


Current Strategies for Selection of Biologic Versus Synthetic Grafts for Hemodialysis Access


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Disclosure


- Consultant LeMaitre
- Consultant Gore




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Biologic versus Synthetic

Structural	Functional
<ul style="list-style-type: none"> • Anatomical differences • Graft Incorporation • Ease of Handling • Degradation • Biocompatibility • Timing of Cannulation • Loop Graft configuration 	<ul style="list-style-type: none"> • Patency • Occlusion/Stenosis • Infection rates • Inflammation • Steal Syndrome




What about Patient's Choice and Costs ???



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Arterio-venous graft (AVG) Access for Hemodialysis Controversies and Challenges


- Insertion of AVG remains the only option when AVF have been exhausted apart from the long term central venous catheterization
- Vascular replacements have been used for over 60 years with synthetic polymers (first autologous saphenous vein (SV) graft implemented in 1967 by Favaloro et al.)
- Expanded PTFE (ePTFE): 1969, W.L. Gore patented ePTFE, a microporous material, biostable and has a non-reactive surface, making it a good choice for vascular grafts



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Vascular Grafts Originate from Four Sources:


1 synthetic polymers	}	Prosthetic/Synthetic Grafts
2 xenogeneic tissues		
3 allogeneic or autologous tissues	}	Biologic Grafts
4 engineered tissues		



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Synthetic Grafts


- **PTFE, ePTFE** (Polytetrafluoroethylene , Venoflo II)
- **Impra or Goretex** (Modified PTFE)
- **Hemasite** (Titanium device, transcatheter button)
- **Vectra** (self sealing 3 layered polyetherurethane-urea vascular access)
- **Acuseal** (Gore), **Flixene** (Getinge)
- **InnAVasc Graft** (clinical trials)



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Biologic Grafts/ Biohybrid Grafts

- Greater Saphenous Vein (Autogenous or Homologous)
- Denatured homologous vein (DHV) grafts
- Cryopreserved venous homografts (saphenous or femoral vein)
- Denatured arterial homografts (Nexian AVX)
- Human umbilical vein
- Bovine mesenteric vein (ProCol)
- Bovine carotid artery graft (Artegraft)
- Denatured bovine collagen prosthesis (Omniflow only in Europe and Canada)
- Modified bovine ureteric graft (Synergraft)
- Genetic Engineer vascular graft (Humacyte)


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Ideal Vascular Graft for Hemodialysis Patients

- Easy to handle
- Closely mimic the native vessels
- Non-thrombogenic
- Immunologically inert
- Resistance to infection
- Resistant to puncture trauma
- Able to retain tensile strength
- Manufactured at a reasonable cost


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Best Material Controversy between Biologic versus Synthetic material for arteriovenous graft








- ❖ no large prospective, randomized trials
- ❖ the materials have been used under different circumstances
- ❖ the methods for reporting patency have not been uniform



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Arteriovenous Graft Challenges 101

- While all the hemodialysis AV grafts have performed well , each of these types of vascular grafts have vastly different outcomes in vivo, with **patency, infection, steal syndrome, and degradation (aneurysm formation)** presenting as the most frequent challenges.
- The most common cause of hemodialysis av graft thrombosis is venous outflow stenosis


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VASCULAR GRAFTS STRENGTHS & WEAKNESSES						
	Polymer grafts	Autologous vessels	Xenografts	Cryografts	TEVG	
Off the shelf	High	Low	High	Medium	High	
Resistance to thrombosis & intimal hyperplasia	Low	Medium	Medium	Medium	Medium	
Durability	High	Medium	Low	Low	High	
Compliance	Low	High	Medium	High	High	
Regenerative capacity	Low	High	Medium	Medium	High	
Intraoperative	Medium	High	Low	Medium	Medium	
Resistance to infection	Low	High	Medium	Medium	High	



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Outflow Venous Stenosis

Venaflo

- Venaflo graft has a cuff at the graft venous anastomosis outflow and larger diameter
- Comparison of straight and Venaflo-type cuffed arteriovenous ePTFE grafts show shear stresses on the floor were more pronounced in the straight configured shunts compared to the cuff which correlate with intimal hyperplasia





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Outflow Venous Stenosis

Spiral Flow AV Graft

- Basis of the hemodynamic environment created by the spiral laminar flow and may be a significant contribution to preventing neointimal hyperplasia and hence AV access graft failure.
- There is no existing published peer reviewed data on the comparison of spiral and standard PTFE in terms of patency rates, cost efficacy and feasibility of use.




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Outflow Venous Stenosis

Gore Hybrid Stent Graft

- Percutaneous venous anastomosis for small outflow vein
- Failure to incorporate and high stent stenosis
- No longer available




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Central Vein Pathology

Herograft

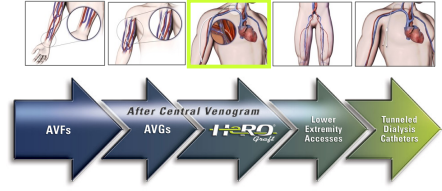
- 1) all AV access options in the upper extremity have been exhausted;
- 2) patient has an appropriately high blood pressure and good cardiac function
- 3) patient has suitable anatomy for HeRO placement consisting of (a) adequate inflow artery and (b) patent or correctable central venous outflow
- 4) patient ESKD life-plan includes long duration on HD (i.e., > 1 year).



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Role of the HeRO Graft in Dialysis Access Algorithm¹



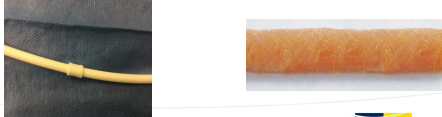
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¹SCVS, 27th Annual Society for Clinical Vascular Surgery Meeting, Orlando, FL, March 2008. Christopher L. Sosa MD, Jean M. Parvizi, MD and Mark H. Goldman, MD
Division of Vascular Surgery, Eastern Virginia Medical School, Norfolk, VA

Bovine Carotid Artery Incorporation

- Bovine Carotid Artery has an outside fibrous tissue that clings onto subcutaneous tissue
- Similar to cuff from tunnelled catheter that incorporates to the tissue better



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High Risk of Infection

- Patients with high risk of infection such as patients under immunosuppression, HIV, obesity, thigh av graft access
- Tissue grafts have decrease incidence of infection when compared to PTFE

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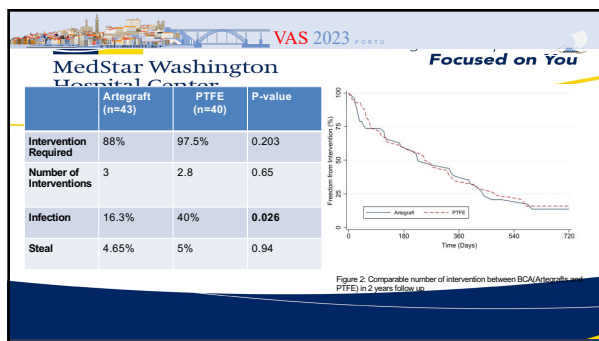
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VAS 2023 PORTO

6 month	Artegraft (n=43)	PTFE(n=40)	P-value
Primary Patency	58.41%	59%	0.82
Primary-Assisted Patency	88.6%	80.6%	0.35
Secondary Patency	94.3%	85.7%	0.23

1 year	Artegraft (n=43)	PTFE (n=40)	P-value
Primary Patency	34.9%	34.1%	0.88
Primary-Assisted Patency	69.7%	54.6%	0.21
Secondary Patency	82.4%	59.1%	0.12



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VAS 2023 PORTO

- Bovine carotid artery grafts have comparable primary, primary-assisted and secondary patency to ePTFE grafts.
- Number of interventions required were also similar in both groups.
- BCA grafts in comparison to ePTFE had fewer infections.
- BCA graft may be a good alternative if not better conduit for HeRO graft insertion in ESRD patients.

- ### Early Cannulation AV Grafts
1. Vectra
 2. Accuseal
 3. Flixene
 4. Rapidax
 5. Avflo (no longer available)
 6. InnAvasc (clinical trials)
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Early Cannulation AV Grafts

<p>Pros</p> <ul style="list-style-type: none"> • Early cannulation promotes decrease catheter use and early removal 	<p>Cons</p> <ul style="list-style-type: none"> • Very thick thus harder to feel thrill • Noncompliant and stiff thus problems with anastomosis with tenting or kinking (newer grafts have thinner walls for doing anastomosis)
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Early cannulation grafts for hemodialysis: An Updated systematic review

Julien AI Shakarchi et al: J Vasc Access 2019 Mar, 20 (2): 123-127

early Cannulation of AVG's with 72 hrs

	FLIXENE	AVFLO	ACUSEAL	VECTRA
Primary patency 12 months	43.3%	58.2%	43.6%	63.7%
Secondary patency 12 months	73.4%	79.2%	70.5%	85.8%

- Conclusion: CONFIRMS EARLY CANNULATION IS NOT DETRIMENTAL ON THE EARLY OUTCOME OF EARLY CANNULATION GRAFT PATENCIES

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Biologic Graft Early Cannulation

Early Cannulation of BCAG Reduces Tunneled Dialysis Catheter-Related Complications: A Comparison of Bovine Carotid Artery Graft Versus Expanded PTFE Grafts in Hemodialysis Access
M. Preston et al. *Comparative Study Vasc Endovascular Surg.* 2019

	142 BCAGs	124 ePTFE Grafts	P value
Graft Cannulation	127 (89.5 days)	42 (33.9 days)	(p<0.01)
2 years primary patency	33%	14%	(p=0.03)
Primary assisted patency	57%	25%	(p<0.001)
2 years secondary patency	55%	33%	(p=0.05)
Complication rates	1.89 (0.24/patient yr)	2.54 (0.48/patient yr)	(p=0.01)
Mean intervention/patient	1.89 interventions	2.76 interventions	(p=0.03)

* BCAG permits earlier cannulation for hemodialysis access with superior primary and primary assisted patency rates compared to ePTFE grafts

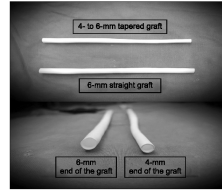



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Steal Syndrome Complication

- Risk factors are diabetes, female sex, coronary heart disease, cerebrovascular disease, and age over 60 as risk factors
- Taper Graft 4mm to 7mm decreasing flow to graft and maintaining flow to hand
- Different sizes with Artegraft but not tapered





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Kinking of Graft

- Ringed synthetic graft prevents kinking especially crossing joints
- Loop grafts tend to kink at the apex
- Biologic grafts do not have this thus important when tunneling graft



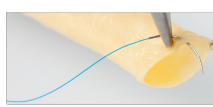


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Aneurysm Formation

Bovine Mesenteric Vein
Thinner Wall



Bovine Carotid Artery
Thicker Wall






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Synthetic Grafts

Polytetrafluoroethylene (PTFE, 1970's) and expanded form (ePTFE)

Pros	Cons
<ul style="list-style-type: none"> Increased porosity Better tissue adhesion Improved pliability vs polyethylene terephthalate (Dacron) Secondary patency 76, 55-59, and 43% 6, 12 and 24 months (H.E., Katzman et al. 2005; K.D. Gibson et al. 2001; T.C. Hodges, 1997) 	<ul style="list-style-type: none"> High incidence of occlusion (myointimal hyperplasia at venous end) Seroma formation High infection rates Suboptimal patency rates Primary patency 28% 1 year (H.E., Katzman et al. 2005)



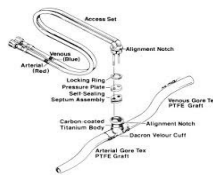
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Synthetic Grafts

Hemasite

- Prosthetic device made of titanium introduced in 1980s
- T shape body that obviates the need for skin puncture
- Major complication is infection with poor long term results





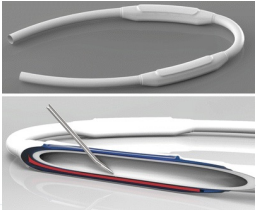
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Synthetic Grafts

InnAVasc Graft (IAVG)

- combines a standard expanded polytetrafluoroethylene (ePTFE) vascular graft with a novel graft modification technology engineered with materials that provide durable, self-sealing cannulation chambers with puncture-resistant posterior and sidewall surfaces
- easier early cannulation without back wall infiltration
- thinner wall for suturing anastomosis
- infection due to cannulating the same areas? Clinical trials ongoing



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Biologic Grafts

Dimethyl sulfoxide cryopreserved cadaver Vein allografts (CRY)

- have been shown to cause broad recipient allosensitization measured by panel reactive antibody PRA assay

Decellularized cryopreserved Synergraft (SYN) cadaver femoral vein allografts

- Been used for past 2 decades
- These allografts are more resistant to infection but significantly more susceptible to aneurysms
- Pros: decrease infection
- Cons: costs, aneurysm formation, specialized storage planning, thawing and preparation time

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Biologic Grafts

Decellularized femoral artery allograft (Nexeon AVX)

- Since thicker wall similar to Artergraft, quicker cannulation and decrease aneurysm formation?
- Prospective study to assess the safety and efficacy of a decellularized human femoral artery allograft (Nexeon AVX) in the creation of [vascular access for hemodialysis](#) in patients with ESRD June 2023 - 2027 100 patients
- Pros: decrease infection, very similar to autologous vessels without harvesting
- Cons: costs

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Autologous Biologic Conduits

Saphenous Vein/Cephalic/Basilic Vein

Pros:

- immunogenicity
- long-term functionality

Cons:

- eliminating the wound care
- operating time burden associated with harvesting patients own vessels

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Biologic Grafts

Genetic Engineered Vascular Graft (Humacyte)

- transform human cells into universally implantable, regenerative tissues using human vascular smooth muscle cells were derived from deceased organ and tissue donors, aged 18–50 years extra cellular matrix, sizes are 6mm x 35-42cm
- Phase 3 trial is a prospective multicenter randomized clinical study of 242 patients comparing primary/secondary patency ATEV 81%/68% and AVF 66%/62% at 6/12 months.
- Pros: lower risk of infection, very similar to autologous vessels without harvesting
- Cons: cost

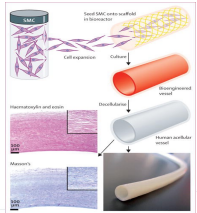
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Biologic Grafts

Humacyte Bioengineering Process

- Cell Transfer** (the cells proliferate and build on extracellular matrix)
- Acellular Tissue Engineered Vessel ATEV Formation** (the cells are fed growth media and subjected to biomechanical stresses)
- Decellularization** (removes cells but retains key ECM protein and structure)



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Summary

- KDOQI Life Plan choose the best access for the patient
- Infection is lower in most Biological Grafts compared to Synthetic Grafts
- Biologic vein graft have increase aneurysmal formation then artery graft
- Costs of Biologic Grafts can be overwhelming
- Genetic grafts superior?
- Multicentre Randomized Control Comparison Studies needed