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### Non-Invasive Cardiac Imaging Modalities

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During recent years, efforts from both the medical and engineering communities have led to enormous advances in the field of noninvasive cardiovascular imaging, strengthening its key role in cardiologic diagnosis making and therapy guidance. The strengths and weaknesses of the new developments in the four main cardiac non-invasive imaging modalities: nuclear imaging, multi-slice cardiac computed tomography (CCT), cardiovascular magnetic resonance imaging (CMR) and echocardiography, will be discussed in the following paper.

#### Nuclear Medicine

Single-photon emission computed tomography (SPECT) uses the gamma radiation of <sup>99</sup>Tc-technetium labelled methoxyisobutylisocyanide (Mibi), a substance, which distributes with the blood flow and is taken up by the myocardial cells like potassium. The detection of stress-induced ischaemia is based on comparing images after two injections, one at peak stress and one under resting conditions. This method is well established in cardiology. ECG gating with usually 8-16 bins per cycle, improves spatial resolution and allows investigation of regional and global function of the LV. Gated SPECT based global function estimates are proven to be highly reproducible.

Recent attempts have expanded regional function assessment by SPECT to the clinical setting of cardiac resynchronisation therapy (CRT). The phase analysis of gated regional myocardial signals has been suggested as a predictor of CRT response and proposed as a criterion for patient selection (Chen 2005). It must be argued, however, that the poor temporal resolution of the technique (ca. 60ms per bin) is sufficient to resolve the short regional functional delays occurring in this disease (20 – 40 ms). Furthermore, assessment of function is limited to the radial motion of the myocardium only, neglecting all other directions of motion and, thus, reflecting the complex myocardial deformation incompletely.

Positron Emission Tomography (PET) uses the co-incidental detection of photons on opposite detectors to reconstruct the distribution of  $\beta^+$ -radiating <sup>18</sup>F-fluorodeoxyglucose in the heart. It is more sensitive than SPECT, has a slightly higher resolution and can quantify perfusion in absolute numbers, which allows the most sensitive assessment of myocardial viability. Higher costs and difficulties due to short-lived tracers explain its limited availability.

The recent development of hybrid PET and CT scanners allow the co-registration of highly resolved anatomical CT data with functional information from PET. Such "fusion imaging" has particular value in oncology, but cardiologic applications have been proposed as well. The added value of such fusion images in the broad cardiologic routine, however, remains to be proven.

#### Cardiac CT

Computed tomography reconstructs a volume data set of regional x-ray attenuation values by advancing a rotating unit of an x-ray source together with several rows of detectors along the long axis of the body. A volume covering the entire heart can nowadays be scanned in a few seconds, thus within a breathhold. Current generation CT scanners allow assessment of coronary artery anatomy noninvasively with a good spatial resolution.

The particular attenuation of x-rays by calcifications results in a very good ability to exclude relevant coronary artery disease but does not allow a sufficiently accurate evaluation of stenosis severity. Therefore, CT angiography (CTA) has been suggested as a tool to rule out coronary artery disease, especially in symptomatic patients with intermediate probability.

Recent developments in the field of cardiac CT focus on improving temporal and spatial resolution as well as volume coverage, paralleled by a reduction of radiation exposure. Currently however, CTA cannot replace selective conventional coronary angiography in the diagnosis of coronary artery disease. Furthermore, a subsequent treatment of a detected stenosis (e.g. by placing a stent) is not possible and would anyway require an additional invasive procedure.

Different patterns of myocardial enhancement have been demonstrated in animal models and humans, early and late, after contrast administration. Although cardiac CT therefore appears capable of detecting myocardial ischaemia and scar tissue, data are still preliminary. Therefore established and radiation-free MR investigations are usually preferred in the clinic.

The use of ionising radiation is a major drawback of nuclear medicine and cardiac CT. A dynamic cardiac radionuclide study and a chest CT examination are equivalent to approximately 2.7, respectively 3.6 years of exposure to natural background radiation (European Commission Referral Guidelines for Imaging, 2000). When choosing any ionising radiation based imaging modality, the principles of "justification, optimisation and responsible use" as stated in CE Euratom Directive 97/43 on health protection of individuals in relation to medical exposure must be followed. According to the above-mentioned referral guidelines, non-ionising techniques should be preferred whenever they give grossly comparable information and are locally available.

#### Cardiovascular Magnetic Resonance Imaging (CMR)

Cardiovascular MRI uses high intensity magnetic fields to influence the spin orientation of atoms in the body. Additional radiofrequency fields introduce a precessional motion of the atoms, the return from which produces a detectable magnetic signal that is used for imaging. CMR generates 3D images of the cardiovascular system with good spatial resolution and contrast. Special sequences for perfusion, blood flow and blood vessel imaging have been developed.

CMR offers excellent anatomic still and cine images of heart and great vessels, accurate measurements of cardiac volumes, mass, ejection fraction, as well as information about myocardial perfusion and fibrosis, blood flow and velocity, while avoiding the use of ionising radiation. An increase in magnetic field strength up to currently 3 Tesla allowed further improvement of image quality. The analysis of myocardial signal intensity several minutes after contrast application (delayed enhancement technique) allows the sensitive and accurate detection of myocardial damage (Fig. 1), which makes CMR the state of the art technique for scar detection (Curtin, 2009).

Coronary magnetic resonance angiography (MRA) has recently improved, but yields a spatial resolution that is currently still inferior to CTA. CMR examinations under ergometric or pharmacologic stress utilise contrast enhanced myocardial perfusion imaging or classic regional wall motion analysis (Nandalur, 2007). Magnetic saturation of the myocardium in a line or grid pattern introduces detectable tissue markers that can be used to quantify myocardial motion and deformation objectively and with good accuracy (tagging). However, the limited temporal resolution of CMR data sets allows no accurate interrogation of fast (e.g. diastolic) events. Analysis of tagging data is tedious, which reserves this technique for research purposes while clinical wall motion assessment relies on the trained eye of the reader.

Fusion of 3D image data sets from either MRI or CT with fluoroscopy data can be used to guide electrical mapping and ablation during electrophysiological studies (Ector 2008). A future real-time CMR guidance of electrophysiological procedures appears possible (Nazarian 2009). The use of CMR is limited in the presence of metal implants and implanted devices. Furthermore, the advantages of this technique are in part balanced by high costs, immobility and the need for time-consuming offline analysis.

### **Echocardiography**

In clinical cardiology, echocardiography is the standard tool for evaluating morphology and function of the heart and the great vessels. Diagnostic and prognostic value has been extensively studied over the years, making it the first line modality in noninvasive cardiovascular imaging. Echocardiography is relatively inexpensive, widely available, portable, fast and accurate. It is therefore integrated in the management guidelines of most cardiovascular disorders. Compared to other modalities, ultrasonic imaging has an excellent temporal resolution. Images are, to a great extent, visually analysed, making diagnostic results observer dependent. Recent developments focus mainly on new ways of quantifying particularly myocardial function and introducing 3D imaging to clinical echocardiography.

### **Myocardial Deformation Imaging**

Assessment of regional and global myocardial function is one of the main goals of almost any echocardiographic examination. Traditional visual interpretation requires a long learning curve and makes results observer dependent. During the last decade, Tissue Doppler Imaging (TDI) and TDI based myocardial deformation assessment emerged as a helpful technique for regional and global function assessment (Fig. 2). Doppler based velocity and deformation imaging have been validated and extensively studied in a variety of cardiac pathologies. They proved to be of particular advantage in the assessment of LV diastolic function, regional dysfunction and LV dyssynchrony.

As the one-dimensional approach of the technique makes it susceptible to misalignment between the ultrasound beam and the motion/deformation direction to be investigated, speckle tracking methods (Fig. 3) were developed as an appealing alternative by different vendors. Speckle tracking is based on the frame-by-frame tracking of image features of the myocardial texture which allows a two-dimensional estimate of myocardial motion and deformation. Applications of the speckle tracking techniques are comparable to those of Doppler measurements. The advantage of an easier and faster post-processing together with the option to generate a plethora of derived parameters is compensated by the somewhat lower temporal resolution of tracking techniques, the difficulty to detect tracking errors and a higher dependence on image quality.

### **Particle Imaging Velocimetry**

Very recently, tracking techniques have also been applied to contrast enhanced intracavitary blood flow. According to data in LV models (Pedrizzetti 2005, Domenichini 2005), first studies show significant changes in intracardiac flow patterns in pathology, e.g. dilative cardiomyopathy (Hong 2008) or mitral valve prosthesis (Faludi 2010).

### **Contrast Echocardiography**

One of the promises of the last decade was echocardiographic myocardial perfusion imaging using echo-contrast agents. However, while contrast echocardiography has proven to be a valuable clinical tool for endocardial delineation in difficult to image patients, accurate echocardiographic perfusion estimates still remain a challenge and are not performed clinically. Likewise, the anticipated option of targeted drug delivery through contrast agents (Bekeredjian 2005) has not yet left its pre-clinical state.

### **Three Dimensional Echocardiography**

Advances in transducer technology have led to 3D transducers with matrix arrays with more than 3,000 elements capable of acquiring echo data from a pyramidal 3D volume. These developments have been facilitated by further advances in circuit miniaturisation, which allowed placing the entire beam former within the handle of the transducer (Bhan 2010). The latest generations of scanners allow the acquisition of a full volume dataset in one cardiac cycle, precluding the need for multiple ECG gated subvolume acquisition followed by online reconstruction with around 20 volumes per second.

The added clinical value of transthoracic 3D echocardiography remains to be proven. The current quality of reconstructed image planes is still inferior to regular images and often insufficient to allow the visual assessment of cardiac morphology. The clearest clinical advantages lies in the quantification of absolute cardiac chamber volumes, mass and ejection fraction, the accuracy and reproducibility of which is now comparable to that of MRI. Furthermore, the 3D approach allows for the first time an accurate echocardiographic assessment of the complex geometry of the right ventricle (Niemann 2007). The recent incorporation of real-time 3DE technology in a transoesophageal probe allows for the first time to image complex 3D structures like mitral valve leaflets in detail with good quality (Sugeng 2008). Its feasibility for more anterior structures like the aortic and tricuspid valves is much lower (Sugeng 2008).

The largest potential of 3D TEE appears to lie in the guidance of percutaneous treatment procedures such as atrial septal defect closures, stented valve implantations and electrophysiological ablation interventions (Budts 2008, Lodato 2009, Balzer 2008). The potential and value of 3D imaging based myocardial function assessment remains to be investigated.

### **Hand-Carried Ultrasound Scanners**

Since a few months, hand-held ultrasound scanners are available from two major vendors. They are designed for triage or focus scans and have currently a limited functionality. First studies, however, have already shown the advantageous use of these devices in a clinical setting (Egan 2008). Further studies are needed to clarify the role of these devices in clinical routine.

#### **Summary**

Cardiac noninvasive imaging is a field that benefits enormously from the fast evolution of technology. Even established classical imaging modalities have been further developed and constantly refined over the past years. While the role of nuclear imaging seems to reach a plateau and the rise of CCT appears to slow down, MRI and echocardiography remain the workhorses of cardiologic imaging and gain more importance in clinical routine. In several clinical settings, different imaging modalities complement each other, emphasising the importance of cardiologists being trained and actively involved in all cardiac imaging modalities.

This became the driving force for a development towards a cardiologic imaging sub-speciality in many European countries. Only this will allow to combine the knowledge about strengths and weaknesses of the different advanced modalities with the specific cardiologic background which is needed to appropriately interpret the findings and to yield an optimal clinical value for the patient.

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