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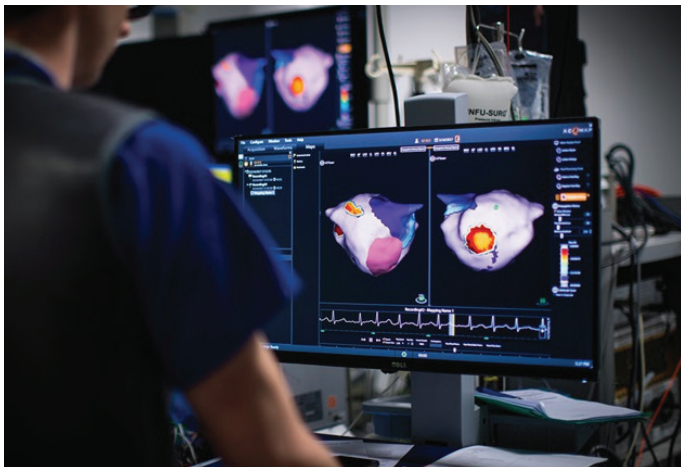
By Reed Miller

ACUTUS MEDICAL INC.'S *ACQMAP* **MULTI-ELECTRODE ELECTROPHYSIOLOGY** mapping catheter has the potential to fundamentally change how arrhythmias are understood and treated, according to Andrew Grace, University of Cambridge, one of the investigators of two studies demonstrating the potential of AcQ-Map to identify non-pulmonary vein targets for atrial fibrillation ablation.



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AcQMap is a catheter-based non-contact cardiac imaging and mapping system.

It acquires up to 115,000 ultrasound data points per minute to rapidly create an anatomic reconstruction of a chamber of the heart and up to 150,000 biopotential samples per second to create a three-dimensional map of cardiac electrical activity of the whole chamber in real-time, according to Acutus. AcQMap earned a CE Mark in 2014 and FDA-clearance in 2017. The company launched it in the US in May 2018 shortly after FDA cleared the *AcQRef* introducer sheath to deliver the AcQMap mapping catheter. *(Also see "US Approvals Analysis: Original PMA Slowdown, De Novo Upswing Among Recent Trends" - , 13 Nov, 2017.)*

Charge-Based Model Versus Current-Based Model

The technology is based on the charge-based model of electrophysiology rather than the current-based model that has dominated electrophysiology for decades, Grace told *Medtech Insight*.

"The key thing here is the reevaluation of the fundamental basis of cardiac electricity and it goes back to the physics that underpin the generation of the electrocardiogram. That has, in my view, been somewhat misinterpreted if for up to 50 years," Grace said.

Günter Scharf, a physicist at the University of Zurich "has exposed the fact that much of the physics that underpins theories of so-called electric cardiology are incorrect," Grace said.

"We've moved away from the current-based model to a charge-based model and this will increase the capability of observing the true sources of the cardiac electrical field which has, obviously, immediate importance to atrial fibrillation and ultimately ventricular fibrillation," he said.

Scharf's insights into the charge-model are of "fundamental scientific interest in terms of relating the generation of the heart beat to what the electrical signals are that are recorded ... There are enormous implications that emerge from this."

Grace, Scharf, and ten other researchers recently published results from DDRAMATIC-SVT, a study of a prototype algorithm for AcQMap, in *The Journal of Clinical Investigation: Insight*. The algorithm processes

multiple non-contact voltage measurements within the cardiac chamber to show a global distribution of charge-density sources across the endocardial surface. The study compared the results of the charge-density mapping to an established computer-simulated model of atrial conduction.

The study demonstrates the feasibility of the charge-density approach, in terms of spatial, temporal, and morphologic metrics, with median spatial errors of 1.73 mm and 2.41 mm for charge-density and voltage, respectively. The median temporal error was less than 0.96 milliseconds and the morphologic correlation was better than 0.90 for both charge-density and voltage.

The activation patterns observed for atrial flutter reproduced those established by contact mapping technologies, but the charge-density approach yielded a four-fold improvement compared to the voltage-based approach, Grace et al. report.

"The First True Maps Of Atrial Fibrillation"

So far, technologies for non-contact mapping of arrhythmias have not been widely adopted outside of the UK, Grace said.

"It just didn't have the capabilities to observe the true sources [of the arrhythmia] and had all kinds of issues with specificity." By contrast, "the AcQMap tool is, obviously, an phenomenal feat of engineering," he said. *(Also see "AF Ablation Procedures Driving CRM Market Expansion" - Medtech Insight, 27 Mar, 2015.)*

"Charge density allows one to exclude the distant confounding signals - the far field noise - that gets in the way of resolving the true sources of the electrical fields. That is the major scientific advance, and then, we showed that that you can get better resolved maps of atrial flutter and there is no controversy about the activation patterns in atrial flutter."

In DDRAMATIC SVT, the charge-density-based global activation maps for hearts undergoing atrial fibrillation showed a reduction in far-field interference compared to existing mapping approaches. The study also showed that ablation of the targets identified by the charge-density-based maps led to slower arrhythmia cycle-lengths and termination of the arrythmia, which "indicates both mechanistic and pathophysiological relevance," according to Grace et al.

Atrial fibrillation is commonly treated with pulmonary vein isolation – a physiology-based approach to blocking the aberrant electrical signals causing the atrial fibrillation by creating a circumferential lesion in the opening of the pulmonary vein.

DDRAMATIC SVT showed AcQMap can help find sources of atrial fibrillation beyond the pulmonary vein, "which is one of the golden objectives of current electrophysiology," Grace said.

Contact mapping technologies cannot find these targets because the signal-directions are constantly changing, he explained.

"You need to get the global map of the total chamber that can only be achieved with non-contact mapping." Grace believes the maps of atrial fibrillation patterns created by AcQMap should be considered "the first true maps of atrial fibrillation. This is an objective that's been pursued by the physiological and the clinical community going back 100 years."

The charge-density cardiac maps produced by Acutus' AcQMap represent "the first true maps of atrial fibrillation," according to Andrew Grace, University of Cambridge.

Grace was also one of the investigators of the 127-patient UNCOVER AF trial, led by Atul Verma of Southlake Regional Health Centre in Newmarket Ontario, evaluating the safety and effectiveness of AcQMap to find non-pulmonary-vein targets for ablation treatment of persistent atrial fibrillation. Results of UNCOVER AF were presented at the Boston AF Symposium in January and will be published in a journal soon, according to Grace.

In the study, treating physicians from 13 different sites used irrigated radiofrequency or cryoablation ablation for pulmonary vein isolation and used irrigated radiofrequency ablation to ablate the non-pulmonary-vein sources of atrial fibrillation identified by AcQMap.

Normal sinus rhythm was restored in 98% of the patients and the mean total procedure time was 4.1 hours. On average, there were five focal, rotational, and/or irregular conduction patterns identified per patient and an average of 4.2 of those patterns were ablated per patient. One year after the procedure, 72.5% of the patients treated only once were free from atrial fibrillation and 93% of the patients were free from atrial-fibrillation after one or two procedures, for an 82.4% reduction of atrial-fibrillation burden, according to Verma et al. The predictors of one-year atrial fibrillation success included the ablation of more than three conduction patterns. Termination of atrial fibrillation to restoration of sinus rhythm predicted a three-times greater likelihood of sinus rhythm at one-year. There were no major safety events.

At the AF Symposium, Verma said, "We have mapped arrhythmias with the same technology for decades without asking if there's a better way to locate ablation targets and deliver a more precise, patient-specific therapy ... The results of the UNCOVER-AF trial demonstrate that with better imaging, we can perform patient-centric ablations with great success, while dramatically improving patient quality of life. This advanced cardiac imaging system paints a complete, high-definition picture in real time and is an important step in advancing the standard of care for AF ablation procedures."

"I think [the AcQMap technology] is going to transform everything," Grace said.

Acutus is also sponsoring RECOVER AF, a 100-patient single-arm, multi-center trial designed to provide clinical data on AcQMap used during the first or second atrial fibrillation retreatment ablation procedures. Acutus and Stereotaxis are co-sponsoring development of a version of Stereotaxis' robotic magnetic navigation system integrated with Acutus' AcQMap. *(Also see "Starts & Stops: CardioFocus Studies HeartLight X3 In Persistent AF; IntraLink Spine Launches Trial Of Low-Back Device In Australia" - Medtech Insight, 17 Mar, 2019.)*

Grace said the reduction in atrial fibrillation shown in UNCOVER AF represents "a 20% increment over results with other approaches.

"He uses it routinely in clinical practice and it has been adopted by six hospitals in the UK's National Health Service because "they're finding it beneficial." But, he acknowledged, a randomized trial will be needed to "truly prove what we would contend anecdotally to be the case, that this is a superior technology."

He also believes AcQMap can help researchers understand the genetic origins of these arrhythmias.

"We can now resolve the signals. It's almost like an *in vivo* protein assay. We can then map it onto genomes and genetics, which are obviously fundamental in the generation of much of atrial fibrillation. So there's all sorts of value that will come out of it," he said. "I think it's going to transform everything."

Privately held Acutus was founded in San Diego in 2011. The company's Series A financing yielded $5.4m from Advent Life, Index Ventures, and its founders. The company closed a $28m Series B funding round in 2013, led by OrbiMed Advisors, LLC along with GE Ventures, with further investments from Index Ventures and Advent Life Science. A a $75m Series C financing announced in 2016 included investments from Deerfield Management Company, Xeraya Capital an undisclosed strategic investor, as well as investments from Advent Life Sciences, OrbiMed, and GE Ventures.

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