ELECTRA

4-5 DÉCEMBRE 202(

**HOTEL VILLA M.
MARSEILLE I FRANCE**

1Ç[èmes] journées françaises
pratiques de rythmologie
& de stimulation cardiaque

**COMITÉ
D'ORGANISATION**

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Maxime GUENOUN, Marseille
Arnaud LAZARUS, Paris
Nicolas LELLOUCHE, Créteil
Jacques MANSOURATI, Brest
Jérôme TAÏEB, Aix-en-Provence

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Apport de l'IA dans le traitement du signal ECG

Théophile Mohr Durdez
CEO, Volta Medical

Persistent atrial fibrillation represents one of the largest unmet needs

75%

of AF patients are persistent AF patients[1] but they represent < 33% of AF ablation procedures[2]

50%- 60%

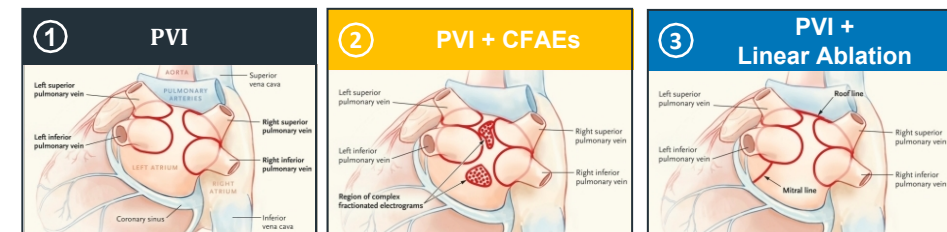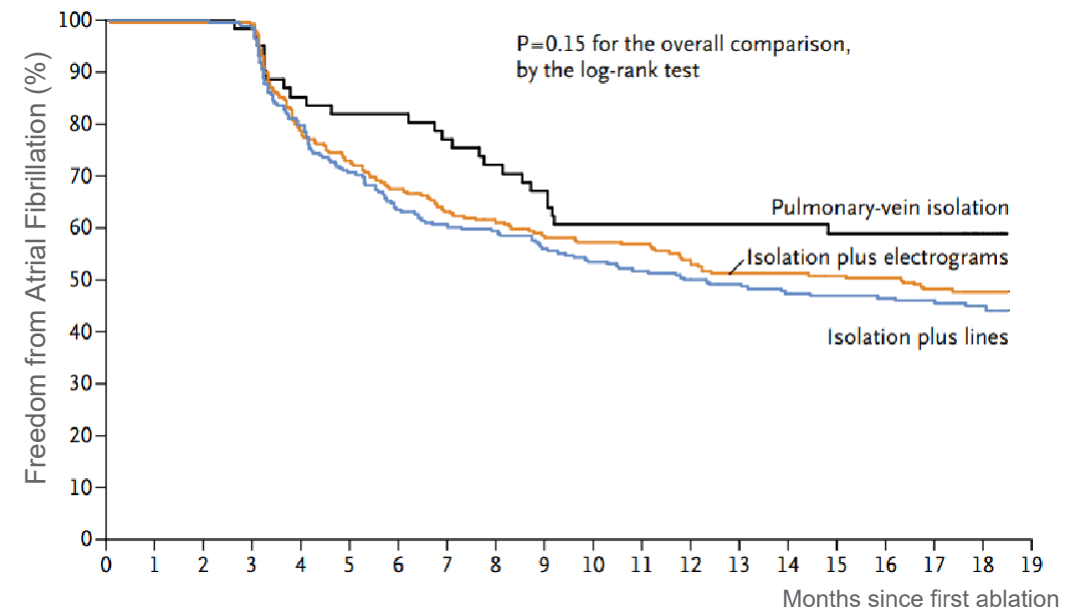Clinical success rates reported in landmark studies for persistent AF[3]

STAR-AF II demonstrated that there is no consistent ablation strategy for persistent AF.[3]

[1]Zoni-Berisso et al. "Epidemiology of atrial fibrillation: European perspective." Clinical epidemiology (2014): 213-220.
[2]Kirchhof et al.. "Catheter ablation in patients with persistent atrial fibrillation." European heart journal 38.1 (2017): 20-26.
[3]Verma, Atul, et al. "Approaches to catheter ablation for persistent atrial fibrillation." New England Journal of Medicine 372.19 (2015): 1812-1822
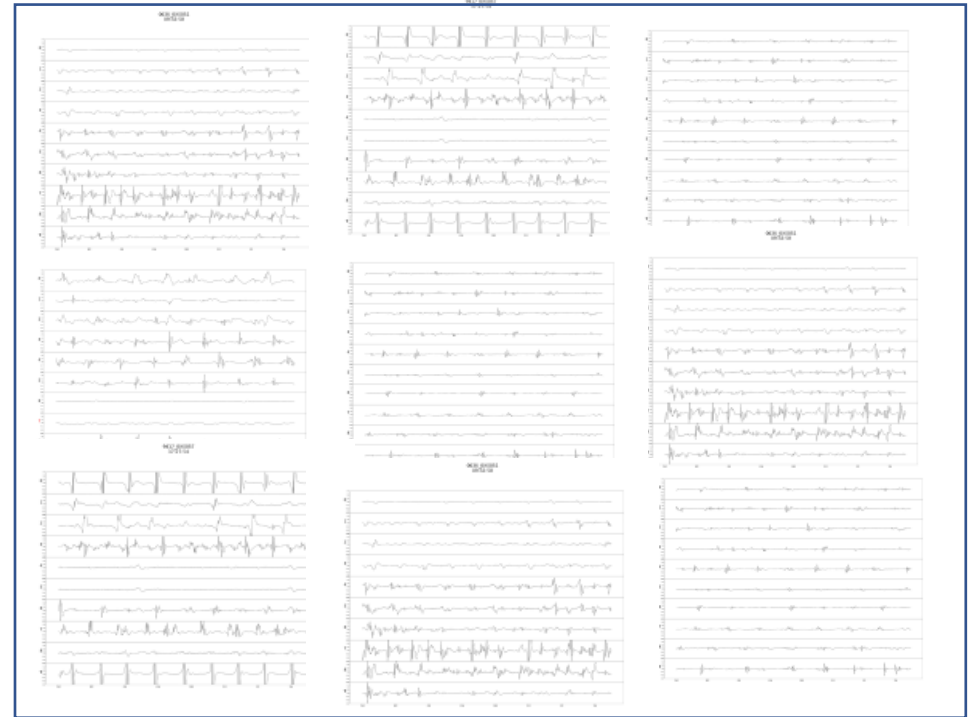
STAR-AF II authors concluded *"**More selective targets** are needed to better characterize an individual patient's specific arrhythmic substrate"*

P=0.15 for the overall comparison, by the log-rank test

Pulmonary-vein isolation
Isolation plus electrograms
Isolation plus lines

Freedom from Atrial Fibrillation (%)

Months since first ablation

① PVI
② PVI + CFAEs
③ PVI + Linear Ablation

VOLTA
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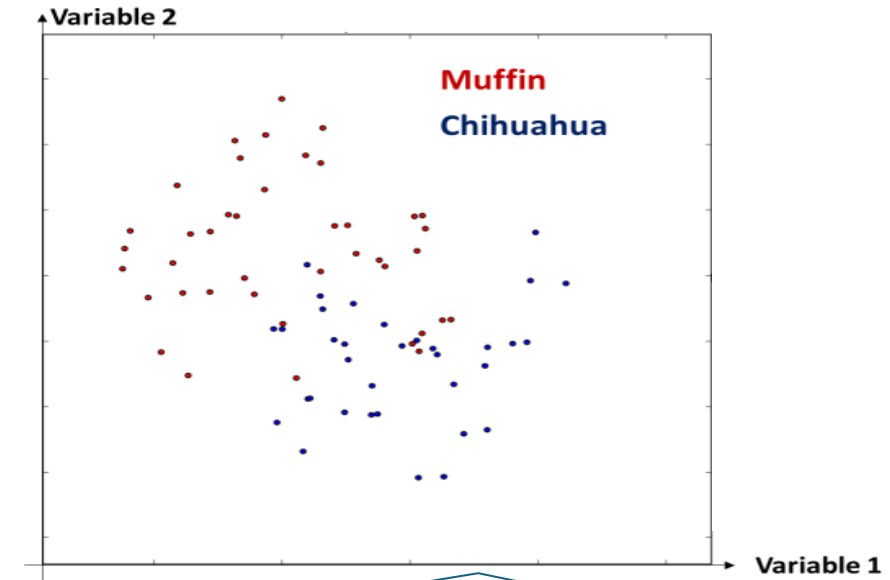# How to automatize complex multiparametric analysis?
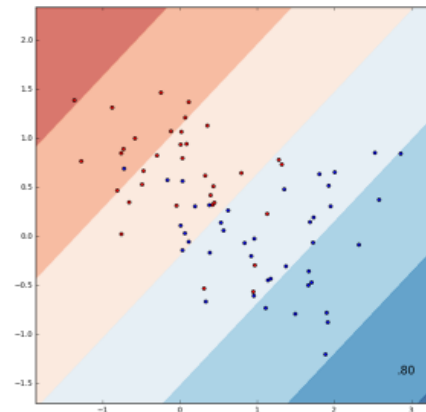

Facial recognition

Intra cardiac EGM analysis

A well trained human brain is very powerful to perform complex multiparametric analysis but it is difficult for conventional algorithms.

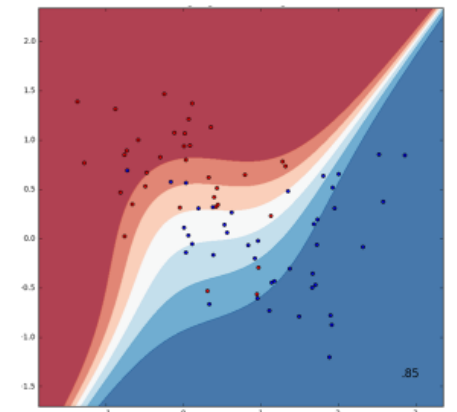# How to automatize complex multiparametric analysis?

Chihuahua or Muffin?

Conventional algorithm:

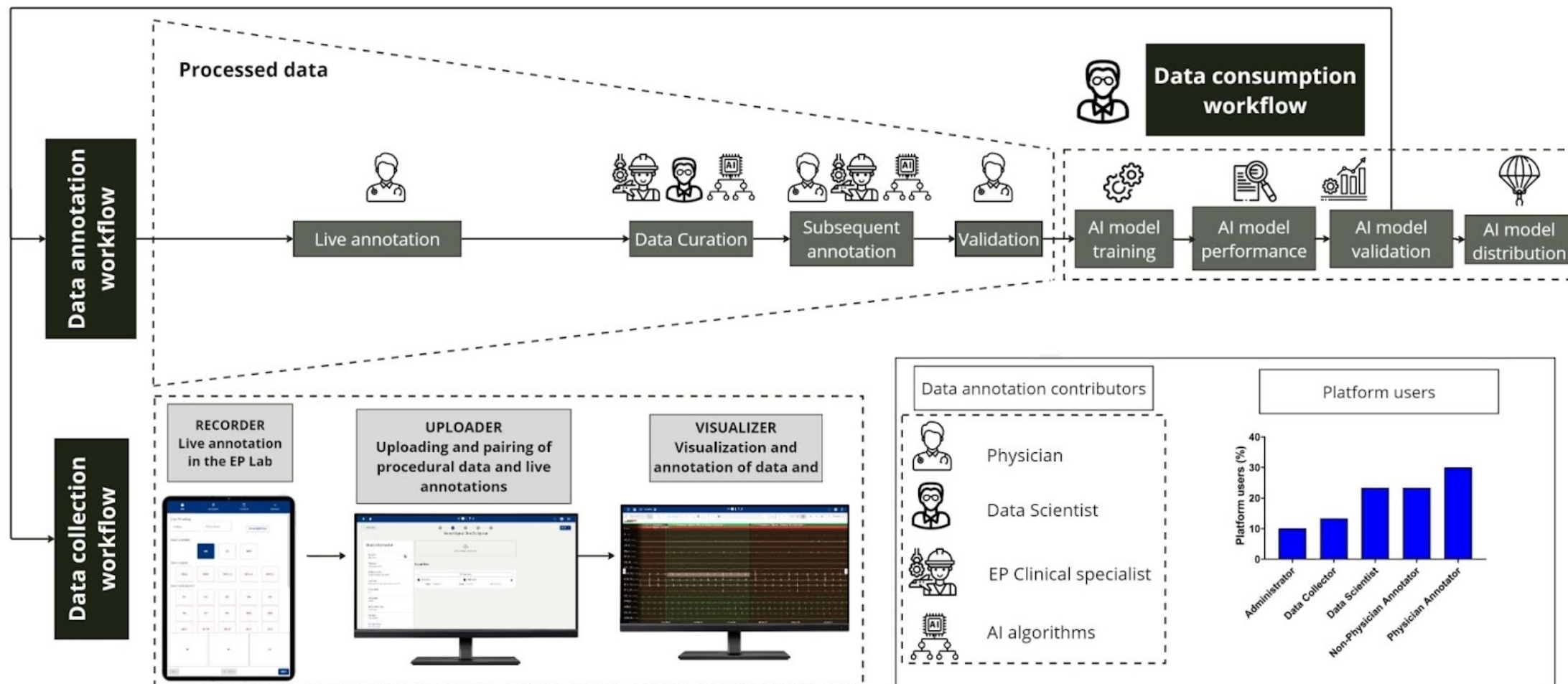(Few) Features & Thresholds are decided by engineers. **Rough boundaries.**

Machine learning algorithm:

Thresholds and a potentially high number of features are automatically extracted from data during training. **Accurate boundaries.**

# Annotation process with the VoltaPlex ecosystem/platform

VoltaPlex Video

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From EGMs Data Management to Enriched Data Ecosystems : Expanding Product Horizons

- Large amount of 3D data collected over the past few years

- Increased mastery of 3D data processing and visualization

- 3D data can be leveraged to :

  o **Offer a better visualization of spatio-temporal dispersion**

  o **Expand our product portfolio**

  o **Strengthening partnerships**
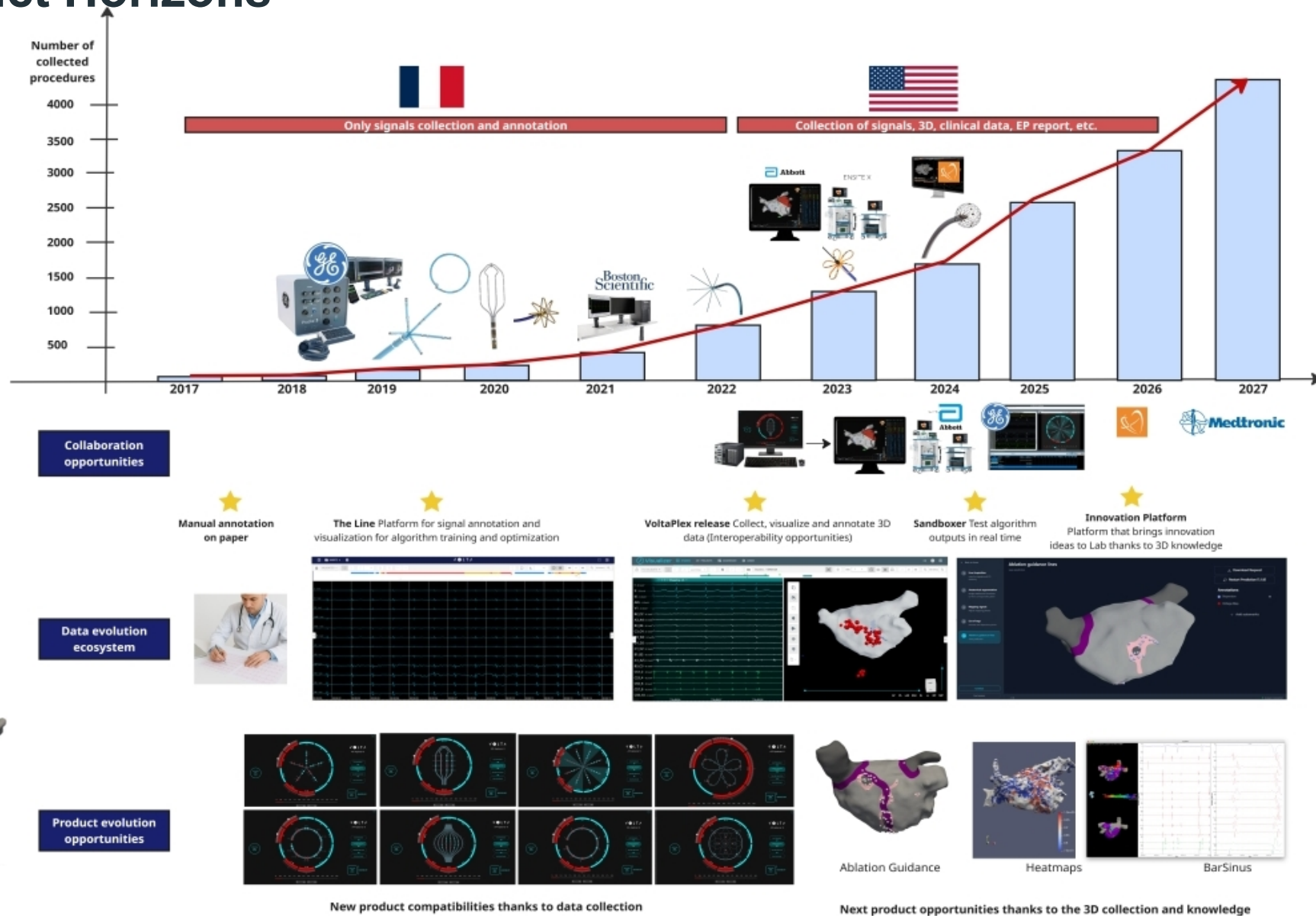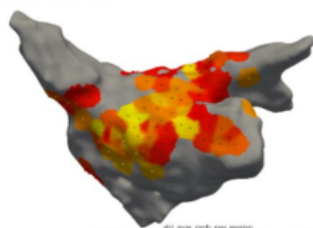
Annotation of dispersed electrograms in procedures that led to termination

Annotation of dispersed electrograms on the VoltaPlex in a region that led to AF termination upon cumulative ablation

INSIDE THE BOX

LARGER & MORE DIVERSIFIED DATABASE

Includes additional cases from EU and US centers annotated by expert electrophysiologists from both geographies

463,610

Annotated EGM samples

Input signal

Trained ML & DL Model

Raw dispersion score p_k

Thresholding

Dispersion detection

Outer frame

Clinical Features

Cycle lengths, activation, fractionation, voltage, spatial components, etc.

Convolutional Features

Classifier

Time & intensity stability analysis

Stability in intensity / Stability in time

Octaray 3-3-3 catheter
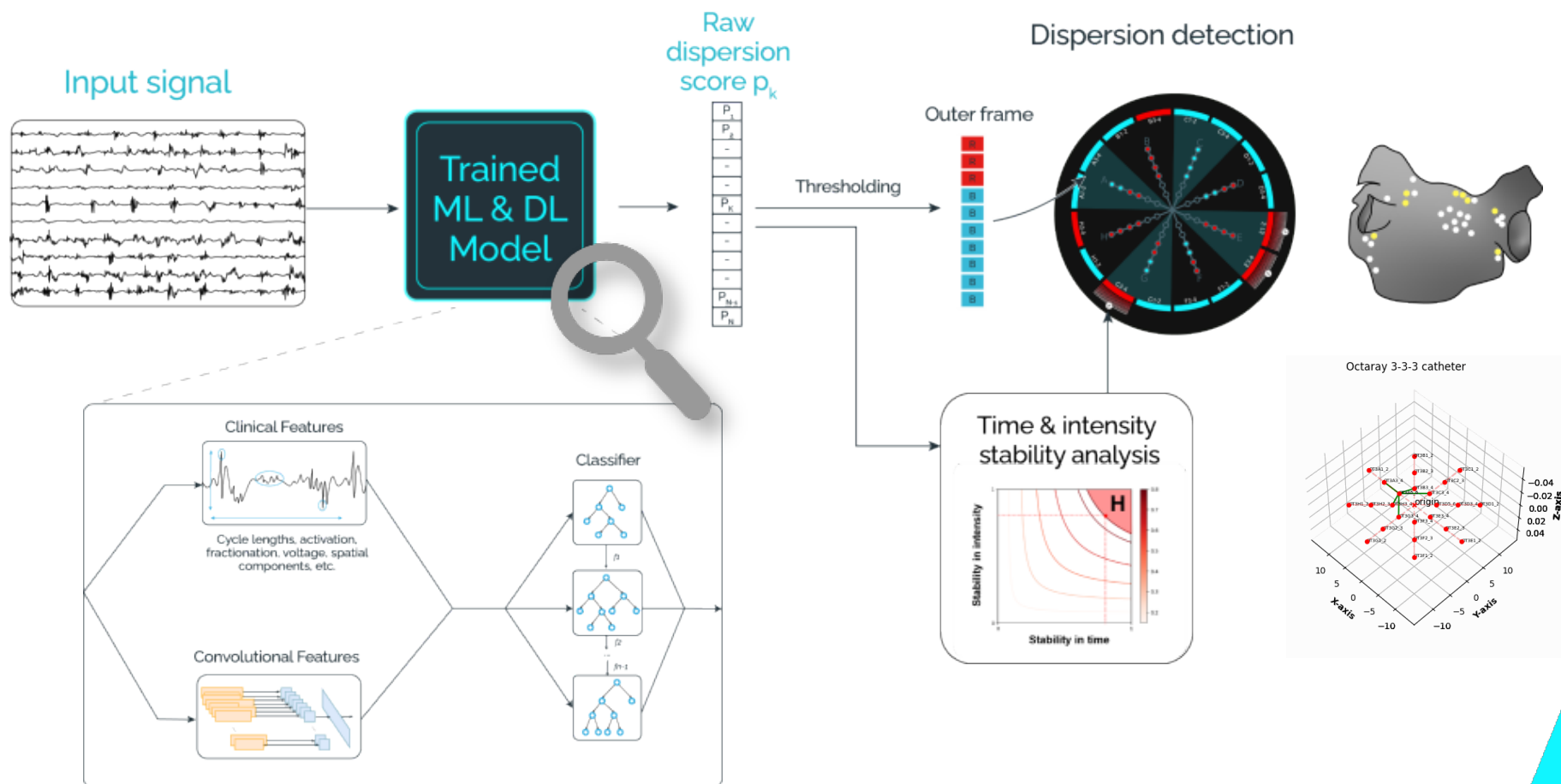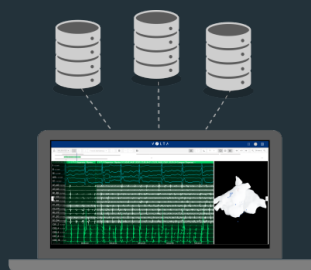
AF-Xplorer II
in Action

3D Mapping System
White and Yellow Dots Correspond to AF-Xplorer II's Tagged Dispersion Areas

Volta AF-Xplorer II
AI Decision Support System Designed to Assess AF and AT Procedures

EP Recording System

Volta's Clinical Evidence Roadmap

Establishing Volta as the Standard of Care in AF

	2017	**2022**	**2024**	**2025**	
	JACC	Journal of Cardiovascular Electrophysiology	nature medicine		
	Published		**Presented at HRS '24 Published in Nature Medicine**	**Results presented at HRS '25**	**Ongoing**
Clinical Study Summary	**Initial Feasibility:** AF Ablation Guided by Spatio-temporal Dispersion w/o PVI	**Volta VX1: Ev-AIFib:** The Preliminary Evaluation of the AI-AF Software Trial	**TAILORED-AF Trial:** Tailored vs. Anatomical Strategy for Persistent AF	**The RESTART Study:** Studying Outcomes for Re-Do AF Procedures	**Clinical Registry** for Patients Treated Using Volta Software
	Multi-Center Prospective Study	**Multi-Center Prospective Study**	**Multi-Center Randomized Controlled Trial**	**Multi-Center Prospective Study**	**Multi-Center Prospective Study**
	3 Sites **105** Patients	**8** Sites **85** Patients	**26** Sites **374** Patients	**21** Sites **92** Patients	**550** Patients
Objective	Spatiotemporal dispersion shows promise in improving ablation efficacy	AF-Xplorer standardizes outcomes across centers	**Volta-guided ablation is superior to standard-of-care for treatment of persistent AF**	**Volta-guided ablation is the best option in subjects presenting with recurrent AF**	**Observe clinical outcomes of Volta's technology in real world situations across multiple centers**

12

TAILORED AF Primary Endpoint Summary

First large RCT to demonstrate superior outcome vs PVI in AF ablation history

88%

70%

Blanking period

nature medicine

Article   https://doi.org/10.1038/s41591-025-03517-w

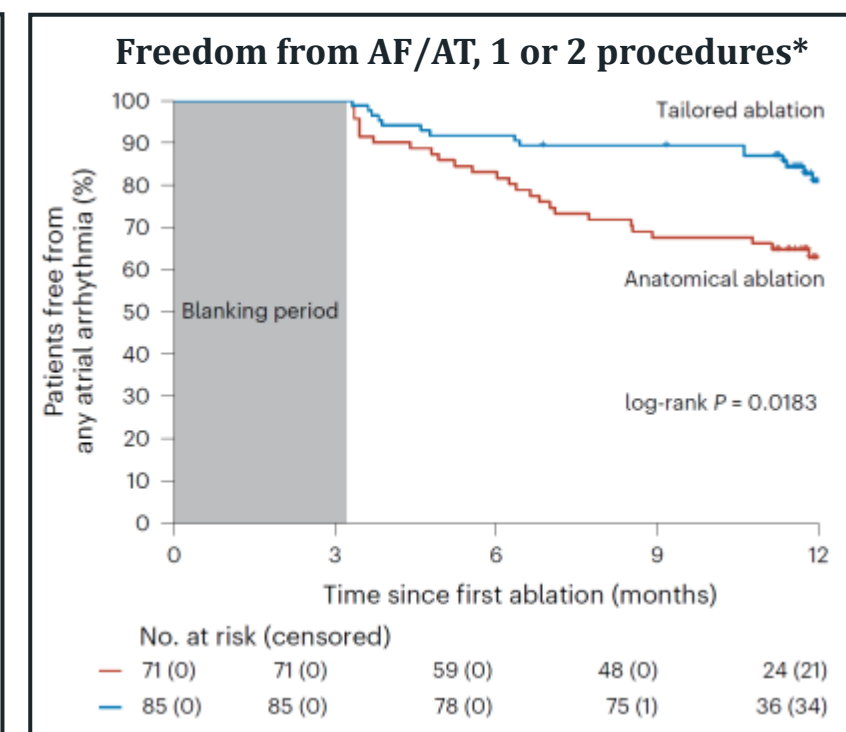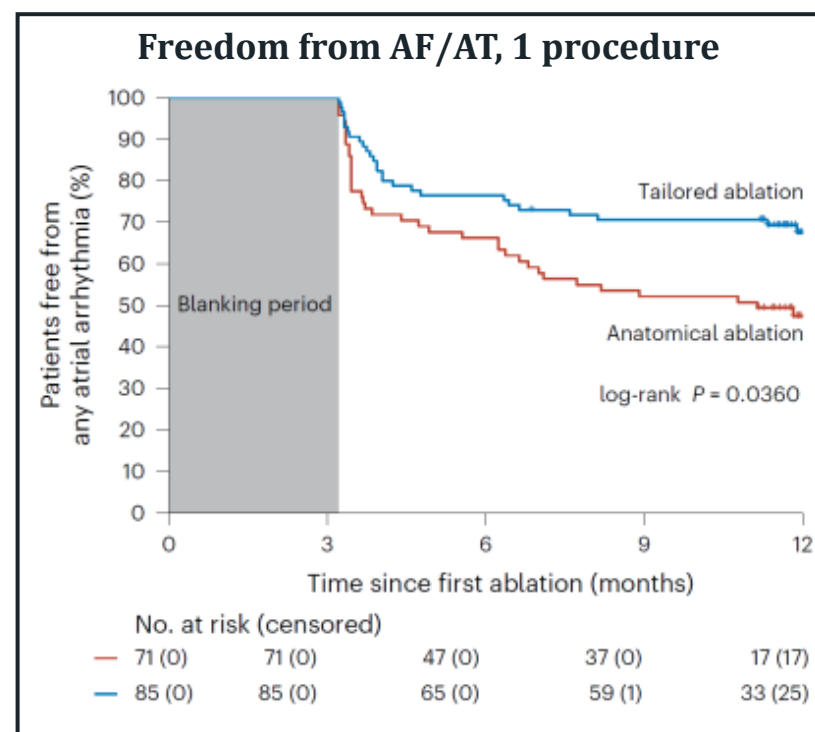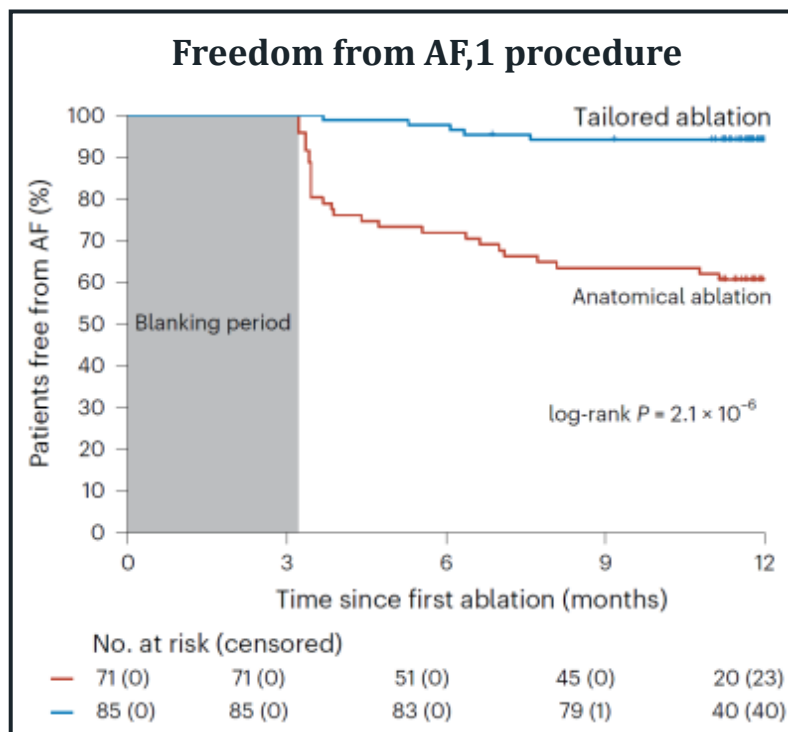**Artificial intelligence for individualized treatment of persistent atrial fibrillation: a randomized controlled trial**

p < 0.0001

13
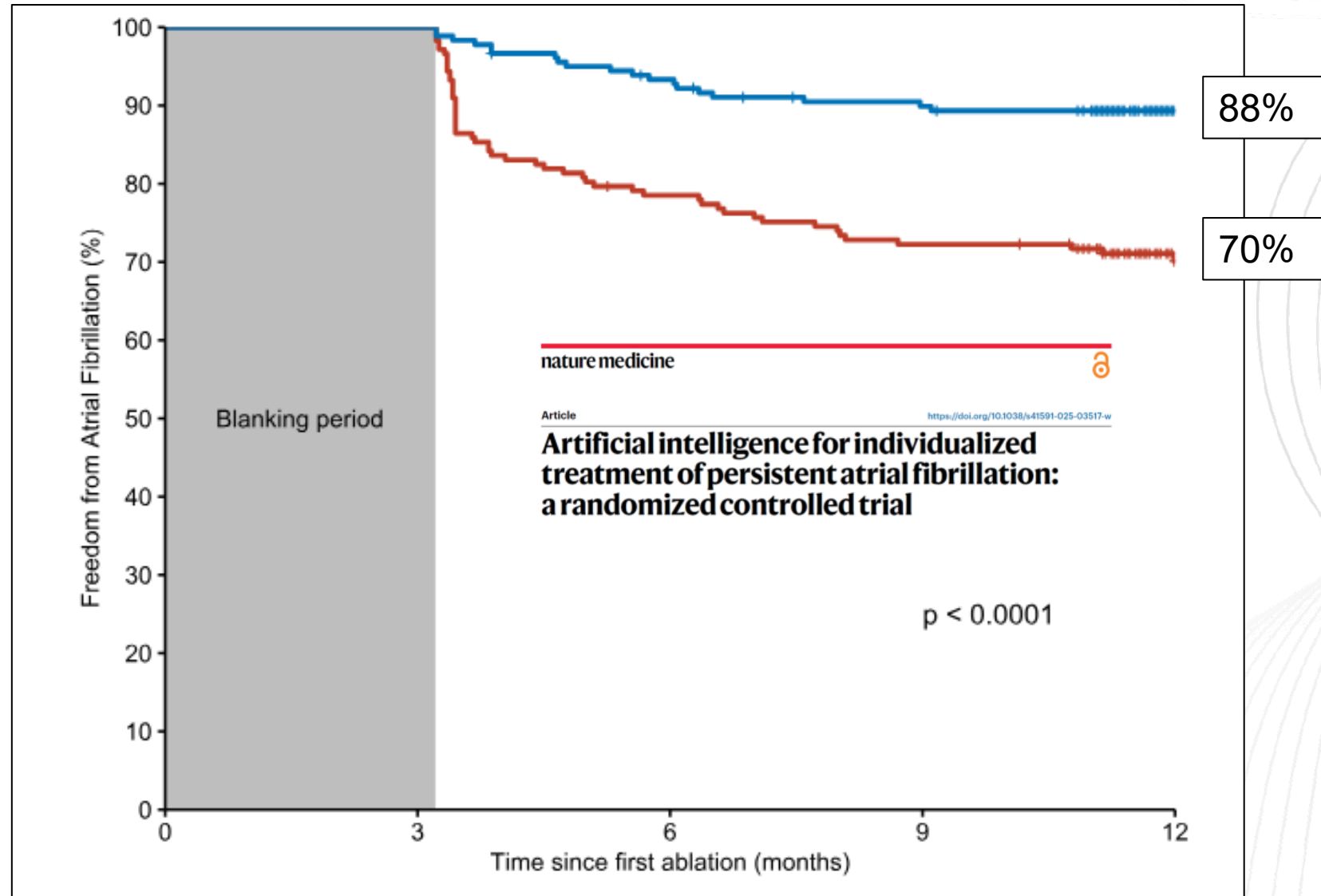
TAILORED-AF : Secondary endpoint

Freedom from any arrhythmia, on/off AADs, at 12 months, per protocol population
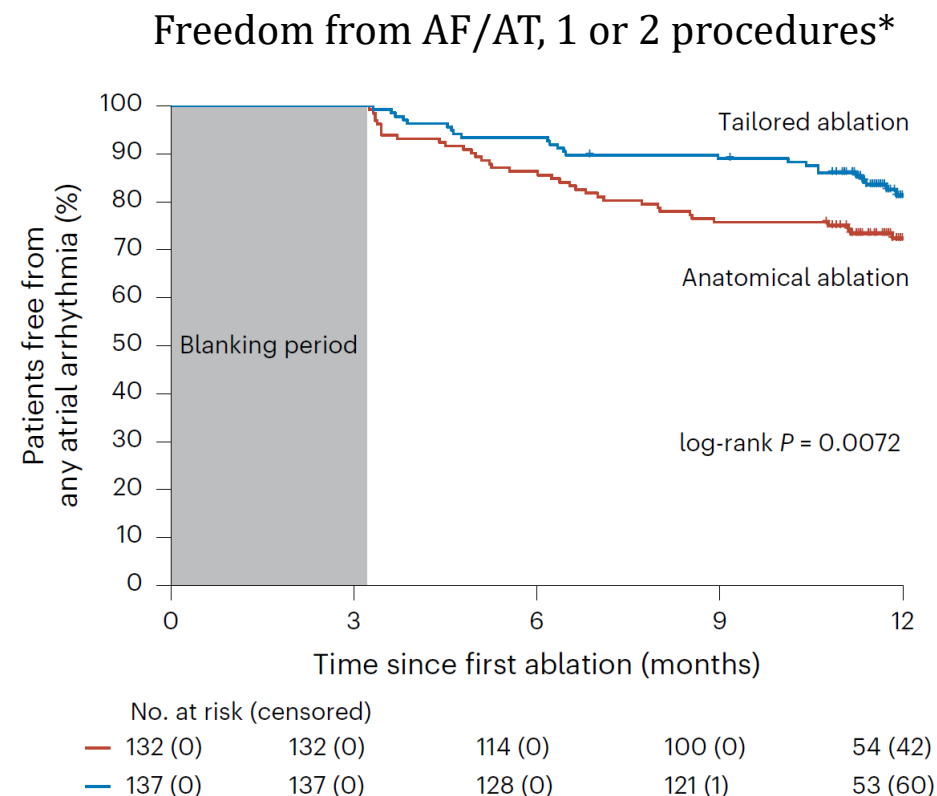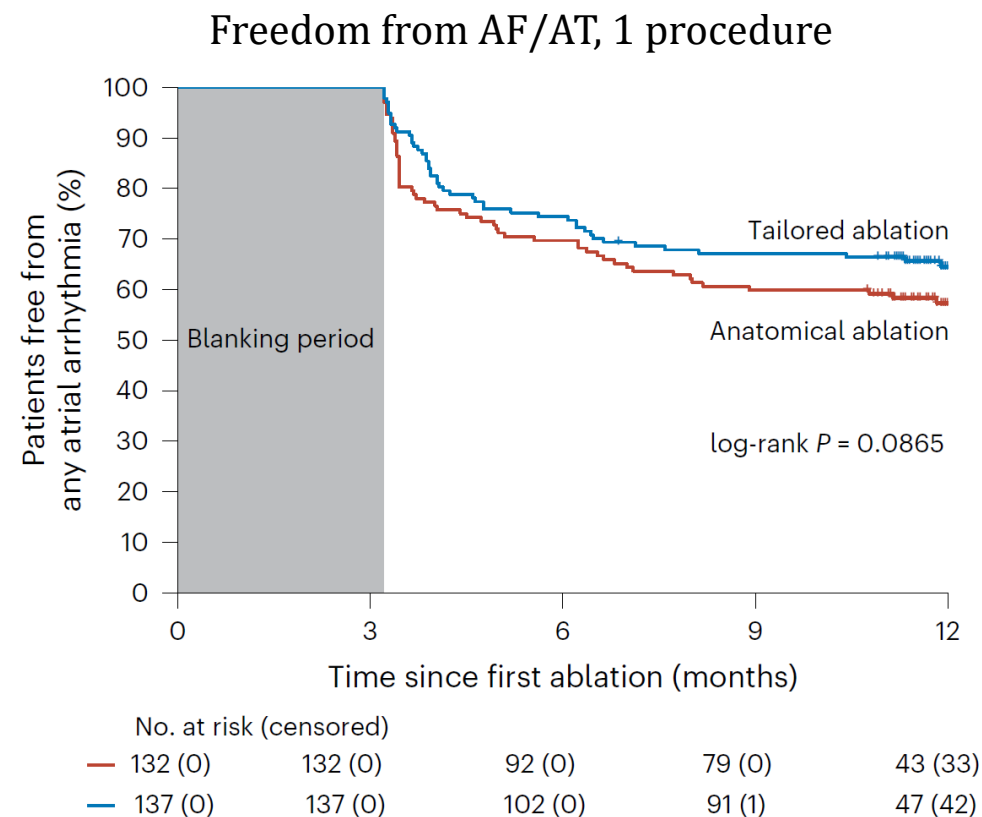
Freedom from AF/AT, 1 procedure

log-rank *P* = 0.0865

No. at risk (censored)

132 (0)	132 (0)	92 (0)	79 (0)	43 (33)
137 (0)	137 (0)	102 (0)	91 (1)	47 (42)

Freedom from AF/AT, 1 or 2 procedures*

log-rank *P* = 0.0072

No. at risk (censored)

|				
132 (0)	132 (0)	114 (0)	100 (0)	54 (42)
137 (0)	137 (0)	128 (0)	121 (1)	53 (60)

Deisenhofer, Isabel, et al. "Artificial intelligence for individualized treatment of persistent atrial fibrillation: a randomized controlled trial." Nature Medicine (2025): 1-8.

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*1.2 procedures/patient

TAILORED-AF : Secondary endpoint

Freedom from arrhythmia, on/off AADs, at 12 months, <u>subjects with AF ≥ 6mo only</u>, per protocol population

Highly significant in prespecified subgroup of patients with persistent AF ≥ 6 months ("truly persistent AF")

Deisenhofer, Isabel, et al. "Artificial intelligence for individualized treatment of persistent atrial fibrillation: a randomized controlled trial." Nature Medicine (2025): 1-8.
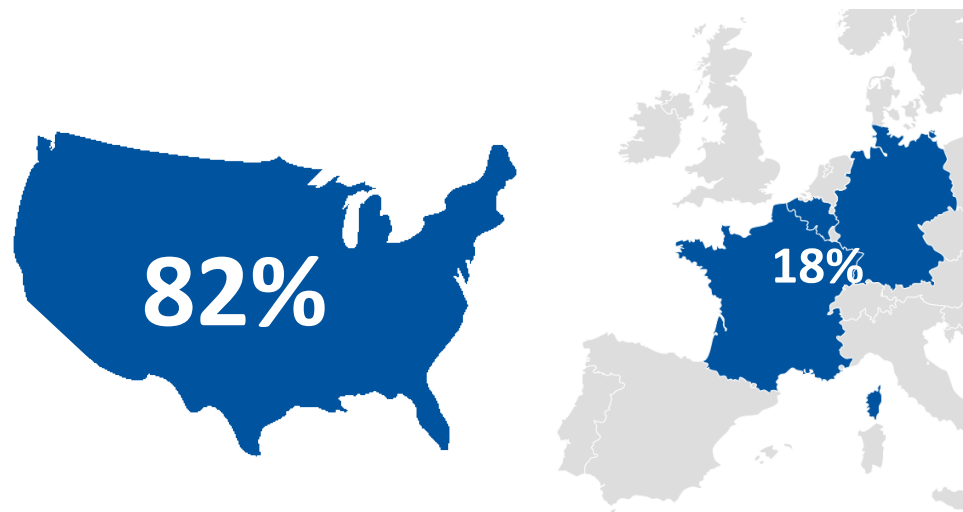
*1.2 procedures/pt

Click to see sub-analysis

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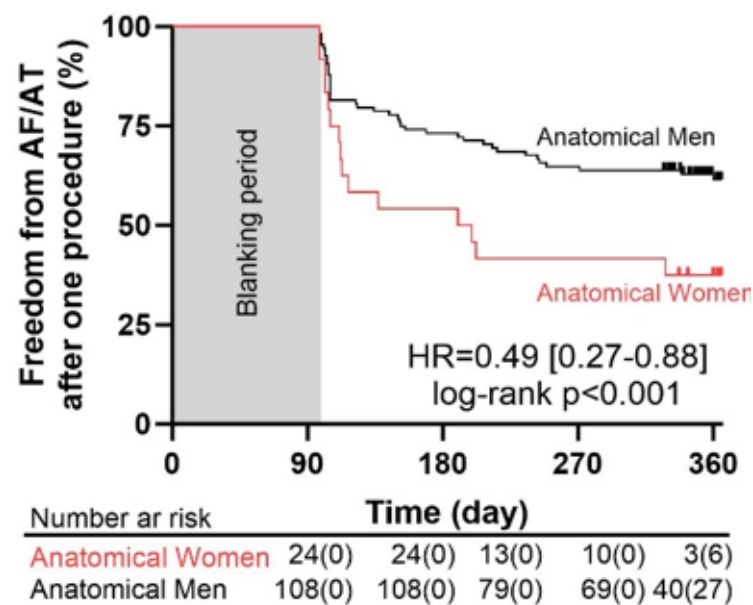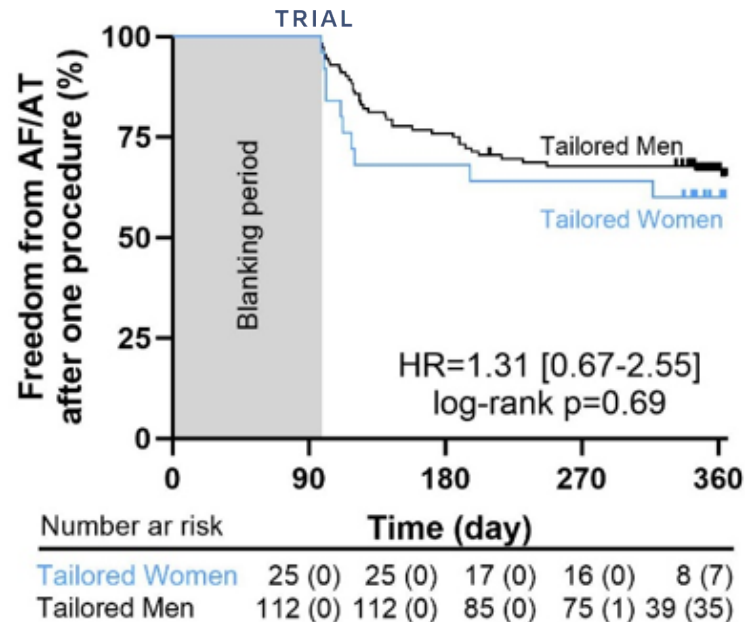
Persistent AF women should get a tailored AI-guided ablation
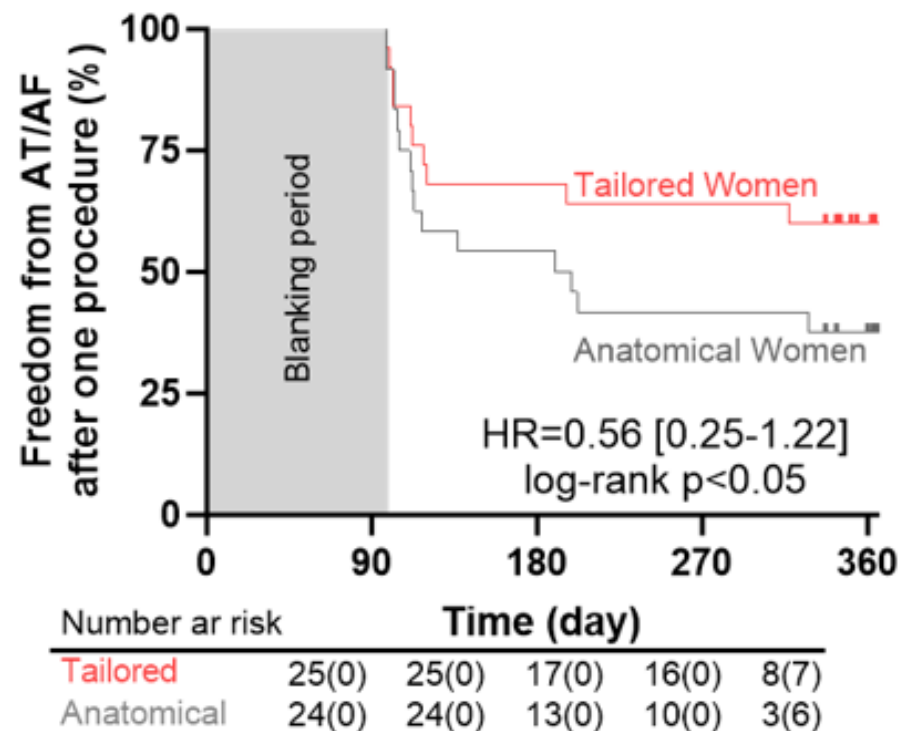
The RESTART trial

- **213 patients consented**
- **29 investigators**
- **20 sites (16 US, 4 EU)**
- **4 countries (82% US patients)**

- **Interventional, single arm, prospective, non-randomized trial**

> **Tailored ablation of AI-detected spatio-temporal dispersion for the treatment of symptomatic AF recurrences in patients with documented isolated PVs**

- **12-month follow-up:**
  - **In-office visits** at 3-, 6- and 12-month
  - **12-lead ECG**
  - **Monitor each F/U: 24-hour (24%) minimum, 2 to 7-day (25%), 14 to 30-day (16%) Holter, cardiac implantable device (26%)**
  - **Quality of life:** AFEQT, SF36
  - **Clinical symptoms**
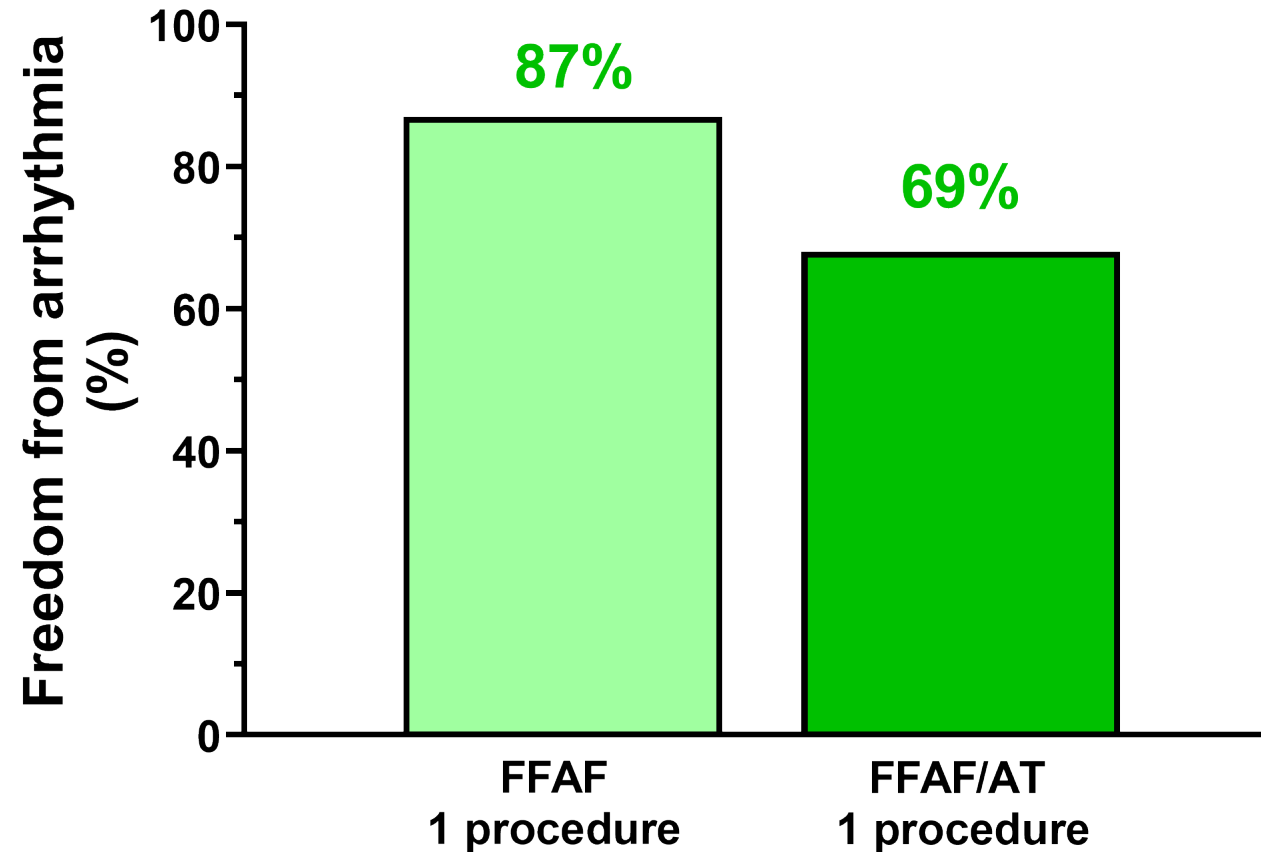
Volta Medical has shown that our solution can increase success in treating these '**complex substrate patients**' in key trials

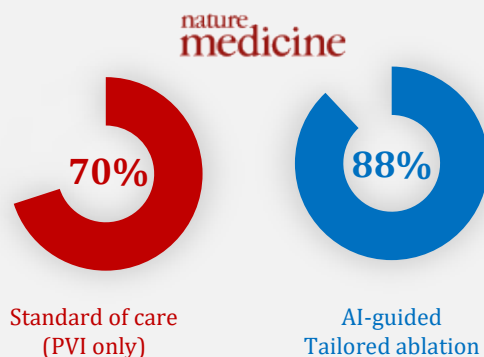## LARGE MARKET, HIGH NEED

The Complex Substrate Patient

PERSISTENT AF

Persistent AF represents 70% of all AF sufferers

Current standard treatment often fails in these patients

The TAILORED-AF Trial RCT

374 patients

26 Sites (8 US, 18 EU)

nature **medicine**

70%
Standard of care (PVI only)

88%
AI-guided Tailored ablation

Freedom from AF, at 12 months after 1 procedure

First large RCT to demonstrate superior outcome vs the standard of care in persistent AF ablation history

WOMEN WITH PERSISTENT AF

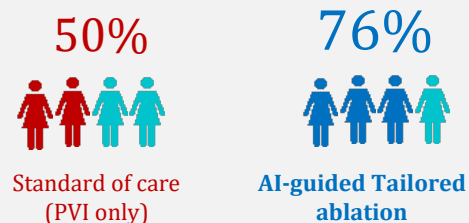Often **more symptomatic** and report **lower quality of life**.

Less likely to **undergo ablation**

Higher AF recurrence levels

Freedom from AF, at 12 months after 1 procedure - Tailored-AF sub-analysis

50%
Standard of care (PVI only)

76%
AI-guided Tailored ablation

Volta improves outcomes after just one procedure in women with persistent AF
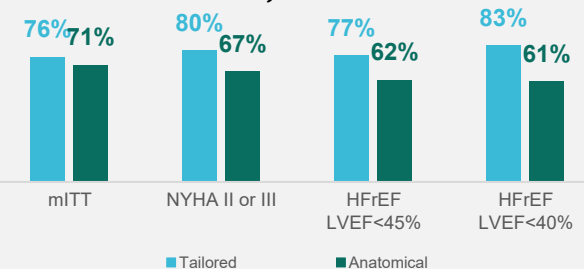
PERSISTENT AF ≥ 6 MONTHS

As AF persists beyond 6 months, outcomes with standard treatment **drop significantly**, while Volta's AI-guided approach maintains **very high success.**

Freedom from AF, at 12 months after 1 procedure - Tailored-AF sub-analysis

Standard of care (PVI)	**61%**
AI-guided Tailored ablation	**91%**

HEART FAILURE

Preliminary subgroup analyses from the TAILORED-AF trial raises the hypothesis that Volta's tailored approach **offers enhanced benefit in patients with heart failure and reduced ejection fraction.**

mITT	NYHA II or III	HFrEF LVEF<45%	HFrEF LVEF<40%
76% 71%	80% 67%	77% 62%	83% 61%

■ Tailored   ■ Anatomical

RE-DO AF PATIENTS WHERE THE STANDARD OF CARE FAILED

The RESTART Trial
Preliminary results presented at HRS 2025

92 patients

20 Sites (16 US, 4 EU)

Patients needing repeat procedures have **no clear treatment path**

Freedom from arrhythmia, at 12 months after 1 procedure - RESTART trial

FFAF	FFAF/AT	FFAF/AT
8	**69%**	PREVIOUS RE-DO TRIALS **39%**
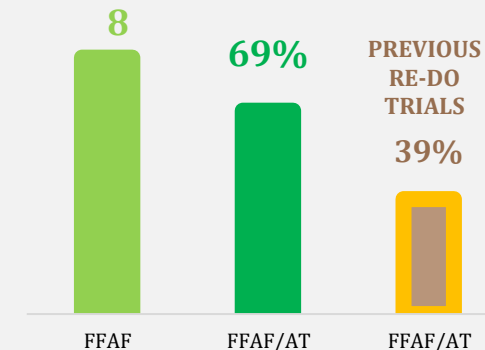
Volta offers a promising approach for re-do patients

Volta Improves Ablation Outcomes for Complex Substrate Patient Populations

Volta's extensive clinical evidence demonstrates its unique ability to treat these patients

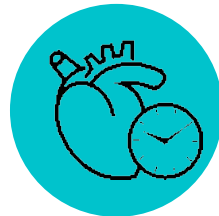COMPLEX SUBSTRATE PATIENTS REPRESENT AFIB's MOST UNDERSERVED COMMUNITIES

| Heart Failure Patients	Persistent AF ≥ 6 months	Women with Persistent AF	Re-do AF Patients with Isolated PVs
TAILORED-AF sub-analysis	TAILORED-AF sub-analysis	TAILORED-AF sub-analysis	The RESTART Trial
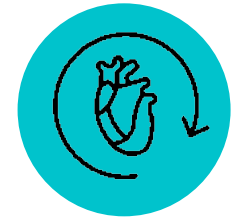
Context

Map with area of interest to be treated
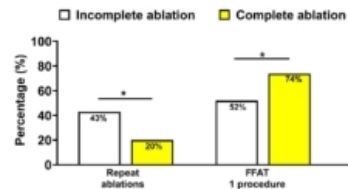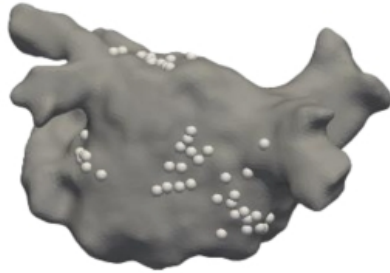
The completeness of the ablation sets are directly correlated with the rate of freedom of any arrythmia

Treatment variability for the same areas of interest
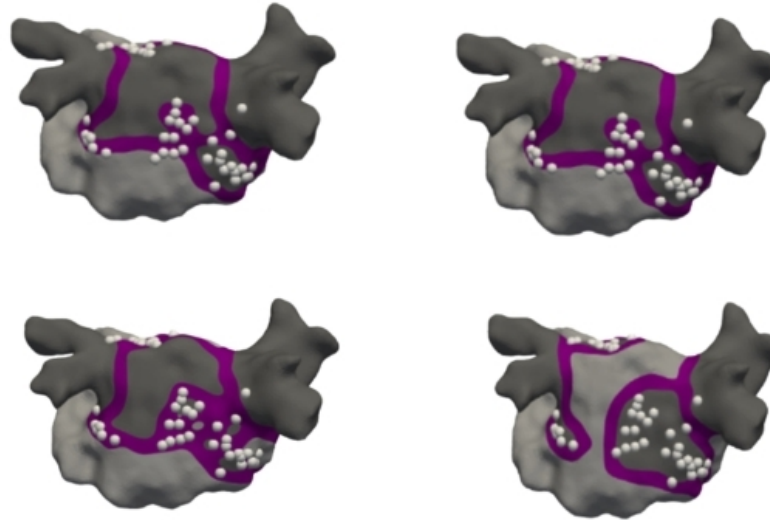
Some operators may not complete their ablation sets resulting in reccurence of arrythmia (either AF or AT)

The variability of treatment leads to varying ablation surfaces, which means that preservation of healthy tissue can be optimized

Standardize treatment
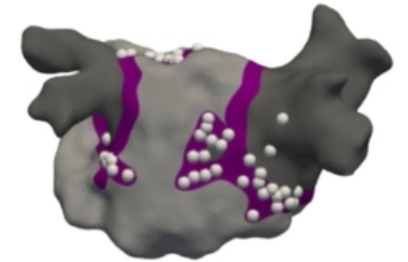
Generate ablation sets across patients in a **standardized manner.**
Equally efficient lesion set, while maximizing preservation of healthy tissue

Ablation guidance prototype (short version)
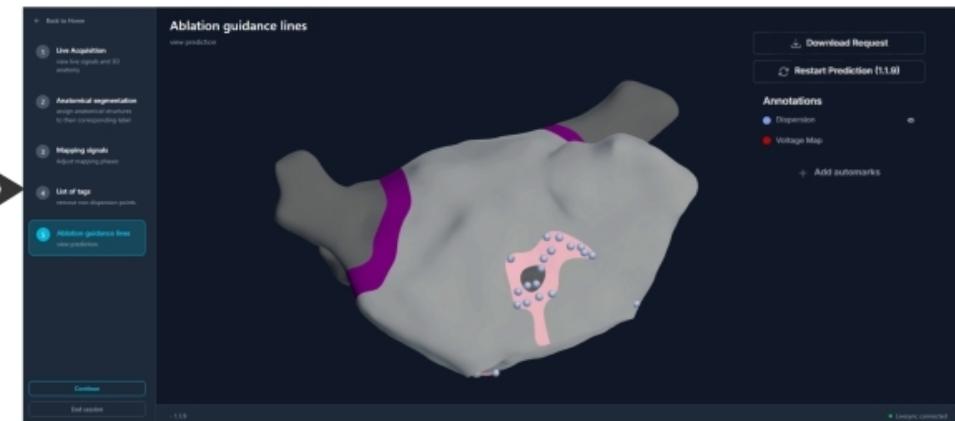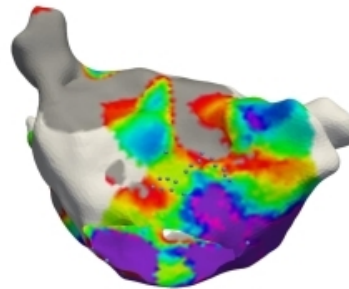
Healthy Tissue preservation

Methodology

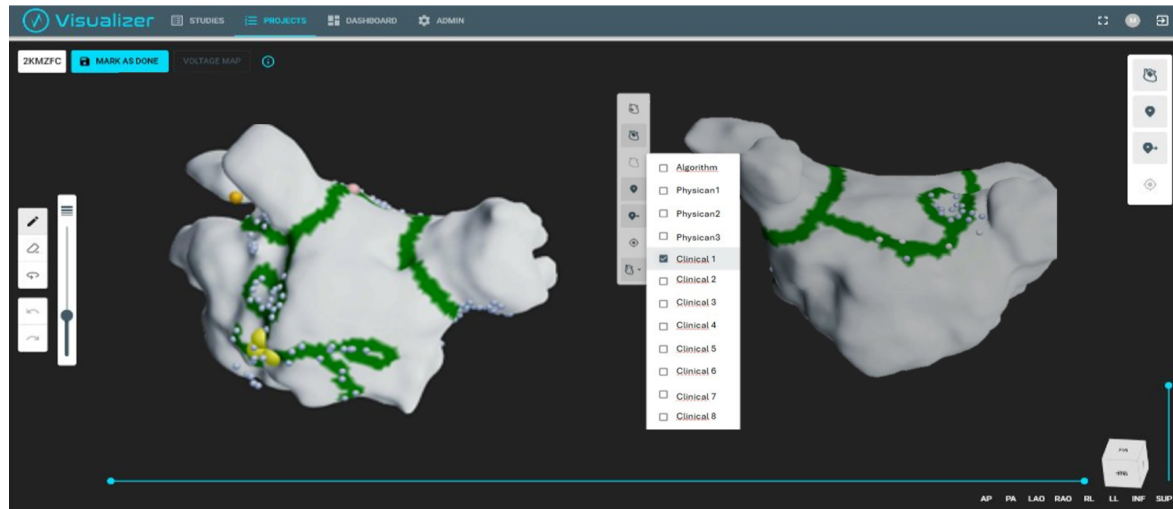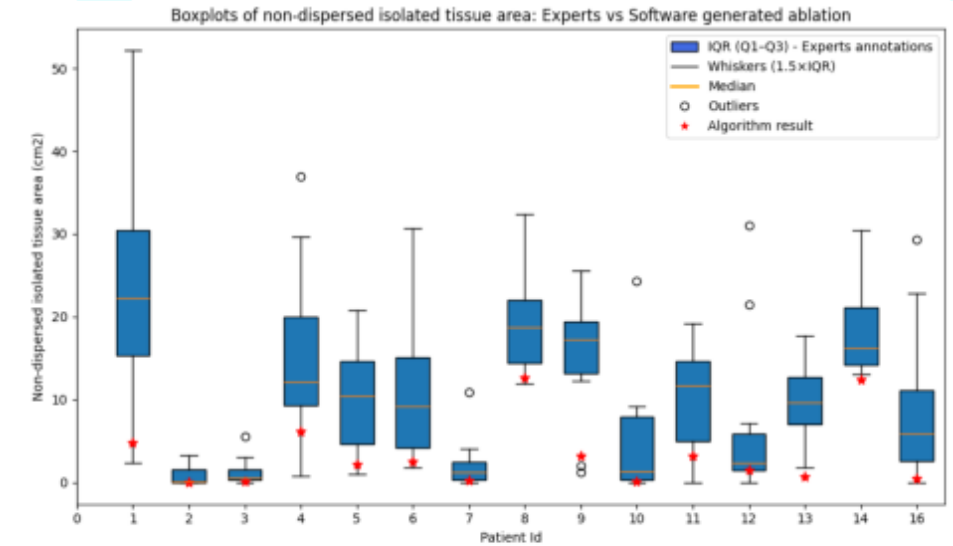- A multi-annotation campaign with 12 annotators (physicians and clinical experts) was performed

- Guidelines : Draw ablation strategy based on the same Ablation Guidance Algorithm inputs
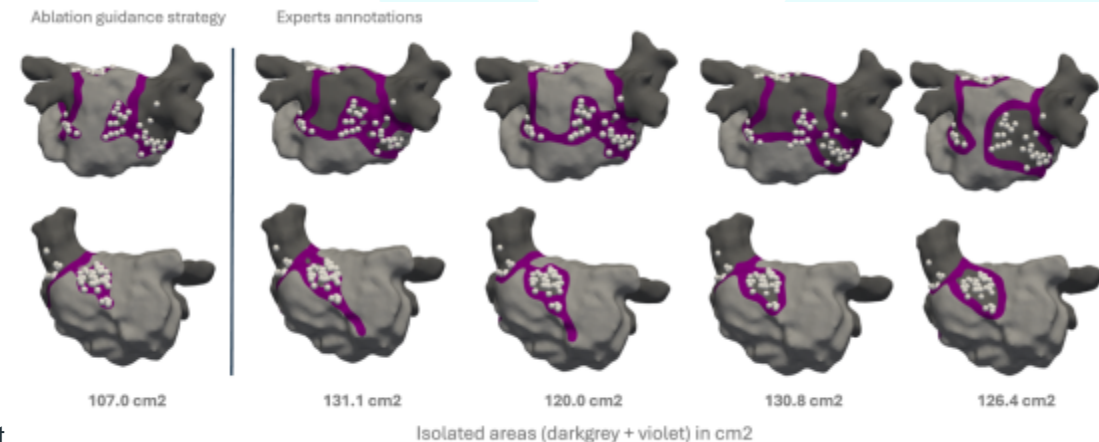
The annotation was done on our data collection and annotation Ecosystem « VoltaPlex

Result

Boxplots of non-dispersed isolated tissue area: Experts vs Software generated ablation

Patient ID	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Average reduction (cm2)	19.1	0.9	1.2	9.4	7.6	9.0	2.0	6.9	12.0	5.1	7.1	5.5	9.0	6.1	1.3	8.7

Example

Ablation guidance strategy   Experts annotations

107.0 cm2   131.1 cm2   120.0 cm2   130.8 cm2   126.4 cm2

Isolated areas (darkgrey + violet) in cm2

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4-5 DÉCEMBRE 2025
VILLA M. - MARSEILLE I FRANCE

19èmes journées françaises
pratiques de rythmologie
& de stimulation cardiaque

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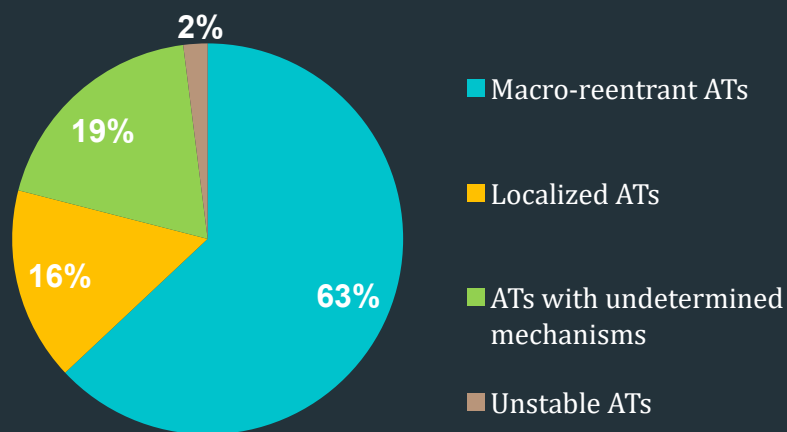Merci pour votre attention!

TAILORED-AF : Repeat procedures Tailored arm

76% Repeat procedures in the Tailored Arm were for ATach (n=43) whereas **86%** of repeat procedures in the Anatomical Arm were for AF recurrences
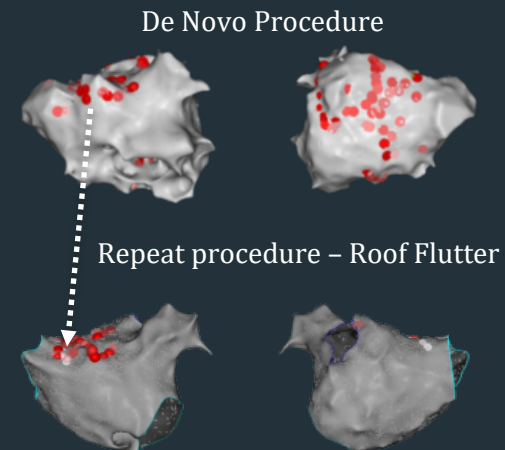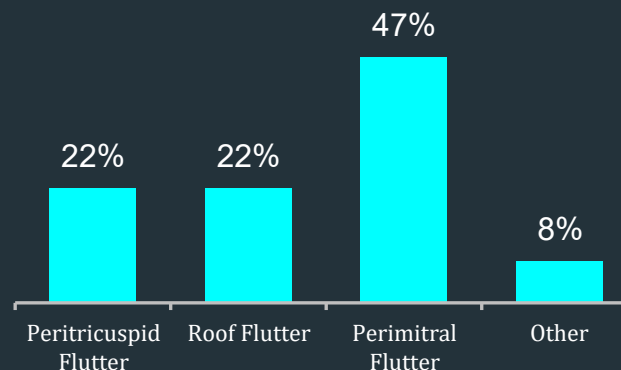
100% Clinical AT termination

■ Macro-reentrant ATs — 63%
■ Localized ATs — 16%
■ ATs with undetermined mechanisms — 19%
■ Unstable ATs — 2%

57 ATs treated during repeat procedures in the Tailored Arm

81% of macroreentries were diagnosed in regions where **dispersion had previously been detected** during the index procedure


- Peritricuspid Flutter — 22%
- Roof Flutter — 22%
- Perimitral Flutter — 47%
- Other — 8%

De Novo Procedure

Repeat procedure – Roof Flutter

100% of Localized AT were diagnosed in regions where **dispersion had previously been detected** during the index procedure.

- Ostium PVs — 22%
- LA — 56%
- RA — 22%
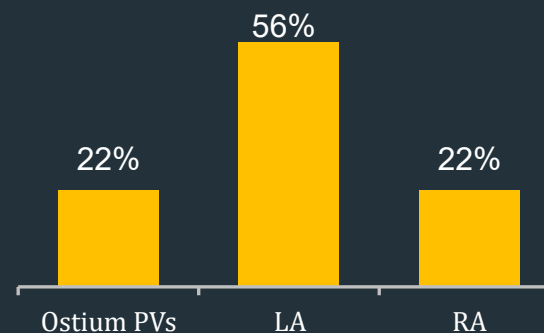
De novo Procedure – Non-contiguous PV isolation

Repeat procedure – Localized AT on Posterior LIPV
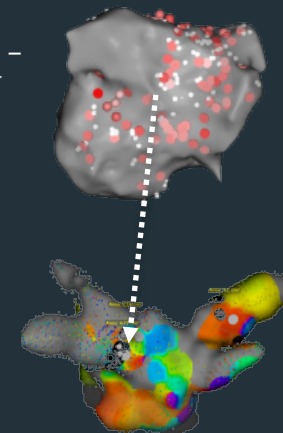
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MEDICAL

Meaningful Increase in Procedure Efficiency When Paired with Newest Ablation Technologies

Multiple factors contribute to a drastic increase in efficiency of Volta-guided procedures:

- Larger mapping catheters

- Volta has improved its interoperability with mapping systems and catheters, making the workflow much easier

- In its latest version, Volta's algorithm has improved in specificity, reducing the size of the detected regions by ~50%

- PFA catheters and newest RF catheters have enabled much faster and larger ablation, drastically reducing ablation time

November 2025 Heart Rhythm publication from Devi Nair on Volta + Affera cases available here

Tailored AF
Procedure time =   178 ± 60 min
N = 187
Year 2022

Year 2024

Investigation	Volta Hyperdrive	Volta + QDOT	Volta + Farawave	Volta + Affera Sphere-9	Volta + Varipulse
N	25	34	19	32	6
Procedure time (min)	**136** ± 36	**127** ± 32	**71** ± 16	**54** ± 11	**88** ± 17

Automated mapping of AF drivers
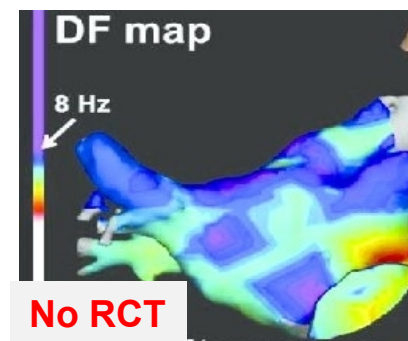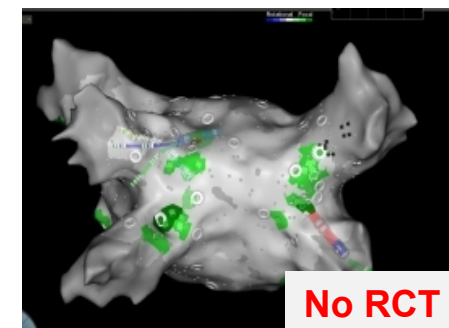
Negative RCT

CFAE
Abbott/BW

Negative RCT

Fibrosis
maps
MRI

DF map

8 Hz

No RCT

DF maps

No RCT

Driver maps (rotors/ focal)
BW
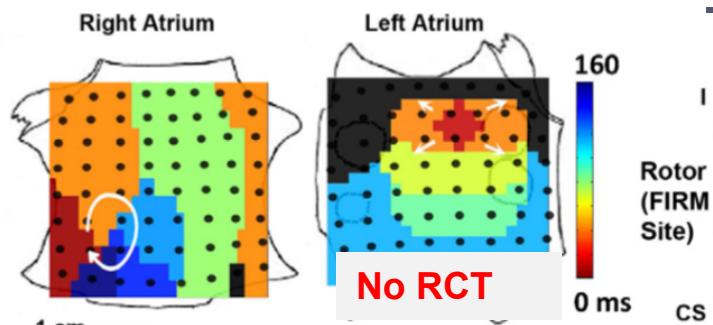
Right Atrium Left Atrium

160

Rotor
(FIRM
Site)

No RCT

0 ms

1 cm

Driver maps (rotors/focal)

No RCT

Driver maps (rotors/focal)
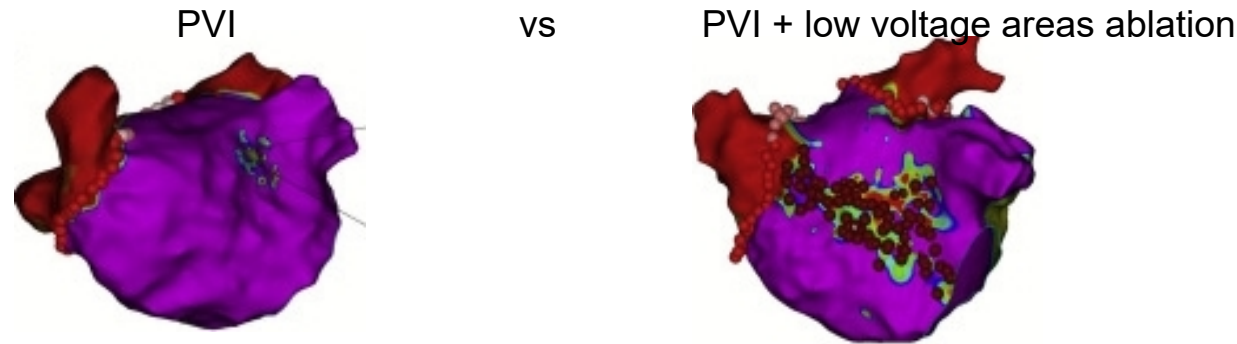

ACUTUS
MEDICAL

70%
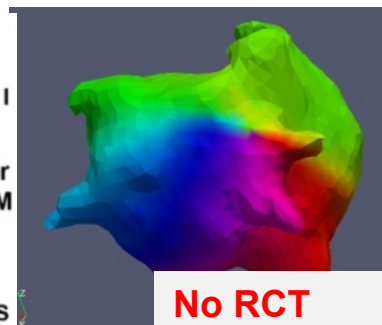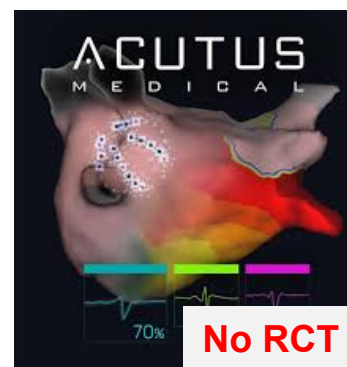
No RCT

Driver maps (rotors/focal)
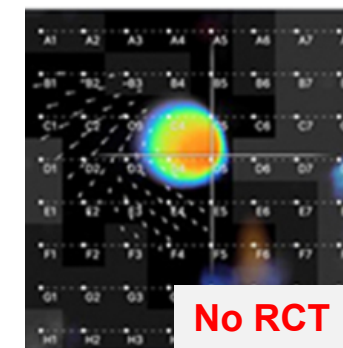
No RCT

Driver maps (rotors/focal)

No RCT-evidence of a superiority in comparison to standard of care in <u>de novo persistent AF</u> ablation

Low voltage-guided ablation: focus on RCT data

PVI   vs   PVI + low voltage areas ablation

- ***STABLE SR II*** *(Yang et al. 2022)*: multicenter RCT (n=300 pst AF) -> **negative**

- ***SUPRESS AF*** *(Masuda et al. 2024)*: multicenter RCT (n=343 pst AF) -> **negative**

- ***SCAR AF*** *(Lepillier et al. 2024)*: multicenter RCT (n=210 pst AF) -> **negative**

- ***ERASE AF:*** multicenter RCT (n=324 pst AF) -> positive

*Strong limitation: (**70%**) without low voltage areas in both arms treated by PVI only.*

The jury is still out about low voltage-guided ablation

Anatomical approach - VOM ethanol infusion national academic RCT data

	Venus *	Plan Marshall **	Prompt AF ***
Centers	12 US	1 french	12 chinese

Ethanol infusion in the VOM seems to improve results of catheter ablation.

Extensive and long procedures

Reproducibility?

Benefit vs PVI after 1 or 2 procedures?

Over or under treatment?

Freedom from atrial arrhythmia

Log-rank P = 0.228
Hazard ratio 0.80 95%CI: 0.56 - 1.15

p = 0.2

Time after the procedure (days)

JAMA
The Journal of the American Medical Association

EHRA

- *Valderabano et al. JAMA 2019*

*** Derval et al. EHRA 2024 (i...
Derval et al. Heart Rhythm 20...
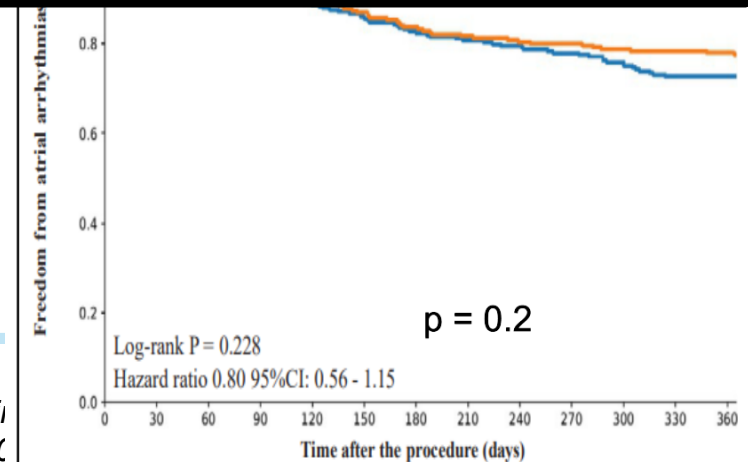
Volta At A Glance

VOLTA'S AI IMPROVES ABLATION OUTCOMES FOR MOST PREVALENT & UNDERSERVED FORMS OF ATRIAL FIBRILLATION

ATRIAL FIBRILLATION (AF) ABLATION

One of the most profitable and highly growing market segment in MedTech

$9Bn Market

COMPLEX AF 73% of the patients — Poor outcomes / Underserved population

VOLTA AF-XPLORER II
AI Software Solution to Guide AF Ablation
CE-marked & FDA cleared

VOLTAPLEX
Unique Data Collection and Annotation Ecosystem

4000+ procedures in the **database**

5,000+ Procedures

30+ Centers

5 Countries

2016 Foundation of Volta Medical

Multidisciplinary Transatlantic Leadership Team with Strong Track Record

R&D, Production, Regulatory & Clinical
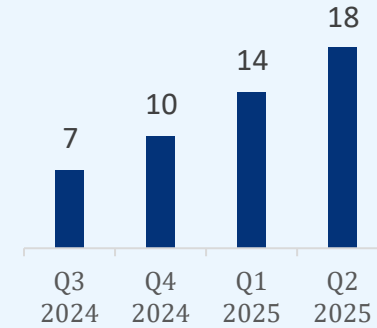
Sales, Marketing & Finance

€90M+ Raised to Date

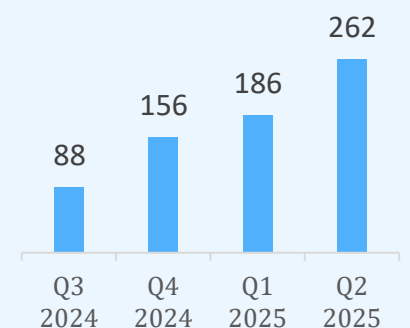LIGHTSTONE VENTURES — GILDE HEALTHCARE — VENSANA CAPITAL

ACCELERATING COMMERCIAL ADOPTION

NB PHYSICIAN ADOPTERS (US)

Q3 2024	Q4 2024	Q1 2025	Q2 2025
7	10	14	18

NB PROCEDURES (US)

Q3 2024	Q4 2024	Q1 2025	Q2 2025
88	156	186	262

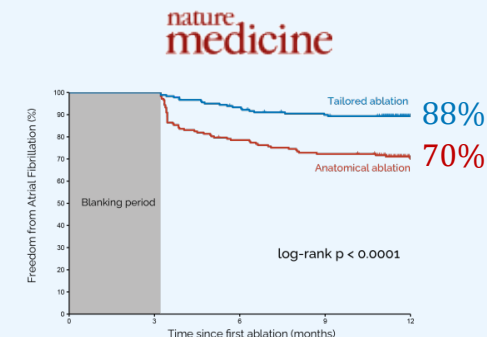### UNPRECEDENTED LEVEL-1 CLINICAL EVIDENCE
Volta provides superior efficacy vs standard-of-care

2024
The TAILORED-AF RCT
Persistent AF Patients

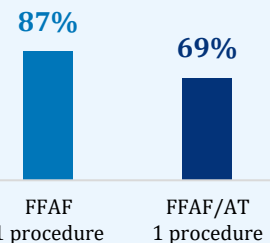nature medicine

Tailored ablation **88%**
Anatomical ablation **70%**
log-rank $p < 0.0001$

2025
The RESTART Trial
Re-Do Patients

Preliminary results presented at HRS 2025

Freedom from arrhythmia at 12 months (n=84)

87% FFAF 1 procedure

69% FFAF/AT 1 procedure

Represents ~50% of the ablation cases

Volta Improves Ablation Outcomes for Complex Substrate Patient Populations

Volta's extensive clinical evidence demonstrates its unique ability to treat these patients

COMPLEX SUBSTRATE PATIENTS REPRESENT AFIB's MOST UNDERSERVED COMMUNITIES

Heart Failure Patients	Persistent AF ≥ 6 months	Women with Persistent AF	Re-do AF Patients with Isolated PVs
TAILORED-AF sub-analysis	TAILORED-AF sub-analysis	TAILORED-AF sub-analysis	The RESTART Trial

AF-Xplorer II Seamlessly Integrates into the Existing Workflow of the EP Lab

AF-Xplorer II Software

3D Mapping System

AF-Xplorer II Console

Bidirectional Digital Communication with Selected Mapping Systems

Or Digital or Analog Communication with EP Recording System

EP Recording System

32
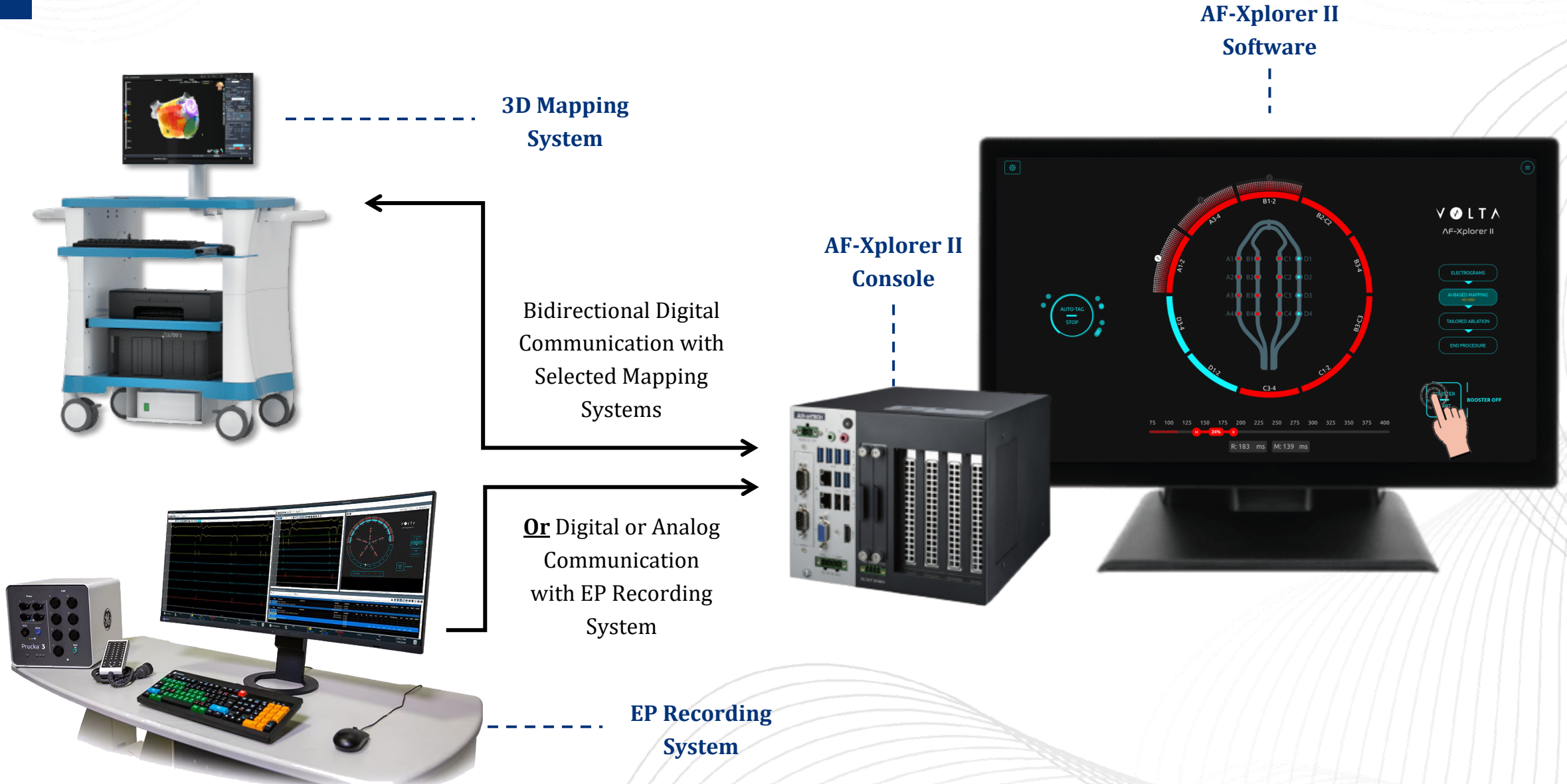
Volta AF-Xplorer™ II represents an evolution into more workflows, use cases, and lab configurations

	VX1	VOLTA AF-Xplorer™	VOLTA AF-Xplorer™ II
Catheter compatibility		Octaray compatibility (10 bipoles)	PFA enablement Octaray 16 bipoles coverage *(with GE CardioLab AltiX Ai.i)*
EP Recording system compatibility (analog)	GE CardioLab Boston LabSystem Pro	GE CardioLab Boston LabSystem Pro	GE CardioLab Boston LabSystem Pro
Digital communication	/	Abbott EnSite X	Abbott EnSite X GE CardioLab AltiX AI.i
Dispersion analysis	Standard dispersion analysis	Standard dispersion analysis	Standard dispersion analysis **High Stability analysis**
Database	274,810 samples Data and annotations from EU	274,810 samples Data and annotations from EU	**832,250 samples** Data and annotations from **EU and US**
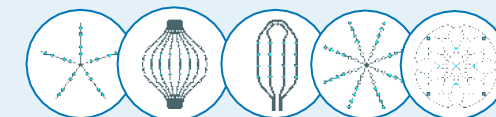
33

Dispersion Extent and AF Termination Sites

- Spatio-temporal dispersion and AF termination **predominantly occurs in the LA.**

- **79%** of patients have dispersion in the RA

- **19%** of termination is observed after ablation in minimally extended **regions of the RA.**

- **100%** of AF Termination occurred **while ablating dispersion regions**
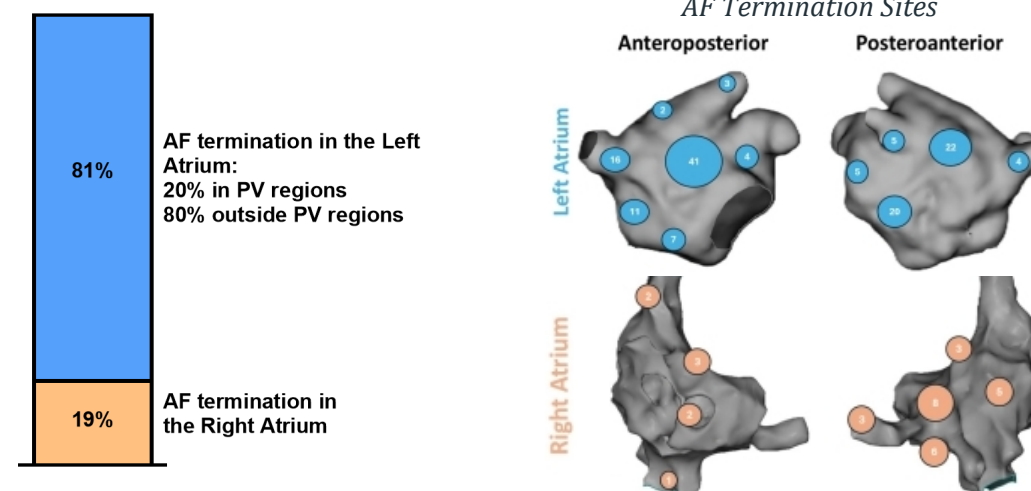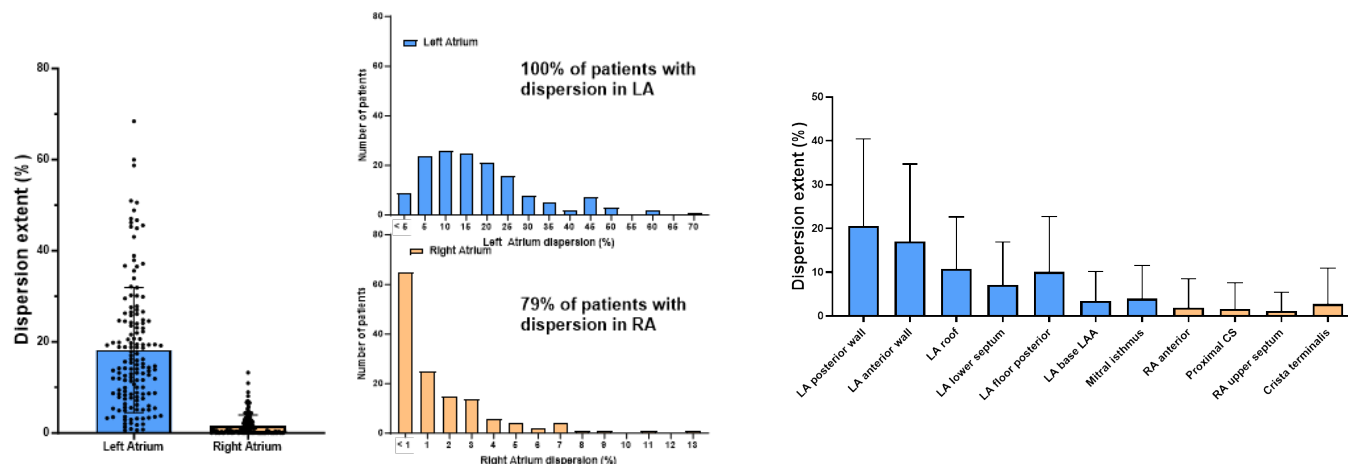
Introducing Volta's AF-Xplorer Technology Platform

Volta's Machine Learning Approach to Improving Identification and Treatment of Complex AF
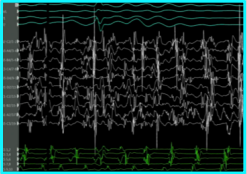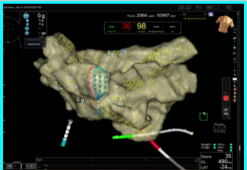
1

Inputs from Existing EP Data Sources

Existing EP Data Inputs Compatible with AF-Xplorer

EP Recording Systems

3D Mapping Systems

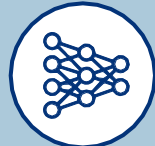AF Mapping Catheters

2

AF-Xplorer Machine Learning Algorithm Processes Data...

V●LTA AF-Xplorer™

Volta's "first of its kind" database of physician-validated EP data is used to train AF-Xplorer's algorithms

Volta's trained machine learning algorithm analyzes data acquired from existing EP data sources

3

...To Identify Regions of Interest in Real-Time

V●LTA AF-Xplorer™

Automatically detects dispersed electrograms in real-time
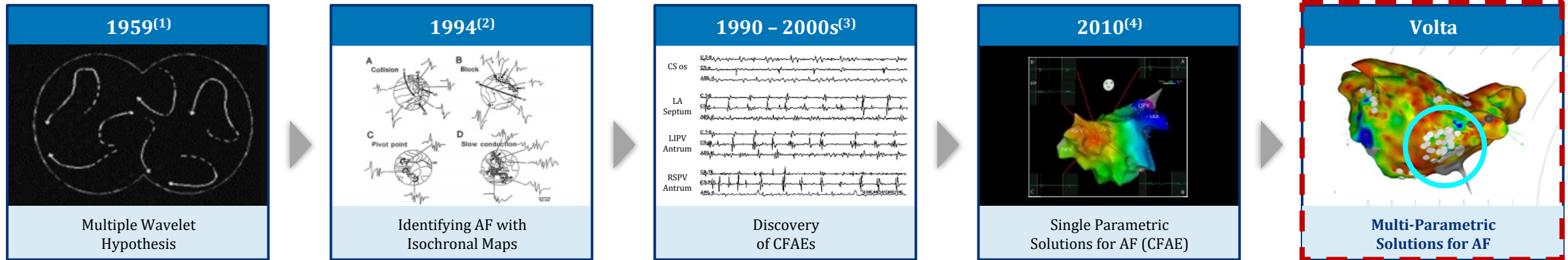
+

Automatically tags dispersion regions on the 3D mapping system interface

AF-Xplorer's Algorithms Work with Existing Tools in the EP Lab to Deliver Clinically Impactful Information and Optimize Catheter Ablation

AF-Xplorer is a Multi-Parametric Solution That Uses AI to Deliver Unprecedented Insights Into the Drivers of AF

Evolution of Identifying Drivers of AF

1959[1]	**1994**[2]	**1990 – 2000s**[3]	**2010**[4]	**Volta**
Multiple Wavelet Hypothesis	Identifying AF with Isochronal Maps	Discovery of CFAEs	Single Parametric Solutions for AF (CFAE)	**Multi-Parametric Solutions for AF**

Spatiotemporal Dispersion: Volta's Multi-Parametric Approach

A patient-unique fingerprint for identifying complex AF

1 Dispersion is a **collection of EGMs that display atypical conduction characteristics** across multiple electrodes

2 Areas of dispersion likely have a role in perpetuating, initiating or sustaining AF**, and studies demonstrate **ablating these areas positively impacts AF catheter ablation outcomes**

Combining AI with Multi-Parametric Data to Personalize AF Ablation

Volta's machine learning algorithms convert vast amounts of complex data into easy to interpret, clinically actionable outputs
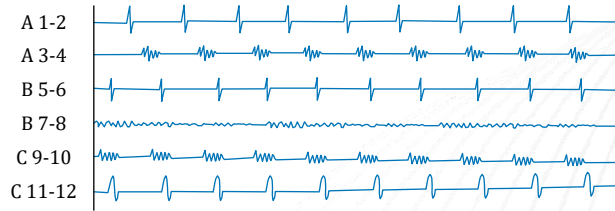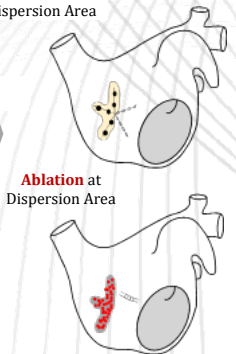
Examples of Spatiotemporal Dispersion
(With or Without Fractionation)

A 1-2
A 3-4
B 5-6
B 7-8
C 9-10
C 11-12

Delineation of a Dispersion Area

Ablation at Dispersion Area

(1) MOE, G. K., & ABILDSKOV, J. A. (1959). Atrial fibrillation as a self-sustaining arrhythmia independent of focal discharge. American heart journal, 58(1), 59–70. https://doi.org/10.1016/0002-8703(59)90274-1.
(2) Konings KT, Kirchhof CJ, Smeets JR, Wellens HJ, Penn OC, Allessie MA. High-density mapping of electrically induced atrial fibrillation in humans. Circulation. 1994 Apr;89(4):1665-80. doi: 10.1161/01.cir.89.4.1665. PMID: 8149534.
(3) Nademanee, K., et al., (2004). A new approach for catheter ablation of atrial fibrillation: mapping of the electrophysiologic substrate. Journal of the American College of Cardiology, 43(11), 2044–2053. https://doi.org/10.1016/j.jacc.2003.12.054.
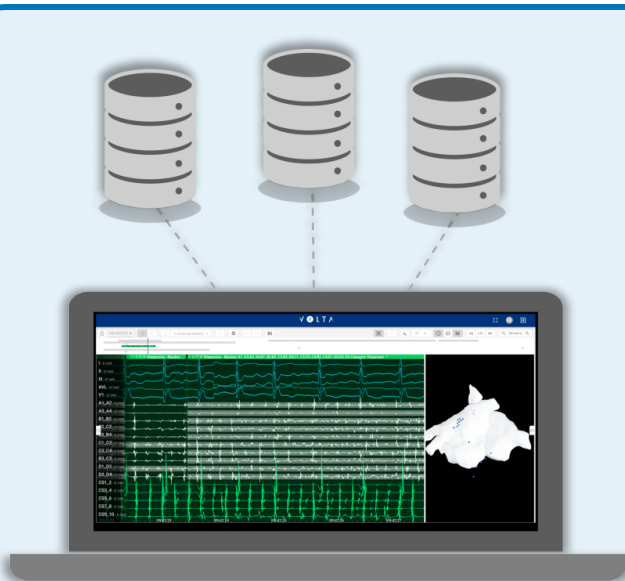(4) Nademanee, K., et al., (2004). A new approach for catheter ablation of atrial fibrillation: mapping of the electrophysiologic substrate. Journal of the American College of Cardiology, 43(11), 2044–2053. https://doi.org/10.1016/j.jacc.2003.12.054.

VoltaPlex: Volta's Proprietary Training Approach for Its Next Generation AI-Based Algorithm

4

Volta's Data-Driven AI Algorithms Assists EPs in the OR When Assessing and Treating Complex AF and AT

1

Volta Collects Physician-Validated EP Data

| Data Captured from Real-Time Events | Patient Epi-Demiological Data | Patient Peri-Procedural Data | Acute and Long-Term Outcomes |

2

Collected Data is Carefully Annotated by Volta's Team of Expert Physicians to Ensure Reliable Outcomes

Unique Data Collection and Annotation Platform Compiled By Volta Over 5+ Years

Annotation of dispersed electrograms on VoltaPlex in a region that led to AF termination upon cumulative ablation

3

Machine / Deep Learning Algorithms Trained and Tested with Peer-Validated Data