

VASA Presentation

Disrupting the Vascular Access Space with Start-ups



F. Nicholas Franano, MD
President and CEO
Flow Forward Medical, Inc

Disclosures

- ▶ Founder, Proteon Therapeutics, Inc.
- ▶ Founder and CEO, Flow Forward Medical, Inc.

How Did I Get Here?

“As a young man I craved factual certainty on the cause of AVF and AVG failure, I thirsted for a solution to the problem of vascular access, and I aspired to fame and fortune - so I became a vascular access physician. This is like becoming an archbishop so you can meet girls.”

- Adapted from Matt Cartmill

Vascular Access is a Big, Costly, Unsolved Problem

Coronary Artery Disease	Drug Eluting Stents, Bypass Grafting
Cardiac Valvular Disease	Surgical Valve Replacement, Percutaneous Valve Replacement and Repair
Thrombotic Stroke	ELVO Thrombectomy, LAA Closure
Hemorrhagic Stroke	Aneurysm Coils and Flow Diverting Stents
Peripheral Arterial Disease	Drug Eluting Stents and Balloons, Bypass Grafting
Aortic Aneurysms	Aortic Stent Grafts and Surgical Aortic Repair
Arrhythmias	Pacemakers, Catheter Directed Ablation
Vascular Access Failure	???

Disruption Often Starts with a Question

- ▶ What if we surgically connect an artery to a vein? Could we access the vein with needles for routine hemodialysis?
- ▶ What if we connect an artery to a vein using an ePTFE tube? Could we access the ePTFE tube with needles for routine hemodialysis?
- ▶ What if we make a large caliber double lumen catheter with a cuff? Could we use that for routine hemodialysis?

What if....

- ▶ What if there a catheter that was highly resistant to infection and thrombosis?
- ▶ What if there were an AVG that had an average primary patency of 2 years?
- ▶ What if there were a way to improve AVF creation that increased average AVF maturation success to $\geq 80\%$ and increased average primary patency to 4 years?

Developing Drugs and Devices for Vascular Access Has Been a Difficult Challenge

Biotechnology and Pharmaceuticals	
Company	Year Founded
Miravant	1989
Angiotech	1999
Corgentech	1999
MGVS	2000
Ark Therapeutics	2001
Afmedica	2002
Lumen Therapeutics	2003
Pervasis	2003
Biovascular	2005
Symic Biomedical	2012

Medical Devices	
Company	Year Founded
Novoste	1992
Vasca	1996
Bioconnect	2006
Phraxis	2008

\$476M of Investments in Vascular Access Companies Currently Developing Drugs and Biologics

Biotechnology, Pharmaceuticals, and Biologics				
Company	Year Founded	Capital Raised	Stage	Notes
Humacyte	2004	\$260M	P3	
Proteon Therapeutics	2001	\$187M	P3	IPO in 2014
Vascular Therapies	2001	\$27M	P3	
Endomimetics	2017	\$2M	Pre-Clinical	
	Total	\$476M		

\$135M of Investments in Vascular Access Companies Currently Developing Medical Devices

Medical Devices				
Company	Year Founded	Capital Raised	Stage	Notes
Lutonix Medical	2007	\$35M	Commercial	Acquired by Bard
TVA Medical	2008	\$34M	Commercial	
Avenu Medical	2010	\$14M	Commercial	
Vascular Flow Technologies	2012	\$14M	Commercial	
Hemosphere	1998	\$9M	Commercial	Acquired by Cryolife
Flow Forward Medical	2010	\$8M	Pre-Clinical	
Laminate Medical	2012	\$8M	Commercial	
Bluegrass Vascular	2011	\$5M	Commercial	
Creativasc	2004	\$5M	Clinical	
InnAVasc Medical	2013	\$3M	Clinical	
	Total	\$135M		

What Approaches Have Companies Taken with AVFs and AVGs?

- ▶ Neointimal Hyperplasia Suppressors
 - Proteon, Vascular Therapies, Symic, Lutonix, Miravant, Angiotech, Corgentech, Ark, Afmedica, Lumen Therapeutics, Biovascular, Novoste
- ▶ Dilating Agents: Flow Forward Medical, Endomimetics
- ▶ Cell Therapies: Pervasis, MGVS
- ▶ Anastomotic Support Devices
 - Laminate Medical, Bioconnect
- ▶ Percutaneous Creation of AVFs
 - TVA Medical, Phraxis, Avenu Medical
- ▶ Improved Grafts
 - Humacyte, InAVasc, Endosphere, Vascular Flow Technologies, Creativasc

What Approaches Have Companies Taken with Catheters?

- ▶ Fully Implantable Catheters
 - Vasca
- ▶ Placement Assistance
 - Bluegrass Medical

Take Home Messages on Financing of Startups

- ▶ Vascular access has been a difficult problem for startups, with few successes, many failures, and few exits
- ▶ Over the last 20 years, investor interest has shifted from AVGs and catheters to AVFs
- ▶ Capital requirements are much higher and time to market is much longer for drugs and biologics than devices
- ▶ Capital remains available for startups developing new vascular access products

What is Driving Investment Interest?

- ▶ Important unmet medical need
- ▶ Most patients experience access failure, time to events is relatively short, relatively easy to run clinical trials
- ▶ KOLs and societies have worked to highlight problem and standardize endpoints
- ▶ CMS and NIH supporting efforts to improve outcomes
- ▶ Problem easy for investors to understand
- ▶ Many investors have family or friends who were on hemodialysis; most heard about their repeated access problems
- ▶ Large number of patients worldwide with vascular access problems
- ▶ Rapidly growing market

\$10B Global Market, Growing at > 5% per year

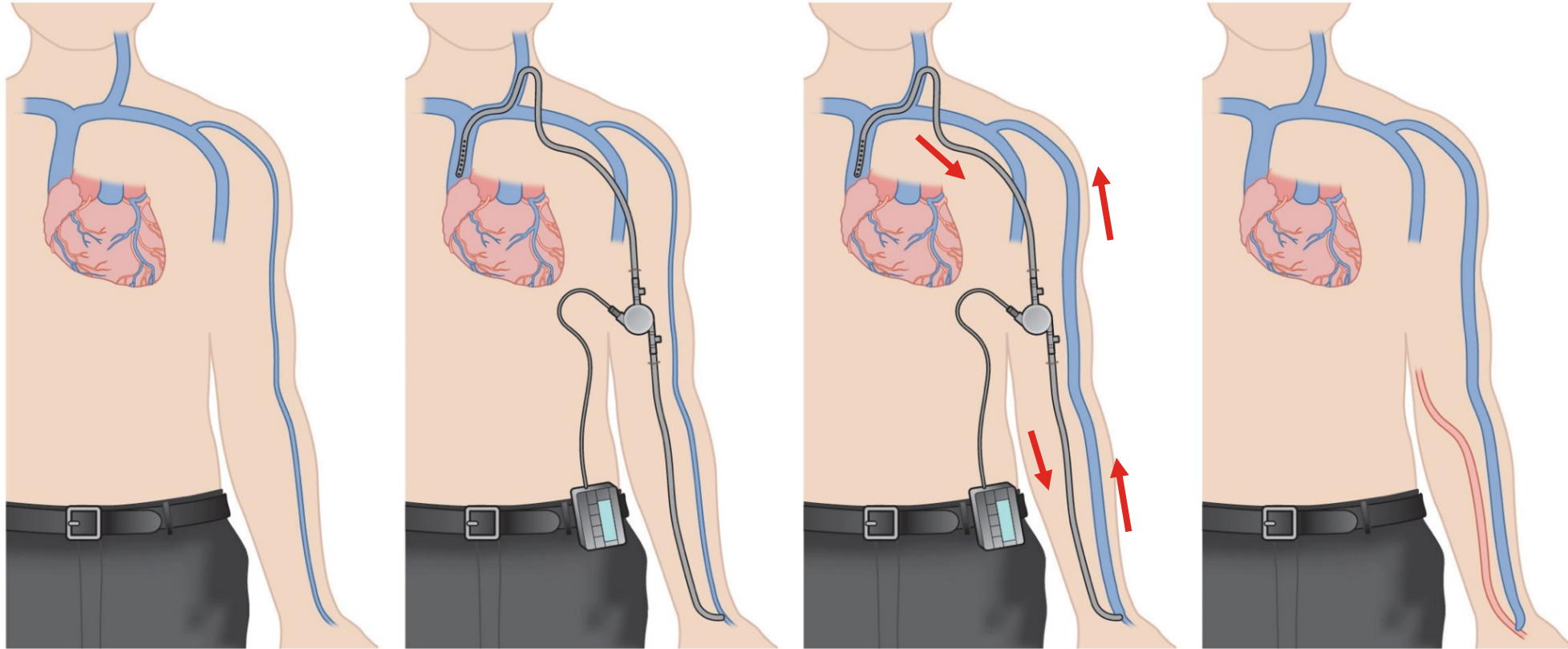
Market	# of Hemodialysis Patients (2020)	ASP (\$)	COGS (\$)	Gross Margin	2020 TAM (\$ billions)	2025 TAM (\$ billions)	2030 TAM (\$ billions)	2035 TAM (\$ billions)
US	529,065	12,000	2,400	80%	2.2	3.0	4.2	5.7
EU	373,132	12,000	2,400	80%	1.5	2.0	2.5	3.2
Japan	380,108	12,000	2,400	80%	1.6	2.0	2.5	3.1
Other	2,220,494	6,000	2,400	60%	5.5	9.1	13.8	19.3
Totals	2,522,000				10.8	16.1	23.0	31.3

Modeled using “ESRD Patients in 2013, a Global Perspective”; Fresenius Medical Care

Key Assumptions:

- Drug or device with \$12K ASP
- 90% of patients eligible to receive treatment when they need a new access site
- 15% of the prevalent patients would need a new access site each year
- No change in the % patients receiving transplant, hemodialysis, or peritoneal dialysis
- No change in the projected need for hemodialysis

What if we Dilate Veins Prior to AVF Surgery?



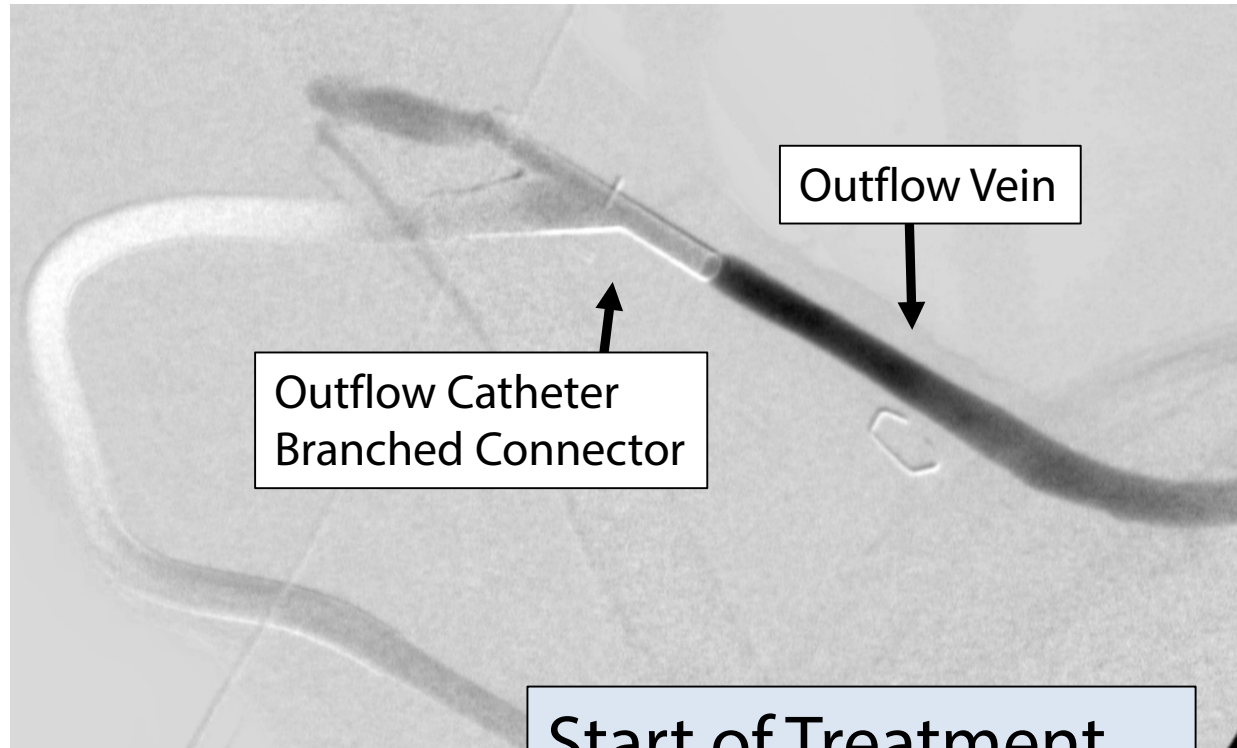
Ineligible
for AVF

1 - 2 Weeks
of Treatment

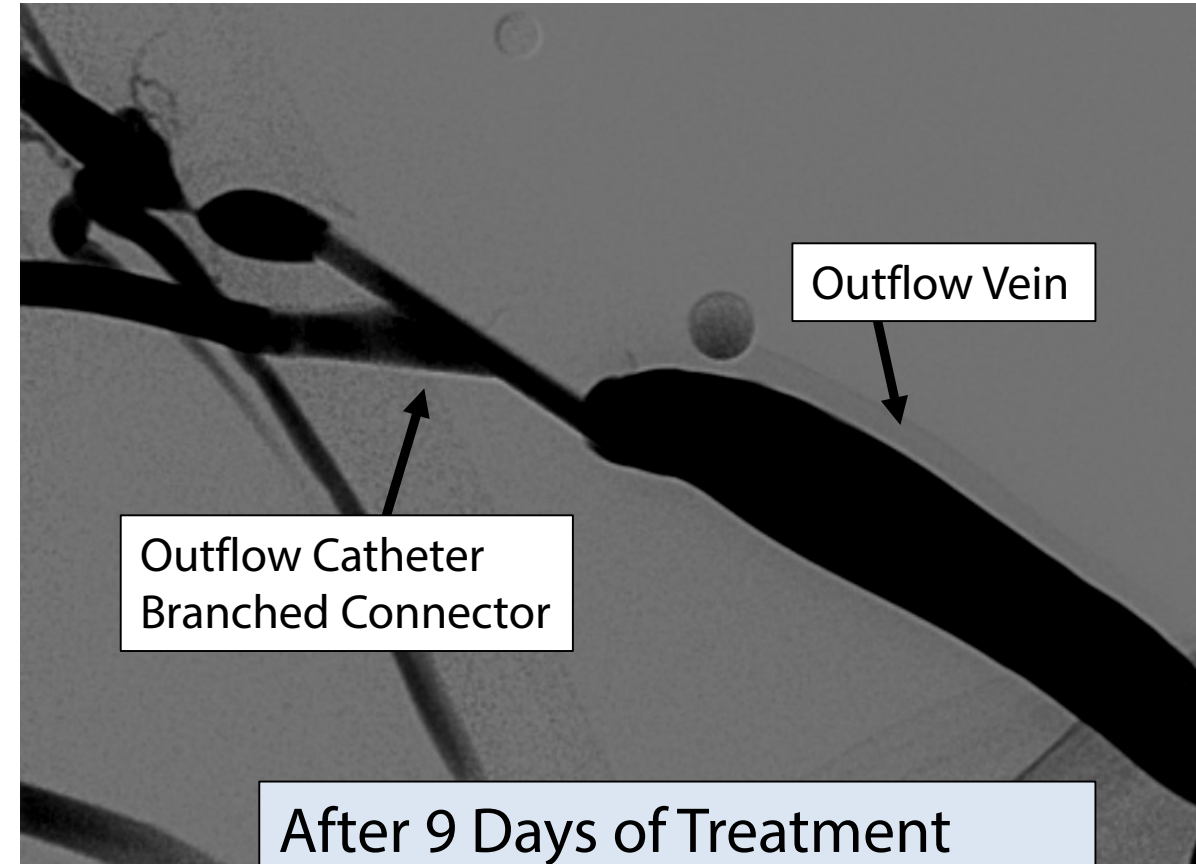
Vein Dilated;
Eligible for AVF

AVF Created

Rapid Outflow Vein Dilation During AFE System Treatment in Sheep

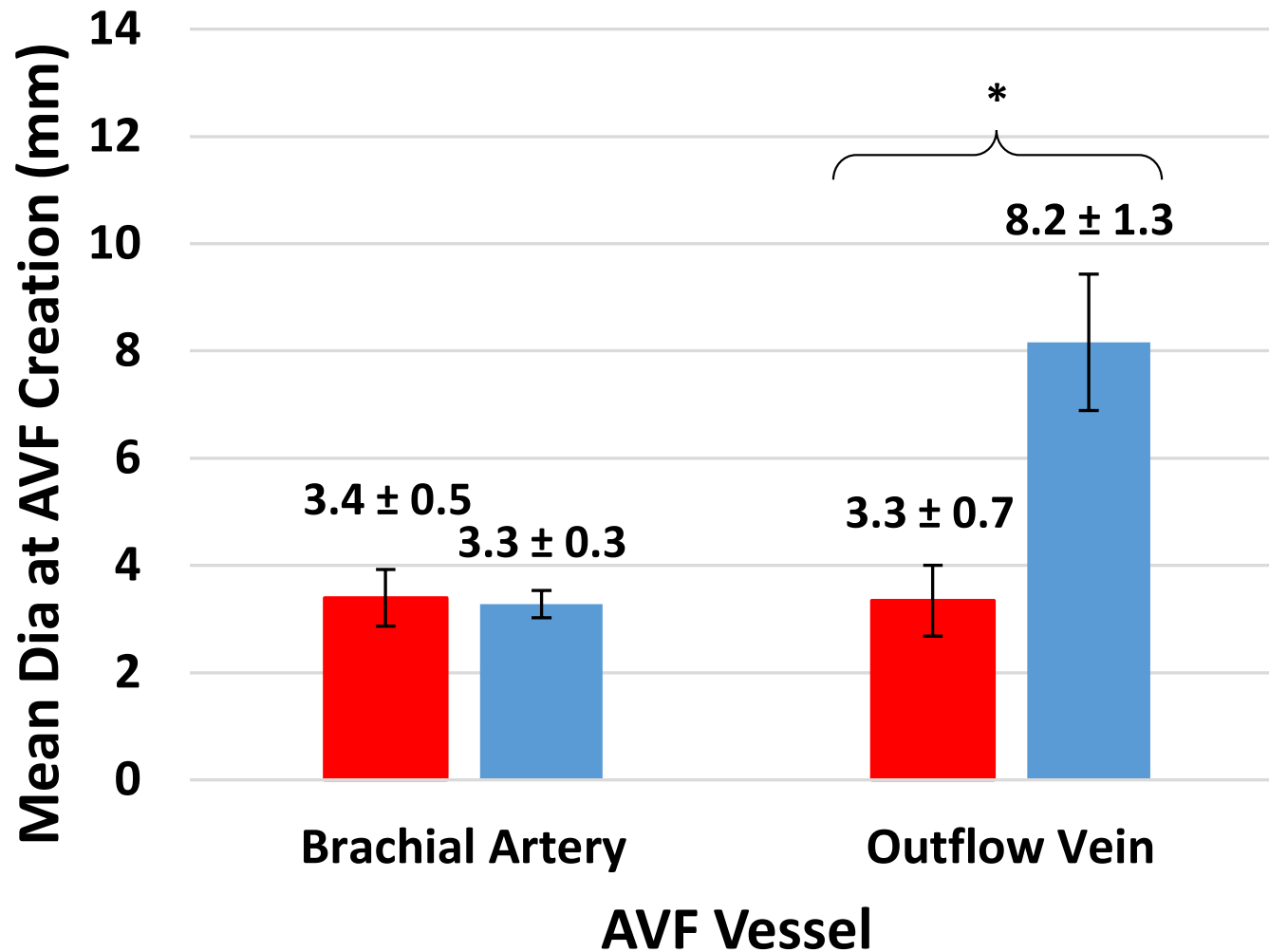


Start of Treatment



After 9 Days of Treatment

AVFs Made with Veins Pre-Treated with AFE System Have Larger Starting Vein Diameters



Outflow veins were significantly larger in AFE-assisted AVFs than in control AVFs at creation, as measured by angiography

■ Control AVF (n=4)

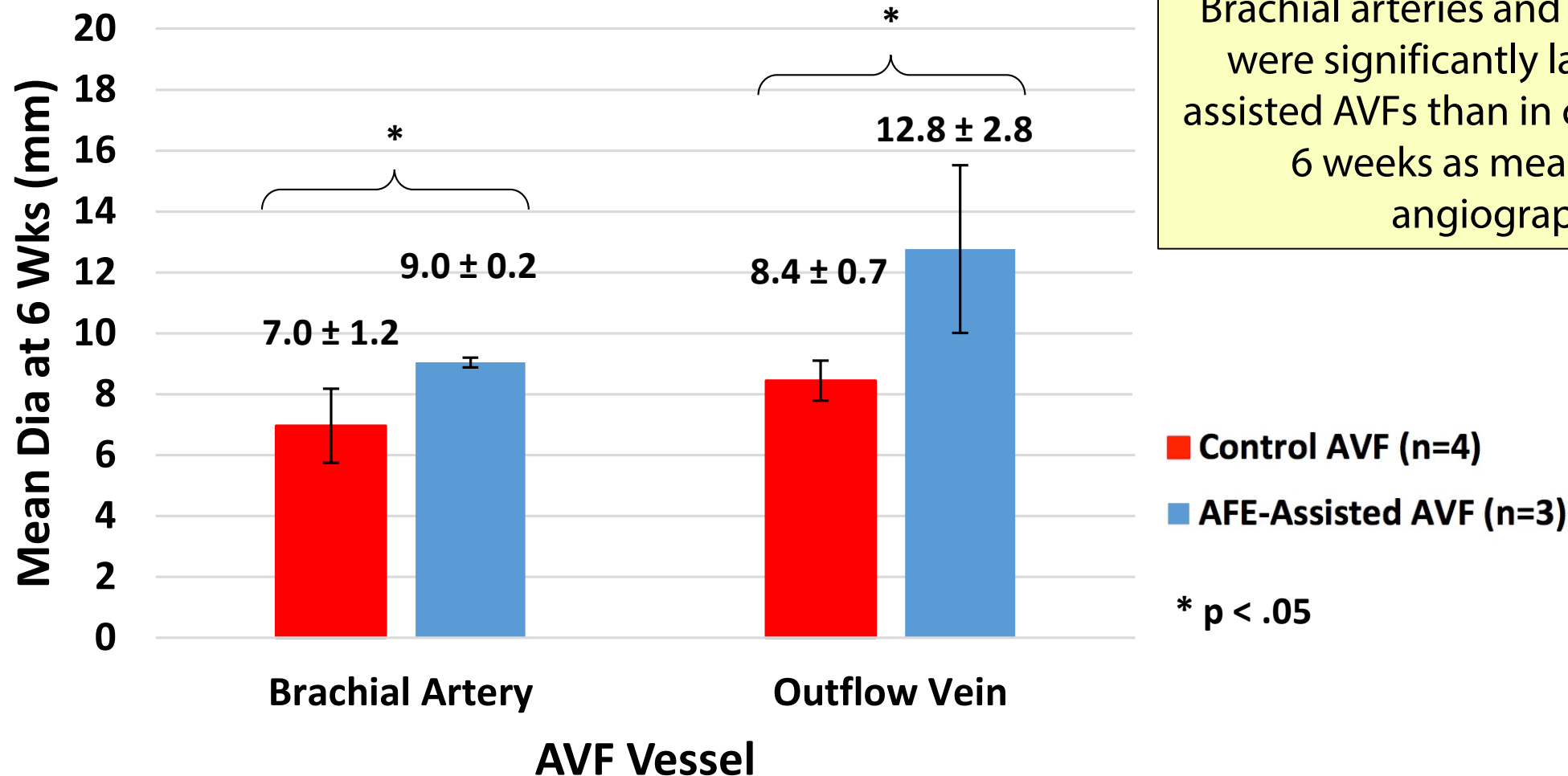
■ AFE-Assisted AVF (n=3)

* p < .05



FlowForward
MEDICAL

AVFs Made with Veins Pre-Treated with AFE System Have Larger Artery and Vein Diameters at 6 Weeks



Brachial arteries and outflow veins were significantly larger in AFE-assisted AVFs than in control AVFs at 6 weeks as measured by angiography

Take Home Messages on Founding Startups

- ▶ Start with a great idea
- ▶ Invest some of your own money
- ▶ Plan all the way to the end
- ▶ Build a great team
- ▶ Raise capital with appropriate terms and valuations
- ▶ Get grants to help fund product development
- ▶ Be prepared to change your product and plan along the way
- ▶ Never compromise your integrity
- ▶ Have fun

Final Thought

One week ago I said that cloning of mammals was years away... it is fun to be alive at this point in history.

Anders Sanberg

Contact Information



F. Nicholas Franano, MD

(913) 730-1651 | nfranano@flowforwardmedical.com