Henry Keynote lecture

Vascular Access: The Story of a Specialty (And a Specialist)

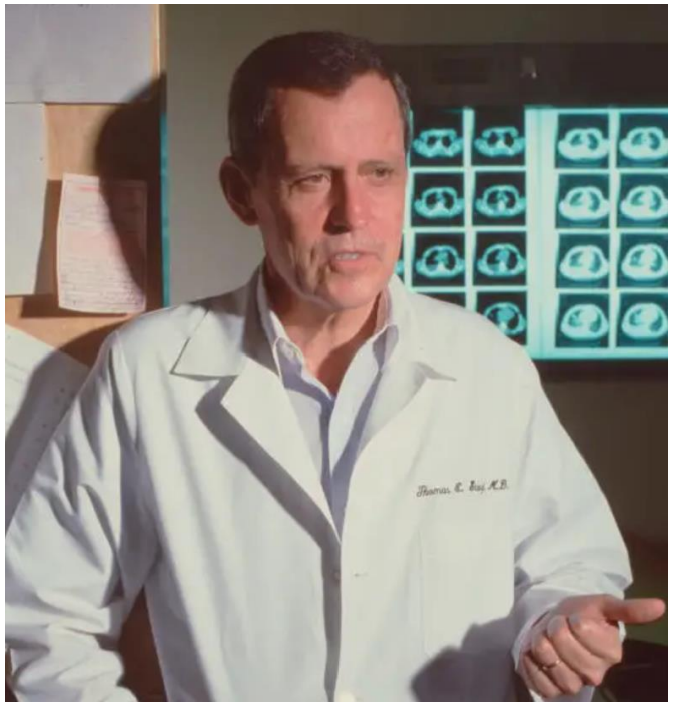
Surendra Shenoy M.D. , Ph. D.
Professor Emeritus
Department of Surgery
Washington University School of Medicine
St. Loui, MO

Disclosures

Medical Advisor - Amplifi Vascular Inc.

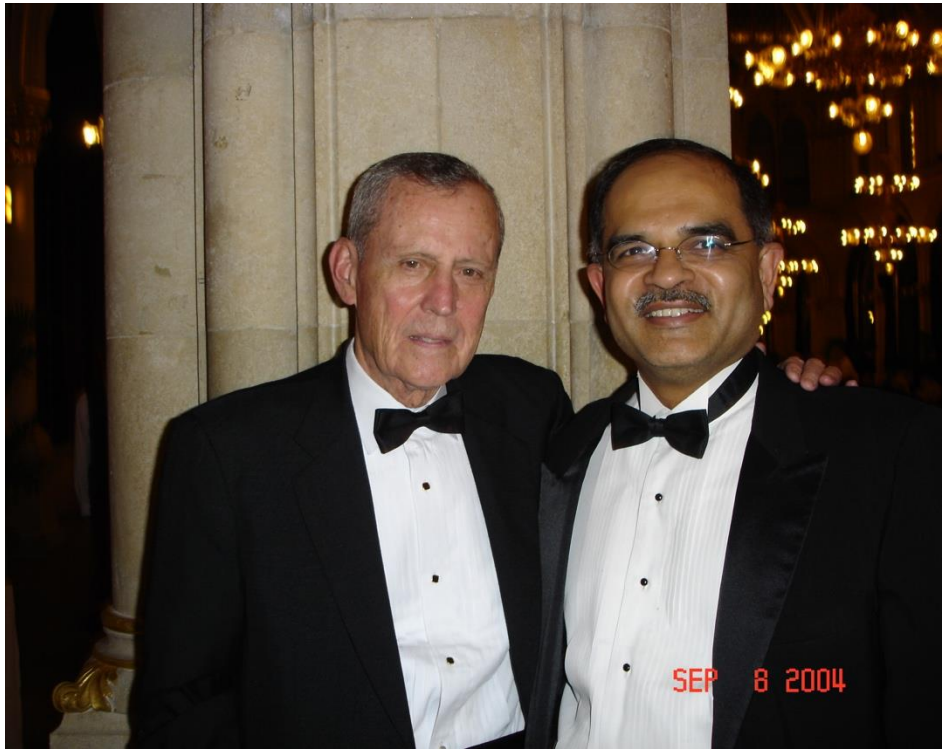
None related to current presentation

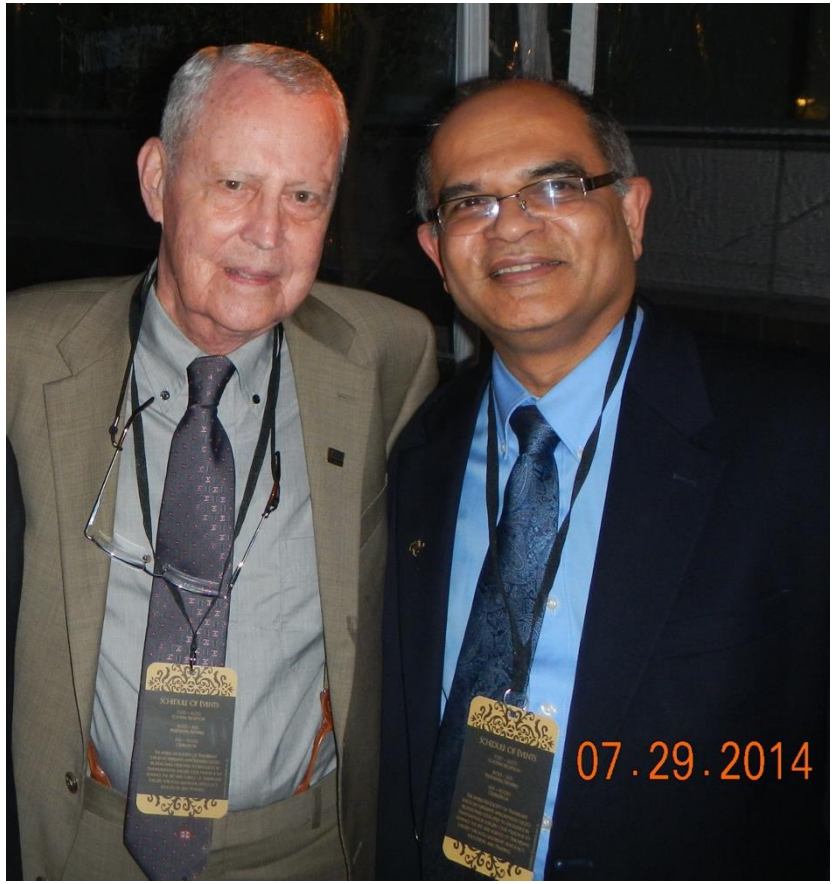
Prof. Thomas Starzl



3/11/1926 – 3/04/2017
Father of modern transplantation

- First attempt liver transplant March 1st 1963
- 1st successful OLTx in July 1967 , Denver, Colorado





- UPMC Over 600 liver transplants in a year in 1985



Introduction

Inception of Gastrointestinal Surgery unit AIIMS -1985

Advanced subspeciality center

(UDDA) Uniform determination of death act of 1981

Transplant fellowship training at WASHU

The Transplantation of Human Organs Act (THOA), 1994

Established transplant program performed vascular access

High AVG prevalence 60-70%

Poor quality CVC, no TDC only Hickman

Poor / non-existent VIR backup

Low AVF prevalence 20-25%

Only major dialysis meeting in the country
Dialysis Access Symposium

Prof. Samiran Nundy
All India Institute of Medical sciences (**AIIMS**), New Delhi

Dhanwate AD Ind J Crit Ca Med 2014; 18: 596-605
Besarab A et. Al. Kid Med 2024;6 : 100871
Simoni G et.al. Neph Dial Trans 1990; 5: 59-61

Dialysis access symposia in the US





Don Lass



Susan Booth

- 1st Vascular Access for Hemodialysis – 1988
- WL Gore Sponsored meeting

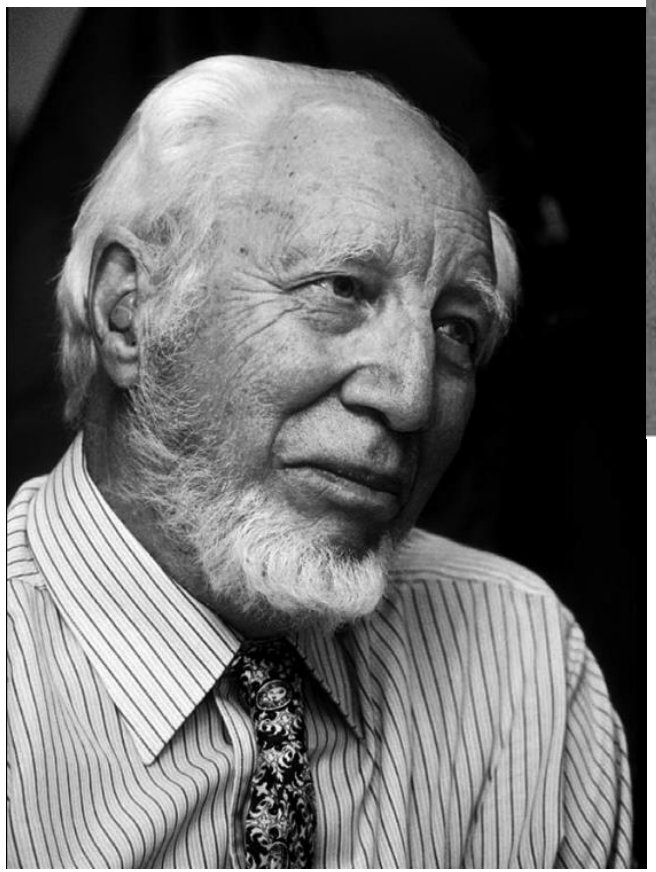


- Compilation of proceedings
- 10Th Vascular Access for HD – 2002
- 1st VASA Hemodialysis Access Symposium 2004
- VASA ‘Mitch Henry lecture’ since 2016

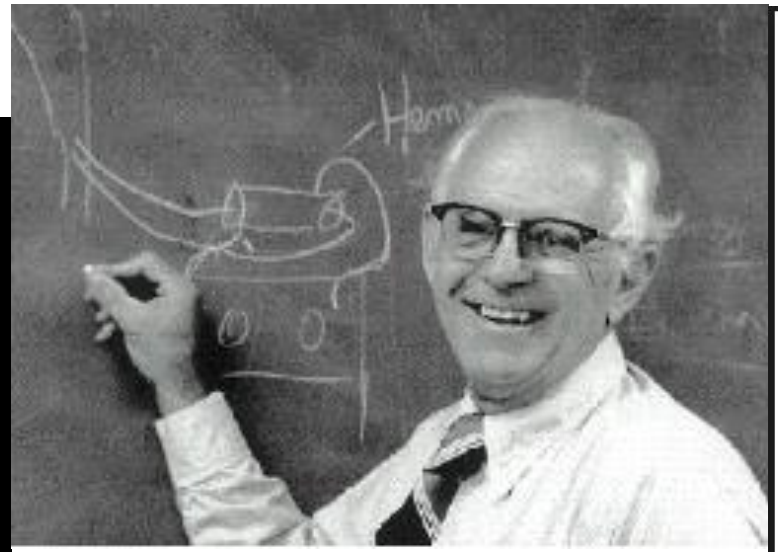


VASA 2004

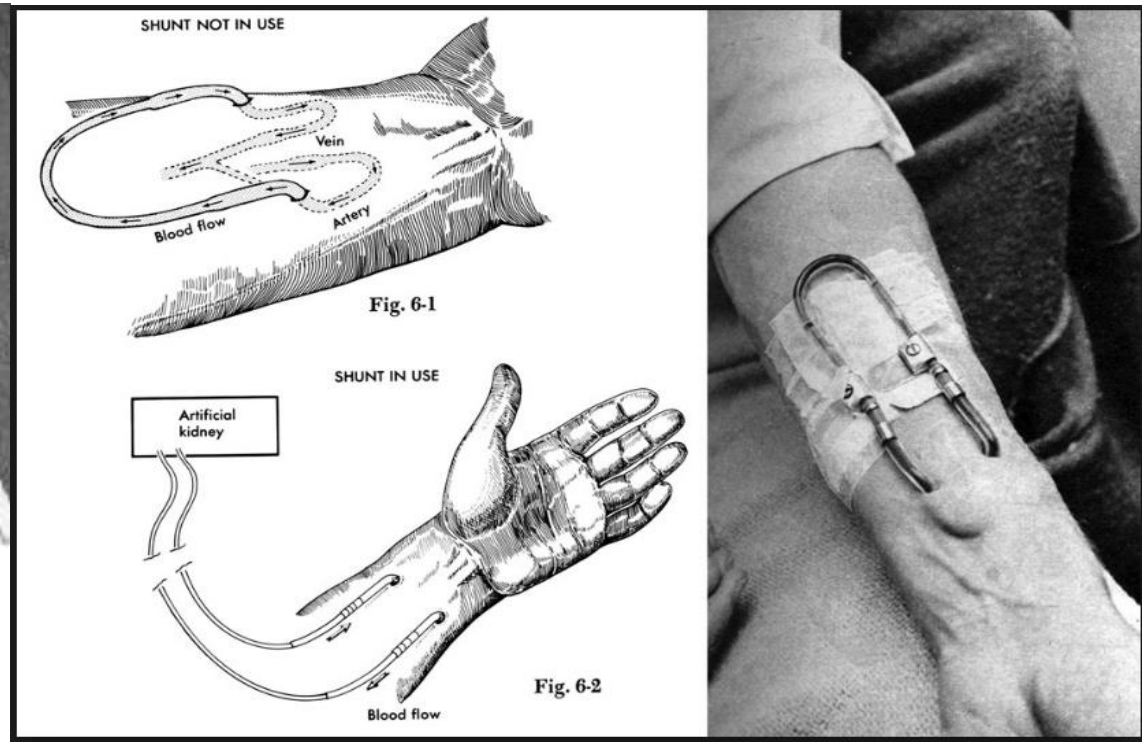
Hemodialysis for renal replacement



Willem Johan Kolff
March 1943



Belding H. Scribner
(1960)



→ **Proof of concept** → **Chronic care modality**

Vascular access – evolution – 1960s – 1990s

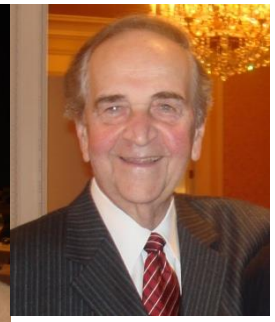




Cimino



Appel



Brescia

Problems

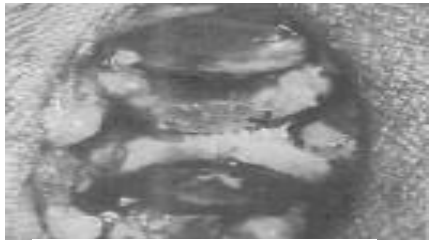
- Limited Anatomic suitability
- Distal venous HTN

Not Universally applicable



Distal venous hypertension

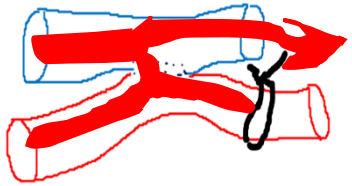




- **Side to side AVF**
- **Distal radial ligation**
- **7-0 silk sutures**

End to side anastomosis

- **Easy to learn**
- **More universally applicable**
- **Minimal distal flow related problems**
- **Inherent risk of failure to mature due to JAS**
- **Varied failure rate (5% - 58%)**



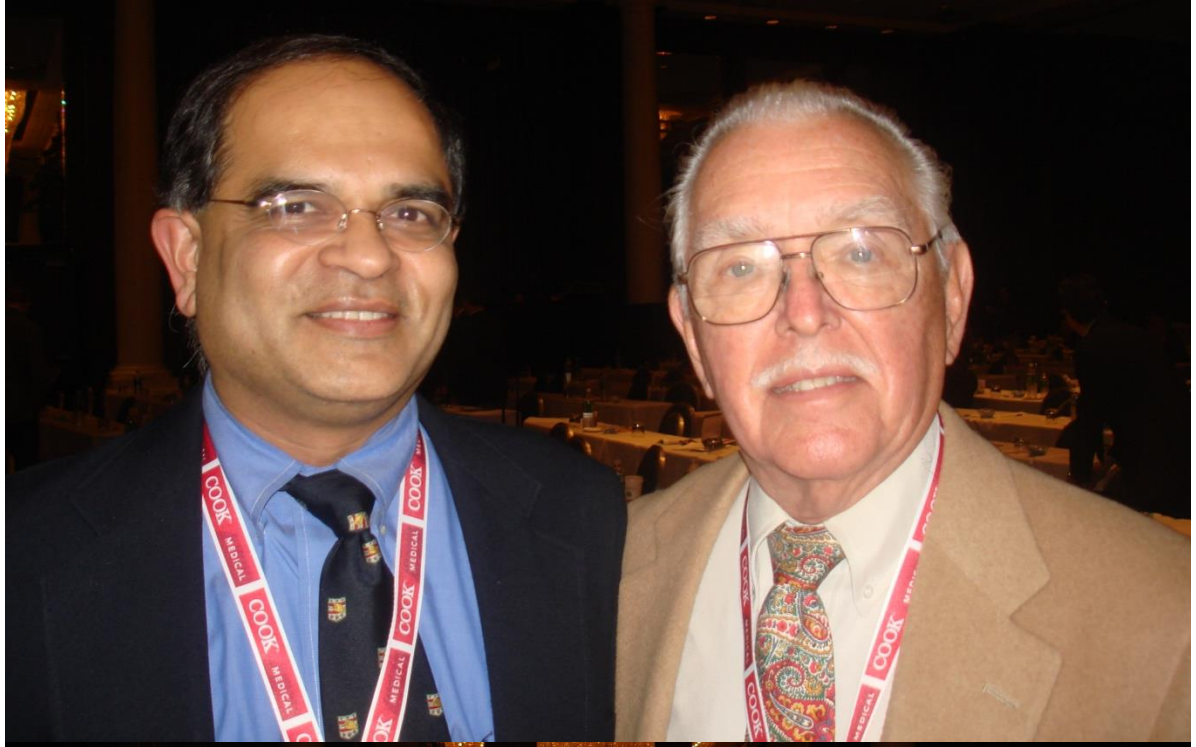


ePTFE Bob Gore in 1969-70

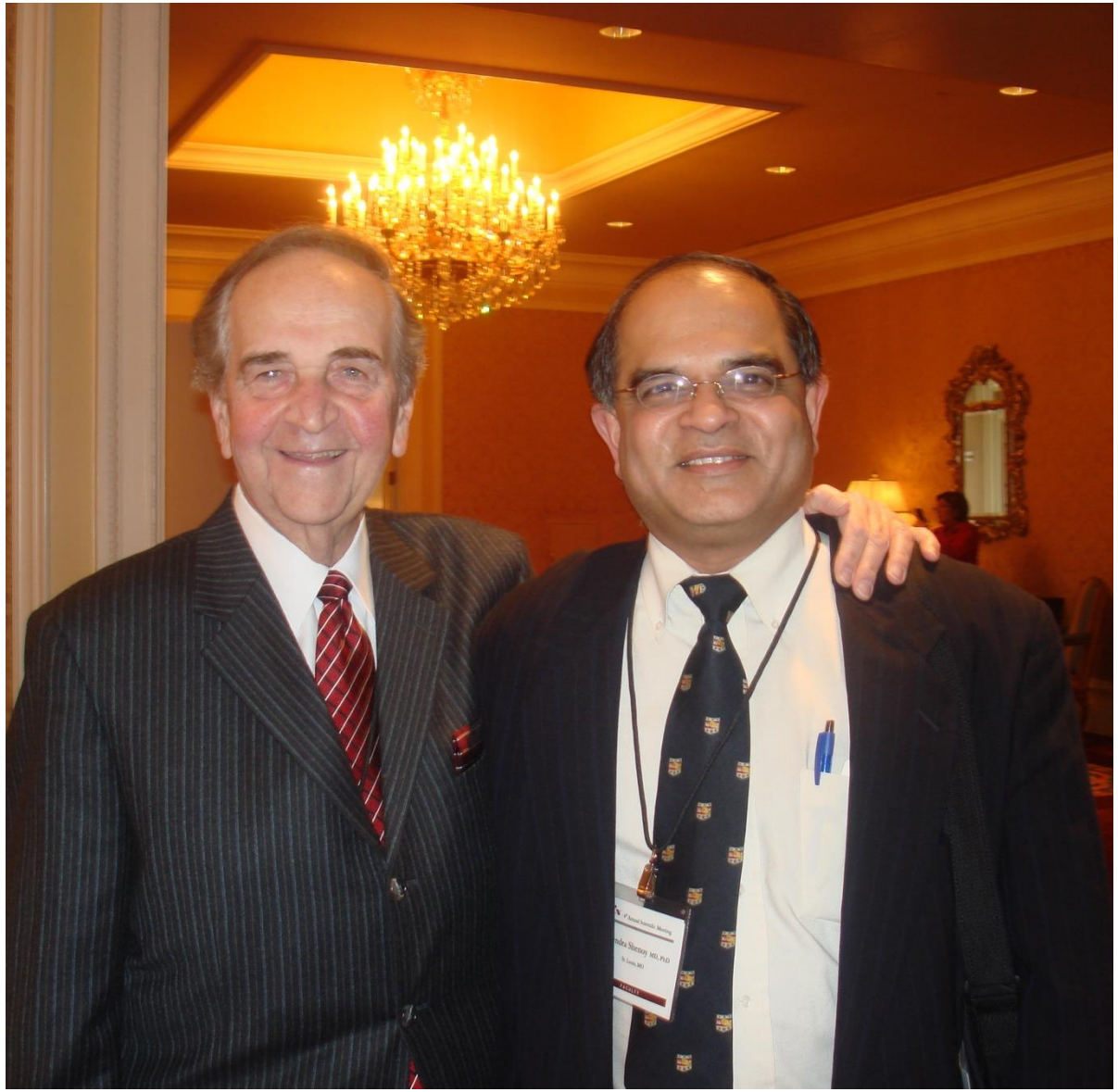
- **Universally applicable**
- **Reliable maturation**
- **Availability of multiple sites**

Section 299I of the Social Security Amendments of 1972

Brescia MJ, Cimino JE, Appel K , Hurwich BJ NEJM;1966:1089
Sperling M et.al. *Dtsch Med Wschr 1967;92: 425-426*
Rohl L, Franz HE, Mohring K et.al. *can J Urol Nephrol 1968; 2: 191-195*
Baker LD et.al. Am Soc Art Int Org (ASAIO) 1976; 22: 382-387
Campbell LD et.al. Am J Surg 1977, 133: 713=716


COOK
MEDICAL


EXIT
COOK



Vascular access evolution 1990s - present

DOQI and KDOQI 1995 -96

National vascular access improvement initiative (NVAII)

‘Fistula first’ breakthrough initiative (FFBI) - 2003

Prevalence of 44% by December 2004!

Can do should not be an indication to do surgery

KDOQI 2006 ‘fistula at all cost may not be a good strategy in some’

‘Fistula first catheter last’ 2014

- **AVF higher failure rate but good once established**
- **AVG easier to establish, has more problems and does not last**

KDOQI 2019 ‘ESKD life plan’

Optimizing use of all modalities developing and periodically revisiting the plan

Lok CE. CJASN 2007; 2 :1043-53
Spergel LM. Sem D 2008; 21: 550-2
KDOQI 2019; AJKD 2020; 75: S1-S164

Overview of progress in ESRD management

Proof of concept (1910-1960) → No reliable access → Acute renal failure management

Stabilization (1960-1970) → Reliable access → AVF, AVG → Chronic replacement modality

Established modality → Assured reimbursement → Social security amendment 1972

Growth and progress of Hemodialysis (1972- present)

Dialyzer technology

Control over blood flow with biofeedback
Ultrafiltration with advanced auto monitoring
On-line hemodiafiltration
Novel membrane technology permeability and biocompatibility
Sorbent technology
Portable dialysis machine
Wearable kidneys

Rapid, galloping improvements

Dialysis access

AV fistulae	AV grafts	Catheters
Change in sites Forearm Upper arm Thigh	Synthetic Autologous Allografts xenografts Bioengineered	Limited application

Relative slow pace of improvement

Vascular access failure

Creation of access precipitates stenosis in the access circuit

Stenosis ⟶ **Stasis** ⟶ **Thrombosis**

Upstream factors ⟶

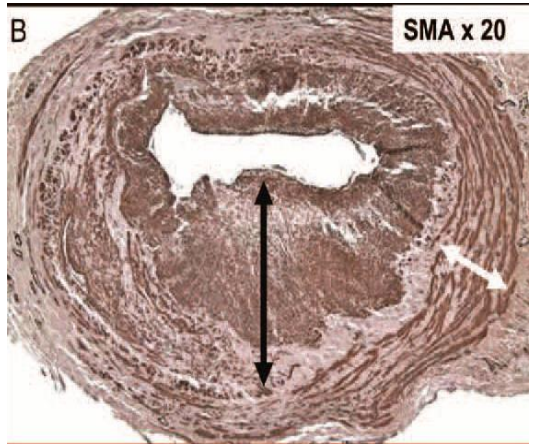
- ➢ Technical: Tissue handling, Suture technique, Clamp injury, vein distention etc.
- ➢ Physiological: Demographics, BP, CO, rheology, vessel size, quality, tissue alignment

↓

Down stream events:

Cellular: **Platelet aggregation, Monocyte /Macrophage infiltration, smooth muscle cell proliferation, extracellular matrix deposition, micro-vessel formation**

Molecular: **Increase expression of cytokines TGF-β1, PDGF, endothelin Altered gene expression prior to the lesion with up regulation of MCP-1, PAI-1, ET-1 Down regulation of TGF-β**



Diskin CJ.N Clin Pra Neph 08;4:628
Tordoir JH Neph Dail Trans'03;18:378
Roy-Chaudhry AJKD 07;50:782;
Vassaloti JA. Sem Dial' 04;17:243
Agarwal A. Am J P Pathol 03; 1759
Woodside KJ AJKD 2018; 71: 793 – 91

Attempts to improve outcome

- **Systemic agents:** Anti coagulants, Antiplatelet, Anti inflammatory etc.
- **Topical agents:** Paclitaxil, Sirolimus, Elastase, endothelial cells etc.

NIDDK workshop in 1998 identified a critical need for research

DAC trial for AVF and AVG

- AVF trial: Clopidogrel reduced thrombosis in new fistulas, it did not increase the number of fistulas that actually became usable for dialysis.
- AVG trial: Aggrenox Trial found that combining aspirin and dipyridamole improved unassisted AVG patency at 1 year(compared to aspirin alone) did not significantly change long-term survival or cumulative graft failure.

Exposed a significant knowledge gap understanding AVF maturation

HFM consortium

- Study the natural history of AVF maturation
- Study the biological and clinical factors

Dember LM. JAMA 2008;299:2164; Peden EK et.al. JVA 2013; 14: 143-51; Lok CE et. al. JAMA 2012; 307; 1809-16; Conte M.S et.al. JVS '09; 50: 1359-68; Paulson WD et.al. NDT 2012; 27: 1219- 24; Al-Jaishi et.el. AJKD 2014;63:464-78

Vascular access failure

Inflammatory response is a innate response to injury necessary for survival of the being

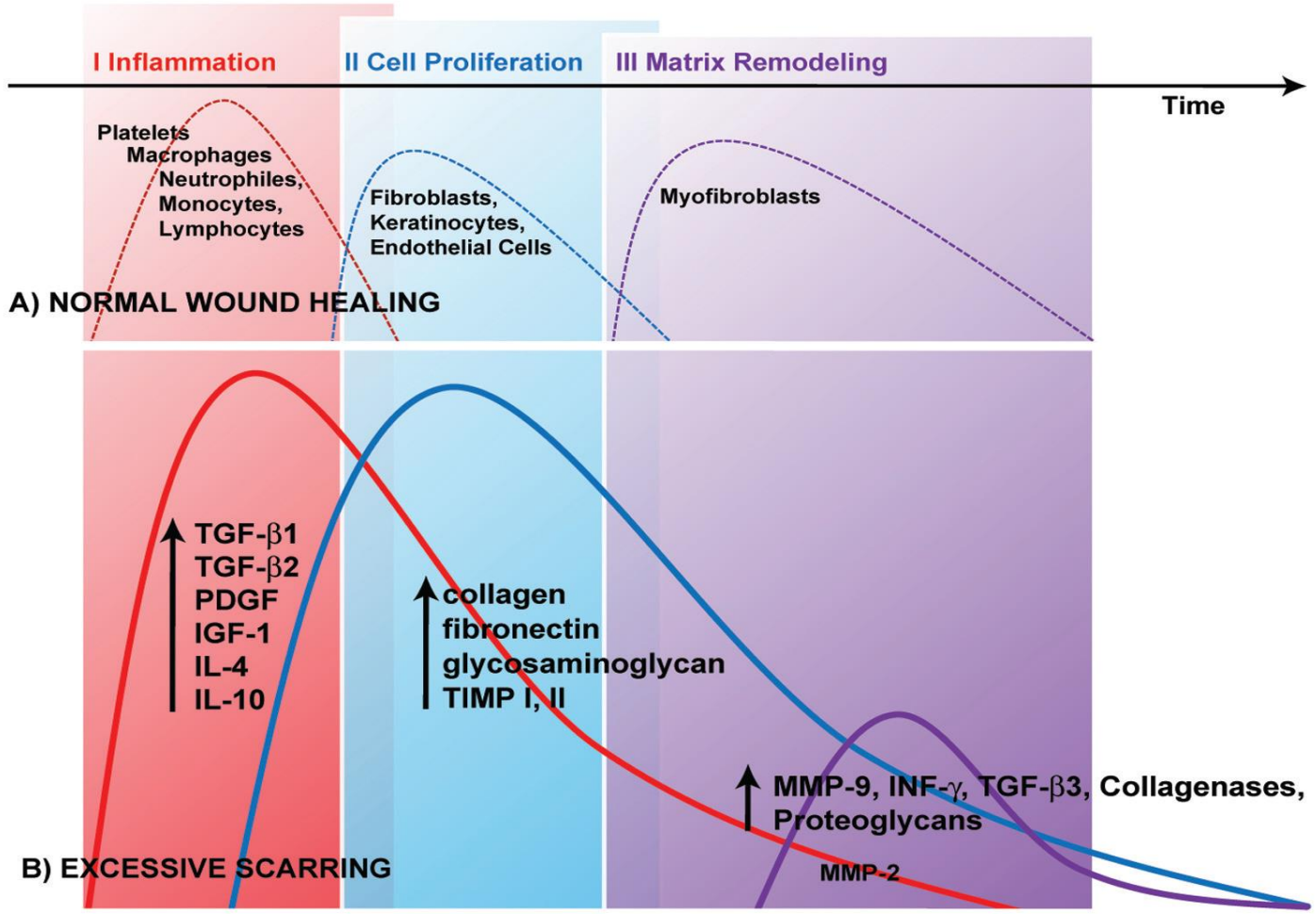
Injury response is similar skin, soft tissue, bones and vessels

‘Intimal thickening is a stereotypic response of vessel wall for any injury’

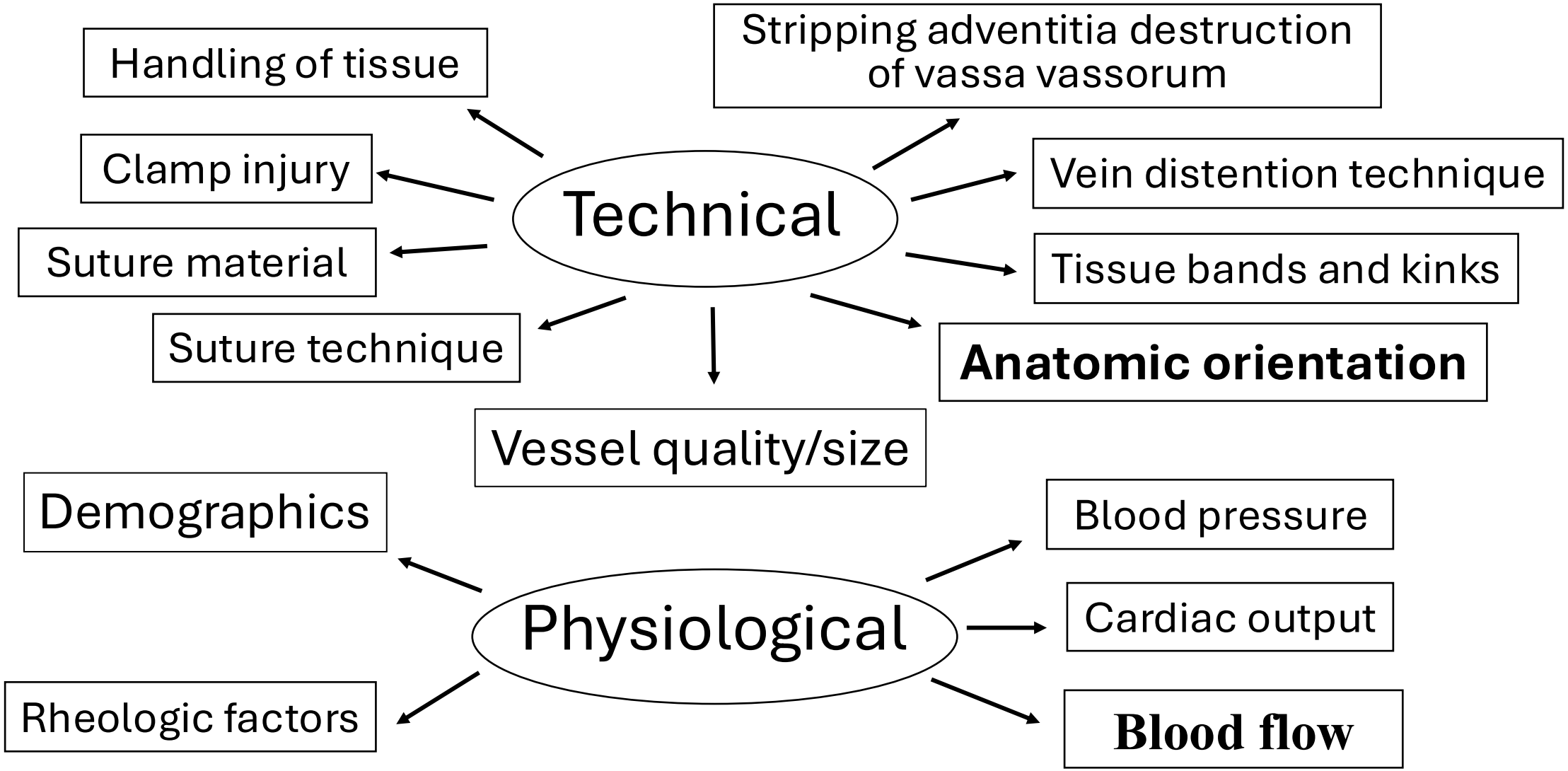
Neointimal response results with any form of vascular injury including infection, inflammation, immune injury, toxic exposure, physical trauma (HTN, balloon catheter) alteration in blood flow

With restoration or normalization of the endothelial cell layer intimal smooth muscle cells can get back to their non proliferative state

‘……..Robbins
Textbook of Basic Pathology

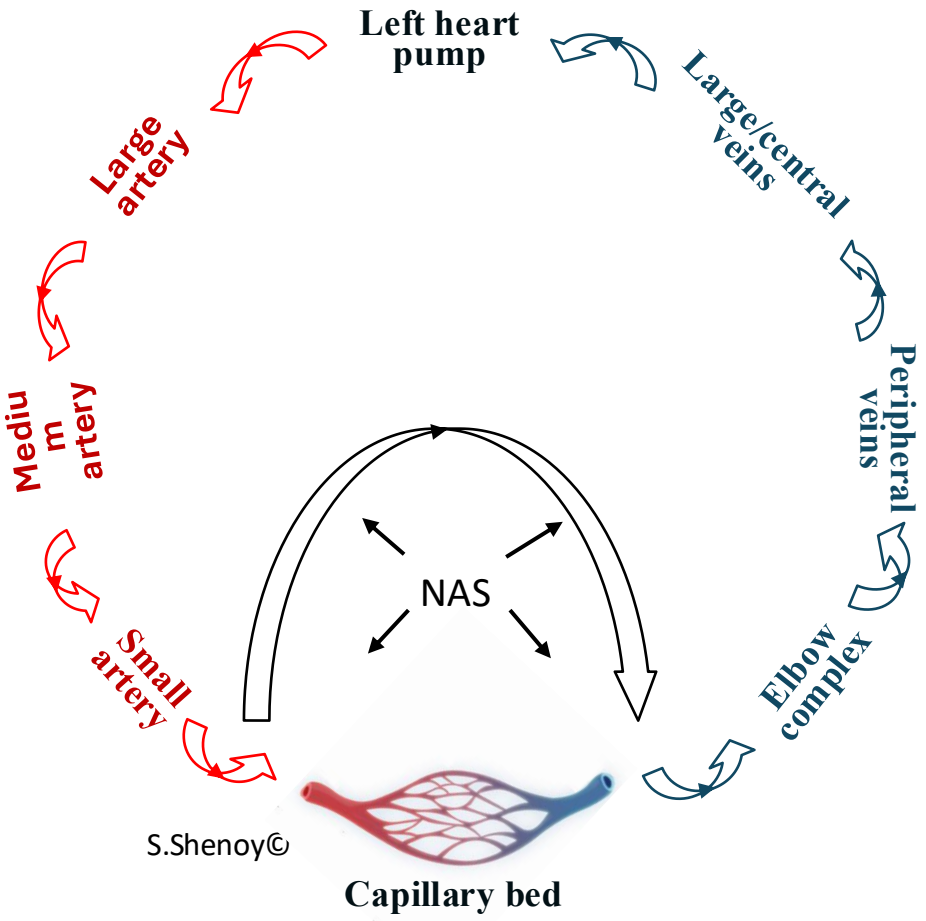


Factors for AVF failure 'upstream events'



Shenoy S. et.al. JVS '03; 28:229
Vassaloti JA. Sem Dial' 04;17:243
Tordoir JH Neph Dail Trans '03;18:378
Dember LM. JAMA 2008;299:2164

Vascular access failure



Creation of AV access produces an acute increase of **20 to 50 times increase** of the blood flow in the outflow vein

AV circuit flow hypothesis

Acute increase in the blood flow caused by AV communication creates flow related 'stress zones' in the vascular access circuit. Shear Stress that exceeds physiological threshold invokes VNH in response to injury. Altering this shear stress with flow modulation mitigate this injury response

.... S.Shenoy

Vascular Access Circuit

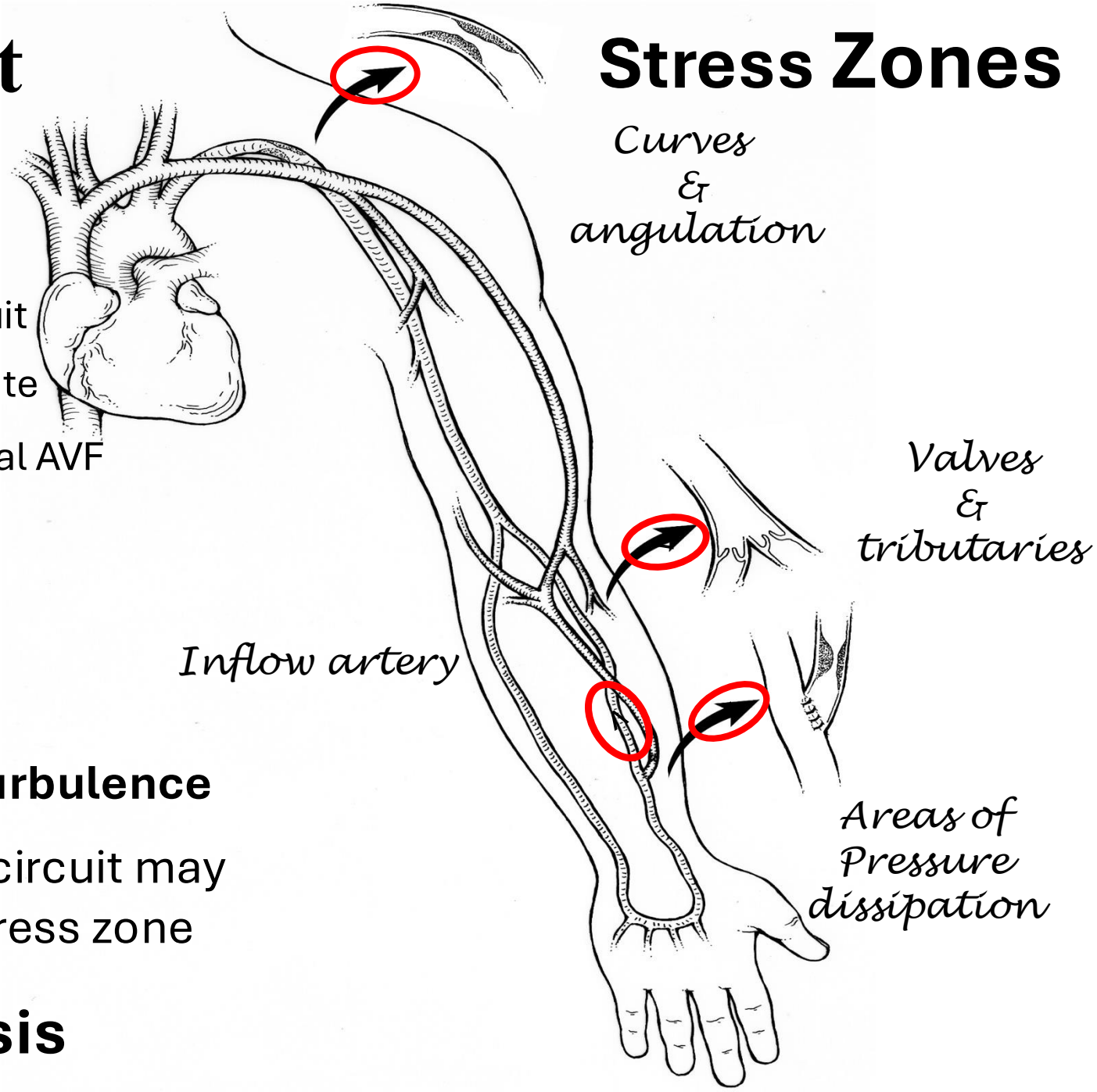
- Area of acute pressure dissipation
  - Juxta anastomotic area
  - Graft vein post anastomotic area
  - Site beyond a stenosis in access circuit
- Curves & angulations: Juxta anastomotic site
  - Juxta anastomotic site in a conventional AVF
  - Swing point in basilic transposition
  - Cephalic arch
- Sites of venous valves
- Areas around **tributary** entry points

CDUS can demonstrate the areas of turbulence

Clinically insignificant stenosis in a circuit may result in significant stenosis in a stress zone

Secondary stenosis

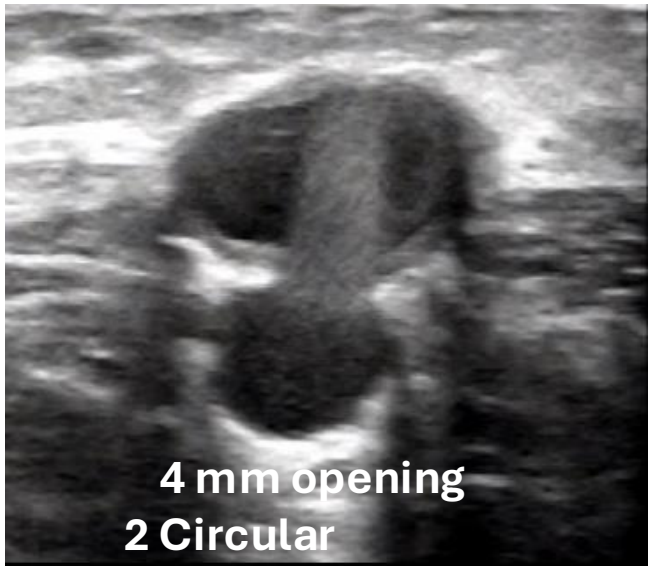
Stress Zones

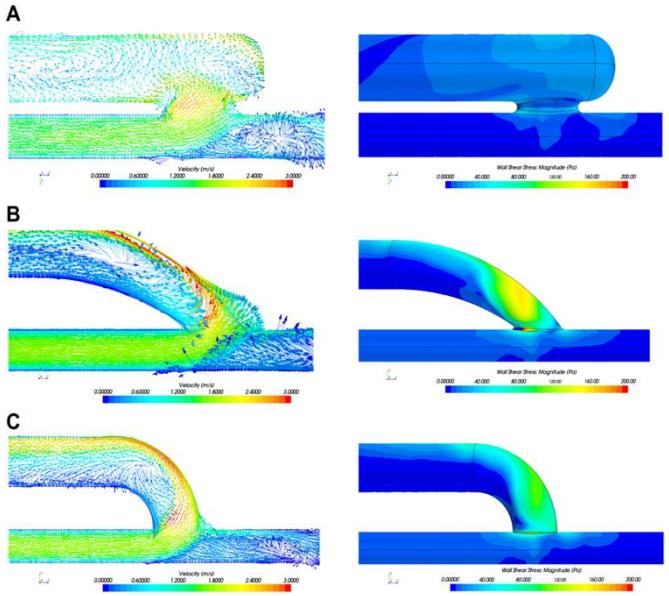


Washington University Single surgeon experience

	Year	Total Access	AV grafts	AV fistulae	% AVF
Pre DOQUI	1993	65	51	14	22
	1996	71	50	21	30
Post DOQUI	1998	158	82	76	48
	1999	154	77	77	50
	2000	125	50	75	60
US lab	2001	104	44	60	58
	2003	83	36	48	57
	2004	106	25	81	77
US by operator	2005	179	26	153	86
	2006	129	17	112	87

Early flow injury concept based intervention





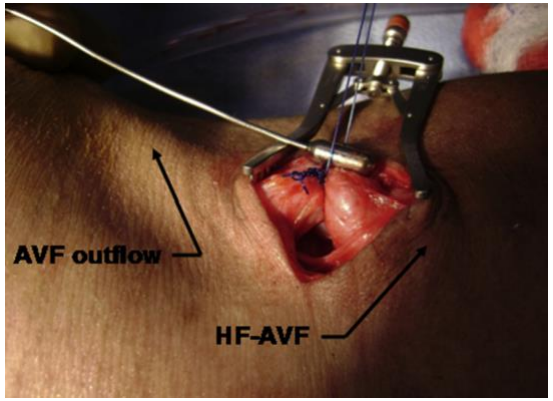
‘Piggy back’ technique - pSLOT

Provide optimal hemodynamics at the anastomotic region

- Avoids angulation
- Provides consistent small anastomosis
- Standardized anastomosis
- Flow from a circular into a circular lumen

Reduced JAS from >30% to <6%

Good long term clinical outcome



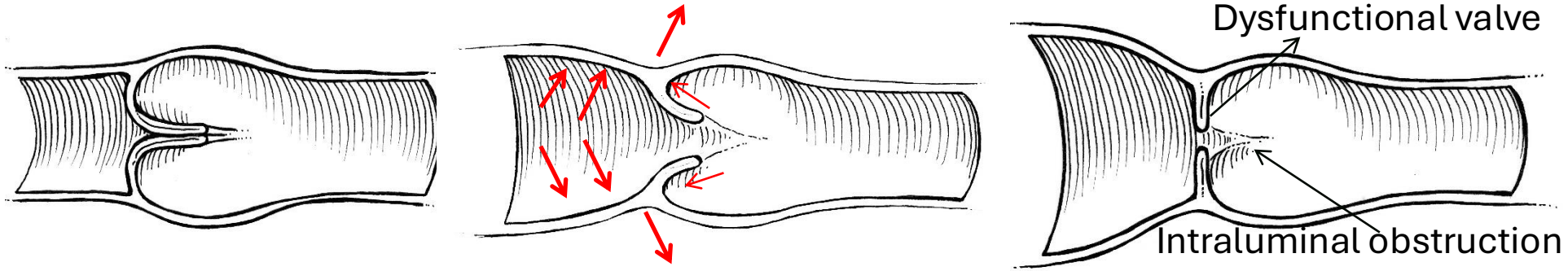
Precision banding for high flow access

Shenoy S. JVA 2007; 3: 152-54
Hull J. JVS 2013; 58:187-93
Darcy M et.al JVA 2017;18:515-521
Gkotsis G et.al. Ann Vasc Surg 2016; 31:85-90

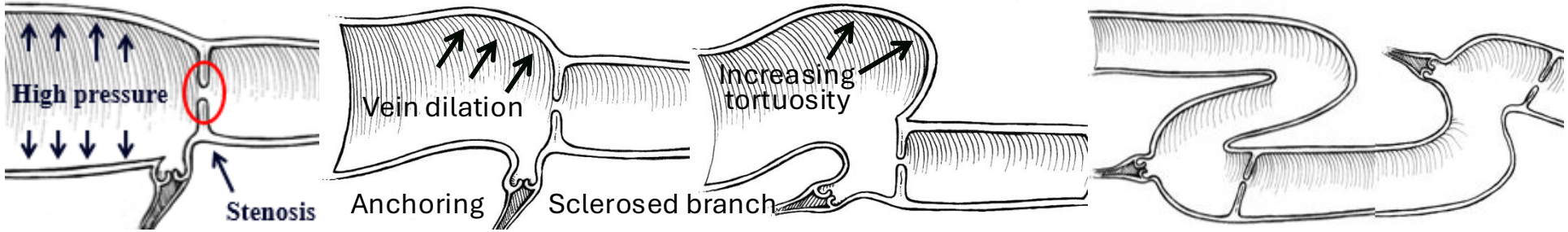
Access failure - Reasons other than JAS

Venous anatomy: contribution of valves and tributaries

Preexisting problems and ‘de novo’ issues



- Tributary + valve induced problems



Outflow Anatomy a major contributor for maturation and long-term function

Access needs close planned follow-up

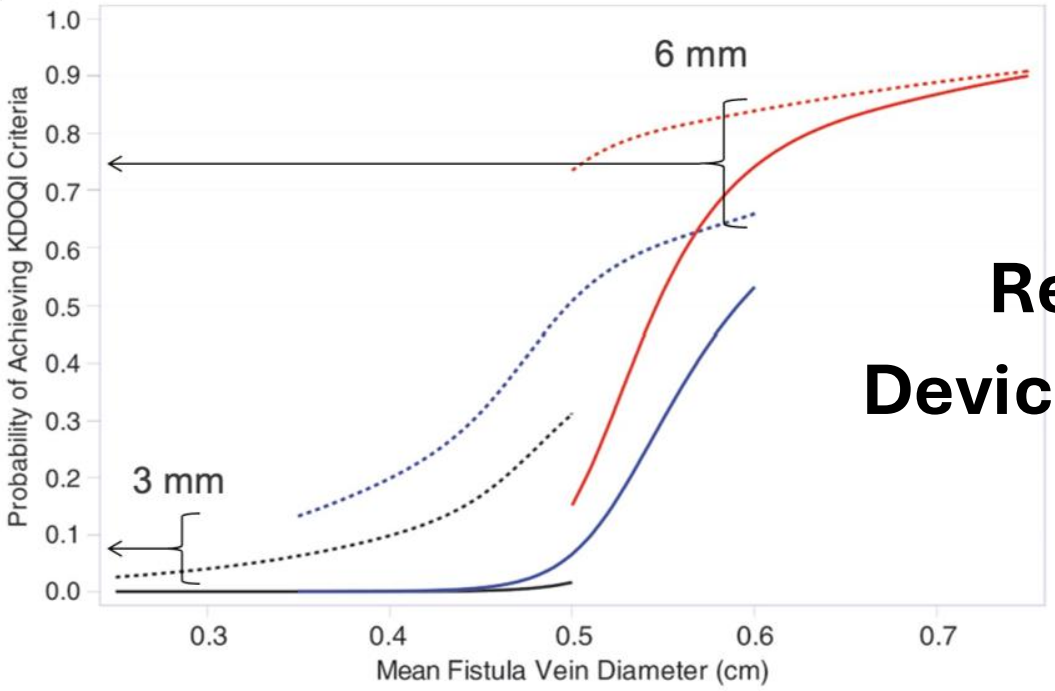
Clinical trial end points in Dialysis Access project

Kidney Health initiative

Phase of life cycle	Creation	Maturation	Initial clinical use	Sustained clinical use	Dysfunction
Duration	Immediate	Weeks	Weeks	Unlimited	Immediate
Direction of movement	→	→	→	↔	
End point	Patent AV access	Physiologically mature AV access	Clinically functional AV access	Uninterrupted clinical use	Restoration and preservation of clinical use

Opportunity to develop studies with device/study specific end points

Beathard GA et.el Clin J Am Soc Nephrol2018; 13: 501–512
Shenoy S et. al. Clin J Am Soc Nephrol 2018;13: 490–494

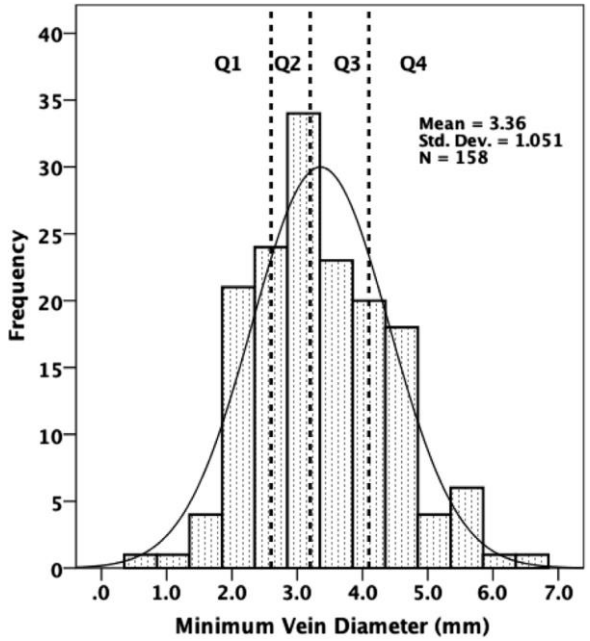


Current state of Vascular Access

Renewed interest in improving out come

Devices to address different aspect of AV access

Probability of maturation increases with size of the vein

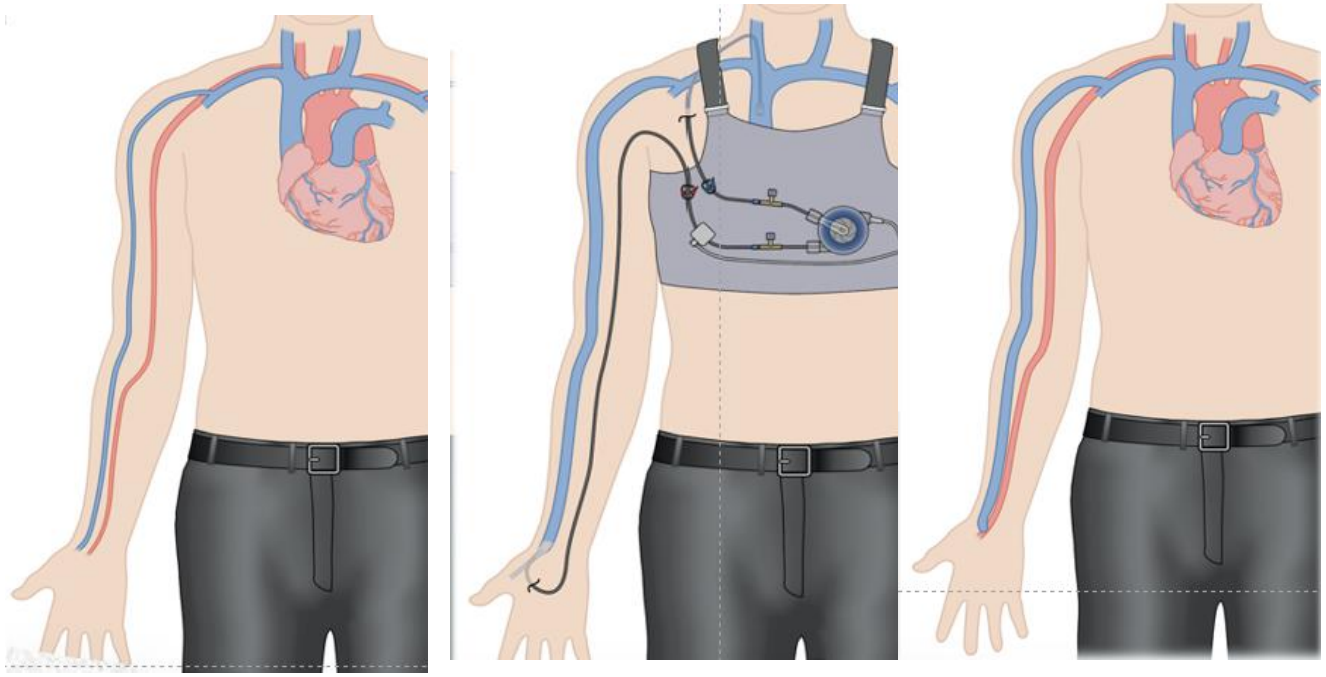


- ❑ 3mm Vein <20% probability of maturation
- ❑ 6mm vein >70% probability of maturation

Vein dilation pre fistula creation

Robbin M., et al. 2016; 279: 620-629;
Dageforde LA *et.al. JVS 2015; 61: 170-176*

Amplifi ™



Portable blood pump worn up to 3 days before AVF is created

- **Promising OUS clinical data**
- **FDA IDE approval**
- **Breakthrough designation**
- **Randomized partially blinded pivotal trial design**

Potential to reduce maturation time

Potential to increase prevalence of radio cephalic fistulae

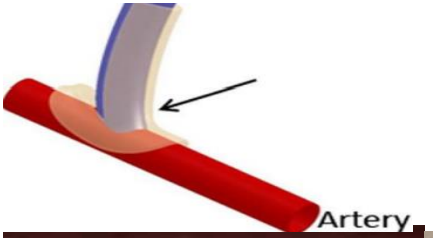
Amplifi vein dilation system is not FDA approved and Not available for commercial sale

AMPLIFI-1 Study (ClinicalTrials.gov ID: NCT07211035)

AV Access Innovation attempts



- Pre creation vein dilation
- AVF creation
- Anastomotic support devices
- Cannulation support device



Amplifi

WavelinQ, Ellipsys, Endoforce

Velocity pAVF System

Topical drug delivery PV-108

VasQ

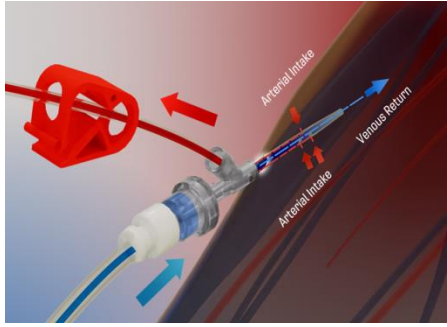
Venostent in pivotal clinical trial

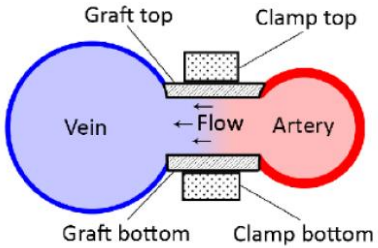
AVF – Voyager, Sonavex

AVG Innavasc graft

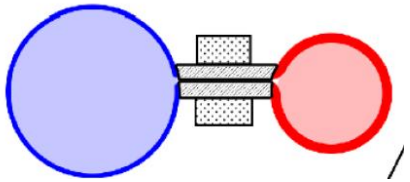
US markers

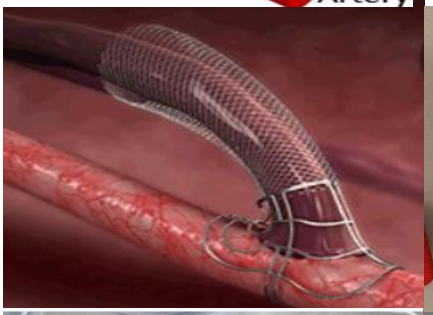
Single needle cannula





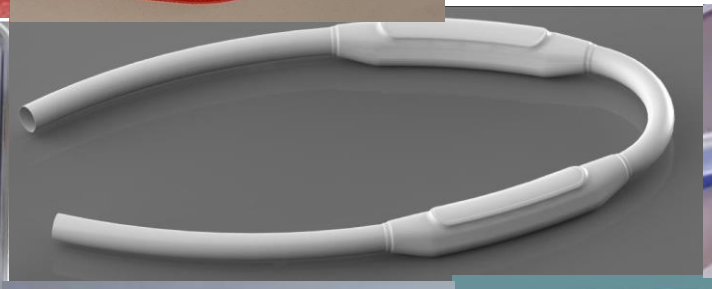






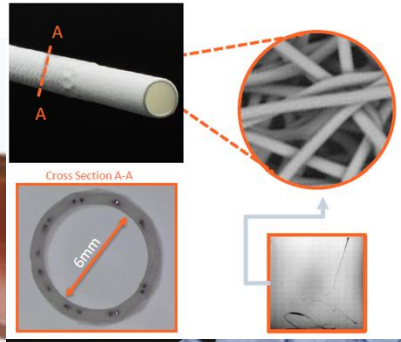


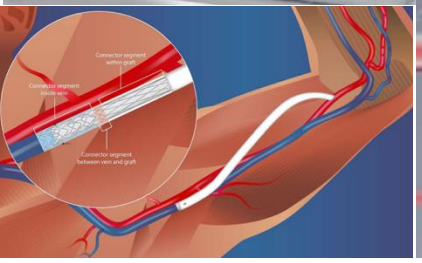


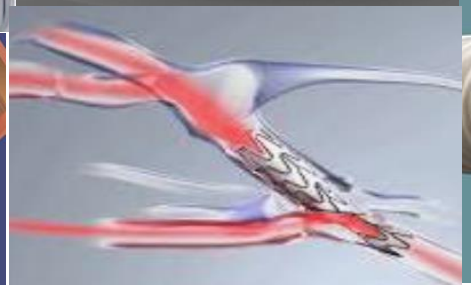






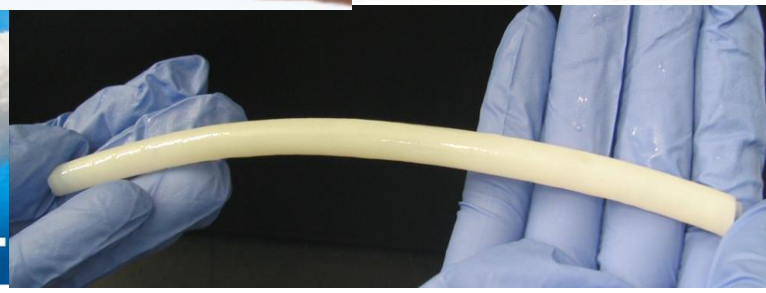












Summary

- Development of Hemodialysis was ‘ proof of concept’ 1910- 1960
- HD became a chronic renal replacement modality with inventio of external/ internal shunts
- Assure reimbursement helped significant improvement in the field
- Compared to dialyzer technology growth in filed of vascular access was stagnant
- Understanding flows with US and CFD along with redefining endpoints have rekindled the R&D in the field








INDIA

Thank You

