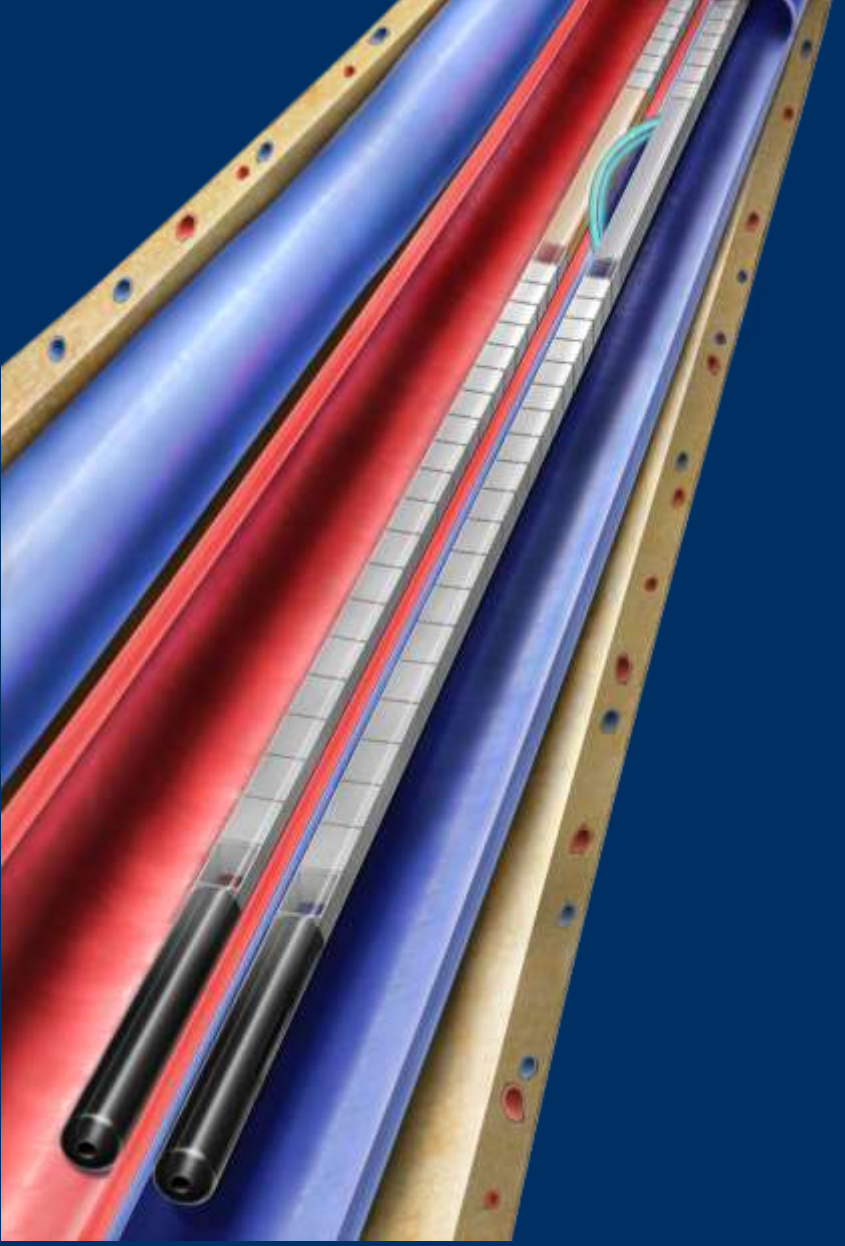

Proven clinical results of AVF creation with WavelinQ™ EndoAVF System

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Disclosure

Speaker name:

Dr Rob Jones

I have the following potential conflicts of interest to report:

☒ Consulting BD Bard, WL Gore, Penumbra.

☐ Employment in industry

☐ Stockholder of a healthcare company

☐ Owner of a healthcare company

☒ Research grant Boston Scientific

☐ I do not have any potential conflict of interest

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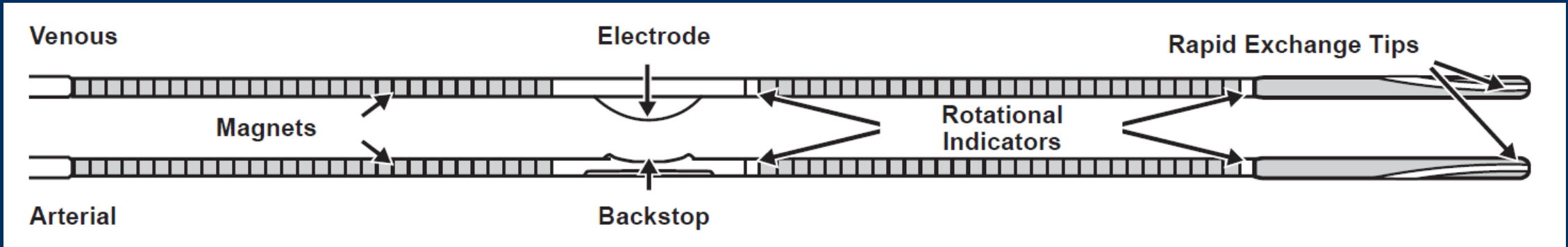
The clinicians have been compensated by Becton, Dickinson and Company to participate in this presentation.

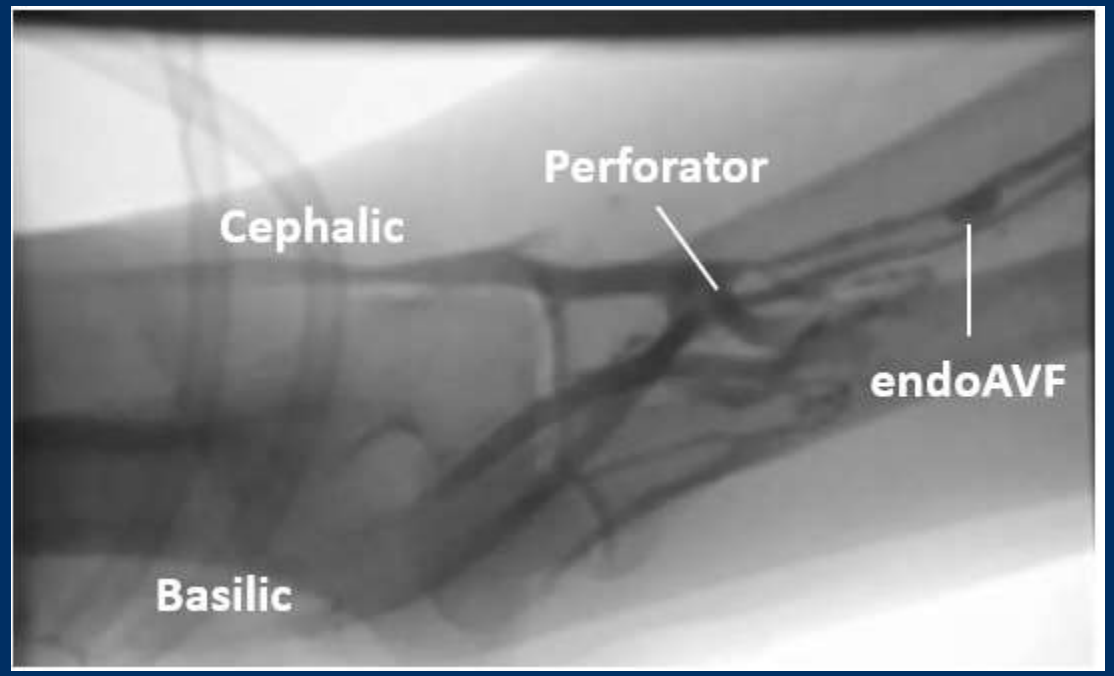
WavelinQ™ EndoAVF System



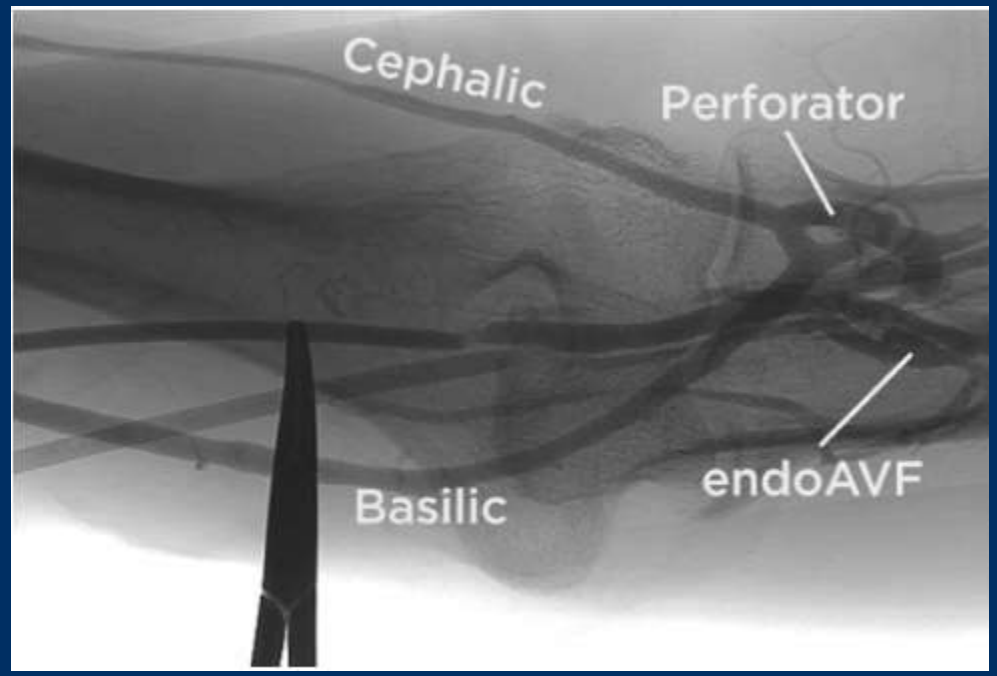
Procedural imaging

Familiar fluoroscopic imaging technology is used with WavelinQ™ EndoAVF System for clear visualization and procedural roadmapping

Radial-Radial



Ulnar-Ulnar



Low-pressure, split-flow AVF

- Multiple outflow vessels can dilate and mature
- Low flow rates through any single vessel
- Minimal vessel trauma
- Preserves future surgical AV fistula site creation options

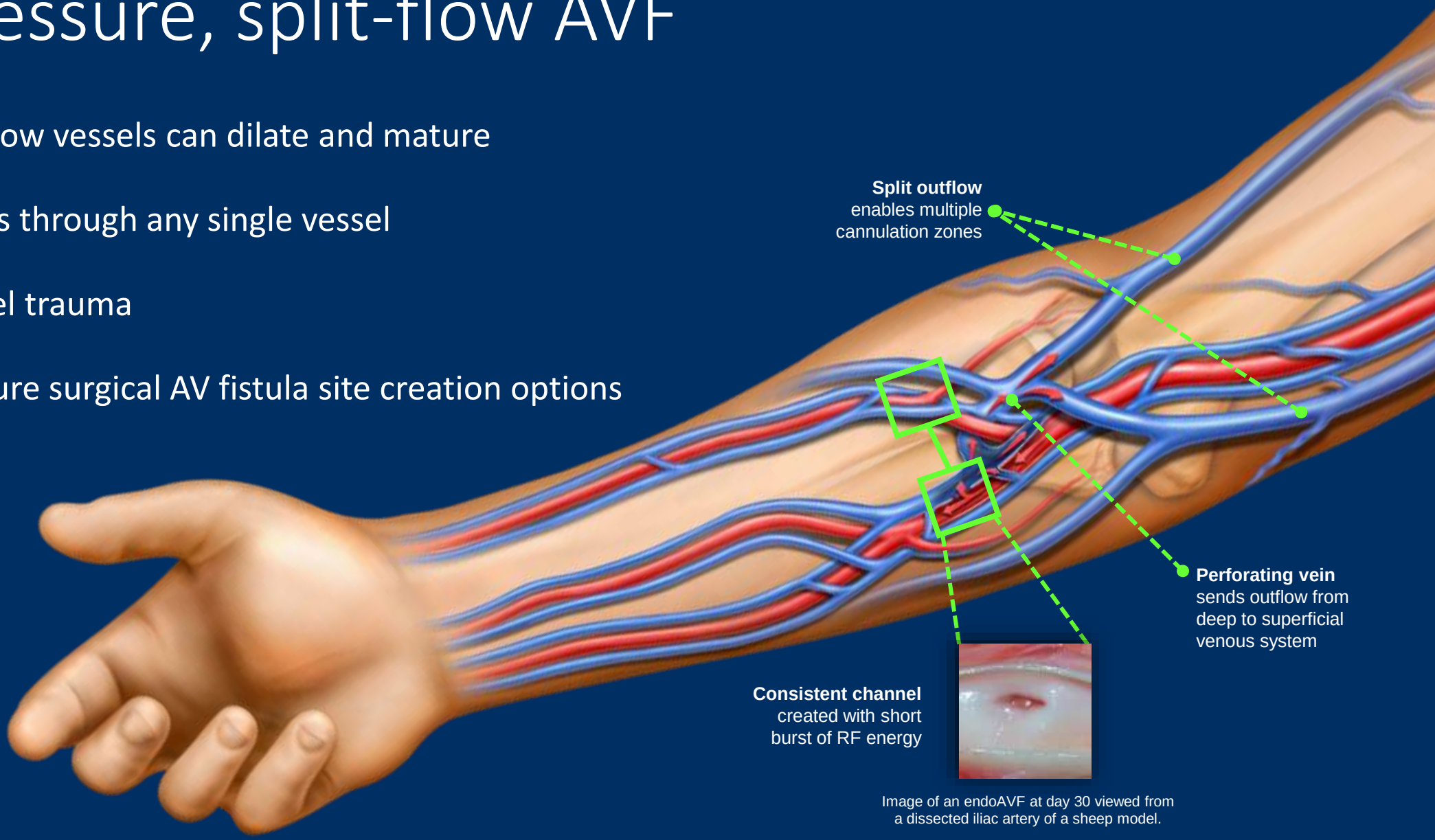


Image of an endoAVF at day 30 viewed from a dissected iliac artery of a sheep model.

Device generations

Generation 1: **WavelinQ™ 6F**

- Two fluoroscopically-guided, **6F** magnetic catheters & a burst of radiofrequency energy create **ulnar-ulnar** EndoAVF via **brachial artery/vein** approach

Generation 2: **WavelinQ™ 4F**

- Two fluoroscopically-guided, **4F** magnetic catheters & a burst of radiofrequency energy create **ulnar-ulnar or radial-radial** EndoAVF via **brachial artery/vein, ulnar and/or radial vein** approaches

BD Clinical program overview

		FLEX	NEAT	EASE	EUR/CA Post-Market	EASE-2
Device(s)	**6F (Gen 1)**	✓	✓		✓	
	4F (Gen 2)			✓	✓	✓
Fistula Location(s)	**Ulnar-Ulnar**	✓	✓	✓	✓	✓
	Radial-Radial			✓	✓	✓
Study Type	**Prospective, single arm**	✓	✓	✓	✓	✓
	Multiple operators	✓	✓	✓	✓	✓
	Multiple centers		✓		✓	
	Single center	✓		✓		✓
Study Details	**Number of patients**	33	60 (+20 roll-in)	32	**100**	24
	Location(s)	Paraguay	Canada, Australia, New Zealand	Paraguay	Germany, UK, Canada	Paraguay
	Status	*Rajan et al. Percutaneous Creation of an Arteriovenous Fistula for Hemodialysis Access (FLEX) JVIR 2015;26:484-490*	*Lok et al. Endovascular Proximal Forearm Arteriovenous Fistula for Hemodialysis Access: Results of the Prospective, Multicenter Novel Endovascular Access Trial Am J Kidney Disease 2017;70(4):486-497*	*Berland et al. Endovascular Creation of Arteriovenous Fistulae for Hemodialysis Access with a 4Fr Device: Clinical Experience from the EASE Study Annals of Vascular Surgery 2019;60:182-192*	Completed	Completed

FLEX Study

- **Design:** Prospective, single center feasibility study to evaluate the use of 6F percutaneous system for the creation of endoAVFs in patients who require hemodialysis
- **Sample size:** 33
- **Key Findings/Takeaways:**
  - Proof of concept that hemodialysis access can be successfully created with an endovascular catheter-based approach

Endpoint	Result	Definition
Technical Success	97%	Creation of a patent connection between the proximal ulnar artery and the adjacent vein, with brisk flow demonstrated by angiography and absence of appreciable extravasation
Functional Cannulation at 6 months	88.6%	Dialyzed using 2-needle cannulation for at least two-thirds of dialysis sessions over a consecutive 28-day period.
Patency at 6 months	96%	The interval from access placement to thrombosis or abandonment; not triggered by access circuit interventions performed in the absence of occlusion.
Mean time to fistula maturation	58 days	Considered mature when the treating nephrologist clinically assessed the fistula and considered the flow(brachial artery flow rate greater than or equal to 500 mL/min) and vein diameter (>4 mm) to be adequate to support dialysis
Device-Related Serious Adverse Events	3% (1/33)	% of patients with one or more serious device-related adverse events within 3 months of creation

1. Rajan et al. Percutaneous creation of an arteriovenous fistula for hemodialysis access. J Vasc Interv Radiol. 2015 Apr;26(4):484-90.

NEAT Study

- **Design:** Prospective, multi-center study to evaluate the WavelinQ™ 6F EndoAVF System when used to create an endoAVF in hemodialysis patients
- **Sample size:** 60
- **Key Takeaways:**
  - EndoAVF reliably created in larger sample size and 84% cumulative patency at 12 months

Endpoint	Result	Definition
Procedural Success	98%	EndoAVF successfully created, confirmed by angiography
Functional Cannulation	64%	Dialyzed using 2-needle cannulation for at least two-thirds of dialysis sessions over a consecutive 28-day period.
Primary Patency at 12 months	69%	Time from successful endoAVF creation to the first intervention designed to address thrombosis or stenosis, assist in maturation or cannulation of endoAVF, or endoAVF abandonment
Cumulative Patency	84%	Time from creation to the abandonment of endoAVF
Reinterventions per patient year	0.46	Any intervention required to maintain or re-establish patency
Device-Related Serious Adverse Events	2%	% of patients with one or more serious device-related adverse events within 3 months of creation

1. Lok et al. NEAT. Am J Kidney Dis. 2017 Oct;70(4):486-497

EASE Study

- **Design:** Prospective, single-center study to evaluate the WavelinQ™ 4F EndoAVF System when used to create an endoAVF in hemodialysis patients
- **Sample size:** 32 patients
- **Key Takeaways:**
  - WavelinQ™ 4F EndoAVF System demonstrated 100% technical success with multiple physician users
  - WavelinQ™ 4F Catheters enabled multiple venous access approaches and creation site options (radial-radial and ulnar-ulnar)
  - Enables tailoring of procedure to individual patient anatomy

Endpoint	Result	Definition
Technical Success	100%	EndoAVF successfully created, confirmed by angiography
Functional Cannulation at 6 months	86%	Dialyzed using 2-needle cannulation for at least two-thirds of dialysis sessions over a consecutive 28-day period.
Primary Patency at 6 months	83%	The interval from access placement to thrombosis or abandonment; not triggered by access circuit interventions performed in the absence of occlusion.
Reinterventions per patient year	0.21	Any intervention required to maintain or re-establish patency
Device-Related Serious Adverse Events	0%	% of patients with one or more serious device-related adverse events within 3 months of creation

1. Berland et al. EASE Study. Ann Vasc Surg. 2019 Oct;60:182-192.

European/Canadian Post-Market Study

- **Design:** Prospective, multi-center study to collect post-market data on outcomes of endoAVF creation using the 4F & 6F WavelinQ™ EndoAVF System in Europe and Canada at 12 study sites
- **Sample:** 100 subjects
- **Key Takeaways:**
  - Large study population
  - Seven out of ten subjects were intervention free at 6 months
  - Pre-dialysis subjects able to initiate hemodialysis without a catheter

Endpoint	Results at 6 months	Definition
Procedural Success	94%	94/100 (N=6 endoAVF not created)
Device-Related Serious Adverse Events	3%	3/100 (N=1 pseudoaneurysm w/ 6F brachial access, N=1 compartment syndrome w/ 6F brachial access, N=1 occlusion/stenosis)
Primary Patency	71% ± 5%	Interval of time from access placement until any intervention designed to maintain or re-establish patency, access thrombosis, access abandonment, or the time of measurement of patency
Assisted Primary Patency	81% ± 5%	Interval of time from access placement to thrombosis or abandonment; not triggered by access circuit interventions performed in the absence of occlusion
Secondary Patency	91% ± 3%	Interval of time from access placement until access abandonment, loss to thrombosis, or the time of patency measurement including intervening manipulations (surgical or endovascular interventions) designed to re-establish functionality in thrombosed access
Functional Patency	95% ± 3%	Interval of time from first 2-needle dialysis utilizing access until access abandonment

European/Canadian Post Market Study Continued Reintervention rates

Reinterventions Per Patient Year	All Subjects N=100	Coiling at Index N=73	No Coiling at Index N=27
All Reinterventions	**0.73**	**0.61**	**1.18**
Maturation Reinterventions	**0.36**	**0.31**	**0.55**
Superficialization	0.18	0.14	0.31
Coiling	0.16	0.14	0.24
Ligation of Tributaries	0.02	0.02	0.00
Maintenance Reinterventions	**0.37**	**0.31**	**0.65**
PTA	0.29	0.23	0.47
Stent Placement	0.04	0.02	0.08
Thrombolysis	0.04	0.05	0.00
Thrombectomy	0.02	0.00	0.08

52% fewer reinterventions when coiled at index procedure

Calculated as the total number of reinterventions divided by exposure (where exposure = subjects x mean duration of follow-up)
Each subject may have more than one type of reintervention; the individual rows do not necessarily sum to the summary rows.

European/Canadian Post Market Study Continued Time to hemodynamic maturation

- Maturity defined as brachial inflow ≥ 500 mL/min and outflow diameter ≥ 4 mm
- Not all subjects had an ultrasound assessment to determine maturation at each time point

Fistula Maturation		n/N (%)	95% CI
Time Point	1 Month	63/79 (80%)	69%-88%
	3 Months	59/70 (84%)	74%-92%
	6 Months	47/57 (82%)	70%-91%

European/Canadian Post Market Study Continued Pre-Dialysis Catheter exposure

47 pre-dialysis subjects enrolled

24 initiated dialysis during study follow up

22 were catheter free within 30 days

21 were catheter free at 6-month follow-up

92%
initiated dialysis with WavelinQ™ EndoAVF (22/24)

1. Based upon dialysis log CRF (DA Data)

Other Published Experience

		Inston N et al. WavelinQ Created Arteriovenous Fistulas versus Surgical Radiocephalic Arteriovenous Fistulas? A Single-Centre Observational Study J Vasc Access 2020	Wee IJY et al. A Systematic Review, Meta-Analysis, and Meta-Regression of the Efficacy and Safety of Endovascular Arteriovenous Fistula Creation J Vasc Surg 2019: 1-9	Radosa CG et al. Endovascular Creation of an Arteriovenous Fistula (endoAVF) for Hemodialysis Access: First Results Cardio Inter Rad (2017) 40: 1545-1551	Shahverdyan R et al. Outcomes of Percutaneous Arteriovenous Fistulae Creation by Ellipsys ® and WavelinQ Devices J Vasc Interv Radiol 2020; 31:1365-1372	Zemela MS et al. Real-World Usage of the WavelinQ EndoAVF System Annals of Vascular Surgery 2020
Device(s)	**6F (Gen 1)**	✓	✓	✓		✓
	4F (Gen 2)	✓	✓		✓	
Fistula Location(s)	**Ulnar-Ulnar**	✓	✓	✓	✓	✓
	Radial-Radial	✓	✓		✓	
Study Type	**Prospective**	✓				
	Multiple operators		✓			
	Multiple centers		✓			
	Single center	✓		✓	✓	✓
Study Details	**Number of patients**	N=30 WavelinQ N=40 RCF	N=300 (133 WL)	N=8	N=100 (35 WL)	N=35
	Location(s)	UK	Global	Germany	Germany	U.S.

Independent Research

Inston N et al. WavelinQ Created Arteriovenous Fistulas versus Surgical Radiocephalic Arteriovenous Fistulas? A Single-Centre Observational Study J Vasc Access 2020

Matched Comparative Analysis	WavelinQ™ EndoAVF N=30	Surgical AVF N=40	Definition
Technical Success	96.7%	92.6%	Visualising AV shunt blood flow through the created endoAVF using angiography at completion of the index procedure
Primary Patency at 6 Months	65.5%	53.4%	Time from creation to intervention or abandonment
Secondary Patency at 6 Months	75.8%	66.7%	Time from the creation date to the last needling date before the AVF was abandoned for a new form of access formation

Key Takeaway: WavelinQ™ EndoAVF and surgical creation had similar observations.

Independent Research

Wee IJY et al. A Systematic Review, Meta-Analysis, and Meta-Regression of the Efficacy and Safety of Endovascular Arteriovenous Fistula Creation J Vasc Surg 2019: 1-9

Endpoint	Result	Definition
Technical Success	97.50%	Angiographic evidence of brisk flow within AVF and absence of leakage of blood outside AVF
90-Day Maturation Rate	89.27%	Brachial artery flow rate ≥500 mL/min and the vein diameter >4
6 Month Patency	91.99%	Time from fistula creation until the last follow-up assessment or until fistula failure
12 Month Patency	85.71%	Time from fistula creation until the last follow-up assessment or until fistula failure
Procedure-related complications	5.46%	Any unintended medical occurrence directly arising from the procedure or device from time of procedure initiation to completion

Key Takeaways:

- Meta analysis of seven studies[1], 300 patients
- "Current endovascular AVF systems appear to be effective and safe"

Independent Research

Radosa CG et al. Endovascular Creation of an Arteriovenous Fistula (endoAVF) for Hemodialysis Access: First Results Cardio Inter Rad (2017) 40: 1545-1551

- Single center, n=8

Endpoint	Result	Definition
Technical Success	100%	Angiography as a flow between the proximal ulnar artery and one of the two ulnar veins, and draining into one of the superficial veins in the upper arm.
Median Maturation	63 Days	Brachial artery flow rate was more than 500 ml/min and the vein diameter more than 4 mm according to the National Kidney Foundation (KDOQI) Clinical Practice Guidelines and Clinical Practice Recommendations.
6 Month Patency	100%	Not defined
Procedure-related complications	N=1 minor	Major complications were defined as a serious adverse event which requires pharmacological/surgical treatment or causes prolongation of hospitalization.

Key Takeaway: Initial experience outside of a clinical trial

Other published experience

Shahverdyan et al. Comparison of Outcomes of Percutaneous Arteriovenous Fistulae Creation by Ellipsys ® and WavelinQ Devices J Vasc Interv Radiol 2020; 31:1365-1372

- Retrospective, single-center, single operator review of 100 patients[1] created between December 2017-December 2019

Endpoint	WavelinQ™ EndoAVF System Result N=35	Definition
Technical Success	97%	Post-procedure examination using Doppler ultrasonography demonstrating a patent anastomosis and fistula flow in the DCV and outflow veins
Time to Maturation	71.4% at end of study period	Brachial artery blood flow of ≥500 mL/min with an AVF diameter ≥5 mm
Functional Patency	85.7%	Time from successful 2-needle cannulation until abandonment
Time to First Clinical Use	90 Days	Time to first cannulation
Interventions per patient year	0.46	Average intervention per patient year
SAEs	3/35 (8.6%)	1 arterial bleeding from the brachial artery (access site), 1 pseudoaneurysm, 1 migration of both primary and secondary brachial vein coils
Procedure Time	63 min	Average length of procedure

Key Takeaways:

- Primary endpoints declared by author show no observed differences between treatment groups.
- 65% radial artery to radial vein creation with WavelinQ™ EndoAVF (4F)

1. Primary endpoints defined by author were technical success, time to maturation, functional patency, and time to first clinical use

Other published experience

Zemela MS et al Real-World Usage of the WavelinQ EndoAVF System. Annals of Vascular Surgery. 2021 Jan;70:116-122.

- Retrospective, single center, exploratory analysis of 35 patients who had the WavelinQ™ EndoAVF procedure (6F) at SSM St. May's Hospital between October 2018-July 2019

Endpoint	Result N=35	Definition
Technical Success	100%	Initial fistula creation success rate
Overall Patency at average follow up of 73 days	88%	Not defined
Successful Cannulation at average follow up of 73 days	48%	Patients on dialysis successfully using the endoAVF at follow-up
Procedure time	120 min	Average length of procedure (total room time)
Procedure-related complications	8/32 (25%)	3 hematoma, 3 contrast extravasation, and 1 resolved vessel spasm all resolving spontaneously, and 1 pseudoaneurysm

Key Takeaways:

- Initial U.S. experience with 6F device, outside of a clinical trial
- All consecutive patients included
- 94% ulnar artery to ulnar vein creation with WavelinQ™ EndoAVF

Summary

- Multi-specialty operators leveraging familiar fluoroscopic imaging
- 5 BD clinical studies, 5 independent published studies
- > 325 patients studied globally[1]
- 94%-100% technical success
- 0.21 - 0.73 interventions per year

- *BD is committed to **continued** clinical study of the next generation system in prospective, multi-center, multi-operator studies*

1. As of Jan-12-2021

WavelinQ™ 4F EndoAVF System for ELQ-002

Indications: The WAVELINQ™ 4F EndoAVF System is intended for the cutting and coagulation of blood vessel tissue in the peripheral vasculature for the creation of an arteriovenous fistula used for hemodialysis.

Contraindications: Known central venous stenosis or upper extremity venous occlusion on the same side as the planned AVF creation. Known central venous stenosis or upper extremity venous occlusion on the same side as the planned AVF creation. Known allergy or reaction to any drugs/fluids used in this procedure. Known adverse effects to moderate sedation and/or anesthesia. Distance between target artery and vein > 1.5 mm. Target vessels < 2 mm in diameter.

Warnings: The WAVELINQ™ 4F EndoAVF System is only to be used with the approved commercially available devices specified in the IFU. Do not attempt to substitute non-approved devices or use any component of this system with any other medical device system. The WAVELINQ™ 4F EndoAVF System catheters are single use devices. DO NOT re-sterilize or re-use either catheter. Potential hazards of reuse include infection, device mechanical failure, or electrical failure potentially resulting in serious injury or death. Use caution when performing electrosurgery in the presence of pacemakers. Improper use could damage insulation that may result in injury to the patient or operating room personnel. Do not plug device into the electrosurgical pencil with ESU on. Keep active accessories away from patient when not in use. Do not permit cable to be parallel to and/or in close proximity to leads of other devices. Do not wrap cable around handles of metallic objects such as hemostats. Consult the ESU User's Guide on its proper operation prior to use. Do not use closure devices not indicated to close the artery used for access.

Cautions: Only physicians trained and experienced in endovascular techniques should use the device. Adhere to universal precautions when utilizing the device. Do not kink, pinch, cut, bend, twist, or pull excessively or with excessive force on any portion of the devices. Damage to the catheter body may cause the device to become inoperable. Avoid sharp bends. This may cause the device to become inoperable. Do not pinch or grasp the catheter with excessive force or with other instruments. This may cause the device to become inoperable. Do not bend the rigid portion of the catheter near the electrode or backstop. Do not touch or handle the active electrode. Electrode dislodgement may occur. Always use the hemostasis valve crosser to assist insertion of the venous catheter through the introducer sheath. Insertion into introducer sheath without hemostasis valve crosser may damage electrode. Do not attempt to remove the hemostasis valve crosser located on the venous device. Device damage or fracture may occur.

Precautions: Care should be taken to avoid the presence of fluid on the ESU. Care should be taken during handling of the arterial and venous catheters in patients with implantable cardiac defibrillators or cardiac pacemakers to keep the distal 3 inches of the catheters at least 2 inches from the implanted defibrillator or pacemaker. Care should be taken to avoid attempting fistula creation in a heavily calcified location of a vessel as fistula may not be adequately formed. If the device does not perform properly during the creation of the endovascular fistula it is possible that a fistula will not be created or there may be some vessel injury. Keep magnetic ends of catheters away from other metallic objects which may become attracted and collide with devices.

Potential Adverse Events: The known potential risks related to the WavelinQTM 4F EndoAVF System and procedure, a standard AVF, and endovascular procedures may include, but are not limited to: aborted or longer procedure; additional procedures; bleeding, hematoma, or hemorrhage; bruising; burns; death; eletrocution; embolism; failure to mature; fever; increased risk of congestive heart failure; infection; numbness, tingling, and/or coolness; occlusion/stenosis; problem due to sedation or anesthesia; pseudoaneurysm; sepsis; steal syndrome or ischemia; swelling, irritation, or pain; thrombosis; toxic or allergic reaction; venous hypertension (arm swelling); vessel, nerve, or AVF damage or rupture; wound problem.

Please consult product labels and instructions for use for all indications, contraindications, hazards, warnings and precautions.

CE
0344

WavelinQ™ EndoAVF System for WQ4305

Indications: The WavelinQ™ EndoAVF System is intended for the cutting and coagulation of blood vessel tissue in the peripheral vasculature for the creation of an arteriovenous fistula used for hemodialysis.

Contraindications: Known central venous stenosis or upper extremity venous occlusion on the same side as the planned AVF creation. Known allergy or reaction to any drugs/fluids used in this procedure. Known adverse effects to moderate sedation and/or anesthesia. Distance between target artery and vein > 1.5 mm. Target vessels < 2 mm in diameter.

Warnings: The WavelinQ™ EndoAVF System is only to be used with the approved commercially available devices specified in the IFU. Do not attempt to substitute non-approved devices or use any component of this system with any other medical device system. The WavelinQ™ EndoAVF System catheters are single use devices. DO NOT re-sterilize or re-use either catheter. Potential hazards of reuse include infection, device mechanical failure, or electrical failure, potentially resulting in serious injury or death. Use caution when performing electrosurgery in the presence of pacemakers. Improper use could damage insulation that may result in injury to the patient or operating room personnel. Do not plug device into the electrosurgical pencil with ESU on. Keep active accessories away from patient when not in use. Do not permit cable to be parallel to and/or in close proximity to leads of other devices. Do not wrap cable around handles of metallic objects such as hemostats. Consult the ESU User's Guide on its proper operation prior to use. Do not use closure devices not indicated to close the artery used for access.

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Potential Adverse Events: The known potential risks related to the WavelinQ™ EndoAVF System and procedure, a standard AVF, and endovascular procedures may include, but are not limited to: aborted or longer procedure; additional procedures; bleeding, hematoma, or hemorrhage; bruising; burns; death; electrocution; embolism; failure to mature; fever; increased risk of congestive heart failure; infection; numbness, tingling, and/or coolness; occlusion/stenosis; problem due to sedation or anesthesia; pseudoaneurysm; aneurysm; sepsis; steal syndrome or ischemia; swelling, irritation, or pain; thrombosis; toxic or allergic reaction; venous hypertension (arm swelling); vessel, nerve, or AVF damage or rupture; wound problem.

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