

# Neo-ECHOTIP: A structured protocol for ultrasound-based tip navigation and tip location during placement of central venous access devices in neonates

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## Abstract

Central venous access devices are often needed in neonates admitted to Neonatal Intensive Care Unit. The location of the tip of the central catheter is usually assessed by post-procedural X-ray. However, this strategy is inaccurate and time consuming. Recent guidelines strongly recommend intra-procedural methods of tip location, to increase the cost-effectiveness of the maneuver and to shorten the time between device placement and utilization. In this regard, real-time ultrasound represents the most promising tool for tip navigation and location in neonates. The aim of this paper is (a) to review all the evidence available about ultrasound-based tip navigation and tip location of central catheters in the neonatal population (b) to propose a novel protocol for tip navigation and location (Neo-ECHOTIP) based on such evidence.

## Keywords

Ultrasound, NICU, intensive care, newborn, central venous access, tip location, tip navigation, umbilical venous catheter, epicutano caval catheter

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## Introduction

Central venous access devices (CVADs) are often required in Neonatal Intensive Care Unit (NICU). The proper location of the tip of a CVAD is crucial and it is usually assessed by radiological methods (chest and abdominal X-rays). Such practice is used in up to 80% of NICUs.<sup>1</sup> However, in the last decade, many studies have shown that radiology-based tip location (“tip location”=assessment of the final position of the catheter tip) has some relevant limitations:

1. It is relatively inaccurate. As X-rays do not allow the direct visualization of the veins, the location of the catheter tip is assessed indirectly, that is, using radiological landmarks such as the vertebral bodies, the cardiac silhouette, the diaphragmatic contour, etc.<sup>2–5</sup>

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**Table 1.** Summary of Neo-ECHO tip.

Catheter	Protocol	Probe	Windows
UVC	Tip navigation	Small sectorial probe, 7–8 MHz	Low subcostal longitudinal view
	Tip location	Small sectorial probe, 7–8 MHz	Subcostal longitudinal view
ECCs inserted via veins of the scalp or of the upper limbs	Tip navigation	Linear “hockey stick” probe, 10–14 MHz	Acoustic windows of RaCeVA and RaPeVA
	Tip location	Small sectorial probe, 7–8 MHz	Bi-caval view; four-chamber apical view; long axis view of SVC
ECCs inserted via veins of the lower limbs	Tip navigation	Linear “hockey stick” probe, 10–14 MHz	Short and long axis view of the femoral vein
	Tip location	Small sectorial probe, 7–8 MHz	Subcostal longitudinal view
CICC	Tip navigation	Linear “hockey stick” probe, 10–14 MHz	Acoustic windows of RaCeVA
	Tip location	Small sectorial probe, 7–8 MHz	Bi-caval view; four-chamber apical view; long axis view of SVC
FICC	Tip navigation	Linear “hockey stick” probe, 10–14 MHz and small sectorial probe	Short and long axis view of the femoral vein and subcostal longitudinal view
	Tip location	Small sectorial probe, 7–8 MHz	Subcostal longitudinal view

UVC: umbilical venous catheter; ECC: epicutaneo-caval catheter; RaCeVA: rapid central vein assessment; RaPeVA: rapid peripheral vein assessment; CICC: centrally inserted central catheter; FICC: femoral inserted central catheter.

- It is consistently a post-procedural methodology, since fluoroscopy is not considered appropriate in NICU. Therefore, being post-procedural, it can be used only for tip location and not for tip navigation (“tip navigation”=real-time assessment of the proper direction of the catheter during placement). Also, being a post-procedural method, there is inevitably some delay in reporting the result and there is sometimes the need to reposition the device after the report.
- It is not harmless, since it exposes the neonate to ionizing radiations, which may ultimately be associated with long term damage.<sup>6,7</sup>

Recent guidelines<sup>8</sup> strongly recommend to prefer real-time, intra-procedural methods of tip location, so to increase the cost-effectiveness of the maneuver and to shorten the time between device placement and device utilization.

In adults and in children, intracavitary ECG (IC-ECG) is currently regarded as the gold standard for tip location because it is intra-procedural, accurate, cost-effective, easy to use and easy to learn.<sup>8–10</sup> Unfortunately, IC-ECG is not always easily feasible in newborns, particularly when inserting central venous catheters as epicutaneo-cava catheters (ECC), that are characterized by very small caliber (1–2.7Fr). Also, umbilical venous catheters (UVC) are often inserted in emergency and/or in settings where the use of IC-ECG might be logistically difficult. Last but not least, IC-ECG is not appropriate for tip navigation, at least in neonates.

For these reasons, real-time ultrasound represents the most promising tool for tip navigation and location during placement of central venous access devices in the neonate. In fact, it has several potential advantages:

- It is accurate, since ultrasound visualization of all venous districts is particularly easy in neonates.
- It is a real-time, intraprocedural methodology.
- It is appropriate for both tip navigation and tip location.
- It can be applied to all CVADs used in NICU.
- It is non-invasive, completely safe and readily available.

The aim of this paper is (a) to review all the evidence available about ultrasound-based tip navigation and tip location of CVADs in the neonatal population and (b) to propose a novel protocol for tip navigation and location (Neo-ECHOTIP) based on such evidence. We will discuss separately the three main CVADs used in NICU: umbilical venous catheters (UVC); epicutaneo-cava catheters (ECC); ultrasound-guided CVADs, that is, centrally inserted central catheters (CICC) and femorally inserted central catheters (FICC).

A summary of the protocol is shown in Table 1

## Methods

The literature search performed for this review was done by searching the following:

- Electronic database searches of PubMed, EMBASE, and Google Scholar.
- Cochrane Central Register of Controlled Trials

The terms used in the search were “ultrasound,” “USG,” “point-of-care ultrasound,” “POCUS,” “infant,” “neonate,” “newborn,” “NICU,” “central line,” “umbilical line,” “umbilical catheter,” “umbilical venous catheter (UVC),”

“umbilical arterial catheter (UAC),” “PICC,” “Epicutaneo-caval catheter,” “CICC,” “FICC,” “internal jugular vein,” “Subclavian vein,” “Brachiocephalic vein,” and “Femoral vein” in the past 20 years from 1/1/2000 to 1/1/2021. No language restrictions were applied, and we included all trials, case reports, and case series and filtered the articles by reviewing the abstract.

### Umbilical venous catheter

The umbilical venous catheter (UVC) is one of the most common neonatal CVAD, for two main reasons: (1) it is easy to insert, as it is placed directly into an open vein; (2) it is appropriate for management of critically ill neonates because it can be used for any kind of infusion, including inotropes administration and parenteral nutrition, as well as for blood sampling.<sup>11</sup> However, recent guideline recommends to limit the dwell time to 4 days in order to reduce the risks of infectious and thrombotic complications.<sup>8</sup>

The correct position for the tip of UVCs is at the junction between inferior vena cava (IVC) and right atrium (RA)<sup>12–14</sup>; this tip location appears to be associated with the minimal incidence of UVC-related complications (pleural and cardiac effusion, cardiac tamponade, endocarditis, arrhythmias, liver lesions, portal vein thrombosis, and portal hypertension).<sup>14–16</sup>

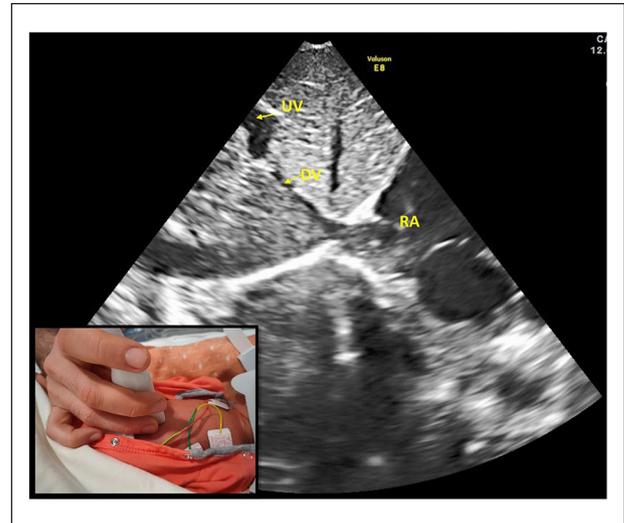
The most widely used practice for UVC insertion includes (a) a pre-procedural length estimation based on anthropometric measurements, nomograms, or formulas based on the weight or the length of the patient,<sup>17,18</sup> followed (b) by a “blind” navigation of the catheter into the venous system and (c) by a final, post-procedural radiological assessment of the tip’s position. Anterior-posterior chest X-ray is still the most used radiological method for this purpose; the vertebral bodies or the cardiac silhouette are the usual radiological landmarks to infer the position of the catheter’s tip.<sup>19,20</sup>

Several recent clinical studies have evaluated the accuracy of real-time ultrasound (RT-US) for tip navigation and location during UVC placement. RT-US use is feasible in any setting, easy to teach, and easy to learn. It is also faster and more accurate when compared to conventional radiology.<sup>21–32</sup>

Furthermore, US can be used in real time avoiding multiple subsequent manipulations of the catheter.

Ultrasound is also useful in the management of UVC, hours or days after placement, to assess any late migration of the catheter tip (secondary malposition), an event that can occur in up to 50% of cases.<sup>31,32</sup> Secondary malposition it is also associated with pleural and cardiac effusion, cardiac tamponade, endocarditis, liver lesions, portal vein thrombosis, portal hypertension which can be properly diagnosed with ultrasound.

**RT-US for UVC: Evidence from the literature.** Several studies have evaluated the accuracy of US for UVC tip location.



**Figure 1.** Subcostal longitudinal view. The pathway of fetal umbilical venous flow from the umbilical vein (UV) to the ductus venosus (DV), and further on to the junction between inferior vena cava (IVC) and right atrium (RA).

According to most authors, the tip can be successfully located in 95%–100% of all patients. Different probes have been used:

- Linear probes, 12–13 MHz.<sup>22,25,27</sup>
- Micro-convex probes, 7–8.5 MHz.<sup>22,27</sup>
- Small sectorial probes.<sup>21,29</sup>

The subcostal longitudinal view was the most common acoustic window, though some authors adopted also complementary windows such as the apical four-chamber view and the parasternal short-axis view.<sup>21,29</sup> A saline flush was used in some studies as a complimentary aid to enhance tip visualization.<sup>21,25,29</sup> Only one study reported the use of US for tip navigation.<sup>33</sup>

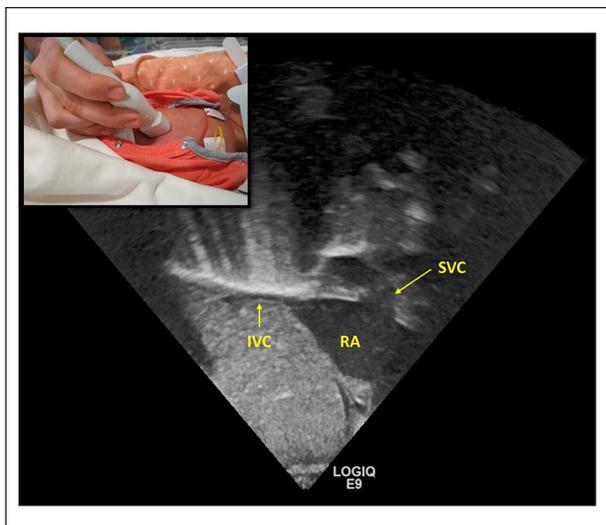
**Our proposal: Neo-ECHOTIP for UVC.** Our Neo-ECHOTIP protocol for UVC placement includes both real-time ultrasound-based tip navigation and real-time ultrasound-based tip location.

Tip navigation protocol:

**Probe:** Small sectorial probe, 7–8 MHz.

**Acoustic window:** Subcostal longitudinal view. This view allows to visualize the pathway of fetal umbilical venous flow from the umbilical vein to the ductus venosus, and further on to the junction between IVC and RA. See Figure 1.

**Procedure:** During catheter insertion, the tip is visualized as it passes through the umbilical vein, the ductus venosus, and the IVC. A small pressure with the probe may facilitate the lineup between the ductus venosus



**Figure 2.** Subcostal longitudinal view. The inferior vein cave (IVC), the right atrium (RA) and the superior vein cave (SVC) are clearly visible.

and the IVC, increasing the odds to direct the catheter into the proper position.<sup>33</sup>

#### Tip location protocol:

*Probe:* Small sectorial probe, 7–8 MHz.

*Acoustic window:* Subcostal longitudinal view. This view allows to visualize the IVC and the RA. See Figure 2.

*Procedure:* The tip is followed until it reaches the target zone, that is, the junction between the IVC and the RA. A small flush of normal saline (0.5–1 ml) can improve the visualization of the tip.

*The position of the UVC tip should be checked after 24 h, so to exclude secondary malposition due to subsequent migration.*  
*Training issues.* Even though US-based placement of UVC has been proved to be accurate, effective, and safe, many neonatologists still consider the chest X-rays as the gold standard technique for tip location of umbilical vein catheters, probably because the training for RT-US is perceived as long and difficult. This is not true: training for RT-US for UVC has been shown to be simple and feasible.<sup>23,26,28,34</sup>

#### Epicutaneo-caval catheter

Epicutaneo-caval catheter (ECCs) are CVADs inserted via superficial veins of the limbs or of the scalp; they are frequently used in NICU to administer parenteral nutrition and drugs not suitable for the peripheral route.<sup>35</sup> They are not appropriate for blood sampling or blood transfusion,

because of their small caliber (1–2.7 Fr) and their low flow (1–2 ml/min).

ECCs are usually placed at the bedside, after a length estimation based on anthropometric measurements, via “blind” tip navigation, using anatomical landmarks for tip location. For ECCs inserted from the upper part of the body, the commonly adopted anatomical landmark is the mid-point between xiphoid process and jugular notch. For catheters inserted from the lower part of the body, the anatomical landmark is the xiphoid. At the end of the maneuver of ECC insertion, post-procedural tip location is usually assessed by chest X-ray<sup>36</sup>: the correct tip position is approximately 1 cm outside the cardiac silhouette in pre-term infants and 2 cm for term infants,<sup>37,38</sup> as this position is believed to be related to a lower incidence of cardiac tamponade.<sup>39</sup> Though, chest X-ray allows only a very rough estimation of the tip location, based on relatively unreliable radiological landmarks.

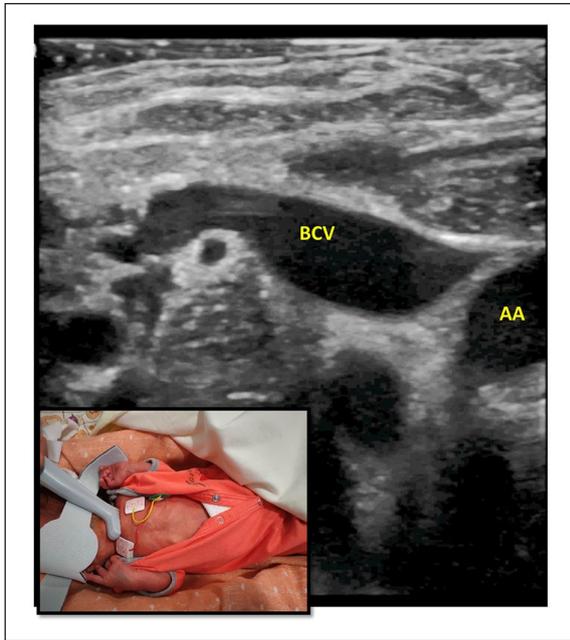
In the last decade, many clinical studies have investigated ultrasound as a reliable tool for tip location for ECCs.<sup>5,26</sup> RT-US is non-invasive, safe, and—being an intra-procedural method—reduces the need of catheter repositioning.<sup>26,40,41</sup> Unfortunately, ultrasound-based tip location of ECCs requires a more advanced training if compared to RT-US for UVC placement: the clinicians should develop a basic expertise in target neonatal echocardiography and in the protocols of US-based visualization of peripheral and central veins (rapid central vein assessment (RaCeVA), rapid peripheral vein assessment (RaPeVA), and rapid femoral vein assessment (RaFeVA)).<sup>39,42</sup> As ECCs are prone to secondary malposition (late tip migration: 30%–35% of cases), ultrasound may be also used for periodic evaluation of the tip’s position.<sup>4</sup> Furthermore, secondary malposition it is also associated with pleural and cardiac effusion, cardiac tamponade, endocarditis, extravasation, deep vein thrombosis which can be properly diagnosed with point-of-care ultrasound.

*RT-US for ECC tip location: Evidence from the literature.* Several clinical studies have evaluated the accuracy of US for tip location during ECC placement. In such studies, the tip was successfully located in a variable percentage of cases, as the percentage of success apparently reaches 100% only when the operator is highly trained.<sup>5,40</sup>

Different probes have been used:

- Linear probe, 12–13 MHz.<sup>26</sup>
- Small sectorial probe.<sup>39</sup>

Different acoustic windows have been used: apical four chamber-view; parasternal long and short axis view; long axis view of superior vena cava (SVC); subcostal longitudinal view of IVC (for catheter inserted from lower limbs). A saline flush has been used in several studies to achieve a better visualization of the catheter tip. No study in the



**Figure 3.** Shows part of the RaCeVA protocol. Left brachiocephalic vein (BCV) is visualized in long axis. Part of the aortic arch (AA) is also evident.

literature has investigated ultrasound-based tip navigation during ECC placement.

*Our proposal: Neo-ECHOTIP for ECC.* Our Neo-ECHOTIP protocol for ECC placement includes both real-time ultrasound-based tip navigation and real-time ultrasound-based tip location. Two different approaches are considered depending on the insertion site.

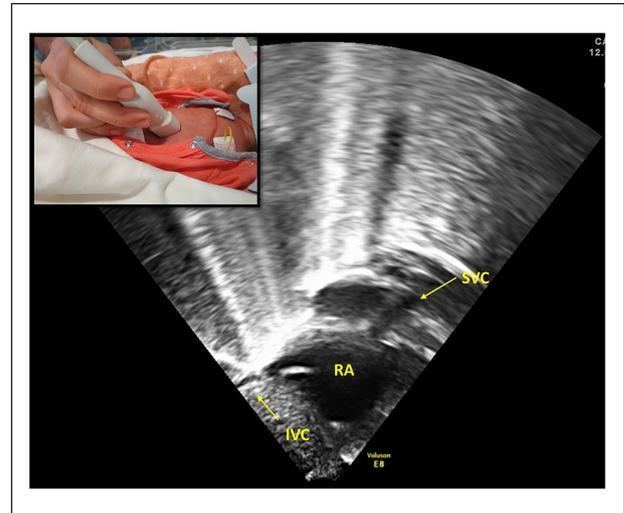
- (1) Protocol for ECCs inserted via veins of the scalp or of the upper limbs

Tip navigation protocol:

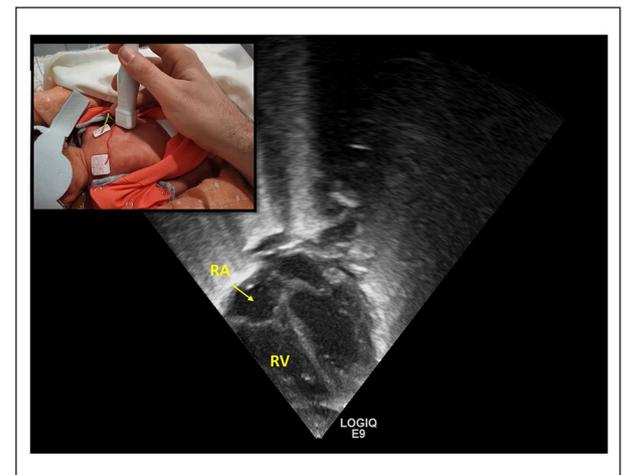
*Probe:* Linear “hockey stick” probe, 10–14 MHz.

*Acoustic windows:* The protocol includes the acoustic windows of RaCeVA<sup>9,10,43</sup> and RaPeVA.<sup>10,43,44</sup> Figure 3 shows the left brachiocephalic vein, part of the RaCeVa protocol.

*Procedure:* The RaPeVA protocol help in progression of the catheter through the arm’s deep veins. The RaCeVA protocol is used for tip navigation of the catheter into the subclavian vein, the brachio-cephalic vein and the SVC, to prevent primary malposition (such as inside the internal jugular vein) during the maneuver of insertion. The RaCeVA protocol can also easily visualize an ECC inserted into scalp veins as it passes through the internal jugular vein, the brachiocephalic vein and the SVC.



**Figure 4.** Subcostal longitudinal view (“bi-caval” view). The inferior vein cave (IVC), the right atrium (RA) and the superior vein cave (SVC) are clearly shown.



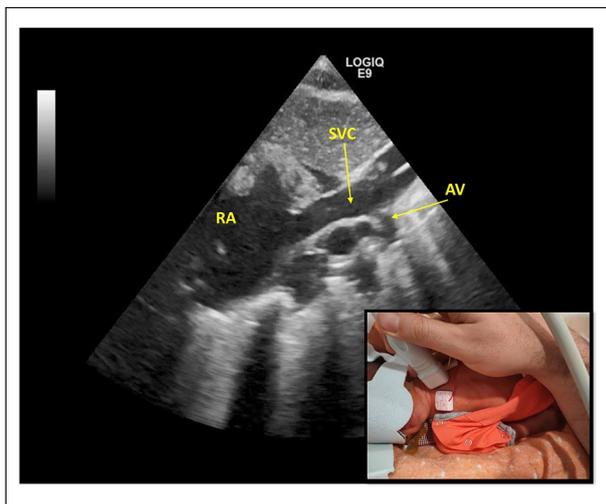
**Figure 5.** Four-chamber apical view. The four chambers of the hearth are clearly visible. The right atrium (RA) and the right ventricle (RV) are visualized on the right side.

Tip location protocol:

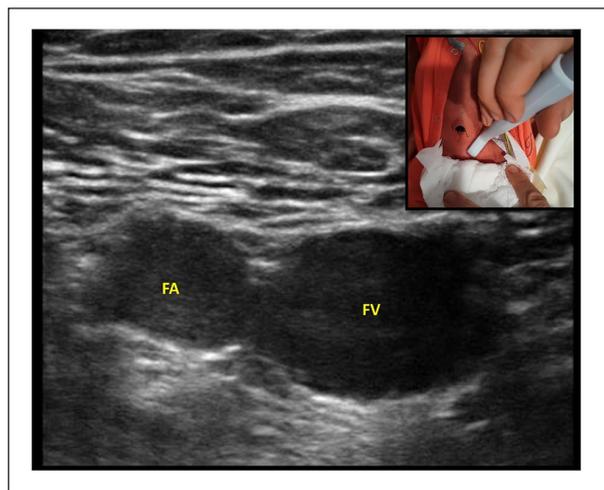
*Probe:* Small sectorial probe, 7–8 MHz.

*Acoustic windows:* At least three different windows have been used to locate the catheter tip. The most useful ones are the subcostal longitudinal view (“bi-caval” view, Figure 4); the four-chamber apical view (Figure 5); the parasternal, long axis view of SVC (Figure 6).

*Procedure:* The catheter tip is followed until it reaches the target zone, that is, the transition between SVC and RA. A small flush of normal saline (0.5–1 ml) may help visualizing the tip.



**Figure 6.** Long axis view of superior vein cave (SVC). SVC is visualized in its long axis into the right atrium (RA). The Azygos vein (AV) is also shown.



**Figure 7.** Short axis view of the femoral vein (FV) femoral artery (FA) shown.

- (2) Protocol for ECCs inserted via veins of the lower limbs

Tip navigation protocol:

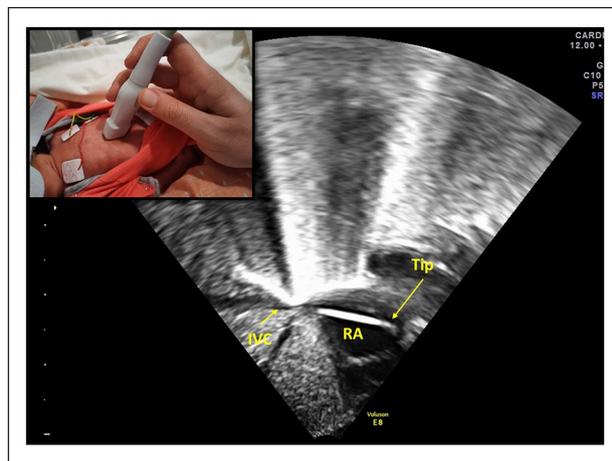
*Probe:* Linear “hockey stick” probe, 10–14 MHz.

*Acoustic window:* Short and long axis view of the femoral vein.<sup>43</sup> See Figure 7.

*Procedure:* During ECC insertion, the catheter tip is visualized into the femoral vein and into the iliac vein.

Tip location protocol:

*Probe:* Small sectorial probe, 7–8 MHz



**Figure 8.** Subcostal longitudinal view. The inferior vein cave (IVC) and the right atrium (RA) are shown. The tip of the catheter is visible into the RA.

*Acoustic window:* Subcostal longitudinal view. This view allows visualization of IVC and RA. See Figure 8.

*Procedure:* The tip is followed until it reaches the target zone, that is, the transition between IVC and RA. A small flush of normal saline (0.5–1 ml) may help visualizing the tip.

The tip location should be checked 24–48 h later, so to exclude secondary malposition due to late tip migration.

*Training issues.* Even though US-based tip location of ECC has been proved to be effective and safe, many neonatologists still consider chest X-rays as the gold standard for this purpose. This is partly explained by the advanced training necessary to complete this maneuver with RT-US.

To the best of our knowledge, few data are available about the training needed for performing ultrasound-based tip location of ECCs. Clinical studies on RT-US for tip location of ECCs show a direct correlation between the level of expertise of the clinician and the percentage of successful tip visualization.<sup>45</sup>

In our experience, the minimum training requirements for ultrasound-based tip navigation and tip location of ECCs should include:

1. Basic knowledge of targeted neonatal echocardiography and advanced vascular ultrasound assessment (in particular, the RaCeVA, RaPeVA, and RaFeVA protocols).
2. Advanced theoretical training, including the evaluation of several clinical case scenarios (at least 12 h).
3. Practical training supervised by a neonatologist with expertise in ultrasound-based tip location of ECCs (at least 50 cases).

## Ultrasound-guided CVADs

Power-injectable, 3–4Fr polyurethane catheters can be placed even in preterm neonates,<sup>46–49</sup> by ultrasound guided puncture of the internal jugular or brachio-cephalic vein (CICC) or of the femoral vein (FICC). CICCs and FICCs offer several advantages if compared to ECCs: they allow high flow infusions (1 ml/s), easy administration of blood products, easy blood sampling, and even hemodynamic monitoring (central venous pressure and oxygen saturation of mixed venous blood). For these reasons, such devices represent the optimal venous access in critically ill neonate.

Ultrasound guided placement of CICC and FICC is feasible at any gestational age and birth weight.<sup>9,47,49–55</sup> The only limitation is the internal diameter of the vein: in fact, the international guidelines—such as the WoCoVA-GAVeCeLT-WINFOCUS consensus<sup>56</sup> or the 2021 INS standards<sup>8</sup>—recommend measuring the vein's diameter before catheter insertion, in order to match the vein diameter with the catheter and reduce the risk of venous thrombosis. It is commonly recommended respect the catheter to vein ratio of 1:3. Therefore, a 3Fr catheter requires a vein with an internal diameter of at least 3 mm. A recent prospective study showed that the brachio-cephalic vein is big enough to allow the placement of a 3Fr catheter even in very low weight neonates.<sup>43</sup>

Tip location of CICC and FICC can be performed by IC-ECG: such technique is feasible and reliable even in the neonatal population.<sup>57</sup> However, RT-US can be very useful also during CICC and FICC placement, for several reasons:

1. RT-US allows both tip navigation and tip location.
2. RT-US can easily rule-out primary malposition, such as the accidental direction of the catheter into the opposite brachio-cephalic vein.
3. RT-US is an effective rescue strategy when the intracavitary ECG is not applicable (for instance in newborns with atrial flutter).
4. RT US is the only way to evaluate the tip location of a FICC when the tip is scheduled to be inside the IVC.

*RT-US for CICC/FICC tip location: Evidence from the literature.* Evidence is scarce in the neonatal population. Though, a few studies suggest to use the same probes and acoustic windows used for ECC.<sup>49,55</sup>

*Probes:*

- Linear “hockey stick” probe, 12–13 MHz.
- Small sectorial probe.

*Acoustic windows:*

- Subcostal longitudinal view (bi-caval view).
- Apical view.
- Parasternal, long axis view of SVC.

*Our proposal: Neo-ECHOTIP for CICC and FICC.* Our Neo-ECHOTIP protocol for CICC/FICC placement includes US-guided venipuncture, US-based tip navigation and US-based tip location.

Neo-ECHOTIP for CICC insertion is as follows.

### 1. Tip navigation protocol:

*Probe:* Linear “hockey stick” probe, 10–14 MHz.

*Acoustic windows:* Same acoustic windows of the RaCeVA protocol,<sup>9,10,43</sup> including proper visualization of the brachio-cephalic veins in long axis on both sides.

*Procedure:* During CICC placement, the brachio-cephalic vein and the SVC should be clearly visualized.

- The needle is visualized during the venipuncture.
- The guidewire is visualized as it passes into the brachio-cephalic vein and into the SVC. It is recommended at this stage also to rule out pneumothorax.
- The micro-introducer is visualized inside the brachio-cephalic vein.
- The catheter is visualized inside the brachio-cephalic vein and then inside the SVC.

### 2. Tip location protocol:

*Probe:* Small sectorial probe, 7–8 MHz

*Acoustic windows:* Three different windows are recommended to locate accurately the tip of the catheter. The most useful ones are the subcostal longitudinal view (“bi-caval” view), the four-chamber apical view, and the long axis view of SVC.

*Procedure:* Follow the catheter tip until it reaches the target zone, that is, the transition between SVC and RA. A small flush of normal saline (0.5–1 ml) may help confirming the tip position.

Neo-ECHOTIP for FICC insertion is as follows. Tip navigation can be divided in two steps.

### 1. Tip navigation protocol—STEP 1:

*Probe:* Linear “hockey stick” probe, 10–14 MHz

*Acoustic window:* Short and long axis view of the femoral vein.

*Procedure:* During FICC placement, the femoral vein should be clearly visualized.

- The needle is visualized during the venipuncture.
- The guidewire is visualized as it passes through the femoral vein (long axis).
- The micro-introducer is visualized inside the femoral vein.

- The catheter is visualized inside the femoral vein and then inside the iliac vein.

## 2. Tip navigation protocol—STEP 2:

*Probe:* Small sectorial probe, 7–8 MHz.

*Acoustic window:* Subcostal longitudinal view. It's mandatory to visualize properly the IVC.

*Procedure:* The catheter tip is visualized as it passes through the IVC.

If hemodynamic monitoring is not required, the catheter tip of the FICC is placed below the renal veins<sup>9</sup>: in such case, “tip navigation STEP 2” is also a tip location technique.

## 3. Tip location protocol:

*Probe:* Small sectorial probe, 7–8 MHz.

*Acoustic window:* Subcostal longitudinal view, so to visualize IVC and RA.

*Procedure:* The catheter tip is visualized as it reaches the target zone, that is, the transition between IVC and RA. A small flush of normal saline (0.5–1 ml) may help visualizing the tip.

Table 1 summarizes the whole protocol of tip location and tip navigation giving information about the probe and the acoustic windows.

## Conclusions

Our proposal of a Neo-ECHOTIP protocol for improving the placement of CVADs in NICU is strongly based on evidence from many published clinical studies. We have tried to integrate different clinical experiences and structure them in order to develop a stepwise and standardized procedure, potentially useful to perform both ultrasound-based tip navigation and tip location, in all central venous access devices currently used in NICU.

Some of these maneuvers are easy and require only a minimal training, while some others imply a well-trained operator with more than basic knowledge in the field of vascular ultrasound and echocardiography. Thus, training is the main open question, and we suggest that more evidence should be published about the proper training required for achieving appropriate skills of real-time ultrasound for CVAD insertion in neonates.

Nonetheless, current evidence and common sense suggest that ultrasound-based tip location will have an increasingly important role for CVAD in NICU, considering its many advantages in terms of accuracy, cost-effectiveness and safety.

## Author contributions

MP and GB made a substantial contribution to the concept or design of the work; GB drafted the article and MP revised it critically for important intellectual content. DGB, DE, EI, AL, and GZ revised and approved the final version of the manuscript improving significantly the intellectual content. VD Made a substantial contribution to the design of the work; revised the available literature and approved the manuscript in its final form.

## Declaration of conflicting interests

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