

Evaluation of the Airglove™, An Air-Regulated Thermal-Venodilatory Device Facilitating the Cannulation of Patients With Difficult Venous Access

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Abstract

Background

Difficult venous access (DVA) can prevent delivery of life-saving intravenous (IV) fluids and medication. The Airglove™ was developed to facilitate IV access, circumventing DVA in chemotherapy patients, as current warm-water immersion (WWI) methods are sub-optimal.

Methods

This study had two parts; EAGLE-1, an observational, proof-of-concept study and EAGLE-2, a prospective, cross-sectional comparative study. EAGLE-1 recruited 80 adult participants undergoing chemotherapy for cancer with DVA where venous cannula insertion success rate was evaluated using Airglove™. EAGLE-2 was carried out on 34 adult healthy participants where the degree of venodilation by WWI and AirGlove™ in three veins; cubital-fossa cephalic vein, cubital-fossa median vein and the third dorsal carpal vein on both arms were measured using the GE Logic S8 multi-frequency linear-array transducer (L6-15MHz), two-dimension B-mode ultrasound. Baseline measurements were taken at 23°C, forearms were warmed to 38°C using the two modalities prior to ultrasound assessment.

Results

An IV cannulation success-rate of 87.5% was achieved with the Airglove™ in EAGLE-1. The EAGLE-2 study demonstrated significant venodilation enhancement in all veins examined ($p < 0.001$, 95% C.I) using the Airglove™. BMI, percentage body-fat, age, gender, or blood-pressure did not significantly influence the degree of venodilation.

Conclusions

Airglove™ enabled a significant percentage of successful cannulations in participants with DVA in EAGLE-1. EAGLE-2 demonstrated that Airglove™ significantly enhanced venodilation compared to WWI. There may be potential for Airglove™ to be considered in specific clinical settings where DVA is encountered.

Introduction

Failure in gaining intravenous (IV) access is common in those undergoing chemotherapy, the obese population, IV drug users and patients with chronic medical problems leading to peripheral venous collapse. The importance of IV access is highlighted in the 2010 National Hospital Ambulatory Care Survey, where over one quarter (35.2 million) of all emergency-department attendances in the United States result in the placement of an IV cannula for parenteral fluid administration¹. However, when

traditional routes are compromised, additional methods such as intraosseous infusion, central IV catheters and other more invasive approaches are available ².

Previous studies have shown where IV access failure occurs, in patients who have “difficult venous access” (DVA), ultrasound-guided methods have proven superior^{3,4,5,6,7}. However, ultrasound equipment is expensive, not widely available at most hospitals for this purpose and very few clinical staff are trained in its use. Furthermore, bedside ultrasound equipment in most hospitals in the UK are only able to image in a single plane, meaning that the operator is only able to either view the vein in the short or long axis but not both simultaneously. There have been advances in bi-plane imaging, however this is costly and not widely available⁸. Thus, there is scope for more simple, cost-effective tools to facilitate venous access in DVA patients in an outpatient setting.

For DVA patients, most chemotherapy units in the United Kingdom immerse the patient’s forearm in a container of warmed-water or by running the patient’s arm under a warm-water tap. Convection of heat from warmed water onto skin causes vasodilation on activation of the sympathetic pathway, thus dissipating excess heat from the surface of the skin ⁹. Venodilation by this method is transient but serves the primary purpose of allowing staff to gain IV access, enabling administration of drugs for chemotherapy, and delivering life-saving fluids, nutrition and medication.

There are important limitations to the warm-water immersion (WWI) method; maintaining accurate and safe temperature controls (risk of scalding) can be challenging, sterility of the method cannot be ensured especially within a cohort with significant risks of immune-compromise, risks of water spillage and the potential distress to patients. For this reason, the Airglove™ (Fig. 1 a, b, c, d) was developed. This device directs warmed air over the forearm within a single-use polyurethane-glove, causing venodilation with precise thermal regulation in three-minutes, to facilitate easier venepuncture or cannulation without the need for specialist training.

A “Medical Technologies Innovation briefing” document has been developed by The National Institute for Health and Care Excellence (NICE) on the recommended use and application of the Airglove™ ¹⁰. In the EAGLE study, we evaluated the utility of the Airglove™ in a cohort of patients undergoing chemotherapy and subsequently compared the degree of venodilation by the Airglove™ relative to the WWI method in the upper limbs of healthy individuals.

Results

EAGLE-1

The median age of participants from the cancer-chemotherapy group in EAGLE-1 was 68.5 years and 67.5% of the participants were women (Table 1). Unexplained weight loss is a common feature in patients upon initial cancer diagnosis thus no participant in this cohort had a BMI > 25. Most (81.25%) of the cancer-chemotherapy participants were within the normal BMI range (18.5–25.0), Mann-Whitney U

analysis indicated that BMI was not a contributory factor to cannulation failure in EAGLE-1 ($p = 0.784$) and adiposity, a feature normally contributing to DVA was not relevant in this cohort (Table 1).

Participants were on various chemotherapy treatments for a variety of cancer presentations (Table 1). Extravasation is a known risk factor during venous access and delivery of chemotherapy drugs, with vesicant drugs carrying the highest risk^{11,12}.

The common observation of participants with DVA in EAGLE-1 was that the forearm of those participants was cold-to-touch (80%), and clinicians involved in EAGLE-1 proposed the cause may be peripheral venoconstriction (Table 1). Another subjective observation by clinical staff in EAGLE-1 was that two patients had very fragile veins (Table 1). "Fragile veins" is a fairly common clinical feature noted in elderly patients undergoing chemotherapy in whom there is a loss of subcutaneous fat or lack of tone, causing the veins to move and roll under the skin when a venous cannula is inserted.

Five patients had multiple IV lines delivering chemotherapy with multiple bruises from past venepuncture attempts, therefore limiting the number of IV-accessible veins for chemotherapy (Table 1). Two patients also had lymphadenectomy or axillary lymph node clearance (Table 1); usually the insertion of peripheral venous cannula is contraindicated in the ipsilateral arm where axillary lymph-node clearance has been performed, due to increased risk of infection¹³. IV-access for chemotherapy is therefore carried out mainly in the contralateral arm for those patients.

Success in IV cannulation deployment in participants with DVA following use of Airglove™.

The use of Airglove™ resulted in an 87.5% success rate in deployment of a venous cannula among participants with DVA undergoing chemotherapy for cancer (Table 1). A comparative study investigating the use of WWI vs Airglove™ was not carried out in EAGLE-1 since ethical approval was only granted for a proof-of-concept observational study solely for the use of Airglove™. Discussions with colleagues from other chemotherapy centres using WWI placed the overall success rate of IV-cannula placement after WWI in patients with DVA at around 65% (LGD personal communication).

The failure rate of Airglove™ in enabling insertion of a venous cannula in the forearm was 12.5% (Table 1). A total of 21.25% of patients undergoing chemotherapy were also on treatment with corticosteroids. Corticosteroids are frequently prescribed in patients undergoing chemotherapy and this class of drugs also causes venoconstriction, thus potentially further complicating IV-access in patients with DVA. However, we were able to gain venous access in 15 of these patients on the first attempt with the use of the Airglove™. Only two patients could not be cannulated, even after a second attempt, due to poorly visible and impalpable veins. With the Airglove™, 77.50% of participants with DVA in EAGLE-1 showed visibly enhanced dilation of their veins.

Survey questionnaires by clinical staff involved in EAGLE-1 using the Airglove™ to deploy venous cannula suggested various subjective factors contributing to the success or failure in cannulation (Table 2). These

factors are subjective viewpoints of 25 members of experienced clinical staff with an average of over 15 years of clinical experience.

EAGLE-2 demonstration of the degree of venous dilatation by ultrasound

Baseline demographics of participants in EAGLE-2 are shown in Table 3. The median age of participants was 40.6 ± 12.36 years, 69% of participants were women (total number of participants = 34). The Shapiro-Wilks test showed that age, BMI and percentage body-fat data was normally distributed. The independent means T-test ($p < 0.05$, 95% C.I.) showed no observable effect of age-bias, BMI or percentage body-fat on the degree of venodilation by the two methods (Airglove™ or the WWI method).

Increases were noted in the median diameter from baseline values in all veins measured by both modalities, although significantly enhanced venodilation was noted using Airglove™ (Fig. 2). Increases in average diameter of all veins (both arms) being measured in this study, subtracted from baseline values are shown in Fig. 3, the Airglove™ showed significant difference in venodilation compared to the WWI in all veins ($p < 0.001$ 95% C.I.).

Discussion

The results of this study are an important prelude for future in conducting a nationwide-randomised clinical trial where the efficacy of Airglove™ will be evaluated in patients undergoing chemotherapy. The device may be of potential use in emergency departments, PET-scanning labs, radiology and cardiac-catheterisation suites, general wards, care of the elderly wards and paediatric units, and whenever patients with DVA are encountered.

The median age-group of participants in EAGLE-1 was in the seventh decade, this conforms to the median age of participants in other adult chemotherapy units in the UK¹⁴. Younger age-group chemotherapy patients are not treated at MTW-Trust, since this subset of patients have unique needs due to the rapid development in their physical, cognitive, psychological, social, and experiential framework¹⁵, such needs are best addressed at other specialist centres, explaining why this subset was under-represented in this study.

The use of corticosteroids is common in cancers as an anti-inflammatory and adjuvant in treatment¹⁶, to offset the effects of spinal cord compression in cancer metastasis¹⁷, to reduce the feeling of nausea and vomiting in cancer¹⁸, and sometimes to enhance appetite and wellbeing¹⁹. However, the use of corticosteroids is also well-known to cause systemic vasoconstriction via the adrenergic system²⁰ which could potentially decrease the chances of a successful cannulation. A total of 17 out of 80 participants in EAGLE-1 were prescribed corticosteroids for various clinical reasons. Only two patients from this cohort did not respond to Airglove™-mediated venodilation.

One widely known cause for failure in gaining venous access is the increased level of adiposity which is directly correlated with BMI ^{21,22,23}. Approximately, 81.25% of the cancer-chemotherapy cohort in our study (EAGLE-1), had an average BMI between 18.5–25 (Table 1), therefore adiposity was not a significant confounding factor in that cohort. It also appears that adiposity was not a significant confounding factor in our healthy cohort population in EAGLE-2 since the average BMI among participants was 25. However, we acknowledge that further studies are warranted to investigate the venodilatory effect in participants with significant adiposity to establish optimal parameters in that cohort.

Although the use of Airglove™ was demonstrated to be successful in EAGLE-1, it was appropriate to carry out an empirical study where the actual degree of venodilation by Airglove™ was determined in comparison with WWI, the current widely used standard venodilation method in chemotherapy units across the UK. In EAGLE-2, we show that the Airglove™ causes statistically significant venodilation, measurable by ultrasound, compared to the WWI method (Fig. 3, $p < 0.001$, CI: 95%).

While the WWI method is widely used, it has numerous issues of concern which are obviated by the Airglove™ including:

- i. water spillage on clothing of patients is common and distressing.
- ii. difficulty adjusting to a suitable temperature reproducibly, without risk of scalding.
- iii. it is non-sterile, while the Airglove™ method employs a double-walled, single-use-glove.
- iv. it is a significant inconvenience due to need for removal of some clothing; patients who are peripherally venoconstricted often complain of feeling cold.
- v. the convection cooling effect from moisture causes constriction of vessels after immersion.
- vi. vi) it is difficult to maintain minimal contact during the current pandemic using the WWI method, whereas the Airglove™ method allows use and disposal of the sterile glove.

Venous or arterial access devices in patient groups that require regular venous access for transfusions or delivery of medication are available, such as use of tunnelled central venous catheters (e.g. Hickman®, Broviac®, Groshong® or Neostar® lines) ²⁴, arterio-venous fistula, peripherally inserted central catheters (PICC) ²⁵, central vascular access devices (CVAD) ²⁶ or portacaths ²⁷. However, these methods are invasive, require specialist medical or surgical team intervention and considerable post-procedural, specialist-nurse-led after-care is often warranted. Furthermore, insertion of some of these ex-vivo devices have been associated with increased risk for deep vein thrombosis (DVT) ^{28,29}, although these risks can be reduced with appropriate patient-centred risk-stratification and prior medical management; DVT prophylaxis with intravenous heparin ³⁰. Other devices have been reported to facilitate easy venous access, such as the AccuVein AV300, which uses infrared light to highlight haemoglobin within blood-vessels, however it does not venodilate veins ³¹. However, subsequent trials that have been conducted produced conflicting results ^{32,33}.

This study has demonstrated that while enhanced venous dilatation is achieved using both modes of forearm-warming, the Airglove™ showed a significant advantage over the WWI method in all the vessels measured (Figs. 2 and 3). The additional major benefits of the Airglove™ are that it is reproducible, sterile, patient-friendly, and simple to use, without the need for specialist training. The Airglove™ has been evaluated by the NICE Medical Technologies Evaluation Programme (MTEP), producing a MedTech Innovation Briefing (MIB) which supports NHS and social care commissioners and staff when they are evaluating new medical devices¹⁰. The MIBs are commissioned by NHS England in line with the 5-year Forward View policy documents, which help accelerate innovation in new treatments and diagnostics and help key personnel in decision making. We anticipate that although use of the Airglove™ in this study has been slanted towards the chemotherapy cohort with DVA, it could be considered in other clinical situations where DVA is encountered. Particularly, we envisage that since the design of the Airglove™ uses a sterile-single use inflatable-glove, it will be pertinent in the current coronavirus pandemic (COVID-19) where sterility is paramount.

Methods

Study design, institutional review, ethical approvals and participants' eligibility criteria

The study acronym: the EAGLE study, was shortened from "Efficacy of Air-GLovE in difficult venous access". The study was carried out in two parts (Fig. 4). The first, an observational, proof-of-concept study for Airglove™ (EAGLE-1), recruited a total of 80 informed and consented participants from patients (inclusion-exclusion criteria; Table 4) attending the chemotherapy unit at Maidstone Hospital, Kent. Approvals for the EAGLE-1 study were granted by the local research ethics committee and the R&D Department at MTW Trust, Kent, England, UK.

The second part, EAGLE-2, was a prospective, cross-sectional, comparative study on 34 appropriately consented participants, where the degree of venodilation of the Airglove™ vs. WWI was determined by ultrasound in three veins of the forearm (Fig. 5). EAGLE-2 was approved by the institutional ethics committee (reference number: HLS/PSWAHP/18/168) and run at the clinical simulation unit of Glasgow Caledonian University, Scotland, UK. All participants to the study (EAGLE-1 and EAGLE-2) met the inclusion-exclusion criteria (Table 4) and written informed consent was obtained in accordance with the requirements of current good clinical practice (GCP) and the ethical standards of the responsible committee on human experimentation (institutional), and with the Helsinki Declaration of 1975, as revised in 2000 and 2008.

EAGLE-1 study

Evaluation of the Airglove™ on participants undergoing chemotherapy

The Airglove™ was evaluated on a total of 80 participants (demographics described in Table 1) undergoing chemotherapy at the Chemotherapy unit, Maidstone Hospital (MTW Trust), Kent, with DVA (inclusion-exclusion criteria in Table 4). The endpoint was set as the overall successful insertion of a

venous-cannula (maximum two attempts) following the use of Airglove™. Total number of participants were recruited to the study over a period of one month and cannulation was carried out by a single qualified nurse to avoid operator bias. EAGLE-1 study questionnaires were completed by the operator of the Airglove™ and a total of 25 clinical staff in the chemotherapy unit normally performing venous-cannulation. Aspects and features frequently contributing to cannulation success or failure from the questionnaires are tabulated in Table 2.

EAGLE-2 study

Pre-assessment of volunteers

Blood-pressure (from both arms), age, height, weight, BMI, percentage of body-fat (using bioimpedance-analysis (BIA) measured with a Tanita Body composition analyser (TBF-300M) across the lower limbs) and hydration status (assessed clinically by capillary refill, dryness of mucus membranes, jugular-venous-pressure) were recorded prior to venodilation and ultrasound measurements.

Interventions

Warmed-water Immersion (WWI) method of venodilation

The upper limbs (to the level of mid-humerus) of participants were immersed in a container filled with a mix of cold-and warm tap-water to 38.5°C for 3 minutes in the WWI method. Water temperature was verified using a Tanma 72-2060 digital thermometer. Arms were towel-dried, and the degree of venodilation was assessed by ultrasound.

Airglove™ method of venodilation

A single-use, double-walled, polyurethane-balloon (Green Cross Medico, Scotland) was inflated around the forearm using the Airglove™ to 38.5°C at setting number-3 (Fig. 1c) for 3 minutes and then removed. The degree of venodilation was assessed by ultrasound.

Ultrasound assessment of venous dilation by Airglove™ vs. WWI

No invasive procedure, such as cannulation or venepuncture, was carried out on participants in EAGLE-2. Ultrasound assessment of veins was performed prior to and following the Airglove™ and WWI warming methods. Volunteers were placed in a semi-recumbent position while ultrasound measurements were taken from each arm, devoid of external circumferential compression-pressures such as tight clothing or watches.

Three markings, aligning with common IV cannulation sites, were made on the upper limbs: i) the prominent veins proximal to the base of the middle-digit on the dorsum of the hand (dorsal-metacarpal), ii) lateral side of arm, 5 cm proximal to the skin crease of cubital fossa, to mark cephalic vein in arm (CV

at cubital fossa), and iii) medial side of arm at the skin crease of cubital fossa to mark the median-cubital vein (MCV near cubital fossa).

Ultrasound examination of the veins in the forearm was performed by a single sonographer, using a GE Logic S8, (software version R2, revision 1.1, GE Healthcare, USA) with multi-frequency linear array transducer (L6-15MHz). Measurements of each vein were recorded to 0.01 cm accuracy, using two-dimensional B-mode scanning in a transverse plane. On frozen annotated images, antero-posterior (AP) measurements were recorded at the skin-marked vessel sites, from inner anterior wall to inner posterior wall (or intima to intima) to facilitate repeatability (Fig. 2).

Baseline ultrasound measurements were recorded at 23°C ambient room temperature. The WWI method was deployed as described above and ultrasound measurements conducted on all three marked sites. Participants were rested for 30 mins before testing with Airglove™ and ultrasound measurements were recorded on the same three marked sites. This process was repeated on the opposite limb. WWI and Airglove™ venodilation (temperature setting #3, Fig. 1c) were set at 38.5°C for uniformity, enabling comparison. The first warming method used first on each participant was randomised and carried out by one of our team members.

Blinding in EAGLE-2

Blinding was achieved by physical concealment of onscreen diameter measures at time of scan, also ensuring the sonographer was unaware of the venodilation warming method used for participants. Vein diameter measurements were retrospectively recorded for statistical analysis.

Statistical analysis and sample size calculations

Personal communication with colleagues from chemotherapy units in the UK indicated a 65% cannulation-success rate for patients with DVA using the WWI method (LGD personal communication). Hence, the alternative hypothesis was formed that cannulation-success rate with Airglove™ in EAGLE-1 may approximate or exceed the success rate set for the WWI method, and the null-hypothesis was set as cannulation-success would be successful only half of the time (50%). Employing the pwr.p.test module (in R ver.3.60)³⁴, a minimum sample-size of 77 participants was needed for a cannulation success rate of 65%, powered at 85% to correctly accept the alternative hypothesis at the $p = 0.05$ significance level.

The EAGLE-2 study which enrolled 34 participants, exceeded the minimum sample size of 24 required for 90% power, with $\alpha = 0.05$ and the ideal anticipated Cohen's "d" effect size of 0.833, calculated using the "pwr.T.test" module (in R ver.3.60, within RStudio ver.1.2.1335).¹⁰¹¹ Mean venodilation by WWI and Airglove™ for input into the "pwr.T.test" script was determined from previous pilot studies carried out at the Sir Geraint Evans Wales Heart Research Institute, Cardiff. Normality of data was determined using the Shapiro-Wilks test in SPSS (ver.25) prior to employing the independent means T-test. The paired samples T-test was used to compare the degree of venodilation between Airglove™ vs WWI.

All statistical analysis was carried out with SPSS (ver.25; IBM Corp), SciPy module (ver.1.3) for Python (ver.3.7.2) and R (ver.3.60), with $P < 0.05$ considered as statistically significant.

Patient and public involvement in this study

The study protocol and questionnaire forms were circulated to members of the Kent Lung Awareness Charity (UK Charity no. 1166445; <http://kentlungawareness.weebly.com>), a charity group consisting of families, friends and supporters of those who had succumbed to various lung diseases including primary and secondary lung cancers. Opinion was also gathered from various lay members of the EAGLE steering committee formed initially at Cardiff University.

Declarations

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Author Contributions

LGD designed the study, clinically examined & assessed participants, carried out the ultrasound measurements for the preliminary study, supervised clinical and scientific teams, submitted application to NICE-MEDTECH, wrote expert review for NICE, carried out the statistical analysis, wrote the manuscript. EG assessed participants, assisted in study design, recruited participants, carried out the ultrasound measurements at GCU and applied for ethics permissions. PS & TMM advised on statistical analysis and reviewed manuscript. DMD assisted in study design and reviewed manuscript. SJack assisted in study design, liaised with regulatory bodies, assisted in application to NICE and reviewed the manuscript. ZY, CDL, FAL and SAH advised on design of study, were part of the steering committee of the study and reviewed manuscript.

Competing interests

All authors, except S Jack in this manuscript declare that they have no conflicting interest. S Jack is an employee of Green Cross Medico Ltd (Scotland).

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Data availability

All data relevant to the study are included in the article.

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Tables

Table 1 Demographic and study information of participants in EAGLE-1 study. Pertinent demographic and key information on the chemotherapy-participant cohort in EAGLE-1. The main causes for classification of DVA in this cohort are listed along with data on cannulation failures and success.

Participant information – EAGLE-1	number of participants, percentage (n=80)
Median age	68.50 ± 13.38 years
Youngest participant	33 years
Oldest participant	87 years
Effect of age on cannulation failure/success using Airglove™	p=0.180
-	
<u>Gender</u>	
females	54 (67.5%)
males	26 (32.5%)
Cannulation failure (males vs females) using Airglove™	3 vs 6
Cannulation success (males vs females) using Airglove™	23 vs 48
Effect of gender on cannulation failure/success using Airglove™	p=0.784
-	
<u>BMI of participants</u>	
18.5-25	65 (81.25%)
>25	15 (18.75%)
Effect of BMI on cannulation failure/success using Airglove™	p=0.784
-	
<u>Proportion of cancers by system among participants</u>	
Breast	13 (13.7%)
Digestive/gastrointestinal	21 (22.1%)
Genitourinary	5 (5.3%)
Gynaecologic	25 (26.3%)
Head and neck	3 (3.2%)
Haematological	6 (6.3%)
Lung	6 (6.3%)
Skin	1 (1.1%)
-	

Chemotherapy drug use by risk of extravasation (vesicant, irritant, neutral)

participants on vesicant only type drugs	16 (20.0 %)
participants on irritant only type drugs	28 (35.0 %)
participants on combination of vesicant & irritant drugs	22 (27.5%)
participants on neutral type drugs in causing extravasation.	14 (17.5%)

Key observations of participants with DVA in EAGLE-1:

1. Forearm “cold-to-touch”, peripheral venoconstriction	64 (80.0 %)
2. Fragile veins	2 (2.5 %)
3. Multiple lines of chemotherapy and multiple needle-punctures	5 (6.25 %)
4. Very small, fine and thread veins	7 (8.75 %)
5. Node-clearance on one arm and few “good” veins on the other arm due to repeated venepuncture.	2 (2.50 %)

Cannulation success and failure with Airglove™:

Participants with cannulation success	70 (87.5%)
Participants with cannulation failure	10 (12.5%)
Participants on corticosteroids	17 (21.25%)
Participants with cannulation failure and on corticosteroids	2 (2.50%)
Effect of corticosteroids on cannulation success/failure using Airglove™	p=0.610

Table 2. Subjective opinion of clinical-staff observing patients and carrying out venous-cannulation for key causes contributing to cannulation failures. The following factors are ranked in order of importance by the consensus opinions of clinical staff.

Possible contributory factors to failure of deployment of venous cannula listed from subjective opinions from clinical staff in EAGLE-1

- Older age of participant
- High BMI
- Cancer-type by system
- Gender
- Prescribed use of steroids
- Limbs cold to touch.
- No visible or palpable veins prior to warming
- Fragile veins
- Bruising, therefore limiting sites available for new cannula deployment.
- Very thin veins
- Multiple IV lines present and therefore fewer sites for successful cannulation
- Previous history of extravasation
- Sub-optimal temperature setting to effect venodilation
- Prescribed chemotherapy drugs by risk of extravasation (vesicant, irritant or neutral)

Table 3. Information on participants in EAGLE-2 study.

The median values for the demographic information quoted here are \pm standard deviation (S.D). All participants were assessed and confirmed to have normal hydration status (capillary refill time within 2 seconds, normal jugular venous pressure, wet mucous membranes). None of the participants in this study were under treatment for clinical hypertension.

Participant information – EAGLE-2	± S.D. (n=34)
Median age	40.6 ± 12.36 years
Percentage females in study	69%
Average weight	72.1 ± 16.6 kg
Average B.M.I.	24.96 ± 4.68 (kg/m ²)
Average percentage body fat	22.59 ± 9.41 %
Average systolic blood pressure (right arm)	122.71 ± 16.49 mmHg
Average systolic blood pressure (left arm)	123.34 ± 15.33 mmHg
Average diastolic blood pressure (right arm)	77.71 ± 10.60 mmHg
Average diastolic blood pressure (left arm)	77.49 ± 13.00 mmHg

Table 4. The inclusion and exclusion criteria used in recruitment of participants to the EAGLE study.

Participants to EAGLE-1 were recruited from staff and student population at the Chemotherapy Unit at Maidstone Hospital, Kent, England, UK. Participants to EAGLE-2 were recruited from a healthy staff and student population at the Glasgow Caledonian University, Scotland, UK. Written informed consent was obtained from all participants.

Inclusion & exclusion criteria for participants in EAGLE-1	
Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none"> · Participants > 17 years old · Participant currently undergoing treatment for cancer and needing a venous cannula for the administration of chemotherapy treatment · Patient with difficult venous access – (DVA) based on the following criteria: <ul style="list-style-type: none"> § 2 or more attempts to cannulate without using Airglove™ or the WWI method by a person proficient in phlebotomy § Target vein not palpable · Able to give written informed consent · Able to understand and respond to questions from the questionnaire helped by the responsible researcher 	<ul style="list-style-type: none"> · Participants < 17 years old · Participant not currently undergoing treatment for cancer and not needing a venous cannula for the administration of chemotherapy treatment · Patient without DVA · Participants not able to give written informed consent · Participants not able to comprehend or respond to the questionnaire forms even with help from the responsible researcher

Inclusion & exclusion criteria for participants in EAGLE-2	
Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none"> · Participants > 17 years old · Able to give written informed consent · Able to understand and complete questionnaire forms independently 	<ul style="list-style-type: none"> · Participants < 17 years old · Participants with cancer and/or undergoing chemotherapy · Participants with DVA · Participants with lymphoedema in either hand · Participants with pre-existing Raynaud’s disease · Participants with Diabetes (Type 1 & 2) · Participants with generalised anxiety disorder · Participants with diagnosis of hypertension · Participants with any cardiovascular disease, previous stroke, episodes of DVT, recent treatment for venous thromboembolism (VTE), recently administered heparin, participants on warfarin or any anticoagulant treatment (including NOACs). · Participants not able to give written informed consent · Participants not able to comprehend or complete questionnaire forms independently

Figures

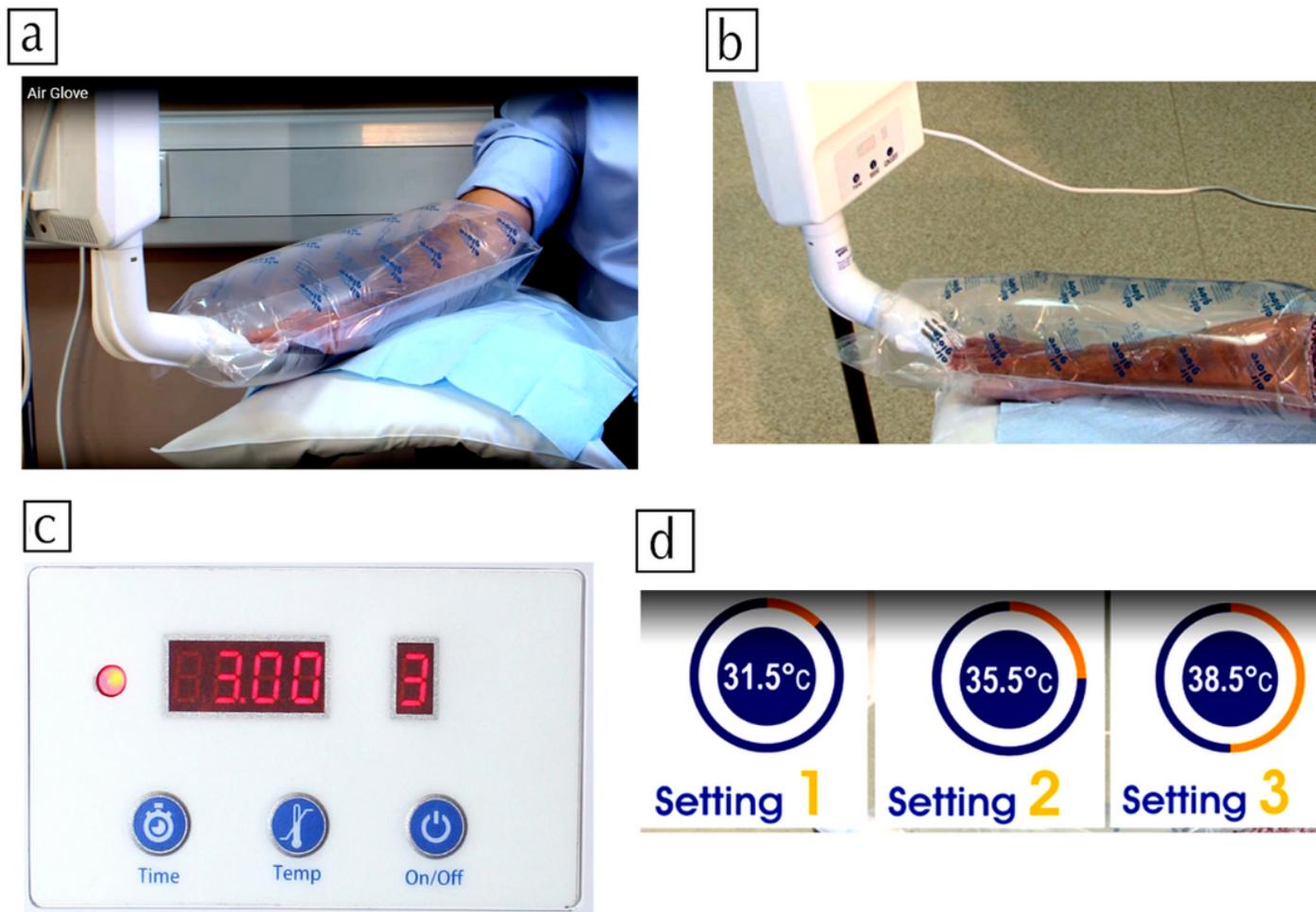


Figure 1

The Airglove™ device used in the EAGLE study and the overall schematic of the study. (a) The Airglove™ device is shown here attached to the forearm of a consenting volunteer with an inflatable double-walled glove. (b) Close-up from a different angle showing the Airglove™ device, where the inflatable glove fits snugly over the arm of the same volunteer. (c) The control panel of the device, showing the digital read-out stating a 3 min countdown indicating the duration of warming at temperature setting number “3”. (d) Three temperature settings are allowed on this device: 31.5oC, 35.5oC and 38.5oC. Participants in this study were subjected to warmth of 38.5oC (setting number 3).

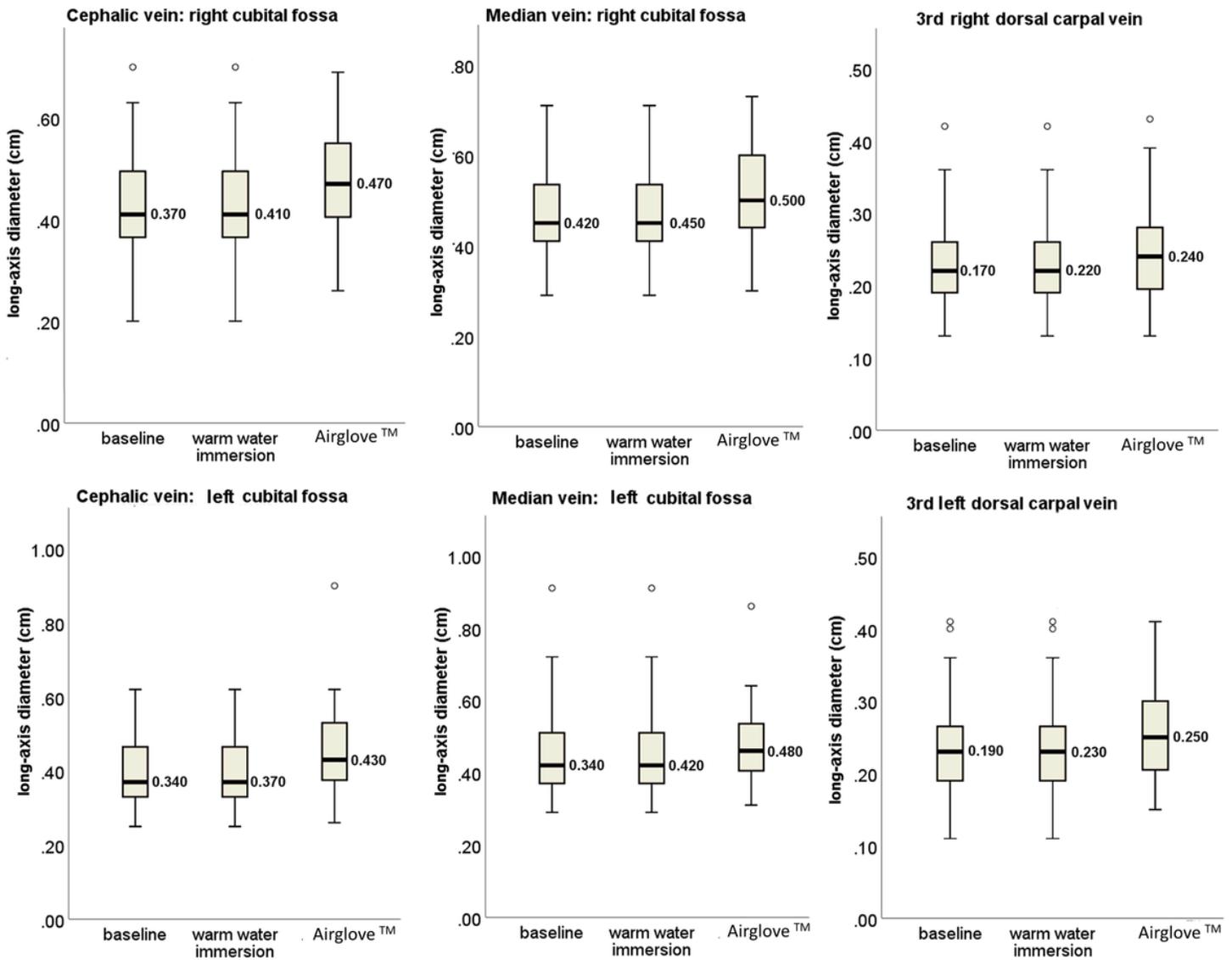


Figure 2

Boxplots showing comparison between baseline venous diameter and increase in venous dilatation via the warm water immersion (WWI) method and Airglove™. The bottom and top edges of the boxes represent the first (25%) and the third (75%) quartile of the long-axis diameter measurements by ultrasound. Veins typically are elliptical; the long axis diameter was selected for preserving consistency in measurements. The whiskers represent the minimum and the maximum measurements in the dataset. The dark-rimmed open-circles represent suspected outlier measurements of the long-axis venous diameter and were determined with the threshold of less than or greater than 1.5 times the lower and upper interquartile range (IQR) limits, respectively. Median values are displayed next to the middle line of each box, reflecting the mid-point of each dataset. The increase in venous diameter from the Airglove™ is more pronounced in all the veins measured compared to the WWI method.

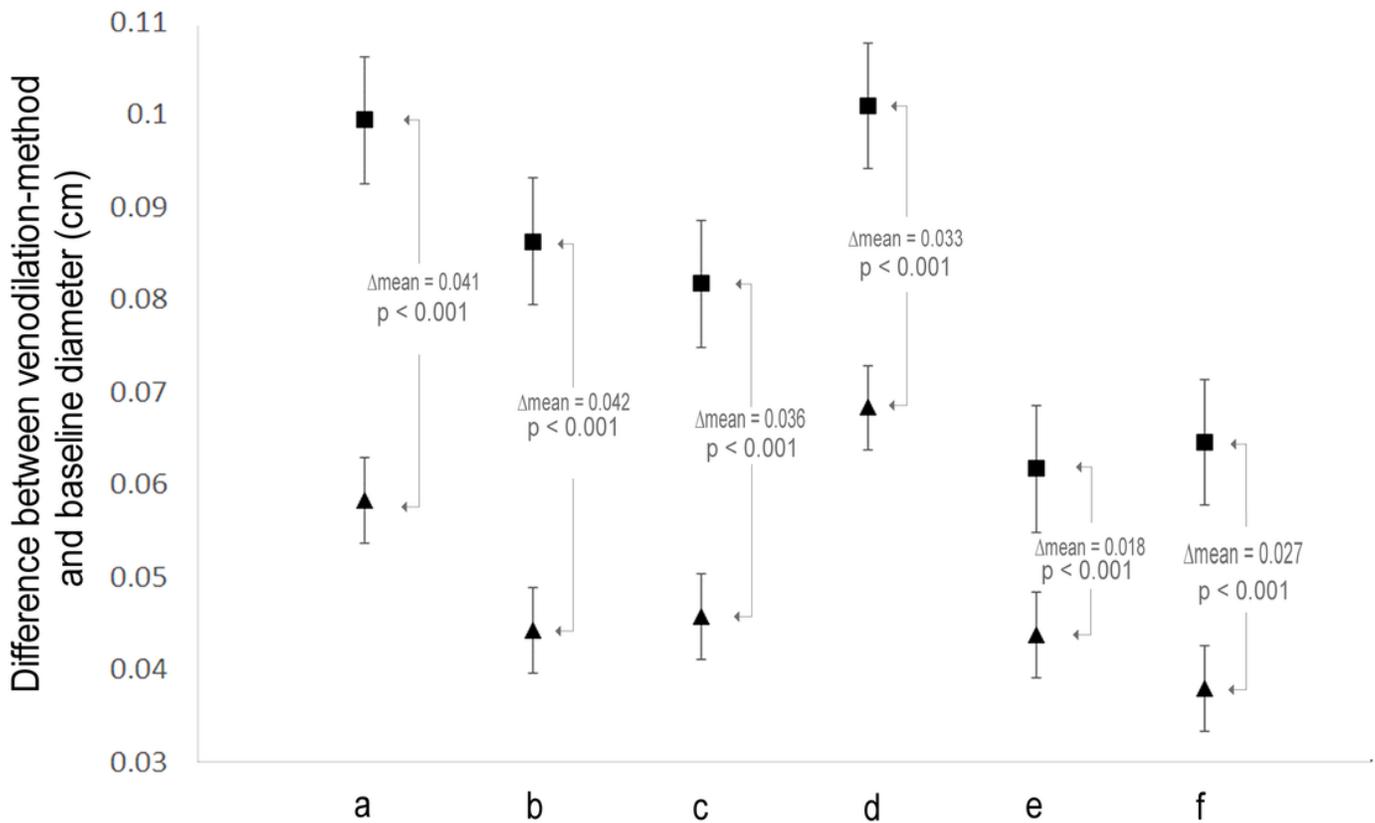


Figure 3

The calculated increase in venous diameter; comparing Airglove™ vs WWI method. Difference in mean values subtracted from baseline diameter measurements by ultrasound from venodilation either by Airglove™ (displayed as shaded boxes; \blacksquare) or the WWI method (shown as shaded triangles; \blacktriangle). The veins being measured are labelled as follows: (a) the right cubital-fossa cephalic vein, (b) the left cubital-fossa cephalic vein (c) the right cubital-fossa median vein, (d) the left cubital-fossa median vein, (e) the 3rd right dorsal carpal vein and (f) the 3rd left dorsal carpal vein. The difference between the baseline-subtracted-means via the Airglove™ vs the WWI method is shown as Δ mean and all p-values determined using the paired sample T-test were < 0.001 at 95% C.I.

EAGLE STUDY

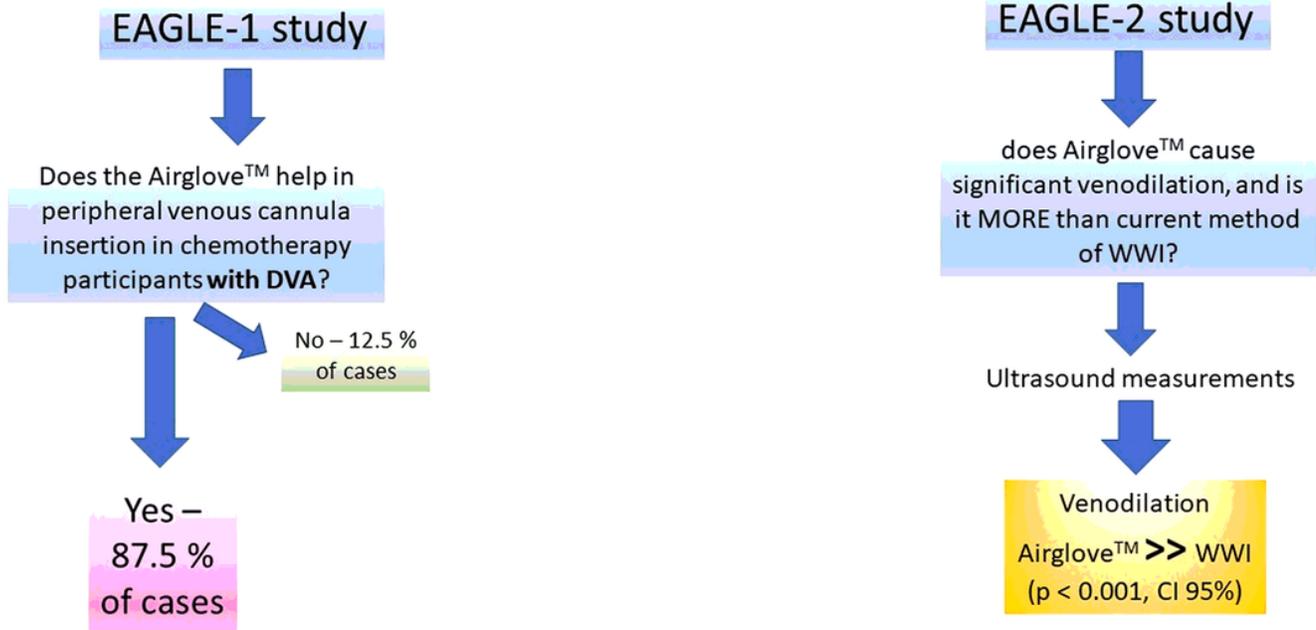


Figure 4

Overall flowchart summarising the EAGLE study.

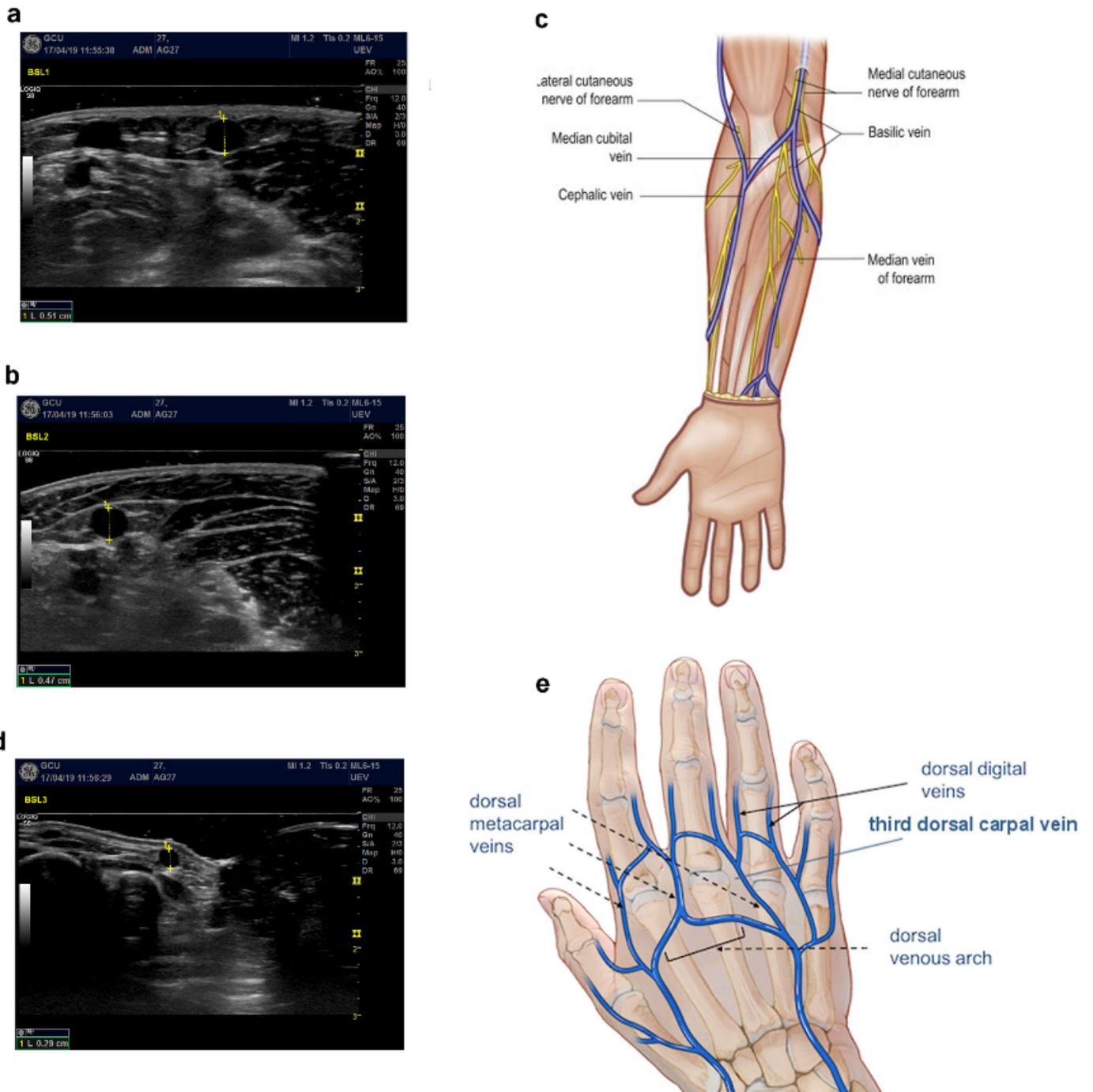


Figure 5

Ultrasound images of the veins being evaluated in this study. (a) The cephalic vein and (b) the median-vein in the cubital fossa as imaged by ultrasound and represented in the (c) line-drawing. (d) The 3rd dorsal vein in the wrist (carpal) and (e) the accompanying line drawing illustrating the location of this vein in the hand. Venous structures were confirmed by applying colour-flow doppler.