Three-Dimensional Ultrasound for Image-Guided Mapping and Intervention

Methods, Quantitative Validation, and Clinical Feasibility of a Novel Multimodality Image Mapping System

Yasuo Okumura, MD, PhD; Benhur D. Henz, MD; Susan B. Johnson, BS; T. Jared Bunch, MD; Christine J. O’Brien; David O. Hodge, MS; Andres Altman; Assaf Govari; Douglas L. Packer, MD

Background—Multiple factors create discrepancies between electroanatomic maps and merged, preacquired computed tomographic images used in guiding atrial fibrillation ablation. Therefore, a Carto-based 3D ultrasound image system (Biosense Webster Inc) was validated in an animal model and tested in 15 atrial fibrillation patients.

Methods and Results—Twelve dogs underwent evaluation using a newly developed Carto-based 3D ultrasound system. After fiducial clip markers were percutaneously implanted at critical locations in each cardiac chamber, 3D ultrasound geometries, derived from a family of 2D intracardiac echocardiographic images, were constructed. Point-source error of 3D ultrasound-derived geometries, assessed by actual real-time 2D intracardiac echocardiographic clip sites, was 2.1±1.1 mm for atrial and 2.4±1.2 mm for ventricular sites. These errors were significantly less than the variance on CartoMerge computed tomographic images (atria: 3.3±1.6 mm; ventricles: 4.8±2.0 mm; *P*<0.001 for both). Target ablation at each clip, guided only by 3D ultrasound-derived geometry, resulted in lesions within 1.1±1.1 mm of the actual clips. Pulmonary vein ablation guided by 3D ultrasound-derived geometry resulted in circumferential ablative lesions. Mapping in 15 patients produced modestly smaller 3D ultrasound versus electroanatomic map left atrial volumes (98±24 cm³ versus 109±25 cm³, *P*<0.05). Three-dimensional ultrasound-guided pulmonary vein isolation and linear ablation in these patients were successfully performed with confirmation of pulmonary vein entrance/exit block.

Conclusions—These data demonstrate that 3D ultrasound images seamlessly yield anatomically accurate chamber geometries. Image volumes from the ultrasound system are more accurate than possible with CartoMerge computed tomographic imaging. This clinical study also demonstrates the initial feasibility of this guidance system for ablation in patients with atrial fibrillation. (Circ Arrhythmia Electrophysiol. 2008;1:110-119.)

Key Words: ablation ■ mapping ■ 3D ultrasound imaging

During the past 10 years, technology to fully “register” cardiac activation to actual anatomic images has evolved in an effort to facilitate complex anatomy-based ablation. Electroanatomic or impedance-based mapping systems merge preacquired, segmented computed tomographic (CT)/magnetic resonance imaging volume data sets and accompanying multidimensional maps by matching specific anatomic fiducial points seen on both anatomic and physiological renderings and simultaneously displaying them within the same coordinate system.¹⁻⁸

Although displaying an ablation catheter and integrating its position within CT/magnetic resonance imaging geometry is possible, the accuracy of the integrated 3D geometry is highly dependent on image quality and, more importantly, on the merge process.¹⁻⁸ Errors may stem from changes in cardiac chamber volume or rhythm occurring between the time of 3D anatomic image acquisition and electroanatomic mapping in the electrophysiology laboratory. Gating of image acquisition to the cardiac cycle and respiratory phase may also affect rendered volumes, as may anesthesia administered in the electrophysiology laboratory.

Clinical Perspective see p 119

Alternatively, techniques that provide high-definition real-time anatomic images should mitigate those factors contributing to matching errors. Recently, an ultrasound-based 3D imaging modality has been developed to guide catheter navigation. This system creates anatomically accurate volumes from real-time 2D intracardiac echocardiographic (ICE) images facilitating interventional navigation within target
cardiac chambers. Nevertheless, the accuracy and utility of this system have not been established. This study was therefore undertaken to (1) validate the accuracy of integrated 3D ultrasound imaging, (2) compare the accuracy of catheter manipulation using this approach with that of merged CT image–based navigation, and (3) assess the clinical utility of 3D ultrasound image–guided intervention in patients with atrial fibrillation (AF).

Methods
The authors had full access to and take full responsibility for the integrity of the data. All authors have read and agreed to the manuscript as written.

Animal Validation Study
Twelve mongrel dogs (30 to 40 kg) were studied according to a protocol approved by the Mayo Foundation Institutional Animal Care and Use Committee, with general methods described previously. After deep anesthesia was established, positive-pressure ventilation (rate 14/min, inspiration:expiration=1:2) instituted, vascular access was percutaneously obtained. Surface ECGs and blood pressure were continuously monitored. Transseptal catheterization to a coronary sinus (CS) atrial electrogram for atrial imaging and to the R wave of V1–3 for ventricular imaging. Although the 2D ICE segments of 2D ultrasound images were acquired during ECG gating (21%). A single gated image was displayed on the system’s resident “Ultrasound Viewer,” from which the endocardial surface contour was manually drawn on the basis of echointensities at the blood and tissue interface (Figure 1A). Each surface contour was thereby stored as a series of individual electroanatomic mapping points delineating each planar anatomic shape. By repeating this process, a family of chamber contours was acquired, collated into a complete volume rendering using point–to-point component interpolation. D, Complete LA and PV geometry created from individual volume components. LA indicates left atrium; LAA, left atrial appendage; PV, pulmonary vein; RS, right superior; RI, right inferior; LS, left superior; and LI, left inferior.

3D Volume Rendering With Intracardiac Ultrasound
An electroanatomic location sensor was incorporated into the ICE catheter tip to allow the establishment of (1) tip location in 3D space, (2) tip direction, and (3) the origin and direction of the 2D ICE sector image. Ultrasound images were relayed to the CARTO XP system (CartoSound) and displayed within the same coordinate system as the subsequently generated electroanatomic maps. Three-second acquisitions were gated at 80% of the R-R interval for atrial and at 0% of the R-R interval (R wave) for ventricular imaging during the end-expiratory phase.

The axial CT images were transferred to the electroanatomic mapping system equipped with CartoMerge Image Integration Software (Biosense Webster). The surface reconstruction of the RA with superior vena cava, left atrium, PVs, RV, and LV were segmented from each chamber volume through a 3-step process as described previously. Individual implanted clips within each chamber were also segmented to serve as specific, predetermined 3D CT anatomic fiducial points.

Figure 1. Three-dimensional ultrasound geometry creation. A, 2D ICE view of the LA with endocardial perimeter (left) and simultaneously rendered endocardial contour (right), B, Collated multiple LA perimeters created with multiple catheter rotations. C, Overall segmented volume using point-to-point component interpolation. D, Complete LA and PV geometry created from individual volume components. LA indicates left atrium; LAA, left atrial appendage; PV, pulmonary vein; RS, right superior; RI, right inferior; LS, left superior; and LI, left inferior.
process, the “tag points” reflecting each implanted clip “insertion site” were manually drawn from repeated ICE images onto the 3D ultrasound-derived geometries to serve as “blindable” anatomic surface markers for use in validation studies (pink-unfilled circle) (Figure 2A). Other electroanatomic points were also acquired by using a separate mapping catheter and registered to the reconstructed 3D ultrasound volume, all registered within the same coordinate system as the ICE images (Figure 1D).

**Baseline Validation Study**

After the completion of 3D ultrasound geometry and annotation with clip sites, the accuracy of image acquisition was assessed via 2 validation methods, after at least 10 minutes of elapsed time. For the first method (“inside-out” validation, Figure 2), real-time 2D ICE and fluoroscopy were used for establishing “gold standard” localization of the inserted clips at specific “insertion sites.” The operator then positioned a 4-mm-tip standard electroanatomic mapping catheter to that 2D ICE–based insertion site, and a point reflecting that electroanatomic location was independently acquired and annotated onto the 3D ultrasound–derived geometry (blue-filled circle). The position error of inside-out validation was defined as the shortest distance between the 2D ICE/fluoro–based clip insertion site and the clip tag point created visually after 3D ultrasound geometric rendering (blue-filled circle versus pink-unfilled circle) (Figure 2C).

For the second method (“outside in” validation, Figure 3), the opposite approach was utilized. The mapping catheter was placed at an apparent clip “tag point” (pink-unfilled circle) on the 3D ultrasound-derived geometry, while the operator was blinded to the real-time 2D ICE/fluoroscopic images, and this apparent clip “tag point” of origin was marked with a yellow-filled circle (Figure 3A). This tag point was then compared with the corresponding actual clip insertion site established by repositioning the Carto mapping catheter under direct 2D ICE/fluoroscopic guidance (blue-filled circle). The position error of the “outside in” validation was defined as the shortest distance from this 3D ultrasound-based tag point origin to the corresponding 2D ICE/fluoro-based clip insertion site (yellow-filled circle versus blue-filled circle) (Figure 3B).

**Variance of Merged 3D CT and 3D Ultrasound-Derived Images**

To verify the actual point-source position error of the merged CT volume images, the reconstructed CT datasets were coregistered with the 3D ultrasound–derived geometries (Figure 4). For the validation, 3 merge methods were performed. First, preimplanted clip sites, established by 2D ICE/fluoroscopy (blue-filled circle), and their corresponding reconstructed CT clips on the CT image (red-filled ellipse) were marked as landmark pairs (Figure 4A). A resident Carto algorithm was then used to approximate the 3D ultrasound volumes and CT images by matching those landmark pairs (“landmark

---

**Figure 2.** Inside-out validation of 3D geometry. A, 2D ICE image used to produce collated LA contours showing clip insertion site (arrow, pink-unfilled circle) with tag point clip drawn into 3D geometry (red-unfilled ellipse). B, Inside-out validation showing catheter (blue-filled circle) positioned at clip insertion site. C, CartoSound rendering of multiple collated perimeters used to create LA geometry. Also shown are the drawn red-unfilled ellipse created with 3D volume acquisition, the actual clip insertion site (pink-unfilled circle), and catheter tip position (blue-filled circle).

**Figure 3.** Outside-in validation of 3D geometry. A, Catheter positioning guided only by 3D ultrasound image (yellow-filled circle). B, Comparison of catheter tip positioned under 2D ICE guidance (blue-filled circle), and tip location from 3D ultrasound (yellow-filled circle). Also shown is the drawn insertion site (pink-unfilled circle) at the clip (red-unfilled ellipse).
merge,” Figure 4B). Second, global surface matching was automatically performed to fit the CT surface reconstruction and 3D ultrasound geometry surface contours by rendering the smallest overall average distance of the 2 surface datasets (“surface merge,” Figure 4C). Finally, a manual iterative process was performed to minimize the average distance of individual landmark pairs on the basis of overall geometry and position of PVs and LA (“adjusted merge,” Figure 4D). In the 3 merge methods, the position error of the CT images was defined as the distance between landmark pairs (red-filled ellipse versus blue-filled circle). This CT image–based position error was compared to the corresponding error from the clip insertion site (blue-filled circle) to the 3D ultrasound–based tag point origin (yellow-filled circle) as previously described in the outside-in validation.

Observed and Actual Ablation Site Validations

In all dogs, the 4-mm-tip standard mapping catheter was navigated to the site of each clip tag point as guided by the 3D ultrasound–derived geometry, again while the operator was blinded to the 2D ICE/fluoroscopic images (outside-in validation). A single radiofrequency energy delivery (60 seconds, 50 W, 60°C) was directed at each tag point reflecting the apparent clip location.

The utility of 3D ultrasound–derived geometry for guiding linear ablation (each ablation: 30 seconds, 50 W, 60°C) was also examined. Creation of a mitral isthmus line was guided in 6 dogs by both LA and LV volumes. Thereafter, circumferential PV ablation (right superior PV [n=8] and superior branch of left superior PV [n=8]) was guided by 3D ultrasound–derived LA and PV geometries. Subsequently, after VF induction with high-rate burst pacing and animal exsanguination all under deep anesthesia, the relationship between implanted clip markers and ablative lesions was evaluated. The position error was based on 2 measurements (Figure 5): (1) distance between the center of the clip insertion point and the center of the lesion and (2) the distance between the center of the clip insertion point and the edge of the lesion.
Linear ablation accuracy was assessed by circumferentiality of PV ablation, continuity of mitral isthmus line, gap number and distance, and presence of ablation lesions inside the PVs on gross inspection.

**Clinical Study of 3D Ultrasound Image Accuracy and Guided Ablation**

Fifteen AF patients also underwent clinical electrophysiological evaluation according to previously described methods. These patients were identified from an institutional review board–approved database study. An Authorization to Use and Disclose Protected Health Information form was on file before retrospective analysis of this prospective cohort. After vascular access was obtained, catheters for recording and pacing were positioned in the RA, RV, and CS. A 10F ICE catheter was positioned via the right femoral vein and advanced into the LA. Intravenous heparin was given to maintain an activated clotting time advanced into the RA. Double transseptal catheterization was performed under ICE guidance and mapping and Lasso catheters advanced into the LA. Intravenous heparin was given to maintain an activated clotting time >300 seconds during the procedure.

The 3D ultrasound images of the LA and PVs were acquired and processed according to the same methods as deployed in the canine studies. These were compared with acquired standard electroanatomic mapping datasets as previously described. The outside-in validation was also performed as described in the animal validation methods. In brief, 4 anatomic points (venoatrial junction of each PV) on the 3D ultrasound geometry and subsequent electroanatomic mapping were marked with yellow-filled circles. These tag points were then compared with the fiducial corresponding anatomic sites (blue-filled circle) based on an independent 2D ICE slice.

In all patients, wide area circumferential ablation around each pair of ipsilateral PVs was undertaken with the use of an open irrigated 7F, 3.5-mm-tip catheter. Radiofrequency energy was delivered (each ablation: 15 to 30 s, 25 to 40 W, 40°C, irradiation flow 17 to 30 mL/min) until PV isolation was accomplished. Catheter navigation was guided by 3D ultrasound imaging with limited use of 2D ICE/fluoroscopic images. If venoatrial electric disconnection was not achieved with the wide area circumferential ablation, additional Lasso-guided segmental ostial ablation, targeting sites of electric breakthroughs, was performed.

**Statistical Analysis**

All statistical analyses were performed with SAS 9.1.3. Continuous variables were presented as mean±SD, and comparisons between groups were completed by using 2-sample t test. Because remaining analysis included multiple observations from the same dog or patient, the Generalized Estimating Equation models were used to adjust for potential effects of repeated measurements in each dog. Values of P<0.05 were considered statistically significant. In the setting of multiple comparisons, the Bonferroni method was also used, with a P<0.008 taken as significant.

**Results**

**Creation of Canine 3D Ultrasound–Derived Geometry**

The RA with the neighboring superior vena cava (n=12), LA with all 4 individual PVs (n=12), RV (n=10), and LV (n=10) were all readily rendered as segmented 3D ultrasound volumes. A 3D ultrasound–derived geometry was created by a family of 51±18 2D ICE RA contours, 22±5 superior vena cava contours, 22±5 contours for the LA, 7±4/8±3 contours for each PV/left atrial appendage, 36±11 contours for the RV, and 31±7 contours for the LV. Total rendering time was 23±9 minutes for the RA, 26±9 minutes for the LA, 22±11 minutes for the RV, and 18±6 minutes for the LV, respectively. Importantly, the overall rendering time significantly shortened with experience from a total of 29±7 minutes in the first 7 dogs to 15±4 minutes in the later 5 dogs (P<0.0001). Of the implanted clip markers, 23 RA clips, 24 LA clips, 27 RV clips, and 22 LV clips were all successfully rendered.

**Table 1. Position Errors of the “Inside-Out” and “Outside-In” Validations**

<table>
<thead>
<tr>
<th></th>
<th>RA (mm)</th>
<th>LA (mm)</th>
<th>RV (mm)</th>
<th>LV (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inside</td>
<td>2.3±1.2 (0–4.4)</td>
<td>1.9±1.4 (0–4.5)</td>
<td>1.9±1.4 (0–4.8)</td>
<td>2.0±1.9 (0–6.2)</td>
</tr>
<tr>
<td>Outside</td>
<td>2.2±1.2 (0–4.0)</td>
<td>2.1±1.1 (0–4.4)</td>
<td>2.3±1.1 (0–4.4)</td>
<td>2.5±1.4 (0–6.0)</td>
</tr>
</tbody>
</table>

Ranges are given inside parentheses. P=NS between cardiac chambers.
visualized by 2D ICE imaging and their position registered to the 3D ultrasound–derived geometries.

Baseline Validation Study

With 96 registered clips used for analysis, the overall position error between the clip insertion sites, as established by 2D ICE/fluoro–guided electroanatomic navigation (gold standard) and clip site tag points annotated on the 3D ultrasound–derived geometry (inside-out validation), was 2.0±1.5 (range 0 to 6.2) mm. For each chamber, the error was 2.3±1.2 (range 0 to 4.4) mm in the RA, 1.9±1.4 (range 0 to 4.5) mm in the LA, 1.9±1.4 (range 0 to 4.8) mm in the RV, and 2.0±1.9 (range 0 to 6.2) mm in the LV (P=NS between cardiac chambers, Table 1).

Conversely, the overall position error between clip tag points, previously annotated on the 3D ultrasound–derived geometry, and actual 2D ICE/fluoro–based catheter tip/insertion site (gold standard), was 2.3±1.2 (range 0 to 6.0) mm (outside-in validation). Individually, the error was 2.2±1.2 (range 0 to 4.0) mm for RA, 2.1±1.1 (range 0 to 4.4) mm for LA, 2.3±1.1 (range 0 to 4.4) mm for RV, and 2.5±1.4 (range 0 to 6.0) mm for LV (P=NS between cardiac chambers, Table 1).

Ablation Accuracy Assessment

All ablative lesions targeting the implanted 23 RA and 24 LA clips were seen on gross pathology. Twenty-six of the 27 clips in the RV and 18 of the 22 clips in the LV were also used for guidance validation. Radiofrequency energy delivery–created lesions, which were 4.6±1.6 mm wide and 6.1±2.1 mm long, showed overall position errors of 1.1±1.1 mm (range 0 to 4.3 mm) from the center and 0.5±0.9 mm (range 0 to 4.0 mm) from the edge of the ablative lesions. For the individual cardiac chambers, position errors for the center versus edge of the lesions were 1.1±1.1 (range 0 to 3.5)/0.5±0.8 (range 0 to 3.0) mm RA lesions, 1.3±1.3 (range 0 to 4.3)/0.8±1.1 (range 0 to 4.0) mm LA ablation sites, and were 0.9±1.1 (range 0 to 3.0)/0.4±0.7 (range 0 to 2.2) mm in RV and 1.1±0.9 (range 0 to 3.5)/0.1±0.3 (range 0 to 1.0) mm in LV lesions (P=NS between cardiac chambers for the lesion center, Figure 5, Table 2).

Comparison of the Accuracy of Merged 3D CT and 3D Ultrasound–Derived Images

Examples and results of the position errors derived from the CT image merged to 3D ultrasound–derived geometry counterparts are shown in Figure 4 and Table 3. After Carto landmark merge was performed, the position error from the 2D ICE/fluoro–based clip insertion site (gold standard) to the apparent clip site on the actual CT image was 2.9±1.1 (range 1.1 to 5.2) mm for atrial and 4.2±1.6 (range 1.4 to 8.4) mm for ventricular sites, respectively. The average global surface mismatch between the 3D ultrasound versus CT images was 2.3±0.5 mm for atrial and 2.8±0.6 mm for ventricular comparisons. The surface merge process minimized the global mismatch between the 3D ultrasound versus CT images to a 1.7±0.4 mm atrial error and 2.1±0.7 mm ventricular error (P<0.001 for both chambers versus landmark merge) but accentuated the point-source position error at each clip to 5.4±2.5 (range 0.8 to 12.0) mm for atrial sites and 6.6±3.1 (range 1.7 to 15.4) mm for ventricular sites (P<0.001 for chambers versus landmark merge). The point-source error after the surface merge was 2.5-fold larger than that guided by 3D ultrasound–derived geometry counterpart [atria: 2.1±1.1 (range 0 to 4.4) mm; ventricles: 2.4±1.2 (range 0 to 6.0) mm]. In contrast, the adjusted merge clip position error at atrial sites was 3.3±1.6 (range 0.8 to 6.5) mm and 4.8±2.0 (range 1.6 to 8.9) mm at ventricular sites, with a global surface mismatch of 2.0±0.5 mm and 2.7±0.7 mm, respectively. Despite the merge method-adjustment, the point-source position errors of the CT images were still significantly larger than when guided by 3D ultrasound–derived geometry (Table 3).

Table 2. Position Errors of the Target Ablative Lesions

<table>
<thead>
<tr>
<th></th>
<th>RA</th>
<th>LA</th>
<th>RV</th>
<th>LV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion center, mm</td>
<td>1.1±1.1 (0–3.5)</td>
<td>1.3±1.3 (0–4.3)</td>
<td>0.9±1.1 (0–3.0)</td>
<td>1.1±0.9 (0–3.5)</td>
</tr>
<tr>
<td>Lesion edge, mm</td>
<td>0.5±0.8 (0–3.0)</td>
<td>0.8±1.1* (0–4.0)</td>
<td>0.4±0.7 (0–2.2)</td>
<td>0.1±0.3 (0–1.0)</td>
</tr>
</tbody>
</table>

Ranges are given inside parentheses. Lesion center: P=NS between cardiac chambers, lesion edge. *P<0.001 vs LV; †P<0.007 vs RV; others, P=NS between cardiac chambers.

Table 3. Position Errors of the CT and the 3D Ultrasound Images

<table>
<thead>
<tr>
<th></th>
<th>Atria Errors, mm</th>
<th>Ventricles Errors, mm</th>
<th>Atria Mismatch, mm</th>
<th>Ventricles Mismatch, mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT MR</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Landmark merge</td>
<td>2.9±1.1* (1.1–5.2)</td>
<td>4.2±1.6* (1.4–8.4)</td>
<td>2.3±0.5 (1.5±1.1–3.2±2.2)</td>
<td>2.8±0.6 (2.0±1.6–4.2±2.9)</td>
</tr>
<tr>
<td>Surface merge</td>
<td>5.4±2.5* (0.8–12.0)</td>
<td>6.6±3.1* (1.7–15.4)</td>
<td>1.7±0.4 (1.1±0.8–2.7±2.5)</td>
<td>2.1±0.7 (1.5±1.3–4.1±2.9)</td>
</tr>
<tr>
<td>Adjusted merge</td>
<td>3.3±1.6* (0.8–6.5)</td>
<td>4.8±2.0* (1.6–8.9)</td>
<td>2.0±0.5 (1.1±0.8–3.2±2.9)</td>
<td>2.7±0.7 (1.8±1.5–4.1±2.9)</td>
</tr>
<tr>
<td>3D ultrasound</td>
<td>2.1±1.1 (0–4.4)</td>
<td>2.4±1.2 (0–6.0)</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

Ranges are given inside parentheses. *P<0.001 vs 3D ultrasound.
Anatomy-Based Ablation Accuracy in Dogs

A representative example of a 3D ultrasound mitral valve isthmus line is shown in Figure 6A and 6B. In 6 dogs, complete mitral isthmus linear lesions were seen without gaps on gross inspection. Figure 6C through 6E show representative examples of a circumferential PV ablation. Navigation for 100% circumferential PV ablation was successfully completed with 3D ultrasound–derived geometries, resulting in 97±4% (range 88 to 100) circumferentiality around the PVs on gross inspection. By review, 0.6±0.7 (range 0 to 2) gaps were observed in the circumferential PV lesions with an average gap size of 2.3±0.7 (range 1.5 to 3.5) mm. In all 8 dogs, circumferential lesions were accurately positioned at the target venoatrial junction, resulting in no lesions inside the PVs. Gross pathological examination showed no complications such as tamponade, cardiac perforation, or injury to the esophagus.

3D Ultrasound Image Rendering and Guided Ablation in AF Patients

Fifteen patients underwent AF ablation during which the utility for mapping with the 3D ultrasound system was assessed. These AF patients had characteristics as described in Table 4. In this process, 58 PVs (including 2 common left PVs) were rendered with the use of 7±3 individual contours. The collated set produced PVs with a volume of 4.3±2.4 cm³.
Each patient also underwent mapping of the LA (total contours: 23±5 contours), with volumes averaging 98±24 cm³ (Figure 7A). Electroanatomic mapping as enabled by catheter manipulation out beyond primary and secondary vein bifurcation (Figure 7B) disclosed PV volumes (total points per PV: 36±13 points) measuring 6.6±4.3 cm³, which were significantly larger than noted with the 3D ultrasound process (P<0.05). Importantly, PV orifice areas derived from the 3D ultrasound geometry were nevertheless larger than created by electroanatomic mapping (3.0±1.4 cm² versus 2.2±0.9 cm², P<0.05). Nonetheless, the LA volumes of electroanatomic mapping (total points: 107±25 points) tended to be larger than those identified by the 3D ultrasound geometry (109±25 cm³ versus 98±24 cm³, P=0.05). For outside-in validation used to compare the 3D imaging methods, 3D ultrasound imaging showed less error (2.1±1.4 mm) than generated with electroanatomic mapping (6.3±3.7 mm) (P<0.05) based on underlying anatomic targets at the venoatrial junction of each PV.

Each patient underwent PV isolation using a wide area circumferential ablation approach (Figure 7C). An average of 14±6 energy deliveries were made around the left PVs, with an average of 13±4 around the right PVs. This was guided by the 3D ultrasound imaging and accompanying registration of the electroanatomic map onto that surface geometry. In all patients, PV entrance/exit block was achieved, although Lasso-guided touch-up lesions were required in 24 of 58 (41%) PVs, similar to that required for Carto map-guided ablation alone.10 In 13 of 15 patients, a LA roof line was fashioned by the right PVs. This was guided by the LA isthmus ablation, and 5 patients underwent additional linear ablation within the LA along the septum or posterior LA wall near the CS. One patient demonstrated a small pericardial effusion, with no other major adverse events. In all patients the 3D ultrasound geometry was the main mode of catheter manipulation. A total of 32±13 minutes were required for CartoSound mapping of the LA with 4 PVs, but the total rendering time was shortened with experience from 41±13 minutes in the first 7 patients to 23±4.7 minutes in the next 8 patients (P<0.0001).

### Discussion

#### Main Findings

This study provides the outcome of an original validation study of a novel integrated imaging approach based on 3D ultrasound–derived geometries for the guidance of ablation. Foremost, this system demonstrated a high level of accuracy during validation and ablation in each cardiac chamber, with navigation 1.5- to 2.5-fold more accurate than possible using a mapping system with merged CT volumes. The 3D ultrasound–derived geometry allowed accurate navigation during complex canine anatomy-based ablations near the PVs. The clinical studies also demonstrate the image accuracy and the initial feasibility of the 3D ultrasound image-guided AF ablation.

#### Validation Study of 3D Ultrasound–Derived Geometry

Two-dimensional ICE imaging is commonly used to precisely display real-time anatomic information.7–9,11,12 In the clinical electrophysiological environment, such imaging is used to monitor (1) catheter positioning, (2) catheter tip/tissue orientation, (3) catheter tip/tissue contact, (4) lesion formation, and (5) microbubble development. The real-time characteristics of the 2D ICE image for detection of cardiac surface contours have prompted the development of this novel integrated 3D ultrasound system. Because differences between real-time 2D ICE-based surfaces and the resulting

### Table 4. Clinical Patient Characteristics

<table>
<thead>
<tr>
<th>Case</th>
<th>Age, y</th>
<th>Sex</th>
<th>AF Type</th>
<th>AF Duration, y</th>
<th>LA Size, mm</th>
<th>Failed AAD, n</th>
<th>Ablation Methods</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>64</td>
<td>M</td>
<td>Persistent</td>
<td>20.4</td>
<td>Normal</td>
<td>1</td>
<td>WACA</td>
</tr>
<tr>
<td>2</td>
<td>76</td>
<td>F</td>
<td>Persistent</td>
<td>4.3</td>
<td>Severe</td>
<td>0</td>
<td>WACA + Roof + MI</td>
</tr>
<tr>
<td>3</td>
<td>52</td>
<td>M</td>
<td>Persistent</td>
<td>9.3</td>
<td>Severe</td>
<td>3</td>
<td>WACA + Roof + MI + AL</td>
</tr>
<tr>
<td>4</td>
<td>66</td>
<td>M</td>
<td>Persistent</td>
<td>10.3</td>
<td>Severe</td>
<td>2</td>
<td>WACA + Roof + MI + AL</td>
</tr>
<tr>
<td>5</td>
<td>51</td>
<td>M</td>
<td>Paroxysmal</td>
<td>8.3</td>
<td>Mild</td>
<td>2</td>
<td>WACA + Roof</td>
</tr>
<tr>
<td>6</td>
<td>51</td>
<td>M</td>
<td>Paroxysmal</td>
<td>3.5</td>
<td>Moderate</td>
<td>2</td>
<td>WACA + Roof + MI</td>
</tr>
<tr>
<td>7</td>
<td>76</td>
<td>M</td>
<td>Persistent</td>
<td>10.4</td>
<td>Severe</td>
<td>4</td>
<td>WACA + Roof + MI + AL</td>
</tr>
<tr>
<td>8</td>
<td>70</td>
<td>M</td>
<td>Persistent</td>
<td>7.4</td>
<td>Normal</td>
<td>2</td>
<td>WACA + Roof + MI + AL</td>
</tr>
<tr>
<td>9</td>
<td>50</td>
<td>M</td>
<td>Paroxysmal</td>
<td>4.4</td>
<td>Normal</td>
<td>1</td>
<td>WACA + Roof + MI</td>
</tr>
<tr>
<td>10</td>
<td>34</td>
<td>M</td>
<td>Persistent</td>
<td>4.4</td>
<td>Severe</td>
<td>1</td>
<td>WACA</td>
</tr>
<tr>
<td>11</td>
<td>51</td>
<td>F</td>
<td>Persistent</td>
<td>4.4</td>
<td>Severe</td>
<td>3</td>
<td>WACA + Roof + MI</td>
</tr>
<tr>
<td>12</td>
<td>51</td>
<td>M</td>
<td>Paroxysmal</td>
<td>1.4</td>
<td>Mild</td>
<td>2</td>
<td>WACA + Roof + MI</td>
</tr>
<tr>
<td>13</td>
<td>78</td>
<td>M</td>
<td>Paroxysmal</td>
<td>2.5</td>
<td>Severe</td>
<td>1</td>
<td>WACA + Roof + MI</td>
</tr>
<tr>
<td>14</td>
<td>66</td>
<td>M</td>
<td>Persistent</td>
<td>11.5</td>
<td>Moderate</td>
<td>2</td>
<td>WACA + Roof + MI + AL</td>
</tr>
<tr>
<td>15</td>
<td>64</td>
<td>M</td>
<td>Persistent</td>
<td>10.5</td>
<td>Moderate</td>
<td>2</td>
<td>WACA + Roof + MI</td>
</tr>
</tbody>
</table>

M indicates male; F, female; AF, atrial fibrillation; LA size, left atrial size (normal ≤ 40 mm, mild 41 to 45 mm, moderate 46 to 50 mm, severe >50 mm); AAD, antiarrhythmic drug; WACA, wide area circumferential ablation; Roof, dome-line from the left to right WACA rings; MI, mitral isthmus line; and AL, additional lines along the septum or posterior LA wall near the coronary sinus.
3D ultrasound rendering may limit image accuracy, validation of this approach was required before its widespread clinical application.

In both animal and human studies, the 3D ultrasound volume renderings showed an acceptable point-source position error of 2 mm, a component of which included electromagnetic location error of <0.8 mm inherent in the system. Factors related to respiratory cycle may also contribute to observed error. Recent studies have shown significant differences in cardiac chamber dimensions occurring over the course of expiration and inspiration. Although such differences were seen during this study, their impact was minimized by comparing 3D ultrasound and CT volumes acquired during the expiratory phase, even though the system did not automatically gate for respiratory cycling. Furthermore, this study showed ≤1 mm resulting error in ablative lesion location, supporting the feasibility and acceptability of this approach to 3D navigation. The size of ablative lesions in this study and their precise positioning suggest this error is not limiting in the radiofrequency ablation arena.

Comparison of the Accuracy of Merged CT and 3D Ultrasound–Derived Images

These data confirm the discrepancies in merged CT/magnetic resonance images reported in recent studies. Several prior integration studies showed a match error of <3 mm as calculated from average global surface match of the registered CT geometry and 3D electroanatomic mapping. Nevertheless, all clinically acquired electroanatomic mapping points used in such a process of surface merging are attached to the closest 3D geometry without regard to any prespecified landmark pairs. Therefore, average global match error would artificially appear small, masking potential single-point error at specific target sites.

In contrast, more recent validation studies focusing on position error at individual target sites showed >5-mm inaccuracies despite favorable average global surface match. The present study confirms that the surface merge alignment with CT-generated images results in larger point-source errors (5.4 ± 2.5 mm for atria and 6.6 ± 3.1 mm for ventricles) as established from the preimplanted fiducial clips, although chamber geometries seemed better aligned, as suggested by the smaller average surface mismatch. Nonetheless, despite manual adjustments, the point-source position error remained larger with CartoMerge guidance than seen using 3D ultrasound geometries.

Such persistent position errors after adequate adjustment of the merge process are likely due to the presence of different chamber conformations in CT and 3D electroanatomic data sets. This can occur because of various LA chamber status changes occurring in the time interval between CT image acquisition and intervention, including changes in volume, rhythm, cardiac cycle, or respiration. Also, the endocardial surface detection of CT/magnetic resonance imaging is achieved by using contrast material and completed by a limited semiautomatic segmentation process. Poor CT image quality at faster heart rates may further increase inaccuracy, particularly during ventricular imaging. In contrast, the 3D ultrasound image volumes have the advantage of real-time confirmation by combined 2D ICE imaging and electroanatomic measurements.

Anatomy-Based Ablation Guided by 3D Ultrasound–Derived Geometry

This study shows the accuracy of 3D ultrasound–guided ablation, which was successful in creating continuous lesions even in the setting of complex anatomy within the small canine LA. As expected, this 3D ultrasound geometry–based approach was also feasible with a variety of AF ablation methods and patient characteristics. The accuracy and feasibility of this approach were confirmed through the validation studies and the qualitative configuration of ablative lesion sets in dogs and the comparisons of the 3D ultrasound geometries and electroanatomic mapping and establishment of PV-antrum entrance block in humans. The clinical data also demonstrated that electroanatomic maps of the LA tended to be larger than 3D ultrasound volumes. This may be partially explained by tissue surface distortions created by manual catheter manipulation. Importantly, the PV orifice was more easily and accurately detectable with 3D ultrasound geometry, as reflected by larger PV orifice areas and smaller errors than seen with electroanatomic mapping. This should allow for more accurate navigation around the PVs, thereby improving the efficacy and safety of AF ablation. Consistent with this, we did not observe any complications such as tamponade, cardiac perforation, or injury to the esophagus or phrenic nerve in the animal and clinical studies. More completely establishing safety and efficacy will require additional larger comparative studies, however.

Study Limitations

There are several technical limitations of this investigation. First, the current system did not allow automatic gating to respiratory cycle. Nevertheless, 79% of images used in the analysis were acquired in late-expiratory phase, and the remaining clips showed no appreciable perimeter changes between inspiration and expiration, thus minimizing the potential impact of this factor. In fact, respiratory cycling made a very small contribution to observed error. Second, the resolution of 2D ICE imaging is less than that of the CT imaging. Possible factors such as acoustic shadowing or incomplete penetration could limit the ability to complete 3D ultrasound rendering. Nevertheless, a prior study from this laboratory showed excellent resolution of tissue structures by 2D ICE imaging at a distance of 0.5 to 8 cm from the tip. Multiple catheter rotations, further ICE catheter insertion or withdrawal, or imaging head angulation also enabled the completion of the 3D ultrasound geometry in all animal and human cases. Third, the 3D ultrasound rendering does not establish catheter tip/tissue contact, except as reflected by the catheter tip color. Because the 3D ultrasound geometry consists of a family of the outlined contours derived from the 2D images, catheter tips at or beyond the 3D ultrasound geometry will still disclose tissue contact, as will the accompanying ICE images. Despite these issues, the 3D ultrasound system provided a robust basis for mapping and ablation, with little inherent error from technical factors, with further feasibility of application demonstrated in the clinical studies.
Source of Funding
This study was supported in part by an unrestricted research grant from Biosense Webster, Inc.

Disclosures
Dr Packer received other clinical and animal research support from Biosense Webster, during the conduct of this study. Dr Packer has also received research grants from Hansen Medical, St. Jude Medical, Boston Scientific, ProRhythm, CryoCath Technologies, and CardioFocus; has received honoraria from Bard EP, CryoCath Technologies, Medtronic, Biosense Webster, Hansen Medical, and St. Jude Medical; has royalty interest in St. Jude Medical; and has served as a consultant to or on the advisory boards of Biosense Webster, Bard EP, Boston Scientific, CryoCath Technologies, Hansen Medical, and SanofiAventis. A. Altman and A. Govari are employees of Biosense Webster. Ms. Johnson receives royalty payment from St Jude Medical. The other authors report no conflicts.

References

CLINICAL PERSPECTIVE
During the past 10 years, technology to fully “register” cardiac activation to actual anatomic images has evolved in an effort to facilitate complex anatomy-based ablation. Although these technologies were widely accepted in the electrophysiology field, multiple factors distort actual anatomic information on 3D electroanatomic maps, impedance maps, or merged computed tomographic (CT) image in guiding ablation. To compensate for inaccuracy on these images, this novel 3D ultrasound system was previously developed. This study examined the accuracy and clinical feasibility of guiding complex anatomy-based ablation in animal and human cases. These data demonstrate that nearly real-time acquired 3D ultrasound images can be used to seamlessly generate anatomically accurate chamber geometries. Quantitative information demonstrates minimal error created by the 3D ultrasound registration system, which was more accurate than seen with quantitative merged CT image analysis or standard electroanatomic mapping. This novel system may provide advantages for complex ablation strategies.
Three-Dimensional Ultrasound for Image-Guided Mapping and Intervention: Methods, Quantitative Validation, and Clinical Feasibility of a Novel Multimodality Image Mapping System
Yasuo Okumura, Benhur D. Henz, Susan B. Johnson, T. Jared Bunch, Christine J. O'Brien, David O. Hodge, Andres Altman, Assaf Govari and Douglas L. Packer

Circ Arrhythm Electrophysiol. 2008;1:110-119; originally published online January 1, 2008; doi: 10.1161/CIRCEP.108.769935
Circulation: Arrhythmia and Electrophysiology is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2008 American Heart Association, Inc. All rights reserved.
Print ISSN: 1941-3149. Online ISSN: 1941-3084

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circep.ahajournals.org/content/1/2/110

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation: Arrhythmia and Electrophysiology can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation: Arrhythmia and Electrophysiology is online at:
http://circep.ahajournals.org//subscriptions/