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iRhythm Builds Momentum Following Large Trial Of AI Approach To ECG Analysis





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► Reed Miller

RESULTS FROM A STUDY OF MORE than 91,000 ECG records collected with iRhythm's Zio ambulatory continuous cardiac monitoring device that demonstrates the successful application of artificial intelligence to ECGs gives the 12-year-old company confidence that it will be profitable very soon.

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Electrocardiography (ECG) data collected by **iRhythm Technologies Inc.**'s Zio ambulatory continuous-care wearable ECG monitor can be analyzed by a "deep learning" artificial intelligence model to detect cardiac arrhythmias as effectively as a panel of expert cardiologists across 12 kinds of cardiac rhythm outputs, according to the results of a 53,549-patient trial.

"Diagnosing arrhythmia is like a needle in a haystack problem," iRhythm Executive VP-Research & Development Mark Day told *Medtech Insight*. "There are just tremendous amounts of ECG data and sometimes only as few as 10 beats over a two-week record ... can be the most meaningful part." Diagnosis of arrhythmia is usually based on short ECG readings, but Zio is a small wireless patch device that patients wear for up to two weeks straight to allow for continuous monitoring. Zio provides the patient and doctor a report based on the data the Zio collects.

He explained that the current algorithms and the current state-of-the-art for arrhythmia detection based on electrocardiography still frequently misses the correct diagnosis, yielding either false positives that erode the clinical



iRhythm's Zio XT ECG Monitor

Source: iRhythm Technologies, Inc.

Two weeks represents about 1.5 million heartbeats, but a patients' arrhythmia may only appear in as few as 10 of those heartbeats. "That's a problem that AI is really well suited to address," iRhythm's Mark Day says.

value of the algorithms or miss or mislabel arrhythmias. "The problem we're really trying to solve is missed diagnosis and mislabeling of annotations that can delay or sometimes confuse clinical therapy," he said.

Day explained that iRhythm's key contribution to this research is "a tremendous amounts of data on cardiology on a single-lead ECG platform and a label dataset, as well as clinical expertise around the meaning and importance of various arrhythmias," while the Stanford group provides the expertise on artificial intelligence and deep-learned algorithms developed for speech and image-recognition.

Results of a new study of Zio and a deep learning network, led by Awni Hannun of Stanford University, are



published in *Nature Medicine*. (Also see “Market Intel: Artificial Intelligence Brings Wave Of Future Health Care Innovation – Embrace it or be Left Behind” - *Medtech Insight*, 28 Jul, 2017.)

The study evaluated the ability of a novel deep neural network to classify 12 rhythm classes – 10 types of arrhythmia plus normal sinus rhythm and “noise” – using 91,232 single-lead ECGs from 53,549 patients who used a Zio single-lead ambulatory ECG monitoring device. The mean and median wear time of the Zio monitor in the study was 10.6 and 13.0 days, respectively.

The deep neural network achieved an average area under the receiver operating characteristic curve of 0.97 when validated against an independent test dataset annotated by a consensus committee of board-certified practicing cardiologists, Hannun et al. report in *Nature Medicine*.

The average F_1 score, which is the harmonic mean of the positive predictive value and sensitivity, for the deep neural network (0.837) exceeded the score for the of average cardiologist (0.780). With specificity fixed at the average specificity achieved by cardiologists, the sensitivity of the deep-neural network was better than the sensitivity achieved by the average cardiologist across all rhythm classes. “These findings demonstrate that an end-to-end deep learning approach can classify a broad range of distinct arrhythmias from single-lead ECGs with high diagnostic performance similar to that of cardiologists,” Hannun et. al report. “If confirmed in clinical settings, this approach could reduce the rate of misdiagnosed computerized ECG interpretations and improve the efficiency of expert human ECG interpretation by accurately triaging or prioritizing the most urgent conditions.”

The Stanford study shows “that there is a path leveraging new algorithm technologies, and deep neural networks in particular, to improve the clinical accuracy of the algorithm ... and to really apply cardiologist-level accuracy throughout such extensive recordings of two weeks of data,” Day said. He pointed out that two weeks represents about 1.5 million heartbeats, but a patients’ arrhythmia may only appear in as few as 10 of

those heartbeats. “That’s a problem that AI is really well suited to address.”

The company is integrating what it learned from the Stanford study into the Zio system “which is just part of our ongoing effort to improve the clinical accuracy and scalability of our service,” Day said. He pointed out that, “while this been shown to be equivalent to physician-level accuracy in no way suggests that it’s a replacement or anything other than a service that will allow physicians to [be more] effective.”

Zio earned US FDA clearance in 2017 for long-term ECG monitoring and results of the mSToPS trial, published in July 2018, show active monitoring with Zio is significantly better at detecting atrial fibrillation than delayed monitoring. The 1,965-patient KP-RHYTHM trial showed that a greater burden of atrial fibrillation, measured with 14-day continuous ambulatory electrocardiographic monitoring with Zio, is associated with a higher risk of ischemic stroke independent of known stroke risk-factors in adults with paroxysmal atrial fibrillation.

In 2017, the EPACS trial showed that early prolonged monitoring with Zio following a stroke or transient ischemic attack is better than 24-Holter monitoring for the detection of paroxysmal atrial fibrillation. (Also see “ACC 2018 Preview: Zoll’s LifeVest, Abbott’s HeartMate 3 And Amplatzer, Late-Breaking Trial Devices” - *Medtech Insight*, 29 Jan, 2018.) Data from the MESA study, published in 2015, Zio can help researchers effectively investigate atrial-fibrillation burden in asymptomatic subjects in community-based studies.

Zio is currently being tested in the SCREEN-AF trial, sponsored by the Population Health Research Institute. The trial is investigating atrial fibrillation-screening in primary care patients using the Zio and Microlife AG’s *WatchBP* home blood pressure monitor that with built-in screening capability.

iRhythm Is Growing Rapidly; Profitability ‘Is Not Far Off’

The collaboration with Stanford on the deep neural network is an example of the investment San Francisco-based iRhythm is making in artificial intelligence to make



ECG analysis more accurate and make its Zio products and service more valuable to physician-customers.

The company is investing in artificial intelligence because it provides “an opportunity to substantially improve the accuracy of ECG analysis, reducing the rate of misinterpretations and inappropriate patient management,” CEO Kevin King said during the company’s Feb. 12 Q4 2018 earnings call. Improved accuracy will lead more patients to use Zio and wear the device longer, which will increase the complexity of each patient’s Zio record. “This means our future AI capabilities will not only accurately diagnose patients with current arrhythmias, but also be capable of predicting a patient’s future risk, allowing for earlier medical treatment and possible prevention,” he said.

“We have a robust pipeline of clinical research, and you can expect to see additional studies coming out of the year that will demonstrate the clinical utility, comparative effectiveness and strength of our Zio platform across a variety of indications,” King said. “In 2019, we look forward to continuing our momentum with strong execution across our business. Confidence in our highly competitive positioning and differentiation includes Zio’s proven superiority, the growing strength of our AI algorithms and data analytics, and the completeness of a platform that routinely creates meaningful value for our customers, large and small.”

For all of 2018, the company reported revenue of \$147.3m – a 55% increase over its 2017 revenue. Gross

margin in 2018 was 73.8% – an 190 basis-point improvement, year-over-year. King credited the success to the performance of its growing sales force – the company expects sales headcount to reach approximately 130 to 140 by year end 2019 – physicians’ increased awareness of the benefits of continuous cardiac monitoring, and the strength of the published clinical data. “We are entering 2019 in our strongest position to date based on Zio’s proven performance and the value our complete solution creates for our customers,” he said.

iRhythm projects revenue for the full year 2019 will grow 36% to 40%, year-over-year, to between \$201m million to \$206m with gross margins between 75% to 76%.

Despite the sales growth, iRhythm reported a net loss in 2018 of \$48.3m, up from \$30.6m in 2017.

“Even when we’re growing at the rates we have been growing, we’re still a relatively small share and we need to continue to invest in the commercial side of our business,” King said during the earnings call. “We’ve got a big pipeline of new indications, new products, new technologies that we’re investing in over time. That said, we’re increasingly confident that there is strong leverage and strong pull-through in our business... The revenue growth rates are continuing to be in the upper tier of our peer groups [and] I’m totally confident [that] as far as profitability, it’s not that far off.”

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