AF | Podium Connection

FEBRUARY 2023

2023 AF SYMPOSIUM (AFS)

AF MARKET INSIGHTS REPORT

This report published by
AF Market Experts, LLC

About the Author

AF Market Experts, LLC ("AFME") was founded by industry veteran Ryan Bachman, who has a total of 16+ years of experience across Wall Street and the EP industry. For four years, Ryan covered the medical device industry as part of the equity research teams at Morgan Stanley and RBC Capital Markets. He then joined Biosense Webster, Inc., the recognized market leader in cardiac ablation, and he spent the next 12 years in various roles of increasing responsibility within Global Strategic Marketing. Across all roles at BWI, his core responsibilities included competitive intelligence and AF market insights.

AFME was founded to share the same level of AF market insights with clients by providing comprehensive coverage from all major AF industry congresses. We bring the AF podium to you.

Legal Disclaimers

TABLE OF CONTENTS

EXECUTIVE SUMMARY

The 28th annual AF Symposium (AFS) was held in Boston, MA from February 2-4, 2023, and attendance appeared comparable to events held before the COVID pandemic. Each year, AFS is one of the best venues for updates on the AF market due to the volume of presentations, the depth of content presented, and the quality of discussions among presenters, panelists, and the audience. The congress provides a breadth of information on technologies from both strategic competitors and start-up companies, with dedicated "Spotlight Sessions" highlighting new products in development from more than 15 start-ups.

Across the congress, the company with the largest podium presence was Biosense Webster, highlighted by four live/recorded case presentations and two late-breaking clinical trial (LBCT) presentations. Please see the summary of live and recorded cases on the next page for more details. Data from the "inspIRE" study in Europe with the VARIPULSE PFA catheter showed 70.9% freedom from atrial arrhythmias at 12 months in the pivotal phase of the trial (Wave 2). The U.S. IDE trial for VARIPULSE ("admIRE") has also completed enrollment. Early preclinical work with a dual-energy, PF/RF application using the STSF catheter was presented and showed deeper lesions vs. PF or RF alone. Data from the U.S. IDE trial for BWI's HELIOSTAR RF balloon were presented for the first time. Freedom from all arrhythmias at 12 months was just 67.7% and safety events in the trial caused much discussion – one death was reported from an atrial bronchial fistula and two permanent phrenic nerve injuries were also reported.

Boston Scientific had a similarly strong presence, and the FaraWave catheter captured the largest podium share of any individual product. To date, over 13,000 commercial cases have been performed in Europe, and the catheter was featured in two live cases. One case included presentation of a prototype software module to fully integrate FaraWave with the Rhythmia mapping system. Data from the U.S. IDE trial for FaraWave ("ADVENT") will be presented later this year at either ESC or AHA. Safety with FaraWave, and PFA in general, was a frequent topic, and recent publications on coronary spasm were discussed the most. The perspectives remain mixed – some physicians were not concerned due to the ability to pre-treat with nitro and others continue to feel that more data are needed.

The two Medtronic Affera PFA catheters, Sphere9 and SpherePVI, were each featured in separate pre-recorded cases, and DiamondTemp was also the subject of multiple posters, although the impact of the posters was low. Although PulseSelect was not presented often during AFS, many physicians referenced the upcoming data presentation at ACC. On Monday March 6, results from the PULSED AF trial will be presented, and it will be the first data set from a U.S. IDE trial investigating PFA.

Also making news during the congress was Philips, which decided to shut down the EPD Solutions business according to local press articles. Philips originally acquired EPD in 2018 for total consideration up to $300 million. The VeriSight Pro ICE catheter continues to be supported by Philips.

Among start up companies, a total of four catheters were presented publicly for the first time at AFS, and all use pulsed field energy. Field Medical introduced the "FieldForce" system during a Spotlight Session. Pulse Biosciences presented the "nsPFA" system in a poster. CardioFocus introduced a new PFA-enabled balloon based on its existing X3 platform. Finally, Arga Medtech reported FIM data from cases with its "multi-configurable catheter" capable of taking different shapes to facilitate different lesion sets. Galaxy Medical received CE Mark in August 2022, and it was disclosed that 300 commercial cases have been completed to date.

Outside of PFA catheters, the CardioNXT iMap mapping system was featured in four posters detailing successful integration with four different ablation catheters from both strategics and start-ups. Finally, a novel mapping system from Anumana-Neutrace was presented at the podium for the first time.

A unique feature of the AF Symposium each year is the inclusion of "Spotlight Sessions" in the agenda. These presentations are only 5 minutes in duration, and they feature an emerging company and its technology under development. Below is a table comparing the companies featured in both the 2023 and the 2022 AF Symposium, along with the physician presenter.

AF Symposium "Spotlight Sessions"

2023		2022	
Featured Company	Presenter	Featured Company	Presenter
Acutus Medical	Dr. Robert Bernat	Ablacon	Dr. David Haines
ADAS 3D Medical SL	Dr. Diego Penela	Aqua Heart	Dr. Srijoy Mahapatra
Anumana-NeuTrace	Dr. Kalyanam Shivkumar	BioSig Technologies	Dr. DJ Lakkireddy
AtriAN Medical	Dr. Vivek Reddy	CardioNXT	Dr. Thomas Kurian
CardioFocus	Dr. David Haines	Cardiva Medical	Dr. Walid Saliba
CardioNXT	Dr. Usman Siddiqui	CathVision	Dr. Mintu Turakhia
CathVision	Dr. Suneet Mittal	Circle Cardiovascular Imaging	Dr. Saman Nazarian
EP Frontiers	Dr. Jonathan Piccini	ElectroPhysiology Frontiers	Dr. Jonathan Piccini
Field Medical	Dr. Usman Siddiqui	Kardium	Dr. Atul Verma
LuxMed Systems	Dr. Jacob Koruth	NeuTrace	Dr. Andrea Natale
MedLumics	Dr. Atul Verma	Philips EPD Solutions	Dr. Lucas Boersma
Volta Medical	Dr. John Hummel	Volta Medical	Dr. Seth Goldbarg

Note: Only companies within cardiac ablation are included. Companies included in both 2023 and 2022 have been highlighted in the same color.

In addition to the Spotlight Sessions, the AF Symposium always includes a strong lineup of live and pre-recorded cases featuring new technology. The table below summarizes the cases featured at the event this year, along with supporting details.

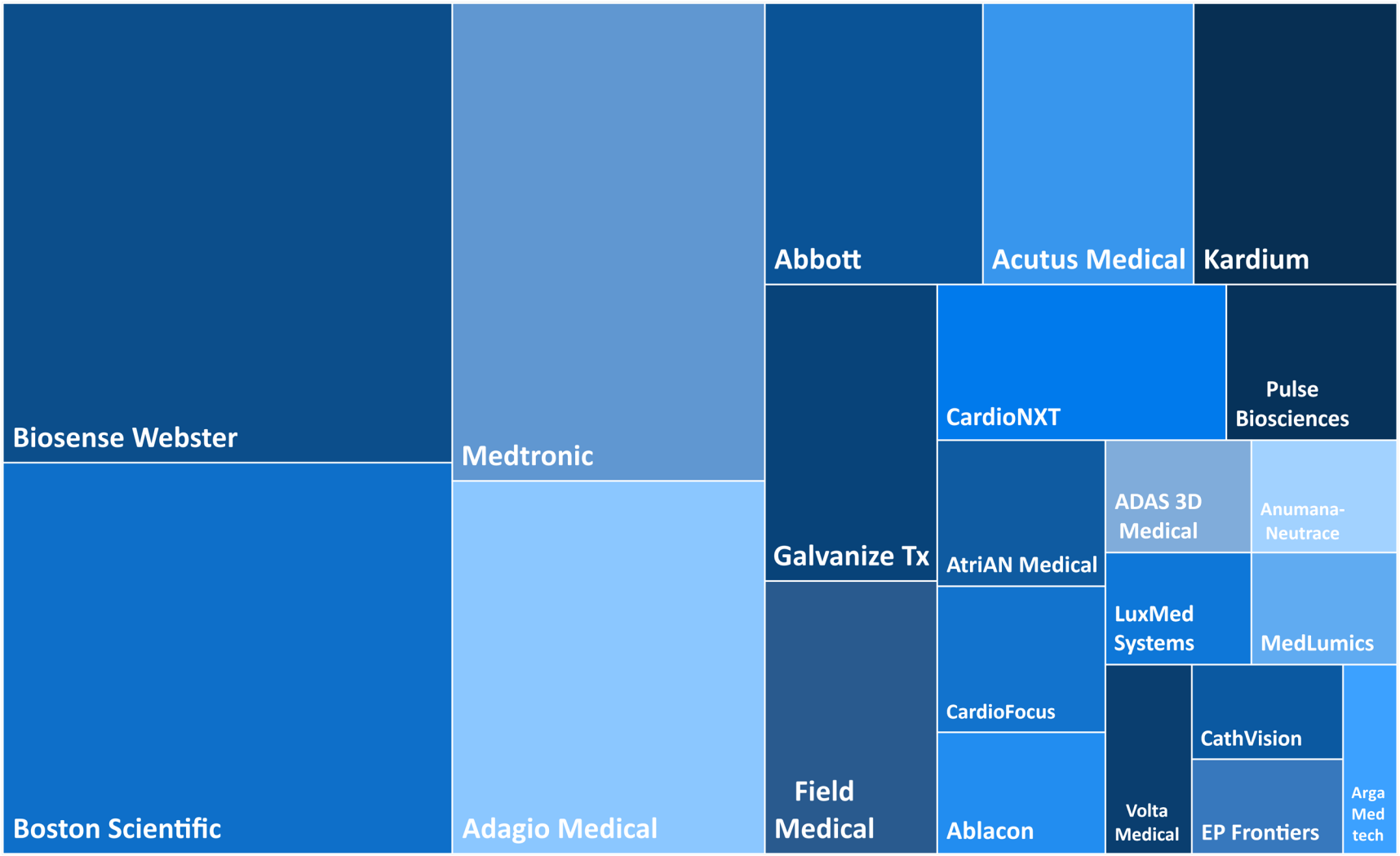
2023 AF Symposium: Live & Pre-Recorded Cases

Event Type	Physician Operators/Presenters	Site of Case	Technologies Featured	Manufacturer
Live	Dr. Daniel Steven	University Hospital Cologne Cologne, Germany	TactiFlex EnSite X Version 2	Abbott EP
Live	Dr. Jean Baptiste Chierchia	Heart Rhythm Management Center Brussels, Belgium	HELIOSTAR	Biosense Webster
Live	Dr. Srinivas Dukkipati	Mount Sinai Medical Center New York, NY	QDOT OctaRay	Biosense Webster
Live	Dr. Mattias Duytschaever	St. Jan Hospital Brugge-Oostende, Belgium	FaraWave	Boston Scientific
Live	Dr. Gabor Szeplaki	Mater Private Hospital Dublin, Ireland	FaraWave Rhythmia	Boston Scientific
Pre-Recorded	Dr. Charles Athill	Sharp Memorial Hospital San Diego, CA	VARIPULSE	Biosense Webster
Pre-Recorded	Dr. Moussa Mansour	Massachusetts General Hospital Boston, MA	VARIPULSE	Biosense Webster
Pre-Recorded	Dr. Kevin Makati	St. Joseph's Hospital Tampa, FL	POLARx FIT	Boston Scientific
Pre-Recorded	Dr. Andreas Rillig	University Heart and Vascular Center Hamburg, Germany	CENTAURI Generator	Galvanize Therapeutics
Pre-Recorded	Dr. Petr Neuzil Dr. Vivek Reddy	Homolka Hospital Prague, Czech Republic	The Globe PF System	Kardium
Pre-Recorded	Dr. Moussa Mansour	Massachusetts General Hospital Boston, MA	Sphere9	Medtronic Affera
Pre-Recorded	Dr. Petr Neuzil Dr. Vivek Reddy	Homolka Hospital Prague, Czech Republic	SpherePVI	Medtronic Affera

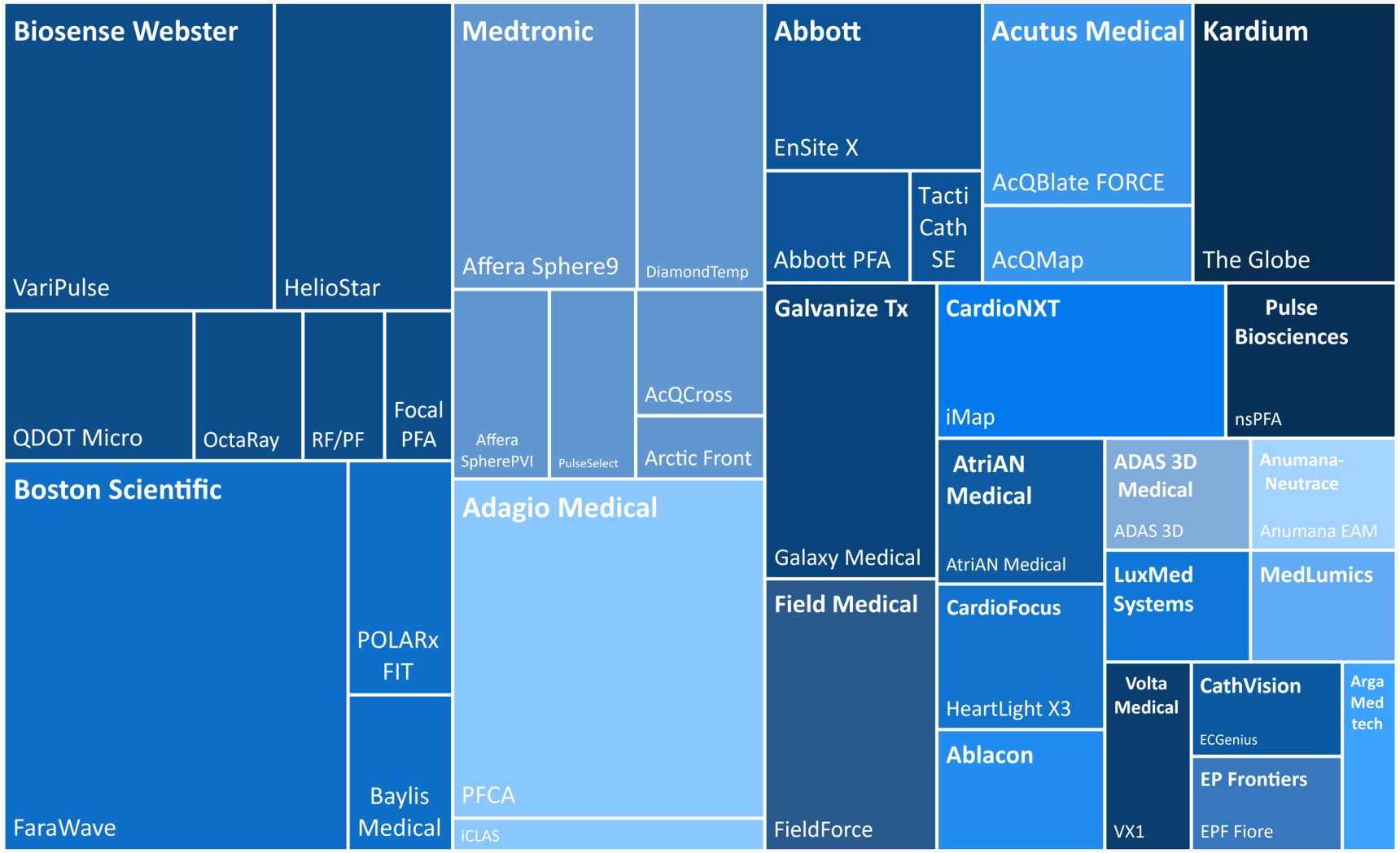
PODIUMSHARE ANALYSIS

The PodiumShare infographics below represent the relative podium presence each Company and individual Product captured during AF Symposium. The size of each area represents the podium share captured: a larger area = stronger podium presence. For the 2023 AF Symposium, Biosense Webster captured the largest podium share as a company (see graph on this page), but Boston Scientific's FaraWave catheter captured the largest podium share of any individual product (next page). Details on the methodology can be found below the graphics.

PODIUMSHARE BY COMPANY



PODIUM SHARE BY PRODUCT



Methodology: AF Podium Connection incorporates a proprietary methodology to score all events that are included in this report. Types of events included in the report are presentations, live cases, and posters, among others. Each type of event receives a score, and we also include a score for the impact of content presented during the event. Finally, each event is tagged for individual products discussed and the respective manufacturer. Scores are then totaled by Company and by Product, enabling the "PodiumShare" calculations across each group.

ABBOTT ELECTROPHYSIOLOGY

Abbott Electrophysiology Website

Summary from AF Symposium

The most important update on Abbott came from Dr. Vivek Reddy, who presented the internally-developed PFA system for the first time. A live case featured the new TactiFlex ablation catheter and EnSite X v2. TactiFlex was mentioned in passing at the podium on several occasions, with several physicians referencing the recent commercial launches in Europe and Japan.

Details from Congress Events

Organized by Product

Abbott PFA

- **Future Directions in Pulsed Field Ablation**
  Vivek Reddy, MD
  Dr. Reddy's presentation contained updates on multiple technologies (ABT PFA, Field Medical, Adagio Medical, and Pulse Biosciences). Notes for each technology are included in the respective company sections in this report.

  - The agenda for Dr. Reddy's presentation included the following topics:
    - PFA + EAM
    - "Field Bending"
    - PFCA
    - Nanosecond PFA
    - LAAC + LAAEI
  - Abbott
    - PFA + EAM topic = novel technology in development by Abbott
      - The catheter was described as having a large basket design with 8 splines
      - The design is "all in one", i.e. it can be used for diagnostics, pacing, and energy delivery
      - It is fully integrated with a magnetic sensor for use with EnSite
    - This catheter has been used pre-clinically and Dr. Reddy said it would start clinical trials later this year

AFME INSIGHTS

This is believed to be the very first presentation of Abbott's internally-developed PFA system. On the Abbott Q4 earnings call in January, CEO Robert Ford said the company originally had two internal PFA programs. After a "bake-off", the company felt stronger about one, which incorporated learnings from currently marketed products. CEO Ford did not discuss the system in any more detail, and he did not provide any estimates for the regulatory timelines.

EnSite X

ERASE-AF: Low-Voltage Myocardium-Guided Ablation Trial of Persistent AF

Part of the sessions sponsored by Abbott
Helmut Pürerfellner, MD

- The ERASE AF trial was published in NEJM Evidence during October 2022 and the abstract can be found here
- This trial compared PVI only vs. PVI + individualized ablation of atrial low voltage myocardium (substrate modification, SM) in PsAF patients
  - Voltage mapping guided the SM ablations
- PVI only = 163pts
- PVI + SM = 161pts
  - ICMs were utilized in a total of 242pts
- PVI + SR was found to be superior to PVI only
  - PVI only recurrences were 50% and PVI + SR recurrences were just 35%
- On his slides, Dr. Purerfellner said that approximately 1/3 of the PsAF patients had significant low voltage substrate and for these patients, PVI alone can achieve only 30-40% complete freedom from AF over 12 months
  - Ablating the low voltage areas eliminates this substrate and can improve outcomes, raising them up to 60-70%

LIVE CASE: AF Ablation with a New Generation Mapping System (TactiFlex & Ensite X Version 2 Abbott)

Daniel Steven, MD, University Hospital Cologne, Cologne, Germany

- EnSite X system used with TactiFlex, the newest ablation catheter from Abbott that features a flexible tip (FlexAbility) with contact force data (TactiCath)
- Dr. Steven said that TactiFlex has only been commercially available in Europe for the last 6 months

AFME INSIGHTS

We expect TactiFlex SE to receive U.S. FDA approval during 2023. In June 2021, Dr. Monica Lo posted on Twitter (here) that the last patient had just been enrolled. Therefore, all 12-month follow should be complete, with only regulatory submission and FDA review remaining.

POSTER: Lesion Durability for AF Ablation Using Voltage and LSI: an LSI Workflow Sub-Study

First Author: Dr. Jasen Gilge
Last Author: Dr. Jesus Almendral

- This poster represents a sub-study from the LSI Workflow study sponsored by Abbott, and three co-authors on the poster are Abbott employees
- 25 patients at 9 sites were retrospectively analyzed and all cases were required to have found one gap after PVI
  - In all lesions, LSI targets, contact force, and average RF power were all the same
- In non durable lesions, the pre-ablation bipolar and unipolar voltage were both significantly higher than in durable lesions
- The authors concluded that baseline voltage could be a key input when deciding RF ablation parameters

- **POSTER: Patterns of Anatomical Approaches to PVI in Initial DYNAMIC-AF Cohort**
  First Author: Dr. Jose Osorio
  Last Author: Dr. Emily Wenzel
  - Dr. Wenzel is an employee of Abbott
  - The DYNAMIC-AF study is non-randomized registry sponsored by Abbott to collect real-world data on the treatment of both PAF and PsAF using RF
  - The total targeted enrollment is 6,000 patients and the current trial entry lists four participating sites as of June 2022
    - The full entry on clinicaltrials.gov can be found here
  - TactiCath SE was used in all 88 procedures included in this poster
  - The main goal of this poster was to report on the lesion strategy used most frequently in anterior and posterior locations
    - In anterior locations, contiguous point by point was by far the most popular approach
    - In posterior locations, non-contiguous point by point was the most frequently used strategy due to concerns about impacting the esophagus
  - First pass PVI success was only 75% and overall acute PVI was 97%

ABLACON

Ablacon Website

Summary from AF Symposium

Ablacon's "electrographic flow" (EGF) mapping technology was featured in a late-breaking clinical trial presented by Dr. Vivek Reddy. In the FLOW AF trial with PsAF patients, freedom from AF at 12 months was 70% when ablating additional targets identified by EGF, in addition to PVI. However, freedom from all arrhythmias (AF/AT/AFL) at 12 months was approximately 50%. The number of patients enrolled was small, with only 46 being randomized to PVI-only (N=24) vs. PVI + EGF (N=22).

Details from Congress Events

- **Late Breaking Clinical Trial: FLOW-AF: A Randomized Controlled Trial of Electrographic Flow-Guided Ablation in Redo Patients with Non-Paroxysmal Atrial Fibrillation**
  Vivek Reddy, MD
  - The full entry on clinicaltrials.gov can be found here
  - EGF Mapping = electrographic flow guided mapping
  - Later in the presentation, Dr. Reddy disclosed that signals were recorded with a "commercially available 64-pole catheter, which suffers from spline splaying"
    - During Q&A, Dr. Reddy disclosed that a proprietary catheter has been designed to eliminate splaying of splines
  - One minute recordings are broken into many segments and each segment analyzed
    - If the same source appears in 27% or more of the segments, it is identified as a target for ablation
  - In the FLOW AF trial, four sites in Europe enrolled a total of 85 patients, with 46 being randomized to EGF guided ablation vs. PVI only
    - The patient population included persistent or long-standing persistent AF (less than 36 months)
    - Only 22 patients received additional EGF guided ablation and 24 received PVI only
      - Two patients withdrew consent and were not included in the analysis
    - In the PVI + EGF arm, 19/20 patients had confirmation of source ablation based on EGF mapping
      - 97.2% freedom from serious adverse events
  - In the PVI-only cohort, less than 20% of patients remained free of AF at 1 year
    - In the PVI + EGF cohort, approximately 70% of patients were free of AF, p=0.04
      - In this cohort, freedom from AF/AT/AFL was approximately 50%

AFME INSIGHTS

Freedom from AF in the PVI-only arm was reported to be just 20% at 12 months, far lower than almost all other recent trials.

- The difference in freedom from AF rates between the two cohorts was highlighted on a slide to be 51%, in favor of EGF-guided ablation

- The mean number of additional ablation targets per patient was approximately the same in both cohorts at 1.3
- Dr. Reddy emphasized that this technology does not require ablation of 10+ sources but generally 1-2 additional sources
- A multi-national randomized controlled pivotal trial will be conducted but Dr. Reddy did not provide estimates as to when it would begin

Q&A

- Dr. Reddy – this is different than phase mapping because this looks at flow
- Dr. Hocini asked about area of ablation for each one of the additional sources identified
  - Dr. Reddy – only measured RF time, not area
- Dr. Hocini also asked about the electrograms seen at the source location
  - Dr. Reddy – they were not analyzed but it is a very interesting question
- Dr. Kalman asked whether or not rotors should be seen with this technology
  - Dr. Reddy – if it flows out, then yes, rotors should be seen. If not, then it is a passive rotor and will not be identified as a source
- Dr. Kalman – what is the mechanism?
  - Dr. Reddy – system is agnostic to the source and whether "it" is focal, rotor, etc. As long as activation is going away from "it", then it a potential source

ACUTUS MEDICAL

Acutus Medical Website

Summary from AF Symposium

The Acutus contact force ablation catheter (AcQBlate FORCE) was featured in both a Spotlight Session and a late breaking clinical trial. However, the trial results reported on treatment of flutter patients - the trial for AF has not yet started. The AcQMap system was presented in two posters, with one comparing the Acutus maps directly to those created with HD Grid + EnSite. No updates were provided on progress with the Acutus PFA technology.

Details from Congress Events

SPOTLIGHT SESSION: The AcQBlate FORCE (AlCath Force) Sensing Ablation Catheter (Acutus Medical)

Robert Bernat, MD

BACKGROUND

AcQBlate FORCE is the same catheter as the legacy Biotronik AlCath Force catheter. Acutus Medical and Biotronik entered a strategic alliance in May 2020 that included access for Acutus in the U.S. to Biotronik's portfolio of ablation catheters. (The original press release can be found here) At the time, none of the Biotronik catheters were approved for commercial use in the U.S. and Acutus has sponsored the IDE trials in support of FDA approval.

- This session was mainly an overview of the catheter features
- AcQBlate FORCE is a focal ablation catheter that features a gold tip electrode with a novel irrigation design
  - Contact force is measured by a single optical fiber
- Data from the catheter are fully integrated into the AcQMap non-contact mapping system
- Dr. Bernat concluded his session with a case presentation

Late Breaking Clinical Trial: AcQForce Flutter Trial Clinical Results: Force Sensing RF Ablation with Low Flow Gold Tip Catheter for Typical Flutter

Gery Tomassoni, MD

- The AcQBlate FORCE system uses a single optical fiber to measure force and contains a gold electrode with 12 irrigation ports
  - Flow rate is 8ml/min for 30W or less and 15ml/min over 30W
- Force data from the catheter can be displayed separately but are also fully integrated with the Acutus AcQMap system

AFME INSIGHTS

Inclusion of this dataset in the LBCT sessions was unusual because presentation of results in flutter ablation are not typically considered "late breaking" - flutter is easier to treat compared to AF.

- Effectiveness was measured as freedom from AFL recurrence off AADs at 30 days
  - In 100 patients, 30-day success was 98%

Q&A

- Dr. Reddy commented that flutter trials are usually done for regulatory reasons
- Dr. Calkins asked if there would be an AF trial
  - Dr. Tomassoni said it has not started yet but will begin in the "near future"

POSTER: The Acute Effect of PVI Upon Left Atrial Conduction – Early Experience with AcQMap Composite Mapping

First Author: Dr. Simon James
Last Author: Dr. Justin Lee

- The authors report experience with the AcQMap composite map algorithm, which calculates the conduction speed of every wavefront analyzed
- Operators define a threshold (0.3 m/s used in this study), and the number of wavefronts below this threshold are counted and visualized on the map
- This feature was used to assess the impact of WACA across the LA, and the early results from these 5 retrospective cases indicate there is an impact beyond just vein isolation
  - However, additional studies are required to confirm the finding

POSTER: Comparing the Accuracy of Novel Composite Software Non-Contact Mapping (NCM) Using AcQMap Catheter to the Conventional HD Contact Mapping Using HD Grid

First Author: Dr. Usman Siddiqui
Last Author: Dr. DJ Lakkireddy

- 14 patients undergoing AF ablation procedures were mapped by both the Acutus AcQMap System and the Abbott EnSite system using HD Grid
- A total of 19 maps were created by each system and then qualitatively compared by 2 electrophysiologists for each patient using AP and PA views
  - 95% agreement (18/19) was seen when comparing propagation mapping between the two systems
    - In the one disagreement, an abnormal substrate was displayed on the AcQMap but propagation on HD Grid was normal
- The poster said these data were the first presentation of intra-procedural maps using two different mapping modes, contact and non-contact

Pulsed Field Ablation Systems: Safety, Effectiveness, and Regulatory Status

Moussa Mansour, MD
Dr. Mansour's presentation contained updates on multiple technologies (BSX FaraWave, MDT PulseSelect, MDT Affera, BWI VARIPULSE, Kardium, Galaxy Medical, Adagio Medical, and Acutus Medical). Notes for each technology are included in the respective company sections in this report.

- Acutus Medical
  - Dr. Mansour described the focal, gold-tip catheter but did not say anything about the current status or expected timelines
    - The Acutus catheter is integrated with the Acutus Mapping system

- **POSTER: Novel Open Architecture 3D Mapping System Compatible With Contact Force Catehter**
  First Author: Dr. Moritoshi Funasako
  Last Author: Dr. Vivek Reddy
  This poster is included in the company sections for both CardioNXT and Acutus Medical
  - This poster reports on the successful integration of the AcQBlate FORCE catheter from Acutus with the iMap system from CardioNXT
    - Co-authors on this poster included one Acutus employee and three CardioNXT employees
  - The CardioNXT iMap system accurately rendered the AcQBlate catheter on the map, including the display of real-time contact force information directly from the Qubic Force Sensing Module
    - iMap is an open system and allows for the use of any diagnostic catheters
  - One of the conclusions on this poster highlighted the fact that contact force-guided RF ablation will now be possible without the need for catheters from Abbott or Biosense Webster
    - The Acutus AcQBlate catheter has not yet been approved by the U.S. FDA

ADAGIO MEDICAL

Adagio Medical Website

Summary from AF Symposium

Adagio Medical sponsored a lunchtime product theater with a total of seven presentations, most of which focused on the PFCA technology that uses both PFA and cryo. In addition to the product theater, PFCA was presented several times during the main sessions. Collectively, there were many discussions, as shown in the PodiumShare results, but no new trial data were presented.

Details from Congress Events

- **Future Directions in Pulsed Field Ablation**
  Vivek Reddy, MD
  Dr. Reddy's presentation contained updates on multiple technologies (ABT PFA, Field Medical, Adagio Medical, and Pulse Biosciences). Notes for each technology are included in the respective company sections in this report.
  - The agenda for Dr. Reddy's presentation included the following topics:
    - PFA + EAM
    - "Field Bending"
    - PFCA
    - Nanosecond PFA
    - LAAC + LAAEI
  - Adagio Medical
    - PFCA was on his agenda but he decided to skip through it since the technology had been presented already by Dr. Verma

- **ADAGIO PRODUCT THEATER**
  - Adagio Medical hosted a product theater on Thursday during lunch, from 12:30 – 1:30
  - A total of seven presentations were given during this event, with four presentations focusing on case reviews

- **Ultra-Low Temperature Cryoablation: The Perfect Launchpad for PFA**
  Dr. Lucas Boersma
  - Dr. Boersma provided a comprehensive overview of the Adagio ultra-low temperature cryo (ULTC) system for AF
    - For ULTC procedures, an esophageal warming balloon is used to prevent injury
  - Dr. Boersma reviewed the recent publication by De Potter et al on the Cryocure 2 Study
    - A link to the full publication can be found here
    - A total of 65 patients were treated, with 44 PsAF patients
  - At 12 month follow up, freedom from AF was 82.6% in the full study and 85.9% in the PsAF cohort

- Three patients had PNP that all resolved over time and no other SAEs were reported
- The U.S. IDE trial is ongoing but Dr. Boersma did not provide any further information

AFME INSIGHTS

The Cryocure 2 study actually resulted in better results for PsAF patients vs. the PAF cohort, which is uncommon in AF ablation trials.

Fundamentals of PFCA and PARALLEL Study Design

Dr. Atul Verma

- The Adagio PFCA system ("Cryopulse") utilizes two energy sources – ultra low cryo and PFA
- Cooled tissue could increase field strength of PFA, perhaps up to 3x the strength
  - Lesion depth can increase from 3-4mm to over 6mm
- A sub-therapeutic freeze is administered, followed by PFA through the same catheter
  - Currently, the cycle starts with a 30 second freeze, but Dr. Verma believes this could be shorter
- The freezing enables continuous tissue contact and allows for fewer pulses due to current amplification
  - Another benefit is reduced muscle contractions and fewer microbubbles
    - Could potentially less coronary spasm as well but this benefit is TBD
- Dr. Verma described the "optimized PFCA" waveform and said it could achieve lesion depths of 10mm+
- PARALLEL Trial = pulsed field ablation and pulsed field cryoabation for persistent AF
  - Adagio announced first patient was treated in October 2022 (press release here), and the full entry on clinicaltrials.gov can be found here
  - According to the trial entry, two sites are actively enrolling patients: McGill University in Montreal (Dr. Verma is PI) and St. Antonius in the Netherlands (Dr. Boersma is PI)

ULTC and PFCA to Treat Ventricular Tachycardia

Dr. Edward Gerstenfeld

- The Adagio catheter for VT has a linear 15mm, 8 electrode ablation element, and it is compatible with a 10Fr sheath
- Dr. Gerstenfeld presented results from the FIM study with Adagio's VT catheter
  - The paper is currently in press at JACC EP and this version can be viewed here
  - 13 patients were enrolled and the average number of lesions per patient was 9.6
  - On a per patient basis, 91% achieved acute non-inducibility post ablation
    - 95% of the clinical VTs identified were successfully ablated across all patients
- Adagio has also modified the VT catheter to deliver PFCA in the ventricle
  - The VT PFCA catheter has a linear 15mm, 6 electrode ablation element (the VT ULTC has 8 electrodes)
  - For each application, a freeze of 30 – 120 seconds is delivered first, followed by a PFA train up to 4000V

- Pre clinical studies have shown a maximum lesion depth in healthy tissue of 22mm
  - In scar tissue, maximum depth was 17mm
- Dr. Gerstenfeld reviewed the work done at his lab investigating the impact of PFA on coronary spasm
  - Animal studies were done with the Adagio VT PFCA catheter on the CTI line
  - Using a field strength that is ~2x the current PFA systems, no spasm occurred with PFCA
    - Dr. Gerstenfeld qualified his remarks by saying there was no spasm "at least to the same degree"
    - Long term data are needed but this approach may mitigate spasm

Clinical Experience with PFCA

Panel review that included case presentations by Dr. Reddy, Dr. Gallagher, Dr. Kowalski, and Dr. Boersma

- Dr. Reddy
  - CARTO used in his case
    - He switched out stylets during the case with PFCA – it is possible to use a different shape of the same catheter in the same case, all while still using PFCA
    - ICE was used to assess bubbles, which were seen "only occasionally", in roughly 20% of the applications
      - The majority of the time, there were no bubbles, which is better than other systems
    - It is still an open question if bubbles matter
- Dr. Gallagher
  - He has only done one case with PFCA but he has done over 20 cases with iCLAS (ULTC catheter)
  - The Adagio PFCA catheter "handles like nMarq"
  - The case being reviewed was completed last week
  - When using PFCA catheter for PWI, his goal is to create "Olympic rings" – a series of circular lesions that will successfully isolate the posterior wall
    - The ablations themselves are faster with PFCA vs. cryo
    - He also believes the initial freeze period with PFCA could be shorter than 30 seconds
- Dr. Kowalski
  - He believes the PFCA catheter is "significantly easier" to maneuver vs. iCLAS
  - 17 total applications of PFCA were performed in his case but the total LA dwell time was just 45 minutes
  - In addition, this was his very first case, which made the dwell time even more impressive to him
    - In the RA, it is possible to do cryomapping first with this catheter
- Dr. Boersma
  - He presented the first case enrolled in the PARALLEL Trial
  - A 25mm stylet was used
  - Early in the case, Philips EPD mapping system was used but only fluoro was used for guidance during the case

---------- *End of Adagio Product Theater notes* ----------

Combined Pulsed Field and Thermal (RF or Cryo) Ablation: Safety and Efficacy

Atul Verma, MD

Dr. Verma's presentation contained updates on multiple technologies (Adagio Medical, BWI PFA). Notes for each technology are included in the respective company sections in this report.

- The concern being addressed with dual-energy approaches is lesion depth because PFA alone cannot always achieve the required depth
  - Repetitive applications of PFA with the Sphere9 have been shown to increase depth, as published by Kawamura et al in Circ AE 2022, but not much beyond 5-6mm
- Goal of dual energy approaches (PFCA, PF/RF) is to increase lesion depth without sacrificing any safety benefits of PFA
- Adagio Medical PFCA
  - Deliver sub therapeutic cryo energy, followed by PF
  - Frozen tissue has higher impedance and ice can be insulating - increases the field for the same magnitude of current
    - Can potentially deliver more energy and achieve greater lesion depth
      - Pre clinical work has shown depths of 10-11mm with PFCA
      - Dr. Verma published this work in JCE and the full article can be found here
    - Ice also mostly eliminates microbubbles

Pulsed Field Ablation Systems: Safety, Effectiveness, and Regulatory Status

Moussa Mansour, MD

Dr. Mansour's presentation contained updates on multiple technologies (BSX FaraWave, MDT PulseSelect, MDT Affera, BWI VARIPULSE, Kardium, Galaxy Medical, Adagio Medical, and Acutus Medical). Notes for each technology are included in the respective company sections in this report.

- Adagio Medical
  - PFCA system with dual PF and cryo energy
  - U.S. IDE trial, PARALLEL, in PsAF just began enrollment

ADAS 3D MEDICAL SL

ADAS 3D Medical Website

Summary from AF Symposium

ADAS was featured in just one podium presentation during the Spotlight Sessions, but the topic of pre-procedural imaging was mentioned frequently at the podium.

Details from Congress Events

- **SPOTLIGHT SESSION: Personalizing AF Ablation Based on CT: Isodistances and Wall Thickness (ADAS 3D Medical SL)**
  Diego Penela, MD
  - Left atrial wall thickness (LAWT) is heterogeneous with a range from <1mm to 5mm
  - LAWT is accurately measured by CT and ADAS 3D software provides segmentations that show wall thickness throughout the LA
    - Resulting ADAS maps are color coded by LAWT to easily visualize thickness by location
    - Color-coded shells are then imported to 3D EAM systems
  - "Isodistance Maps" = new feature on the ADAS platform that measures and projects distances from the LA endocardial surface to extracardiac structures
    - Similar to the LAWT measurements, these distances are color coded and projected onto the ADAS 3D map
    - Example maps were presented with distances projected to the esophagus, SVC, and aortic root
    - This technology was featured in a 2022 publication by Teres et al in the Journal of Interventional Cardiac Electrophysiology
      - Link to publication is here, separate subscription required
    - Isodistance maps can be helpful in planning the ablation strategy and potentially modifying ablation index targets based on measured distances to extracardiac structures, i.e. esophagus
  - ADAS has implemented a machine-learning based automatic segmentation technology to enable faster creation of the LAWT 3D maps
  - "Ablate by LAW" trials used ADAS 3D technology to create 3D maps of the LAWT, which were then integrated in EAM systems. LAWT was then used to determine AI targets for ablation
    - The single center study has been published (link here)
      - 90pts with PAF treated using this strategy
      - Procedure times were 59mins and freedom from recurrence at 25 months was 93%
    - The multi center study was presented briefly
      - Early results were presented on cases in 105 PAF patients at sites across the U.S. (2) and Europe (5)
      - At approximately 7 months follow up, 90% of patients were free of recurrences with no major complications reported

AFME INSIGHTS

During a Q&A session later in the symposium, Dr. David Keane asked the audience to raise their hands if they routinely performed pre-procedural imaging. Approximately half of the audience raised their hands. Although Dr. Keane did not ask specifically about the ADAS system, the response indicated how often pre-procedural imaging is currently being utilized.

ANUMANA-NEUTRACE

Anumana Website

Summary from AF Symposium

The Anumana technology was presented at the podium for the first time during AF Symposium, and the company appears to have developed a novel mapping system. However, Dr. Shivkumar did not provide full details on the system during the Spotlight Session. According to a recent press release, Anumana has acquired NeuTrace, a company featured last year at a Spotlight Session during AFS.

Details from Congress Events

- **SPOTLIGHT SESSION: Artificial Intelligence Enabled Platforms in Cardiovascular Medicine (Anumana-NeuTrace)**
  Kalyanam Shivkumar, MD, PhD
  - Anumana is a portfolio company of nference
  - In November 2022, Anumana acquired NeuTrace, a company featured during the Spotlight Sessions at the 2022 AF Symposium and presented by Dr. Andrea Natale
    - Press release announcing the transaction can be found here
    - A July 2021 press release (here) describes the NeuTrace technology
  - EAGLE study was referenced by Dr. Shivkumar
    - The EAGLE study showed that an AI screening tool demonstrated an ability to predict ejection fraction with "extreme accuracy" based only on the ECG
    - Abstract for EAGLE can be found here
  - Dr. Shivkumar presented a slide that compared "legacy mapping system" vs. "Anumana EAM" in an animal study
    - Based on the slides and Dr. Shivkumar's commentary, it appears the Anumana EAM is a novel mapping system
  - Trials are ongoing to answer several outstanding questions in the treatment of PsAF
  - Details for the trials were not provided and only one trial was found in clinicaltrials.gov for Anumana, Inc. (link to the full entry is here)

ARGA MEDTECH

Arga Medtech Website

Summary from AF Symposium

Clinical data from FIM experience with the Arga PFA system were presented for the first time during AFS. In addition, details on the company's catheter were also provided publicly for the first time. Arga has developed a "multi-configurable catheter" that is capable of taking multiple shapes to complete multiple lesion sets, beyond just PVI. The system delivers a proprietary type of PFA called "coherent sine burst" (CSE). Early acute data with the first uses of the system showed durable PVI of 84% (16/19 veins).

Details from Congress Events

AFME INSIGHTS

The technology in this poster has been developed by Arga Medtech. Co-authors on this poster include both the CEO (David Neale) and the CTO (Randy Werneth).

- **POSTER: PFA Using a Novel Multi Configurable Catheter with Coherent Sine Burst Electroporation: Case Study and Acute Clinical Outcomes for Treatment of PsAF with Long Linear Lesions**
  First Author: Dr. Ante Anic
  Last Author: Dr. Giorgi Papiashvili
  - Coherent Sine Electroporation = "CSE"
  - Advantages of CSE-PFE include the elimination of microbubbles and potentially less skeletal muscle contraction
  - Data were presented from the BURST-AF trial, a FIM pilot study (full entry on clinicaltrials.gov is here)
    - Only one site is listed on the entry (Israeli-Geogrian Medical Research Clinic Helthycore Ltd, Tbilisi, Georgia), but the poster referenced two sites: Site A and Site B
    - No details on the sites were included in the poster but Dr. Anic's site in Split, Croatia is the only other non-U.S. site among the listed authors
  - A total of 12 PsAF patients were treated across the two sites
  - An image of the actual catheter was not included in this poster, but artist renderings and fluoro images from cases showed a total of 8 electrodes
    - The catheter was shaped into a circle for PVI and then straightened out for linear PFA
  - A data table showed ablation results across four different targets (PVI, PWI Superior Line, PWI Inferior Line, and CTI Bidirectional Block) using three different configurations (2 electrodes, 4 electrodes, or 8 electrodes)
    - Acute results from both sites showed 100% first pass PVI (45/45)
    - Acute PWI was also achieved in 4/4 patients
    - First pass acute CTI block achieved in 7/7 patients
  - Remapping data from Site A only were presented and showed durable PVI of only 84% (16/19 veins)
  - CTI remained durable in one patient and superior line PWI remained durable in two linear lesions

AFME INSIGHTS

Dr. Lorenzo first presented the CSE technology from Arga at HRS 2022, and the poster at 2023 AF Symposium is believed to be the first data presentation from clinical use.

ATRIAN MEDICAL

AtriAN Medical Website

Summary from AF Symposium

AtriAN was featured in a Spotlight Session presented by Dr. Vivek Reddy, who presented both an overview of the technology and an update on clinical progress. Currently, AtriAN requires a surgical approach to ablate GPs on the epicardial surface using PFA. Studies to date have included patients undergoing concomitant CABG procedures, and 12-month follow up is ongoing for the first series of 12 patients treated with the technology. Dr. Reddy said next steps include transition to a sub-xiphoid approach to access the epicardial surface.

Details from Congress Events

- **SPOTLIGHT SESSION: Epicardial Ablation of Ganglionated Plexi for the Treatment of Atrial Fibrillation (AtriAN Medical)**
  Vivek Reddy, MD
  - Endocardial PFA has a limited impact on ganglionated plexi (GP)
    - Therefore, AtriAN is developing an epicardial PFA approach
      - This epicardial approach results in closer proximity to the GPs
  - Dr. Reddy said on his slides that "GP neurons are slightly more susceptible to electroporation than myocytes"
  - First generation AtriAN technology uses a surgical approach on the epicardial surface
  - The two catheters presented were the "Glove", a multi-spline catheter in the shape of a grid, and the "Finger", a focal tip catheter with four electrodes pictured
    - Pulses are delivered with EKG gating and saline infusion
    - Currently, the waveform is monopolar at 1000V with a 100 microsecond pulse width
    - One energy pulse is delivered per heartbeat and a total of 60 pulses are delivered per GP
  - Pre clinical data were published in 2022
    - Link to the publication is here
  - The "Nueral AF" study assessed safety and feasibility in 24 patients across two sites (Tbilisi, Georgia and Prague, Czech Republic)
    - Link to the full trial entry on clinicaltrials.gov is here
    - Only 3 of 24 patients actually had AF
  - "Neural AF 2" trial assessed epicardial GP ablation in patients with AF undergoing CABG
    - Link to the full trial entry on clinicaltrials.gov is here
    - Enrollment of 12 patients has been completed at one site in Tbilisi, Georgia and 12-month follow up is ongoing
  - Next steps for the AtriAN technology:
    - Convert from monopolar to bipolar delivery
    - Transition to sub-xiphoid percutaneous approach

- Studies in the planning phase include GP ablation for surgical patients with AF and reduction of post-operative AF
    - The last study on Dr. Reddy's slide ended with a question mark but identified the possibility of investigating AtriAN technology as an adjunctive procedure to percutaneous PVI

Neuromodulation/Vagal Denervation with PFA: Techniques and Impact on Outcome of AF Ablation

Pierre Jais, MD

- Dr. Jais cited the same paper that Dr. Reddy cited during his "Spotlight Session" presentation on AtriAN Medical
    - AtriAN is developing PF technology to specifically ablate the GPs
- Dr. Jais said he would like to see a large study focusing only on GPs – this type of study would answer the question regarding the role of GPs in AF ablation
- During Q&A, Dr. Verma asked Dr. Natale which type of catheter he will use?
    - Dr. Natale – likes larger footprint focal because lesions are deeper but he is not sure what he will use yet
    - Workflow with single shot is appealing
- Dr. Schmidt asked Dr. Jais if he has any data or concerns regarding the aorta?
    - Dr. Jais – no data yet on aortic aneurysm
    - He does not do large PFA on the anterior side and will not until he does have data on aorta

BIOSENSE WEBSTER

Biosense Webster U.S. Website

Summary from AF Symposium

BWI had a strong presence at AFS, as seen by the company reaching the top of our PodiumShare analysis. Technologies from BWI were featured in 2 late-breaking clinical trials and 4 live/recorded cases. Data on the VARIPULSE PFA system were presented for the first time and showed 12-month freedom from atrial arrhythmias of 70.9% in the pivotal phase of the trial (Wave 2). Clinical success, defined as freedom from symptomatic arrhythmias, was 78.9% in Wave 2. Early work with a combined PF/RF approach using STSF to deliver both energies was also presented. Beyond PFA, data from the global IDE with BWI's HELIOSTAR RF balloon were presented. Results showed efficacy of just 67.7%, below what is currently seen with other technologies. In addition, one death and two permanent PNPs were reported in this trial. Finally, the QDOT Micro focal RF catheter was featured in a live case using vHPSD (90W for 4 seconds).

Details from Congress Events

Organized by Product

VARIPULSE

- **Late Breaking Clinical Trial: Paroxysmal AF Ablation Using a Variable-Loop Pulsed Field Ablation Catheter Integrated with a 3D Mapping System: One-Year Outcomes from inspIRE**
  Vivek Reddy, MD
  - Results from this study were simultaneously published online and can be found here
  - The Biosense Webster VARIPULSE PFA catheter was the subject of this study
    - Dr. Reddy referred to the VARIPULSE catheter as a "variable loop circular catheter (VLCC)"
    - The catheter is also irrigated
  - The PFA system includes a multi channel generator and full integration with CARTO
  - Two patient cohorts were presented: Wave 1 feasibility phase (N=40) and Wave 2 pivotal phase (N=186)
    - 13 centers participated across Europe and Canada
  - The trial was stopped early after 83 patients reached 12 month follow-up
  - The PVI workflow includes three applications per location and four locations per vein, for a total of 12 applications per PV, at a minimum
  - Procedure times for Wave 2 were 70 minutes with 44.7 minutes of LA dwell time
    - GA was used in 132 cases (71.0%)
  - Acute PVI was achieved in 97.1% of targeted veins in Wave 2
    - During Q&A, Dr. Reddy said that this result was "disappointing", although it is still just a few percentage point below 100%
  - Zero safety events were reported in either Wave
    - Also saw zero PV stenosis of any kind

- Brain MRIs were done on 39 patients in Wave 1
  - Of the first six patients scanned, four showed silent cerebral lesions (66%)
    - After this result, a 10 second pause between PFA applications was implemented
    - Of the next 33 patients, 4 showed SCLs (12%)
- Freedom from documented atrial arrhythmias at 12 months was 70.9% in Wave 2
  - "Clinical success", defined as freedom from symptomatic AF/AT/AFL recurrence, was 78.9% in Wave 2
- The U.S. IDE trial (the "admIRE" study) has completed enrollment with 362 patients treated

Q&A

- Not many questions were asked following this presentation
- Dr. Reddy mentioned that the system does have a tissue proximity indicator based on impedance
- Dr. Deisenhofer - Is irrigation important?
  - Dr. Reddy – not sure. There is some heat generated, so maybe there is some benefit to irrigation

❖ Pre-Recorded Case: Pulsed Field Ablation for AF Using a Circular Multielectrode Catheter (VARIPULSE Biosense Webster)

Charles Athill, MD, Sharp Memorial Hospital, San Diego, CA

- This case was part of the admIRE study that investigated the VARIPULSE catheter and the TRUPULSE generator
- admIRE has two sequential phases: pilot phase with 20 patients to assess acute safety data and then a pivotal phase with up to 408 patients investigating safety and effectiveness
  - A total of 35 centers have been involved
  - November 16, 2022 = last patient enrolled in the pivotal phase
- Dr. Athill used ICE in his cases
- Waveform is bipolar, biphasic and delivers 1800V
- VARIPULSE catheter is a bidirectional variable loop catheter with 10 electrodes and 4mm spacing
  - Diameter is adjustable from 25mm to 35mm
  - Catheter is also irrigated
  - It is fully integrated with CARTO mapping system
- A total of four locations are targeted per vein: 2 ostial and 2 antral
  - 3 pulses are delivered per location
- Individual electrodes can be turned on and off
- Dr. Reddy said that the ring is asymmetrical and more difficult to maneuver
  - However, it does include a "very robust" mapping system
  - Dr. Athill also said the catheter was "not the most maneuverable"
- Dr. Athill does not show lesion tags for each electrode at each application – "they are annoying"
  - The VisiTags do not add value to VARIPULSE cases
- Dr. Jais commented that there are no signals after the very first delivery – this is an important point

- With PFA, there is a "massive stunning effect", which means operators have to work differently than with RF

- During ablation in the LSPV, he turned off 4 electrodes
- Dr. Reddy explained that flashing electrodes on the CARTO system are actually tissue proximity indicators, based on impedance
- Dr. Nair said that a steerable sheath is definitely needed because of catheter stiffness
  - Dr. Nair also asked about arcing with Agilis if the electrodes are too close
    - Dr. Athill said he used Agilis in this case
    - Dr. Athill said energy delivery is not allowed if active electrodes are still in the sheath
      - He also said the software is not fully updated to where you can see them inside a sheath – now they just turn black
- Dr. Reddy shared his experience with the BWI Vizigo sheath and said there are measures in place to prevent energy delivery when electrodes from the sheath are too close to VARIPULSE
- Unlike with Farawave, Dr. Athill tends not to get too far out into the antrum with VARIPULSE
- The first procedure Dr. Athill performed lasted 100 minutes and now they average about 90 minutes
  - The recorded case presented at the Symposium lasted 81 minutes, with 2 minutes of fluoro
    - LA PFA time totaled 25 minutes with PFA application time of 6 minutes

❖ **Pre Recorded Case: Pulsed Field Ablation for AF Using a Circular Multielectrode Catheter (VARIPULSE Biosense Webster)**
Moussa Mansour, MD, Massachusetts General Hospital, Boston, MA

- The VARIPULSE catheter from BWI is based on the platform from the original nMARQ catheter designed for circular RF ablation
  - Dr. Mansour commented later that the nMARQ catheter did not work with RF but works well with PFA
- VARIPULSE – 8Fr shaft (compatible with Agilis and ViziGo); biphasic, bipolar waveform
- Per protocol, three ablation sequences per position are delivered over 10 seconds
  - Then, rotate catheter and deliver in next position
- Even though electrograms disappear, further ablation is still required to ensure durable lesions are created
- Ablation "tags" are placed on CARTO map in the location of each electrode for each delivery
  - The tags are smaller than traditional tags and appear as dots on the map
  - With 10 electrodes on the catheter and multiple applications per vein, the CARTO map is quickly filled with dots
    - Please see Dr. Athill's commentary above from the case he presented
  - Dr. Mansour said this is "probably a preliminary version of the software" and that over time, the system will probably have a better way of displaying ablation tags
- Dr. Reddy – need to pause between energy deliveries so heat does not accumulate
  - Heat is created. It is a small amount but a pause is need so the heat does not accumulate
- Dr. Jais – this catheter is not an easy one to manipulate but he still uses it

- It is a fantastic demonstration of safety that you can use now for PF because RF energy did not work
- As highlighted in the previous case with VARIPULSE, it is possible to only ablate from selected electrodes on the catheter – can use it to partially ablate in the antrum

- Question from the floor – since the waveform is biphasic, bipolar does algorithm change when different electrodes are selected. Dr. Mansour – yes.

Pulsed Field Ablation Systems: Safety, Effectiveness, and Regulatory Status

Moussa Mansour, MD

Dr. Mansour's presentation contained updates on multiple technologies (BSX FaraWave, MDT PulseSelect, MDT Affera, BWI VARIPULSE, Kardium, Galaxy Medical, Adagio Medical, and Acutus Medical). Notes for each technology are included in the respective company sections in this report.

- Biosense Webster – VARIPULSE
  - Two cases presented during AF Symposium
  - U.S. IDE in PAF, the admIRE study, has completed enrollment
    - Dr. Mansour commented that it was one of the fastest trials to complete enrollment
      - See write up below from Dr. Reddy regarding results with BWI VARIPULSE presented during the LBCT sessions
- Q&A, Panel and Audience Discussion
- The panel discussion included Ksenia Blinova, PhD, Deputy Director, Division of Biomedical Physics, Office of Science and Engineering Laboratories, CDRH, US FDA
  - Dr. Blinova presented at AHA on work their team is doing on PFA at the FDA
- Dr. Hindricks to Dr. Blinova – there will be a flood of new PFA technology in the next few years. What are your expectations in FDA?
  - Dr. Blinova – currently there is not much evidence on tissue specificity and the cell death mechanism is unknown
  - Outstanding questions remain: Is synchronization needed? Are microbubbles concerning?
- Dr. Hindricks – How will you approach dual energy devices?
  - Dr. Blinova – FDA will need clear instructions on when to use each
- Question to the panel – is contact force needed or just contact?
  - Dr. Koruth – contact force measurement depends on tip geometry
    - Data on coupling is needed but force is not
  - Dr. Nakagawa – it is better to have contact force than not have it
    - Dr. Jais responded to this statement by saying it applies only to focal catheters
- Question to panel – do all systems have the same tissue specificity?
  - Dr. Haines – the mechanism of injury is the same across technologies but algorithms differ across systems
    - "Once you've tried one PFA system, you've tried one PFA system"
  - Dr. Reddy – workflow is probably the least important because all systems will be fast
    - Need to see the durability data in order to believe in a particular PFA system

- In terms of safety, Dr. Reddy believes PV stenosis will not be an issue but he is still wondering how PFA impacts it
  - Phrenic nerve can be damaged but very little damage is likely
  - Coronary spasm – all systems likely to have this but the extent could be different

POSTER: Assessment of Optimal Dose Response Using a Circular PFA Catheter

First Author: Dr. Jonathan Hsu
Last Author: Dr. Shephal Doshi

- Four Biosense Webster employees are listed as co-authors on this poster
- The BWI IRE ablation system includes a catheter (VARIPULSE), generator (TRUPULSE), and is fully integrated with the CARTO mapping system
- The study reports on animal studies to determine optimal PFA dosing as compared to RF
- Three groups received different PFA doses: low dose = 1 application, nominal dose = 3 applications, high dose = 6 applications
- Across 12 porcine subjects, acute PVI was successful in 100% of cases with both energy sources
  - Chronic PVI at 28 days was 100% in the PFA group and 83% with RF
- For additional lesion sets that included PW, MI, and LAA, the "low" PFA group did not show 100% durability
  - Both the "nominal" and the "high" PFA groups showed 100% durability across all lesion sets
- PFA was applied directly to the phrenic nerve in all cases but no loss of function was seen as shown by pacing capture after PFA application

Dual Energy RF/PF

Combined Pulsed Field and Thermal (RF or Cryo) Ablation: Safety and Efficacy

Atul Verma, MD
Dr. Verma's presentation contained updates on multiple technologies (Adagio Medical, BWI PFA). Notes for each technology are included in the respective company sections in this report.

- RF followed by PF
  - If tissue is pre-treated with RF, the impedance is actually decreased
    - Question is then whether or not PF can go through the RF tissue and penetrate greater depth
  - Preclinical work with a BWI STSF catheter and PF was presented
    - HPSD RF ablation was performed (50W for 10 seconds)
    - Immediately after RF stopped, PFA applied – 12 pulses, biphasic, monopolar waveform
      - Total lesion depth approached 6mm
- PF followed by RF
  - Reversed the previous workflow
  - Pre treatment with PF prior to HPSD results in deeper RF lesion, up to 6mm also

- HPSD usually results in shallow, "cup shaped" lesions, but pre-treating the tissue with PF creates deeper RF lesion with same RF application
- In a summary table, Dr. Verma showed that lesions from PFA alone were much smaller than lesions created with either PF-RF or RF-PF
  - The table did not include exact numbers, but the PFA lesion depth appeared to be just over 3mm vs. a depth approaching 6mm for PF-RF and just over 5mm for RF-PF
- Dr. Verma emphasized that work with both PF/RF algorithms is still early

Clinical Outcomes with Focal Pulsed Field Ablation Systems

Andrea Natale, MD

Dr. Natale's presentation contained updates on multiple technologies (BWI, Galaxy Medical, and MDT Affera). Notes for each technology are included in the respective company sections in this report.

- Biosense Webster
  - BWI animal data were presented investigating the impact of contact force on PFA lesions when using the STSF catheter and a unipolar waveform
    - The data showed that lesion volume increases with higher contact force
  - Dr. Natale indicated that a version of STSF was being developed that could deliver both RF and PF energy

HELIOSTAR

Late Breaking Clinical Trial: Pulmonary Vein Isolation of Paroxysmal Atrial Fibrillation with Multielectrode Radiofrequency Balloon Catheter: Results From the Global, Multicenter, STELLAR Study

Moussa Mansour, MD

- The Biosense Webstar HELIOSTAR RF balloon catheter was the subject of this study
  - The full entry on clinicaltrials.gov can be found here
- STELLAR is a global IDE study conducted at 36 sites in the U.S., Italy, and China
- A total of 257 patients met eligibility criteria and had the catheter inserted
  - However, Dr. Mansour slide indicated that only 238 patients were treated without "major protocol deviation"
- Total procedure time was 116 minutes with 60 minutes of balloon dwell time
  - RF application time was 8.3 minutes
- Acute PVI was achieved in 100% of patients but a focal catheter was required for touch up ablations in 5.9% of cases
- Freedom from documented recurrence of AF/AFL/AT at 12 months was 67.7%
  - "Clinical success" was defined as time to symptomatic arrhythmia recurrence and this rate was 77.7%
- Freedom from repeat ablation procedures at 12 months was 92.2%
- Safety events included one patient death and two permanent phrenic nerve paralyses
  - The death was due to an atrial bronchial fistula and Dr. Mansour disclosed later that it occurred in a site outside the U.S. An autopsy was not performed.

Q&A

- Dr. Calkins – any more information on the death or permanent PNP?
  - Dr. Mansour – He attributed it to "bad luck" because fistulas are usually atrial-esophageal
    - It is very rare to get an atrial bronchial fistula. This catheter is very powerful and operators must be very careful with positioning
  - Dr. Mansour – The PNP rate is within range of balloon catheters
- Dr. Mansour said that more than 2,000 cases have been completed in Europe to date
- Dr. Reddy on the fistula – there are 1 or 2 reports of bronchial fistula with cryo. With RF, do not need full occlusion – just need to get contact. If operators position without pushing, then atrial bronchial fistula concern will be mitigated
- A physician from the floor was involved in the recent publication of data with HELIOSTAR in a single center study that treated 104 patients
  - The full publication can be found here
  - He said that the manufacturer changed the architecture of the balloon and created a "gen 2" device – he did not know which version was used in this study but thought it was the first one
    - If so, then outcomes could have been impacted

❖ LIVE CASE: AF Ablation Using a Radiofrequency Balloon Catheter (HELIOSTAR Biosense Webster)

Jean Baptiste Chierchia, MD, Heart Rhythm Management Center, Brussels, Belgium

- HELIOSTAR is a 28mm balloon that delivers RF energy
- Must pace phrenic nerve when ablating on the right side because this is a balloon approach
- 10 electrodes are controlled independently
  - Posterior electrodes on every ablation cut off at 15 seconds for safety
  - Anterior electrodes are limited to 45 seconds of ablation time
  - Balloon inflation is measured on a scale from 0 to 1
    - Inflate to 0.7 in order to occlude vein
- On RIPV, pacing was done from the balloon to assess PN capture
  - Dr. Chierchia said that cryo energy is more forgiving
- Dr. Jais has no experience with HELIOSTAR and asked how it compares to cryo?
  - Fast ablation, compliant balloon
- Since it is RF energy, operators need to be more careful with phrenic nerve because RF is less forgiving than cryo
  - With prior cryo experience, this balloon is "easier"
    - Dr. Jais commented that it looks easier and faster
- Dr. Mansour commented that pacing from the balloon itself is a very important feature – it is possible to pace from anterior electrodes in the RSPV
- Case was completed prior to the end of the transmission and Dr. Mansour said they should have given them two cases

Radiofrequency Balloons for AF Ablation

Part of the sessions sponsored by Biosense Webster
Tillman Dahme, MD

- HELIOSTAR RF balloon features 10 irrigated electrodes that are all controlled independently
  - It is fully integrated with CARTO mapping system
- HELIOSTAR enables tailored energy delivery for circumferential or segmental ablation
- Dr. Dahme said the procedure is "mainly fluoroscopy guided"
- Dr. Dahme presented data from his experience using HELIOSTAR in the first 130 patients:
  - 80.2% single shot isolation
  - 10 seconds median time to isolation
  - Freedom from AT/AF recurrence at 12 months was 91% with 90-day blanking period
    - Without blanking period, success was 74.5%
- 1 transient phenic nerve palsy was reported in 130 patients, and this one case resolved within 48 hours
  - Dr. Dahme said that balloon pacing was "forgotten" in this case
- Despite this one case, he did comment that a big advantage of this technology is the ability to pace from all ten electrodes
  - This feature is especially valuable in the RSPV when operators want to pace for phrenic nerve capture
- A dedicated slide was presented on thermal esophageal lesions
  - Esophageal temperature probes were used in all cases, and a temperature above 42°C was seen in 23.8% of cases (31/130)
  - In his conclusion, Dr. Dahme said that he felt esophageal temperature monitoring was "mandatory" in HELIOSTAR cases
  - Esophageal lesions (EDEL) were found in 4.6% of patients (N=6 patients)
    - All lesions healed spontaneously without any AEF
- This balloon is "probably" going in the direction of delivering PF or even dual energy, RF + PF
- During Q&A, Dr. Hocini asked Dr. Dahme if there are data on asymptomatic cerebral emboli with HELIOSTAR
  - Dr. Dahme – Data were not collected on this topic

QDOT Micro

RF Ablation Lesion Assessment with Conventional vs Temperature Controlled Catheters: Update on Ultra High Power Very Short Duration RF Ablation

Part of the sessions sponsored by Biosense Webster
Jose Osorio, MD

- BWI QDOT Micro catheter has been approved by FDA but is NOT commercially available yet
  - Dr. Osorio said it would be available in Europe and the U.S. "hopefully soon"
- Data from the "Q-FFICIENCY Trial was presented

  - The publication is currently in press and can be found here
  - 166 patients were enrolled at 22 U.S. centers
- PVI with vHPSD was performed on all patients but conventional temperature controlled ablation was also allowed for touch up lesions
  - Freedom from all atrial tachycardias at 12 months was 76.7% and "clinical success" was 86.0%
- Is it possible to use index guided ablation with HPSD and vHPSD? (vHPSD = 90W for 4 seconds)
  - Unpublished data from Dr. Nakagawa showed prediction accuracy of 1mm for his ablation index using conventional power with QDOT
  - Data were presented that showed less lesion variability using vHPSD, which leads to the question of whether or not an index is even needed
- An increase in contact force DOES result in different lesion sizes, even in the 4 second application used for vHPSD
  - Publication from Lozano-Granero showed results to support this claim and the abstract can be found here
  - Unpublished data from Dr. Nakagawa and BWI showed significant lesion variability during vHPSD as contact force increased from 10g to 20g to 40g
- During his conclusion, Dr. Osorio said the ablation index for vHPSD is not available yet but it would be a valuable tool
- Inter-lesion distance is also important for vHPSD
  - With only 4 seconds of RF application, it does not last the full respiration cycle
- A new algorithm has been created by BWI to decompose the catheter motion relative to the respiration cycle
  - Dr. Osorio's slide called this the "stability algorithm" and it is used for auto-tagging during vHPSD
  - If stability is lost, even for one or two seconds, it can have a large impact on the lesion during vHPSD
  - This algorithm automatically tags each lesion based on stability criteria filters
    - If all filters are fulfilled for the entire application, the lesion tag is a solid red color
    - If stability is lost, the tag becomes a pink circle with a red line around it
      - This allows the operator to quickly see when a specific lesion did not meet stability criteria

LIVE CASE: Ultra-High Power Short Duration AF Ablation (QDOT & OctaRay Biosense Webster)

Srinivas Dukkipati, MD, Mount Sinai Medical Center, New York, NY

- BWI QDOT Micro catheter features 3 microelectrodes at the tip, 6 total thermocouples (3 distal, 3 proximal) and 66 irrigation ports
- Temperature controlled ablation is delivered in two modalities:
  - QMODE+ = 90W for 4 seconds at 8ml/min irrigation and target temperature of 60°C
  - QMODE:
    - ≤35W at 4ml/min irrigation and target temperature of 45°C
    - >35W at 15ml/min irrigation and target temperature of 45°C
- The catheter has been approved by FDA and Mt. Sinai is the first U.S. center to use it

- ICE and OctaRay also used in this procedure

- Two types of ablation tags are shown on CARTO
  - Images that look like soccer balls indicate ablations made with QMODE + and are usually found in thin tissue with a stable catheter position
  - Red circles indicate ablations made with QMODE and are usually delivered in thicker tissue
- Dr. Reddy commented that 90W is actually less aggressive modality because the lesions are shallow
  - Must also have good stability during full 4 seconds
- Dr. Reddy also commented that durability data with QDOT have not been collected
  - When contact force was introduced, operators had to adapt after finding gaps over time
    - Operators will likely have the same experience with QDOT
- Dr. Natale said he does not use 90W and he believes operators who did use 90W had higher rates of reconnection, anecdotally
- Dr. Reddy – QMODE+ is a “double edge sword”
  - With good stability, lesions are great
  - Without good stability, lesions are not great
    - Dr. Natale said he is not a fan of QMODE+
- Dr. Purerfellner said there have been thousands of cases to date with no esophageal issues
  - He uses smaller tag distance anteriorly
  - Upcoming study to be published in JACC EP showed 90W vs. 50W had no difference in procedure time and efficacy at 6 months (N=180pts)
    - A physician from the floor commented that it better be a lot safer or he would not use it since only a few minutes of procedure time are saved

BOSTON SCIENTIFIC ELECTROPHYSIOLOGY

Boston Scientific Electrophysiology Website

Summary from AF Symposium

Boston Scientific had a strong presence throughout AFS, and the focus was predominantly FaraWave, the top individual product in our PodiumShare analysis. FaraWave has been used in over 13,000 commercial cases in Europe since receiving CE Mark two years ago. At AFS, it was featured in two live cases, one of which showed a protype version of integration with BSX's Rhythmia mapping system. Discussion of the software under development revealed that it will display full catheter visualization, including spline deformation. The Rhythmia system will also display the predicted energy field prior to delivery. Data from the U.S. IDE trial (ADVENT) is expected later this year at either ESC or AHA, according to Dr. Calkins. Finally, safety remains a key topic, and many discussions at AFS focused on coronary spasm. Most comments seemed to indicate physicians are comfortable with the ability to prevent it by pre-treating with nitroglycerin. However, they also acknowledge experience is still early with PFA. Outside of PFA, the next-generation POLARx "FIT" expandable cryoballoon (from 28mm to 31mm) was featured in one live case.

Details from Congress Events

Organized by Product

FaraWave

- **Pulsed Field Ablation Systems: Safety, Effectiveness, and Regulatory Status**
  Moussa Mansour, MD
  Dr. Mansour's presentation contained updates on multiple technologies (BSX FaraWave, MDT PulseSelect, MDT Affera, BWI VARIPULSE, Kardium, Galaxy Medical, Adagio Medical, and Acutus Medical). Notes for each technology are included in the respective company sections in this report.

  - Boston Scientific
    - FaraWave has received CE Mark and over 13,000 commercial cases have been completed to date in Europe
    - The U.S. IDE trial for FaraWave, ADVENT, has completed enrollment of over 450 patients
    - Dr. Mansour said it will "soon" be integrated into a mapping system but further details were not provided
    - Two other catheters are also in development – FaraFlex (large tip focal) and FaraPoint (focal ablation)
    - Data from the MANIFEST PF registry with FaraWave were presented
      - The data were the same as the original presentation by Dr. Reddy at ESC in August 2022
      - Dr. Mansour noted the small number of patients that reached 12-month follow up (<50)
        - Overall efficacy for these patients reaching 12 month follow up was just 68.9%, with PAF efficacy of 73.4% and PsAF efficacy of 58.2%
      - No esophageal injury, PV stenosis, or permanent PNP were reported in 1,334 cases

LIVE CASE: Pulsed Field Ablation for AF Using a Multispline Catheter PFA (FaraWave Boston Scientific)

Mattias Duytschaever, MD, St. Jan Hospital, Brugge-Oostende, Belgium

- The experience at Bruges with various PFA systems:
  - Boston Scientific:
    - Registry with FaraWave = 181 patients
    - FARA-Freedom Trial = 8 patients
    - BEAT-AF Trial = 16 patients
  - Medtronic:
    - PULSED AF Trial = 5 patients
  - Biosense Webster:
    - Some experience but the exact number on his slide was covered by live video feed
- GA was used in this patient it is not always the case
- Per vein, four applications delivered in basket pose and four applications in flower pose
- CARTO used for segmentation and fluoro used for guidance
  - Contact is assessed when splines deform on fluoro, confirmed by electrograms
- Dr. Mansour commented from the podium in Boston that the catheter is not yet integrated with EAM but it will be "soon"
  - Dr. Jais followed this comment by saying the system is extraordinary and has "changed my life"
    - Integration with EAM will help manipulation from left side to the right side of the LA
      - Dr. Jais said that the EAM integration will not change his life
- Dr. Duytschaever said that he has no complaints from patients the day after the procedure
  - In fact, patients usually ask him, "Did you really do a procedure?"
    - Please see the side note regarding this story
    - Dr. Hindricks said this technology will help expand the market to younger patients
      - When it is connected with mapping, it will mark a "new era" for PVI

AFME INSIGHTS

The story shared by Dr. Duytschaever was referenced throughout the rest of the symposium, by multiple physicians. It was used to highlight how easy and painless FaraWave procedures are from the patients' perspective.

LIVE CASE: Pulsed Field Ablation for AF Using a Multispline Catheter (FaraWave Boston Scientific)

Gábor Széplaki, MD, Mater Private Hospital, Dublin, Ireland

- Since April 2022, this site has completed 268 cases with Farapulse
  - Skin to skin procedure time has averaged just 40.0 minutes with 16.1 minutes of fluoro
  - It is a recognized training center with 6 EPs and total annual ablation volume of 800-900 procedures
- This case is showing the first full integration of FaraWave with the Rhythmia mapping system
- LA mapping is done with Orion because the current version of FaraWave cannot map LA

  - The current version of the catheter displays as a loop catheter on Rhythmia
  - Dr. Galvin said the next version of FaraWave will be able to map the LA
- Images were later shown of the true FaraWave geometry being displayed on Rhythmia with dynamic shape changes (see notes later in this session)
- Dr. Hindricks asked if this procedure can be done as an outpatient procedure?
  - Dr. Hindricks then answered his own question and shared his thoughts on outpatient procedures in Germany:
    - Within 5 years, he expects 80% of AF ablations will be done outpatient in Germany
    - Financial incentives have changed and it is now economically possible to transfer almost all procedures to outpatient
- In this case, maneuvering from the left side to the right side was done with the flower pose open
- With a common right pulmonary vein, how do you ablate with this catheter?
  - He chose 31mm since this patient has a small LA and it allows for individualized lesions
- In this case, ablation was done with FaraWave and then the Orion catheter was brought back to map again and confirm PVI
- Discussion on integration of FaraWave with Rhythmia:
  - Dr. Galvin presented a few slides and discussed the integration
  - Currently, splines are not identifiable and the catheter displays as a circle
  - Software under development was used to create maps offline in a post-procedure analysis
    - The new software displayed full catheter visualization and also projected onto the map the predicted electric field to be created before each application
      - The software then showed post application field in red, with overlapping applications displayed as a darker red
      - By visualizing each spline, the system enables the operator to reposition the catheter if splines are too close
      - One image appeared to show a spline turn red when it was too close to the adjacent spline
      - Another image showed that the petals will bend on the Rhythmia map, which could signal placement in the PV ostium
- Dr. Mansour – will integration change your workflow in terms of applications per vein?
  - Dr. Galvin - even after integration, they expect to still use a total of 8 applications per vein
    - He would be “nervous” to apply less energy
- Clinically, they have not experiences any PNP in their experience but they do paralyze during the procedure
- Dr. Neuzil from the floor:
  - He has completed 1,600 commercial cases and 300-400 in studies
  - With atropine, zero cases of asystole and no PNP
    - Dr. Reddy referenced Dr. Hansen’s presentation of permanent PNP that was disclosed during APHRS last year
- Dr. Reddy – do you have any experience with PWI?

- Dr. Galvin – PWI is currently off label with the catheter but they do have experience with MI and it has performed well. Typical lesion set is four applications, two superior and two below
- He has done PWI and the strategy is to create the "Olympic rings" – three applications in the top row between the superior PVs and and two below, between the inferior veins

- Dr. Galvin – they have only had 7 redo procedures to date out of the 268 cases
- Dr. Natale commented from the panel during discussion that he has seen 2 cases in which the FaraWave catheter showed isolation but Orion mapping showed gaps
  - Dr. Keane also commented that FaraWave mapping will likely not be sufficient for PsAF
- Dr. Reddy spent several minutes discussing coronary spasm and started by saying there are two types of spasms:
  - General spasms are possible with all energy sources and publications from Japan have documented spasm with cryo
    - Localized spasms are due to proximity of the catheter to the coronary
  - In the posterior locations, his data has not shown any localized coronary spasms with PFA
  - If location is closer to a coronary (CTI, MI, or potentially anterior near root of aorta), spasm can occur
    - What to do ultimately depends on the frequency of occurrence
    - Dr. Reddy said he will give nitro EVERY time he is near a coronary

Long Term Follow up from the MANIFEST Study

Kars Neven, MD, PhD

- Dr. Neven said that FaraWave is now approved in New Zealand
- He presented the same data from MANIFEST PF that were originally presented by Dr. Reddy at ESC in August 2022
- MANIFEST PF is a real-world survey of commercial cases with FaraWave in Europe
  - Early results were published online in June 2022 and the full publication can be found here
- In this data set, the 12-month freedom from atrial arrhythmias was 73.4% for PAF patients and 58.2% for PsAF
  - Dr. Neven commented that the efficacy was not that bad but not that good either

Real World Experience with a Multielectrode Pulsed Field Ablation System – Single and Multicenter Experience

Melanie Gunawardene, MD

- St Georg in Hamburg started using FaraWave commercially in May 2021
- Mapping is done by impedance and the catheter is displayed as a lasso
- Dr. Gunawardene said it is "easy" to do more than PVI – just retract the wire and "stamp" the PW
- Data from MANIFEST PF were also reviewed by Dr. Gunawardene
- Data from her original presentation at ESC were reviewed again and showed 79% freedom from atrial arrhythmias at 229 days
  - This data set included 279 patients treated across 5 sites in Germany

- Dr. Gunawardene compared the data from MANIFEST PF to a recent meta-analysis published by Shaheen et al
  - The full publication can be found here
  - In this meta analysis, successful PVI was found in 100% of cases and the overall complication rate was 2.23%
- In December 2021, Dr. Gunawardene published the first case report documenting coronary spasm while using FaraWave
  - At AF Symposium in Boston, she discussed the case and said it occurred during the very first month of using the system

Debate: RF and Cryo Will Continue to Have a Role in AF Beyond 2025

Part of the sessions sponsored by Biosense Webster
Pro: Hugh Calkins, MD
Con: Luigi Di Biase, MD, PhD

AFME Insights

This presentation and discussion occurred during the sessions sponsored by BWI. However, the conversation focused on FaraWave, and the notes are therefore included here.

- During his presentation, Dr. Calkins disclosed that data from the BSX U.S. IDE trial for FaraWave, the ADVENT trial, will be presented at ESC (August 25-28) or AHA (November 11-13)
- Dr. Calkins pointed to many reasons that RF and cryo will continue to have a role in AF ablation beyond 2025, including the need to ablate non PV triggers, MI lines, and atypical flutters

Q&A For BWI Sessions

- Dr. Di Biase is not convinced PFA has completely eliminated fistula because it is not a perforation – it happens over time
  - Dr. Mansour said that over 13,000 commercial cases have been performed with FaraWave in Europe since launch, and there has not been one report of AEF
  - Dr. Hocini said it still needs to be assessed in each catheter separately
  - A physician from Belgium shared from the floor that he has seen two cases of AEF with PFA
    - In both cases, a reprocessed esophageal probe was used, and after the events, the probes were analyzed with an electron microscope
    - Bare metal was found to be exposed, which could have caused arcing during PFA
    - After these cases, reprocessed probes are not used and there have been no further AEF complications

Enhancing Efficiency of AF Ablation: Feasibility of Pulsed Field Ablation without General Anesthesia (5S Study)

Boris Schmidt, MD

- The "5S" study does not use general anesthesia in the workflow – sedation only
- Mapping and ablation are done with the same catheter (BSX FaraWave)
- Updated data from the "FLOWER POWER Registry" at his site included 509 patients treated with FaraWave through the Wednesday prior to the conference
  - Mean procedure times across all patients were 35 minutes with 7 minutes of fluoro
  - A total of six different operators are included in this data set
- Procedure times at CCB Frankfurt across other technologies were presented alongside the FaraWave data

- CardioFocus laser balloon procedures average 44 minutes
- Medtronic cryoballoon procedures average 51 minutes
- Point by point RF procedures average 55 minutes

- In the total cohort of 507 cases, Dr. Schmidt reported two transient PNP cases and two strokes
- The two strokes occurred in the beginning experience when they were still using a circular mapping catheter to document PVI
  - They abandoned the use of CMCs and no strokes have occurred since that time
- Dr. Schmidt presented efficacy data from his site in both PAF (83%) and PsAF (64%)
  - Average follow up was 280 days

Safety of Pulsed Field Ablation I: Conduction System, Phrenic Nerve, Coronary Vasospasm and Bronchoscopy

Vivek Reddy, MD

- MANIFEST PF data were reviewed again, with a focus on the topics at hand
- In 1,758 patients, there were zero reports of esophageal events, PV stenosis, or phrenic nerve paralysis
  - Dr. Reddy did show an example of asymptomatic transient phrenic nerve paresis, which recovered fully by the next morning
  - He also referenced, again, the reported permanent PNP presented by Dr. Hansen at APHRS
- Coronary spasm has been published as occurring with other energy sources as well
- A 2021 publication by Nakamura et al found a rate of 0.34% in cryoballoon procedures and 0.04% in RF procedures
  - Overall incidence of spasm in 22,232 patients was found to be 0.19% and all 42 occurrences were relieved with NTG administration
- Since Dr. Gunawardene's original case report in December 2021, several publications have focused on investigating this topic
  - Dr. Reddy presented data from HRS 2022 as reported by Higuchi et al and Koruth et al
  - He recently published his own paper on "remote" vs. "adjacent" PFA and the resulting occurrences of coronary spasm
    - If PFA is done remotely from coronaries, no spasms were seen
    - If PFA is done adjacent to coronaries, subclinical spasms were seen
      - Subclinical spasms can be prevented by administering NTG prior to PFA
- A paper currently in press at JACC EP by Della Rocca et al was reviewed and it found that 2/6 patients who received CTI ablation with FaraWave experienced ST elevation
  - One resolved with nitro and the other patient required CPR + DC shock to resolve
  - Dr. Reddy said the 33% rate in this study is probably an overestimate, but it is also not likely to be 1% either – the actual rate will be somewhere in between
    - Based on these findings, the best strategy needs to be identified:
      - Is prophylactic NTG required in every case or just as needed?
      - What is the best timing and dose for NTG, if it is administered?
- Another outstanding question identified by Dr. Reddy is whether focal catheters will also create the same type of spasms as the flower shape FaraWave

- **Safety of Pulsed Field Ablation II: Microbubbles; Brain MRI; Esophagus/EGD**
  Thomas Deneke, MD
  - The rate of AEF in RF ablations for AF has been reported at 0.02% to 0.2%
  - With PFA, there have been approximately 14,000 clinical cases worldwide and no AEF has been described
  - Two endoscopically detected esophageal lesions (EDEL) were reported in cases using the Galaxy generator and reprocessed esophageal probes that were found to have exposed metal upon investigation post procedure
  - A table was presented comparing rates of SCE/SCL across multiple technologies
    - The rate of SCE was consistently 9-12% across all technologies (Farapulse, Galaxy, Affera, Kardium, and BWI)
    - The one exception was a reported rate of 21% with BWI VARIPULSE, but a footnote explained this rate occurred prior to procedural modifications – after implementation of these modifications, the rate dropped to 12%
  - During the discussion that followed this series of presentations, Dr. Reddy said a "hurricane" of microbubbles can be seen with FaraWave but the SCE rate is 15%
    - Dr. Deneke cited estimated SCE rates for other procedures and TAVR was 50%
    - Since air and emboli produce the same MRI lesions, it is not possible to tell what causes SCL
  - Dr. Deneke concluded his comments by saying that regardless of the cause, he still does not want to have SCE
  - From the floor, Dr. Natale said that he believes SCE is not being driven by PF energy – it is something else, i.e. sheath manipulation, etc.

- **POSTER: PFA Technology for PVI and Left Atrial Posterior Wall Isolation in Patients with AF: Preliminary Experience from an Experienced Ablation Center**
  First Author: Dr. Marco Moltrasio
  Last Author: Dr. Claudio Tondo
  - One Boston Scientific employee is listed as a co-author
  - This poster reported on the first 45 cases performed with BSX FaraWave at Centro Cardiologico Monzino in Milan, Italy
  - PVI was performed with the protocol-defined 8 applications per vein
  - PWI was performed in 13 cases, and all of these cases included the use of 3D mapping
  - First pass isolation per vein was reported to be 100% using only PFA
  - Total procedure time was 86 minutes with 22 minutes of fluoro
    - A mapping system was used in 28 cases (62%)
  - No major procedure-related safety events were reported

POLARx FIT

Pre Recorded Case: AF Ablation Using a New Cryoballon Catheter (Polar Fit Cryo balloon Boston Scientific)

Kevin Makati, MD, St. Joseph's Hospital, Tampa, FL

- The case reviewed was actually a pre-recorded case performed by Dr. Wilbur Su
- Dr. Makati said the POLARx FIT will "soon" be commercialized
- The POLARx FIT is expandable from 28mm to 31mm in diameter
- Dr. Makati explained that the balloon does not become "bigger" but takes a completely different shape altogether – it is shaped to cover the antral portion of the vein
- In this case, six attempts were made to occlude the vein with the 28mm configuration but none were successful
  - One attempt was made after expanding the diameter to 31mm and it was successful
- With larger trunk veins and left common veins, the 31mm configuration is more helpful
- FROZEN AF Trial = U.S. IDE trial for POLARx
  - Last patient will reach 12 month follow up in August 2023
  - The trial was extended with a cohort treated exclusively with the 31mm configuration of POLARx FIT
- On his conclusion slide, Dr. Makati highlighted shorter procedure times, enhanced PV margin of isolation, and a lessened requirement on operator proficiency

AFME INSIGHTS

BSX expects U.S. approval for POLARx in 2H 2023, according to the presentation accompanying Q4 results in January.

POSTER: Voltage Mapping of a Novel 31mm Cryoballoon for PVI to Manage PAF: A Single Center Experience

First Author: Dr. Kevin Makati
Last Author: Nicholas Jordan-Topp

- Two co-authors on this poster are listed as Boston Scientific employees
- Selected data from the Boston Scientific FROZEN AF trial were presented
  - The FROZEN AF trial is the global IDE trial for Boston's POLARx cryoballoon
- According to this poster, total enrollment globally was 435 patients across 44 sites in 10 countries
  - 385 patients were treated with the first generation POLARx and 50 patients were treated with the POLARx FIT balloon, which is expandable to 31mm in diameter
  - Dr. Makati participated in this trial and treated a total of 14 patients, including 8 cases with FIT
- Mapping with Orion was performed pre and post PVI and voltage maps were exported to assess scar burden offline
- Data showed that the 31mm balloon produced significantly larger lesions than the 28mm balloon based on the analysis of scar burden
- The authors noted that the larger balloon allowed greater control of lesion placement while maintaining occlusion
- In all patients, PVI was successful

Baylis Medical

- **POSTER: Comparison of Transseptal Puncture Using a Dedicated RF Wire System Versus a Deployable Mechanical Needle With and Without Electrification**
  First Author: Dr. Jeremiah Wasserlauf
  Last Author: Dr. Bradley Knight
  - A co-author on this poster is employed by Boston Scientific
  - The ex-vivo animal studies in this poster investigated the VersaCross system from Boston Scientific Baylis Medical vs. the AcQCross System recently purchased by Medtronic from Acutus
  - The BSX VersaCross system includes a dedicated sheath and RF generator, while the AcQCross system uses a standard electrosurgical generator
  - The poster concluded that VersaCross showed superior safety and efficacy in achieving transseptal puncture as compared to the AcQCross system
    - Using the electrified AcQCross needle required twice the applications and additional power vs. VersaCross
    - Tissue coring was seen in 50% of the AcQCross TSPs
    - Using the mechanical AcQCross approach required 6x more force than using RF puncture with VersaCross

- **POSTER: Efficient Zero Fluoro Cryoballoon Ablation Using VersaCross Large Access, ICE Guidance, and Workflow Optimization**
  First Author: Dr. Hany Demo
  - A new workflow was investigated that uses the 12.5F VersaCross Large Access (Boston Scientific Baylis Medical) to replace the 8.5F VersaCross Fixed Sheath
  - 54 cases with the new system and workflow were compared to 53 cases using the legacy approach
  - Across both cohorts, acute PVI was achieved in 100% of patients without the use of any fluoroscopy
  - Comparing the new Large Access System to the Fixed Sheath:
    - Transseptal time was 34% faster
    - Time to FlexCath insertion was 31% faster
    - Ablation start time was 41% faster
    - Overall procedure time was 30% faster

CARDIOFOCUS

CardioFocus Website

Summary from AF Symposium

CardioFocus recently shifted its focus to PFA and announced completion of certain preclinical milestones with a prototype PFA balloon based on its current X3 platform. At AFS, Dr. David Haines showed an image of this "PFA balloon" for the first time. Although it was not completely clear, it appears that CardioFocus has placed flexible electrodes on the exterior surface of the balloon in order to deliver PFA. Dr. Haines did not provide any expected timelines for FIM or clinical trials.

Details from Congress Events

- **SPOTLIGHT SESSION: A New Solution for Efficient PVI Achieved Through Conformance, Stability, and Direct Visualization-HeartLight X3 (CardioFocus)**
  David Haines, MD
  - The first generation laser balloon from CardioFocus originally received FDA approval in April 2016
    - Press release with the announcement can be found here
  - Dr. Haines spent considerable time on the features and benefits of the most recent generation laser balloon, the X3, which received FDA approval in May 2020
    - The X3 features the same endoscope as prior generations to provide direct visualization of the cardiac tissue, and "RAPID Mode" enables PVI in as little as 3mins/vein
  - Dr. Haines presented two slides on the topic of PFA with the CardioFocus balloon, and each slide contained an image of the "CardioFocus PFA Balloon"
    - This image is believe to be the first public presentation of the PFA balloon
  - In July 2022, CardioFocus announced completion of certain preclinical milestones with its prototype PFA system, but no image of the catheter was included in the press release
    - A link to the full release is here
  - The image on Dr. Haines' slides during AFS appeared to show flexible electrodes on the exterior surface of the balloon, but it was not fully clear
  - The description of the system included two key features of the balloon-based approach:
    - The insulating effect of the balloon directs the voltage field into the tissue
    - A compliant balloon also ensures electrode-tissue contact
      - No timelines were provided by Dr. Haines for expected FIM or clinical trials

- **POSTER: 1-Year Recurrence In Patients With PAF Undergoing PVI Only Using Cryoballoon vs X3 Laser Balloon Ablation**
  First Author: Dr. Mahmoud Ali
  Last Author: Dr. Atul Bhatia
  - A total of 188 patients received de novo PVI with either cryoballoon (n=111) or X3 (n=77) across three sites
  - Fluoro times were significantly lower in X3 procedures (24mins) vs. cryoballoon procedures (33mins), p<0.001
  - Procedure times were also lower in X3 cases (141mins) vs. cryoballoon procedures (212mins)
    - Overall, procedure times overall were much longer in this study vs. other presentations at AF Symposium in which both laser and cryoballoon procedure times were less than 60mins
  - Freedom from AF was not statistically different between the X3 cohort (77.9% efficacy) and the cryoballoon cohort (78.7%)

CARDIONXT

CardioNXT Website

Summary from AF Symposium

The iMap system from CardioNXT was featured in a Spotlight Session that also included presentation of a new HD basket mapping catheter, "iON." This catheter has 2 EM sensors, 38 high fidelity flat electrodes across six splines, and a diameter of just 1cm. iMap is an open mapping system and four posters at AFS showed successful integration of ablation catheters from both strategics (MDT DiamondTemp) and start-ups (Acutus AcQBlate FORCE, Field Medical, and Pulse Biosciences). CardioNXT has previously reported on successful integration with BSX FaraWave (here).

Details from Congress Events

- **SPOTLIGHT SESSION: Internally Referenced and AI Enabled 3D Mapping and Navigation (CardioNXT)**
  Usman Siddiqui, MD
  - CardioNXT iMap Mapping & Navigation system and MultiLink CS catheter received 510k clearance from the FDA in August 2021
    - The press release can be found here
  - iMap is a hybrid magnetic and impedance mapping system with improved stability – maps do not shift, even after a cardioversion
    - Dr. Siddiqui described it as a "true navigation system"
  - iMap is an open system capable of integrating with any catheters
    - Case videos were shown with the CardiNXT system displaying the following catheters: MDT DiamondTemp, BSX Farawave, and Field Medical
  - The "iON EM Sensor Enabled HD Mapping Catheter" was presented and it is a six-spline miniature basket catheter with a diameter of 1cm
    - The slide described the catheter as having 38 high fidelity flat electrodes and 2 electromagnetic location sensors, delivered through an 8 Fr shaft

- **POSTER: Novel Open Architecture 3D Mapping System Compatible With Contact Force Catehter**
  First Author: Dr. Moritoshi Funasako
  Last Author: Dr. Vivek Reddy
  This poster is included in the company sections for both CardioNXT and Acutus Medical
  - This poster reports on the successful integration of the AcQBlate FORCE catheter from Acutus with the iMap system from CardioNXT
    - Co-authors on this poster included one Acutus employee and three CardioNXT employees
  - The CardioNXT iMap system accurately rendered the AcQBlate catheter on the map, including the display of real-time contact force information directly from the Qubic Force Sensing Module
    - iMap is an open system and allows for the use of any diagnostic catheters

- One of the conclusions on this poster highlighted the fact that contact force-guided RF ablation will now be possible without the need for catheters from Abbott or Biosense Webster
    - The Acutus AcQBlate catheter has not yet been approved by the U.S. FDA

POSTER: HPSD Integrated with Novel 3D Mapping and Navigation

First Author: Dr. Usman Siddiqui
Last Author: Dr. Petr Neuzil
This poster is included in the company sections for both CardioNXT and Medtronic CAS

- This poster reports on the successful integration of the Medtronic DiamondTemp catheter with the iMap system from CardioNXT
    - Two CardioNXT employees are listed as co-authors
- The poster noted that DiamondTemp can only be visualized on two systems, CardioNXT and EnSite Precision from Abbott
- The Abbott system does not localize the tip of the catheter, which could cause accuracy to be off by as much as 1.1mm
- A total of 48 patients were treated with the DiamondTemp catheter being navigated with CardioNXT iMap
- The iMap system also displays data from the DiamondTemp generator in real-time, including temperature
- When used with DiamondTemp, iMap also provides automatic lesion tags after each ablation, and it is the only system that provides this feature
    - If 50°C is achieved for more than 1 second, a red tag is displayed on the map
    - If 45-50°C is achieved for more than 1 second, the lesion tag is pink

POSTER: Novel Nanosecond PFA Compatible with 3D Mapping & Navigation System

First Author: Ashwin Mathur
Last Author: Dr. Vivek Reddy
This poster is included in the company sections for both CardioNXT and Pulse Biosciences

- Three co-authors are employees of CardioNXT and three co-authors are employees of Pulse Biosciences
- This poster reports on successful integration of the “nsPFA catheter” from Pulse Biosciences with the iMap system from CardioNXT
- The “nsPFA catheter” is being presented publicly for the first time at AF Symposium and the integration with CardioNXT has already been completed
- Current PFA systems in development use pulse durations measured in microseconds, but nsPFA uses pulses measured in nanoseconds
    - Potential advantages include less skeletal muscle contraction and less nerve capture
- The poster reports on results from nine animal cases in which the nsPFA catheter was full visualized on the CardioNXT system
    - Accurate tracking and visualization of the catheter orientation was successful

- **POSTER: Unique "FieldBending" PFA Electrode Design with Contact-Force Integrated with Commercial 3D Mapping & Navigation System**
  First Author: Dr. Steven Mickelsen
  Last Author: Dr. Vivek Reddy
  Notes for this poster are included in company sections for both Field Medical and CardioNXT
  - Dr. Mickelsen is the founder of Field Medical, Inc, and one other employee is listed as a co-author on this poster
    - Four co-authors are employees of CardioNXT
  - Field Medical is developing the "FiedForce Ablation System", which includes a novel focal ablation catheter that delivers PFA and also measures contact force using optical sensors
    - The catheter also has an integrated sensor, and a software interface was created to enable iMap to receive both position data and contact force information
  - This poster reported on successful visualization of the catheter on the CardioNXT, in addition to displaying accurate, real-time contact force readings
  - The study did not mention any animal cases as part of the study, so it appears the poster is just reporting successful completion of the interface at this point

CATHVISION

CathVision Website

Summary from AF Symposium

CathVision was featured in a Spotlight Session for the second consecutive year, and Dr. Suneet Mittal presented the technology this year. The "ECGenius System" is a recording system and has been approved by FDA. Four modules are in development and two have been submitted to FDA for approval. Additional modules are also being developed for disease states outside of AF, including VT and SVT.

Details from Congress Events

- **SPOTLIGHT SESSION: The ECGenius Next Generation EP Recording System (CathVision)**
  Suneet Mittal, MD
  - ECGenius System is an FDA approved low-noise recording system
  - Value proposition:
    - Data used to train current AI algorithms is noisy
    - CathVision provides higher fidelity electrogram signals, which can help create better AI outputs for AF ablation
  - "PVI Analyzer" = real time aid in PVI
    - Analyzes signals beat by beat to detect time of isolation based on model
  - "FaST" = focal sources and trigger analysis
    - The "FaST" algorithm was published by Chauhan et al in Heart Rhythm May 2020
      - A link to the abstract is here
    - In this randomized controlled pilot study, freedom from AF was 74% for patients who received additional ablation guided by FaST vs. 51% for PVI only
      - According to Dr. Mittal's slides, CathVision has an exclusive license to this algorithm
  - CARDIALYTICS suite of tools is in development by CathVision and includes a portfolio of four modules
    - PVI Analyzer: "aid in classification of PVI" (under review at FDA)
    - AF Freedom: "clinical outcome prediction"
    - FaST: focal source mapping
    - Signal Complexity: "multiparameter complexity visualization" (under review at FDA)
      - Dr. Mittal said there are two active trials investigating signal complexity
  - Modules are in development for both VT and SVT

ELECTROPHYSIOLOGY FRONTIERS

EP Frontiers Website

Summary from AF Symposium

EP Frontiers was presented publicly for the first time at the 2022 AF Symposium, and Dr. Piccini presented the technology again this year. The EPF catheter has been named "Fiore" and the design remains consistent with last year. FIM is now expected later this year, and the EU pivotal trial is expected to run from 2024 to 2026. Expectations for a U.S. IDE trial were not presented.

Details from Congress Events

- **SPOTLIGHT SESSION: In-Vitro and In-Vivo Preclinical Evaluation of Pulsed Field Ablation with a Circular Linear Ablation Catheter (EP Frontiers)**
  Jonathan Piccini, MD
  - The EPF catheter has been named "Fiore" and features a unique anchor that sits in the pulmonary veins to stabilize the ablation element, called the "CLA" – circumferential linear array
  - The Fiore System includes a custom PFA generator
  - The CLA includes four linear electrodes that fully encircle each PV, enabling true "single shot" ablation
  - Biphasic, bipolar waveforms can be delivered in multiple ways – cross ablation or rotational ablation
  - Benchtop studies with potatoes showed full circumferential lesions can be delivered
  - Pre-clinical swine studies have been successfully completed
  - FIM study is now expected later in 2023
    - The FIM will enroll the first 10 patients in the Czech Republic, followed by an early feasibility study at two sites in the U.S. and two sites in Belgium
  - The EU pivotal trial is expected to run from 2024 – 2026
    - According to Dr. Piccini, this trial will be a prospective, multicenter, single arm study at 20 sites in Europe, with targeted enrollment of 125-150 patients
  - Expectations for a U.S. IDE trial were not discussed

AFME INSIGHTS

Dr. Piccini presented the EP Frontiers technology during a Spotlight Session at the 2022 AF Symposium, and his presentation then was believed to be the first public presentation of the catheter.

During his presentation last year, Dr. Piccini said FIM was expected by year-end 2022.

FIELD MEDICAL

Field Medical Website

Summary from AF Symposium

Field Medical was founded by Dr. Steven Mickelson in 2022 and the technology was presented at the podium for the first time during AFS. Dr. Mickelson was a co-founder of Farapulse, Inc. (formerly The Iowa Approach, Inc.), and he was most recently the Chief Translational Science Officer at Acutus Medical. The "FieldForce" system includes a focal catheter with a proprietary PFA generator, and combined, the technology enables "field bending" to reduce far field stimulation. The catheter also provides contact force data. No expected clinical timelines were provided.

Details from Congress Events

- **SPOTLIGHT SESSION: Field Bending - The Promise of an Effective Second Generation PFA system (Field Medical)**
  Usman Siddiqui MD
  - Dr. Siddiqui described the current, first generation PFA devices as being focused on "a race to market"
  - Technology from Field Medical was characterized as "second generation" PFA, applicable to all atrial arrhythmias in awake patients
    - Applications for VT are also in development
  - Field Medical has developed the "FieldForce Therapy System" which includes a proprietary PFA generator and a magnetically enabled, irrigated focal catheter that provides contact force data
  - The electrode has been designed to optimize focal PFA, including a reduction of far field stimulation
  - The internal electrode is 3mm in size and allows for "field bending" – shape of the field can be altered to avoid far field drop out
    - A series of slides were presented with data from finite element modeling (FEM) of the Field waveform
    - The "FieldBending" electrode produced 81% less far field stimulation than unipolar and 46% less than bipolar
  - Lesions up to 2cm are possible with this technology, based on FEM

AFME INSIGHTS

Dr. Siddiqui's presentation on Friday is believed to be the very first public presentation of the technology under development at Field Medical, a company founded by Dr. Steven Mickelson. Dr. Mickelson most recently worked at Acutus Medical as the Chief Translational Science Officer before founding Field Medical in July 2022. (Press release announcing his departure from Acutus can be found **here**)

- **POSTER: Unique "FieldBending" PFA Electrode Design with Contact-Force Integrated with Commercial 3D Mapping & Navigation System**
  First Author: Dr. Steven Mickelsen
  Last Author: Dr. Vivek Reddy
  Notes for this poster are included in company sections for both Field Medical and CardioNXT
  - Dr. Mickelsen is the founder of Field Medical, Inc, and one other employee is listed as a co-author on this poster
    - Four co-authors are employees of CardioNXT
  - Field Medical is developing the "FiedForce Ablation System", which includes a novel focal ablation catheter that delivers PFA and also measures contact force using optical sensors
    - The catheter also has an integrated sensor, and a software interface was created to enable iMap to receive both position data and contact force information
  - This poster reported on successful visualization of the catheter on the CardioNXT, in addition to displaying accurate, real-time contact force readings
  - The study did not mention any animal cases as part of the study, so it appears the poster is just reporting successful completion of the interface at this point

- **Future Directions in Pulsed Field Ablation**
  Vivek Reddy, MD
  Dr. Reddy's presentation contained updates on multiple technologies (ABT PFA, Field Medical, Adagio Medical, and Pulse Biosciences). Notes for each technology are included in the respective company sections in this report.
  - The agenda for Dr. Reddy's presentation included the following topics:
    - PFA + EAM
    - "Field Bending"
    - PFCA
    - Nanosecond PFA
    - LAAC + LAAEI
  - <u>Field Medical</u>
    - Dr. Reddy described this technology as having one electrode inside and one electrode outside
      - The slide highlighted the ability to deliver energy in an awake patient
      - The technology is still in concept phase and no pre clinical or clinical work has been completed

GALVANIZE THERAPEUTICS (GALAXY MEDICAL)

Galvanize Tx Website – CENTAURI System

Summary from AF Symposium

A pre-recorded case was presented by Dr. Andreas Rilling using the CENTAURI generator with a BWI SMARTTOUCH catheter. This site has completed a total of 30 cases with CENTAURI. The CENTAURI generator has received CE Mark and approximately 300 commercial cases have been completed to date, according to Dr. Mansour's update. Across multiple presentations, expectations for the U.S. regulatory timeline were not discussed.

Details from Congress Events

- **Pre Recorded Case: Pulsed Field Ablation for AF Using a Focal Tip Catheter (Galvanize Therapeutics)**
  Andreas Rillig, MD
  - The CENTAURI generator from Galvanize Therapeutics (formerly Galaxy Medical) was used with the BWI THERMOCOOL SMARTTOUCH catheter
    - The CENTAURI generator has been studied with additional focal catheters, including ABT TactiCath SE and IntellaNav StablePoint
  - Waveform is monopolar, biphasic
  - At his site in Hamburg, Germany, 30 cases have been completed with the Galvanize system
  - Three different settings are available to the operator: 19A, 22A, and 25A
    - PFA applications are QRS-gated
  - For posterior ablations, he uses 22A setting but other sites have used 25A
    - Dr. Rillig ablates for 7-10 seconds for posterior applications
  - Some muscle contraction is seen but "not much"
  - Still have contact force information during case, except during PEF application
    - During application, the catheter is not visualized and there is no contact force data available
  - Catheter stability is high – no jumping
  - Q&A was not allowed for this presentation due to time constraints

- **Pulsed Field Ablation Systems: Safety, Effectiveness, and Regulatory Status**
  Moussa Mansour, MD
  Dr. Mansour's presentation contained updates on multiple technologies (BSX FaraWave, MDT PulseSelect, MDT Affera, BWI VARIPULSE, Kardium, Galaxy Medical, Adagio Medical, and Acutus Medical). Notes for each technology are included in the respective company sections in this report.
  - Galaxy
    - CE Mark received and over 300 commercial cases have been completed
    - Dr. Mansour did not comment on the status of a U.S. trial

Clinical Outcomes with Focal Pulsed Field Ablation Systems

Andrea Natale, MD

Dr. Natale's presentation contained updates on multiple technologies (BWI, Galaxy Medical, and MDT Affera). Notes for each technology are included in the respective company sections in this report.

- Galvanize Therapeutics
  - Previously presented data with the Galvanize Therapeutics' (formerly Galaxy Medical) CENTAURI generator were reviewed
  - The generator is compatible with three leading catheters and durability results were strong with each one – 87% across the three catheters
    - 12 month efficacy data were included in this data set and overall freedom from AF was 84% (38/45)
      - Efficacy in PAF patients was 88% vs. 80% in PsAF

Role of Contact Force Sensing in Pulsed Field Ablation

Hiroshi Nakagawa, MD, PhD

- Preclinical data were presented with the CENTAURI generator from Galvanize Therapeutics using the ABT TactiCath SE catheter
- This study investigated the impact of contact force on PFA lesion size
- Dr. Nakagawa concluded that tissue contact is required for PFA when using biphasic, monopolar waveforms
  - With the same PF dose, lesion depth increases with increasing contact force, from 2mm to 8mm
  - The study also found that a decrease in impedance with PFA does not correlate with lesion depth
- During his presentation, Dr. Nakagawa highlighted the lack of microbubbles on ICE when using this system, and he noted that it is completely different than RF

KARDIUM

Kardium Website

Summary from AF Symposium

Data from Kardium were featured in a late-breaking clinical trial presented by Dr. Vivek Reddy, and the data showed strong durable PVI (99%) with multiple PF applications from The Globe catheter. Dr. Reddy also co-led a pre-recorded case with Kardium along with Dr. Petr Neuzil. In his comprehensive update, Dr. Moussa Mansour said a total of 69 patients have been treated to date with The Globe (PFA application), and a global IDE trial across the Europe, Canada, and the U.S. is expected to start this year.

Details from Congress Events

- **Late Breaking Clinical Trial: AF Ablation Using a Novel "Single-Shot" Map-and-Ablate Spherical Array Pulsed Field Ablation Catheter: Impact of Application Repetition on Durability of PV Isolation**
  Vivek Reddy, MD
  - Dr. Reddy began with a comparison of the legacy "G3" system vs. the new generation "G4" system, both of which were used during this study
    - G4 features the same 30mm array, i.e. no changes were made to the ablation element
    - G4 has a smaller sheath size (16Fr vs. 19Fr), improved handle controls, improved air management, and improved mapping features
      - Mapping now includes HD activation and propagation maps
      - Mapping is impedance based
  - The Globe is orientation independent – "just get there" was the phrase used by Dr. Reddy
  - Electrodes are selected individually for each application, and Dr. Reddy said the goal was to select a "train track", which looks like two rows of electrodes around the vein
  - The PULSE EU study enrolled a total of 59 patients, with 11 patients in Group one receiving a single PF dose using the G3 system and 48 patients in Group 2 treated with one of two protocols:
    - 10 patients were treated with the G3 system and received 3 individual applications of 10 seconds each
    - 38 patients were treated with the G4 system and received one, extended application of ~30 seconds
      - It appears this "one" application was actually a combination of the three individual applications delivered together in one automated train
    - ICE was used in all procedures and no esophageal management strategy was employed
  - Across all patients pulse delivery time was measured in seconds and averaged under 60 seconds

AFME INSIGHTS

Early durability data from the PULSE EU study were presented in a poster by Dr. Vivek Reddy during AHA 2022. That poster only reported on 10 patients from "Group 2" that received repetitive applications. Despite the small number of patients, repetitive applications showed a clear benefit at 90-day remapping – 100% of veins remained durably isolated in Group 2 vs. just 62.5% in Group 1 that received one PF application.

- In 7 patients that received PVI + PWI + MI with the Globe, pulse delivery time was 112 seconds

- Procedure times in Group 2 averaged 82 minutes
- Acute PVI was achieved in all patients across both Groups
  - Durable PVI in Group 1 was 63% per vein and 30% per patient
  - Durable PVI in Group 2 was 99% per vein and 95% per patient
- Only one safety event was reported – a drug responsive case of pericarditis in Group 2
- 43 patients were assessed for esophageal lesions and none were found
- Brain MRIs found 18.8% of patients treated with G3 had SCLs but only 5% of patients treated with G4
  - The results were published simultaneously online and the abstract can be found here
- Limitations of this study = single center experience (Homolka, Prague) with three operators
- The U.S. IDE trial is expected to begin enrollment soon

Q&A

- Are additional lesions possible?
  - Dr. Reddy – it is early but experience is encouraging
    - PWI was successful in all three patients and one MI was also successful, which will be shown tomorrow in a case review
- Dr. Reddy – no clinical spasm was seen but it does need to be assessed

❖ **Pre Recorded Case: Pulsed Field Ablation for AF Using a Spherical Multielectrode Catheter (Kardium)**

Petr Neuzil, MD, PhD and Vivek Reddy MD, Homolka Hospital, Prague, Czech Republic

- At his institution, Homolka Hospital, 69 cases have been completed to date with The Globe PF System
- This recorded case is one of the most recent cases from last month – a PsAF patient of >1 year
- FLOW Maps indicate whether or not contact has been achieved
- CONTACT Maps are more precise and confirm contact
  - Dr. Reddy explained that these maps use temperature, not impedance
  - Low level current is injected and this causes heating of the tissue
  - Each of the 122 electrodes has a thermocouple and the temperature readings after the current is injected indicated if the catheter is in contact with tissue (small temperature rise) or blood (no temperature rise)
  - The rate of cooling is another indicator for contact – blood will show quicker cooling of the electrode vs. tissue contact
- Fluoro and ICE are both used to guide opening of the sphere
  - Dr. Neuzil said that opening the catheter is “stressful”
- On the map, geometry is distorted but Dr. Neuzil “doesn’t care” – only need to see gaps
- Total duration of one pulse train is ~30 seconds according to Dr. Neuzil
- The mapping system marks the location of each electrode where PF was applied
  - With 122 available electrodes, the map is quickly filled with small dots from each lesion tag
- In this case, PVI was completed, followed by PWI

  - MI also done and Dr. Neuzil said that 5 patients total received MI line in his experience
  - Two of these patients were remapped and showed durable block
- It is possible to pace from any element on the catheter
- For these cases, Dr. Reddy said the protocol did not allow for shooting of the coronaries
- Dr. Kottkamp commented from the panel:
  - In a single position, PVI is almost guaranteed
  - The Globe is a platform catheter – after PVI, it is possible to do PWI, MI, and voltage mapping
    - Dr. Kottkamp said the electrograms from The Globe look like bipolar electrograms

Pulsed Field Ablation Systems: Safety, Effectiveness, and Regulatory Status

Moussa Mansour, MD

Dr. Mansour's presentation contained updates on multiple technologies (BSX FaraWave, MDT PulseSelect, MDT Affera, BWI VARIPULSE, Kardium, Galaxy Medical, Adagio Medical, and Acutus Medical). Notes for each technology are included in the respective company sections in this report.

- <u>Kardium</u>
  - 69 patients treated to date with Kardium
  - Global IDE trial to start during 2023 for PAF and PsAF across sites in the U.S., Canada, and Europe

LUXMED SYSTEMS

LuxMed Systems Website

Summary from AF Symposium

Technology from LuxMed has been presented at industry congresses as far back as 2015, according to the company website. At 2023 AFS, Dr. Jacob Koruth presented updates during a Spotlight Session that included images of two catheters that we believe have not been presented at the podium previously – "OptoSpider" and "HexaClaw". Dr. Koruth said each catheter will include the core LuxMed technology to assess tissue viability in real time, which could potentially enable lesion assessment immediately following energy delivery. No regulatory timelines were discussed during the presentation, however.

Details from Congress Events

- **SPOTLIGHT SESSION: Ablation with Real-Time Optical Lesion Assessment (LuxMed Systems)**
  Jacob Koruth, MD
  - NADH is an enzyme that represents cellular vitality and measuring this enzyme can assess whether tissue is viable or not
  - LuxMed is developing a prototype focal catheter compatible with RF and PF that includes a light source to interrogate tissue in real time
    - Returned light from the tissue is analyzed by spectrometer and displays tissue NADH characteristics
      - Observing a decrease of NADH indicates lesion is being formed
  - Pre clinical animal data from HRS 2019 were presented again
    - Lesions were predicted with 87% accuracy by fellows who only looked at NADH signals
  - Catheter can be used to sweep over a lesion set after it has been completed, in order to look for gaps
    - The system is not just looking at electrograms; it is analyzing the content of the actual tissue
  - According to Dr. Koruth, the LuxMed platform will be based on a focal catheter compatible with both RF and PF
  - First generation technology was only forward-looking, but the second generation "OmniView" catheter assesses tissue from multiple directions
  - Work is being done with robotic magnetic ablation catheters
  - The long-term goal at LuxMed is to develop a large footprint catheter and a single shot catheter optimized for PVI
    - Each catheter will be able to assess tissue viability in real time
    - Two images were shown on Dr. Koruth's slide and the two trademarked names were "OptoSpider" and "HexaClaw"

MEDLUMICS

MedLumics Website

Summary from AF Symposium

The "PulseView" system was presented during a Spotlight Session and preclinical data showed that the proprietary "PS-OCR" technology can also assess tissue birefringence following PFA. Dr. Atul Verma said that the system (catheter + generator) is now progressing to FIM studies, but he did not provide an expected timeline.

Details from Congress Events

- **SPOTLIGHT SESSION: Predicting Durability of PFA Lesions Using an Optically Guided Catheter (MedLumics)**
  Atul Verma, MD
  - MedLumics technology is based on PS-OCR (polarization sensitive optical coherence reflectometry)
    - PS-OCR enables the following:
      - Direct confirmation of tissue contact and stability
      - Direct assessment of lesion progression
      - Direct assessment of gaps by identification of healthy vs. ablated tissue
  - "AblaView" = RF catheter system
  - "PulseView" = PF catheter system
  - PulseView includes a PFA generator that delivers a bipolar, biphasic waveform through a focal catheter that is also equipped with the optical system that measures tissue birefringence
  - Key outstanding question is whether or not PS-OCR will work with PFA
    - Yes – tissue can lose up to 20% of its birefringence seconds after PFA
  - Once lesion set has been completed, the catheter can be dragged over the lesions to assess birefringence
    - Loss of birefringence = durable lesion
  - Preclinical animal studies intentionally left gaps in the lesion sets to assess ability of PS-OCR to measure lesion durability
    - Animal studies concluded that system is 91% accurate in determining complete, durable lesions, independent of electrogram loss
      - Sensitivity = 93%
      - Specificity = 82%
  - Dr. Verma concluded his presentation by saying that the technology is now "moving into FIH studies", but no timeline was provided

AFME INSIGHTS

MedLumics co-sponsored with Galaxy Medical the "One-Day PFA School" that occurred in conjunction with ESC in 2022.

MEDTRONIC CARDIAC ABLATION SOLUTIONS

Medtronic Cardiac Ablation Solutions – U.S. Website

Summary from AF Symposium

The Medtronic Affera catheters were presented multiple times and referenced throughout the symposium. Pre-recorded cases were presented with both the large tip "Sphere9"catheter and the single-shot "SpherePVI" catheter. Both catheters are fully integrated with the Affera mapping system. Several physicians referenced the upcoming PulseSelect data presentation at ACC, which will results from the first completed IDE trial with PFA. Dr. Mansour also said the internally-developed PulseSelect would "soon" be integrated with the recently-acquired Affera mapping system. DiamondTemp was featured in three posters, but the impact was low – one reported results in flutter patients and one focused on legacy benchtop data.

Details from Congress Events

Organized by Product

Affera Sphere9

- **Pre-Recorded Case: Pulsed Field Ablation for AF Using a 9mm Lattice-Tip Catheter PFA Sphere (Affera/Medtronic)**
  Moussa Mansour, MD, Massachusetts General Hospital, Boston, MA
  - The MDT Affera Sphere9 catheter was used in this case, along with an Agilis sheath
  - Sphere9 can map and ablate with the same electrodes, and pacing is also available
  - Both RF and PF delivery available
  - One feature of the mapping system is the automatic filtering out of PAC's and changes in rhythm during map creation
    - This feature enables map creation without significant editing
  - The mapping system is a sensor-based magnetic mapping system
    - The Sphere9 catheter has 2 sensors, one distal and one proximal
  - In this case, Dr. Mansour showed how it is possible to pace from the catheter in order to identify the location of the phrenic nerve, which was then tagged on the map
    - Dr. Reddy commented how important it is to tag the phrenic nerve when using RF
  - Dr. Mansour said he believes that eventually there will be no benefit to using RF
  - Catheter is able to assess contact – a white dot on the tip of the basket changes in size to indicate contact quality
  - Lesion assessment algorithm can be set to user preferences, i.e. set own parameters for the tags
    - The algorithm is based on temperature from the electrodes and distance between lesions
    - If the line between tags on the map is blue, then the distance between lesions exceeds the defined parameters – must go back and ablate in this case
  - Dr. Reddy referenced a paper in JACC EP that is still in press that describes the commercial use with PFA

- In this paper, 2/6 patients with CTI line also had ST elevations, which was presumed to be spasm
  - One of the patients fibrillated but both fully recovered
    - No further details on this paper were provided by Dr. Reddy

- Dr. Mansour did an MI line in this case and is doing more now
  - Why? Dr. Valderrabano's paper on Vein of Marshall ablation showed superiority
  - Plus, with this catheter, the MI line is easy, so he does it
- Activation is displayed on the map <u>while</u> mapping is done so the operator does not have to wait
  - Dr. Mansour said this was another nice feature of the mapping system

Pulsed Field Ablation Systems: Safety, Effectiveness, and Regulatory Status

Moussa Mansour, MD

Dr. Mansour's presentation contained updates on multiple technologies (BSX FaraWave, MDT PulseSelect, MDT Affera, BWI VARIPULSE, Kardium, Galaxy Medical, Adagio Medical, and Acutus Medical). Notes for each technology are included in the respective company sections in this report.

- <u>Medtronic – Affera</u>
  - Two catheters have been developed by Medtronic Affera: Sphere9 and SpherePVI
  - Fully integrated with proprietary mapping system
  - U.S. IDE for Sphere9 in PsAF patients has completed enrollment

Future Directions in Pulsed Field Ablation

Vivek Reddy, MD

Dr. Reddy's presentation contained updates on multiple technologies. Notes for each technology are included in the respective company sections in this report.

- The agenda for Dr. Reddy's presentation included the following topics:
  - PFA + EAM
  - "Field Bending"
  - PFCA
  - Nanosecond PFA
  - LAAC + LAAEI
- <u>PF Mapping – MDT Affera Sphere9</u>
  - Dr. Reddy finished his presentation with case examples of PF mapping using Sphere9
    - This topic has been presented many times over the last few years
  - Delivering a sub-therapeutic dose of PF allows operators to assess location prior to delivering therapy

Clinical Outcomes with Focal Pulsed Field Ablation Systems

Andrea Natale, MD

Dr. Natale's presentation contained updates on multiple technologies (BWI, Galaxy Medical, and MDT Affera). Notes for each technology are included in the respective company sections in this report.

- <u>Medtronic Affera Sphere9</u>
  - Dr. Natale presented a broad overview of the technology and emphasized the importance of "stacking" the lesions as close together as possible

- Data under review from Dr. Reddy et al were presented showing 1-year clinical outcomes with Sphere9
  - A total of 178 patients were treated with both RF/PF and PF/PF using three different waveforms
  - Across all patients, 1-year freedom from AF/AFL/AT was 78.1%, which was similar for both PAF patients (78.3%) and PsAF (77.9%)
    - Results were also similar across energy modalities, with success in the PF/PF cohort of 77.3% and in the RF/PF group, success was 79.1%
  - Dr. Natale singled out one KM curve for the PsAF cohort treated with only the PULSE3 waveform (optimized waveform)
    - Efficacy at one year in the cohort was 84.8%
- In his conclusion, Dr. Natale emphasized that remapping studies are essential for every system in order to optimize the dose

Pulsed Field Ablation Beyond the Pulmonary Veins: Posterior Wall and Mitral Isthmus Ablation

Ante Anic, MD

- Dr. Anic presented an extensive review of prior publications on PFA, with multiple technologies
- A series of slides illustrated the use of Medtronic Affera Sphere9 catheter for PVI + MI + PWI
- When discussing PFA for MI, Dr. Anic said coronary spasm is completely preventable by using nitro, but operators must not forget to use it
  - For MI, focal PFA catheters are better options vs. single shot designs

Affera SpherePVI

Pre Recorded Case: Pulsed Field Ablation for AF Using a Large Diameter Lattice-Tip Catheter (Affera/Medtronic)

Vivek Reddy, MD & Petr Neuzil, MD, PhD, Homolka Hospital, Prague, Czech Republic

- The Affera SpherePVI catheter was used in this pre-recorded case
  - Adjustable diameter catheter up to 35mm, controlled by a slider on the handle
- OTW but it can be moved without wire
- Mapping system is ONLY magnetic – all catheters have a magnetic sensor
  - Two sensors on the catheter, proximal and distal
    - Everything else on the map is interpolated
  - Mapping system is “pretty good”
- Workflow calls for four applications per vein
  - After each application, a green shadow appears on the map to designate where energy was delivered
- The catheter is not rotated between applications because of the design:
  - The catheter has six segments but the whole lattice is one big electrode – ablate from all segments of the catheter on every application

- Dr. Verma asked a question from the floor – which Affera catheter will you use, 9mm ("Sphere9") or PVI ("SpherePVI")?
  - Dr. Reddy – for the first time procedures, singe shot will eventually win
    - 90% of his cases NOW are point by point
    - PVI catheter takes less work and is easier
- Dr. Verma – 9mm catheter allows for flexibility and he will stick with point by point workflow
  - "We will have almost too much choice"
- Question to panel – with 100% durable PVI, what efficacy would you expect?
  - All said ~80%, with range up to 90%
- Dr. Anic – question on application strategy and whether it is consecutive or if there is a break?
  - Dr. Reddy – He does pause between applications because of concern over heat accumulation

PulseSelect

Pulsed Field Ablation Systems: Safety, Effectiveness, and Regulatory Status

Moussa Mansour, MD

Dr. Mansour's presentation contained updates on multiple technologies (BSX FaraWave, MDT PulseSelect, MDT Affera, BWI VARIPULSE, Kardium, Galaxy Medical, Adagio Medical, and Acutus Medical). Notes for each technology are included in the respective company sections in this report.

- Medtronic – PulseSelect
  - PulseSelect is the internally-developed catheter based on the legacy PVAC system
  - Dr. Mansour said this catheter would be integrated with the Affera mapping system "soon"
  - Long term results from the U.S. IDE trial will be presented at ACC 2023 in March

DiamondTemp

Diamond Tip Temperature Controlled Catheter Ablation for AF

Part of the sessions sponsored by Medtronic

Usman Siddiqui, MD

- Medtronic has branded "RealTemp" technology to include (i) temperature controlled ablation, (ii) diamond cooling, and (iii) high resolution electrograms
- Cases with DiamondTemp are heavily dependent on ICE
- Dr. Siddiqui presented multiple case videos, all of which highlighted the use of ICE, the DiamonTemp GUI, and using the catheter with NavX
- A novel ICE stabilization device was presented, designed by the team at Dr. Siddiqui's lab
  - The device appears to be mounted to the patient table and is used to "hold" the ICE catheter in place during a procedure
- The integration with CardioNXT was presented, and this integration has been presented many times before

  - The CardioNXT system displays data from the DiamondTemp console directly onto the CardioNXT map
  - The CardioNXT system also has a feature to auto-tag lesions based on the maximum temperature achieved during RF application
- The DiamondTemp catheter samples temperature 50 times per second

❖ **POSTER: Novel Temperature-Controlled RF Diamond-Tip Ablation System to Treat Atrial Flutter: Acute Results from the DiamondTemp Global Registry**
First Author: Dr. Massimo Tritto
Last Author: Dr. Phillipp Sommer

- The registry is sponsored by Medtronic, and three Medtronic employees are co-authors on this poster
- The poster contained data on 55 cases at 14 sites across 9 countries, all of which used DiamondTemp to treat CTI-dependent atrial flutter
  - Total procedure times were 49 minutes with 14 minutes of fluoro
  - Acute efficacy was achieved in 100% of patients
  - Two adverse events were reported: one groin hematoma and one AT prior to discharge

AFME INSIGHTS

Results in treating atrial flutter are not typically presented at industry congresses as the focus of these events tends to be treating AF and VT

❖ **POSTER: Characterizing Lesion Morphology of a Novel Diamond-Tip Temperature-Controlled Irrigated RF Ablation Catheter**
First Author: Dr. Tarvinder Dhanjal
Last Author: Michael Getman, MS

- Two co-authors are Medtronic employees, including the last author
- The poster reported on a benchtop model that investigated lesion morphology in excised porcine endocardium
- According to these data, it takes just 10 seconds to create a lesion with a width of 6.1mm and a depth of 2.9mm
  - Target temperature was set at 60°C with a maximum power of 50W
  - After 60 seconds, the average lesion was 5.6mm deep and 7.1mm wide

AFME INSIGHTS

The DiamondTemp catheter was approved by the U.S. FDA in January 2021 (press release here). Presentation of benchtop data two years after regulatory approval is not typically seen.

❖ **POSTER: HPSD Integrated with Novel 3D Mapping and Navigation**
First Author: Dr. Usman Siddiqui
Last Author: Dr. Petr Neuzil
This poster is included in the company sections for both CardioNXT and Medtronic CAS

- This poster reports on the successful integration of the Medtronic DiamondTemp catheter with the iMap system from CardioNXT
  - Two CardioNXT employees are listed as co-authors
- The poster noted that DiamondTemp can only be visualized on two systems, CardioNXT and EnSite Precision from Abbott
- The Abbott system does not localize the tip of the catheter, which could cause accuracy to be off by as much as 1.1mm
- A total of 48 patients were treated with the DiamondTemp catheter being navigated with CardioNXT iMap
- iMap also displays data from the DiamondTemp generator in real-time, including temperature

- When used with DiamondTemp, iMap also provides automatic lesion tags after each ablation, and it is the only system that provides this feature
  - If 50°C is achieved for more than 1 second, a red tag is displayed on the map
  - If 45-50°C is achieved for more than 1 second, the lesion tag is pink

Arctic Front

❖ **POSTER: Cryoballoon Ablation for AF with Lead-Free Zero Fluoroscopy Approach Integrating Pulmonary Vein Hemodynamics, Intracardiac Imaging, and 3D Mapping: A Four Year Single Center Experience**
First Author: Brandon Doty
Last Author: Dr. Devi Nair

- St. Bernards Healthcare in Jonesboro, AR reported data for this poster
- The zero-fluoro workflow includes ICE guidance for transseptal puncture, occlusion assessment using ICE and color flow, and 3D mapping to confirm PVI, among other steps
- The poster reported on a retrospective analysis of 433 cases
  - Mean procedure times were 49 minutes and mean LA dwell time was 36 minutes
  - Procedural complication rates were reported as follows:
    - Effusions 0.6%
    - Phrenic nerve dysfunction 1.3%
    - Phrenic nerve palsy 0.8%
    - Esophageal injury 0%
    - All cause mortality 0.5%

AcQCross

Acquired from Acutus Medical in 2022

❖ **POSTER: Comparison of Transseptal Puncture Using a Dedicated RF Wire System Versus a Deployable Mechanical Needle With and Without Electrification**
First Author: Dr. Jeremiah Wasserlauf
Last Author: Dr. Bradley Knight

- A co-author on this poster is employed by Boston Scientific
- The ex-vivo animal studies in this poster investigated the VersaCross system from Boston Scientific Baylis Medical vs. the AcQCross System recently purchased by Medtronic from Acutus
- The BSX VersaCross system includes a dedicated sheath and RF generator, while the AcQCross system uses a standard electrosurgical generator
- The poster concluded that VersaCross showed superior safety and efficacy in achieving transseptal puncture as compared to the AcQCross system
  - Using the electrified AcQCross needle required twice the applications and additional power vs. VersaCross
  - Tissue coring was seen in 50% of the AcQCross TSPs
  - Using the mechanical AcQCross approach required 6x more force than using RF puncture with VersaCross

PHILIPS EPD SOLUTIONS

- **Highlights of the Latest Advances in the Philips KODEX-EPD System (EPD Systems-A Philips Company)**
  Andreas Rillig, MD
  - This presentation title was included in the agenda but did not occur
  - Press reports indicated that Philips decided to shut down the EPD Solutions organization
    - One article on this development can be found here

PULSE BIOSCIENCES

Pulse Biosciences Website

Summary from AF Symposium

PFA technology from Pulse Biosciences was presented publicly for the first time at AFS. Pulse is a small publicly traded company (PLSE) that has developed proprietary nano-pulse IRE technologies originally targeted for applications in dermatology. In November 2022, the company announced a shift in corporate strategy to focus on cardiac ablation (press release here). During AFS, Dr. Vivek Reddy presented the "nsPFA" system, which includes a new catheter design. A poster also showed that successful integration of this catheter with the CardioNXT iMap system has already been achieved. Preclinical work has been completed but no timelines were provided for FIM.

Details from Congress Events

Future Directions in Pulsed Field Ablation

Vivek Reddy, MD

Dr. Reddy's presentation contained updates on multiple technologies (ABT PFA, Field Medical, Adagio Medical, and Pulse Biosciences). Notes for each technology are included in the respective company sections in this report.

- The agenda for Dr. Reddy's presentation included the following topics:
  - PFA + EAM
  - "Field Bending"
  - PFCA
  - Nanosecond PFA
  - LAAC + LAAEI
- Pulse Biosciences
  - All current PFA systems are working on the scale of micro-seconds, according to Dr. Reddy
  - A novel system is delivering pulses in duration of nano-seconds, "nsPFA"
  - A catheter image was presented and also shown displayed on a mapping system (see note to the right)
  - The catheter has five splines and looked like a PentaRay that is completely flat against the tissue
    - Two concentric circles connect all five splines
  - nsPFA has been cleared by FDA for applications in dermatology and elsewhere but it is not approved for cardiac ablation
  - Pre-clinical work completed by Dr. Koruth at Mt. Sinai showed lesion depths up to 8mm are achievable with this system

AFME INSIGHTS

Based on the separate press release issued jointly by CardioNXT and Pulse Biosciences, the mapping system in Dr. Reddy's presentation is assumed to be CardioNXT.

- **POSTER: Novel Nanosecond PFA Compatible with 3D Mapping & Navigation System**
  First Author: Ashwin Mathur
  Last Author: Dr. Vivek Reddy
  This poster is included in the company sections for both CardioNXT and Pulse Biosciences
  - Three co-authors are employees of CardioNXT and three co-authors are employees of Pulse Biosciences
  - This poster reports on successful integration of the "nsPFA catheter" from Pulse Biosciences with the iMap system from CardioNXT
    - The "nsPFA catheter" is being presented publicly for the first time at AF Symposium and the integration with CardioNXT has already been completed
  - Current PFA systems in development use pulse durations measured in microseconds, but nsPFA uses pulses measured in nanoseconds
    - Potential advantages include less skeletal muscle contraction and less nerve capture
  - The poster reports on results from nine animal cases in which the nsPFA catheter was fully visualized on the CardioNXT system
    - Accurate tracking and visualization of the catheter orientation was successful

VOLTA MEDICAL

Volta Medical Website

Summary from AF Symposium

Dr. John Hummel presented a comprehensive review of the Volta Medical technology that included discussion of a new module in development, "AF-Xplorer". This module will include auto-tagging when used with EnSite X and it will also include integration with BWI's OctaRay catheter. Regulatory timelines were not presented. In a separate press release, Volta announced completed enrollment for the TAILORED-AF trial, a multi-center RCT that included 370 patients. The company is planning two additional trials – RESTART for redo procedures and a clinical registry. Across these three trials, over 960 patients will be enrolled.

Details from Congress Events

- **SPOTLIGHT SESSION: Software and Clinical Update on Volta AI Technology for Complex AF (Volta Medical)**
  John Hummel, MD
  - Early publication on the Volta technology was presented – Seitz et al, JACC EP 2017 (full publication can be found here)
  - VX1 software analyzes data from four standard mapping catheters (Lasso, HD Grid, PentaRay, Orion) to identify ablation targets
  - Ev-AIFib Trial – published last year in JCE (link to full publication can be found here)
    - 85 PsAF patients enrolled across 8 sites and treated by 17 operators using three mapping systems (CARTO, Ensite, Rhythmia)
    - At 12 month follow up, 86% of patients remained free of AF after one procedure, and 54% remained free of AF/AT
  - Clinical trial roadmap for Volta Medical VX1 software:
    - Tailored-AF Trial – multi center randomized controlled trial with 370 patients
      - Prior to the congress, Volta issued a press release announcing completion of enrollment in this trial (press release is here)
    - RESTART Trial – multicenter prospective study with 92pts investigating VX1 in redo procedures
      - This trial is expected to start enrolling soon and the full trial entry can be found here
    - Clinical Registry – targeted enrollment of 500 patients
      - In total, these trials are expected to enroll over 962 patients
  - Pipeline includes "AF-Xplorer" software module:
    - Auto-tagging of the Volta regions of interest on EnSite X
    - Integration with BWI OctaRay
  - This module does not have regulatory clearance in any geography and expected timelines were not provided by Dr. Hummel

OTHER TOPICS

Future Directions in Pulsed Field Ablation

Vivek Reddy, MD

Dr. Reddy's presentation contained updates on multiple technologies. Notes for each technology are included in the respective company sections in this report.

- The agenda for Dr. Reddy's presentation included the following topics:
  - PFA + EAM
  - "Field Bending"
  - PFCA
  - Nanosecond PFA
  - LAAC + LAAEI
- LAAC + LAAEI
  - A technology was described as altering an LAAO device currently in EU trials to enable it to deliver PFA, which would electrically isolate the LAA while also occluding it
    - Dr. Reddy commented that it can be debated whether this should be done but he presented the technology
    - No company was disclosed for this technology, but Aurigen Medical is developing a device that is similar in concept (http://aurigenmedical.com/)
    - Pre clinical work has been completed in 20 animals and acute LAA isolation was achieved in 100% of cases

Same Day Discharge Following AF Ablation: Optimal Workflow, Logistics, & Outcomes

Part of the sessions sponsored by Medtronic

Daryl Wells, MD

- Dr. Wells shared his center's experience with transitioning to same day discharge (SDD) at Swedish Heart and Vascular in Seattle, WA
- The initial target for system-wide SDD after AF ablation was 50%
  - Currently, they send 90% home on the same day
- Dr. Wells said they do not use vessel closure devices, which could make this percentage even higher

Debate: PVI is Sufficient for Catheter Ablation of Persistent AF: Implications of CAPLA vs ERASE AF

Part of the sessions sponsored by Medtronic

Pro: Jonathan Kalman, MD

Con: Andrea Natale, MD

- Dr. Kalman presented a long series of publications showing that PVI alone provides similar results in PsAF patients as PVI plus additional ablations
  - He said the issue is not the procedure but the endpoint – a 30 second burden underestimates procedure success
- Dr. Natale presented many points to support his statement that the CAPLA trial failed due to trial design:
  - Sample size was too low
  - Power setting was too low

- Box lesion strategy has 63% rate of reconnection

Q&A For Medtronic Sessions

- Dr. Natale said his approach for PsAF ablation using PFA instead of RF does NOT work
  - With PFA, lesions need to be stacked, which cannot be done with his approach to PWI that includes many, many ablation points
- Dr. Marrouche to Dr. Siddiqui – would you use DiamondTemp catheter for all RF procedures?
  - Real time visualization with ICE is key
- Dr. Mansour – with SDD data, will AF ablation move out of the hospital?
  - Dr. Wells referenced the recent cuts in physician payments and said they may cause the shift to happen "soon"
  - He also said there are "pockets" of ASC use with cryo and mentioned Alaska – no further details provided
    - Dr. Natale said that PFA will accelerate this trend

Best Abstract Award 2023: Very Long-Term Outcome of Atrial Fibrillation Ablation

Roger A. Winkle, MD

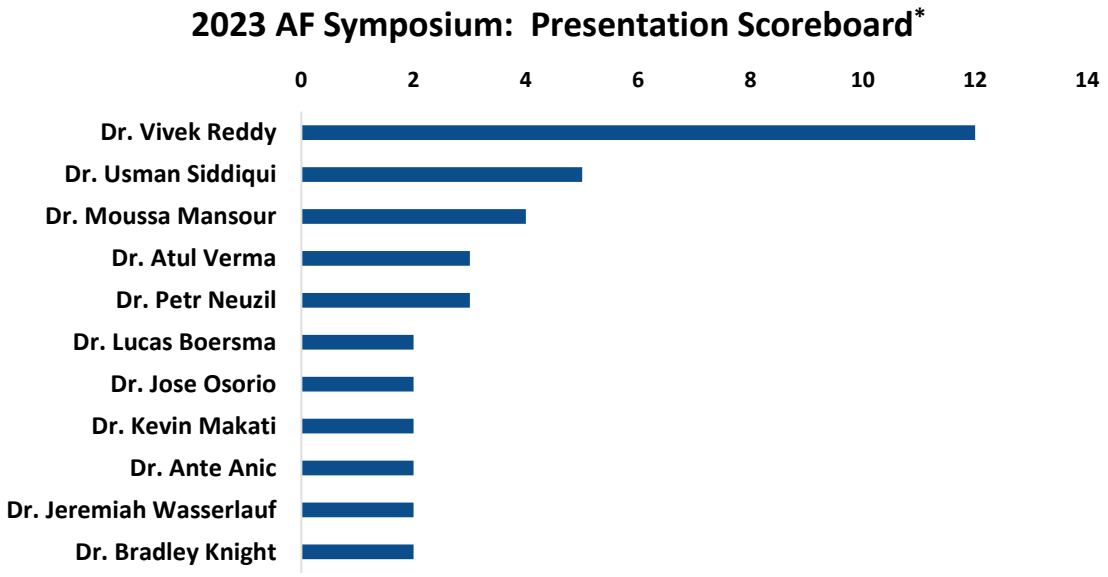
- Long term data set from his site in Palo Alto, CA includes 5,200 consecutive patients who received a total of 7,145 ablations from October 2003 through December 2021
- All procedures done with RF
- In general, his data show about 2% failure per year over time
  - The data also show very little progress in outcomes for long-standing PsAF patients
- At 16 years follow up, success in PAF patients after the initial ablation was ~50%
  - For PsAF, success was less than 30% and for long-standing PsAF, success was below 20%
  - Results were also segmented by catheter type, and contact force technology resulted in better results than both open irrigated (non-contact force) and "solid big tip" catheters
- A total of just 3 patients required tamponade surgery, but Dr. Winkle made a point of saying that all 3 patients would have died if their procedures had been done in the ASC setting
  - See note to the right
- Across eras, there is no statistical difference in the rate of major complications
- Dr. Winkle concluded by saying that we might be bumping up against the limit of AF ablation, even with new tools

AFME INSIGHTS

During the 2023 AF Symposium, the topic of AF ablation in ASCs came up several times, and Dr. Winkle is clearly not in favor of the procedure migrating outside the hospital.

PRESENTATION SCOREBOARD

The "Presentation Scoreboard" tracks the number of times an individual physician is included in this report as either a presenter or an author on a poster.
For poster presentations, only first and last authors are included.
The Scoreboard is updated for each individual congress and also for year-to-date totals in each calendar year.



** A total of 53 individuals are counted with one presentation. Due to formatting constraints, only physicians with more than one presentation are included in this table.*

ABBREVIATIONS & ACRONYMS

ABT	Abbott
ACE	asymptomatic cerebral emboli
AEF	atrial esophageal fistula
AF	atrial fibrillation
BSX	Boston Scientific
BWI	Biosense Webster
CABG	coronary artery bypass graft surgery
CE Mark	Conformite Europeenne
CF	contact force
CMC	circular mapping catheter
CTI	cavotricuspid isthmus
EAM	electroanatomic mapping
EDEL	endoscopically detected esophageal lesion
FDA	Food and Drug Administration
FEM	finite element modeling
FIH	first in human
FIM	first in man
Fr	French
GA	general anesthesia
GUI	graphical user interface
HPSD	high power short duration
ICE	intracardiac echo
KM	Kaplan Meier
LA	left atrium
LV	left ventricle
MDT	Medtronic
MDT CAS	Medtronic Cardiac Ablation Solutions
MI	mitral isthmus
mins	minutes
mos	months
NTG	nitroglycerin
OTW	over the wire
PAF	paroxysmal atrial fibrillation
PFA	pulsed field ablation
PFCA	pulsed field cryoablation
PI	primary investigator
PN	phrenic nerve
PNP	phrenic nerve palsy
PsAF	persistent atrial fibrillation
pts	patients
PVI	pulmonary vein isolation
PWI	posterior wall isolation
RA	right atrium
RV	right ventricle
SAE	serious adverse events
SCE	silent cerebral emboli
SCL	silent cerebral lesion
SDD	same day discharge
SVT	supraventricular tachycardia
TBD	to be determined
TSP	transseptal puncture
TTI	time to isolation
ULTC	ultra low temperature cryoablation
vHPSD	very high power short duration
VT	ventricular tachycardia

AF Market Insights Reports are published by AFME, LLC

www.afmarketexperts.com