Summary, conclusions and future perspectives
SUMMARY

In recent years, a number of new cardiac interventional procedures have been introduced. For atrial fibrillation (AF), catheter ablation procedures have been refined and are now considered a good treatment option in patients with drug-refractory AF. In cardiac pacing, cardiac resynchronization therapy (CRT) is now standard of care in patients with drug-refractory heart failure. At the same time, CRT may also be beneficial in patients with heart failure after long-term RV apical pacing. Finally, new percutaneous procedures for valvular heart disease have been introduced for patients that are deemed inoperable. At the same time, various imaging modalities have been further developed and important advances have been made in the integration of different imaging modalities.

The aim of the present thesis was to explore the role of multimodality imaging in cardiac interventional procedures. In Part I, the integration of different imaging modalities during catheter ablation procedures for AF was studied. In addition, the effects of these procedures on left atrial (LA) and left ventricular (LV) size and function were investigated. Part II studied the effects of right ventricular (RV) apical pacing on LV dyssynchrony and mechanics, and the effect of upgrade to CRT. Finally, in Part III the role of imaging in new percutaneous procedures for valvular heart disease was explored.

PART I: Catheter ablation for atrial fibrillation

The first part of the thesis focused on catheter ablation procedures for AF. These procedures are performed in an increasing number of patients worldwide. For these procedures, accurate visualization of the LA and pulmonary veins (PVs) is of critical importance. Chapter 2 reviews the different imaging modalities that are available for the assessment of LA and PV anatomy. In daily clinical practice, conventional transthoracic echocardiography is most frequently used to assess LA size and volumes. Three-dimensional imaging techniques such as magnetic resonance imaging and multi-slice computed tomography (MSCT) are mainly used to assess PV anatomy before catheter ablation of AF. In addition, intracardiac echocardiography may be a valuable tool during these procedures. Finally, the integration of MSCT and electroanatomic mapping during catheter ablation procedures is discussed.

Chapter 3 is a clinically oriented review on the use of imaging in the work-up of patients with AF, and provides an overview on the role of imaging in catheter ablation procedures. In the evaluation of patients with AF, associated conditions such as coronary artery disease, valvular heart disease and heart failure should carefully be analyzed. The various imaging modalities that are available for this are reviewed in this chapter. In addition, relevant issues before catheter ablation (detection of thrombi, assessment of LA and PV anatomy) and available imaging techniques are discussed. Finally, an overview of the different imaging modalities that can be integrated to guide catheter ablation procedures is provided.
In Chapter 4, the feasibility of the integration of MSCT images and electroanatomic mapping was tested in 16 patients undergoing catheter ablation for drug-refractory AF. The fusion of pre-procedural acquired MSCT images and electroanatomic maps may facilitate catheter ablation procedures by improved visualization of critical structures such as the PVs. A new image integration module (CartoMerge™) was used to merge the two imaging modalities using dedicated registration algorithms. After fusion of the two images, the mean distance between all mapping points and the MSCT image was $2.1 \pm 0.2$ mm (range 1.7 – 2.8). The integrated image was subsequently used to guide the catheter ablation. This study demonstrates that it is feasible to integrate MSCT images and electroanatomic maps. Image integration can facilitate catheter ablation procedures by improved visualization of important anatomical structures.

The findings of the previous study were extended in Chapter 5. In this study, the feasibility of the integration of intracardiac echocardiography, electroanatomic mapping and MSCT was tested. For this purpose, a newly developed intracardiac echocardiography probe, with an incorporated Carto™ navigation sensor located at its tip, was used. After positioning of the catheter in the right atrium, electroanatomic maps were created by drawing endocardial contours on the real-time intracardiac echocardiography images. Seventeen patients (13 men, mean age 56 ± 8 years) referred for catheter ablation for AF were studied. A mean of 31.1 ± 8.5 contours were used to create the 3D maps of the LA and PVs, and the mean distance between the contours and the MSCT image (registration accuracy) was $2.2 \pm 0.3$ mm. Furthermore, a good agreement between intracardiac echocardiography and MSCT for the assessment of PV anatomy and PV diameters was noted. In conclusion, the feasibility of the integration of intracardiac echocardiography, electroanatomic mapping and MSCT was clearly demonstrated in this study.

Chapter 6 focused on PV anatomy assessment with MSCT before catheter ablation, and its impact on the outcome of the ablation procedures. A total of 100 patients undergoing catheter ablation for AF were evaluated with MSCT. Pulmonary vein anatomy was classified as ‘normal’ or ‘complex’ based on the absence or presence of additional PVs or common ostia (single insertion of PVs). Furthermore, LA dimensions were assessed in three directions. Complex PV anatomy of the left-sided and right-sided PVs was present in 26% and 22% of patients, respectively. Mean LA diameter in the anterior-posterior direction was 41 ± 7 mm. Interestingly, the presence of right-sided complex PV anatomy was associated with an improved outcome of the catheter ablation procedure ($OR = 0.149 \ [0.038-0.576]$, $p=0.006$), whereas LA dilatation was associated with a worse outcome ($OR = 1.083 \ [1.009-1.162]$, $p=0.027$). This study underlines the importance of pre-procedural PV and LA anatomy assessment. Favorable anatomy may have impact on the outcome of catheter ablation procedures.
In the following studies, the effect of catheter ablation procedures on LA and LV size and function were investigated. We hypothesized that successful elimination of AF results in reverse remodeling of the LA. The study described in Chapter 7 included 57 patients treated with catheter ablation for AF. At baseline and after three months follow-up LA size and volumes were assessed with conventional 2D echocardiography. In patients who maintained sinus rhythm during follow-up (n=39), LA size significantly decreased, whereas in patients with recurrence of AF (n=18) LA size increased. In addition, a decrease in LA end-diastolic volume (from 37 ± 9 ml to 31 ± 7 ml, p<0.01) and LA end-systolic volume (from 59 ± 12 ml to 50 ± 11 ml, p<0.01) was noted in patients who maintained sinus rhythm during follow-up. These findings were confirmed in Chapter 8. In this study, real-time 3D echocardiography was used to assess LA size and volumes. This technique may be more accurate and reproducible than conventional 2D echocardiography for assessment of LA volumes. In addition to LA size and volumes, LA function was assessed at baseline and follow-up (mean 7.9 ± 2.7 months). Based on minimum and maximum LA volume, and LA volume just before atrial active contraction, LA function (total emptying fraction, active emptying fraction and passive emptying fraction) was assessed. Significant improvements in LA active function (from 22 ± 8% to 33 ± 9%, p<0.01) and LA reservoir function (from 116 ± 45% to 152 ± 54%, p<0.01) were noted in patients who maintained sinus rhythm. In contrast, LA function showed a trend towards deterioration in patients who had recurrence of AF.

From the abovementioned studies, it appears that LA reverse remodeling may occur after catheter ablation for AF. The following study aimed to elucidate the clinical and echocardiographic determinants of LA reverse remodeling (Chapter 9). Reverse remodeling was defined as ≥15% reduction in maximum LA volume at follow-up. Tissue Doppler imaging was used to assess LA systolic and end-diastolic strain, representing LA expansion function and LA active contraction function, respectively. The study population (n=148) was divided according to the presence or absence of LA reverse remodeling at follow-up (‘responders’ [n=93] or ‘non-responders’ [n=55]). In the responders, a significant increase in LA systolic strain was noted from baseline to follow-up (from 19 ± 8% to 22 ± 9%, p<0.05), whereas no change was noted in the non-responders (from 14 ± 6% to 15 ± 8%, p=NS). Interestingly, LA systolic strain at baseline was the strongest predictor of LA reverse remodeling (OR 1.089; 95% CI 1.014-1.169, p=0.019). This study suggests a close association between LA reverse remodeling after catheter ablation and LA strain.

Finally, in Chapter 10 the long-term effects of catheter ablation on LV function were studied. In this study, speckle-tracking echocardiography was used to assess LV strain in 3 directions (radial, circumferential and longitudinal). This technique may detect more subtle abnormalities in LV systolic function, as compared with conventional parameters such as LV ejection fraction. A total of 78 patients (mean LV ejection fraction 60 ± 7%) were included in the study. After 13.8 ± 4.7 months follow-up, 54 patients maintained sinus rhythm, whereas 24 patients had
recurrence of AF. In the patients who maintained sinus rhythm, LV circumferential strain and LV longitudinal strain significantly improved from baseline to follow-up (from -18.3 ± 3.2% to -20.4 ± 3.8%, p<0.001 and from -18.8 ± 2.7% to -19.6 ± 2.6%, p<0.001, respectively). In contrast, LV circumferential strain remained unchanged and LV longitudinal strain significantly deteriorated in patients with recurrence of AF. This study demonstrates that LV strain improves in patients with preserved LV ejection fraction that are successfully treated with catheter ablation for AF.

**PART II: Ventricular pacing and dyssynchrony**

The second part of this thesis focused on cardiac pacing and mechanical dyssynchrony. In Chapter 11, an extensive review of the available evidence on the effects of RV apical pacing on LV function and dyssynchrony is provided. Large randomized trials on the selection of pacing mode have demonstrated an association between long-term RV pacing and deterioration of LV systolic function and heart failure. These negative effects may be related to the presence of LV dyssynchrony. Several studies have demonstrated that the upgrade from RV apical pacing to biventricular pacing results in (partly) reversal of the detrimental effects of RV pacing. In addition, there is increasing evidence that ‘de novo’ CRT may be preferred over RV apical pacing in patients requiring high amounts of ventricular pacing.

The long-term effects of RV apical pacing on LV function, LV dyssynchrony and heart failure symptoms were studied in Chapter 12. For this purpose, 55 patients were studied 3.8 ± 1.7 years after atrio-ventricular node ablation and pacemaker implantation. Left ventricular dysynchrony was assessed with conventional 2D echocardiography: with the use of M-mode echocardiography the septal-to-posterior wall motion delay was assessed as a measure of intraventricular dyssynchrony. A delay ≥130 ms was used to define significant LV dyssynchrony. In addition, tissue Doppler imaging was used to assess the septal-to-lateral delay at follow-up. At baseline, none of the patients exhibited ventricular dyssynchrony. However, in 27 patients (49%) LV dyssynchrony was present at long-term follow-up. Importantly, LV ejection fraction significantly decreased in patients with LV dyssynchrony (from 48 ± 7% to 43 ± 7%, p<0.05), whereas it remained unchanged in patients without LV dyssynchrony (from 49 ± 6% to 49 ± 8%, p=NS). In addition, NYHA functional class deteriorated in patients with LV dyssynchrony (from 1.8 ± 0.6 to 2.2 ± 0.7, p<0.05), whereas it improved in patients without LV dyssynchrony (from 1.7 ± 0.7 to 1.4 ± 0.5, p<0.01). This study demonstrates that patients may develop significant LV dyssynchrony after long-term permanent RV apical pacing. Importantly, the development of LV dyssynchrony is associated with a deterioration of LV function and functional class.

After these findings, a subsequent study was conducted to investigate if LV dyssynchrony is induced acutely (Chapter 13). For this purpose, 25 patients undergoing electrophysiological testing for supraventricular arrhythmias, and 25 control subjects were studied. At baseline and after at least 5 minutes of RV apical pacing, LV function and dyssynchrony were assessed.
Speckle-tracking echocardiography was used to assess global LV longitudinal strain, LV dysynchrony and LV twist. At baseline, the 25 patients and 25 control subjects were comparable with regard to LV function and LV synchrony (median 21 ms vs. 20 ms, p=NS). However, during RV apical pacing, a significant decrease in LV ejection fraction was noted (from 56 ± 8% to 48 ± 9%, p=0.001). In addition, the time difference between the earliest and the latest activated segments (representing LV dyssynchrony) significantly increased in the study population (from 21 ms [10, 53] to 91 ms [40, 204], p<0.001). In 36% of the patients significant LV dyssynchrony (≥130 ms) was present. In addition, deterioration in LV global longitudinal strain and LV twist was noted after onset of RV apical pacing. Thus, the detrimental effects of RV apical pacing may (partly) occur immediately after onset of pacing.

In patients with significant LV dyssynchrony immediately after onset of pacing or at long-term follow-up, ventricular synchrony may be restored with biventricular pacing (or CRT). For optimal benefit of CRT, the site of latest activation (maximum dyssynchrony) should be identified. Speckle-tracking echocardiography was used in 58 patients with permanent RV apical pacing to detect the site of latest activation in the study described in Chapter 14. Furthermore, the effect of upgrade from RV apical pacing to CRT was studied in a subset of patients. Before RV pacing, similar time-to-peak strain was noted among six LV segments (mean 371 ± 114 ms). However, after long-term RV apical pacing, heterogeneity in time-to-peak strain was noted. Most frequently, the lateral and posterior segments of the LV wall were the site of latest activation (31% and 25%, respectively). This delay resulted in significant LV dyssynchrony in 57% of the patients. Unfortunately, no clinical parameters at baseline could predict LV dyssynchrony. Importantly, 11 patients underwent an upgrade from RV apical pacing to biventricular pacing. In these patients, LV dyssynchrony disappeared and LV ejection fraction significantly improved from 30 ± 8% to 39 ± 7% (p<0.001) after upgrade to CRT. Thus, the detrimental effects of RV apical pacing may (partly) be reversed by CRT.

In Chapter 15 the effect of RV pacing on myocardial oxidative metabolism and efficiency was studied. A total of 10 pacemaker patients (mean age 62 ± 17 years) were studied with the use of echocardiography and positron emission tomography during pacing-OFF (sinus rhythm or atrial pacing) and pacing-ON (RV pacing). Left ventricular dyssynchrony was studied with tissue Doppler imaging and speckle-tracking echocardiography. Myocardial blood flow, oxidative metabolism and myocardial efficiency were derived from the positron emission tomography images. During RV pacing, global myocardial blood flow and oxidative metabolism did not change significantly in the overall study population. However, different effects on cardiac metabolism and efficiency were observed according to the presence or absence of LV dyssynchrony during RV pacing. In patients with LV dyssynchrony during pacing-ON (n=6) a significant decrease in myocardial efficiency was noted (from 78.11 ± 25.35 mmHg·l/g to 60.40 ± 13.93 mmHg·l/g, p<0.05), whereas in patients without LV dyssynchrony (n=4) no significant
change was noted (from 73.55 ± 24.78 mmHg·l/g to 75.32 ± 31.33 mmHg·l/g, p=NS). The presence of LV dyssynchrony during RV pacing appears to be associated with a worsening of LV oxidative metabolism and efficiency. From the abovementioned studies, it becomes clear that assessment of ventricular dyssynchrony in patients with RV pacing has important clinical implications. The presence of LV dyssynchrony is associated with deterioration of LV function, impaired oxidative metabolism and functional status.

PART III: Percutaneous valve procedures

The third part of this thesis focused on percutaneous valve procedures. In recent years, a number of new transcatheter procedures have been introduced to treat severe mitral regurgitation (MR) and aortic stenosis (AS). Various imaging modalities may be of great value for these procedures, in particular for the selection of patients. The various percutaneous valve procedures are reviewed in Chapter 17.

In Chapter 18, MSCT was used in 105 patients to assess coronary sinus anatomy. The relation between the coronary sinus, the mitral valve annulus and the coronary arteries is of critical importance for percutaneous mitral valve procedures that use the coronary sinus to remodel the mitral valve apparatus. The third part of this thesis focused on percutaneous valve procedures. In recent years, a number of new transcatheter procedures have been introduced to treat severe mitral regurgitation (MR) and aortic stenosis (AS). Various imaging modalities may be of great value for these procedures, in particular for the selection of patients. The various percutaneous valve procedures are reviewed in Chapter 17.

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Finally, in Chapter 16, the prevalence of ventricular dyssynchrony in patients with arrhythmogenic right ventricular dysplasia (ARVD) was studied. Arrhythmogenic right ventricular dysplasia is an inherited disease characterized by fibrofatty infiltration of the myocardium. This infiltration may result in electrical conduction delay and mechanical dyssynchrony. However, the prevalence of mechanical dyssynchrony in ARVD has not been studied yet. A total of 52 patients (mean age 41 ± 12 years, 22 men) with ARVD and 25 healthy controls were studied. Transthoracic echocardiography was used to assess ventricular volumes and tissue Doppler imaging was used to determine the extent of mechanical dyssynchrony using time-to-peak systolic velocity (TSV) of the RV free wall, the interventricular septum and the LV lateral wall. Significant RV dyssynchrony was defined as a difference between the RV free wall and interventricular septum of >2 SD above the mean value for control subjects. Mean difference in TSV between the RV free wall and interventricular septum (ΔTSV) was 26 ± 15 ms in the controls (resulting in a cut-off value of 56 ms for RV dyssynchrony) and 55 ± 34 ms in the ARVD patients (p<0.001). In 26 ARVD patients (50%) RV dyssynchrony was present, with RV remodeling rather than electrocardiographic abnormalities.

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the mitral valve annulus. Unfavorable anatomy may result in inefficient remodeling and may impair coronary blood flow. In the present study, a highly variable relation between the coronary sinus and the mitral valve annulus was noted. The coronary sinus was located along the LA wall in the majority of the patients (mean distance 5.1 ± 2.9 mm). Importantly, the circumflex artery coursed between the coronary sinus and the mitral valve annulus in 68% of the patients. In addition, it was noted that the minimal distance between the coronary sinus and the mitral valve annulus was significantly larger in patients with MR as compared with patients without MR (mean 7.3 ± 3.9 mm vs. 4.8 ± 2.5 mm, p<0.05). In patients with large distance between the coronary sinus and mitral valve annulus, or in patients where the circumflex artery courses between the two structures, percutaneous mitral valve procedures may not be feasible. Therefore, MSCT provides important information for the selection of patients for these procedures.

The evaluation of the mitral valve with MSCT was further explored in Chapter 19. The subvalvular apparatus and mitral valve geometry (mitral valve tenting height and leaflet tethering) was evaluated in 151 patients, including 29 patients with moderate to severe MR. An asymmetric deformation of the mitral valve was observed in patients with MR. In these patients, an increased posterior leaflet angle was noted at the central (44.4 ± 11.9°) and the posteromedial (35.9 ± 10.6°) levels. In addition, mitral valve tenting height was significantly increased in patients with MR, compared with patients without MR at these levels (central level: 6.6 ± 1.4 mm/m² vs. 5.3 ± 1.3 mm/m², p<0.001; posteromedial level: 5.4 ± 1.6 mm/m² vs. 4.1 ± 1.2 mm/m², p<0.001). This study demonstrates the value of MSCT in the evaluation of anatomical and geometric characteristics of the mitral valve.

The remaining of the studies focused on percutaneous aortic valve procedures. In Chapter 20, an extensive review of the available studies on percutaneous aortic valve procedures is provided. The majority of these studies clearly demonstrate high procedural success rates, low 30-day mortality and good prosthesis function during follow-up. In addition, the recommendations on selection of patients for percutaneous aortic valve procedures are reviewed in this chapter. At present, these procedures are only recommended in patients with symptomatic, severe AS that are deemed inoperable. Finally, the use of various imaging modalities in the selection of patients, performing aortic valve procedures and follow-up is reviewed.

Multi-slice computed tomography is one of the imaging modalities that may provide important information on aortic valve anatomy before percutaneous valve procedures. Therefore, the anatomy of the aortic root was assessed with MSCT in 169 patients referred for non-invasive coronary angiography (including 19 patients with moderate to severe AS) in Chapter 21. In addition to the extent and location of valvular calcifications, standardized measurements of the aortic root were performed. Reconstructed MSCT images were used to assess the aortic annulus diameter in two directions. The orientation of the reconstructions was similar to the image orientation that is used during the actual percutaneous valve implantation. Furthermore,
the distance between the aortic annulus and the ostia of the coronary arteries was measured. These parameters may have great impact on prosthesis sizing and on the feasibility of the procedure. Interestingly, an oval shape of the aortic annulus was noted, with a mean diameter of 26.3 ± 2.8 mm on the coronal view, and 23.5 ± 2.7 mm on the sagittal view. Large variation in the distance between the aortic annulus and the left coronary ostium (mean 14.4 ± 2.9 mm, range 7.1 to 22.7 mm) and the right coronary ostium (mean 17.2 ± 3.3 mm, range 9.2 to 26.3 mm) was noted. Importantly, the length of the coronary leaflet exceeded this distance in up to 49% of the patients. This may increase the risk of coronary occlusion during percutaneous valve procedures. Thus, MSCT may provide important information for the selection of patients for percutaneous aortic valve replacement.

These findings were confirmed in a group of 26 patients with severe AS referred for percutaneous aortic valve replacement (Chapter 22). Before the percutaneous valve implantation and after 4 months follow-up, MSCT images were analyzed using the same measurements as in the previous study. Measurements of aortic annulus diameters with MSCT, echocardiography and fluoroscopy were compared. In addition, the stent diameter and the distance between the left coronary artery and the stent wall were assessed. Mean distance between the aortic annulus and the left coronary ostium was 15.0 ± 3.0 mm. Comparable results for aortic annulus diameters were noted with different imaging modalities: mean difference between MSCT and transthoracic echocardiography was -0.3 mm (95% confidence interval -1.1 to 0.6 mm). After percutaneous aortic valve replacement, the prosthesis extended above the coronary ostia in 50% of the patients. In addition, in 78% of the patients a circular deployment of the prosthesis was noted. Importantly, no association was found between the aortic annulus shape and the proportion of patients who developed perivalvular aortic regurgitation. This study clearly demonstrates the value of MSCT in the pre-procedural assessment and follow-up of patients with severe AS referred for percutaneous aortic valve replacement.

CONCLUSIONS AND FUTURE PERSPECTIVES

The studies described in the present thesis explore the role of multimodality imaging in cardiac interventional procedures. In recent years, exciting advances have been made in the invasive treatment of AF, cardiac pacing and the percutaneous treatment of valvular heart disease. The selection of patients for these procedures, the procedures themselves and the follow-up of patients may be greatly facilitated by the use of imaging modalities. Importantly, the integration of different imaging techniques may enhance visualization of critical anatomic structures during the interventional procedures.
Catheter ablation for atrial fibrillation

Careful identification of LA and PV anatomy is of critical importance for successful catheter ablation of AF. Importantly, the anatomy of the PVs and LA has impact on the outcome of the catheter ablation procedure. Different imaging modalities are available for assessment of LA and PV anatomy. Unfortunately, each imaging modality also has its drawbacks. Image integration may overcome the limitations of each separate imaging modality by combining the different techniques. The studies in the present thesis demonstrate that the integration of different imaging modalities is feasible, and provides additional information during the catheter ablation procedure. Future studies are needed to further explore image integration in the electrophysiology laboratory. Large randomized trials are needed to assess the impact of image integration on the outcome of AF ablation procedures. In addition, in the near future new imaging techniques such as rotational angiography (providing real-time 3D fluoroscopic images comparable to MSCT) and real-time magnetic resonance imaging (in a hybrid suite) may have great impact on AF ablation procedures.

Furthermore, the present studies demonstrate that successful catheter ablation of AF results in reverse remodeling of the LA and improvement of LA and LV function. Unfortunately, the exact pathophysiologic mechanism remains to be determined. Furthermore, it remains unclear whether the maintenance of sinus rhythm results in reverse remodeling, or vice versa (‘chicken or egg’). Additional studies are therefore needed to find predictors of reverse remodeling, and pre-clinical studies may contribute to a better understanding of this phenomenon. It may well be that the amount of fibrosis in the LA plays an important role in the outcome of catheter ablation procedures. Pre-procedural evaluation of LA scar with dedicated imaging techniques may then be of great value. Finally, assessment of LA scar and ablation lesions using magnetic resonance imaging after the procedure may provide important information on the effect of catheter ablation procedures on LA and LV function.

Ventricular pacing and dyssynchrony

The detrimental effects of long-term RV apical pacing as demonstrated in large pacing mode trials and smaller observational studies may be related to the induction of LV dyssynchrony. The present studies demonstrate that about half of the patients with long-term RV apical pacing develop significant LV dyssynchrony and exhibit deterioration of LV function. The presence of LV dyssynchrony during RV pacing is also associated with worsening of cardiac oxidative metabolism and efficiency. By restoration of synchronous contraction, CRT may (partly) reverse the detrimental effects of long-term permanent RV apical pacing. Importantly, LV dyssynchrony may be present immediately after onset of RV apical pacing. Finally, from the present studies it has become apparent that significant ventricular dyssynchrony is also present in up to 50% of patients with ARVD. More studies are needed to clarify the underlying mechanism, and the clinical implications of these findings.
With regard to RV pacing and ventricular dyssynchrony, a number of important questions remain unanswered, and need to be addressed in future studies. For example, why do some patients develop significant LV dyssynchrony with RV pacing, while others do not? Both patient- and pacemaker-related parameters that may predict the development of mechanical dyssynchrony and deterioration of cardiac function need to be identified. Is acutely induced LV dyssynchrony associated with deterioration of LV function during follow-up? Should future studies confirm that there is a relation between acutely induced LV dyssynchrony and worsening of LV function and functional class at long-term follow-up, assessment of LV dyssynchrony at pacemaker implantation may have important implications. Biventricular pacing may then be considered in patients with significant LV dyssynchrony immediately after onset of pacing. Furthermore, screening for LV dyssynchrony on a regular basis in patients with conventional RV pacing may identify patients that may benefit from upgrade to CRT.

**Percutaneous valve procedures**

In recent years, a number of exciting procedures and prostheses have been introduced for the percutaneous treatment of severe valvular heart disease. The present studies demonstrate that cardiac imaging provides critical information for percutaneous valve procedures. In particular, MSCT plays an important role in the selection of patients referred for these procedures. This 3D imaging technique clearly visualizes the relation between the coronary arteries, coronary veins and affected valves. Both for percutaneous mitral valve procedures using coronary sinus annuloplasty and transcatheter aortic valve replacement, this relation is of utmost importance. Furthermore, MSCT allows visualization of the prosthesis, and the relation with surrounding structures, after implantation.

Future studies will need to address a number of important issues. The long-term durability of the prostheses and favorable long-term clinical outcome needs to be demonstrated. At the same time, more studies comparing percutaneous and surgical treatment of valvular heart disease are warranted. The results of the PARTNER trial (The Placement of AoRTic TraNscaThetER Valve Trial) comparing percutaneous and surgical aortic valve replacement in 350 patients are eagerly awaited. This trial may add important evidence on the role of percutaneous valve procedures in the treatment of patients with severe AS. Should future studies demonstrate equal or superior efficacy and long-term durability, it may well be that the indication for percutaneous valve procedures is expanded. This is of particular interest when considering the percutaneous ‘valve-in-valve’ concept in patients with degenerated aortic bioprostheses. Finally, more studies are needed to examine the ability of different imaging modalities to improve the safety of percutaneous valve procedures. In particular, the feasibility of image integration during percutaneous valve procedures needs to be studied.