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ORIGINAL ARTICLE

Point-of-care ultrasound for neonatal central catheter positioning: impact on X-rays and line tip position accuracy

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Abstract

Objective of the study was to compare number of X-rays performed for neonatal central line tip positioning when real-time US is used compared to X-ray only, and to assess consequences on position accuracy, irradiation and cost. Retrospective monocentric cohort study conducted at Evelina London Children's Hospital Neonatal Unit over 6 months. Study was conducted during implementation of US for line tip localisation with formulation of US protocol. Tip position on X-ray was reviewed by one neonatologist and one radiologist and inter-rater agreement calculated. Criteria for good, satisfactory or inadequate position of the tip were defined. Estimated effective radiation dose and cost for each X-ray was determined. Two hundred seventy-four lines were inserted (nPICC, UVC, UAC). Eighty-three lines were scanned with US (US group); 191 lines were not (no-US group). Number of X-rays performed was significantly lower in the US group: 1.19 vs. 1.5 (p 0.001), related to a significantly lower percentage of lines requiring multiple X-rays (38.7% no-US group vs. 19.9% US group; p 0.004). Accuracy was higher in US group with more lines at cavoatrial junction (p 0.05) and was significantly increased with US use for lines inserted from lower limbs (22.9% and 76.2%, p 0.001). Inter-rater agreement was strong ($k > 0.8$). US group received lower mean radiation dose ($p < 0.001$) and cost related to X-ray was significantly reduced (p 0.001).

Conclusion: Real-time US use for line tip positioning in the NICU significantly decreased the number of X-rays performed and was associated with better-positioned lines, decreased irradiation and cost.

What is Known:

• *The use of point-of-care ultrasound (PoCUS) by critical care providers in neonatology has increased in recent years. International guidelines advocate for the use of PoCUS as valid guidance to practical procedures in neonatology.*

• *Central catheters (umbilical catheters and neonatal peripherally inserted central catheters) are among the most commonly used devices to support NICU patients. Proper positioning is crucial to avoid complications and PoCUS has high sensitivity and specificity in accurately determining line tip position. The current standard practice for line tip position confirmation in neonatology is still conventional radiography despite multiple evidenc suggest significant inaccuracy of X-ray compared to ultrasound.*

What is New:

• *PoCUS implementation for line tip positioning leads to a significant decrease in the number of X-rays performed, in radiation effective dose and costs. PoCUS evaluation of central catheters significantly increases the accuracy of the final line tip position with more lines at the cavoatrial junction.*

• *Training is fundamental for univocal interpretation of ultrasound images and an effective learning strategy is being proposed.*

Keywords Point-of-care ultrasound · Neonatology · Vascular access · Central catheters

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Abbreviations

BW	Birth weight
DV	Ductus venosus
GA	Gestational age
IVC	Inferior vena cava
LLL	Left lower limb
LUL	Left upper limb
NICU	Neonatal intensive care unit
nPICC	Neonatal peripherally inserted central catheter
PoCUS	Pont-of-care ultrasound
RA	Right atrium
RLL	Right lower limb
RUL	Right upper limb
SVC	Superior vena cava
UAC	Umbilical arterial catheter
US	Ultrasound
UVC	Umbilical venous catheter

Introduction

Point-of-care ultrasound (PoCUS) is bedside ultrasonography performed by clinicians in real time, integrated within the patient's clinical condition with a problem-based approach. It offers rapid and replicable diagnostic imaging at affordable costs with greater portability and adaptability to context and users [1]. The use of PoCUS by critical care providers has increased in recent years. However, neonatologists have been slower to incorporate this tool into practice [2]. Recent international guidelines on PoCUS applications in children and neonates advocate for the use of PoCUS as an important adjunct to the clinical decision-making process as well as valid guidance to practical procedures in neonatology [3].

In the NICU, monitoring, lifesaving treatments and nutrition are provided through central catheters which are most commonly umbilical venous and arterial lines (UVC, UAC) and neonatal peripherally inserted central catheters (nPICC). Proper positioning of the catheter is recommended to decrease risk of complications, which can be life-threatening, such as cardiac tamponade [4, 5]. The current standard for line tip positioning is conventional radiography [6, 7]. X-ray is a post-procedural method which estimates the position of the line tip based on static landmarks like the cardiac silhouette or the diaphragm level [8]. Nevertheless, recent evidence suggested significant inaccuracy of X-ray and the higher sensitivity and specificity of real-time US in accurately determining line tip position [9–15].

The primary objective of our study was to define if US performed to assess line tip positioning in neonates will impact the number of X-rays, without compromising the accuracy of the final position. Secondary objectives were to identify factors which would impact the performance of US and to quantify the potential reduction in ionising radiation exposure and costs.

Materials and methods

This study is a monocentric retrospective cohort study conducted at Evelina London Children's Hospital (ELCH) Neonatal Unit, London (UK), a tertiary neonatal and multidisciplinary paediatric hospital, admitting 6600 deliveries per year, with high-risk pregnancies maternity on-site. The study had institutional governance approval. We used routinely collected clinical data and explicit informed consent was not sought for this reason.

All newborns with umbilical lines and/or nPICC inserted between 1st October 2018 and 31st March 2019 were included. Demographic and line characteristics data were collected from electronic patient's records (BadgerNet®) and comprised gestational age at birth (GA), birth weight (BW), date and type of catheter inserted, indication and site of insertion for nPICC lines. For the analysis, one episode was defined by insertion of one line, which could be either an umbilical venous or arterial catheter (UVC, UAC) or a nPICC. Gestational age subgroups were divided as follows: extreme preterm (23–27 weeks), preterm (28–31 weeks), moderate/late preterm (32–36 weeks) and term (≥ 37 weeks). X-ray data were obtained from Picture Archiving and Communication System (PACS®) and were the total number and type of X-ray performed for each episode (chest, abdomen or chest and abdomen).

UVCs used were Vygon® double-lumen 4Fr or 5Fr. Three different types of nPICC were available: single lumen Vygon Premicath® 1Fr (28G), single lumen Vygon Nutriline® 2Fr (24G) and double-lumen Vygon Nutriline Twinflo® 2Fr (24G). The length of insertion of the catheters was calculated using the Shukla and Ferrara formula for UVCs [16] and external anatomical measurements for nPICCs: from the insertion point to the sternal notch then from sternal notch to the right second intercostal space if inserted from upper extremities, or to the xiphoid process if inserted from lower extremities [8].

A consultant radiologist (KHJ) was involved early in the development of the US protocol and worked collaboratively with 3 consultants neonatologists trained in line US tip assessment (15 years, 1 year and 1 year of experience respectively). This involved agreement on US probes, settings, views, training and regular collaboration with the experienced and trained neonatologists. Training consisted in 1 h formal teaching followed by practical supervision by one of the 3 consultant neonatologists experienced in line tip US assessment. For completion of training, 10 scans for nPICC lines, UVC and UAC respectively had to be performed, including 2 under direct supervision and 8 clip reviews. During the study period, all scans were performed by the 3 trained neonatologists or by a junior doctor in training supervised by one of them during examination. During the study period, all scans were performed by the 3 trained neonatologists or by a junior doctor in training supervised by one of them. In practice, a 8C convex probe from a LOGIQe US ultrasound machine (GEHealthcare®) was used. Once the operator had inserted the catheter at the desired length and before securing the line, a second operator located on the other side of the patient, positioned the US probe covered with sterile gel below the sterile drapes.

The main views used for each catheter are described in Fig. 1. For each line, 2 to 3 different views were obtained to ensure findings could be confirmed on multiple views: for UVC, a subxiphoid ductus venosus view and a left long axis parasternal view on the right atrium (RA); for nPICC lines in inferior vena cava (IVC), an axial view, an abdominal longitudinal IVC view and a 4 chambers view; for nPICC lines in superior vena cava (SVC), a modified bi-caval view and a 4 chamber view. The modified bi-caval view, described here for the first time, was obtained by starting with a left parasternal long axis view, followed by a right inferior probe tilt and a cranial rock (video 1). This view allows a good visualisation of the lower portion of the SVC and the RA-SVC junction. Good position for UVC on US was defined as the line tip seen at the junction of the RA with the ductus venosus (DV)/IVC and for nPICC line at the RA-IVC/SVC junction. UAC catheters were visualised on subxiphoid transverse and longitudinal views focused on the abdominal and thoracic aorta. Aim was to position the tip at or within 1 cm above the level of the diaphragm. Three criteria had to be met to confirm that line tip seen on the screen was not an artefact or any other part of the line (i.e. curl): (i) tip seen at the good position as defined above, (ii) small mobilisation of the line by the catheter operator leading to small movements of the line tip seen on the US screen and (iii) positive bubble test for all lines except UAC (small bubbles arising from the line tip and filling the RA after flushing the line with 0.3 ml of 0.9% saline solution). For lines in the IVC or SVC, the tip was usually brought backward slowly into the large vessel, at 0.3 to 0.5 cm to the RA entry, to allow visualisation of the bubbles in the large vessel, confirming that the identified tip was the actual tip of the catheter. For upper and lower limb nPICC, the limb used for insertion was flexed and extended at all joints to ensure the furthest point of insertion of the line tip was visualised. Once the catheter was considered to be in a good position by the US operator, the catheter operator secured the line.

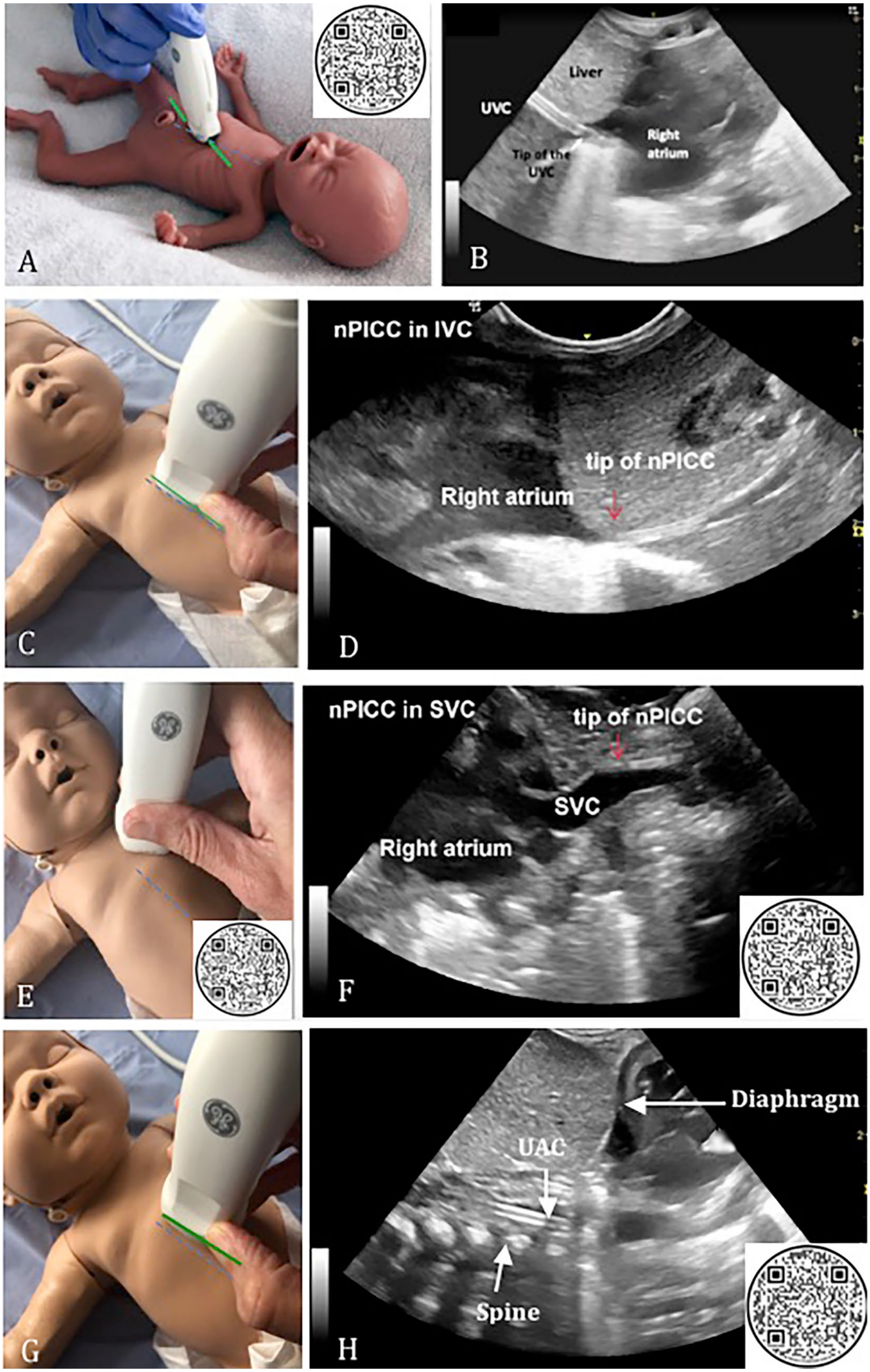
Chest and/or abdominal X-ray was performed for each line as gold standard, whether the line was checked with US or not. To ensure that the potential decrease in number of X-rays secondary to US use would not be at the expense of lower position accuracy, line tip location on all X-rays was reviewed and criteria for good, satisfactory and inadequate position were defined (Table 1). X-ray landmark criteria used for UVCs and lower limb nPICC lines was the junction between the diaphragm and the RA. For upper extremities, adequate line tip position was the SVC-RA junction on the cardiac silhouette. For upper extremities, the cardiac method was used. For each line episode, a neonatologist and a radiologist (VMP and KHJ) independently reviewed all X-rays and defined the position according to the criteria in Table 1. The definition was based on the landmarks for SVC-RA and IVC-RA junction on X-ray as well as the practical aspects of line management. The definitions were used for the purpose of the study only. They were based on the landmarks for SVC-RA and IVC-RA junction on X-ray as well as the practical aspects of line management. Lines were defined as satisfactory when their tip was not sitting in a good position but was detected in a large vessel (SVC or IVC) where the risk of severe complications was considered as extremely low [17]. These lines were kept in same position and not adjusted. Inter-observer agreement was calculated.

To estimate the radiation exposure resulting from each X-ray, the effective dose (mSv) for patients aged 0–1 year was calculated using the exposure factors derived from the standard protocols used in our hospital: 60 kV, 2 mAs, FID 115 cm. The estimated effective dose was 0.0223 mSv for chest X-ray, 0.0132 mSv for abdominal X-ray and 0.0287 mSv for chest and abdominal X-ray. The estimation was performed by the principal physicist of our hospital using DEFORM® software. For each line episode, the total estimated effective dose was calculated. The total cost of each X-ray was also determined.

The population was divided into two groups: "US group" comprised all the lines scanned with US and videos recorded prior to X-ray. Lines that were evaluated with X-ray only or when US did not allow proper visualisation of the line tip were defined as "no-US group". Similar subgroups were defined according to the type of line inserted: US/nPICC, no-US/nPICC and US/UVC, no-US/UVC.

Statistical analysis

Data were analysed using IBM SPSS Statistics® software (version 20.0). Data were expressed as mean (95% CI), median and percentage as appropriate. Data were compared using the Mann–Whitney *U* test for non-normally distributed data or chi-squared test as appropriate. Cohen's *k* was used to evaluate the inter-rater reliability between two operators for categorical variables. p value ≤ 0.05 was considered statistically significant.


A
Liver
UVC
Tip of the UVC
Right atrium
B
C
nPICC in IVC
tip of nPICC
Right atrium
D
E
nPICC in SVC
tip of nPICC
SVC
Right atrium
F
G
Diaphragm
UAC
Spine
H

◂**Fig. 1** US views and probe positioning. (**A**) and (**B**) UVC view: the probe is placed vertically below the sternum (blue dashed lines) and slowly rotated clockwise until the ductus venosus can be seen (plain green line). (**C**) and (**D**) nPICC in IVC. (**E**) and (**F**) nPICC in SVC (modified bi-caval view, see video): the first view is a left parasternal long axis view, then the probe is tilted downward and rocked up (**G**) and (**H**) UAC view

Results

Between 1st October 2018 and 31st March 2019, 274 lines were inserted in 144 newborns and were distributed as followed: 142 nPICC lines (78 Nutriline®, 24 Premicath®, 10 Twinflo® and 30 not specified), 92 UVC and 40 UAC (Fig. 2). No significant difference in the frequency of US use was found between the first and the second 3 months of the study period (*p* 0.29).

Population characteristics are shown in Table 2 and did not differ significantly between the US and the no-US groups (Table 3) as well between different subgroups (nPICC, UVC and UAC).

A total of 386 X-rays were performed: 220 for nPICC lines, 120 for UVC and 46 for UAC. The mean number of X-rays per line for the whole population was 1.41 (95% CI 1.33–1.49) and the median was 1. As displayed in Table 3, the total number of X-rays performed in the US group was significantly lower than in the no-US group (*p* 0.001). More lines required 2 or more X-rays in the no-US group compared to the US group (38.7% versus 22.9%, 0.004) (Fig. 3). In two cases in the US/UVC group, catheter was visualised in the liver allowing the prompt removal of the line based on US findings and avoiding X-ray. Population characteristics for UAC are not reported in Table 3 for more clarity in the table; mean GA in the UAC subgroup was 30.15 weeks (95% CI 28.16–32.14). Mean BW was 1688 g (95% CI 1312–2064 g). No further analysis was performed on UAC group, as number of US/UAC episodes was too small ($n=2$).

Percentage of lines in the correct position on X-ray (good or satisfactory) was significantly higher in the US group than in the no-US group (76.9% versus 69.1%, *p* 0.05), including significantly more lines in good position (69.2% vs. 59.1%; *p* 0.05) and fewer lines in inadequate position (23.1% vs. 30.9% lines; *p* 0.05) (Table 3). Similar results were found in the nPICC and UVC subgroups (Table 3). There was a significant difference in position accuracy according to the limb where nPICC lines were inserted for the whole population, with significantly higher position accuracy in the upper limbs (Fig. 4). In the no-US/nPICC subgroup, the position accuracy was significantly decreased when the line was inserted in the lower limbs (*p* 0.008) (Fig. 4A, B). In contrast, position accuracy was high in the US/nPICC subgroup whatever the insertion site was (good or satisfactory RUL 88.2%, LUL 100%, RLL 93.7%, LLL 80%) (*p* 0.65). Accuracy significantly improved with the use of US for lines in IVCs (*p* 0.001) while it did not vary significantly for lines in SVC (*p* 0.2) (Fig. 5).

The agreement between an experienced neonatologist (VMP) and a radiologist for the assessment of the line position accuracy on X-ray was strong in the whole population and in the nPICC and UVC subgroups (*k* 0.8) (Table 3). The final agreement between the two operators did not vary significantly with the GA or with the type of line inserted.

The mean effective radiation dose (mSv) per episode estimated for all the X-rays performed in our series was 0.0330 mSv (95% CI 0.0307–0.0353). US group received significantly less radiation dose compared to no-US group ($p<0.001$) (Table 4). Similar results were found in nPICC and UVC subgroups.

A cost-effectiveness analysis was also performed and showed that the total cost for X-rays in our series was £20,212.4 (mean £87.78, 95% CI £81.01–£94.56). Mean X-ray cost per episode was significantly higher for the no-US group compared to US group (£94.42 vs. £75.04, *p* 0.001) (Table 4). Similar results were found in nPICCs and UVC subgroups.

Discussion

Our work suggests that the use of US to assess line tip position led to a significant reduction in the number of X-rays, irradiation and cost, associated with an improvement in line position accuracy, especially for nPICCs inserted from the lower limbs.

Our data confirmed results from previous studies, showing that integration of US in the assessment of line tip position resulted in a significant decrease in X-ray requirement, for both UVCs and nPICCs [2, 3, 13, 18, 19]. A prospective randomised controlled study by Katheria et al. involving

Table 1 Criteria used to evaluate line tip position at X-ray for UVC and nPICC

	UVC	nPICC
Good	At the RA-IVC junction (diaphragm method)	In IVC/SVC, < 0.5 cm from RA-IVC/SVC junction (cardiac method)
Satisfactory	< 0.5 cm from RA-IVC junction	In IVC/SVC, > 0.5 cm from RA-IVC/SVC junction
Inadequate	Either > 0.5 cm in the heart or > 0.5 cm below the RA-IVC junction	> 0.5 cm in the heart or at mid-clavicular level with no US documentation

Table 2 Population characteristics

General population characteristics (144 newborns)	
Gestational age, mean in weeks (95% CI), [range]	31.97 (31.05–32.89), [23–42]
Gestational age subgroups, number (%)	
Extreme preterm (23–27 weeks)	41 (28.5%)
Preterm (28–31 weeks)	33 (22.9%)
Moderate/late preterm (32–36 weeks)	28 (19.4%)
Term (≥ 37 weeks)	42 (29.2%)
Birth weight, mean in grams (95% CI), [range]	1904 (1718–2089), [490–4895]
Lines inserted per patient, mean (95% CI)	1.88 (1.72–2.04)
Number of lines per patient, number (%)	
1 line	66 (45.8%)
2 lines	40 (27.8%)
3 lines	29 (20.1%)
4 lines	7 (4.9%)
5 lines	2 (1.4%)
Reason for line insertion (%)	
Parenteral nutrition	61.6%
Haemodynamic monitoring/blood sampling	15.8%
Prostaglandins infusion	9.5%
Clear fluids infusion	6.7%
Inotropes administration	4.3%
Exchange transfusion/dilutional exchange	1.2%

49 patients displayed a reduction in the number of X-rays from 2 to 1 (p 0.001) when US was used to identify nPICC tip position [20]. Another prospective randomised study by Fleming and Kim focusing on UVC showed a significant reduction in the mean number of X-rays per patient from 4.1 in the standard group (16 patients) to 2.3 in the ultrasound group (15 patients). In this study, however, both anteroposterior and latero-lateral X-ray views were performed for each line, accounting for the high initial number of X-rays per patient [21]. A recent pre/post-intervention study by Rubortone et al. confirmed a reduction in the number of X-rays requested for UVC position confirmation in the post-intervention phase when US was used (92.3% vs. 32.1%; $p < 0.0001$). However, a potential bias was the choice of the confirmatory method (X-ray or US) which was left to the attending neonatologist and was not standardised [22]. Our findings confirm these trends, in a bigger sample size. Moreover, although mean number of X-rays required was significantly different between US and no-US groups, a median of 1 X-ray was required for each line episode. Our results thus showed that important clinical benefit of US was to reduce the number of episodes requiring multiple X-rays. In 2 US/UVC episodes, US also showed that the line was not in the ductus venosus but wrongly placed in the liver allowing prompt removal of the line without any X-ray. For some other lines inserted from upper limbs, US allowed direct visualisation of the line progressing into a wrong vessel, most frequently the internal jugular vein. Such misplacement was corrected by line mobilisation, gentle head positioning and redirection of the line into the SVC under US guidance, avoiding multiple X-rays. This US navigation and location of the tip has been recently well described and studied within a new protocol named Neo-ECHOTIP [23]. This suggests that by identifying misplaced lines earlier, US avoids the use of multiple X-rays but also prevents complications when lines inaccurately appear to be in the correct vessel on X-ray [10–12, 24]. Another advantage of US is the use of serial US to detect line migration. Franta et al. have reported that 50% of UVC migrate, both into the heart or out into hepatic vessels [11]. Following this report and case-reviews of fluid extravasation incidents secondary to UVC migration in our unit, we have adopted a new protocol which requires follow-up US 24 h and 3 days after insertion for all UVCs.

More lines were found in good position in the US group. The main contributor for position inaccuracy in our study was the absence of US use for nPICCs. Additionally, we have identified a difference in malposition rates according to the limb used for insertion. Catheters inserted from the lower limbs resulted in a less accurate position on X-ray compared to upper limb catheters, but accuracy significantly improved with US use. This could be explained by the easier technique required to view line tip in IVC with US compared to SVC—which may require some echocardiography skills—, and the poor accuracy of external landmarks for lines in IVC [25]. Additional observation was the

Table 3 Demographics, number of X-rays, position accuracy and inter-rater agreement among whole population, US and no-US groups and subgroups

	All lines 274 lines		***p* value**	**nPICC** 142 lines		***p* value**	**UVC** 92 lines		***p* value**
	US 83 lines (30.3%)	**No-US** 191 lines (69.7%)		**US** 43 lines (30.3%)	**No-US** 99 lines (69.7%)		**US** 38 lines (41.3%)	**No-US** 54 lines (58.7%)	
Gestational age (wks) mean (95% CI), median	30.67 (29.43–31.92), 30	30.59 (29.79–31.38), 29	NS	30.14 (29.29–30.99), 30			31.54 (30.33–32.76), 30		
Gestation age subgroups			NS						
Extreme preterm	31 (37.3%)	76 (39.8%)		56 (39.4%)			31 (33.7%)		
Preterm	19 (22.9%)	48 (25.1%)		40 (28.2%)			21 (22.8%)		
Moderate/late preterm	16 (19.3%)	25 (13.1%)		23 (16.2%)			13 (14.1%)		
Term	17 (20.5%)	42 (22%)		23 (16.2%)			27 (29.4%)		
Birth weight (g) mean (95% CI), median	1772 (1513–2030), 1305	1643 (1495–1790), 1240	NS	1547 (1387–1707), 1240			1889 (1643–2135), 1387		
Number of X-rays mean (95% CI), median	1.19 (1.07–1.32), 1	1.5 (1.40–1.61), 1	0.001	1.26 (1.06–1.45), 1	1.68 (1.51–1.84), 2	0.001	1.11 (0.94–1.27), 1	1.44 (1.27–1.62), 1	0.02
Number of X-rays for each line			0.004			0.01			0.03
0 X-ray	2 (2.4%)	0					2 (5.3%)	0	
1 X-ray	67 (80.7%)	117 (61.3%)		35 (81.4%)	49 (49.5%)		31 (81.6%)	34 (63%)	
2 X-rays	11 (13.3%)	56 (29.3%)		6 (14%)	37 (37.4%)		4 (10.5%)	16 (29.6%)	
3 X-rays	2 (2.4%)	15 (7.9%)		1 (2.3%)	10 (10.1%)		1 (2.6%)	4 (7.4%)	
4 X-rays	1 (1.2%)	2 (1%)		1 (2.3%)	2 (2%)		0	0	
5 X-rays	0	1 (0.5%)		0	1 (1%)		0	0	
Agreement on position (Cohen's kappa)	0.80			0.80			0.80		
Line position X-ray			0.05			0.003			0.35
Good	69.2% (54)	52.1% (98)		79.1% (34)	45.5% (45)		55.9% (19)	40.4% (21)	
Satisfactory	7.7% (6)	17% (32)		11.7% (5)	28.3% (28)		2.9% (1)	5.8% (3)	
Bad	23.1% (18)	30.9% (58)		9.2% (4)	26.2% (26)		41.2% (14)	53.8% (28)	

high rates of nPICCs lines already in good position without US use when inserted from upper limbs, supporting the use of current external landmarks for lines in SVC. Findings in literature are rare on this topic. One of the largest retrospective study published by Wrightson and colleagues showed, in contrast to our results, that of the 626 nPICCs studied, 69 (11%) did not have a centrally located tip at the time of removal; 9.2% were inserted from upper extremities compared to 1.8% from lower limbs. Good position was defined as nPICC in SVC at T2–T4 level and in IVC at the level of the diaphragm [26]. We recommend further studies looking at the role of US to reduce lines misplacement and complications, which would include a comparison between upper and lower limbs. As US training required to identify tip line position in IVC is easier, this could potentially open the field to a more generalisable skill among neonatologists. Additionally, the National Association for Neonatal Nurses report that catheters inserted from lower-extremity

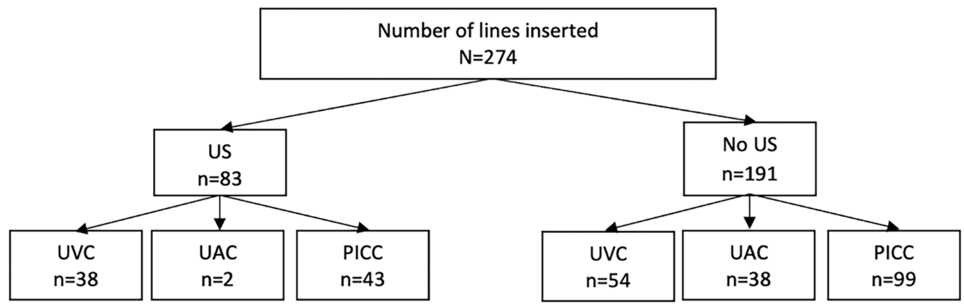


Fig. 2 Study flowchart

vessels are associated with lower complications rates, especially the right saphenous vein, which is associated with lower malposition rates [27]. We would thus suggest that, when multiple veins are suitable and US can be used, lower limb should be prioritised. Moreover, we suggest checking nPICC position in real time to evaluate the tip movements according to limb position, as limbs movements might cause involuntary line tip migration into the heart [8] increasing the risk of cardiac tamponade. The line can then be secured according to the limb position which brings the tip the closest to the heart, which is most often the flexed position for lower limbs [21].

Estimated mean effective radiation dose was significantly lower in the US group ($p < 0.001$). The impact of US use in reducing radiation exposure in newborns has been demonstrated for lung US [28] but not for neonatal catheter positioning. Despite cumulative risk for cancer for a single X-ray might be low [29], it is known that newborns are especially vulnerable because of higher mitotic activity, greater radiosensitivity and longer lifetime to manifest consequences of radiation exposure [30, 31]. Therefore, in line with heightened awareness of radiation safety and radiation dose as low as reasonably achievable (ALARA), every effort should be made to embrace alternative imaging modalities.

By reducing the number of X-rays, it was also shown that US use was cost-effective with a cost saving of £19.33 per line. The cost of a POCUS examination for line tip evaluation has not been calculated for this study as the service had just been implemented. However, this would need to include training time, clinician time to perform each POCUS examination as well as the cost, support and maintenance of the US machine.

This observation has been reported for lung US but to our knowledge, no other neonatal studies have reported central catheters cost-effectiveness analysis [32].

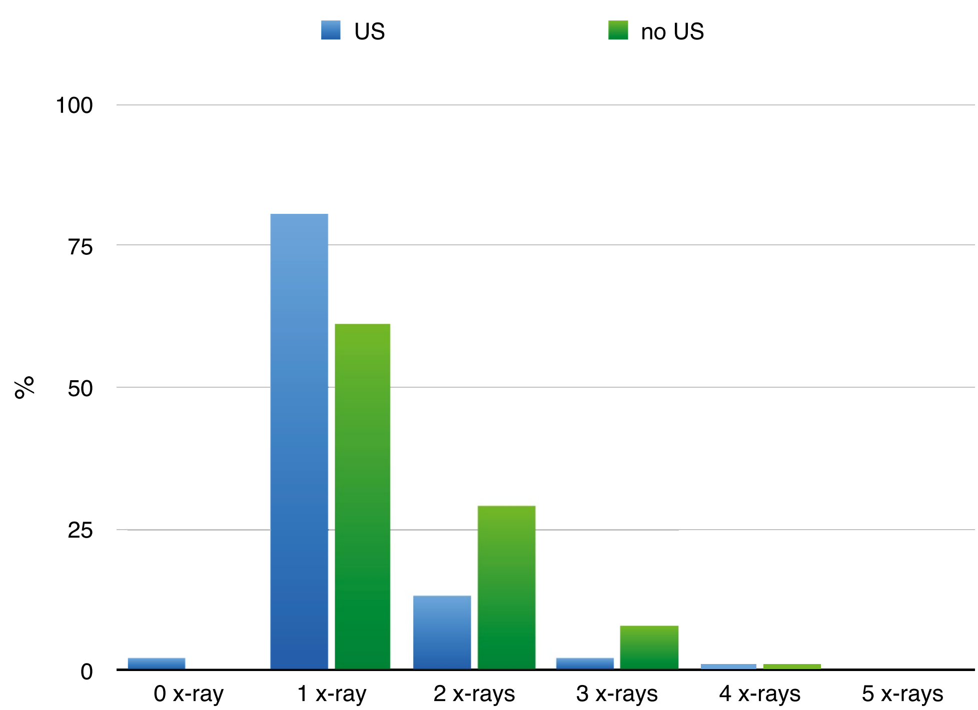


Fig. 3 Number of X-rays required for the evaluation of the line tip position

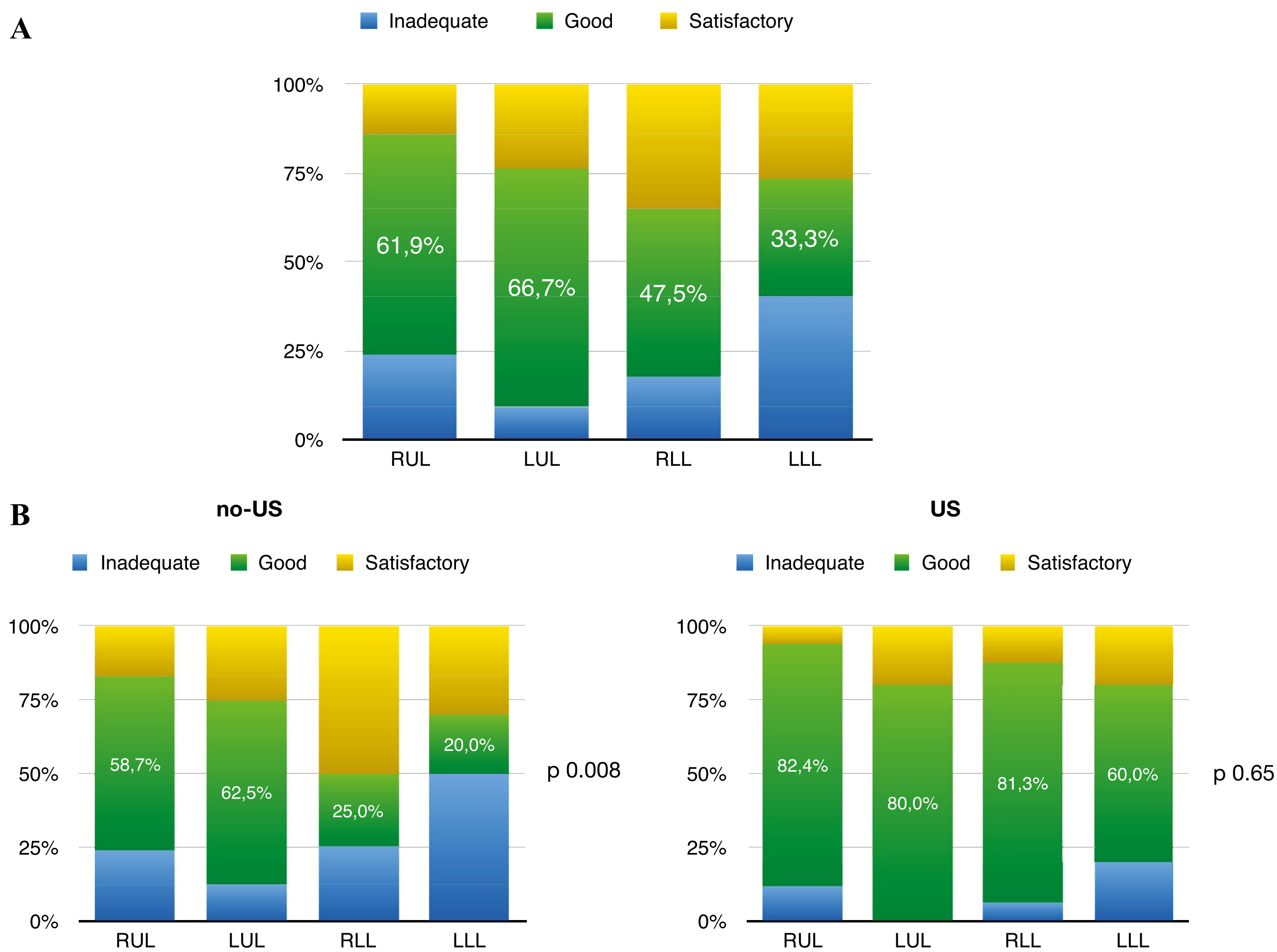


Fig. 4 Position accuracy on X-ray according to the limb used for insertion in the whole nPICC group (**A**) and in no-US/nPICC and US/nPICC subgroups (**B**)

Limitations

Our study is monocentric therefore the reproducibility in other clinical settings is to be determined. Its retrospective nature did not allow a randomisation of patients in the US or no-US group causing an uneven distribution of patients in each group. However population characteristics were similar between the two groups. The sample size is one of the largest reported in the literature and we reasonably believe that, despite the monocentric and retrospective nature, our results might be of significant interest. The allocation of the patient into each group (US vs. no-US) was based on the presence of a skilled US operator at the time of line insertion, and this should not have a significant impact on the results. UACs were removed from our analysis, as only 2 patients had US. In our experience, UACs were almost always determined to be in good position at X-ray, as the window of good position is wider and pre-insertion measurements were generally reliable. Moreover, thoracic aorta and UAC tip were frequently hidden by B-lines artefacts created by RDS which made the UAC tip more difficult to precisely assess. Also, no bubble test was performed for UACs as bubbles were flowing in opposite direction from the catheter. However, we suggest that use of US for UAC should be properly assessed in further studies. Although conventional radiography was considered as gold standard for line tip positioning in our study, this might have provided inaccurate results. X-ray relies on surrogate or anatomical markers which do not allow direct visualisation of the line tip within anatomical structures. Provided that good visualisation is possible, we suggest that US performed by properly trained operators should be the new gold standard for line tip positioning in routine neonatal practice.

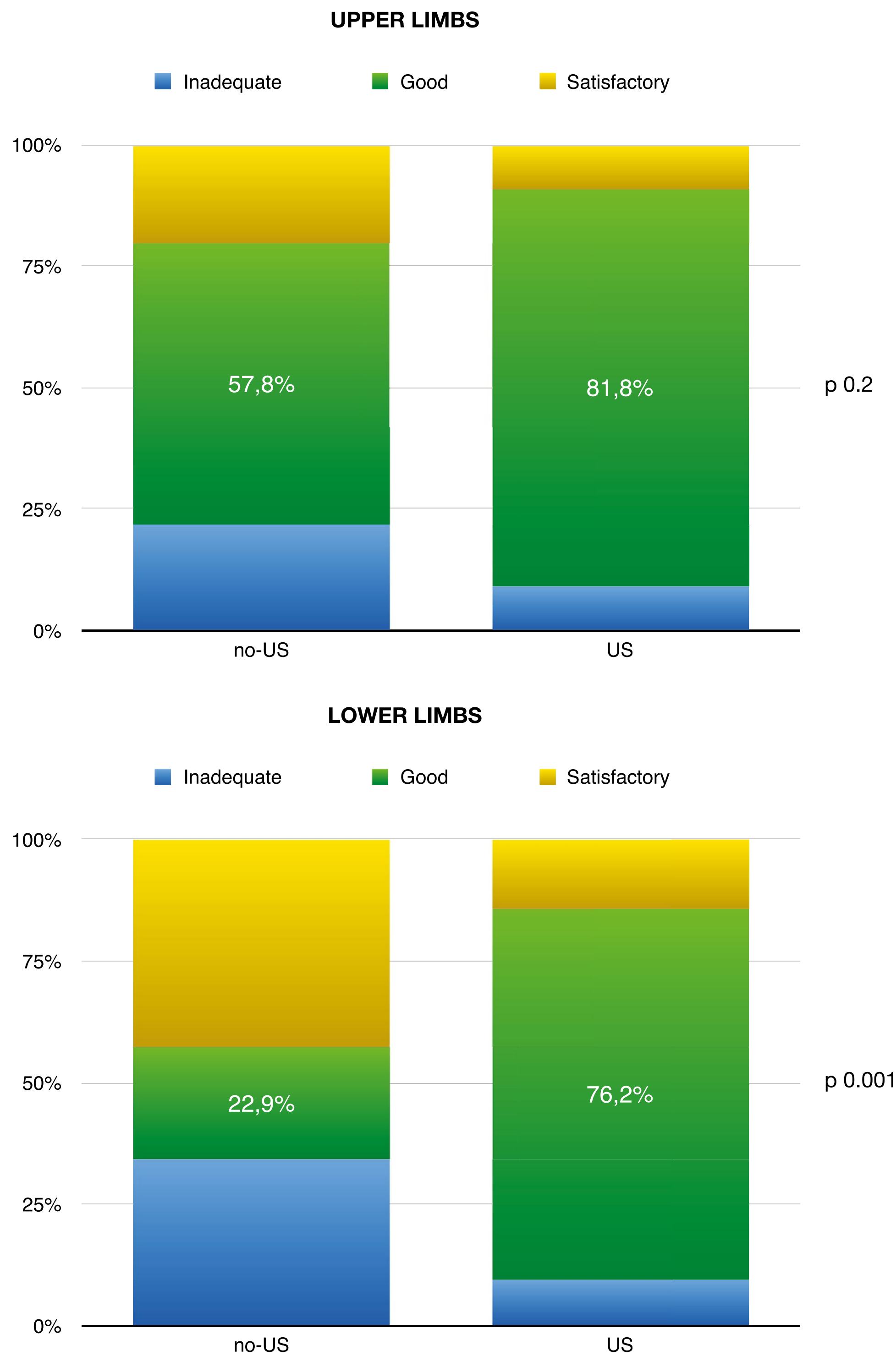


Fig. 5 Difference in accuracy between upper and lower limbs whether US is used or not

As a conclusion, our study suggests that US implementation for line tip positioning could lead to a significant decrease in the number of X-ray and radiation, combined with a higher position accuracy. These results need to be confirmed in further randomised controlled trials. Timing of procedure, consequences on catheters-associated complications (CLABSI, mechanical complications etc.) also need to be assessed further. It is of paramount importance, for the adequacy of this examination, to be performed by appropriately trained doctors who are able to univocally interpret the

Table 4 Effective radiation dose and costs

	All US	All no-US	*p* value	US/nPICC	No-US/nPICC	*p* value	US/UVC	No-US/UVC	*p* value
Effective dose (mSV) mean (95% CI), median	0.0277 (0.0245–0.0310), 0.0287	0.0358 (0.0327–0.0388), 0.0287	<0.001	0.0230 (0.0186–0.0274), 0.0223	0.0326 (0.0289–0.0364), 0.0264	0.001	0.0334 (0.0291–0.0378), 0.0287	0.0414 (0.0364–0.0464), 0.0287	0.03
Cost of X-ray (£) mean (95% CI), median	75.09 (65.49–84.69), 86	94.42 (85.52–103.33), 86	0.001	54.07 (43.37–64.77), 54	78.02 (68.77–87.27), 54	0.001	100.19 (87.29–113.10), 86	123.89 (107.78–140), 86	0.068

results. However, no accredited neonatal curriculum in this field has been published until now, and neonatal US mentors are critically lacking. Curriculum and training implementation remain the main challenge to move forward. We have proposed an effective learning strategy, which is successfully integrated into the teaching programmes and daily clinical practice of a level III NICU and that has shown promising prospective for its application of a larger scale.

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Authors' contributions All authors contributed to the study conception and design. VMP, HK and EM performed all the ultrasounds. HJ and VMP reviewed the X-rays. Data collection was performed by VMP, EM and SR. Data analysis was performed by SR and EG. The first draft of the manuscript was written by SR and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Availability of data and material The datasets generated and analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval The study had institutional governance approval and no ethical approval was required.

Consent to participate Routinely collected clinical data were used and explicit informed consent was not sought for this reason.

Consent for publication The authors affirm that routinely collected clinical data were used for this study and explicit informed consent for publication was not sought for this reason.

Conflict of interest The authors declare no competing interests.

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