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## CT Imaging to Assess the Left Atrial Appendage Anatomy: Clinical Implications

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### 1. Introduction

The left atrial appendage (LAA) is a highly complex anatomical structure distinct from the rest of the left atrium from an embryologic, anatomic, and pathophysiologic standpoint. While the LAA is a remnant of the embryonic left atrium, the remaining of the left atrial cavity derives from an outgrowth of the pulmonary veins. From a pathophysiologic perspective, the LAA is not just an embryologic remnant. Rather, it plays a significant role in the thromboembolic risk associated with atrial fibrillation, and is a demonstrated trigger site of atrial tachyarrhythmias. Moreover, LAA regulates normal cardiac physiology through functional receptors that influence heart rate, and secretes natriuretic peptides in response to change in left atrial pressure. In recent years, the study of LAA anatomy and its relationship with surrounding structures has gained increasing interest, as transcatheter techniques of LAA exclusion and radiofrequency ablation of left atrial tachyarrhythmias have been increasingly implemented.

Multidetector computerized tomography (CT), with its capability to distinguish among small density differences in structures attenuation, is emerging as the noninvasive reference test to image the LAA and define its anatomy and topographic relationships.

This chapter will review the role of CT to image the LAA, discussing the clinical implications different LAA morphologies detected at CT imaging.

### 2. Anatomy and physiology of the LAA

The LAA originates from primordial atrial tissue and is a remnant of the embryonic left atrium. The LAA lies in the left atrioventricular sulcus atop the proximal portion of the left circumflex artery; posteriorly it has a close relationship with the left superior pulmonary vein, with a distance between the ostia of these two structures (i.e., ridge) varying from 5.8 to 23.7 mm (Su et al., 2008). Another structure that have relationship with the epicardial lateral aspect of the LAA is the left phrenic nerve, which risks to be damaged when the LAA is approached during epicardial procedures (Sanchez-Quintana et al., 2005).

The shape of the LAA has significant variability. Anatomical studies have described the LAA as a long, narrow, tubular, and hooked structure (Kitzman et al., 1988, Sharma et al., 1988). Significant age- and sex-related differences in macroscopic anatomy have also been reported (Veinot et al., 1997).

In more than two-thirds of cases, the LAA consists of two or more lobes, which are usually located in different planes. This has important clinical implications when the LAA is studied to rule out intracavitary thrombus. Indeed, failure to image all the lobes or incomplete visualization of a lobe may account for under- or over-diagnosis of LAA thrombosis. The lobes extend toward the atrioventricular groove and the basal surface of the left ventricle.

The ostium of the LAA is typically elliptical, with a long diameter ranging from 10 to 24.1 mm and a short diameter ranging from 5.2 to 19.5 mm (Su et al., 2008). The length of the LAA ranges from 20 to 45 mm (Veinot et al., 1997), and the average distance between the ostium and the point at which the LAA change its orientation is 7 to 12 mm (Su et al., 2008).

The LAA is lined by a single layer of endothelium and contains pectinate muscles with a course perpendicular to its long axis. The thickness of the pectinate muscles is variable, and areas with deficient myocardium have been described on the anterolateral wall close to the mitral valve (Su et al., 2008), at an average distance of 4 mm from the LAA ostium. In these areas, the LAA may reach a minimum thickness of 0.5 mm, and particular care should be taken to avoid perforation during invasive procedures.

From a physiologic perspective, the LAA is not just an embryologic remnant.

It contains functional stretch-sensitive receptors that influence heart rate, and secretes natriuretic peptides in response to change in atrial pressure. A quantitative analysis of atrial natriuretic peptides (ANP) contained in excised LAAs revealed a content of approximately 30% of all cardiac ANP (Chapeau et al., 1985). Experimental studies have demonstrated that infusion of fluid in the LAA result in increased heart rate, diuresis and natriuresis; this further supports a significant role of the LAA in regulating normal cardiac physiology (Kappagoda et al., 1972a, Kappagoda et al., 1972b).

The LAA has a distinct pattern of contraction, and shortens to a greater extent than the rest of the left atrium. The pattern of normal blood flow in the LAA has been extensively studied with transesophageal echocardiography (Garcia-Fernandez et al., 1992, Pollick & Taylor, 1991). The LAA empties with a typical biphasic pattern; with a first passive phase that occurs in protodiastole and a second active phase that occurs during left atrial contraction. Therefore, pathophysiological changes leading to either decreased diastolic performance of the left ventricle or absence of left atrial contraction (or both), may lead to incomplete emptying of the LAA and thrombus formation.

### **3. Role of the LAA in cardiac pathophysiology**

The LAA is the site most commonly associated with thrombus formation in patients with atrial fibrillation. The reasons why during atrial fibrillation thrombus occurs most frequently in the LAA and spare other regions, including the right atrial appendage, are incompletely understood. Transesophageal echocardiography studies have reported that up to 98-100% of atrial thrombi occurring during atrial fibrillation derive from the LAA (Leung et al., 1994, Manning et al., 1994). The variants of LAA structure and function have been studied in relation to thrombus formation and stroke.

The LAA size is associated with increased thromboembolic risk (Somerville & Chambers, 1964). Studies with transesophageal echocardiography have reported occurrence of spontaneous echocontrast and smoke-like effect most likely in patients with larger LAA (Pollick & Taylor, 1991). Thus far, no data have linked different shapes of the LAA to the thromboembolic risk of patients with atrial fibrillation.

The hemodynamic function of the LAA is also important in relation to the thromboembolic risk of patients with atrial fibrillation. To this regard, three LAA flow patterns have been described: type I characterized by a regular biphasic emptying pattern, and occurring in sinus rhythm; type II characterized by a saw-tooth emptying pattern, and occurring in some patients with atrial fibrillation; type III without any active emptying pattern and typically occurring during atrial fibrillation. The latter pattern is associated with the highest incidence of spontaneous echocontrast and thrombus (Garcia-Fernandez et al., 1992).

The arrhythmogenic role of the LAA in triggering atrial tachyarrhythmias is a matter of increasing interest (Di Biase et al., 2010b, Miyazaki et al., 2011, Takahashi et al., 2005). Our group has recently reported that up to one third of patients presenting for repeat catheter ablation of atrial fibrillation actually have the LAA as the triggering site for atrial fibrillation (Di Biase et al., 2010b).

## 4. CT imaging of the LAA: Clinical implications

### 4.1 CT imaging to diagnose LAA thrombosis

Transesophageal echocardiography is the imaging modality of choice to diagnose LAA thrombosis. Studies of comparison with intraoperative observations have disclosed a sensitivity and specificity of transesophageal echocardiography of 100% and 99%, respectively, with a positive and negative predictive values of 86% and 100% (Manning et al., 1995). However, transesophageal echocardiography is semi-invasive. Multidetector cardiac CT is emerging as a powerful diagnostic tool to detect LAA thrombosis (Kim et al., 2007, Patel et al., 2008, Shapiro et al., 2007, Singh et al., 2009, Tang et al., 2008, Tani et al., 2003).

Tani et al. evaluated the usefulness of CT for detecting LAA thrombi in patients with chronic atrial fibrillation as compared to transesophageal echocardiography (Tani et al., 2003). In this study, 96 patients with chronic atrial fibrillation underwent CT scan either in the standard supine position (71 cases) or in the prone position (25 cases). A LAA filling defects, defined as a clearly circumscribed area with lack of contrast enhancement in the LAA, was diagnosed in 13 (18%) patients undergoing CT in the supine position, and in 4 (16%) of those undergoing CT in the prone position. Transesophageal echocardiography confirmed LAA thrombi in 9/13 patients in whom CT was performed in the supine position, and in 4/4 of those who undergo CT in the prone position. In conclusion, CT was demonstrated to high sensitivity and specificity to diagnose LAA thrombosis, especially when it was performed in the prone position.

Shapiro et al. have compared the diagnostic performance of CT with that of transesophageal echocardiography to diagnose LAA thrombosis or spontaneous echocontrast (Shapiro et al., 2007). Overall, 43 patients were included in the study; of these, 10 (23%) had evidence of LAA thrombosis at transesophageal echocardiography, while 11 (26%) patients had spontaneous echocontrast without LAA thrombus. Cardiac CT failed to detect 3 of 10 thrombi (sensitivity, 70%; negative predictive value, 90%) and misclassified 6 of 33 filling defects (specificity, 82%; positive predictive value, 54%). Interestingly, in each of the 6 false-positive computer tomographic cases, the TEE revealed spontaneous echo contrast.

The role of CT to rule out LAA thrombosis has been also extensively evaluated in patients undergoing atrial fibrillation ablation (Table 1). These patients frequently undergo both transesophageal echocardiography to exclude thrombus and CT to define pulmonary vein anatomy.

Study	N. Pts	Prevalence LAA thromb.	Sens.	Spec.	PPV	NPV
Kim et al. 2007	223	15 (6.7%)	93%	85%	31%	99%
Tang et al. 2008	170	11 (6.5%)	36%	94%	29%	96%
Singh et al. 2009	51	2 (3.9%)	100%	96%	50%	100%
Martinez et al. 2009	402	9 (2.2%)	100%	92%	23%	100%

N. = number; Pts = patients; Thromb. : thrombosis; Sens. = sensitivity; Spec. = specificity; PPV = positive predictive value; NPV = negative predictive value.

Table 1. Diagnostic accuracy of LAA filling defects on CT in diagnosing LAA thrombosis (assessed by transesophageal echocardiography) in selected studies of atrial fibrillation ablation.

Kim et al. have evaluated the accuracy of CT detect LAA filling defects in patients undergoing pulmonary vein antrum isolation (Kim et al., 2007). Overall, 223 patients were included in the study. CT identified LAA filling defects with a sensitivity, specificity, positive and negative predictive values of 93%, 85%, 31% and 99% respectively, as compared to TEE (Kim et al., 2007).

These results have been recently confirmed by Martinez et al. in a cohort of 402 patients (Martinez et al., 2009). Overall, 362 patients (91%) had no evidence of a filling defect by CT or left atrial spontaneous echo contrast or thrombus by transesophageal echocardiography. In 40 patients, a LAA filling defect was detected by CT, which was confirmed as thrombus in 9 patients. The estimated sensitivity and specificity were 100% and 92%, respectively, with a positive and negative predictive values of 23% and 100%, respectively. Notably, in the Martinez’s paper, most patients (91%) actually had no evidence of any LAA filling defect at CT or thrombosis at transesophageal echocardiography.

In fact, the incidence of LAA thrombosis in patients undergoing catheter ablation of AF has been reported low also by our group in a previous study (Khan et al., 2008). We assessed the incidence of LAA thrombosis in a prospective study including 1,221 patients undergoing pulmonary vein antrum isolation. All patients received a CT before the ablation procedure; 601 received a transesophageal echocardiography and all patients who had LAA filling defects at CT received also a transesophageal echocardiography to confirm the presence of LAA thrombosis. Overall, 9 patients had LAA filling defects on CT scan, but only 3 of these had LAA thrombosis on transesophageal echocardiography. Notably, 2 of these patients had chronic atrial fibrillation with an average left ventricular ejection fraction of 48%, and 1 patient had paroxysmal atrial fibrillation with severe left ventricular dysfunction (ejection fraction = 25%). These data support that patients with paroxysmal atrial fibrillation and normal left ventricular ejection fraction have very low incidence of LAA thrombosis, and CT alone is likely to be sufficient in these patients to reliably rule out LAA thrombosis (Khan et al., 2008).

The introduction of atrial fibrillation ablation under therapeutic warfarin has significantly changed the scenario of pre-procedural screening for LAA thrombosis (Di Biase et al., 2010a). We have recently reported that when ablation is performed without therapeutic warfarin discontinuation and patients had at least 4 weeks of international normalized ratio consistently >2, even pre-procedural transesophageal echocardiography can be avoided, as



already it is the common practice for electrical cardioversion of persistent atrial fibrillation (Fuster et al., 2011).

4.2 CT imaging for transcatheter LAA exclusion

Percutaneous transcatheter exclusion of the LAA is an important strategy to virtually eliminate the thromboembolic risk of atrial fibrillation and avoid the need for long-term oral anticoagulant therapy. This technique has been developed as an alternative to surgical ligation or amputation, which have been demonstrated very effective in reducing the risk of thromboembolism associated with atrial fibrillation. Three devices have been specifically designed for percutaneous LAA exclusion: the Percutaneous LAA Transcatheter Occlusion (PLAATO; ev3, MN, USA), the WATCHMAN® LAA device (Atritech Inc., MN, USA) and the AMPLATZER® Cardiac Plug (AGA Medical, MN, USA). The effectiveness and safety of LAA exclusion with the WATCHMAN® device has been demonstrated in a large international trial (Figure 1). The PLAATO has been withdrawn from the market in 2006. At that time most of the published reports suggested acceptable efficacy and safety profiles; the formal reason provided by the company for the withdrawal of the device was the over-large financial investment projected to obtain clinical approval (Ostermayer et al., 2005). The AMPLATZER® device is currently undergoing active investigation in a prospective trial (NCT01118299); this device has several important differences with the WATCHMAN® and may be useful for different subsets of patients (Table 2).

Specification	AMPLATZER®	WATCHMAN®
Manufacturer	AGA Medical, MN, USA	Atritech Inc., MN, USA
FDA Approval	No	No
CE-Mark	Yes	Yes
Sizes	8 sizes (16 mm to 30 mm)	5 sizes (21 mm to 33 mm)
Delivery sheath size	9-13 French	12 French
Transesophageal echo guidance	Recommended	Recommended
Device retrieval	Possible before release	Possible before release
Oral anticoagulants	Not necessary	Recommended at least 45 days
Initial dual antiplatelet therapy	Yes	Yes (after oral anticoagulant)
Long-term antiplatelet therapy	No	Recommended

Table 2. Characteristics of commercially available percutaneous occlusion devices for the LAA.

Percutaneous LAA exclusion is most reasonably indicated for patients with significant risk of thromboembolic complications (i.e., CHADS<sub>2</sub> score ≥2) who are unable to tolerate anticoagulants because of increased risk of bleeding complications or poor compliance. An accurate imaging assessment of the LAA and its relationship with surrounding structures is of utmost importance for percutaneous LAA exclusion. As mentioned, the LAA is closely associated with the left aortic sinus and, therefore, with the ostium of the left coronary artery. Particular care should be exercised when choosing the size of a LAA occlusion device, since oversizing the device may result in compression of the left circumflex artery.

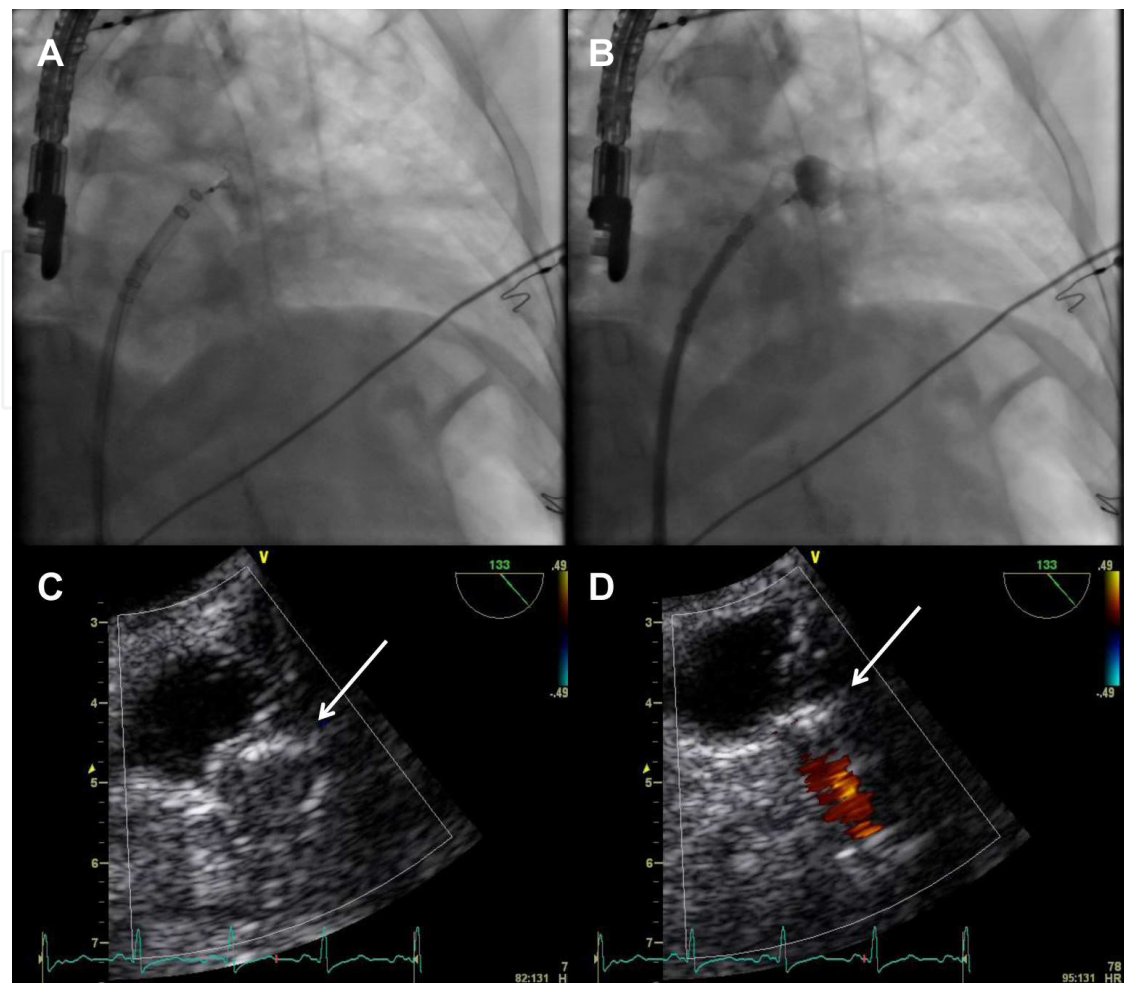


Fig. 1. Placement of a WATCHMAN® left atrial appendage exclusion device. Panels A and B show transcatheter deployment (Panel A) and contrast injection (Panel B) in the left atrial appendage, without evidence of contrast leaking. The correct positioning of the device is confirmed by real-time transesophageal echocardiography (Panels C and D), which confirms absence of leaking by Color Doppler study (Panel D).

With regard to the shape of the LAA, it is important to remark that the ostium of this structure is typically elliptical, while all available occluders have a round shape. This may well account for incomplete sealing of the orifice and leakage from the LAA. More than two-thirds of the LAA have two or more lobes originating from a common opening; usually different lobes are positioned in different anatomical planes. The distance between the LAA orifice and the point at which the LAA first deviates from its original course (LAA neck) range from 7 to 12 mm; this distance is very important for a correct device deployment (Su et al., 2008).

A correct imaging assessment of the LAA is crucial to plan for LAA device closure. Transesophageal echocardiography is required to define the size and shape of the LAA; the ostium, neck, and depth of the LAA. The zone of device landing is usually the junction between the proximal third and the medial third of the LAA, and can be easily assessed with transesophageal echocardiography.

Cardiac CT is of valuable aid in evaluating the shape of the LAA and in defining its relationships with surrounding critical structures.

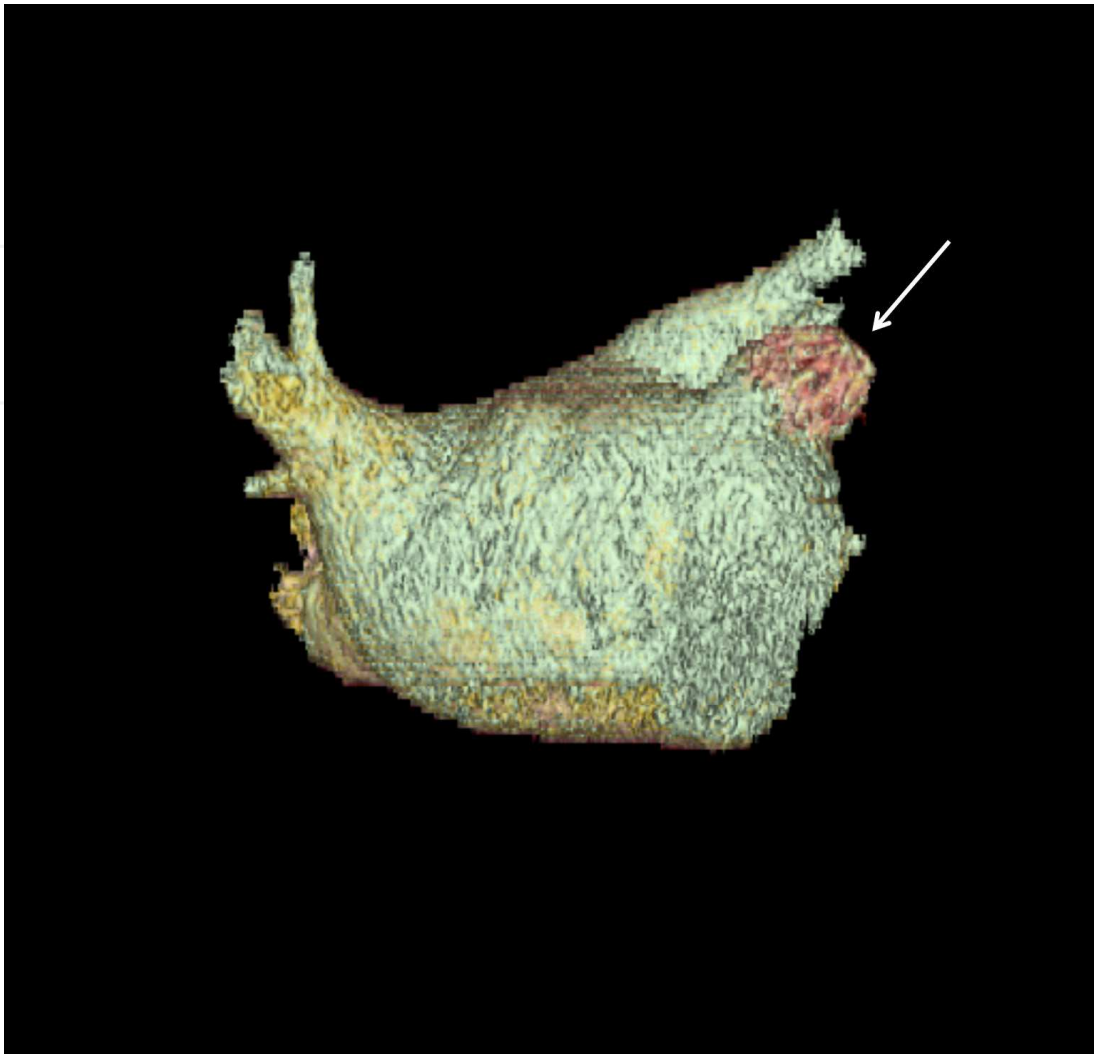


Fig. 2. Antero-posterior CT imaging of the left atrium after WATCHMAN® device placement (Arrow).

As mentioned, the ostium of the LAA is in close proximity to both the left superior pulmonary vein and the left aortic sinus, from which the left coronary artery arises. CT studies have demonstrated that the LAA ostium can be located at different levels relative to the left superior pulmonary vein ostium, namely, above the left superior pulmonary vein, in the same plane, or underneath it.

In the latter case, the LAA is in the closest contact with the circumflex coronary artery (Su et al., 2008). In this case, particular care should be taken with implantation of percutaneous LAA exclusion devices or with radiofrequency catheter ablation, since damage to the circumflex artery can occur.

In a recent study, our group investigated the LAA morphology in 612 patients, evaluating the reproducibility of different measurement methods for determining the size of the LAA orifice in different cardiac phases.

In particular, the LAA morphology, the relationship with the left pulmonary veins, the LAA volume, number of lobes, the angle of the first LAA bend, the distance from the first bend to the LAA orifice, and the distance between the LAA orifice and the septum were studied on three-dimensional CT images (Wang et al., 2010).



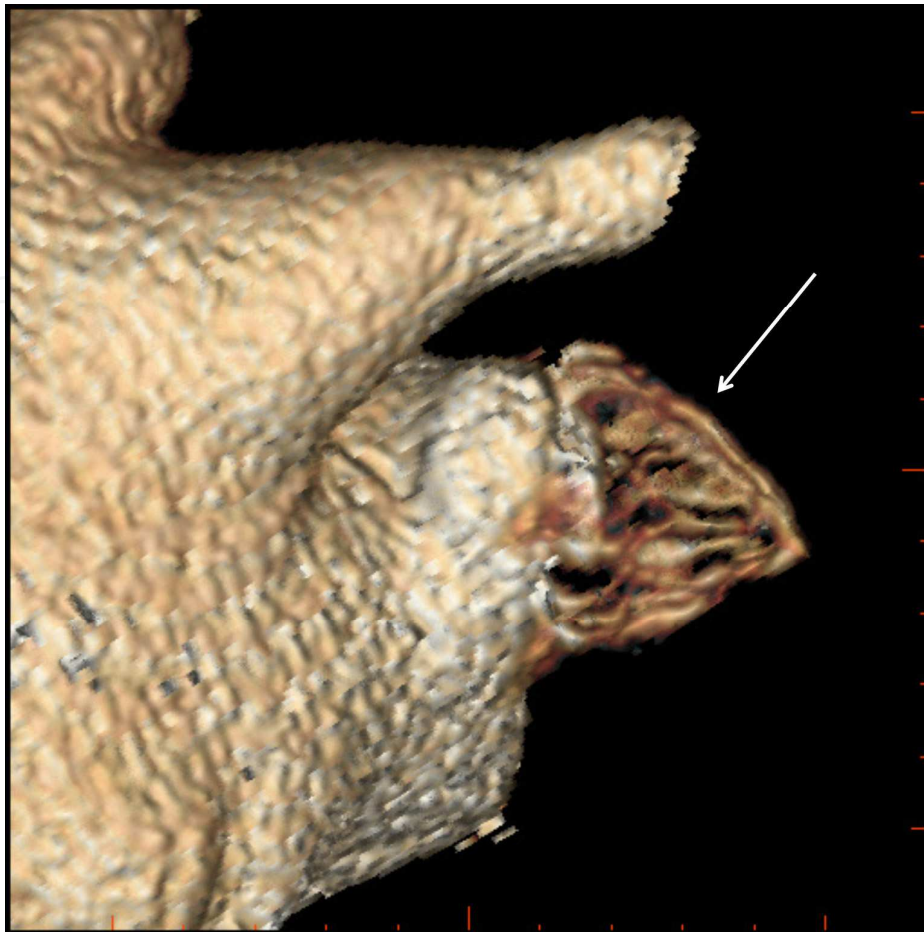


Fig. 3. CT detail of the WATCHMAN® device correctly positioned in the left atrial appendage.

The LAA morphology was initially classified on the basis of the presence of an obvious bend, giving to the LAA an appearance similar to a chicken wing (18.3% of cases).

In the absence of an obvious bend, the LAA was classified as: 1) windsock shaped (46.7%), with 1 dominant lobe; 2) cauliflower shaped (29.1%), that has limited overall length with more complex internal characteristics; 3) cactus shaped (5.9%), with a dominant central lobe and secondary lobes extending from the central lobe in both superior and inferior directions (Figure 4).

The approximate LAA length, defined as length of the primary lobe only from the LAA orifice to the LAA apex was  $45.8 \pm 12.1$  mm and the LAA volume was  $8.8 \pm 5.6$  mL. An obvious bend in the primary lobe was seen in 73.2% of patients, with an angle of the first bend of  $97.6 \pm 20.3$  degrees.

Analysis of the LAA ostium showed a round shape only in 5.7% of cases, with the majority of LAA presenting an elliptical shape (68.9%). The diameters of the ostium in the horizontal, coronal, and sagittal plane were  $18.5 \pm 4.9$  mm,  $20.6 \pm 4.4$  mm, and  $17.0 \pm 4.0$  mm. Long- and short-axis diameters were  $25.4 \pm 5.5$  mm and  $16.8 \pm 4.5$  mm, respectively. Interestingly, these diameters showed minimal changes during different phases of the cardiac cycle in sinus rhythm (maximal change 1 to 2 mm), while no change was observed during atrial fibrillation.

Our study shed additional light on the complex anatomy of the LAA, which is crucial for a correct positioning of LAA occlusion devices. Those factors may include the distance

between the fossa ovalis where the transseptal access is obtained to the base of the LAA, the LAA shape, its anatomic relationships with the left pulmonary veins, the distance between the ostium and the first bend, and the shape and dimension of the LA orifice.

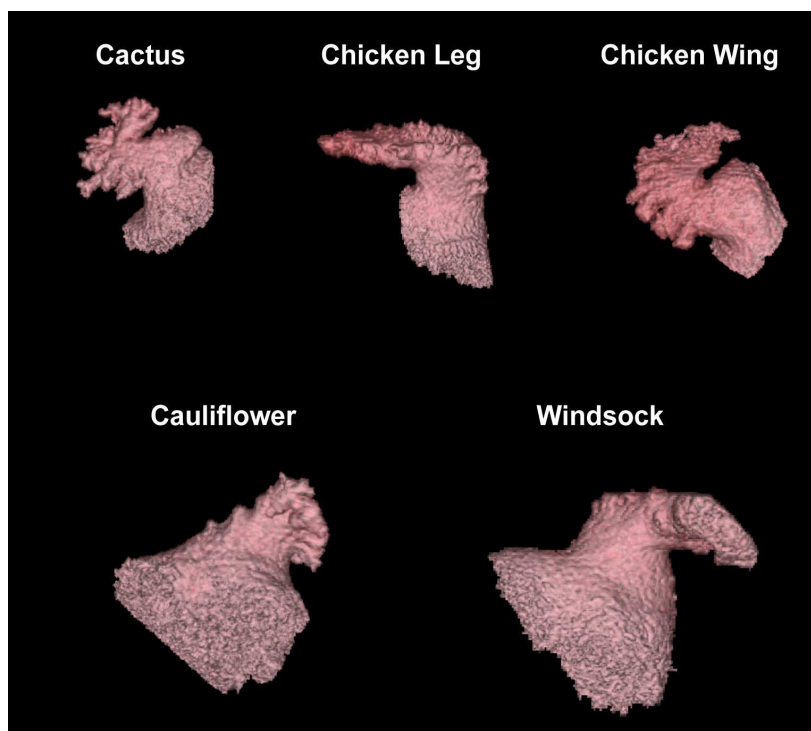


Fig. 4. Different shapes of the left atrial appendage as assessed by cardiac CT imaging.

## 5. Conclusions

CT is an accurate tool to non-invasively detect LAA thrombosis. Moreover, it allows an accurate assessment of the LAA anatomy. Different parameters such as the morphology and diameter of the LAA orifice, the shape of the LAA, and the angle of the LAA bend can be accurately defined by CT. All these parameters are crucial for a correct positioning of LAA occlusion devices.

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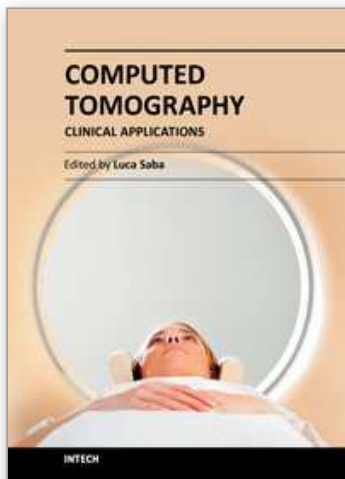
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## **Computed Tomography - Clinical Applications**

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Computed Tomography (CT), and in particular multi-detector-row computed tomography (MDCT), is a powerful non-invasive imaging tool with a number of advantages over the others non-invasive imaging techniques. CT has evolved into an indispensable imaging method in clinical routine. It was the first method to non-invasively acquire images of the inside of the human body that were not biased by superimposition of distinct anatomical structures. The first generation of CT scanners developed in the 1970s and numerous innovations have improved the utility and application field of the CT, such as the introduction of helical systems that allowed the development of the "volumetric CT" concept. In this book we want to explore the applications of CT from medical imaging to other fields like physics, archeology and computer aided diagnosis. Recently interesting technical, anthropomorphic, forensic and archeological as well as paleontological applications of computed tomography have been developed. These applications further strengthen the method as a generic diagnostic tool for non-destructive material testing and three-dimensional visualization beyond its medical use.

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