First-in-Human Study of the Saranas Early Bird™ Bleed Monitoring System for the Detection of Endovascular Procedure Related Bleeding Events

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Disclosure Statement of Financial Interest

Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below

- Abbott Vascular
  - Consultant, Speaker Fees
- Abiomed
  - Consultant/advisor, speaker fees
- Boston Scientific
  - Consultant
- Cardinal Health/Cordis
  - Consultant, Speaker Fees
- Cardiovascular System Inc.
  - Consultant, Speaker Fees, Research Grant
- Edwards LifeSciences
  - Consultant, Speaker Fees, Proctor, Research Grant
- Medtronic
  - Consultant, Speaker Fees
- Opsens
  - Consultant
- Penumbra
  - Research Grant
- Pi-Cardia
  - Equity, Consultant
- Puzzle Medical
  - Equity, Consultant
- Soundbite Medical Inc.
  - Equity, Consultant
- SIG.NUM
  - Equity, Consultant
- SARANAS
  - Consultant
- TRYTON Medical Inc.
  - Consultant, Speaker Fees, Research Grant

Why The Need For Early Bleed Detection?

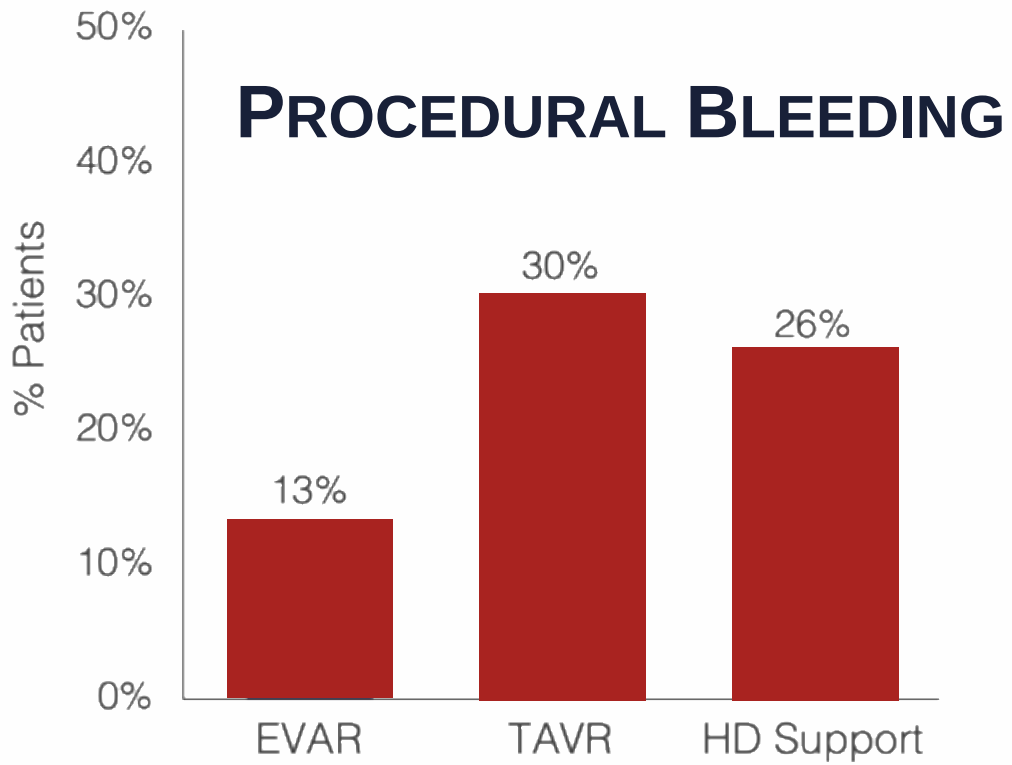
BLEEDING IS FREQUENT

In a study looking at >17,000 large-bore transcatheter interventions from the National Inpatient Sample Database

1 in 5

patients had a bleeding complication

> *While transcatheter technology will continue to improve to reduce bleeding risk, increased adoption of the devices in the hands of inexperienced operators will counterbalance this*



Redfors B et al. JAMA Cardiol. 2017;2(7):798-802.

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Why The Need For Early Bleed Detection?

JAMA Cardiology | Brief Report

Mortality, Length of Stay, and Cost Implications of Procedural Bleeding After Percutaneous Interventions Using Large-Bore Catheters

Björn Redfors, MD, PhD; Brendan M. Watson, MD, PhD; Thomas McAndrew, PhD; Emilie Palisaitis, BSc; Dominic P. Francese, MPH; Mehdi Razavi, MD; Jordan Safirstein, MD; Roxana Mehran, MD; Ajay J. Kirtane, MD, SM; Philippe Généreux, MD

3X

INCREASE MORTALITY

2X

LENGTH OF HOSPITAL STAY

60%

INCREASED HEALTHCARE COST

Redfors B et al. JAMA Cardiol. 2017;2(7):798-802.

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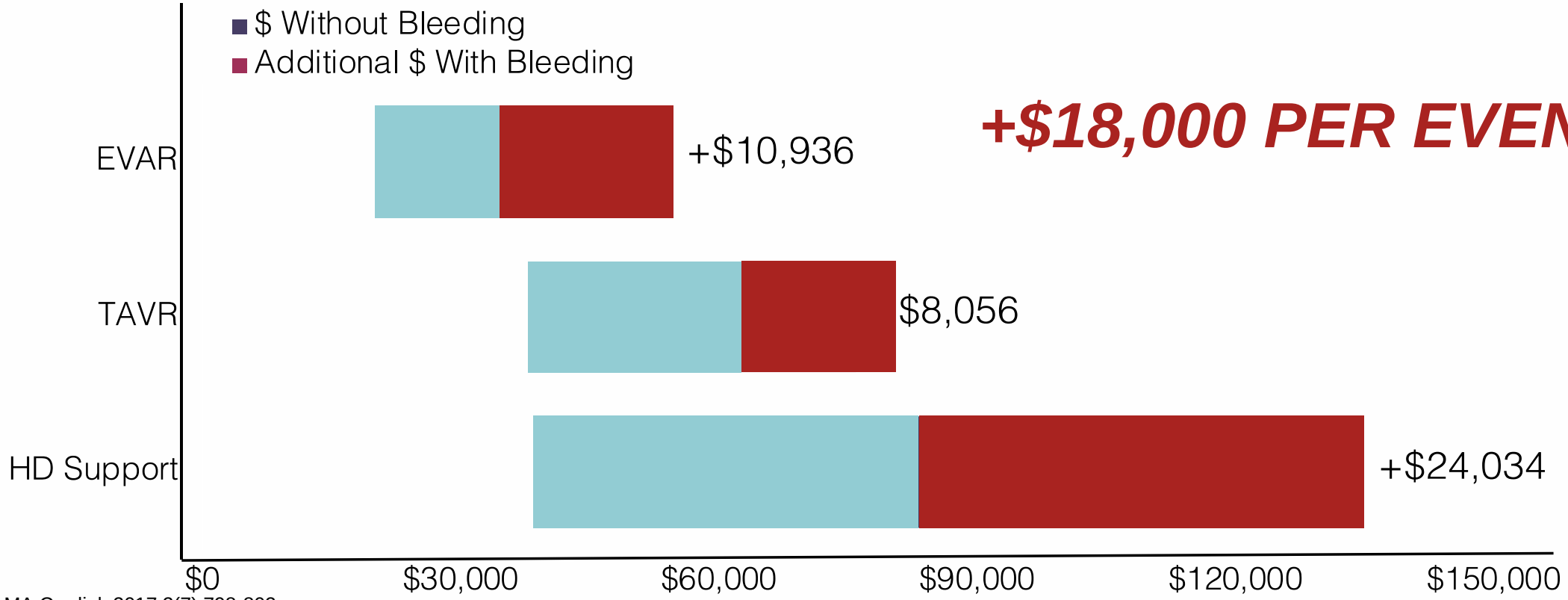
Why The Need For Early Bleed Detection?

BLEEDING ADDS TREMENDOUS COST



+$18,000 PER EVENT

Redfors B et al. JAMA Cardiol. 2017;2(7):798-802.

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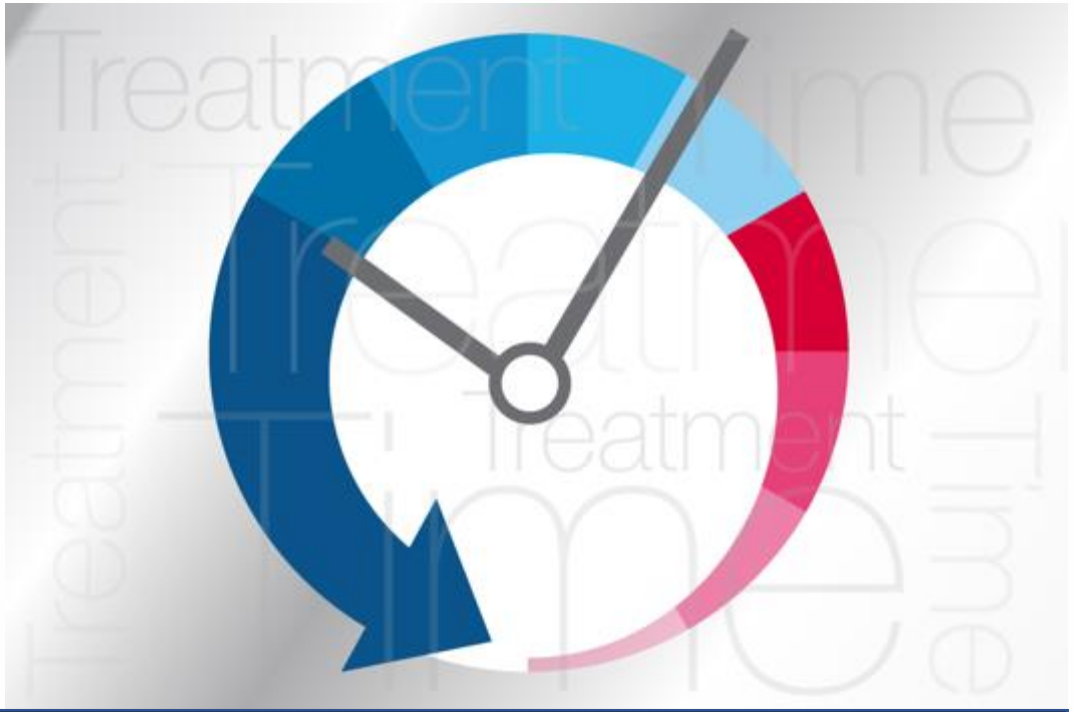
Current Paradigm: Wait for Symptoms

- **Current protocol relies on symptomatology for detection, which can take hours to develop.**
- ***~40% of retroperitoneal bleeds presented with hemorrhagic shock*.**



Addressing onset & progression of bleed complications <u>early</u> may significantly reduce clinical cascade and mitigate downstream costs

Eisen A et al. Retroperitoneal Bleeding after Cardiac Catheterization: A 7-Year Descriptive Single-Center Experience. Cardiology 2013;125:217-222.

seamless integration
into current workflow

actionable alerts
for clinical intervention

feels like, works like
current standard of care

EARLY BIRD™ BLEED MONITORING SYSTEM

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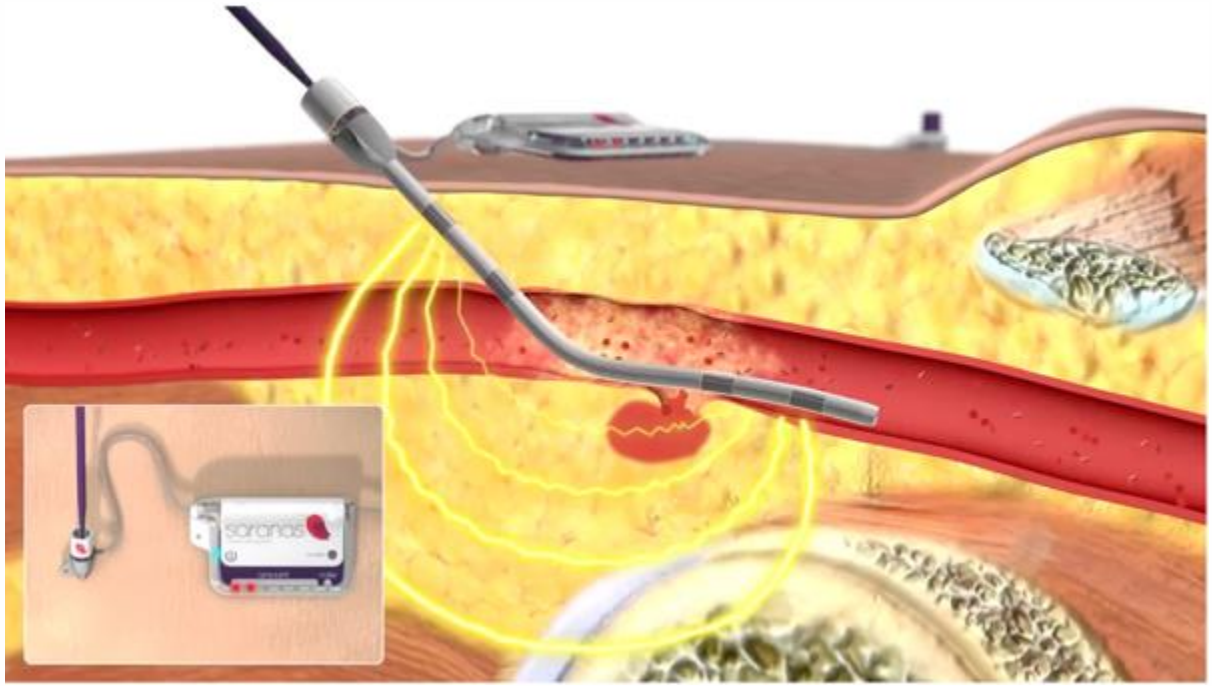
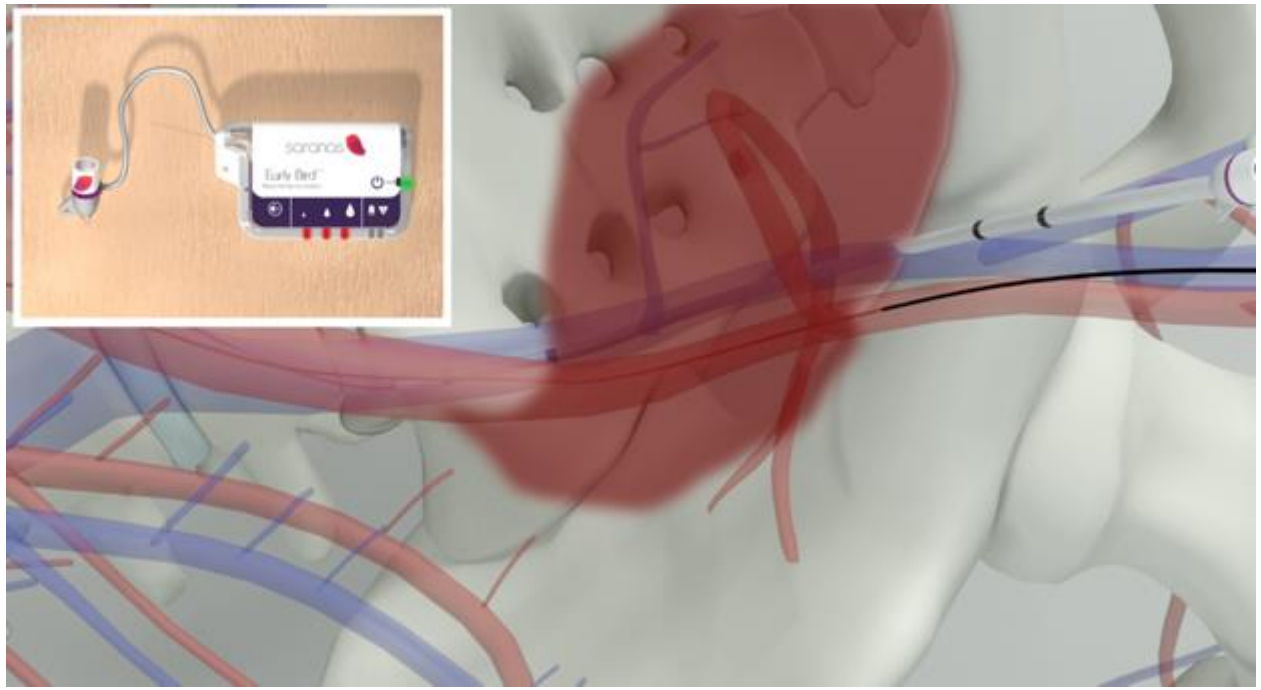
BLEED MONITORING WITH BIOIMPEDANCE



ACCESS SITE BLEED



RETROPERITONEAL BLEED

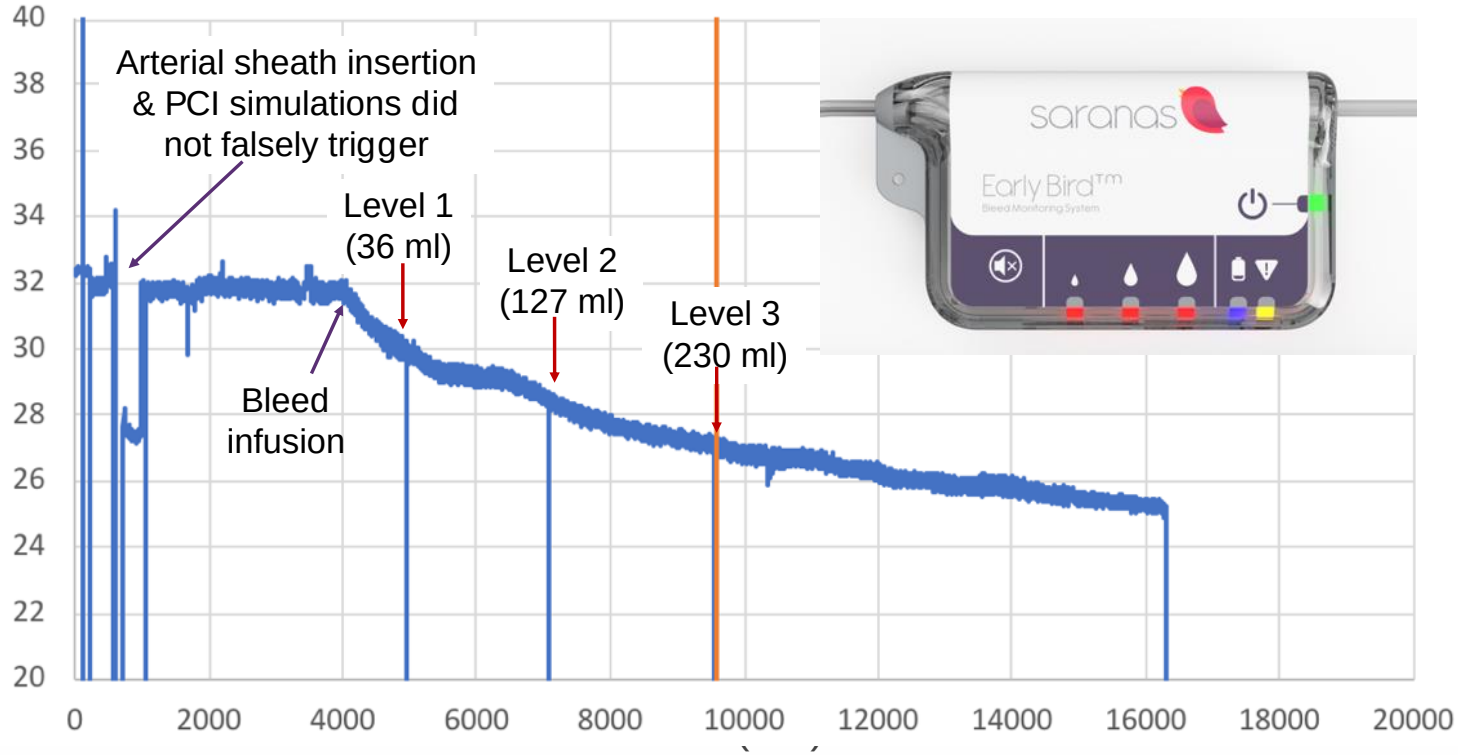
SUCCESSFUL ANIMAL VALIDATION STUDY

100% SENSITIVITY AND 100% SPECIFICITY

PRECLINICAL TESTING

58
individual animals

3
prototype iterations



FDA DE NOVO GRANTED MARCH 1, 2019

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ROBUST BIOIMPEDANCE SIGNAL

ALGORITHM ACTIVELY DETECTS BLEED PROGRESSION

Level 1

48 ml bleed

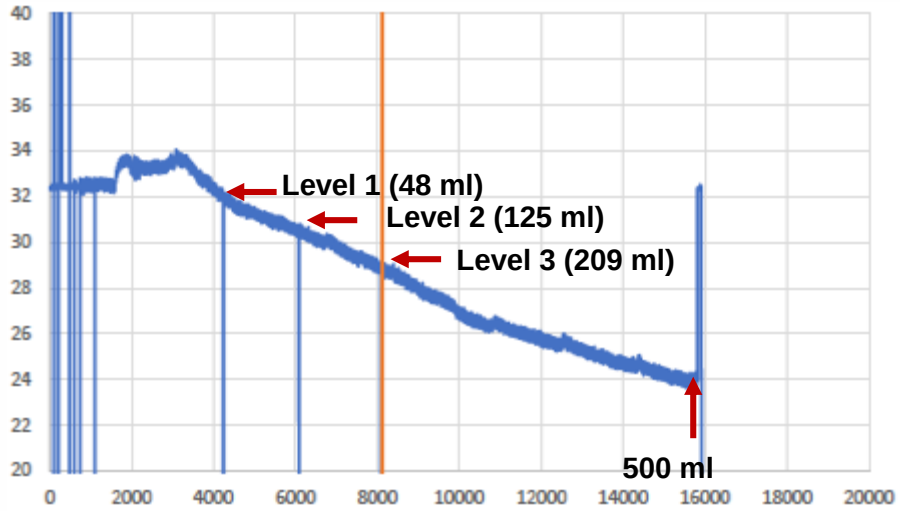
Level 2

125 ml bleed

Level 3

209 ml bleed

Bleed Signature



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EARLY BIRD First-in-Human Study

Investigational Product	Saranas Early Bird Bleed Monitoring System (EBBMS)
Subject Population	Patients undergoing endovascular procedure via arterial or venous access
Study Objectives	To evaluate the safety and accuracy of the Saranas EBBMS for the detection of access site related internal bleeding events during endovascular procedures
Primary Endpoint	**Level of agreement in bleeding detection between the Saranas EBBMS and post-procedural computerized tomography (CT)**
Study Design	Prospective, multicenter, observational
Key Inclusion Criteria	• ≥18 years of age • Planned endovascular procedure such as transcatheter aortic valve replacement (TAVR), balloon aortic valvuloplasty, percutaneous coronary intervention, complex or high-risk percutaneous coronary intervention requiring hemodynamic support device (Impella 2.5, Impella CP, and ECMO), endovascular aortic repair (EVAR), or any other endovascular procedures requiring arterial or venous access.

EARLY BIRD First-in-Human Study

Planned endovascular procedure

↓

Informed consent/Eligibility/Screening procedures/Enrollment

↓

Pre-procedure CT (contrast or non-contrast CT; optional)

↓

Endovascular Procedure
Introduce and activate Saranas EBBMS first
Perform endovascular procedure

↓

Post-procedure monitoring with Saranas EBBMS for up to 12 hours
Prior to EBBMS removal:
CT scan non-contrast and blood sample (core lab review)

↓

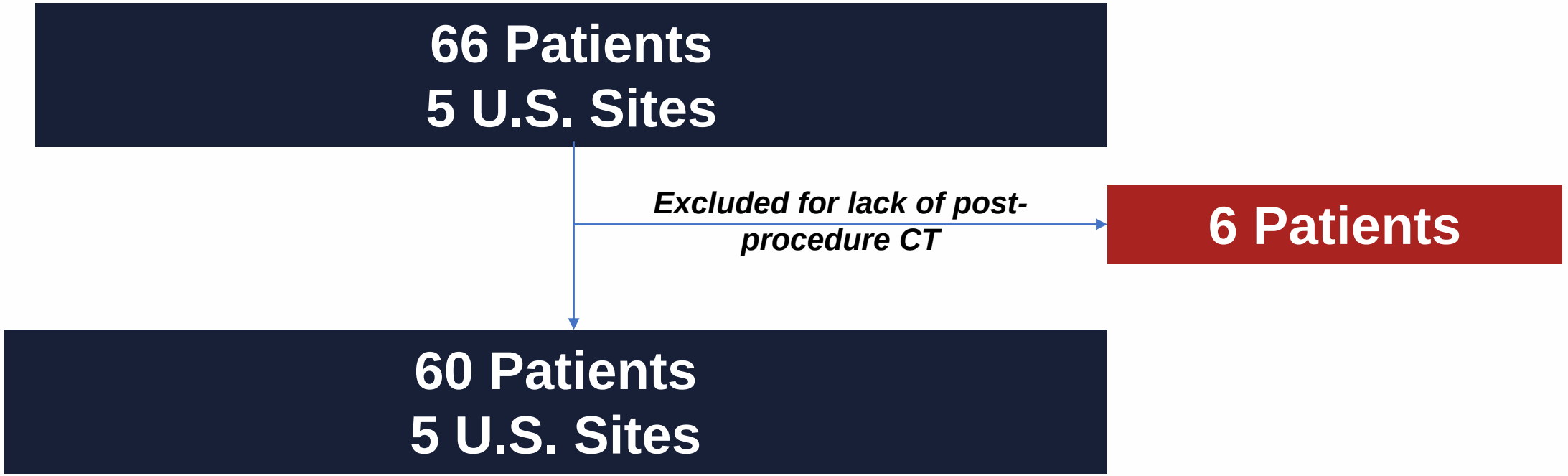
Remove Saranas EBBMS and send for data analysis

↓

Clinical follow-up, post-EBBMS and pre-discharge blood sample

EARLY BIRD First-in-Human Study

Enrollment from August 2018 and December 2018



Endovascular Procedures (n=60)

TAVR self-expandable	24 (40%)
TAVR balloon-expandable	16 (27%)
Percutaneous coronary Intervention	8 (13%)
Impella Hemodynamic Support	5 (8%)
Balloon Aortic Valvuloplasty	4 (7%)
Mitral Clip	1 (2%)
TMVR	1 (2%)
EVAR	1 (2%)

Procedure Characteristics: Access Details (n=60)

Early Bird Bleed Monitoring System	
6F	32 (53%)
8F	28 (47%)

Access Sheath Index Procedure	
6F	1 (2%)
7F	2 (3%)
8F	6 (10%)
12F	4 (7%)
14F	28 (47%)
16F	17 (28%)
18F	1 (2%)
24F	1 (2%)

EARLY BIRD BLEED DETECTION (n=60)

No Bleed Detected		35% (n=21)

EARLY BIRD BLEED DETECTION (n=60)

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Level 1		**33% (n=20)**

EARLY BIRD BLEED DETECTION (n=60)

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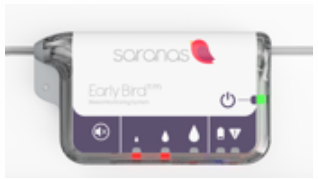
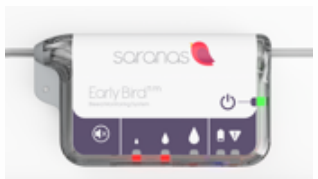
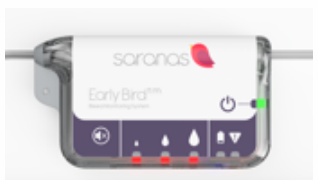
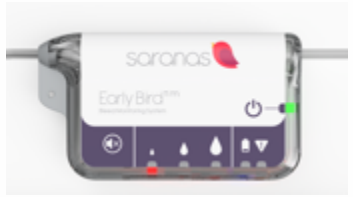
Level 1		**33% (n=20)**
Level 2		**25% (n=15)**

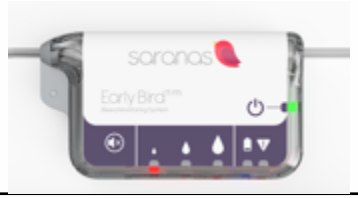
EARLY BIRD BLEED DETECTION (n=60)

No Bleed Detected		35% (n=21)
Level 1		**33% (n=20)**
Level 2		**25% (n=15)**
Level 3		**7% (n=4)**

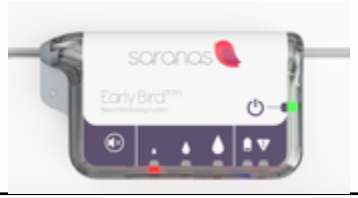
EARLY BIRD BLEED DETECTION (n=60)

Early Bird Bleed Detection	
Level 1	
Level 2	
Level 3	

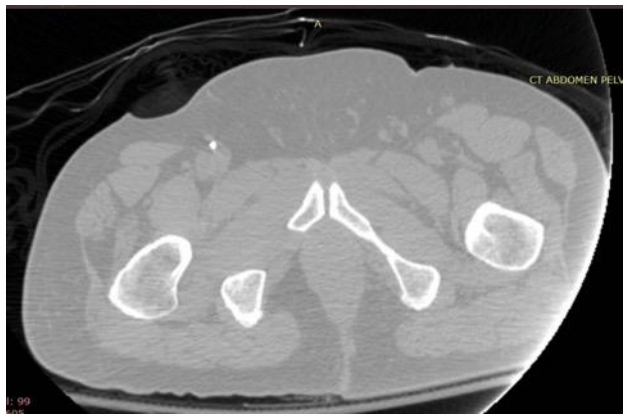
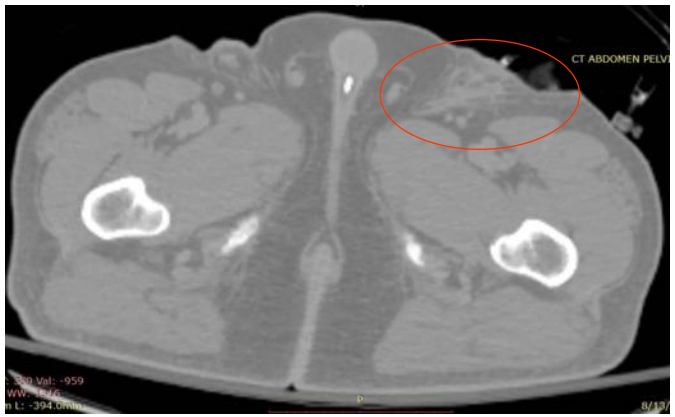
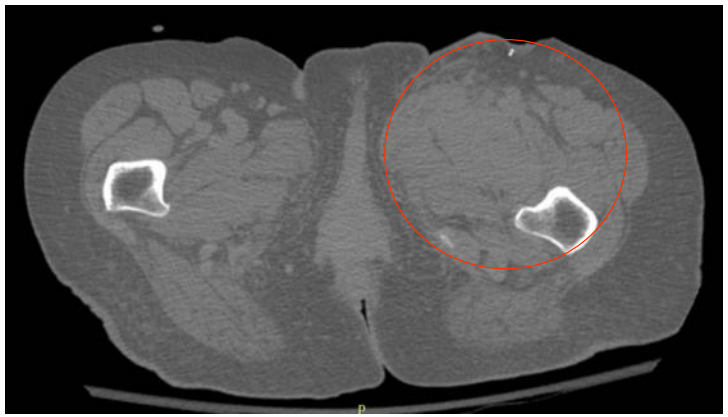
EARLY BIRD BLEED DETECTION (n=60)

Early Bird Bleed Detection	Intra-Procedure (31%)
Level 1 	25.6% (n=10)
Level 2 	2.6% (n=1)
Level 3 	2.6% (n=1)

EARLY BIRD BLEED DETECTION (n=60)

Early Bird Bleed Detection	Intra-Procedure (31%)	Post-Procedure (69%)
Level 1 	25.6% (n=10)	25.6% (n=10)
Level 2 	2.6% (n=1)	35.9% (n=14)
Level 3 	2.6% (n=1)	7.7% (n=3)

CT FINDINGS: Independent Core Lab Analysis

NORMAL	INFILTRATION	HEMATOMA	RETRO
			
4/60 (6.7%)	34/60 (56.7%)	22/60 (36.7%)	0/60 (0%)

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EARLY BIRD First-in-Human Study

PRIMARY ENDPOINT COHEN'S KAPPA* (κ) = 0.84

*Kappa strength of agreement: <0=none; 0-0.20=slight; 0.21-0.40=fair; 0.41-0.60=moderate; 0.61-0.80=substantial; *0.81-1.00=almost perfect*

EARLY BIRD First-in-Human Study

PRIMARY ENDPOINT COHEN'S KAPPA* (κ) = 0.84

	Level 1	Level 2	Level 3
Cohen's Kappa (κ)	1.00	0.81	1.00
PPV	100%	92%	100%
Specificity	100%	75%	100%

*Kappa strength of agreement: <0=none; 0-0.20=slight; 0.21-0.40=fair; 0.41-0.60=moderate; 0.61-0.80=substantial; ***0.81-1.00=almost perfect***

The EARLY BIRD First-in-Human Study

Conclusions (1)

- Among a population of all-comer patients undergoing a broad variety of endovascular procedures, ***The EARLY BIRD Bleed Monitoring System was safe and easily incorporated in standard flow of work.***
- Among the study population, sub-clinical ***bleeding events were frequent, with more than 1/3 of patients presenting with a hematoma at the access site*** as detected by CT.
- ***The EARLY BIRD Bleed Monitoring System triggers*** notification in 65% of patients, with ***~1/3 at level 2 and 3 of bleed severity.***

The EARLY BIRD First-in-Human Study

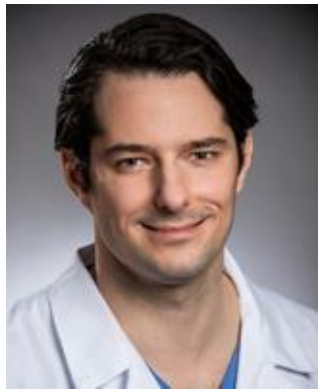
Conclusions (2)

- Among patients triggering a bleed detection response from the EARLY BIRD Bleed Monitoring System, ***~1/3 occurred during the procedure, and ~2/3 after the procedure***, suggesting initiation or progression of bleeding after the procedural period.
- Severe bleeding events such as retroperitoneal bleed or life-threatening bleeding were non-existent in our cohort, most likely the reflection of high experienced operators, but also suggesting that the detection, notification and awareness of early sub-clinical bleed could have led to these favorable outcomes.
- Whether the ***systematic use of the EARLY BIRD Bleed Monitoring System*** could lead to a significant reduction in bleeding complication during endovascular procedure remains to be determined

The EARLY BIRD First-in-Human Study
Conclusions (3)

- *Among a population of all-comer patients undergoing a broad variety of endovascular procedures, the EARLY BIRD Bleed Monitoring System was safe, easily incorporated in standard flow of work, and demonstrated the capacity to detect bleeding before the progression to a more severe or symptomatic phase.*

Thanks to all the sites!



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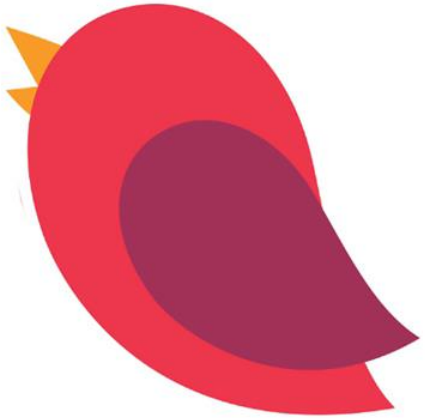

Early Bird™

Bleed Monitoring System