CT sizing for left atrial appendage closure is associated with favourable outcomes for procedural safety

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Aims
We evaluated the utility of computerized tomography (CT) with respect to sizing work-up for percutaneous left atrial appendage (LAA) closure, and implications for procedural safety and outcomes.

Methods and results
Contrast-enhanced multi-detector CT was routinely conducted to guide sizing for LAA closure in addition to transoesophageal echocardiography (TOE). Procedural safety and efficacy were prospectively assessed. Across 73 consecutive cases there were no device-related procedural complications, and no severe leaks. Systematic bias in orifice sizing by TOE vs. CT was significant on retrospective analysis (bias −3.0 mm vs. maximum diameter on CT; bias −1.1 mm vs. mean diameter on CT). Importantly, this translated to an altered device size selection in more than half of all cases, and median size predicted by CT was one interval greater than that predicted by TOE (27 mm vs. 24 mm). Of particular note, gross sizing error by TOE vs. CT was observed in at least 3.4% of cases. Degree of discrepancy between TOE and CT was correlated with LAA orifice eccentricity, orifice size, and left atrial volume. Mean orifice size by CT had the greatest utility for final Watchman device-size selection.

Conclusions
In this single-centre registry of LAA closure, routine incorporation of CT was associated with excellent outcomes for procedural safety and absence of major residual leak. Mean orifice size may be preferable to maximum orifice size. A particular value of CT may be the detection and subsequent avoidance of gross sizing error by 2D TOE that occurs in a small but important proportion of cases.

Keywords
left atrial appendage closure • LAA • CT • safety • procedural hazard • Watchman

Introduction
The prevention of stroke and systemic embolism remains an overarching consideration in the management of individuals with atrial fibrillation. No satisfactory pharmacological strategy is currently available for individuals where the risks of long-term oral anticoagulation (OAC) are prohibitive. Percutaneous closure of the left atrial appendage (LAA) has an emerging role in this setting.1 Implantation is not free of complications however, with both randomized studies and recent registry data reporting a significant procedural hazard of ~2–8%.1,4 and perhaps even higher in a recent European survey of individual centres.5 Measures that reduce the risk of procedural complications thus merit particular consideration in this emerging technology.

A correct sizing of the LAA orifice is an important stage in procedural planning, with transoesophageal echocardiography (TOE) typically playing a key role in this regard.6 Evaluation of this complex structure by two-dimensional imaging is challenging however. Recent data have reported discordant measurements by TOE in comparison with isotropic datasets such as multi-detector computerized tomography (CT).7,8 These data were primarily acquired from individuals undergoing procedures unrelated to LAA closure however and thus could not report whether device-size selection was altered, and/or

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clinical outcomes were not reported. Moreover, current vendor recommendations are based upon 2D-TOE measurements and as such may not be immediately transferrable to CT measurements. The utility of CT in LAA orifice sizing thus remains uncertain. We sought to evaluate: (i) procedural outcomes of percutaneous LAA closure following a routine incorporation of CT-guided sizing, and (ii) a comparison of TOE vs. CT with respect not only to LAA sizing, but also the clinical relevance with regards to device-size selection.

**Methods**

**Patient selection**

A registry was prospectively established for all consecutive individuals undergoing LAA occlusion under our care between July 2010 and December 2015. Eligible individuals were those with an indication for anticoagulation in atrial fibrillation as determined by a CHA2DS2-VASc risk score ≥2 but in whom the risks of long-term OAC were deemed to be prohibitive.

**CT imaging**

Pre-procedure contrast-enhanced multi-detector CT (dual-source FLASH high-pitch spiral, 2×128 slice, Siemens Definition) was used to evaluate the left atrium (LA) and LAA. Temporal resolution was 75 ms with a gantry rotation time of 0.28 s, detector collimation of 128×0.6 mm, pitch of 3.4 and tube voltage of 100–120 kV according to body habitus. A volume of 50 ml of contrast (Omnipaque 350, GE Healthcare, Buckinghamshire, UK) was delivered via the antecubital vein with a 50 ml saline flush at 5 ml/s. Automated contrast bolus tracking with a region of interest placed in the LA was triggered at 100 Hounsfield units. Where LAA opacification was noted to be suboptimal at the time of image acquisition, a second delayed-phase image (~30 s) that was localized to the appendage could be acquired to facilitate the distinction between thrombus vs. incomplete filling.

**CT sizing of the LAA orifice**

Multi-planar reconstruction was used to obtain orthogonal views of the neck of the LAA and thus a double-oblique en face view of the orifice (Figure 1). Thin-slab views on CT were used for measurements. Orifice sizing was in accordance with vendor guidelines. Thus for sizing of intra-appendage devices (Watchman, Boston Scientific Corporation, MA or WaveCrest, Coherex Medical, UT) the orifice was at the neck immediately distal to the circumflex artery/at the mitral annulus and a point ~15±5 mm from the tip of the limbus, but reflecting as closely as possible the site where the proximal aspect of the closure device would be expected to lie. For sizing of an ostial closure device (Amplatzer, St. Jude Medical, MN) the orifice was the landing zone ~10 mm distal to the LAA ostium. In each case the major axis, minor axis and perimeter were identified. Mean diameter could then be derived from orifice perimeter. 3D volume- and endoscopic-rendering allowed further appreciation of morphology and spatial associations of neighbouring structures.

**TOE sizing of the LAA orifice**

Transoesophageal echocardiography and fluoroscopy at the time of procedure under general anaesthesia provided complementary assessment of LAA size, morphology, and the exclusion of thrombus. TOE was conducted by either of two imaging cardiologists with extensive experience across the spectrum of a mature cardiac structural interventional program. The identification of LAA orifice in relation to limbus, ostium, circumflex artery and mitral annulus was as described above for CT sizing, with careful evaluation during a comprehensive sweep of transducer planes (0°–20°, 40°–60°, 80–100° and 120–140°). Orifice size by TOE was taken as the largest orifice diameter obtainable from a meticulous review of all views.

**LAA occlusion procedure**

All procedures were conducted in concert by an interventional cardiologist and electrophysiologist via femoral venous access under general anaesthesia. Trans-septal puncture was followed by unfractionated intravenous heparin at a dose of 70–100 IU/kg, target activated clotting time >250 s. Images from both CT and TOE were considered side-by-side to determine orifice size. Closure device-size was selected with reference to manufacturer sizing guidelines that typically recommend an over-sizing of ~20%, with a preference for larger size-interval in intermediate cases. Deployment was guided in real-time by TOE and fluoroscopy, and gentle traction was used to test stability. Device anchoring, compression and any residual leak were evaluated by TOE across multiple transducer planes immediately after final deployment. The pericardial space, mitral regurgitation, pulmonary venous inflow and left ventricular contractility were also inspected closely prior to procedural conclusion. Transthoracic echocardiography (TTE) was conducted within 12-h post-procedure to further confirm the absence of complications. TOE under conscious sedation was conducted next at 45-day post-procedure. Patients received aspirin 100 mg and clopidogrel 75 mg once for 1-month post-procedure (pre-procedural loading doses 300 and 600 mg, respectively, in anti-platelet naïve individuals). In the absence of severe residual leak (≥5 mm), this was then converted to aspirin monotherapy. Routine outpatient review was at 6 weeks, 6 months, 1 year, and then annually or as appropriate to on-going clinical requirements.

**Prospective evaluation of outcomes**

Procedural complications and the severity of any residual leak were prospectively documented at the conclusion of the procedure and at follow-up TOE. A peri-device leak of ≥3 mm was regarded as significant,
and ≥5 mm as severe.1 Events specifically sought at outpatient follow-up were stroke, transient ischemic attack, systemic emboli, any other clinical event potentially related to the occluder device, and cardiovascular or unexplained death. Only face-to-face consultations were accepted for the purpose of confirming the absence of adverse events. Statewide government healthcare registries were also interrogated to further ensure that no unscheduled acute admission had occurred, and the general practitioner was contacted if any individual was lost to follow-up.

Retrospective comparison of LAA orifice size by CT vs. 2D TOE

Left atrial appendage sizing methodology as well as device-size intervals vary significantly according to which of the three devices is implanted (Amplatzer/Amulet, Watchman or Wavecrest). A prospective comparison of CT vs. TOE measurements used during the procedure across our full cohort was therefore not feasible, and was also potentially susceptible to bias as operators had access to both modalities during measurements. To allow meaningful and unbiased comparisons of LAA sizing according to imaging modality, we now repeated all CT and TOE measurements of the LAA orifice but in a blinded and anonymized fashion, and specifically for the orifice relevant only to a Watchman device (the sizing methodology of which is particularly well described). For this orifice we measured in each case: (i) maximum orifice diameter on 2D-TOE (the current standard for sizing), (ii) maximum orifice diameter by CT, and (iii) mean orifice diameter by CT derived from orifice perimeter/π. Discrepancies between each CT diameter vs. TOE were then determined.

Measurements were performed by the same clinicians who were undertaking these prospectively in the LAA closure program. Imaging datasets that were not sufficiently comprehensive or that were uninterpretable were not evaluated.

Retrospective comparison of predicted device-size

The impact of LAA sizing approach on occluder device-size selection was evaluated next. For this purpose, a predicted Watchman device size by 2D-TOE was determined in accordance with standard recommendations,10 and compared with the device size derived by a similar process but using mean or maximum diameters on CT. Sizing discrepancy between imaging modalities was a difference of at least one Watchman device-size interval. A difference of two or more device-size intervals was deemed a gross device-sizing discrepancy; a 6-mm difference as such is deemed a gross device-sizing discrepancy. Assessments of orifice diameter by CT derived from orifice perimeter/π. Discrepancies between each CT diameter vs. TOE were then determined. Measurements were performed by the same clinicians who were undertaking these prospectively in the LAA closure program. Imaging datasets that were not sufficiently comprehensive or that were uninterpretable were not evaluated.

Potential causes for sizing discrepancies by TOE vs. CT

To explore factors that might increase the likelihood of discrepant measurements by TOE vs. CT, we evaluated associations that might be relevant to the complexity of the LAA orifice. Relevant variables included LAA orifice size, LAA orifice eccentricity, LA volume, age, gender, history of hypertension, office systolic and diastolic blood pressures, left ventricular ejection fraction, pulmonary artery systolic pressure as estimated by TTE, and chronicity of AF (paroxysmal vs. non-paroxysmal). Eccentricity index was calculated from CT measurements by \( \frac{1 - \text{minor diameter}}{\text{major diameter}} \). LAA orifice size was determined by orifice perimeter on CT. LA volume was measured on CT by biplane area-length equation.

Left ventricular ejection fraction was determined from pre-procedure transthoracic echocardiogram by modified Simpson’s biplane method.

Optimal measurement tool

Patients undergoing Watchman closure-device implantation were identified from our prospective registry. The Watchman device-size predicted by our retrospective blinded measurements (TOE maximum diameter, CT maximum diameter or CT mean diameter) could then be compared with the device-size actually used in each case, allowing us to identify which individual approach was most likely to match the eventual implant size. Although this analysis represents sizing choices at two separate time points, they were performed by the same clinicians undertaking them prospectively in the LAA closure program.

Statistical analyses

Continuous variables are expressed as mean± SD or median as appropriate, and categorical variables as a percentage. Variables were compared using t test or Wilcoxon matched-pairs signed rank test as appropriate. Bland–Altman plot was used to determine bias and limits of agreement of measurements according to imaging modality. Correlation was tested by Pearson’s correlation coefficient (GraphPad Prism v6, CA). A statistical significance threshold of 0.05 was accepted for hypothesis testing.

Results

Patient and procedural characteristics

A total of 73 patients without contraindications were submitted for LAA closure. Mean CHA2DS2-VASc score was 4.4. Important predictors of stroke including age ≥75, congestive heart failure, and previous ischemic stroke were recorded in 57.5%, 41.1% and 28.8% of patients, respectively. Other relevant patient characteristics and indications are listed in Table 1. Device implantation was successfully achieved in all 73 individuals (100%). Mean duration of follow-up was 25.0 months, with a total 151.9 patient-years of follow-up. CT imaging incurred a mean radiation dose-length product of 167.6 mGy cm (estimated effective dose 2.3 mSv).

Prospective registry of procedural hazard

There were no acute device-related procedural complications in this cohort. Specifically, there were no instances of cardiac perforation or new pericardial effusion, nor were there any instances of device embolization, migration, peri-procedural embolic events or procedural death (Table 2). One patient presented with a self-resolving pericarditis 6-day post-procedure but without any effusion and did not require any intervention. Two individuals developed femoral puncture-site hematoma that prolonged inpatient stay. The first required treatment with factor IX in view of a known hemophilia. The second individual required packed red-cell transfusion, and also developed lower limb deep vein thrombosis at a later date that was attributed to the period of immobility. None required endovascular intervention however. At the conclusion of the procedure no patient exhibited a severe residual peri-device leak ≥5 mm on TOE, nor did any follow-up TOE reveal new severe leak ≥5 mm.

Retrospective comparison of LAA orifice sizing by imaging modality

Left atrial appendage opacification by our protocol was sufficient to allow evaluation in all but one CT study. In 6.8% of TOE studies the
stored images did not record all four standard planes of the LAA and thus were not analysed. Maximum diameter by 2D-TOE was 21.8 ± 3.9 mm, whereas maximum orifice diameter by CT was 24.8 mm ± 4.4 mm (bias vs. TOE of +3.0 mm, limits of agreement ±1.7 to 7.7 mm, P < 0.0001, Figure 2). Mean diameter by CT was 23.0 mm ± 4.1 mm (bias vs. TOE of +1.1 mm, limits of agreement −3.1 to 5.4 mm, P < 0.001, Figure 3).

### Retrospective comparison of device-size selection by imaging modality

Device-size selection based on TOE (the current standard) vs. mean or maximum diameters on CT was compared. Median Watchman device size was 24 mm by TOE, 27 mm by mean diameter on CT, and 27 mm by maximum diameter on CT. Selection of Watchman device size by mean CT diameter would match that by TOE in 45.8% of cases, but would differ by one sizing interval in 50.8% of patients and by two intervals in 3.4%. Selection of Watchman device size by maximum CT diameter would match that by TOE in 25.4% cases, but would differ by one sizing interval in 54.2% of patients and by two intervals in 20.4%.

### Optimal measurement approach

For those individuals undergoing Watchman device closure, the device size actually implanted was used as the reference to determine which of our blinded unbiased measurements was most likely to be concurrent. No patient in this subgroup had a significant peri-device leak ≥3 mm, and thus none were excluded from comparison. Device-size predicted by mean orifice diameter on CT was most likely to match actual device size implanted (73.7% of cases). Device-size predicted by maximum diameter on TOE was least likely to match (42.1% of cases). Device-size predicted by maximum orifice diameter on CT was of intermediate utility, matching in 57.9% of cases.

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### Table 1  Baseline patient characteristics

<table>
<thead>
<tr>
<th>Risk factors for stroke</th>
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<tbody>
<tr>
<td>Mean age (years)</td>
<td>76.3</td>
</tr>
<tr>
<td>Heart failure</td>
<td>41.1%</td>
</tr>
<tr>
<td>Mean LVEF (%)</td>
<td>53.5</td>
</tr>
<tr>
<td>Hypertension</td>
<td>84.9%</td>
</tr>
<tr>
<td>Mean SBP (mmHg)</td>
<td>135.9</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>26.0%</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>28.8%</td>
</tr>
<tr>
<td>Vascular disease</td>
<td>38.4%</td>
</tr>
<tr>
<td>Female gender</td>
<td>43.8%</td>
</tr>
<tr>
<td>Mean CHADS2 score</td>
<td>2.7</td>
</tr>
<tr>
<td>Mean CHA2DS2-VASc score</td>
<td>4.4</td>
</tr>
</tbody>
</table>

Indications for closure

- Gastrointestinal bleeding: 24.7%
- ICH: 21.9%
- Other major bleeds: 15.1%
- Comorbid bleeding propensity: 17.8%
- Bleeding with poorly controlled INR: 8.2%
- OAC declined (family bereavement on OAC): 5.5%
- Intolerant of OAC: 4.1%
- Recurrent stroke despite OAC: 2.7%

### Table 2  Procedural safety and efficacy

<table>
<thead>
<tr>
<th>Device</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amplatzer Cardiac Plug</td>
<td>48.0%</td>
</tr>
<tr>
<td>Watchman device</td>
<td>26.0%</td>
</tr>
<tr>
<td>WaveCrest Occluder</td>
<td>26.0%</td>
</tr>
</tbody>
</table>

Procedural hazard

- Device-related complication: 0%
- Arteriovenous fistula: 0%
- Significant hematoma: 2.7%
- Residual leak ≥5 mm: 0%
- Residual leak 3–4.9 mm: 10.3%
- No leak or leak <3 mm: 89.7%
- Mean leak size: 0.77 mm

Efficacy

- Implantation rate: 100%
- Embolic event rate: 3.9/100 PYFU
- Embolic event excl. TIA: 1.3/100 PYFU
- Predicted embolic event rate*: 8.5–9.9/100 PYFU
- Cardiovascular death: 2.0/100 PYFU
- Composite stroke/SE/death**: 4.6/100 PYFU

Outcomes for procedural safety and efficacy of LAA closure.

*Predicted event rate derived according to individual CHADS2-VASc scores and follow-up duration.9

**Composite end-point for efficacy as defined by the PROTECT-AF trial of stroke, systemic embolus, or cardiovascular or unexplained death.2

PYFU, patient-years follow-up; SE, systemic embolus.
Factors associated with discrepant orifice size between TOE vs. CT

Discrepancy between maximum diameters on TOE vs. CT was positively correlated with the degree of LAA orifice eccentricity ($r = 0.34$, $P < 0.01$, Figure 4), LAA orifice size as measured by perimeter ($r = 0.28$, $P = 0.03$, Figure 5), and LA volume ($r = 0.39$, $P < 0.01$, Figure 6). In contrast, factors such as age, gender, history of hypertension, systolic and diastolic blood pressure, LV ejection fraction, pulmonary artery systolic pressure and paroxysmal AF did not correlate with the degree of discrepancy in measurements (Table 3).

Table 3  Associations with sizing-discrepancy

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean (cm)</th>
<th>Coefficient of correlation ($r$)</th>
<th>Significance, $P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAA orifice perimeter</td>
<td>7.3</td>
<td>+0.34</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>LAA orifice eccentricity</td>
<td>0.19</td>
<td>+0.28</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>LA volume (ml)</td>
<td>136.9</td>
<td>+0.39</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>LA volume index (ml/m²)</td>
<td>68.8</td>
<td>+0.30</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Age (years)</td>
<td>76.3</td>
<td>+0.01</td>
<td>0.9</td>
</tr>
<tr>
<td>Male gender (%)</td>
<td>56.2</td>
<td>−0.06</td>
<td>0.6</td>
</tr>
<tr>
<td>Paroxysmal AF (%)</td>
<td>24.7</td>
<td>−0.06</td>
<td>0.7</td>
</tr>
<tr>
<td>History of hypertension (%)</td>
<td>84.9</td>
<td>−0.05</td>
<td>0.7</td>
</tr>
<tr>
<td>Office SBP (mmHg)</td>
<td>135.9</td>
<td>−0.15</td>
<td>0.3</td>
</tr>
<tr>
<td>Office DBP (mmHg)</td>
<td>76.9</td>
<td>−0.23</td>
<td>0.1</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>51.6</td>
<td>−0.11</td>
<td>0.4</td>
</tr>
<tr>
<td>PASP (mmHg)</td>
<td>33.7</td>
<td>+0.04</td>
<td>0.8</td>
</tr>
</tbody>
</table>

Patient, left atrial, and left atrial appendage parameters and their correlation with magnitude of discrepancy between measurements on 2D-TOE vs. CT (maximum LAA orifice diameters).
Embolic events and cardiovascular deaths
Six events that were likely to be embolic occurred in six individuals over the total 151.9 patient-years of follow-up [event rate 3.9 per 100 patient-years of follow-up (Table 2), comparing favourably with a predicted event rate of 8.5–9.9 per 100 patient-years based on CHADSVasc scoring].1 Four of these were transient ischemic attacks without residual deficit at 24 h, and one was a cerebrovascular accident. The sixth experienced acute ischemia of a lower-limb requiring invasive management, with left atrial thrombus also confirmed at subsequent TOE although not clearly adherent to the device. Of note, this occurred in the setting of small-cell lung cancer requiring chemotherapy as well as recent deep-vein thrombosis and pulmonary emboli, pointing to a highly pro-thrombotic milieu in this individual. Separately, one patient presented 8 months after closure with diplopia and features consistent with an internuclear ophthalmoplegia. Cerebral imaging here revealed diffuse small-vessel disease in the setting of long-standing hypertension, and an embolic aetiology was felt to be unlikely. One further patient experienced spontaneous intracranial hemorrhage (ICH) 2 years after LAA closure, with prior spontaneous ICH being the contraindication for OAC prior to closure. Three cardiovascular deaths were recorded (event rate 1.98 per 100 patient-years of follow-up), in all cases due to pre-existing heart failure in individuals aged >75 years and in all cases >1 year after LAA closure. Embolic events were not associated with the presence or severity of peri-device leak.

Discussion
The routine integration of pre-procedural multi-slice CT into the work-up for LAA closure is a novel strategy, and the procedural outcomes in such a program have not previously been reported. In this prospective single-centre registry of 73 consecutive individuals, multi-modality imaging that included CT allowed a particularly comprehensive evaluation and sizing of the LAA with low additional radiation burden. Two observations can be made in this cohort. Firstly, highly favourable outcomes were observed with respect to procedural hazard. Secondly, sizing of the LAA orifice according to CT vs. TOE were frequently divergent, with clinically relevant impact on device size selection. These two observations now merit further discussion.

Procedural safety
A key observation in this cohort was the absence of any device-related complications. By contrast, large studies and registries have reported device-related complication rates of 2.2–6.7%.1,2,13 In none of our cohort did we observe a severe residual leak ≥5 mm, device migration or device embolization, despite the inevitable learning curve inherent to a novel technique. While a number of factors will contribute to procedural hazard, sizing errors in particular may be implicated in the occurrence of complications.14 This leads us to speculate that a superior sizing of the LAA orifice by CT may at least in part account for the zero device-related procedural hazard reported here. Although this hypothesis clearly cannot be confirmed in an observational dataset, important differences in measurements between the two modalities proved clinically relevant including with respect to device-size selection, and as such warrant closer scrutiny.

Discrepant LAA orifice sizing by 2D TOE vs. CT
We noted firstly that LAA orifice size by 2D-TOE was not universally interchangeable with diameters derived by CT, an observation that has also been noted by others.2,15 More importantly however, sizing discrepancies also appeared to be clinically relevant (albeit on analyses that were retrospective); device-size selection differed in more than half of all cases, and in the case of Watchman device-size selection the median size in this cohort was 3 mm greater by CT than by 2D-TOE. Of particular note, even though the averaged numerical bias between TOE diameter vs. a ‘gold standard’ of mean CT diameter was relatively modest at 1.1 mm, gross sizing error was still observed in an important proportion of cases (3.4%). The key utility of CT may thus extend beyond a modestly improved sizing accuracy, with the greatest safety benefit in fact being a detection and avoidance of occasional gross sizing errors by TOE.

Optimal sizing tool
We and others have previously documented the typically eccentric and irregular nature of the LAA orifice.1,6,17 The mean eccentricity index in this cohort was significant at 0.19. As such, it is questionable whether the current reliance on maximum orifice diameter for device sizing is the most appropriate approach. A mean orifice diameter may be more intuitive, given the circular nature of current occluder devices that will consequently be expected to deform the orifice to a more circular shape. Parallels can be drawn in this regard from international experiences with transcatheter aortic valve intervention, where mean orifice diameters appear to confer important advantages over planar maximal diameters,18 particularly in the setting of significant eccentricity.19 In support of this hypothesis, we observed that device-sizing based on mean diameter by CT was most likely to match the actual device size implanted, albeit on retrospective analysis. As such, these data further highlight the potential advantages of the routine incorporation of a multi-planar imaging dataset into procedural workup. 3D-TOE might arguably provide equivalent data in this regard with the advantage of obviating additional modalities, but unfortunately we did not routinely acquire 3D-TOE datasets to test this hypothesis.

Potential predictors of sizing discrepancy between TOE vs. CT
Sizing errors of an orifice by TOE may be attributable to the inherent limitations of two-dimensional ultrasound such as a poorer spatial resolution, difficulties in accurately obtaining a true central maximal plane through the orifice, or perhaps even hemodynamic factors related to anaesthesia or conscious sedation. Factors related to individual patients or the LAA itself might also be relevant however, and we evaluated these in further detail. We observed that LAA orifice eccentricity, LAA orifice size, and LA volume were correlated with greater tendency to discrepancies between maximum dimensions by 2D-TOE vs. CT. This suggests that an increasingly complex and larger LAA orifice along with increasing remodelling of the LA may pose particular challenges to accurate sizing by a two-dimensional
modality. As such, patients with such characteristics may benefit in particular from CT evaluation. However, apart from LA volume these parameters may be difficult to identify in an office-based evaluation, and thus a routine rather than selective use of CT may continue to be preferred.

Corroborating studies
Although the utility of CT has not previously been systematically evaluated with respect to procedural outcomes, there are other data supporting a wider use of such a multi-modality approach. In one small registry where a proportion of patients underwent either MRI or CT work-up prior to LAA closure by the Amplatzer device, procedural hazard was also very low. Another group has reported via abstract format the favourable outcomes in nine patients where closure was guided by a novel three-dimensional printed model of the LAA derived from CT. Echocardiography clearly plays an essential role in the complementary evaluation of the LAA and is indispensible in terms of real-time guidance of closure. The importance of dynamic images must also not be under-estimated in the evaluation of this complex and variable cul-de-sac structure, and we do not advocate a complete replacement of TOE-based sizing by CT. However, these studies and our data support the hypothesis that the addition of CT to the work-up of LAA closure may improve procedural safety over 2D-TOE in isolation.

Limitations
We have speculated that CT-guided sizing of the LAA may contribute to favourable safety outcomes during percutaneous closure, but such an assertion can of course only be properly tested by randomized controlled study. However, a scrutiny of associations from real-world observational data is both logical and necessary in the stepwise evaluation of an emerging technology. The single-centre origin of our data and relatively small numbers are also important limitations. As such, any number of aspects of our protocol may have influenced procedural hazard to an even greater extent than CT. One such aspect might be the simultaneous presence at implantation of two cardiologists with combined expertise thus in both percutaneous structural interventions and invasive electrophysiology. This approach is certainly not unique to our centre however, nor do other aspects of our protocol deviate particularly from consensus recommendations. Out of necessity, the component of our study evaluating sizing discrepancies between TOE vs. CT was retrospective and as such these measurements may differ from those used prospectively. Retrospective measurements were performed by the same group of clinicians conducting these prospectively, however. Finally, we unfortunately did not document the frequency at which the initial device-size proved incorrect and mandated sizing exchange before final deployment; such data would provide important information on the 'first-time right' accuracy of individual modalities which may have important cost-efficacy implications.

Conclusion
Multi-modality imaging of the LAA that routinely incorporated CT was associated with excellent procedural safety during percutaneous closure in this small single-centre study. Eccentricity and size of the LAA orifice may be implicated in sizing discrepancies between 2D-TOE and CT, which in turn frequently translates into an altered device-size selection. A particular advantage of CT may be its ability to detect (and thus allow avoidance of) gross sizing errors by 2D-TOE. Routine integration of CT into the work-up of LAA closure may thus improve outcomes in this emerging intervention, but further prospective studies are warranted.

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