary angiography is severely hampered by a significant variability (up to 50%), both within and between observers, in defining the anatomic relevance of stenoses [5,6], as underlined by a poor correlation with postmortem coronary anatomy [7,8]. In addition, angiographic findings are not able to predict the physiologic relevance of a coronary stenosis [6,9–12]. Therefore, it has become the clinical standard to require proof of ischemia by a non invasive test before considering revascularization procedures [13,14]. This limitation also applies to computed tomography angiography, as any assessment of coronary luminology by means of a purely morpho-anatomical method must remain poor at predicting the functional relevance of a stenosis [10].

Hybrid imaging – the future

An accurate, non invasive technique for the evaluation of CAD should provide complementary information on coronary anatomy and the severity of the pathophysiologic lesion. Currently, the integration of functional and morphological information is performed by mentally combining the findings obtained by coronary angiography with those from myocardial perfusion imaging (MPI). Unfortunately, the planar nature of the coronary angiography projections and the axial slice-by-slice display of cardiac MPI render a subjective integration difficult, leading to inaccurate allocation of the coronary lesion to its subtended myocardial territory. There have been several attempts to fuse conventional coronary angiography with MPI [15–17]. This approach does not allow non invasive preplanning of the intervention, as information on the coronary anatomy is obtained only during conventional coronary angiography. In addition, the time-consuming process of fusing coronary angiography with MPI is not helpful in rapid decision-making during a current intervention. Consequently, this approach has not been adopted into daily clinical routine. Ideally, the complementary information should be obtained completely non invasively, permitting proper planning of the elective intervention.

We have recently shown that combination of MPI with multislice CTA is a feasible and interesting new approach for non invasive complementary morpho-anatomical and functional assessment of CAD [18,19], providing useful information for clinical decision-making [20]. These very encouraging preliminary data suggest that hybrid imaging has the potential to be integrated into clinical practice, eventually leading to a reduction in the frequency or overuse of angioplasty and stent placement, a key
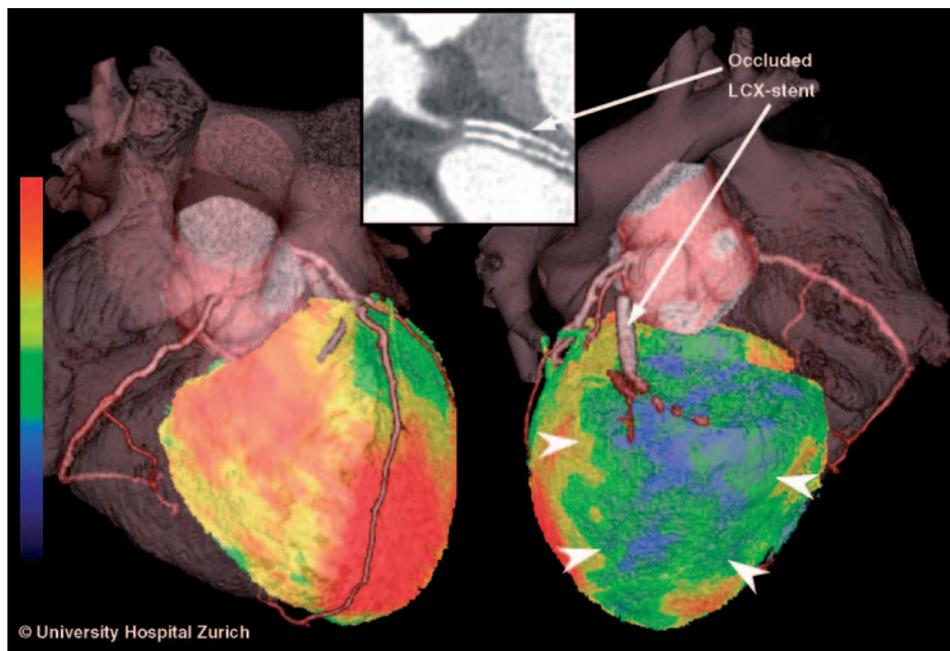

Figure 1. The arrowheads on the right image denote a lateral infarction without uptake of [^{18}F]-fluorodesoxyglucose (blue and green area), indicating lack of viability in the territory subtended by the stented left circumflex coronary artery with an occluded stent (LCX-stent).

cost driver in interventional cardiology practice. Occasionally, in patients in whom the lesion anatomy is unsuitable for angioplasty, bypass surgery may be considered directly, without the need for further pre-operative diagnostic coronary angiography [21].

Future role of positron emission tomography/computed tomography for the assessment of viability

A mismatch between decreased flow and preserved uptake of [18F]-fluorodeoxyglucose (FDG) represents the classical finding diagnostic for hibernating myocardium, as established 20 years ago in the seminal work by Tillisch and coworkers [22]. Although, at first, hibernating myocardium was considered to have reduced resting blood flow, newer data have demonstrated that patients frequently have normal resting flow, whereas flow reserve is reduced. To improve the description and understanding of these two situations, the term 'chronic and repetitive stunning' was suggested for left ventricular dysfunction in the presence of normal resting flow, the term 'hibernation' remaining reserved for the situation of chronic left ventricular dysfunction with reduced resting flow. Current debate now suggests that chronic stunning and hibernation may represent two ends of the spectrum of chronic ischemia. The real issue in the clinical management of hibernation remains the prediction of improvement in function, but also encompasses prognosis after revascularization.

Several techniques are used for viability testing, including nuclear imaging (PET or SPECT), dobutamine stress echocardiography, and magnetic resonance imaging. Most clinical experience has been gained with nuclear techniques, which rely upon assessment of perfusion, cell integrity, and metabolism, as opposed to dobutamine testing, which relies upon assessment of contractile reserve. Pooled data have demonstrated that nuclear imaging is more sensitive for the detection of viable myocardium, particularly in severely depressed left ventricular function. This may be attributable to the fact that contractile reserve may no longer be preserved (ischemic damage of the contractile apparatus), whereas other markers of viability, metabolism, and cell membrane integrity may still be found. The greater sensitivity of FDG scanning seems to be of clinical importance, as it has been clearly shown that patients with viable tissue, who will not undergo revascularization, have an unfavorable outcome compared with both those who undergo revascularization and those without viable tissue. Patients with a very small amount of viable tissue, who did not undergo revascularization because the extent of their left ventricular function was estimated to be too small to permit improved

ventricular function, had the greatest annual mortality and worst outcome over 8 years of follow-up [23]. As most of these patients died from sudden cardiac death, hibernating myocardium seems to be a dangerous substrate of arrhythmic focus. Viability testing could be used in the future to identify those patients who would benefit most from the expensive procedure of insertion of an implantable cardioverter-defibrillator. This may be best achieved by using hybrid scanning of FDG PET with CT angiography (*Figure 1*). This technique offers correct assignment of viable and dysfunctional myocardial segments to the territory of the occluded artery, allowing correct decision making with regard to revascularization of the cardioverter-defibrillator implant, without need for perfusion scanning. ■

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