Arteriovenous Fistula Surveillance Using Tomographic 3D Ultrasound‡

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WHAT THIS PAPER ADDS

A well functioning arteriovenous fistula (AVF) is essential for haemodialysis, but despite regular duplex ultrasound (DUS) surveillance significant numbers of AVFs fail. Up to 83% of sonographers suffer repetitive strain injury (RSI) from high volumes of scanning. DUS and tomographic 3D ultrasound (tUS) are equally accurate at detecting AVF complications compared with fistulography. tUS has excellent intra- and interobserver agreement and is significantly quicker than DUS at detecting potential AVF complications. tUS may represent improved capacity, a reduction in RSI, shorter waiting times, and better service for patients. tUS could be an important test for AVF surveillance but further work is needed.

Objective: A well functioning arteriovenous fistula (AVF) is essential for haemodialysis. Despite regular duplex ultrasound (DUS) a significant number of AVFs fail. Tomographic 3D ultrasound (tUS) creates a 3D image of the AVF that can be interpreted by the clinician. DUS, tUS, and fistulograms were compared for the identification and measurement of flow limiting stenosis.

Methods: Patients with AVF dysfunction on routine Transonic surveillance, defined as (1) $>$ 15% reduction in flow on two consecutive occasions, (2) $>$ 30% reduction in flow on one occasion, (3) flow of $<$ 600 mL/sec, (4) presence of recirculation, underwent DUS. AVF tUS imaging was performed prior to fistulography. All fistulograms were reported by the same consultant radiologist and tUS images by the same vascular scientist blinded to the fistulogram results. Maximum diameter reduction in all stenoses were measured using all three imaging techniques.

Results: In 97 patients with 101 stenoses, the mean ($\pm$ standard deviation [SD]) severity of stenosis was 63.0 $\pm$ 13.9%, 65.0 $\pm$ 11.6%, and 64.8 $\pm$ 11.7% for the fistulograms, DUS, and tUS respectively. The mean ($\pm$ SD) time between ultrasound and fistulography imaging was 15.0 $\pm$ 14.5 days. Assuming the fistulogram as the "gold standard", Bland—Altman agreement for DUS was −1.9 $\pm$ 15.5% (limit of agreement [LOA] −32.2 − 28.4) compared with −1.7 $\pm$ 15.4% (LOA −31.9 − 28.4) for tUS. Median ($\pm$ interquartile range) time to complete the investigation was 09:00 $\pm$ 03:19 minutes for DUS and 03:13 $\pm$ 01:56 minutes for tUS ($p < .001$).

Conclusion: DUS and tUS were equally accurate at detecting AVF complications but tUS investigation requires less skill and was significantly quicker than DUS.

Keywords: Arteriovenous fistula surveillance, Fistulography, Duplex imaging, Tomographic 3D ultrasound (tUS)
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INTRODUCTION

In the UK, haemodialysis remains the most frequent renal replacement therapy, and in 2018 5 731 new individuals started receiving haemodialysis.[1] A well functioning arteriovenous fistula (AVF) is essential for most patients on haemodialysis while they await renal transplant, if appropriate, but the annual cost is over £35 000/patient).[2]

Turbulent blood flow leading to high shear stress within the AVF is thought to lead to intimal damage causing flow limiting stenoses or aneurysmal changes. When undetected and untreated, these stenoses lead to AVF thrombosis, the patient's lifeline. AVF thrombosis is the single most frequent cause of morbidity in patients on haemodialysis.[3] For this reason, AVF surveillance is important with angioplasty recommended when stenoses $>$ 50% are detected.[4] Despite regular duplex ultrasound (DUS) surveillance to detect AVF complications, up to 50% of AVFs fail within a year.[5–7]

DUS is cheap and safe and allows measurement of flow dynamics in the calculation of stenosis severity, which

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cannot be estimated by fistulogram.[3] However, DUS needs to be reported by skilled ultrasound operators who are able to build a mental picture of the AVF. Being operator dependent, DUS may be prone to error.[8–10] Clinicians rely on these written reports and, in the absence of substantial trust between the clinicians and the vascular scientists, invariably further imaging will be required prior to treatment. Equally importantly, there is a national shortage of skilled ultrasound operators with DUS requiring approximately 20 minutes/patient to acquire the image and 10 minutes for each report. Additionally, up to 83% of the sonographers suffer repetitive strain injury (RSI),[11–13] emphasising the importance of new technologies that require less skill, less time to acquire, and which can be interpreted directly by clinicians.

Tomographic 3D ultrasound (tUS) is a high resolution, tracked free hand, 3D ultrasound system, which works by frame grabbing the images from a standard DUS system.[14] Sensors are attached to the standard DUS transducer to track its position as it is swept over the vessel, allowing imaging of the entire length of the artery or vein in seconds. The DUS images are acquired and processed by the tUS computer into a near real time 3D image. The software generates reconstructed volumes of the AVF within seconds, which can then be viewed in any orientation allowing precise measurement of the severity of any stenosis.

DUS and tUS with fistulography were compared, as the gold standard, for the identification and measurement of flow limiting stenosis (Fig. 1). The time taken to acquire the DUS and tUS images was also recorded.

MATERIALS AND METHODS

Patients in whom AVF dysfunction was suspected on clinical grounds, or at routine surveillance using Transonic flow measurement, underwent DUS if one of four criteria were met: (1) $>$ 15% reduction in access flows on two consecutive occasions, (2) $>$ 30% reduction in access flow on one occasion, (3) access flow of $<$ 600 mL/sec, (4) presence of recirculation. Consecutive patients who had $>$ 50% stenosis detected by DUS were recruited. All patients provided informed written consent and the study protocol was approved by the National Research Ethics committee (18/LO/0100).

Patients who met one of the four criteria above and had $>$ 50% stenosis (determined by velocity measurements, B-mode images and volume flow[15] identified on DUS, using B mode, colour flow, and spectral Doppler modes), underwent fistulogram with or without angioplasty. This was carried out using Axiom Artis fluoroscopy set (Siemens Healthineers, Frimley, UK), with images acquired at 3 frames / sec. Contrast was hand injected via either a 6F sheath side arm or through 4F catheters using Visipaque 270 (GE

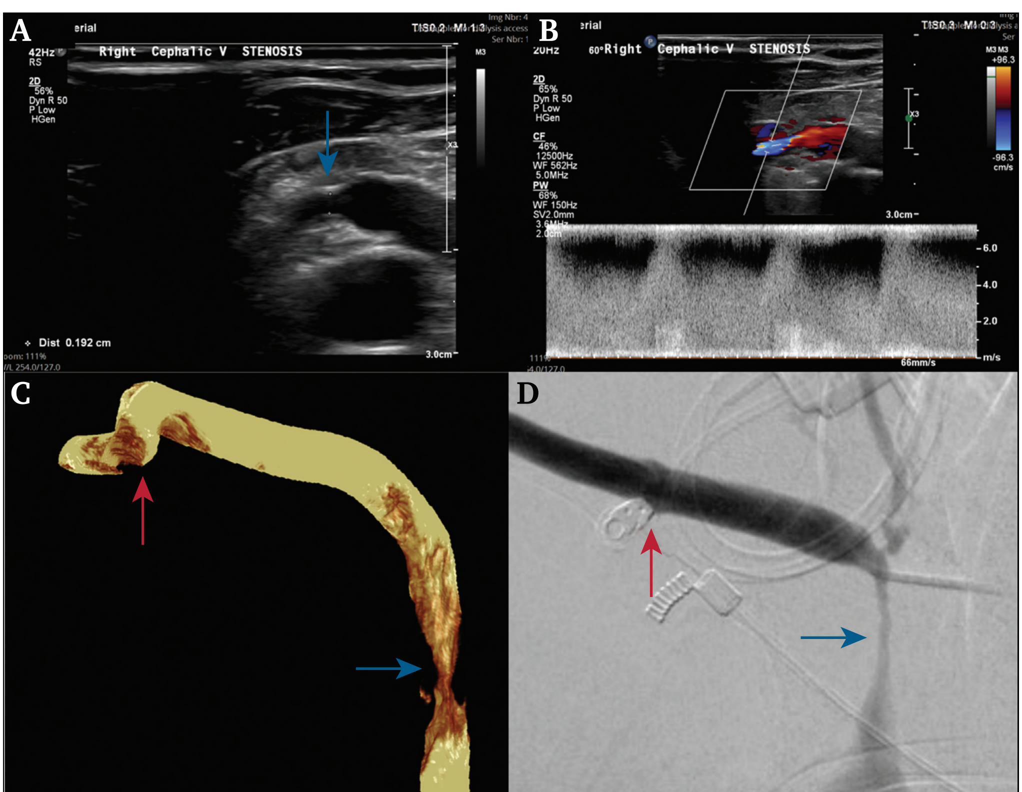

Figure 1. Arteriovenous fistula (AVF) stenosis in a single patient by imaging modality. (A) B-mode duplex ultrasound (DUS) image of a right cephalic vein stenosis of 75.6%. (B) Colour and spectral doppler image of the same stenosis. (C) Tomographic 3D ultrasound (tUS) image of the same cephalic vein stenosis of 67.6%. (D) Fistulogram image of the same cephalic vein stenosis of 90%. Red arrows indicate the same point within each image where the vessel is kinked. Blue arrows indicate the cephalic vein stenosis.

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healthcare, Chalfont St Giles, UK) diluted 50% with 0.9% saline. Prior to fistulogram, a tomographic 3D ultrasound (tUS) was performed using a 9 MHz transducer and a DUS instrument (Affinity 5g, Philips UK Ltd, Guildford, UK) with the tUS sensors attached (PIUR imaging GmbH, Vienna, Austria). tUS images were acquired in transverse section using B mode ultrasound settings with separate images of the inflow vessel, outflow vessel and anastomosis. From the wrist to as far proximally as could be visualised, a minimum of three tUS scans, of the full vessel length, were recorded per patient: one of inflow, one of the outflow, and another of the complete anastomosis including junction and a small section of each inflow/outflow vessel. The vascular scientists were able to repeat the scan if required. The acquisition of the DUS and tUS images was performed by one of three specifically study trained and tUS experienced vascular scientists. The time to perform all the duplex and tUS scans was recorded.

The fistulogram, reported by a single consultant interventional radiologist blinded to the DUS and tUS results, was used as the gold standard measure of severity of stenosis against which DUS and tUS were compared. The stenosis severity, calculated by diameter reduction calculations on tUS, was measured by a single experienced vascular scientist blinded to the results of DUS and fistulography. Each individual tUS image was reviewed (i.e., images were not combined or fused) to identify the stenosis location. If the stenosis was visible on more than one scan, the "best" scan was chosen at the discretion of the only reporting vascular scientist. Repeat analysis was performed by a second blinded vascular scientist.

Statistical analysis

Descriptive statistics (mean and standard deviations) were used for severity of stenosis per imaging modality. tUS intra- and interobserver agreement was assessed using interclass correlation (ICC). ICC estimates and their respective 95% confidence (95% CI) intervals were calculated based on a single measurement, absolute agreement, two way mixed effects model. A p value $< .050$ was considered significant. Bland–Altman agreement was used to establish measurement error for each modality using fistulography as the gold standard. Interclass correlation was calculated using SPSS statistics v22 (IBM Corp., Armonk, NY, USA). Descriptive statistics, Bland–Altman agreement, and all graphs were created using GraphPad Prism v7 (GraphPad software Inc., La Jolla, CA, USA).

RESULTS

One hundred and twenty-seven patients referred for fistulogram were recruited, of which 30 were excluded from analysis. Of the 30, two patients could not be cannulated and no comparative fistulogram could be taken. In 24 of the

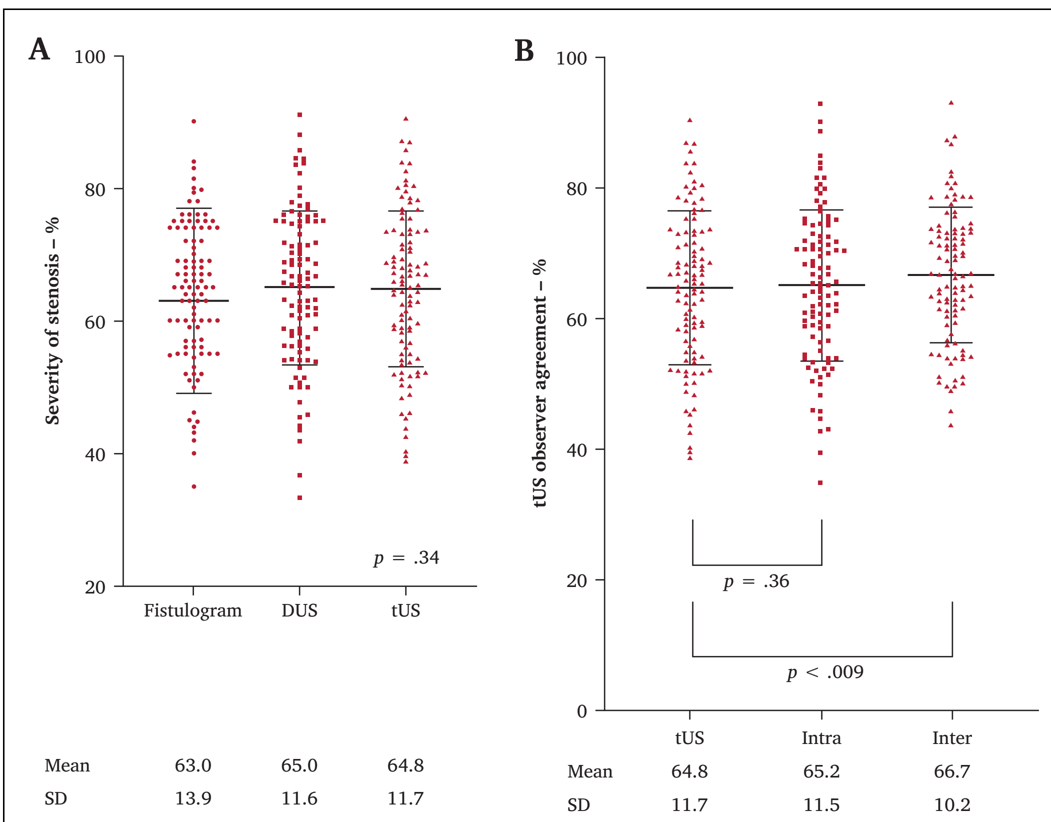

Figure 2. (A) Mean and standard deviation of arteriovenous fistula stenosis severity by fistulography, duplex ultrasound (DUS) and tomographic 3D ultrasound (tUS). (B) Mean and standard deviation of tUS severity of stenosis compared with intra- and interobserver agreement. SD = standard deviation.

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30 patients the radiologist was unable to adequately measure severity of stenosis. This was due to vessel tortuosity in 2D images in 20 cases and in four cases was because the catheter occluded the lumen in severely tight stenoses resulting in no luminal contrast for measurement. Additionally, tUS images were non-diagnostic on two occasions and an axillary vein stenosis was missed in a further case. In one patient the radial artery occluded between the ultrasound scans and fistulogram date. Evaluable results were available for comparison in 97 patients who had 101 stenoses (three patients had multiple stenoses).

Of the 97 AVFs, 26 were in the right arm and two had previously been revised (one brachiocephalic, one radiocephalic). Forty-five were radiocephalic, three were ulnarcephalic, 25 were brachiocephalic, and 24 were brachiobasilic transpositions. The mean (± SD) time between duplex/tUS scans and fistulogram was 15.0 ± 14.5 days. The mean (±SD) stenosis severity (Fig. 2) was reported at 63.0 ± 13.9%, 65.0 ± 11.6% and 64.8 ± 11.7% for the fistulograms, DUS, and tUS respectively, $p = .34$ (no significant difference).

Intra- and interobserver agreement for tUS was good and excellent with ICC values of 0.92 (95% CI 0.89 − 0.95, $p = .36$) and 0.77 (95% CI 0.66 − 0.84, $p < .009$) respectively (Figs 3 and 4). Bland—Altman agreement for intra-observer error was −0.4 ± 4.5% (limit of agreement [LOA] −9.3 − 8.5) compared with −2.0 ± 7.4% (LOA −16.48 − 12.53) for interobserver error (Figs 3 and 4). DUS and tUS agreed closely with the fistulogram for the severity of stenosis. With the fistulogram as the gold standard, Bland—Altman agreement (Fig. 5) for DUS was −1.9 ± 15.5% (LOA − 32.2 − 28.4) compared with −1.7 ± 15.4% (LOA −31.9 − 28.4) for tUS. Bland—Altman agreement for tUS where DUS is the gold standard was 0.2 ± 12.75% (LOA −24.8 − 25.2) (Fig. 5). Median (± interquartile range) time to acquire the DUS and tUS images (Fig. 6) was 09:00 ± 03:19 minutes and 03:13 ± 01:56 minutes respectively ($p < .001$).

DISCUSSION

The results demonstrate that tUS achieved the same accuracy in identifying and measuring the severity of stenoses

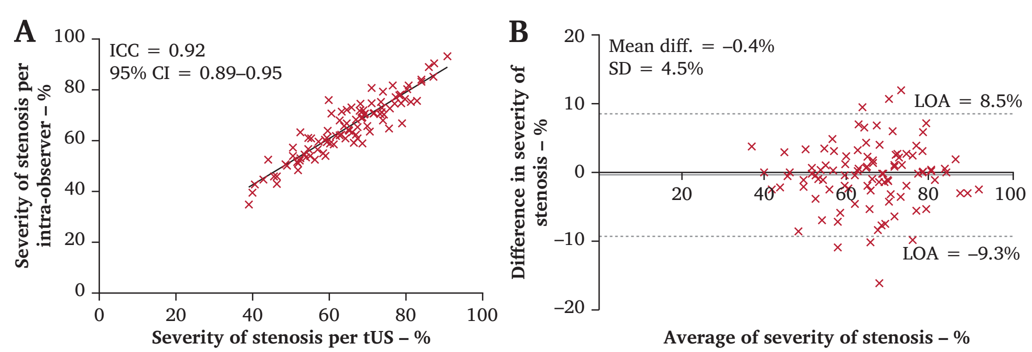

Figure 3. (A) Intraclass correlation (ICC) for intra-observer assessment of arteriovenous fistula stenosis severity as measured by a single observer using tomographic 3D ultrasound (tUS). (B) Bland—Altman assessment for intra-observer agreement of stenosis percentage by one observer using tUS. CI = confidence interval; SD = standard deviation; LOA = limit of agreement.

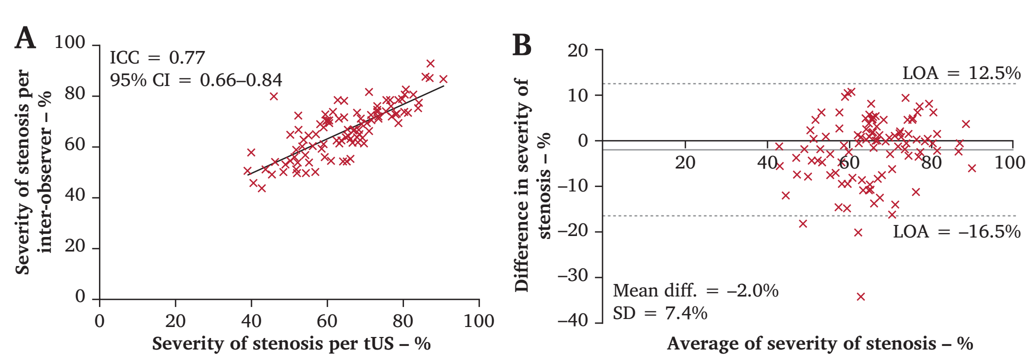

Figure 4. (A) Intraclass correlation (ICC) for interobserver assessment of arteriovenous fistula stenosis severity as measured by a single observer using tomographic 3D ultrasound (tUS). (B) Bland—Altman assessment for interobserver agreement of stenosis percentage by one observer using tUS. CI = confidence interval; SD = standard deviation; LOA = limit of agreement.

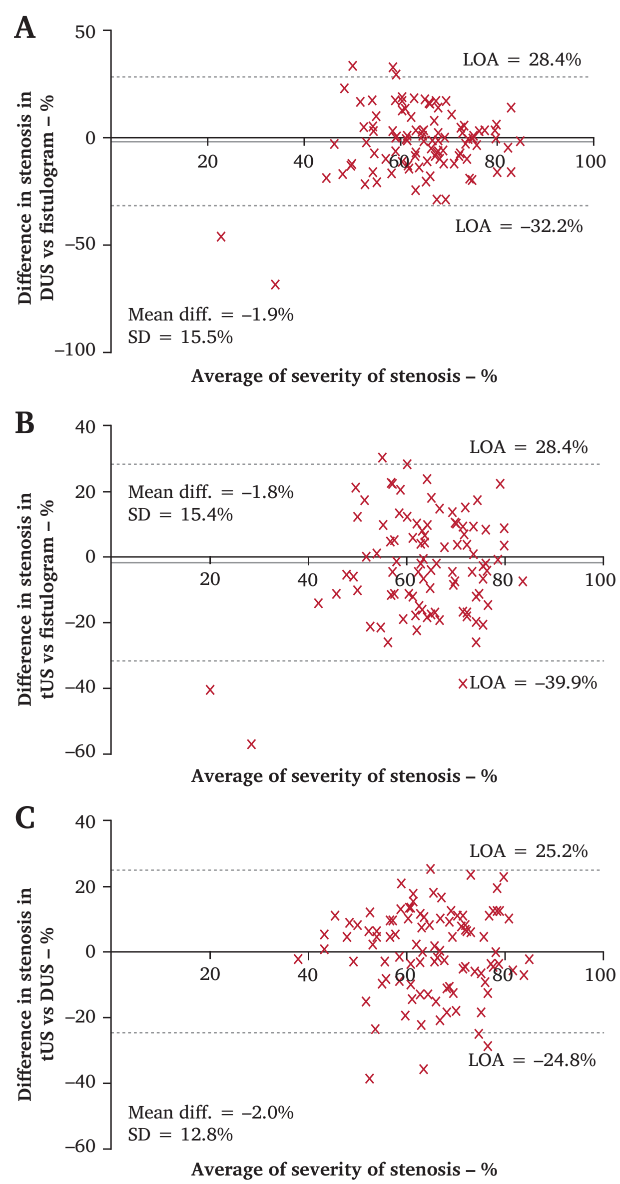

Figure 5. Bland–Altman agreement for (A) duplex ultrasound (DUS) and (B) tomographic 3D ultrasound (tUS) compared with fistulography as the gold standard and (C) tUS compared with DUS as the gold standard in the measurement of arteriovenous fistula stenosis. SD = standard deviation; LOA = limit of agreement.

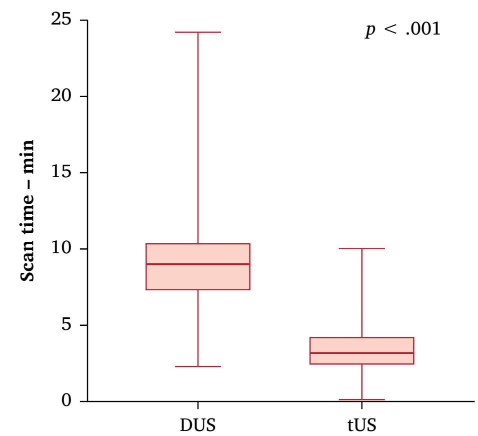

Figure 6. Median and interquartile range of the scan time for duplex ultrasound (DUS) and tomographic 3D ultrasound (tUS) recorded by one vascular scientist.

involving the AVF compared with fistulography, but compared with DUS, tUS images took less than half the time to acquire. With further research, potentially tUS may be an important test for routine AVF surveillance. The relatively less skill and shorter time required to assess the AVF by tUS compared with standard DUS, has added benefits for both the patient and the workforce representing a potential increased scanning capacity and decreased RSI risk.

The 24 cases in which it was not possible to adequately measure the severity of the stenosis plus the two failed cannulation cases are recognised flaws of invasive 2D imaging like fistulography. This failure rate clearly documents why the use of diagnostic fistulography is inappropriate when ultrasound techniques are more than adequate. In all 24 instances a stenosis was identified with ultrasound and fistuloplastied with an improvement in AVF function and Transonic flow seen at dialysis. The two instances of non-diagnostic tUS images were the result of superficial aneurysmal disease and loss of skin contact. This is a documented limitation of all ultrasound techniques, including tUS, but downstream volume flow measurements detected a haemodynamically significant stenosis.

tUS acquires images taken in the transverse, anteroposterior plane. Scanning aneurysmal AVF disease with tUS, as with DUS, is challenging where excessive amounts of ultrasound gel are needed. Even then, it is possible to have partial loss of contact between the probe and the skin degrading the image quality. Although tUS is compatible with most commercially available ultrasound systems, and uses software specifically generated for vascular surgery, it remains limited by the same constraints as standard DUS. In addition to aneurysmal disease, acoustic shadowing as a result of calcification, also remain a challenge for all ultrasound techniques.

RSI in vascular scientists/Sonographers is related to total scanning time and the leaning/twisting of the sonographer for certain examinations.[12] Implementing methods that reduce risk and improve workforce occupational health has previously been recommended.[11,13] The shorter time and lower operator skill required for tUS should reduce RSI. It may also be possible for AVF imaging to be undertaken by dialysis staff with minimal training to improve departmental capacity of the Vascular Laboratory through fewer or faster scans but may provide easier access at markedly less cost.

Based on a potential saving of 05:47 minutes per patient, a total time saving in 97 patients could have been 8 hours 46 minutes if tUS was used for surveillance instead of DUS. Using the current UK reimbursement tariff that assumes a DUS takes 20 minutes on average, it is estimated that an additional 26 patients could have been scanned.[16]

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Fundamentally, tUS could improve departmental capacity, reduce RSI and shorten waiting lists. While the exact clinical protocol for the use of tUS in AVF imaging needs determining, it is important to recognise the advantages of DUS. The haemodynamic information presented by DUS through colour and spectral Doppler can still be valuable. One such solution may be to perform the morphological map with tUS and then use DUS for targeted assessment for specific haemodynamic information, but with the use of Transonic measurements this may not be needed. This could also hinder the adoption of tUS by less experienced operators.

Further work must as a priority assess the value of tUS when used by less experienced operators in the dialysis unit, while the scans would need to be sent to a vascular scientist to report in the short term. Although not formally documented in this study, the processing time per patient is currently around 10 − 15 minutes and requires an experienced vascular scientist. With the development of artificial intelligence, it may become possible to automate that step meaning AVF patients may not need an additional visit to the vascular laboratory for further imaging in the future.

Although DUS is known to have has a role in predicting AVF maturation,[17] perhaps tUS also opens new methods of interpretation that may further improve outcomes. Traditionally, DUS can be used to detect changes in volume flow within an AVF.[18] Advances in dialysis equipment now mean that this volume flow can easily be detected during dialysis, avoiding the need for patients to travel to the Vascular Laboratory for additional testing.[19] Although it is known that changes in Doppler volume flow (mL/min) are predictive of AVF failure,[18] tUS presents new ways to sensitively measure changes within the AVF. By being 3D, tUS opens up the possibility of AVF volume (cm^3) measurements. Further assessment via randomised control trials should be used to assess the role of tUS like those performed with traditional DUS to further outline its role in vascular access creation.[18] Future work should focus on AVF volumes and their correlation with maturation rates and future complications as they may represent a potential early warning. It is clear that volume is sensitive to small changes, but a threshold needs establishing.

Conclusion

DUS and tUS are equally accurate at detecting complications compared with fistulography in AVF surveillance. Tomographic 3D ultrasound has excellent intra and interobserver agreement and requires less skill to perform. tUS is significantly quicker than standard duplex at detecting potential AVF problems, representing an improved capacity and reduced repetitive strain risk. The results suggest that tUS could be an important AVF surveillance test but further work is needed.

AUTHOR CONTRIBUTIONS

S.R., A.H., and C.M. achieved the funding and ethics for this project. S.R., C.M. and R.C. designed the study. K.S. and S.K. performed tUS image analysis. S.L. measured the angiograms. S.R. performed data interpretation and the statistical analysis plus interpretation and drafted the manuscript for critical review by all authors. Final approval and critical revision of intellectual content was completed by R.C. and C.M.

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CONFLICT OF INTEREST

Charles McCollum is a founder of PIUR imaging GmBH.

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