At HRS, Topera Topples Conventional Wisdom About Atrial Fibrillation

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Topera Medical questions the assumptions underlying current therapies for atrial fibrillation. Sanjiv Narayan, MD, PhD, the electrophysiologist who founded Topera, has developed a means of identifying focal sources of aberrant electrical activity called rotors, and in late breaking clinical trials at the 2013 annual meeting of the Heart Rhythm Society, was able to show a definitive link between their ablation and treatment success.

Atrial fibrillation has always been frustratingly resistant to a cure. Even among the so-called easiest groups of patients, those with paroxysmal atrial fibrillation (which is intermittent and terminates on its own), conventional ablation procedures using radiofrequency or some other energy modality to scar the heart and isolate the instigating electrical impulses (or triggers) provide long-term freedom from AF only 50% of the time. The search for better efficacy is compelling because patients that suffer from atrial fibrillation have a five to seven-fold increased risk for stroke.

While much of the cardiology industry has tried to improve the results by incrementally improving the therapies, Topera Medical Inc. challenges the assumptions upon which therapy has been based. (See "Device Companies Follow New Map To Atrial Fibrillation" — Medtech Insight, December 2012.) Back in 2011, Topera’s scientific founder, electrophysiologist Sanjiv Narayan, MD, PhD, of the department of medicine at the University of California, San Diego, and the Veterans Affairs Medical Center in San Diego was a lone voice at the Heart Rhythm Society’s (HRS) 32nd annual scientific sessions. At the time, Narayan presented study results that concluded that there were previously theorized but never before seen sources of AF that drive and sustain arrhythmias. At this year’s annual meeting Narayan was flanked by a chorus of electrophysiology professionals carrying the same tune.

Atrial fibrillation is typically treated based on an anatomical, rather than a physiologic treatment strategy. That is, physicians have isolated the pulmonary vein, or targeted the roof of the left atrium as a treatment strategy, without truly identifying the source of the aberrant electrical signals. For whatever reason, those anatomical strategies resulted in lackluster efficacy for patients with paroxysmal atrial fibrillation even after retreatments, and very little efficacy for the harder-to-treat persistent AF patients further along in the course of their disease. Topera has apparently revealed the reason.

Topera developed a new electrophysiologic mapping technology, called RhythmView, for identifying focal sources of atrial fibrillation called rotors. These rotors resemble miniature electrical hurricanes in the heart; they’re organized in the center but chaotic in the periphery.

In August 2012, Narayan published the results of a first-in-man study called CONFIRM, in which the efficacy of treatments in patients in whom those rotors were ablated (a strategy the company calls FIRM, for Focal Impulse and Rotor Modulation) along with conventional pulmonary vein isolation, was far superior to that of patients treated just by pulmonary vein isolation.

Patients treated with ablation guided by the Topera mapping technology enjoyed 82% freedom from recurrent AF, compared to a 45% rate for conventional pulmonary vein isolation at a median
follow-up period of 273 days. All patients were mapped by RhythmView, but the control group maps were not available until after the completion of their procedure.

As a follow-up to CONFIRM, a sub-group analysis hinted that in those patients that were free of atrial fibrillation after only undergoing pulmonary vein isolation, rotors had been coincidentally located near the pulmonary vein and ablated, suggesting the possibility that the success of pulmonary isolation alone was due to the serendipitous ablation of the specific rotors rather than the blocking of triggers from the pulmonary veins.

Late-breaking results presented at the recent Heart Rhythm Society meeting in Denver supported those conclusions. A small, 31-patient study at five centers called PRECISE studied the use of the RhythmView system to identify and treat rotors in patients with paroxysmal atrial fibrillation. This time, only the rotors were targeted for ablation; the pulmonary veins were not isolated. At one year, 83% of the patients were free of atrial fibrillation. This compares to an expected success rate of about 50% from conventional treatments.

Topera’s CEO Edward Kerslake, PhD, says this year’s HRS industry meeting was a tipping point for the company. At the recent meeting, Narayan was no longer the sole advocate for FIRM. There were some 21 presentations about Topera’s technology, many by researchers not affiliated with the company. Several important conclusions emerged from the research that show that FIRM is not just interesting science, but a modality with the potential to improve outcomes in patients with AF.

Two studies were presented by Vijay Swarup, MD, of the Arizona Heart Rhythm Center. In one, he noted that rotors are not transient, meandering signals; they’re stable in their location for thousands of cycles, which makes them good targets for treating and alleviating AF. Second, rotors are located in diverse locations in both atria with perhaps as many as 30% located in the right atrium. Says Kerslake, “If you suppose that 20%-30% of the sources are in the right atrium and you’re only treating the left, well, you’re looking for the light switch in the wrong room.”

But the real point, he says, is that such variability calls for a technology robust enough to find rotors in every patient. The horse race is on, Kerslake says, and other companies believe they’re finding rotors. “Showing a rotor in a human is scientifically interesting, but not clinically relevant, unless you can map every patient that comes into the hospital. If it only works in the very simple cases, where there is a single rotor that is all-encompassing and you can practically see it from 50 feet, that is not valuable.” Kerslake says Topera has now mapped more than 300 patients. “Our system has demonstrated that we can find these rotors in every single patient, with an ability to differentiate the multiple simultaneous rotors that are found in the majority.”

At the meeting, a presentation by Robert Kowal, MD, of Baylor University Medical Center, demonstrated that multiple sites new to FIRM ablation achieved results similar to those achieved by Narayan, so the method is reproducible. Finally, a presentation based on the work of Jonathan Steinberg, MD, of Valley Health System’s Arrhythmia Institute (in Ridgewood, NJ), demonstrated that some of his worst cases of persistent AF, patients who tended to generally relapse into AF within a week of their treatments, returned to sinus rhythm after the procedure, and have maintained normal rhythm out to a year so far.

Kerslake says the RhythmView system, which has 510(k) clearance, has been used at 14 sites across the US. “Those sites continue to do early work with us as we refine the system in preparation for the full commercial launch in the US planned or the second half of this year.” The company awaits 510(k) clearance on a proprietary mapping catheter called FIRMap, which is designed to achieve better tissue contact with improved distribution of the signal-capturing electrodes than the off-the-shelf-catheter it used in the CONFIRM study.

In late April, Topera raised approximately $25 million from a Series C venture round with private investors, an undisclosed strategic investor, and the venture capital firm New Enterprise Associates (NEA). In conjunction with the financing, NEA partner Justin Klein, MD, joined the board. [See Deal] Klein states, “As an investment, it is a rare occasion when we find an opportunity to apply a diagnostic technology – where its use in a procedure imparts very little incremental risk to the patients – that can have such a profound impact on improving the overall efficacy of a treatment in a growing market with a significant unmet clinical need.”