

Bedside 3D ultrasound fistula maturation assessment by non-expert sonographers provides equivalent accuracy to formal duplex sonography: A prospective clinical trial

Lannery Lauvao¹, Jason Burgess², Devin O'Brien-Coon³, Tyson Rogers⁴, Alex Yevzlin⁵  and Jason Beaver⁶

The Journal of Vascular Access
1–11

© The Author(s) 2024

Article reuse guidelines:

sagepub.com/journals-permissions

DOI: 10.1177/11297298241287609

journals.sagepub.com/home/jva



Abstract

Background: EchoSure is an automated point-of-care 3D ultrasound (3DUS) designed to be used by dialysis technicians without advanced ultrasound training. The EchoMark/EchoSure System is a two-part system comprised of a bioresorbable implant, EchoMark, and a diagnostic ultrasound imaging platform, EchoSure. EchoSure was designed to enable any healthcare personnel in a dialysis clinic setting to obtain non-invasive, direct measurements of flow and vessel parameters that are critical quantifications used in the assessment of AVF maturation and readiness for hemodialysis cannulation.

Objective: In this pilot feasibility study, we sought to explore whether use of an automated 3DUS could enable fistula assessment by non-experts and obtain measurement accuracy comparable to expert sonographer Duplex.

Method: This was a 20 subject prospective multicenter trial conducted at four sites in the United States. All subjects had an EchoMark implanted under their AVF during the fistula creation procedure. Subjects were evaluated at 2-weeks post-op with EchoSure and Duplex, followed by monthly assessments until either the 4-month visit or until radiographic maturation was achieved, whichever was longer. Beyond monthly ultrasound assessments, clinical follow-up continued every 6 months between months 6 and 24.

Result: Technical success of EchoMark implantation was demonstrated in 100% of subjects. Technical success of EchoSure was 99% across all scans. The mean percent difference in flow rate measurements between EchoSure and Duplex was -9.2% with a standard deviation of 38.1% compared to a mean percent difference of -15.7% with a standard deviation of 35.5% between Duplex measurements taken at the cannulation zone and brachial artery. Pearson correlation between EchoSure and Duplex was 0.708 versus 0.716 for the two Duplex measurements. Radiographic maturation was achieved in 70% of study subjects by 30 days and continued to rise to 90% through 90 days and 95% through 180 days after baseline.

Conclusion: This study demonstrates the feasibility and accuracy of an automated 3D ultrasound system for assessment of maturation at the dialysis bedside by non sonographers.

Keywords

AV fistula, dialysis access, ultrasound, point of care, maturation, sonography

Date received: 7 June 2024; accepted: 3 September 2024

¹Mana Vascular Clinic, Glendale, AZ, USA

²Surgical Specialists of Charlotte, Charlotte, NC, USA

³Departments of Plastic Surgery and Biomedical Engineering, Johns Hopkins University, Baltimore, MD, USA

⁴NAMSA, Minneapolis, MN, USA

⁵Sonavex, Baltimore, MD, USA

⁶Surgery Center South, Dothan, AL, USA

Corresponding author:

Alex Yevzlin, 3927 County Road JJ, Black Earth, WI 53515, USA.

Email: ayevezlin@gmail.com

Introduction

There are 726,000 Americans and nearly 4 million patients worldwide with end-stage renal disease (ESRD) that require dialysis three times per week to survive.^{1,2} The health care costs associated with ESRD are substantial: since 2019, the Medicare costs for ESRD alone accounted for 7% of the total CMS budget, exceeding \$50 billion per year.³ The incidence of ESRD is also steadily increasing because of the growing prevalence of comorbid and causative conditions such as hypertension and diabetes, particularly in the elderly population.

Over 80% of HD patients begin dialysis through a central venous catheter.³ Robust evidence links each day of additional catheter dependence time to a higher risk of infection, thrombosis, and a doubled risk of mortality. Biologically, most fistulas reach vascular maturity by as soon as 4 weeks after surgery. However, identification that a fistula is ready for cannulation attempts by physical examination alone is difficult and has only a 21% specificity.⁴

While physical examination in isolation has limited utility, particularly when employed by non-physicians, ultrasound enables non-invasive, accurate assessment of radiologic readiness of a fistula for cannulation. In countries such as Japan where frequent ultrasound scans are done, 94% of fistulas are used within 4 weeks.⁵ However, ultrasound is complex and user-dependent, and in real-world American health care settings, dialysis-bedside ultrasound scanning has never gained traction. Instead, patients are typically required to go to separate sonographer appointments at a different health care site. The ESRD population faces significant financial and healthcare disparities. As a result, compliance with these visits is quite low and average time to autogenous AV fistula use remains far longer than necessary.⁶ The average time of clinical maturation in the U.S. is reported to be more than 6 months.^{7,8}

EchoSure is an automated point-of-care 3D ultrasound (3DUS) designed to be used by dialysis technicians without advanced ultrasound training. A resorbable polymeric marker with high ultrasound echogenicity (EchoMark) is placed under the fistula during the AVF creation procedure, then at dialysis clinic visits, the 3D ultrasound probe is placed over the general region of the fistula. Measurements of sonographic parameters correlated to AVF maturity are performed automatically. In this pilot feasibility study, we sought to explore whether use of an automated 3DUS could enable fistula assessment by non-experts and obtain measurement accuracy comparable to expert sonographer Duplex through 6 months.

Methods

Background

This study received an Investigational Device Exemption (IDE; G210264) from the United States Food and Drug



Figure 1. Photo of EchoMark (left), EchoMark LP (center), and EchoMark XS (right) next to a U.S. Quarter, Nickel, and Dime.

Administration (FDA). Subsequently, the study received IRB approval by WCG IRB (20215466).

Design of system

The EchoMark/EchoSure System is a two-part system comprised of a bioresorbable implant, EchoMark, and a diagnostic ultrasound imaging platform, EchoSure. EchoSure was designed to enable any healthcare personnel in a dialysis clinic setting to obtain non-invasive, direct measurements of flow and vessel parameters that are critical quantifications used in the assessment of AVF maturation and readiness for hemodialysis cannulation. The system deskills the process to obtain ultrasound-based measurements of flow and vessel configuration such that they can be obtained during a patient's regular dialysis appointments and be immediately transmitted to their surgeon or nephrologist via a Health Insurance Portability and Accountability Act (HIPAA) compatible cloud.

EchoMark (Figure 1) is an implantable, echogenic, bioresorbable fiducial marker comprised of 70:30 poly(L-lactide-co-caprolactone; PLC), a well-established bioresorbable polymer. EchoMark has special geometry that ensures any two-dimensional cross-sectional ultrasound image is unique. This is an important feature to allow for the companion device, EchoSure, to function reliably. Additionally, EchoMark's novel manufacturing process creates a closed-cell foamed structure throughout the part that yields a highly echogenic (bright) signal in ultrasound images. Both features provide localization and orientation information about the marked vessel when scanned with the EchoSure ultrasound system that facilitate ultrasound data collection for the quantification of the marked vessel's volumetric blood flow rate, diameter, and depth. This, in turn, allows relatively unskilled and untrained personnel to acquire vessel at the bedside, thereby obviating the need for additional appointments with an imaging specialist.

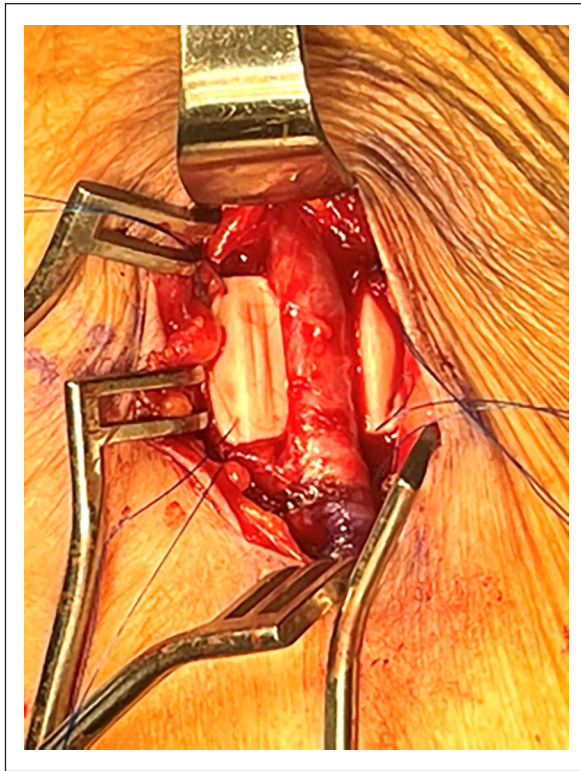


Figure 2. Photo of EchoMark LP under fistula.

The EchoMark is implanted under the fistula during the AVF creation procedure. The surgeon selects the appropriately sized EchoMark and places it under the outflow vein of the fistula after the anastomosis of the vein to the artery has been completed and sutures it into place to prevent

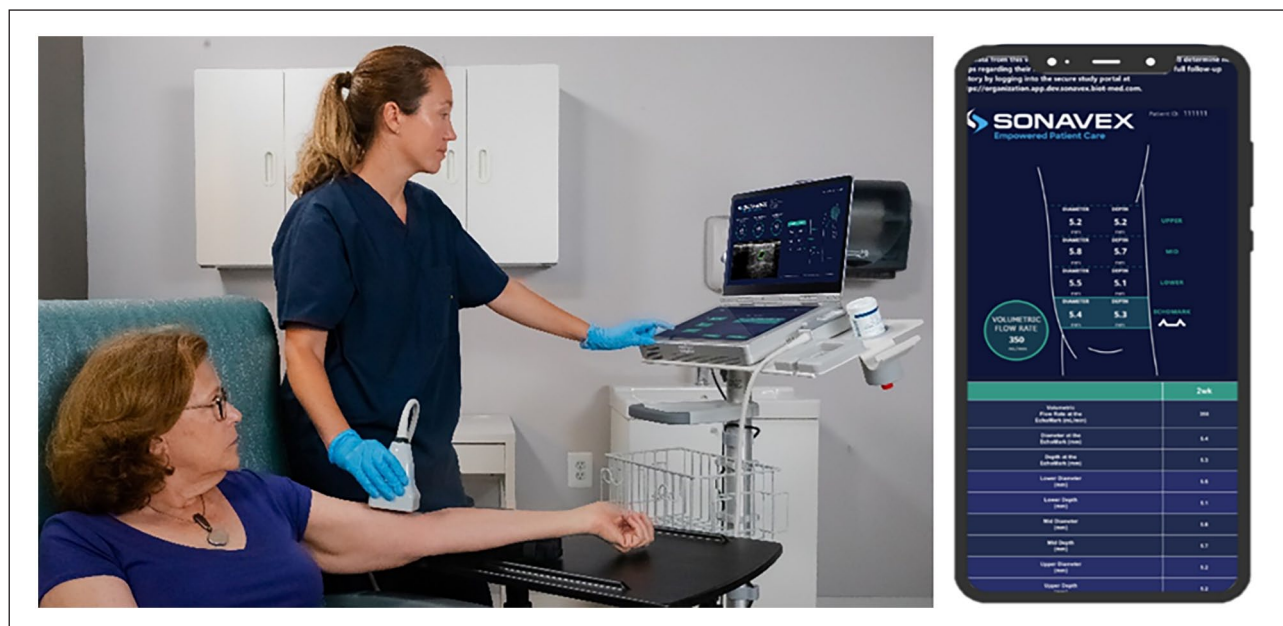
migration. The vessel resides in the channel of the EchoMark between its two peaks (Figure 2).

EchoSure is a portable automated diagnostic ultrasound imaging device that includes the EchoSure Ultrasound, the EchoSure AVF Software Application, and the EchoSure Probe (Figure 3). The EchoSure Probe is a mechanized linear transducer that can conduct volume acquisition of ultrasound data, such that the user simply needs to place the probe in the general region of the target rather than in a precise location. These features enable health care personnel without ultrasound experience to position the EchoSure probe quickly and reliably for a successful scan without consideration of technique.

The EchoSure AVF Software Application is designed with a simple user interface that walks the user through scanning with step-by-step instructions. Several aspects of the scan process, such as gain and pulse repetition frequency (PRF) selection, are automated to further reduce the need for user input. With each scan session, EchoSure AVF automatically calculates and reports volumetric flow, diameter and depth of the AVF at the EchoMark and three segments along the cannulation zone. Members of the patient's care team can receive emails with the scan summary containing the same information as displayed on the system via encrypted transmission (Figure 3). Additional information on the EchoMark/EchoSure System and results from a pilot benchtop study were published previously in this journal.⁹

Clinical trial protocol

This was a 20 subject prospective multicenter trial conducted at four sites in the United States. Eligible patients were adults aged 18–85 years with life expectancies



exceeding 18 months who were referred for the creation of a new upper arm fistula. Vessel diameters for inclusion were minimal vein diameter of 2.5 mm (without tourniquet) and minimum artery diameter of 3 mm. Key exclusion criteria were patients with three previously failed AVFs, a history of steal syndrome, recent infections, diagnosed bleeding disorder, active malignancy, existing access, those who are immunocompromised or immunosuppressed, and those receiving a forearm fistula.

Trial structure

All subjects had an EchoMark implanted under their AVF during the fistula creation procedure. Subjects were evaluated at 2-weeks post-op with EchoSure and Duplex, followed by monthly assessments until either the 4-month visit or until radiographic maturation was achieved, whichever was longer. Beyond monthly ultrasound assessments, clinical follow-up continued every 6 months between months 6 and 24. In this publication we report on the results through the 6-month follow-up visit.

The primary safety endpoint was defined as the composite of new major device-related adverse events (MAEs) at 30 days post EchoMark implantation, as adjudicated by the Clinical Events Committee (CEC), including: device or procedure-related death, device-related infection, device-related interventions, device-related hospitalizations, fistula failure, fistula rupture, and aneurysm. The primary effectiveness (feasibility) endpoint was technical success, defined as the successful implantation of the EchoMark implant and the ability to determine blood flow, diameter and depth measurements using the EchoSure diagnostic ultrasound system. Technical success was assessed from baseline to 4 months post-op. Additionally, time to radiographic maturation was captured as an endpoint and time to clearance for cannulation was collected. Radiographic maturation was defined as a fistula with volume flow of 500 mL/min and 5 mm diameter on ultrasound imaging; imaging was captured at all follow-up visits until 150 days. Clearance for cannulation was determined by the Principal Investigator's (PI's) assessment of the ultrasound data, patient history, and physical exam.

Ultrasound measurements

The study also included several sonographic endpoints for comparison of EchoSure versus Duplex measurements of flow, diameter, and depth. Triplicate measurements were taken for EchoSure, Duplex scans at the EchoMark location, and Duplex scans in the cannulation zone of the AVF. For additional context, a single brachial artery Duplex measurement was collected.

For the volume flow analysis, EchoSure flow was compared to Duplex flow in the cannulation zone. To provide a comparison, Duplex measurements at the cannulation zone

Table 1. Baseline demographics.

	Study subjects (n = 20)
Age	Mean = 64.3 (40–80)
Gender	
Male (n (%))	13 (65)
Female (n (%))	7 (35)
Race	American Indian/Alaska Native = 1 (5%) Black or African American = 6 (30%) White = 11 (55%) Unknown or not reported = 2 (10%)
Ethnicity	Hispanic or Latino = 6 (30%) Not Hispanic or Latino = 14 (70%) Unknown or not reported = 0 (0%)
Height (inches)	
Mean (range)	68 (58.5–78)
Weight (lbs)	
Mean (range)	202 (137–384)
BMI	
Mean (range)	31 (22.7–43.5)
History of smoking	Never = 10 (50%) Past = 7 (35%) Current = 3 (15%)
Diabetes	None = 2 (10%) Type 1 = 0 (0%) Type 2 = 18 (90%)
Hypertension	18 (90%)
Congestive heart failure	5 (25%)
Peripheral artery disease	0 (0%)
Prior hemodialysis therapy	9 (22%)
Stage of CKD	Stage 4 = 5 (25%) Stage 5 = 15 (75%) Unknown = 0 (0%)

were also compared to Duplex measurements in the brachial artery. For diameter, EchoSure measurements were compared to Duplex measurements at the EchoMark. For depth, EchoSure measurements were compared to measurements collected by an independent RVT using the same image to ensure the exact anatomic location was analyzed by both approaches. This approach minimized the impact of varying depths along the fistula.

RVTs and EchoSure users were educated on the importance of not compressing the vessels during scans.

Statistical methods

Triplicate measurements by EchoSure (version 1.4.0) and Duplex ultrasound were compared by analyzing the nine unique measurement pairs from each patient visit among study subjects. Agreement between measurement pairs was assessed with the Bland-Altman method and correlation was assessed using Pearson's method. Agreement of

Duplex ultrasound measurement to itself at two different locations served as a point of reference. Due to higher flow rates having higher measurement variability, the Bland-Altman analyses assessed agreement of the percent difference in measurements rather than the absolute difference to reduce heteroscedasticity. The percent difference for each measurement pair was calculated as the difference divided by the mean. A linear random effects repeated measures model was used to estimate the contribution of patient, visit, measurement method, and residual variance components to total variability. The variance components analysis of flow rate used a log base 10 transformation to address heteroscedasticity. Radiographic maturation and clearance for cannulation were analyzed as time-to-event variables using the Kaplan-Meier method. To be conservative, fistula failure prior to reaching the radiographic maturation or clearance for cannulation was treated as not reaching the outcome of interest over all 180 days of the analysis follow-up period. Analyses were performed using SAS version 9.4.

Results

Demographics (see Table 1).

This paper presents feasibility study data on 20 study subjects enrolled after completion of the roll-in phase. Four sites participated with enrollments of 11, 5, 4, and 1 study subjects.

Primary safety endpoint

There were zero adverse events from the above list reported after EchoMark implantation from all subjects at the primary timepoint.

Other safety endpoints

There was one event occurring within 30 days of implantation that required reintervention or hospitalization. This subject was diagnosed with mild steal syndrome, which resulted in a banding procedure. This incidence (5%) aligns with what is reported in the literature.

The following endpoints will be reported once all subjects have reached their 12 month visit and are still in progress. The information below captures the data collected to date. Four of the twenty subjects reported a reduction in blood flow, which were the result of stenosis or thrombosis. Two subjects were treated with angioplasty. In one of the other two with a failed fistula, the fistula was ligated and EchoMark was explanted due to the lack of future utility. Two of twenty subjects experienced infiltrations within the first 12 months, though zero experienced a hematoma requiring procedural intervention.

Zero subjects experienced the inability to use EchoSure due to migration or early resorption of EchoMark. One

subject reported pain. This was one of the two subjects with a failed fistula. While the final endpoint will be reported once all subjects reach 12 months, to date there have been zero instances of infection.

Though not all subjects have reached 12 months, there have been six reported MAEs across five subjects to date. One of the interventions was a fistulogram for a potential aneurysm segment (confirmed to not be an aneurysm), another was a fistulogram for a non-maturing fistula, and the remainder were fistula failures.

Overall, 3 of 20 fistulas failed (15%), favorable compared to the 30%–61% failure rate commonly reported in literature and databases. Furthermore, one of the three failures occurred after the fistula was cleared for cannulation.

Primary effectiveness endpoint: Technical success

Technical success of EchoMark implantation was demonstrated in 100% of subjects. Technical success of EchoSure was 99% across all scans.

EchoSure-Duplex measurement correlation

Bland-Altman plots showing agreement between EchoSure and Duplex measurements of flow and diameter are shown on the bottom left of Figures 4 and 5, respectively. The bottom right of each figure shows agreement between Duplex measurements at two separate locations for comparison. Summary statistics describing the Bland-Altman analysis and Pearson correlation comparing measurements made with EchoSure versus Duplex are shown in Table 2. The mean percent difference in flow rate measurements between EchoSure and Duplex was -9.2% with a standard deviation of 38.1% compared to a mean percent difference of -15.7% with a standard deviation of 35.5% between Duplex measurements taken at the cannulation zone and brachial artery. Pearson correlation between EchoSure and Duplex was 0.708 versus 0.716 for the two Duplex measurements.

For diameter, the mean percent difference between EchoSure and the Duplex measurement was -2.5% with a standard deviation of 15.9% compared to a mean percent difference of -2.0% with a standard deviation of 25.1% between Duplex measurements taken at the EchoMark and cannulation zone. Pearson correlation between EchoSure and Duplex was 0.832 versus 0.529 for the two Duplex measurements.

For depth, the mean percent difference between EchoSure and the Corelab measurement was 17.3% with a standard deviation of 23.0% compared to a mean percent difference of -34.3% with a standard deviation of 36.0% between Duplex measurements taken at EchoMark and Corelab measurements. Pearson correlation between EchoSure and Corelab was 0.855 versus 0.536 for the Duplex and CoreLab measurements.

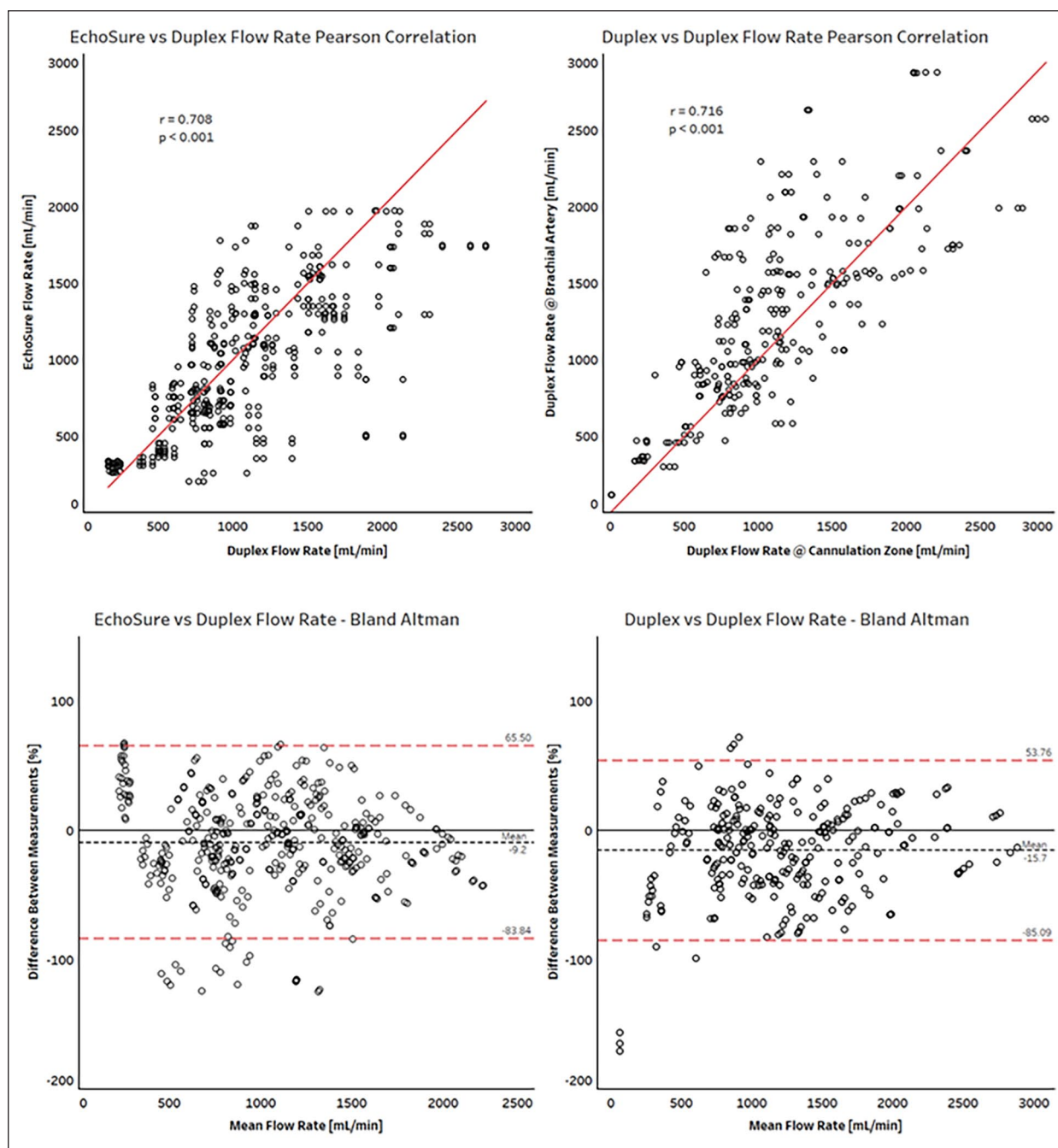


Figure 4. Pearson correlation (top) and Bland-Altman (bottom) plots of flow rate agreement. EchoSure versus Duplex at Cannulation Zone (left) and Duplex at Cannulation Zone versus Duplex @ Brachial Artery (right).

EchoSure-Duplex variance analysis

The standard deviation provides a measure of the degree of variation associated with each factor. The degree of variation for each factor was additionally measured by the percent of total variation explained. The repeated measures variance components analysis results are displayed in Table 3. For flow, the variation between the EchoSure measurement at the EchoMark and the Duplex ultrasound measurement at the

cannulation zone accounted for 13.3% of the total variation present in the data, comparable to the 12.0% proportion of variation accounted for by variation between Duplex ultrasound measurements. Standard deviations were also comparable between these two different pairs of flow rate measurement methods at 0.132 and 0.120 on the log base 10 scale, respectively. For vessel diameter, the standard deviation was 0.026 mm between EchoSure and Duplex ultrasound

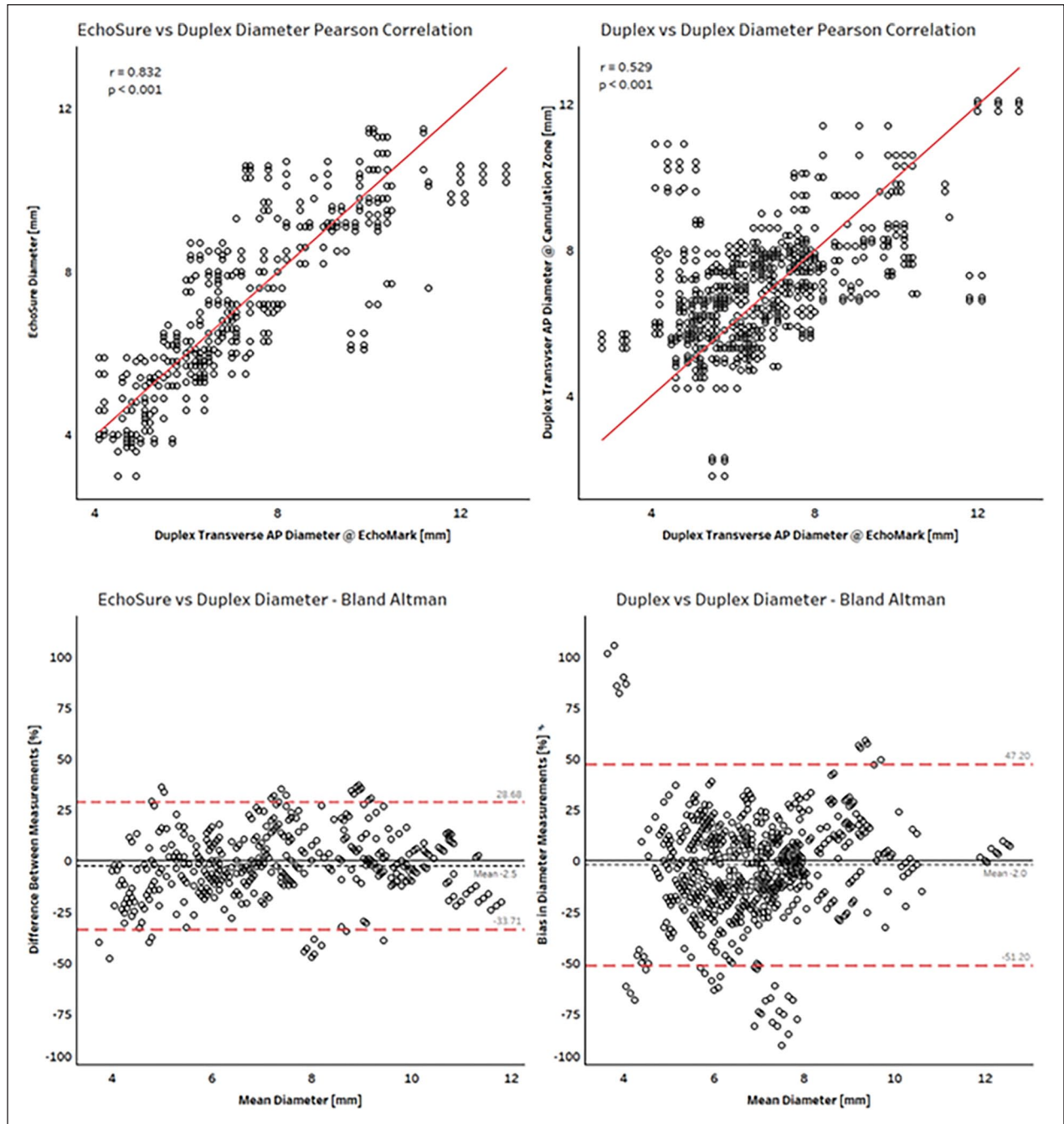


Figure 5. Pearson correlation (top) and Bland-Altman (bottom) plots of diameter agreement. EchoSure versus Duplex at EchoMark (left) and Duplex at EchoMark versus Duplex @ Cannulation Zone (right).

measurements at the EchoMark which accounted for 5.0% of the variation. This variation compared favorably with the standard deviation of 0.080mm between Duplex ultrasound measurements at the EchoMark and cannulation zone which accounted for 39.0% of the total variation. Finally, for vessel depth, the standard deviation was 0.611mm between EchoSure and CoreLab measurements at the EchoMark which accounted for 9.8% of the variation. This variation compared favorably with the standard deviation of 0.968mm

between Duplex ultrasound at the EchoMark and CoreLab measurements at the EchoMark which accounted for 25.9% of the total variation.

Maturation outcomes

Fistula maturation outcomes for study subjects are shown in Figures 6 and 7. These plots present the proportion of subjects that reached radiographic maturation and cannulation

Table 2. Bland Altman agreement between EchoSure versus Duplex compared to Duplex versus Duplex.

Measure	EchoSure Assessment Mean $\pm$ StdDev (lower LOA, upper LOA) Pearson correlation	Duplex Assessment Mean $\pm$ StdDev (lower LOA, upper LOA) Pearson correlation
Flow	$-9.2\% \pm 38.1\%$ ($n=343$) (-83.8% , 65.5%) 0.708*	$-15.7\% \pm 35.5\%$ ($n=362$) (-85.2% , 53.9%) 0.716**
Diameter	$-2.5\% \pm 15.9\%$ ($n=371$) (-33.7% , 28.7%) 0.832 [^]	$-2.0\% \pm 25.1\%$ ($n=545$) (-51.2% , 47.2%) 0.529 ^{^^}
Depth	$17.3\% \pm 23.0\%$ ($n=303$) (-27.8% , 62.5%) 0.855 [†]	$-34.3\% \pm 36.0\%$ ($n=303$) (-104.8% , 36.3%) 0.536 ^{††}

LOA: Bland-Altman limit of agreement.

*EchoSure versus Duplex at Cannulation Zone.

**Duplex at Cannulation Zone versus Duplex at Brachial Artery.

[^]EchoSure versus Duplex at EchoMark.^{^^}Duplex at EchoMark versus Duplex at Cannulation Zone.[†]EchoSure versus CoreLab.^{††}Duplex at EchoMark versus CoreLab.**Table 3.** Repeated measures variance components analysis.

Measure	Methods compared	Variance components	Standard deviation	Percent of variation
Flow (log l0 mL/min)	EchoSure @ EchoMark, DUS @ Cannulation Zone	Between subject	0.223	38.3
		Between visit	0.244	45.9
		Between methods	0.132	13.3
		Between repeated measurements	0.057	2.5
	DUS @ Cannulation Zone, DUS @ Brachial Artery	Between subject	0.269	60.0
		Between visit	0.172	24.4
		Between methods	0.120	12.0
		Between repeated measurements	0.066	3.6
Diameter (mm)	EchoSure @ EchoMark, DUS @ EchoMark	Between subject	0.106	81.4
		Between visit	0.038	10.4
		Between methods	0.026	5.0
		Between repeated measurements	0.021	3.2
	DUS @ EchoMark, DUS @ Cannulation Zone	Between subject	0.097	57.4
		Between visit	0.000	0.0
		Between methods	0.080	39.0
		Between repeated measurements	0.024	3.6
Depth (mm)	EchoSure @ EchoMark, Corelab	Between subject	1.763	81.7
		Between visit	0.244	1.6
		Between methods	0.611	9.8
		Between repeated measurements	0.514	6.9
	DUS @ EchoMark, Corelab	Between subject	1.585	71.0
		Between visit	0.000	0.0
		Between methods	0.958	25.9
		Between repeated measurements	0.329	3.1

Bold rows indicate the variance due to imaging modality.

clearance over 180 days of follow-up. Radiographic maturation was achieved in 70% of study subjects by 30 days and continued to rise to 90% through 90 days and 95% through 180 days after baseline. Cannulation clearance occurred in most study subjects between 30 and 90 days during which

time the proportion of patients with cannulation clearance increased from 5% to 85% and continued to rise to 90% through 180 days after baseline. As shown in Figure 8, for subjects that reach unassisted maturation, volumetric flow rapidly increases to >500 mL/min within 30 days.

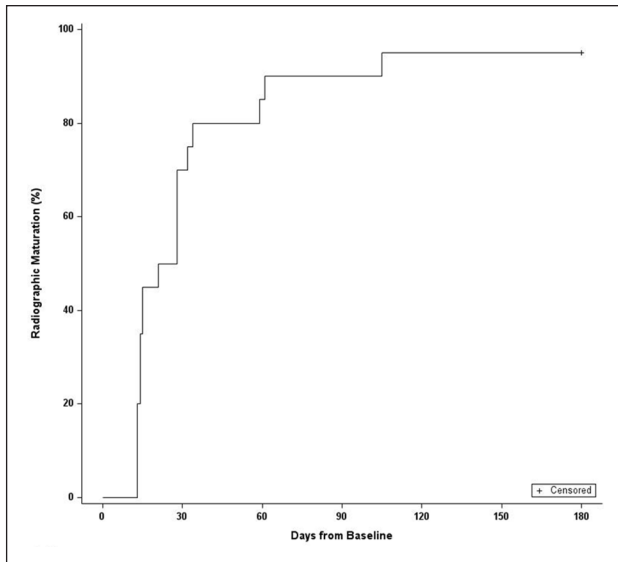


Figure 6. Radiographic maturation by follow-up time through 180 days.

N is the number of subjects under observation who have not yet reached radiographic maturation

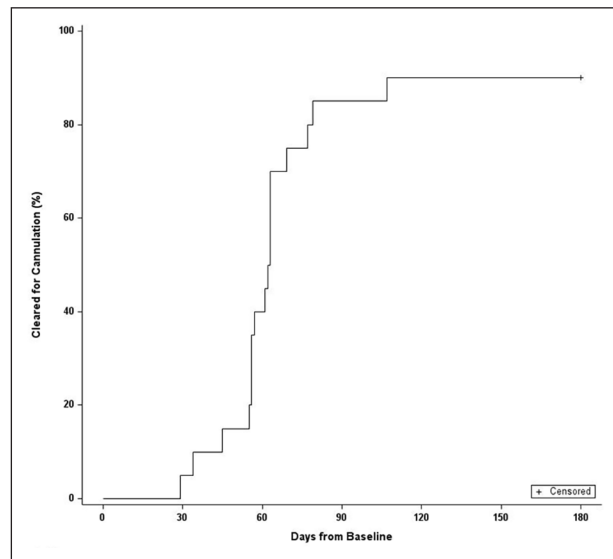


Figure 7. Cannulation clearance by follow-up time through 180 days.

N is the number of subjects under observation who have not yet been cleared for cannulation.

Discussion

Maturation times in real-world clinical environments consistently lag physiologically feasible maturation times by many months. In typical practice, patients are often required to travel to an outpatient imaging laboratory for an ultrasound by a certified sonographer or Registered Vascular Technologist (RVT). Compliance with these appointments outside patients' standard dialysis sessions is

quite poor: estimated at 12%–33%.⁵ As a result, in the U.S., over half of patients remain on a CVC 6 months after initiating HD, and the average time until a new AVF is used is over 7 months.^{6,7} Closing the gap between potential fistula readiness for use and actual average cannulation times offers enormous clinical impact, yet efforts to promote faster AVF usage have had little effect. A reliable method of evaluating whether a new fistula is ready for cannulation attempts in the dialysis clinic has the potential to break longstanding barriers to improved ESRD patient care.

It has previously been shown in a benchtop setting that automated 3D ultrasound can be used by dialysis technicians to obtain similar measurements to standard 2D Duplex ultrasound assessments conducted by expert sonographers.⁶ In this work, we extended these results to perform an assessment of the feasibility and safety of the surgical marker/3D ultrasound system for accurate sonographic evaluation of AV fistulas in patients.

Intraoperative implantation of the marker appeared relatively straightforward. Successful placement was achieved in all cases. Similarly, the marker displayed excellent biocompatibility, with no cases of device-related adverse events, infections, or cases of migration. Fistula failure rates of 15% in this study compare favorably to historical failure ranges in the 30%–61% range.^{10–16}

The value associated with collecting ultrasound data in the dialysis clinic has been previously described, but duplex ultrasound is known to have some degree of operator and machine variability, particularly with regards to estimation of volumetric flow rate, which have been estimated to range from 27% to 46%.^{17–19} Despite this, the agreement of EchoSure with Duplex was remarkably high when assessed against measurements comparing Duplex to itself. For volume flow, diameter, and depth EchoSure-Duplex concordance exceeded Duplex-Duplex concordance. Despite expected variation across different ultrasound users and patient anatomies, the fact that scan success rates were over 99% suggests that it is feasible for non-sonographers to use automated ultrasound in a health care setting with live patients. Most importantly, the system was able to accurately detect maturity as early as a formal DUS scan, but in a context where it could be performed at routine dialysis session visits by the existing staff. Radiographic maturation was identified at a median of 18 days (mean 29), suggesting that a large margin for reduction in maturation can be achieved.

Strengths of this study include a prospective design, multi-center enrollment and rigorous methodology and tracking of outcomes including the use of a blinded radiology adjudicator. Weaknesses include the fact that the study design meant that scans had to be conducted in a location where a sonographer could also perform a regular Duplex ultrasound (i.e., not at the dialysis bedside). Similarly, the frequency of scans was limited by this requirement, and

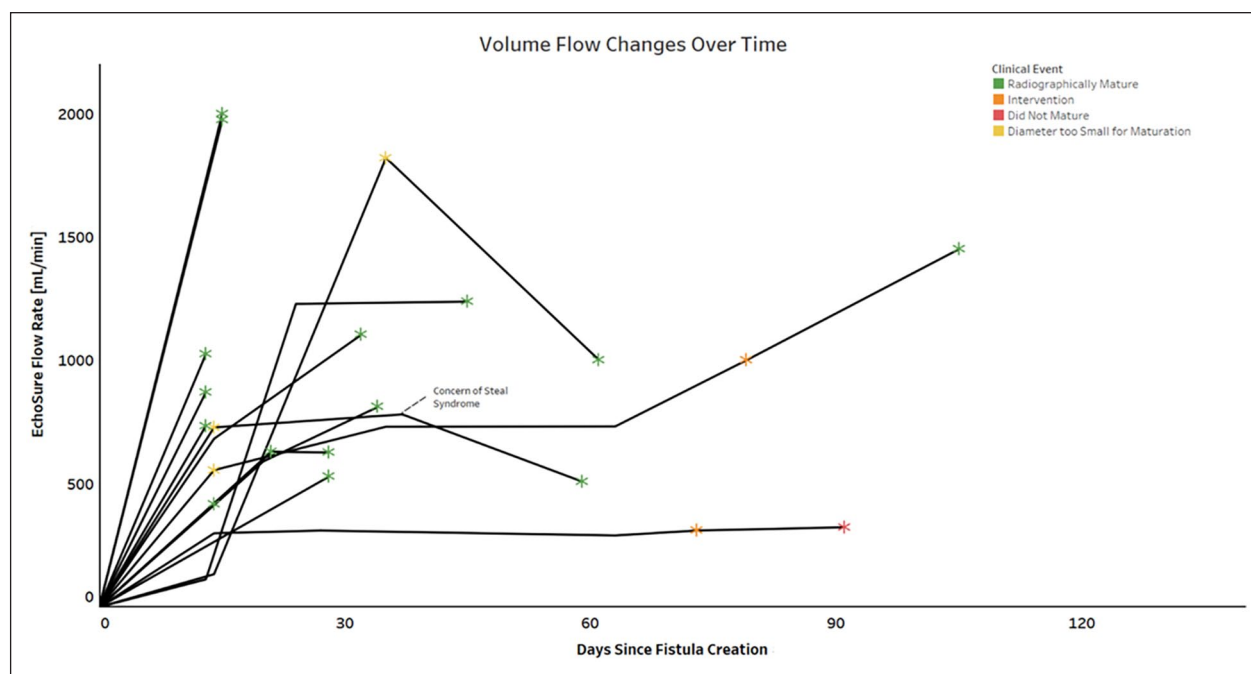


Figure 8. Fistula volume flow over time.

thus the true EchoSure-identified time to maturation would probably be faster than that seen here.

Another limitation is that Duplex ultrasound is not an ideal “gold standard” for comparison. Given the known measurement errors previously described, Duplex does not represent a true “ground truth” measurement for comparison to EchoSure. Even for skilled sonographers, results are meaningfully impacted by small changes in probe positioning, caliper location, probe compression of the vessel, and other factors. Venous compression is a well-known limitation of Duplex ultrasound. In our study, we endeavored to compare the EchoSure maturation parameters of the fistula at the EchoMark location, which is implanted under the venous segment of the fistula, to those of Duplex in the same location. EchoSure-derived measurements for depth were compared to measurements collected by a CoreLab using the same images. By using the same images, any difference in true anatomic depth driven by minor disparities in probe location were eliminated. For flow analysis, however, post-hoc measurement standardization is not possible and Duplex volume flow data was collected in the cannulation zone. The use of Duplex as a comparison assumes that when Duplex and EchoSure are marginally discordant, Duplex is correct, though benchtop data suggests EchoSure is closer to measuring true flow rates. However, the clinical utility and success of current Duplex techniques for fistula maturation assessment is clear, and the high degree of agreement between Duplex and EchoSure offers robust assurance of accurate maturation prediction.

Upper arm fistulas were chosen for study in this pilot trial because upper arm fistulas represent the

majority of all AV fistulas and because the EchoMark device in its current iteration is only available in a size that is compatible with upper arm venous anatomy. A new smaller EchoMark is now available and compatible with forearm fistulas. This smaller size will be studied in subsequent trials. In addition, we will report the clinical endpoints through 24 months in a subsequent publication.

In considering the potential financial impact of the technology, we first evaluated the current cost to manage a patient dialyzing through a catheter compared to a patient dialyzing through a fistula. When factoring in the incidence and cost associated with hospitalization from bloodstream infections and catheter exchange procedures due to dysfunction, the incremental cost is an extra \$160 per day. Therefore, as little as a 2-week improvement in time to maturation yields more than \$2000 of cost savings.²⁰ While final pricing has not been established, it will be a fraction of the economic value created by the device.

In summary, this study demonstrates the feasibility and accuracy of an automated 3D ultrasound system for assessment of fistula maturation at the dialysis bedside by non-sonographers. A 304-subject randomized controlled trial is currently underway, which will capture time to maturation, time to catheter removal, patency, and other longer-term outcomes.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This study was funded in part by Sonavex, Inc. Research reported in this publication was supported by the National Heart, Lung, And Blood Institute of the National Institutes of Health under Award Number R44HL147423. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

ORCID iD

Alex Yevzlin  <https://orcid.org/0000-0001-5213-8376>

References

- Centers for Disease Control and Prevention. *Chronic kidney disease in the United States, 2019*. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, 2019.
- Bello AK, Okpechi IG, Osman MA, et al. Epidemiology of haemodialysis outcomes. *Nat Rev Nephrol* 2022; 18: 378–395.
- Johansen, Johansen KL, Gilbertson DT, Li S, et al. US Renal Data System 2023 Annual Data Report: Epidemiology of kidney disease in the United States. American journal of kidney diseases : The official journal of the *National Kidney Foundation* 2024; 83: A8–A13.
- Ferring M, Henderson J and Wilmink T. Accuracy of early postoperative clinical and ultrasound examination of arteriovenous fistulae to predict dialysis use. *J Vasc Access* 2014; 15(4): 291–297.
- Pisoni RL, Zepel L, Port FK, et al. Trends in US vascular access use, patient preferences, and related practices: an update from the US DOPPS practice monitor with international comparisons. *Am J Kidney Dis* 2015; 65(6): 905–915.
- Lynch SK, Ahanchi SS, Dexter DJ, et al. Patient compliance limits the efforts of quality improvement initiatives on arteriovenous fistula maturation. *J Vasc Surg* 2015; 61: 184–191.
- Johansen KL, Chertow GM, Foley RN, et al. US Renal Data System 2020 Annual Data Report: Epidemiology of kidney disease in the United States. *Am J Kidney Dis* 2021; 77 (4 Suppl 1): A7–A8.
- Woodside KJ, Bell S, Mukhopadhyay P, et al. Arteriovenous fistula maturation in prevalent hemodialysis patients in the United States: a national study. *Am J Kidney Dis* 2018; 71(6): 793–801. Erratum in: *Am J Kidney Dis* 2018; 72(2): 314.
- Calotta NA, Astor BC and Ross JR. Automated 3D ultrasound enables novice users to measure arteriovenous fistula maturation parameters with comparable accuracy to conventional duplex by trained sonographers: results of a benchtop study. *J Vasc Access* 2023; 24(6): 1398–1406.
- Huber TS, Berceli SA, Scali ST, et al. Arteriovenous fistula maturation, functional patency, and intervention rates. *JAMA Surg* 2021; 156(12): 1111–1118.
- Dember LM, Beck GJ, Allon M, et al. Dialysis Access Consortium Study Group. Effect of clopidogrel on early failure of arteriovenous fistulas for hemodialysis: a randomized controlled trial. *JAMA* 2008; 299(18): 2164–2171.
- Robbin ML, Greene T, Allon M, et al. Hemodialysis Fistula Maturation Study Group. Prediction of arteriovenous fistula clinical maturation from postoperative ultrasound measurements: findings from the hemodialysis fistula maturation study. *Am Soc Nephrol* 2018; 29: 2735–2744.
- Sheth RA, Freed R, Tavri S, et al. Nonmaturing fistulae: epidemiology, possible interventions, and outcomes. *Tech Vasc Interv Radiol* 2017; 20(1): 31–37.
- Masengu A, Maxwell AP and Hanks JB. Investigating clinical predictors of arteriovenous fistula functional patency in a European cohort. *Clin Kidney J* 2016; 9(1): 142–147.
- Bleyer AJ, Scavo VA, Wilson SE, et al. A randomized trial of vonapanitase (PATENCY-1) to promote radiocephalic fistula patency and use for hemodialysis. *J Vasc Surg* 2019; 69(2): 507–515.
- Peden EK, Lucas JF, Browne BJ, et al. PATENCY-2 trial of vonapanitase to promote radiocephalic fistula use for hemodialysis and secondary patency. *J Vasc Access* 2022; 23(2): 265–274.
- Zierler RE, Leotta DF, Sansom K, et al. Analysis of factors influencing accuracy of volume flow measurement in dialysis access fistulas based on Duplex ultrasound simulation. *Vasc Endovascular Surg* 2019; 53(7): 529–535.
- Roca-Tey R, Ibeas J, Moreno T, et al. Spanish Multidisciplinary Vascular Access Group (GEMAV). Dialysis arteriovenous access monitoring and surveillance according to the 2017 Spanish Guidelines. *J Vasc Access* 2018; 19(5): 422–429.
- Carroll J, Colley E, Cartmill M, et al. Robotic tomographic ultrasound and artificial intelligence for management of haemodialysis arteriovenous fistulae. *J Vasc Access*. Epub ahead of print 23 November 2023. DOI: 10.1177/11297298231210019.
- Mohr BA and Trovillion PJ. Economic value of preventing central venous catheter sepsis infections with early cannulation arteriovenous grafts (ECAVGS) compared to non-ECAVGS. *Value Health* 2015; 18(3): A42.