

## Cardiovascular imaging 2013 in the International Journal of Cardiovascular Imaging

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It has become a tradition to provide the annual overview of the published papers in the International Journal of Cardiovascular Imaging in the year 2013. Particularly, this last year we have published many more manuscripts than in previous years, covering the well-known areas of X-ray angiography, intravascular imaging, echocardiography, nuclear cardiology, magnetic resonance imaging and computed tomography. In 2013, the Asian Society of Cardiovascular Imaging published two ASCI Supplements with Adjunct Editor Yeon H. Choe and Guest Editors Byoung W. Choi, Hajime Sakuma and Jongmin Lee.

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### X-ray angiography

Over the course of 2013 a number of interesting papers over various areas of interest were published in the field of X-ray angiography.

### FFR

In the group of Molloy, Takarada et al. [1] carried out an in vivo validation in eight anesthetized swine of an image-based technique using first-pass distribution analysis of the contrast distribution and scaling laws to assess the fractional flow reserve (FFRa), and tested this technique against a flow-probe based FFRq and pressure-wire FFRp; data was acquired at maximal hyperemia in LAD arteries. They concluded that a linear relationship exists between the angiographic FFRa and the gold standard flow-probe based FFRq ( $FFRa = 0.97 \times FFRq + 0.06$ ,  $r^2 = 0.80$ ,  $p < 0.001$ ), but that there are still differences between the flow-based FFRq and the pressure-derived FFRp, especially at low values ( $FFRp = 0.657 \times FFRq + 0.313$ ,  $r^2 = 0.710$ ,  $p < 0.0001$ ).

### Renal dysfunction

In the paper by Burchardt et al. [2] the authors investigated the incidence of early renal function deterioration within 12–18 h after the administration of iodine contrast media in patients scheduled for elective coronary angiography, who were intravenously and orally hydrated. This was a single-center retrospective analysis in a total of 319 patients enrolled over a period of 16 months. They concluded that impairment of renal function 12–18 h after contrast agent administration may result in no change or an increase of creatinine and blood urea nitrogen (BUN) and glomerular filtration rate (GFR). The phenomenon was detected in

13–28 % of their patients. These results need to be confirmed in a larger prospective trial.

### Rotational angiography

Park et al. [3] investigated the feasibility and accuracy of 3D rotational angiography (3DRA) to determine the anatomy of the left atrium (LA) and pulmonary veins (PVs) compared with cardiac computed tomography (CCT) and trans-thoracic echocardiography (TTE) in a population of 102 patients. They concluded that this intra-procedural imaging resulted in 3DRA LA volumes ( $120 \pm 32$  mL) being greater than those found by CCT ( $109 \pm 35$  mL) or TTE ( $64 \pm 23$  mL), although with high correlations. Furthermore, there is a limitation with 3DRA in optimally delineating the lateral ridge between the LLA and LSPV.

### Stents

In a study including 414 patients Jin et al. [4] studied the effect of StentBoost Subtract (SBS) on the radiation dose during PCI; in 177 patients SBS was used, in the remaining 237 patients not. Although the dose area product (ADP), fluoroscopy time and cine frames in the SBS group was significantly increased, multiple linear regression analysis showed that SBS imaging has no significant impact on radiation dose.

### Syntax score

Brkovic in the team of Beleslin [5] investigated the possible additive prognostic value of the SYNTAX score over other existing scores in patients with STEMI undergoing primary PCI. This retrospective observational study included 209 consecutive patients with STEMI referred for primary PCI. A total of 6 scores were evaluated (GRACE, TIMI, ZWOLLE, CADILLAC, PAMI and of course SYNTAX). The authors concluded that the SYNTAX score improves prognostic performance over well-established clinical scores, except for the CADILLAC risk score. Furthermore, the long-term survival in patients after STEMI depends less on detailed angiographic characterization of coronary lesions, but more on clinical characteristics, myocardial function and basic angiographic findings as provided by the CADILLAC score.

### Intravascular imaging

The year of 2013 repeated the success of 2012 with high quality papers in intravascular imaging. In almost every issue of “The International Journal of Cardiovascular Imaging” an insightful paper involving intravascular

imaging was present. We would like to start this year’s review by revisiting our prediction and call for papers from last year. In addition to papers that utilize the unique aspects of intravascular imaging, namely high spatial resolution and tissue characterization features, for investigating devices and vessel biology. Last year we also requested papers with real world application of these methods for guiding therapy. Several groups reacted to this request and submitted various papers with clinical application of intravascular methods. A total of five papers were selected and for the first time we are very excited to add a new family of papers on this review: “Clinical application of Intravascular Imaging”.

### Device evaluation

Staico et al. [6] presented data in very late stent follow-up (5 years) interrogated by OCT. The BioMatrix stent had lower percent lumen stenosis with similar low rate of uncovered strut as compared to a bare metal stent (S-Stent). In light of recent observations of neo-atherosclerosis higher prevalence in DES, we would like to suggest for the authors to publish data on the tissue characterization of these stents.

Do we need dedicated bifurcation stents? Gil et al. [7] make a case for dedicated bifurcation stent design with the BiOSS stent. The authors elegantly demonstrate less luminal compromise and plaque re-distribution at the level of the side-branch and reinforce the mechanistic aspect that conventional stents do not take into consideration vessel tapering and may result in carina and plaque shift.

Costa et al. [8] also provide some insights on bifurcation lesions, by performing IVUS pre-intervention 1,1,1 Medina classification. The authors demonstrate high prevalence of negative remodeling at the ostium of the side branch and eccentric plaque distribution, mostly located opposite to the carina, which corresponds to regions of low shear stress. These findings may contribute even further to design and concept of dedicated bifurcation stents.

### Atherosclerosis and vessel biology

Are CTOs different in plaque composition compared to non-occlusive stenosis? This intriguing question has important clinical relevance. Guo et al. [9] evaluated plaque composition in chronic total occluded lesions versus non-occlusive lesions. This has a particular interest and relevance as the field of CTO evolves with new devices beyond better guidewires. Surprisingly CTOs had similar plaque composition with the exception of less dense calcium, and this may reinforce the data in which percent calcification functions as a predictor of unsuccessful CTO treatment.

Can stent coverage as defined by OCT predict physiology? Assessment of stent coverage by OCT has resulted in several publications in the past recent years. Stent coverage has been utilized as a surrogate for risk of stent thrombosis. Won et al. [10] looked at this metric from a different angle; can stent coverage predict vessel reactivity? The response to acetylcholine was indifferent to the percent of stent coverage. OCT is unable to directly visualize endothelial layer and particularly if this layer is functional. Overall coupling of molecular imaging to our current imaging armamentarium would be a big leap forward.

Is the radial approach free of vascular complications? Not by OCT! Di Vito et al. [11] investigated acute and chronic vessel changes after the radial approach. The authors identified more than one third of intimal tear acutely and significant intimal thickening chronically. This is an important finding particularly considering the trend to more radial procedures and close monitoring is warranted if any of these findings may predict clinical endpoints like loss of radial pulse.

#### Clinical application of intravascular imaging

Can anatomy predict physiology? We asked for papers with correlation between physiology and intravascular imaging and Pawlowski et al. [12] responded with a very well conducted paper with more than 70 intermediate lesions interrogated with both FFR and OCT. By ROC analysis the authors identified a threshold of MLA = 2.05 mm<sup>2</sup> as the highest accuracy compared to FFR. Is 87 % accuracy good enough? It is at least probably one of the best correlations ever reported and we look forward for more data. Is coronary FD-OCT safe? A very practical approach is reported in a single center experience by Lehtinen et al. [13]. The authors not only corroborate the safety of the method, but identify a learning curve that relates with higher success rate of the method after 50 cases were performed in the center. Can we predict edge dissections with OCT? Although the data suggest good outcome in the vast majority of patients with edge dissections [14] as identified by OCT, some of these cases may result in clinical events and the question becomes: is edge dissection preventable? Reith et al. [15] demonstrated that presence of eccentric plaque at the landing zone is an important predictor of edge dissection and this information may be considered when selecting the stent length. Is it all about spatial resolution? Liu et al. [16] compared accuracy of longitudinal measurement of FD-OCT versus IVUS and demonstrated better accuracy and reproducibility with FD-OCT. This can be explained in part by the exponential higher pullback speed of FD-OCT, which makes the method less susceptible to heart motion longitudinal movement. Can OCT guide additional interventions for

atherothrombotic material intra-stent? Protrusion of atherothrombotic material intra-stent is frequent, particularly in ACS situations. Di Giorgio et al. [17] demonstrated reduction of the atherothrombotic material with additional balloon dilatation, proving feasibility and paving the way for a large study on the topic.

As of last year we want to encourage research applications of intravascular imaging to help research and development of better techniques, device and medical therapy. In addition to reinforce the need to continuous application of these methods in our clinical daily care and we highly welcome papers with real world application of these powerful methods. One more time we would like to thank you the contributors: the success and increasing impact factor of this journal is a direct consequence of the quality of your work.

#### Echocardiography

As in previous years, many excellent papers have been published in 2013 in the International Journal of Cardiovascular Imaging using different echocardiographic modalities, focusing on various clinical scenarios. In fact, far too many to discuss all of them in detail. We therefore focused on echocardiographic studies exploring the boundaries of dobutamine stress echocardiography, diastolic dysfunction and finally novel echocardiographic technologies.

#### Dobutamine stress echocardiography

Traditionally, wall motion scoring is done visually during stress echocardiography, however novel strain imaging techniques allow quantification. Yu et al. [18] evaluated whether they could detect abnormalities in strain, strain rate, and dyssynchrony by applying 2-dimensional speckle tracking echocardiography in patients with severe coronary artery disease (CAD) during early stages of dobutamine stress echocardiography. Thirty-four patients with angiographically documented severe 3-vessel CAD and preserved left ventricular (LV) ejection fraction were compared with 42 control patients without evidence of CAD. Circumferential and longitudinal strain, strain rate, and LV synchrony using standard deviation of time to systolic peak strain and strain rate were analyzed with 2-dimensional speckle tracking echocardiography at rest and at intermediate doses of dobutamine stress echocardiography. Compared with control subjects, patients with CAD showed lower circumferential strain rate and significantly lower longitudinal strain and strain rate at intermediate doses; these values were also compromised at peak dose. The standard deviation of longitudinal time to systolic peak strain at intermediate dose was significantly

greater in patients with CAD than in control patients. The 2-dimensional speckle tracking echocardiography derived strain and strain rate detected myocardial dysfunction and asynchrony in patients with CAD during intermediate doses of dobutamine stress, with minimal changes in regional wall motion abnormalities at this stage. Gong et al. [19] combined 2-dimensional speckle tracking echocardiography with low-dose dobutamine stress echocardiography to evaluate myocardial viability in 42 patients with acute myocardial infarction. Speckle tracking was used to measure radial, circumferential and longitudinal end-systolic strain and peak systolic strain rate. The movement of each segment was observed by routine echocardiography at 1, 3 and 6 months after percutaneous intervention, and its improvement over time was the criterium of viable myocardium. Only longitudinal strain and longitudinal strain rate at rest and low dose dobutamine stress echocardiography emerged as independent predictors of viable myocardium. The sensibility of speckle tracking in conjunction with low dose dobutamine stress echocardiography was similar to dual isotope simultaneous acquisition single photon emission computed tomography for detecting viable myocardium in patients with myocardial infarction but the specificity and accuracy were higher. Elmayergi et al. [20] evaluated the test–retest reliability and the normal dose–response relationship of echocardiographic measures of LV contractile function to low dose dobutamine stress in healthy individuals. Thirty healthy volunteers underwent dobutamine stress echocardiography on 2 occasions, separated by 14 days. LV ejection fraction, longitudinal strain and strain rate could be measured during dobutamine stress imaging with a high degree of test–retest reliability, and may be of clinical value when serial follow up of dobutamine stress echocardiography measures of LV performance is indicated over time. Nguyen et al. [21] performed a quantitative systematic review assessing the use of dobutamine stress echocardiography in detecting CAD and predicting perioperative and long term cardiac events in patients undergoing liver transplantation. Seven studies were identified, including a total of 580 patients. Dobutamine stress echocardiography had a limited accuracy for the detection of CAD in candidates for orthotopic liver transplantation. However, among those selected for transplantation, the negative predictive value of dobutamine stress echocardiography for both perioperative and long term cardiac events is high.

#### Diastolic function

Yodwut et al. [22] hypothesized, that recent developments in real-time three-dimensional echocardiographic (RT3DE) imaging technology that allow dynamic quantification of both LV volume and 3D myocardial deformation, could be

utilized to objectively assess diastolic dysfunction. Trans-thoracic RT3DE datasets were acquired in 76 subjects, including 20 normal controls, 16 mild diastolic dysfunction, 20 moderate diastolic dysfunction and 20 severe diastolic dysfunction. Images were analyzed using prototype software (TomTec©) that performs 3D speckle tracking to generate time curves of LV volume and segmental myocardial strain. Indices of diastolic function were calculated: volume at 25, 50 and 75 % of filling duration (FD) in percent of end-diastolic volume (volume index, LVVi), and rapid filling volume (RFV) fraction. Temporal indices included: FD in % of RR, and rapid filling duration (RFD) in % of FD. LVVi and RFV fraction showed a biphasic pattern with the severity of diastolic dysfunction characterized by an initial decrease (grade 1), a pseudo-normalization (grade 2), and then an increase above normal (grade 3). Filling duration progressively decreased with severity of diastolic dysfunction. RFD was significantly increased in all 3 groups compared to normals. After normalization by peak systolic values, all strain components showed a linear pattern with the severity of diastolic dysfunction, suggesting potential clinical usefulness. This is the first study to show that current RT3DE technology allows combined quantitative analysis of LV volume and 3D myocardial strain, which is sensitive enough to demonstrate differences in myocardial relaxation in patients with different degrees of diastolic dysfunction. Roos et al. [23] studied the relationship between LV diastolic dysfunction and increased arterial stiffness in patients with diabetes mellitus. In 142 asymptomatic patients with diabetes mellitus, diastolic function was assessed with echocardiography. Arterial stiffness was evaluated measuring the aortic pulse wave velocity (PWV) whereas wave reflection was assessed measuring central systolic blood pressure (cSBP), central pulse pressure (cPP), and augmentation index (AIx) with applanation tonometry. PWV was independently associated with LV diastolic dysfunction grade ( $\beta = 0.76$ ,  $p = 0.03$ ). In contrast, measures of wave reflection, cPP, cSBP and AIx were independently related with E/A ratio, but not with the LV diastolic dysfunction grade. Parameters of arterial stiffness and wave reflection are associated with echocardiographic indices of diastolic function in asymptomatic patients with diabetes mellitus. Therapies that prevent progression of arterial stiffness and reduce late-systolic pressure overload may help to reduce the prevalence of LV diastolic dysfunction in this population. Wuthiaropas et al. [24] studied the impact of cardiac rehabilitation on diastolic function and conducted a prospective study of CAD patients referred for 3-month outpatient rehabilitation, with pre-rehabilitation and post-rehabilitation echocardiograms. Three-month, exercise-based cardiac rehabilitation was associated with improved LV diastolic function in half of the patients.

Further large studies are needed to clarify the effect of cardiac rehabilitation on diastolic dysfunction in patients with CAD. AlJaroudi et al. [25] assessed the prognostic value of diastolic dysfunction in low-risk adults beyond Framingham risk score. Diastolic dysfunction was assessed in a standardized method and in accordance to relevant guidelines by using a combination of echocardiographic variables including transmitral inflow pattern, pulmonary venous flow pattern and mitral annular velocities assessed by tissue Doppler. The study cohort consisted of 1,039 patients, 346 patients (33.3 %) had diastolic dysfunction. After a mean follow-up time of 7.3 years, 71 patients died. Adjusting for age, gender and race, diastolic dysfunction remained an independent predictor of all-cause mortality with hazard ratio 2.03 and similarly after adjusting for Framingham risk score (hazard ratio 2.73,  $p = 0.0002$ ).

### New technologies

Three-dimensional (3D)-imaging provides important information on cardiac anatomy during electrophysiological procedures. A beat to beat 3D visualization of cardiac anatomy by intracardiac echocardiography (ICE) was developed and tested in phantoms and animals by Stapf et al. [26]. During a single heartbeat, the ICE-catheter was rotated and 2D-images were acquired. Reconstruction into a 3D volume and rendering by prototype software was performed beat to beat. After experimental validation using a rigid phantom, the system was tested in an animal study and afterwards, for quantitative validation, in a dynamic phantom. Acquisition of beat to beat 3D-reconstruction was technically feasible. However, twisting of the ICE-catheter shaft due to friction and torsion was found and rotation was hampered. Also, depiction of catheters was not always ensured in case of parallel alignment. Beat to beat 3D-ICE-imaging is feasible. However, shape and dimension of static and moving objects cannot always be displayed with necessary steadiness as needed in the clinical setting. As catheter depiction is also limited, clinical use seems impossible. Ruddox et al. [27] evaluated the diagnostic accuracy of pocket-sized cardiac ultrasound when used by unselected internal medicine residents with minimal training. Left ventricle and pericardium were of first priority. Pocket-sized ultrasound examination performed by residents with minimal training could provide a suitable means of ruling out cardiac pathology. It is however not a satisfactory tool for identifying patients with various cardiac disorders.

### Nuclear cardiology

In 2013 different excellent paper in the field of nuclear cardiology were published in the journal. In this review we

selected a few papers on the topics of detection of plaque burden, CAD, ischemic cardiomyopathy and rare cardiac disorders including infectious endocarditis and cardiac sarcoidosis.

### Detection of plaque burden

Positron emission tomography (PET)/CT imaging potentially allows to evaluate vessel wall inflammation and calcified plaque burden across different vascular beds. Two larger studies on this topic were published in the journal in 2013. In the study by Strobl et al. [28] 315 patients, free of cardiovascular disease, underwent whole body 18F-fluorodeoxyglucose (FDG) PET/CT examinations. Blood pool-corrected standardized uptake values of FDG (TBR) and the calcified plaque score (CPS) were determined in different vascular beds including the thoracic and abdominal aorta, the carotid arteries and the iliac arteries. The main findings can be summarized as follows: (1) the TBR was mainly related to advanced age (>65 years) and male gender, while the CPS was more closely associated with cardiovascular risk factors including hypertension, diabetes and smoking and (2) the impact of cardiovascular risk factors on vessel wall inflammation and calcified plaque burden differed across vascular territories. In a second study by Morbelli et al. [29], 80 oncologic patients underwent 18F-NaF PET/CT examinations to evaluate both visual calcium load by CT as well as molecular calcium depositions by 18F-NaF PET. The arterial 18F-NaF uptake was measured by drawing regions of interests comprising the arteries on each slice of the transaxial PET/CT and normalized to blood 18F-NaF activity to obtain the target-to-background ratio (TBR). The main findings can be summarized as follows: (1) 18F-NaF uptake was significantly correlated with classical risk factors including diabetes, smoking and hypertension while visible calcium deposition (measured by CT) was only related to age and (2) the regional distribution of 18F-NaF uptake was different when compared to macroscopic arterial calcifications. These 2 studies clearly demonstrate: (1) the potential value of molecular imaging for the evaluation of different vascular beds; and (2) given the contradictory results of the relationship between cardiovascular risk factor burden and visible calcium deposition, the need for further larger scale studies to evaluate the true impact of risk factors on visible calcium deposition and inflammation.

### Coronary artery disease

The use of stress-only gated SPECT myocardial perfusion imaging has been proposed in the setting of evaluation of CAD when stress images are normal as this would reduce radiation exposure and costs. Ferreira et al. [30] evaluated

the outcome of 790 patients with suspected or known CAD who had normal myocardial stress only perfusion gated SPECT images. Images were considered as normal if a homogeneous myocardial distribution of the tracer was associated with a normal LV ejection fraction. After an average follow-up of 3.6 years, the main predictors for cardiac events were advanced age, diabetes, history of CAD and type of stress protocol (exercise test vs. adenosine). A very low cardiac event rate was documented (1 % after 1 year follow-up). This larger study confirms that a normal stress gated-SPECT study is associated with an excellent short-term (1–3 years) prognosis and that this approach can be used in daily practice in a broader spectrum of patients with suspected or known CAD to reduce radiation exposure and costs.

### Ischemic cardiomyopathy

Positron emission tomography with <sup>18</sup>F-fluorodeoxyglucose (FDG) in combination with an evaluation of myocardial perfusion by PET or SPECT imaging, provides a precise identification of viable and non-viable myocardium and is therefore an important investigation in patients with reduced LV function in whom the need of revascularization is considered. Uebleis et al. [31] evaluated the prognostic significance of combined myocardial perfusion SPECT and FDG-PET viability scanning in a larger series of patients (244) with ischemic cardiomyopathy (LVEF  $\leq$  45 %). Percent scar tissue and SPECT/PET mismatch (% mismatch) were calculated and correlated with event-free survival (hard end-point of all-cause mortality during a median follow-up of 33 months) according to the type of therapy (medical therapy with/without revascularization) provided after imaging. The results indicated that: (1) SPECT/PET mismatch and the interaction of SPECT/PET mismatch with early revascularization were independent predictors for death due to all causes; and (2) a threshold of  $\geq$  5 % SPECT/PET mismatch predicted best which patients benefitted from early revascularization in terms of long-term survival. These results are in-line with many previous papers on this topic but the authors used the stronger endpoint of all-cause mortality. The lack of randomization was, however, a major limitation.

In patients with reduced LVEF and increased QRS duration, cardiac resynchronization therapy (CRT) is an established option to reduce morbidity and mortality. Dyssynchrony analysis by several different imaging modalities may provide additional information for the selection of these patients. Also the size of scar present in the lateral wall of the LV has been shown in some studies to predict response to CRT. Lalonde et al. [32] evaluated the potential value of gated blood pool SPECT phase analysis of the lateral wall of the LV for prediction of CRT

response. 49 patients underwent both gated blood pool SPECT as well as FDG viability and Rubidium-82 perfusion PET scans prior to CRT implantation. Phase analysis was performed on the gated blood pool SPECT data to extract amplitude values used to define amplitude size and amplitude score parameters. Scar size and scar score were obtained from the PET scans and then compared to the amplitude parameters in the lateral wall. The ability of amplitude parameters to predict response to CRT was also investigated and compared to scar parameters. The main results can be summarized as follows: (1) amplitude size in the lateral wall showed overall modest correlations with PET-derived lateral wall scar size ( $r = 0.51$  for all patients,  $r = 0.64$  for ischemic patients); and (2) lateral wall amplitude based parameters had an overall similar accuracy as PET lateral wall scar parameters in predicting CRT response in ischemic patients. Clearly further studies are needed to assess its reproducibility in serial imaging and whether these measurements can further contribute in patient selection and follow-up before and after CRT implantation.

### Rare cardiac disorders

Infectious endocarditis is a serious condition with a high morbidity and mortality. In the diagnostic work-out of these patients, it is not only important to evaluate cardiac manifestations, but also to identify the portal of entry and detect extra cardiac infectious manifestations. For the latter, FDG PET/CT has been proposed as a potential new tool. Ozcan et al. [33] assessed the usefulness of a PET/CT study in patients with infectious endocarditis as a supplemental method to standard work-up in evaluating primary and distant infective foci. They retrospectively identified a cohort of 72 endocarditis patients which had an FDG PET/CT performed and in which the findings were assessed in relation to the routine work-up, which served as the “gold standard”. Of the 159 infectious lesions, FDG PET/CT identified 64 of these and suggested another 50, resulting in an overall sobering sensitivity (40 %) and positive predictive value (56 %) for detecting both cardiac and extra cardiac infective foci. However, when excluding lungs and organs with high physiological FDG-uptake/secretion, the sensitivity increased to 87. These findings indicate that FDG PET/CT may be an additional tool in detecting extra cardiac infections in these patients, particularly in organs with low physiological glucose uptake.

Cardiac sarcoidosis is a rare disease that has however a higher risk for lethal arrhythmias. F18-FDG/PET has been proposed as a new way to identify myocardial involvement in patients with sarcoidosis. Paz et al. [34] presented a series of cases in which they illustrate the novel applications of cardiac PET using F18-FDG and N13-ammonia

radiotracers in the evaluation and treatment of arrhythmias associated with cardiac sarcoidosis. These promising applications include defining the cause of the arrhythmia, identifying arrhythmias that will be amenable to medical management, and guiding therapy using serial scanning.

### Magnetic resonance imaging

There were a number of advances in cardiovascular MRI in 2013. Saeed et al. [35] studied a pig model of micro infarction and found global and regional wall LV dysfunction were comparable to occlusion and reperfusion injuries. Coronary microemboli were found to have an acute impact on LV function. The reproducibility of CMR derived LV volume and function measurements were improved using a semi-automatic threshold-based segmentation algorithm [36]. In a confirmatory study of highly trained asymptomatic male endurance athletes, myocardial mass was increased in participants having ECG abnormalities independent of late gadolinium enhancement (LGE) [37]. In another confirmatory study, aortic stiffness in patients with diabetes mellitus was assessed with CMR by PWV and compared to echocardiography diastolic function indices and LV and left atrial strain rate [38]. A significant correlation was found. LV dysfunction was also assessed by CMR and compared to invasive coronary flow reserve (CFR) in allograft heart transplant patients with vasculopathy [39]. While there was no significant difference in CFR, in patients having vasculopathy, the peak filling rate was found to be lower. Feature tracking was used to demonstrate reduced global longitudinal and radial strain in patients with normal ejection fraction after aortic coarctation repair [40]. A real-time radial k-space balanced SSFP pulse sequence was proposed for evaluation in patients whom breath-hold and good quality ECG cannot be achieved [41]. Phase contrast imaging of the right ventricular outflow track was used to obtain systolic flow acceleration in patients with pulmonary arterial hypertension [42]. A significant correlation was found with invasively measured maximum  $dP/dt$  and found to be a predictor of cardiovascular events. Exclusion of the trabeculae and papillary muscle in the right ventricle (RV) blood pool decreased the end diastolic volume, the end systolic volume and stroke volume while increasing the ejection fraction and end diastolic RV mass compared to inclusion in patients with tetralogy of Fallot [43]. Inter-observer agreement improved of RV mass improved with exclusion. In related work, axially derived measurements of RV volume and function were found to have better reproducibility compared to short axis values whereas RV EF was not found to be significantly different by the two methods for patients with complete transposition of the

great arteries repaired with atrial switch [44]. Strain-encoded MR was found to have good correlation with RV EF and brain natriuretic peptide in patients with pulmonary hypertension [45]. Myocardial strain assessed by displacement encoding with stimulated echoes (DENSE) was found to reliably identify contractile abnormalities in segments exhibiting LGE in patients with CAD [46]. The ratio of the cross-sectional biventricular area at end diastole measured at end-inspiration and end-expiration was found to be a reliable index for biventricular interdependence in patients with surgically confirmed constrictive pericarditis [47]. Cardiac magnetic resonance was used to predict responders and long-term survival following CRT and found to be effective for both wide and narrow QRS complex patients [48]. The latter represents a group that may particularly benefit from receiving CMR as echocardiography does not predict responders as well.

The reproducibility of cardiac and liver  $T2^*$  measurements in patients with thalassemia major was assessed with two different software packages [49]. Both were found to be reproducible with slight differences in the values which were judged not be clinically significant. The heterogeneity of myocardial iron deposition in response to chelation therapy in patients with transfusion-dependent anemias was assessed [50].  $T2^*$  was found to be lowest in the mid anterior septum and highest in the apical inferoseptum. The apical inferoseptum exhibited the most improvement with chelation therapy.

$T2$ -weighted imaging was used to compare the area of myocardium at risk following non-ST-elevation myocardial infarction to the Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease Score and found to correlate well with slight underestimation by MRI [51]. Gender differences in LGE were examined in patients following acute myocardial infarction [52]. While scar size was not different amongst genders with similar risk profiles, the size of microvascular obstruction was smaller in women. LGE was assessed in patients receiving an implantable cardioverter-defibrillator following myocardial infarction [53]. No difference was seen for recipients for primary versus secondary prevention. A dog model of Duchenne muscular dystrophy was examined by MRI for diffuse myocardial damage [54]. While there were no significant functional differences compared with controls, there was increased perfusion in the dog model with decreased retention coefficient. In another study, myocardial fibrosis was assessed by LGE and compared with quality of life measures in patients with non-ischemic cardiomyopathy [55]. No association was found. The pattern of nulling on the inversion scout sequence was found to be predictive of myocardial amyloid infiltration in a retrospective analysis of 39 patients [56]. The presence of myocardial edema as evidenced by  $T2$ -weighted images

but not LGE was found to be predictive of the presence of viral genome in the peripheral blood in patients with viral myocarditis [57]. In related work, the elimination of T2 weighted images or early gadolinium enhancement was found to reduce the sensitivity of MRI for diagnosing acute myocarditis [58].

T2 mapping was found to be more sensitive than T2-weighted imaging for detection of myocardial edema following reperfusion of myocardial infarction in a small series of patient [59]. In a series of contrast-enhanced CMR patients, 3T was found to be superior to 1.5T for perfusion imaging and LGE [60]. The safety of CMR following percutaneous coronary interventions was confirmed in a retrospective study of 211 patients [61].  $^{23}\text{Na}$  chemical shift imaging and gadolinium enhancement of myocardial edema were found to correlate in an isolated rat model [62].

There were several papers relating to vascular imaging by MRI. Intraplaque hemorrhage was assessed in carotid MRI to identify high risk patients [63]. It was found to be an independent predictor of cardiovascular events. Regional aortic stiffness was assessed in a healthy Asian population by PWV and found to have the highest value in the descending aorta increasing with age [64]. The stability of respiratory motion was found to influence image quality of free-breathing 2D black-blood coronary MRI [65]. Gadobenate dimeglumine and gadoverset trisodium were compared for 3T whole heart coronary MRA [66]. Godofosvest was found to show slightly better performance. Asymmetry of aortic valves was found to affect comparison of MRI to transthoracic echocardiography [67]. Breath-hold versus, non-breath-hold phase contrast imaging was compared in the ascending aorta [68]. Wide differences were found suggesting that the techniques are not interchangeable. The feasibility of flow-gated radial phase-contrast imaging in the presence of weak flow was demonstrated in a small series of patients suggesting use with arrhythmia or weak ECG signals [69].

The dose response of the intravascular contrast agent gadofosveset trisodium for quantitative myocardial perfusion was assessed for 1.5 and 3 T in healthy volunteers [70]. The optimal dose was determined to be 0.00375 mmol/kg at 1.5 T and 0.0075 mmol/kg at 3 T. A new method for quantification of regional myocardial blood flow was validated in swine and applied to humans [71]. Global myocardial blood flow was assessed in the coronary sinus using the myocardial mass. The index of the first pass signal intensity upslope was then indexed to the upslope of the entire LV myocardium. Regional myocardial perfusion was estimated as the product of the indexed upslope and global myocardial blood flow. Good agreement was found compared with  $^{13}\text{NH}_3$ -PET.

## Computed tomography

Over the last few years, the clinical diagnostic utility of cardiovascular CT has expanded significantly, which has been reflected in many articles in the journal. Looking forward, evaluation and publication of advances in three areas are important: *safe data acquisition, novel technical developments supporting novel clinical applications, and eventually demonstration of impact on clinical decision making and outcome*. The following summary of articles published in the 2013 issues of the journal are organized along these goals.

Computed tomography is associated with exposure to ionizing radiation and potentially nephrotoxic contrast material. Major advances in recent years have been reduction of radiation and contrast media exposure. Several related manuscripts have been published in the journal: Burchardt et al. [72] examined the incidence of early renal-function deterioration within 12–18 h after administration of iodine contrast media in 319 patients, scheduled for elective coronary angiography, who were intravenously and orally hydrated. The data suggest that early deterioration of renal function may occur in 13–28 % of all patients.

Komatsu et al. [73] examined application of low-tube voltage (80 kV) for coronary CTA in 154 patients with low body weight. The amount of contrast media (CM) was chosen with a CT number-controlling system. The amount of CM for 80 kV/280 HU, 80 kV/350 HU, and 120 kV/350 HU groups were  $10 \pm 4$ ,  $15 \pm 7$ , and  $30 \pm 6$  mL, respectively. There was no significant difference in image quality between the groups and the amount of CM and effective dose was lower for 80 kV CCTA than for 120 kV CCTA.

Chen et al. [74] used software to simulate reduced radiation exposure in images from 93 consecutive clinical coronary CTA studies, reconstructed with standard filtered back projection (FBP) and adaptive iterative dose reduction in three-dimensions (AIDR3D). The results suggests that a 50 % reduction in radiation dose can be achieved with adaptive iterative dose reduction software with image quality that is at least comparable to images acquired at standard radiation exposure and reconstructed with filtered back projection.

Technical and clinical advances in imaging are often interrelated. Optimally, novel clinical indications can be supported by hard- and increasingly software improvements. Examples of technical advances are novel detector material, dual-source scanners, and wide-detector systems, but also novel data analysis: Kazakauskaitė et al. [75] examined a scanner system with high-definition detector material (HDCT) and iterative image reconstruction algorithm in comparison to a standard definition CT (SDCT)



scanner. 93 consecutive patients underwent HDCT, and were compared to a matched group of patients who had undergone SDCT. The mean image quality score from HDCT versus SDCT was comparable ( $2.02 \pm 0.68$  vs.  $2.00 \pm 0.76$ ) and mean effective radiation dose did not significantly differ between HDCT ( $1.7 \pm 0.6$  mSv, range 1.0–3.7 mSv) and SDCT ( $1.9 \pm 0.8$  mSv, range 0.8–5.5 mSv;  $p = \text{n.s.}$ ). A subsequent paper from the same group examined application to obese patients: In 70 overweight and obese patients segment-based image revealed marginally better scores for HD-ASIR compared to SD-FBP ( $1.5 \pm 0.43$  vs.  $1.8 \pm 0.48$ ;  $p < 0.05$ ) [76]. The estimated effective radiation doses were similar,  $2.3 \pm 0.1$  and  $2.5 \pm 0.1$  mSv (HD-ASIR vs. SD-ASIR respectively).

Dual-source scanners allow imaging with higher temporal resolution but also low dose acquisition using a high-pitch mode: Bischoff et al. [77] examined if higher-pitch imaging is feasible for vascular access imaging (in the context of TAVR) using current single source scanners. Patients with severe symptomatic aortic valve stenosis underwent CT imaging for planning purposes prior to TAVI. 20 patients in each group were examined with a 2nd generation DSCT system using a high-pitch scan mode (pitch value 3.4), or a 128-slice SSCT system, using a high-pitch scan mode (pitch value of 1.7) both with 60 ml of contrast agent. Image quality of the aortic valve, the ascending aorta, the coronary artery ostia, the iliofemoral arteries and overall image quality showed a minor but significant difference in the overall image quality score with lower image quality in SSCT ( $3.5 \pm 0.6$ ) when compared to DSCT ( $3.85 \pm 0.4$ ;  $p = 0.037$ ).

Wide-detector scanners allow prospective coronary imaging in a single heart-beat, reducing step artifact as initially described in the journal in 2008 [78]. Yoo et al. [79] assessed the image quality of coronary CT angiography (CTA) with a 320-detector system (640-slice) reconstructed by adaptive iterative dose reduction (AIDR) in comparison with the conventional filtered back-projection (FBP). CTA images of 51 patients were scanned at the lowest tube voltage suggested by an automatic exposure control system. Mean effective radiation dose was  $2.0 \pm 1.0$  mSv. The AIDR 3D reconstruction algorithm reduced image noise by 39 % compared with the FBP without affecting CT density, improving SNR, CNR, and interpretability.

Chen et al. [80] examined the accuracy of vasodilator stress CMR and coronary CTA in 151 consecutive subjects referred for suspected obstructive CAD. Vasodilator stress CMR was performed on a 1.5 T scanner. CTA was performed on a 320-detector row system. Subjects were followed for cardiovascular events and downstream diagnostic testing over an average period of  $450 \pm 115$  days. Stress CMR and coronary CTA were highly concordant and negative test

results, using a reference standard including quantitative invasive angiography, conferred an excellent prognosis. The event-free survival for patient with negative test results was 97 % for CMR and 99 % for CTA.

Optimization of acquisition technique was discussed in the context of CT-perfusion imaging: Bischoff et al. [81] examined optimal timing of single-phase first-pass stress CTP acquisitions in 16 patients with known or suspected CAD, who underwent invasive coronary angiography with FFR measurements and time-resolved CTP protocol under adenosine stress, performed on a dual-Source CT scanner. From the stress CTP data, time-attenuation curves both in known ischemic myocardium (angiographic coronary artery stenosis with FFR below 0.75), as well as in non-ischemic reference myocardium were derived.

Soft-ware related innovation, which is increasingly important, was described in the context of motion and strain imaging with CT: Tavakoli et al. [82] reported a new method to detect 3D motion and strain from cardiac CT images. The method was validated by using manual tracking of the cardiac CT landmarks and comparison to the cardiac tagged magnetic resonance imaging (MRI) and 2D B-mode echocardiography strain values of the same patients and demonstrated good agreement.

Yang et al. [83] described successful validation of a fully automatic centerline extraction algorithm for coronary arteries in CTA images.

Examples of novel clinical applications include valvular heart disease (including transcatheter valve replacement and prosthetic valve endocarditis), HOCM, and aspects of coronary imaging. For transcatheter procedures including transcatheter aortic valve replacement (TAVR), pre-operative imaging plays an important role. It includes vascular access [6] and the aortic root: Examining 105 consecutive patients with symptomatic severe aortic valve stenosis, Marwan et al. [84] evaluated the correlation between CT parameters and the degree of post-procedural aortic regurgitation (AR). Compared to patients with  $AR < 2$ , patients with  $AR \geq 2$  showed more severe calcification of the aortic annulus as well as higher aortic valve Agatston scores.

Lehmkuhl et al. [85] evaluated the inter-individual variance and the variability of aortic root dimensions during the cardiac cycle using computed tomography (CT) in 56 patients with severe aortic stenosis prior to transcatheter aortic valve implantation (TAVI). The data demonstrates that the systolic effective diameter, as measured by ECG-gated CT, represents an appropriate parameter for sizing the aortic annulus. In about 70 % of the patients with relevant paravalvular leaks the finally implanted prosthesis (based on echocardiography) was too small according to the CT based calculated ED.

Anticipating future transcatheter approaches for mitral valve repair/replacement other papers described the mitral

annulus with CT: Gordic et al. [86] compared mitral annular dimensions with echocardiography and contrast-enhanced cardiac CT in 28 patients with moderate and severe functional mitral regurgitation (FMR) and controls. Using an advanced visualization, segmentation, and image analysis software, the area, intercommissural distance (CC), septolateral distance (SLD), and the anterior and posterior circumference of the MA were measured in diastole. The results provide in vivo human CT data on MA dimensions in normals and patients with FMR.

Imaging of or Prosthetic Valve Endocarditis (PVE) and HOCM is a domain of echocardiography: In this context, Habets et al. [87] examined the potential complementary diagnostic value of CTA to transthoracic and transesophageal echocardiography (TTE/TEE) in 28 patient with PVE. For diagnostic accuracy the reference standard was surgical findings or clinical follow-up. CTA resulted in a major diagnostic change in six patients (21 %) mainly driven by novel detection of mycotic aneurysms by CTA. Furthermore, treatment changes occurred in seven patients (25 %) compared to clinical routine workup.

In patient with HCM, the gold standard imaging modality of myocardial fibrosis (IF) is cardiovascular magnetic resonance (CMR) with late gadolinium enhancement (LGE-CMR). In a validation study Langer et al. [88] examined 24 patients, of whom 14 demonstrated fibrosis by LGE-CMR. Patient- and segment-based sensitivity in fibrosis identification with MDCT was 100 and 68 %, respectively.

Because coronary CTA can visualize occluded vessel segments, pre-procedural CT imaging can be used for planning in patient with chronic total occlusion: Rolf et al. [89] examined 30 patients with chronic total coronary artery occlusions prior to PCI for CTO. Three-dimensional volume-rendered images of the occluded coronary artery were displayed in the catheterization lab during PCI to guide the advancement of the wire. PCI success, defined as the ability to advance the guide wire into the distal lumen with thrombolysis in myocardial infarction III flow was significantly higher than in patients with compared to those without prior coronary CTA [matched: CT 88 % (22/25) vs. no CT 64 % (16/25)  $p = 0.03$ ].

While the primary focus of the journal is clinical imaging, a smaller number of experimental papers discussed aspects of pre-clinical imaging with CT: Saeed et al. [90] described the use MDCT for assessing the effects of coronary microemboli on pre-existing acute myocardial infarct (AMI) based on data in an animal model. MDCT successfully identified perfusion, LV function and viability in comparison to pathology.

Moritz et al. [91] examined the potential of micro-CT to detect localized areas of decreased or increased vascularity in coronary arterial walls in an animal model. Numburi et al. [92] evaluated the optimal C-arm computed tomography

(CT) protocol for transcatheter aortic valve implantation (TAVI) in an animal model.

The impact of imaging findings on clinical outcome was a topic of several papers. Park et al. [93] compared the prognostic power of clinical parameters, biomarkers and imaging parameters in predicting cardiovascular outcome in a large population of 5,182 asymptomatic participants in South Korea. MACE events including cardiac death, acute coronary syndrome and stroke and were found in 1.3 % during median follow up period of 48 months. Various multivariate models including C-reactive protein, Framingham risk score (FRS), coronary artery calcium score and degree of coronary artery stenosis showed that FRS and degree of coronary artery stenosis were independent predictors for future MACE.

While this data extends the known predictive value of CTA to asymptomatic populations, it should not be understood as a justification for use of CTA for risk assessment, a practice not supported by current clinical guidelines.

**Conflict of interest** None.

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