Changes of Pulmonary Vein Orifice Size and Location throughout the Cardiac Cycle: Dynamic Analysis Using Magnetic Resonance Cine Imaging

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Dynamic Pulmonary Vein Analysis. ***Introduction:*** **Anatomically guided left atrial ablation is used increasingly for treatment of atrial fibrillation (AF). Three-dimensional mapping systems used for pulmonary veins (PV) encircling ablation procedures anticipate a stable size and position of the PV orifice. The aim of the current study was therefore to analyze changes of PV orifice size and location throughout the cardiac cycle using cine magnetic resonance imaging (MRI).**

Methods and Results: **Twenty-five healthy volunteers were studied using a 1.5 Tesla MRI system. MR angiograms were acquired with a breath-hold three-dimensional fast-spoiled gradient-echo imaging (3D FSPGR) sequence in the coronal plane before and after gadolinium injection. Maximum intensity projections and multiplanar reformations were performed to reconstruct images of the PV. Bright blood cine imaging in the axial view was acquired by a steady-state free precession pulse sequence. Twenty bright blood images were obtained per cardiac cycle. The axial (anterior-posterior) PV orifice diameter was measured in all 20 images. For analysis of PV movement the location of the orifice posterior edge was plotted on scale paper.**

PV orifice size depends on the stage of the cardiac cycle with the largest diameter in late atrial diastole and a mean decrease of 32.5% during atrial systole. Location changes of the PV orifice are in the range of up to 7.2 mm and larger in the coronal (lateral-medial) than in the sagittal (anterior-posterior) direction.

Conclusion: **PV orifice size and location is not as stable as anticipated by three-dimensional mapping systems used for PV encircling left atrial ablation procedures. RF application close to the presumed orifice location should therefore be avoided to minimize the risk of PV stenosis.** *(J Cardiovasc Electrophysiol, Vol. 16, pp. 582-588, June 2005)*

magnetic resonance imaging, pulmonary vein, atrial fibrillation, dynamic change

Introduction

Catheter ablation of the pulmonary veins (PV) recently emerged as a new treatment option for patients with atrial fibrillation (AF).[1-5] There are two main technical approaches to PV isolation. First, the segmental ostial ablation under guidance of a circumferential mapping catheter, which is placed in the PV orifice.[6-11] Second, the creation of linear ablation lesions in large circuits around the PV orifices under guidance of a three-dimensional mapping system.[12-14] In contrast to the segmental ostial ablation, the circumferential left atrial ablation is mainly guided by anatomical instead of electrophysiological information. Three-dimensional mapping systems anticipate a stable position and size of the PV orifice.[15-17] The location and diameter of the PV orifice, however, may change during the cardiac cycle with potential impact on safety and efficacy of the ablation procedure. Magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) have been proven powerful tools for evaluation of PV anatomy before and after PV ablation.[18-23] Dynamic changes of PV orifice size and location have not been evaluated by means of MRI so far. The aim of the current study was to analyze changes of PV orifice size and location throughout the cardiac cycle using cine MRI.

This study was supported in part by National Institutes of Health grant 1RO1-HL-64795.

Presented in part at the American Heart Association Scientific Sessions 2003, Orlando, Florida.

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Received 24 October 2004; Revised manuscript received 19 December 2004; Accepted for publication 4 January 2005.

doi: 10.1111/j.1540-8167.2005.40724.x

Methods

Study Subjects

Twenty-five healthy volunteers (13 men) were studied. None had a history of cardiovascular disease, hypertension, or lung disease. Their mean age was 47 ± 7 years (range 29–59 years). The study was approved by the Johns Hopkins University institutional review board. All subjects gave informed written consent.

Magnetic Resonance Angiography

A 1.5 Tesla MRI system (Signa Horizon LX; GE Medical Systems, Milwaukee, WI) with a body coil or a torso phased-array coil was used. Images were obtained before and after contrast-medium (0.2 mmol/kg gadolinium-diethyl triamine pentaacetic acid) was injected. MR angiograms were acquired with a breath-hold three-dimensional fast-spoiled gradient-echo imaging (3D FSPGR) sequence in the coronal plane. Imaging parameters were as follows: TR/TE 3.7–4.6 per 1.2–1.6 ms; flip angle 30–40°; receiver band width 62.5 kHz; field of view 36–40 × 34–36 cm; slice thickness 2.2–2.4 mm; number of partitions 34–42; matrix 256 × 160–192. Zero filled interpolation was performed in the slice direction to obtain images every 1.1–1.2 mm, and in plane zero filling resulting in a final matrix of 512 × 512. Source images were transferred to a workstation (Advantage Windows 4.0, GE Medical Systems). Maximum intensity projection (MIP) and multiplanar reformations (MPR) were performed to reconstruct images of the PV.

Magnetic Resonance Cine Imaging

Bright blood cine imaging in the axial view was acquired by a steady-state free precession pulse sequence. The following imaging parameters were used: TR = 1 RR interval, slice thickness 5 mm, no interslice gap, field of view = 32 cm, 15–20 seconds breath-hold time. Twenty bright blood images were obtained per cardiac cycle. The temporal resolution for the cine images was 40–50 ms and the spatial resolution 1.4 mm. Images were analyzed at a workstation (Advantage Windows 4.0, GE Medical Systems). The axial (anterior-posterior) PV orifice diameter was measured in all 20 images. The anterior PV orifice was defined as the point where the contour of the left atrium makes an angle to create the PV orifice. From here, a rectangular line was drawn posterior to define the posterior boundary of the PV orifice. For analysis of PV movement the location of the orifice posterior edge as given by the MRI scanner coordinates was plotted on scale paper. By doing this, 20 points for each PV were obtained on scale paper representing the PV orifice movement throughout the cardiac cycle. The distances between the points furthest apart in the coronal and sagittal directions were then measured for each PV.

Statistical Analysis

Variables are given as mean ± standard deviation. Parameters of PV diameter and location changes between the four individual PV were compared using a Student's *t*-test. A P value <0.05 was considered statistically significant. The intraobserver variability of MRI measurements was 0.9 ± 0.8 mm, and the interobserver variability was 1.3 ± 1.2 mm.

Results

Anatomical Characteristics

MR angiography analysis showed normal PV anatomy (Fig. 1) with 2 left and 2 right PV in 20 of 25 subjects. The anatomical variant of a common orifice of the left-sided PV was observed in three subjects. An additional PV between the right superior and right inferior PV (right middle PV) was found in two subjects. One subject exhibited the presence of two additional right-sided PV, a right middle and a right top PV, which originated above the right superior PV and extended posteriorly and upward. This anatomical variant has been referred to as "right top pulmonary vein."[23]

PV Diameters and Changes Throughout the Cardiac Cycle

MR cine imaging analysis of the PV could be performed in all subjects; the right superior and left inferior PV could be analyzed in all, and the right inferior PV in 23 of 25 patients. The left superior PV however could only be analyzed in 9 of 22 patients due to its upward course, which did not allow accurate measurement in the axial MRI projection. Figure 2 shows a representative example of MR cine images at two different stages; at the end of left atrial diastole with maximum left atrial volume just before beginning of left atrial contraction (left side) and at the time of minimum PV

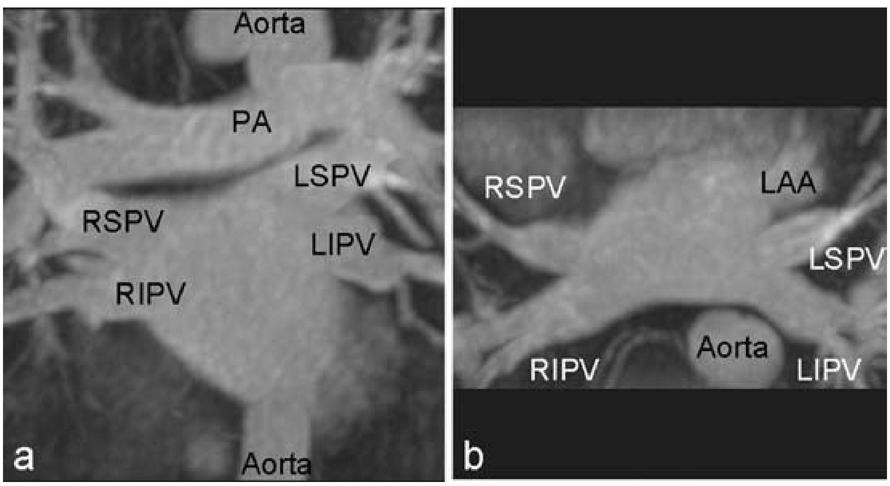

Figure 1. *Magnetic resonance angiography of normal pulmonary vein and left atrial anatomy. Three-dimensional reconstructions using maximum intensity projections (MIP). Oblique coronal view with a slice thickness of 46mm. A: Oblique axial view with a slice thickness of 30 mm, resembling a view from the feet of the subject. The large slice thickness as well as tilting of the imaging plane enable visualization of all four pulmonary veins on a single image. PA = pulmonary artery; RSPV = right superior pulmonary vein; RIPV = right inferior pulmonary vein; LSPV = left superior pulmonary vein; LIPV = left inferior pulmonary vein; LAA = left atrial appendage.*

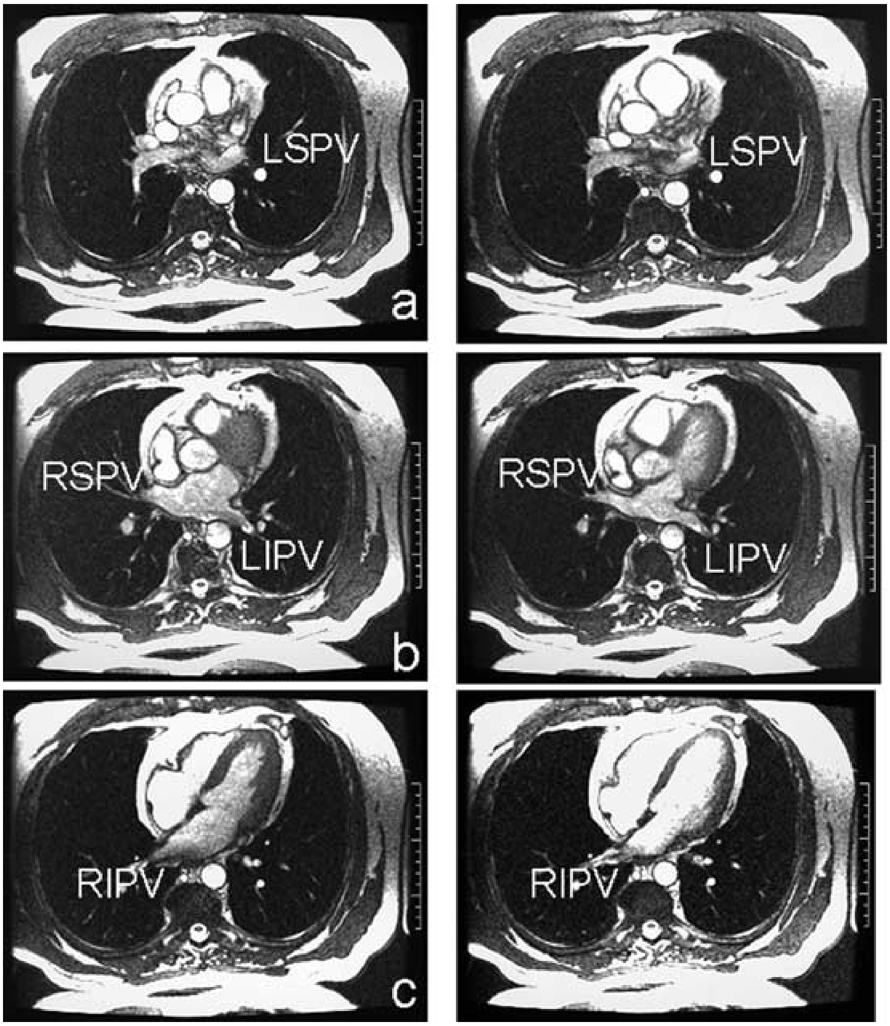

Figure 2. *Magnetic resonance bright blood cine images in the axial view with a slice thickness of 5 mm. Pulmonary veins are shown at the left atrial end-diastolic time (left side) and at the time of minimum pulmonary vein diameter (right side). A = Left superior pulmonary vein; B = Right superior and left inferior pulmonary vein; C = Right inferior pulmonary vein.*

orifice diameter (right side). Analysis of PV orifice size at 20 different consecutive stages of the left atrial cycle revealed a characteristic pattern with two down-strokes of the PV orifice diameter curve (Fig. 3). The PV orifice size is expressed as the percentage of the value at left atrial end-diastolic time (time 1 on x axis) in this figure. Noteworthy, PV diameter decreased in parallel to left atrial contraction indicating active contraction of the PV wall musculature rather than passive filling patterns secondarily to left atrial pressure changes. As shown in Figure 4, mean PV orifice diameter in axial view throughout the left atrial cycle was 11.9 $\pm$ 2.4 mm for right superior PV, 13.1 $\pm$ 3 mm for right inferior PV, 11.9 $\pm$ 1.8 mm for left superior PV, and 8.6 $\pm$ 2.3 mm for left inferior PV. The mean diameter of the left inferior PV orifice was significantly smaller than the mean orifice diameter of the three other PV. The PV orifice diameter reduction during atrial systole, as compared to end-diastolic diameter, was 39 $\pm$ 9% for right superior PV, 31 $\pm$ 9% for right inferior PV, 32 $\pm$ 6% for left superior PV, and 28 $\pm$ 7% for left inferior PV. The individual difference between the largest and the smallest diameter was between 5.7 mm in the case of the right superior PV and 2.8 mm in the case of the left inferior PV. It was significantly smaller in the left inferior PV than in the other three PV.

Changes of PV Location Throughout the Cardiac Cycle

The extent of movement of the posterior edge of the PV orifice throughout the left atrial cycle is shown in Figures 5 and 6. In general, PV orifice movements in the coronal direction (lateral-medial) are significantly larger than movements in the sagittal direction (anterior-posterior) (Fig. 6). Movements in the coronal direction are largest in the left superior PV and smallest in the right inferior PV. Movements in the sagittal direction are largest in the right superior PV and smallest in the left inferior PV. Regarding the coronal direction, there is a significant difference between the right superior PV and right inferior PV and between both inferior PV. Regarding the sagittal direction, there is a significant difference between the left inferior PV and the right-sided PV.

Discussion

Main Findings

There are several important findings in the present study. First, this study demonstrates that PV orifice size and location can be analyzed by means of MR cine imaging. Second, PV

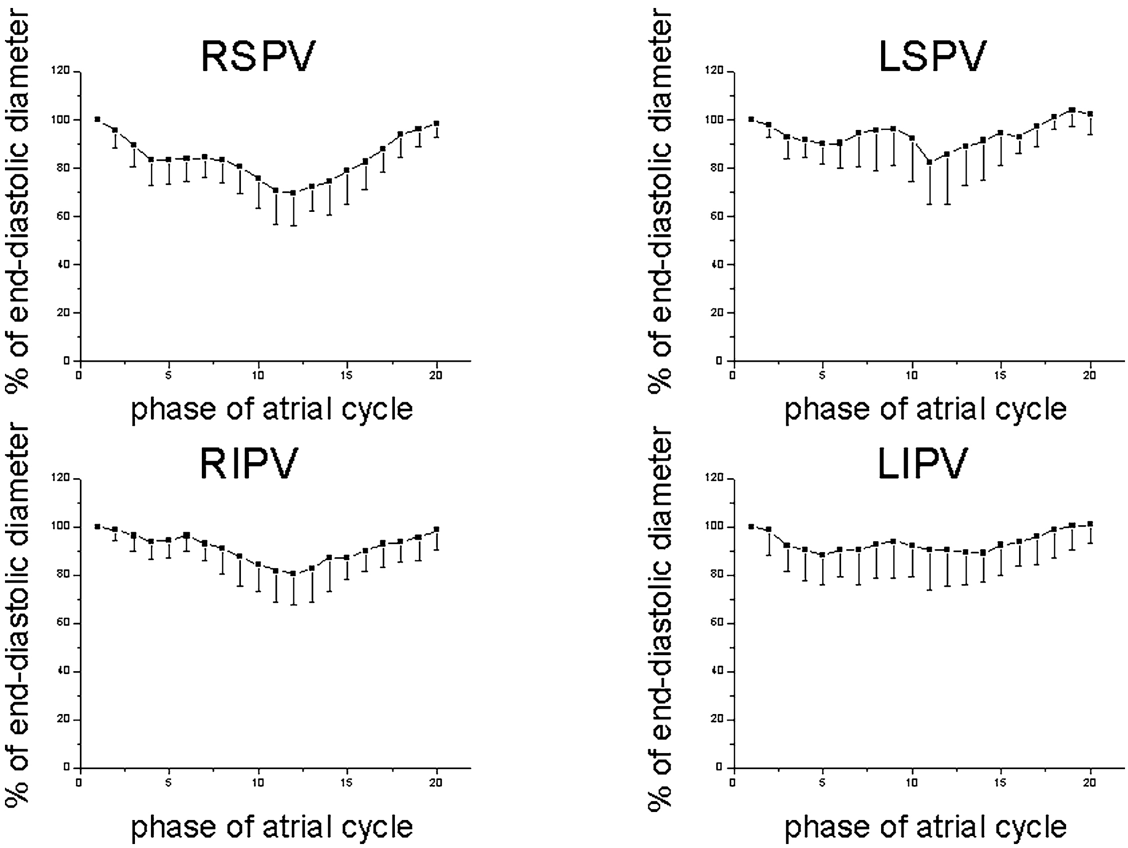

Figure 3. *Pulmonary vein orifice diameter change throughout the left atrial cycle. The diameters are expressed as the percentage of the value at left atrial end-diastolic time (time 1 on x axis). Left atrial end-diastolic time was determined as the time of maximum left atrial volume just before left atrial contraction. RSPV = right superior pulmonary vein; RIPV = right inferior pulmonary vein; LSPV = left superior pulmonary vein; LIPV = left inferior pulmonary vein.*

orifice size changes considerably throughout the left atrial cycle. Third, location changes of the PV orifice are in the range of up to 7.2 mm and larger in the coronal (lateral-medial) than in the sagittal (anterior-posterior) direction. Fourth, PV diameter decreases in parallel to left atrial contraction indicating active contraction of the PV wall musculature rather than passive filling patterns secondarily to left atrial pressure changes. It seems possible that the amount of PV orifice contraction correlates with the amount of ostial PV musculature. In this case cine MR imaging could facilitate an estimation of the amount of ablation energy necessary for ostial catheter ablation.

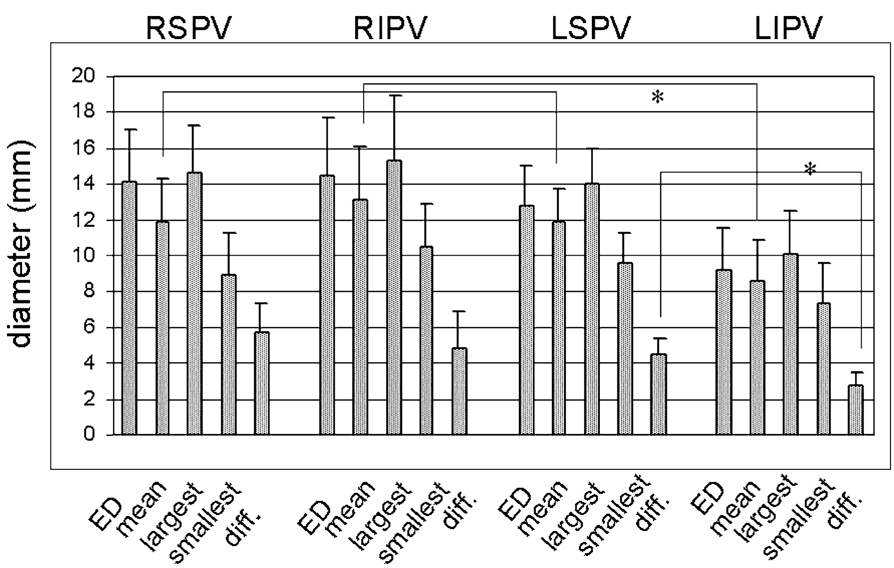

Figure 4. *Pulmonary vein orifice diameter change throughout the left atrial cycle. Shown are the end-diastolic (ED), mean, largest, and smallest pulmonary vein diameter as well as the difference between the largest and smallest diameter (difference). RSPV = right superior pulmonary vein; RIPV = right inferior pulmonary vein; LSPV = left superior pulmonary vein; LIPV = left inferior pulmonary vein. *P value <0.05.*

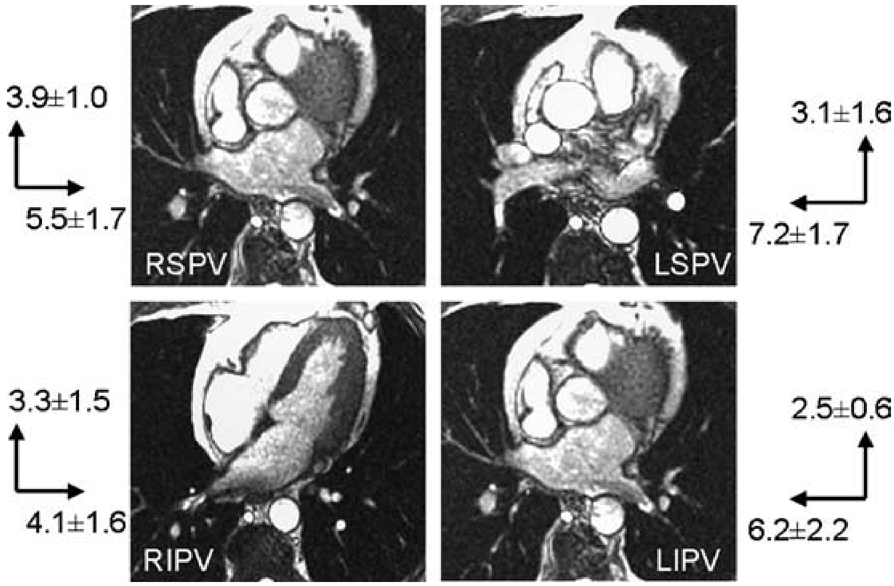

Figure 5. *Pulmonary vein orifice location changes throughout the left atrial cycle. Shown are the extent of movements (mm) of the posterior edge of the pulmonary vein orifice in the sagital direction (vertical arrows) and in the coronal direction (horizontal arrows). RS = right superior pulmonary vein; RI = right inferior pulmonary vein; LS = left superior pulmonary vein; LI = left inferior pulmonary vein.*

Current Approaches for AF Ablation

Strategies for catheter ablation of AF have changed significantly since identification of the PV as important triggers of AF by Haissaguerre and colleagues.[1-3] The initial approach of focal ablation targeting arrhythmogenic triggers was replaced subsequently by empiric isolation of the PV at the atrio-venous junction.[6-11] Pappone and colleagues developed a different technique of AF ablation, creating circumferential linear lesions around the PV orifices under the guidance of a three-dimensional mapping system.[5,12] Current three-dimensional mapping systems provide a spatial resolution between less than 1 and 2 mm. This approach of left atrial instead of PV junction catheter ablation is increasingly used by other institutions as well.[13,14] Potential advantages are the lower risk of PV stenosis as well as a higher success rate for patients with persistent instead of paroxysmal AF.[13] Three-dimensional orientation during the ablation, however, is more difficult, partly due to the fact that a mapping catheter is usually not placed into the PV orifice. Three-dimensional mapping systems used for the technique of left atrial ablation anticipate a stable position and size of the PV orifice.[15-17] Location and diameter of PV orifice however may change during the cardiac cycle with potential impact on safety and efficacy of the ablation procedure. Left atrial ablation in some distance from the PV orifice will not be influenced by PV orifice diameter changes in the range of a few millimeters. It is however sometimes difficult to keep adequate distance from the PV orifice for example when ablating the left atrium between the left superior PV and the left atrial appendage.

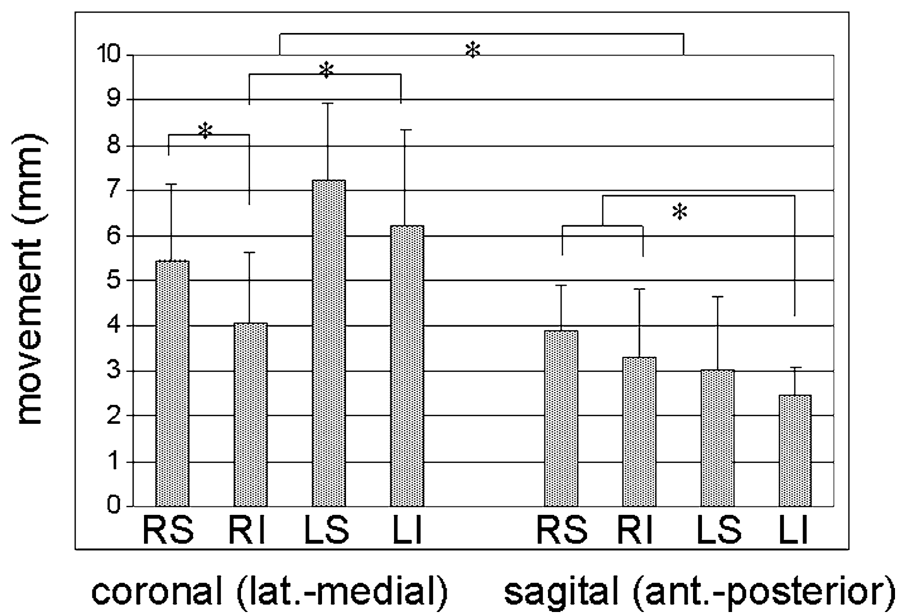

Figure 6. *Pulmonary vein orifice location changes throughout the left atrial cycle. Shown are the extent of movements of the posterior edge of the pulmonary vein orifice in the coronal direction (left) and in the sagital direction (right). RS = right superior pulmonary vein; RI = right inferior pulmonary vein; LS = left superior pulmonary vein; LI = left inferior pulmonary vein.* **P value <0.05.*

In these circumstances it is therefore important to stay as far away from the PV orifice as technically possible. Sometimes reduction of RF energy might be considered.

Current three-dimensional mapping systems give the wrong impression of a static size and shape of the analyzed heart chamber without consideration of systolic and diastolic changes. Another approach for depicting a heart chamber and showing the ablation catheter in relation to it is real-time MRI-guided electrophysiology study and ablation.[24] It has the advantage that the pictorial information provided by the system is not reconstructed but real. Another potential advantage is that the complete information about one heart chamber can be acquired much faster compared to the mostly used contact-mapping systems. Real-time MRI for catheter ablation purposes is however still experimental and not yet available in the clinical setting.[24]

Pulmonary Vein Imaging

Different modalities are available for imaging of the PV. Methods used during the ablation procedure consist of selective contrast angiography[25,26] as well as intracardiac or transesophageal echocardiography.[27–30] In contrast, computed tomography[31,32] and gadolinium-enhanced magnetic resonance angiography[18–23] are performed and analyzed in advance of the ablation procedure. There is only one previous report of the use of MRI for dynamic analysis of PV diameter throughout the cardiac cycle[33] (see below).

Dynamic Analysis of PV Size and Location

Our results demonstrate that MR cine imaging can be used for dynamic analysis of PV orifice size and location. PV orifice size depends on the stage of the cardiac cycle with the largest diameter in late atrial diastole and a mean decrease of 32.5%. The minimum diameter is reached early in the second half of the left atrial cycle. The left inferior PV exhibited significantly less change of orifice size than the other three PV; the difference between the largest and smallest orifice diameter was only 2.8 mm, compared to 5.7 mm in the case of the right superior PV.

MRI cine imaging was also used to track the posterior edge of the PV orifice. It was found that the posterior PV orifice moves significantly more in the coronal direction (lateral-medial) than in the sagittal direction (anterior-posterior). The largest coronal movement was found in the left superior PV (7.2 mm) and the largest sagittal movement in the right superior PV (3.9 mm). The smallest sagittal movement was found in the left inferior PV (2.5 mm).

We cannot deduce from our results whether PV orifice movements are due to PV contraction, left atrial contraction or left ventricular forces. It is likely that there is not a single mechanism behind PV movement, but rather more than one influence.

Previous Studies on Pulmonary Vein Dynamics

There are only very few previous studies on dynamic changes of the PV. Gefter and colleagues also used cine MR imaging (GRASS technique) to measure dynamic changes of pulmonary arteries and veins.[33] Fluctuations in PV were less pronounced than in arteries and not given in exact numbers. The authors stated that the results are descriptive and semiquantitative. In contrast to our study, only the inferior PV were analyzed and the proximal PV rather than the PV orifice was measured. Another method was used by Chiang and colleagues.[34] They performed transesophageal echocardiographic M-mode evaluation in 12 dogs for analyzing dynamic changes of the PV orifice diameter. They found that the peak PV diameter difference throughout the cardiac cycle was between 26 and 49% with a mean of 35%, which is very similar to our results. They also reported a similar pattern compared to our results with narrowing of the PV orifice during left atrial contraction and extension during left atrial diastole.

Limitations

The present study was performed in healthy volunteers rather than in AF patients. It demonstrates the degree of PV orifice diameter and location changes of normal subjects. It is therefore unclear if the results can be applied to patients referred for catheter ablation of AF. Another limitation of the study is that it provides no information about PV orifice diameter and location changes during ongoing AF. It is likely that changes of PV orifice size and location are most pronounced in healthy subjects with no structural and functional changes of PV and left atrium. So the results of this study likely indicate the upper range of dynamic changes, which can be expected during catheter ablation of AF. Patients with chronic AF can be expected to have the least changes of PV orifice size and location changes. Cardiac comorbidities resulting in volume and/or pressure overload of the left atrium can also be expected to impair normal dynamics of PV orifice size and location.

Due to the MRI image acquisition technique we were only able to analyze PV diameter change and movement in the axial view. The present study therefore cannot demonstrate the complex three-dimensional patterns of PV orifice diameter and location changes during the cardiac cycle. PVs are not round but rather oval in shape.[18,21] It is therefore possible that PV orifice size is even more variable in a superior-inferior direction. Attempts to perform three-dimensional reconstructions of cine images and subsequently to analyze PV diameter change in the coronal projection were not successful due to significant loss of image quality.

Clinical Implications

This study demonstrates that PV orifice size and location is not as stable as anticipated by three-dimensional mapping systems used for PV encircling left atrial ablation procedures. RF application close to the presumed orifice location should therefore be avoided to minimize the risk of PV stenosis. Based on our findings we would recommend that a 5-mm distance from the presumed PV orifice should be kept at least during PV encircling ablation at all times.

One can predict that PV orifice diameter change is considerably less during AF because of the lack of active PV contraction. It is also likely that the PV orifice location is more stable during AF compared to sinus rhythm. One can therefore conclude that ablation is safer during ongoing AF compared to sinus rhythm.

Seeing the results of our study showing considerable location changes of the PV orifice it can be explained why there is often the impression that a circumferential mapping catheter moves in and out of the PV orifice. In this case the circumferential catheter apparently keeps a stable position but the PV orifice moves along the long axis of the catheter. In this case ablation at the level of the circumferential catheter increases the risk of PV stenosis.

Due to the fact that the size of the PV orifice is considerably variable during the left atrial cycle, comparison of PV orifice size before and after ablation by means of cine MRI or fast CT should be performed during the same phase of the cardiac cycle.

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