

# Contrast enhanced ultrasound as a new tool to estimate the performance of midline catheters in the single patient

Antonio Gidaro , Francesco Casella, Francesca Lugli, Chiara Cogliati, Maria Calloni, Federica Samartin, Nicola Brena and Guido Pace

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## Abstract

**Background:** Contrast enhanced ultrasound (CEUS) through MicroBubbles Time (MBT) (time from infusion of saline with addition of micro-bubbles of air to visualization of first bubbles in right atrium (RA), visualized by subxiphoid or apical echocardiography) is an alternative to Intracavitary ECG and chest X-ray in evaluation of tip location in central venous catheters.

**Objective:** To evaluate feasibility and variability of CEUS in peripheral catheters (Midline-MC) in a cohort of patients and in a subgroup where tip location was also performed through chest X-ray. Secondary outcomes were verifying the correlation between MBT and distance between tip of MC and RA (anthropometric and radiological measures), body mass index (BMI), vein diameter at point of insertion.

**Methods:** Patients with insertion of MC were enrolled in this prospective cohort. After catheter insertion, CEUS was performed recording MBT.

**Results:** One hundred thirty-two MCs were inserted, 45 performed Chest X-ray. MBT wasn't feasible in 7 (5%) because of low quality echocardiographic images. Subcostal view was available in 114 patients (91.2%), while 11 patients (8.8%) were examined through apical four-chamber view. Mean MBT in the whole population was  $2.3 \pm 0.8$  s. Significant correlation between anthropometric and radiological measures, BMI and MBT was found. 32.8% of MC had a MBT  $\leq 2$  s.

**Conclusions:** CEUS could be useful to estimate tip position. Our study showed how 2 s is not a suitable cutoff to confirm central catheter's tip.

## Keywords

Midline catheter, contrast enhanced ultrasound, MicroBubbles Time, tip's location, catheter related thrombosis

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## Introduction

Peripheral venous catheters (PVCs) make up a heterogeneous group of devices. We can mainly divide this group based on length of catheter into three categories: short cannulas ( $<6$  cm); long peripheral cannulas (a.k.a mini midlines) (8–10 cm) and midline catheters (20–25 cm).<sup>1</sup> Despite this great diversity, recent guidelines<sup>2</sup> for appropriate use of venous accesses address PVCs almost as a single entity, greatly reducing their potential. PVC choice is now based on the expected length of therapy.<sup>2</sup> Among PVCs, MCs should have the best performances because in certain patients their tip can almost reach the subclavian vein. In central venous catheters (CVCs)<sup>3,4</sup> an alternative

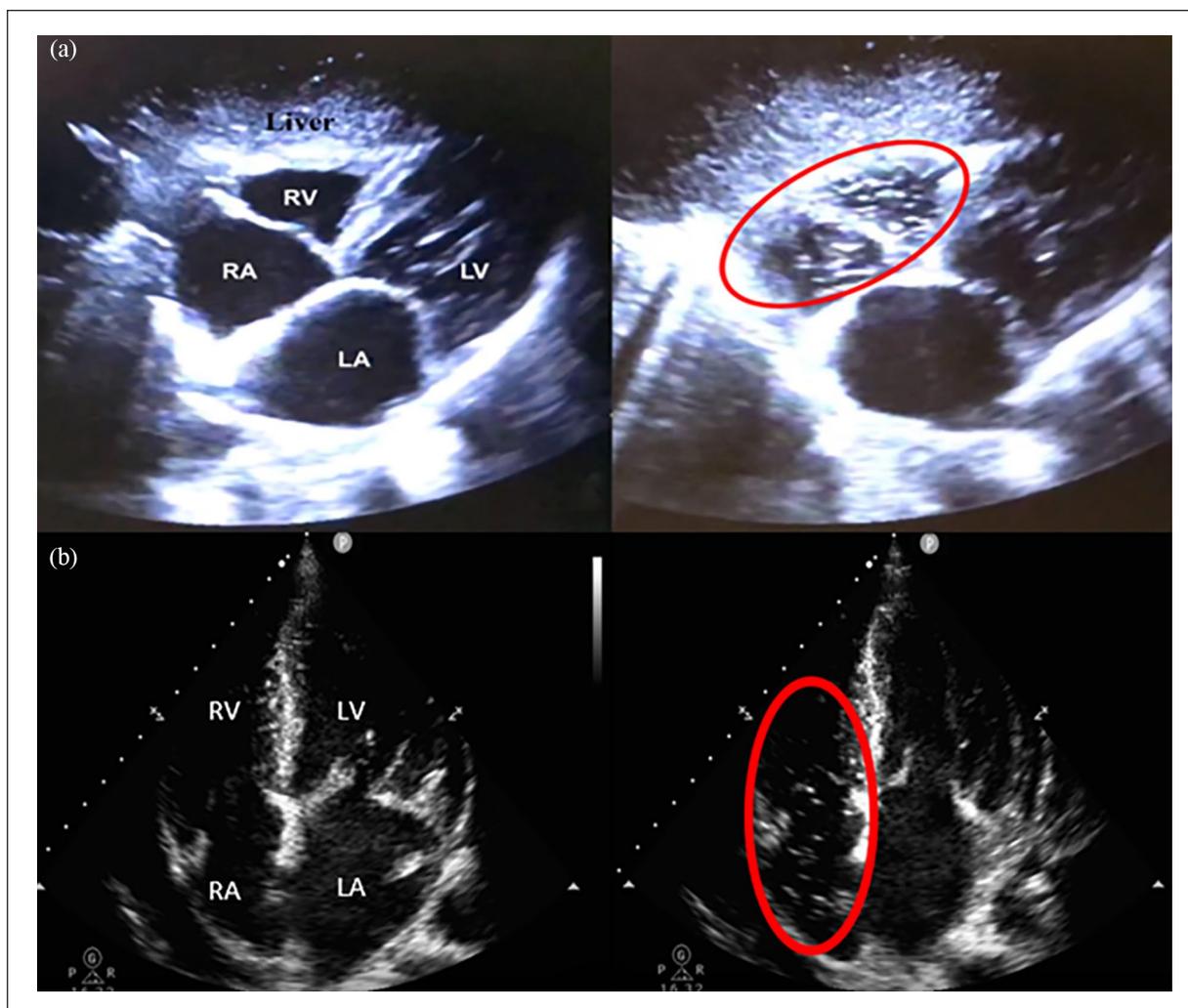
to Intracavitary ECG and chest X-ray (CXR) to evaluate tip location is the assessment of vein flow through contrast enhanced ultrasound (CEUS): a MBT (rapid infusion of saline with the addition of micro-bubbles of air, visualized by subxiphoid or apical echocardiography) (Figure 1) less

Department of Biomedical and Clinical Sciences "Luigi Sacco," University of Milan, Luigi Sacco Hospital, Milan, Italy

### Corresponding author:

Antonio Gidaro, Department of Biomedical and Clinical Sciences "Luigi Sacco," University of Milan, Luigi Sacco Hospital, Via G.B. Grassi N° 74 H. Sacco, Milan 20157, Italy.

Email: gidaro.antonio@asst-fbf-sacco.it



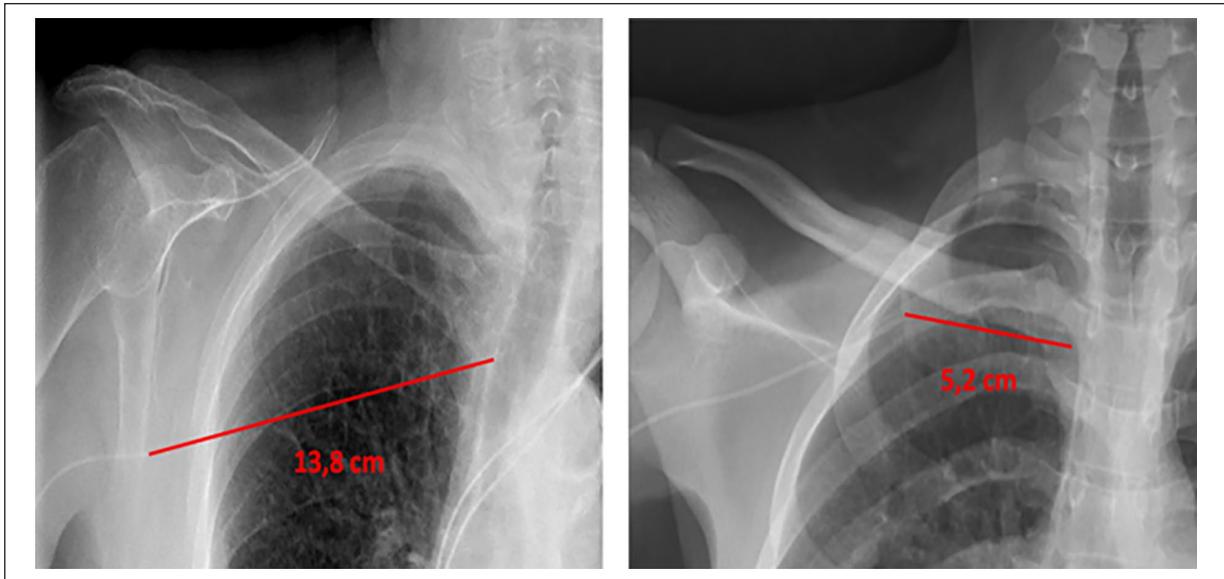
**Figure 1.** Transthoracic echocardiography of the heart: (a) subcostal view and (b) apical four-chamber view which shows the transit of microbubbles through the right chambers.

than 2 s is indicative of a correct tip location.<sup>5</sup> Recently, GAVeCeLT Working Group for Vascular Access in COVID-19<sup>6</sup> suggested the use of bedside transthoracic echocardiography (TTE) for tip location by using probes with convex or sectorial transducers and adopting the microbubbles test. Bedside ultrasonography with microbubble test can theoretically be useful in Midline catheters placement by allowing an estimate of catheter's tip location.

The primary outcome of this study was to analyze the feasibility and the variability of flow time in MCs using CEUS in a cohort of patients and in a subgroup with radiological tip location through chest X-Ray. Secondary outcomes were: to verify the presence or absence of a correlation between MBT and the following parameters: radiographic distance between tip of MC and RA (Figure 2), distance between tip of MC and right atrium (RA) (anthropometric measures), body mass index (BMI), vein diameter at the point of insertion.

## Materials and methods

We consecutively enrolled patients who underwent MC implantation (MedComp 4 F × 20 cm, single lumen, power injectable) at Luigi Sacco Hospital between October 2018 and December 2019. MC were inserted in patients who had a difficult intravenous access (DIVA) and an expected need of intravenous therapy longer than 6 days. All MCs insertions were performed following the “Safe insertion of PICCs (SIP)” bundle recommendations.<sup>7</sup> In particular, the catheter to vein ratio was consistently lower than 1:3,<sup>2,8</sup> and suture less securement was adopted in all groups. All MCs were used for infusion of peripherally compatible drugs. The Institutional Review Board of our University Hospital (Luigi Sacco Hospital, University of Milan, Italy) approved the study protocol. All the enrolled patients expressed and signed an informed consent. We gathered data regarding patients' BMI, distance from the catheter's insertion point to the RA (by measuring the distance from the exit site to the ipsilateral



**Figure 2.** CXR measure of the distance from the tip of the MC to the sternoclavicular joint.

clavicle–sternal articulation plus adding 10 cm for the access from the right arm or 15 cm for the access from the left arm (Ocado Technique)<sup>9</sup>, insertion procedure (cannulated vein, vein diameter, MBT), administered therapy, and catheter dwell time. Radiographic distance between tip of MC and RA (measured from the tip of the catheter to the sternoclavicular joint and then adding 10 cm for the MCs inserted in the right arm and 15 cm for those inserted in the left arm—Figure 2) was recorded if, for clinical reasons, a chest X-Ray was performed during catheter dwell time. After inserting MC we measured the MBT by performing the microbubbles test<sup>10</sup>: injection of 5 mL of a contrast agent compounded by 90% saline and 10% air, mixed with a three-way stopcock by exchange of saline/air mixture between the syringes. A time from injection to the visualization of the first bubbles in the RA was evaluated for study purpose. A first operator started timer when contemporary injecting contrast agent, and stopped time when the first microbubble appeared in the RA. A second operator, with high expertise in bedside echocardiographic exam, visualized RA during MBT test for all the patients. Three measures were performed for each patient and the mean was used as result of MBT. Subcostal view (Figure 1(a)) was considered the first choice for RA visualization, apical four-chamber view (Figure 1(b)) was used as a second option when subcostal view was not feasible. Subcostal view and apical four-chamber view were acquired according to American Society of Echocardiography (ASE) guidelines<sup>11</sup>; pictures of subcostal and apical four-chamber views were included in Figure 1.

### Statistical analysis

Kolmogorov-Smirnov test was done to evaluate the normality of distribution of data. Qualitative data were expressed as number and percentage. Quantitative data

were expressed as mean, standard deviation. Student *T*-test and Mann-Whitney test (for non-parametric data) were used for comparison between whole population and the subgroup with a performed chest X-Ray. *p*-Value less than 0.05 was considered statistically significant.

Two Logistic regression model were used:

- 1) for assessing correlation between MBT (dependent variable) and BMI, radiographic distance between tip of MC and RA and vein diameter (independent variable).
- 2) for assessing correlation between MBT (dependent variable) and BMI, distance from the catheter's insertion point to the RA and vein diameter (independent variable).

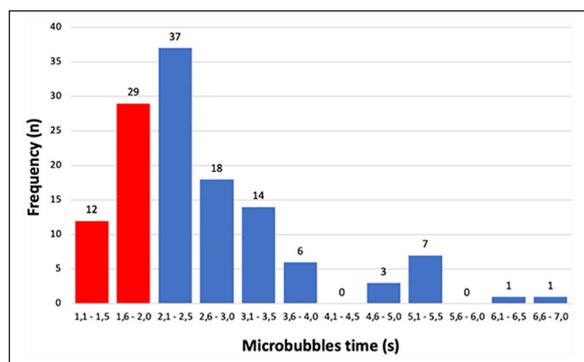
Data from the study were stored and analyzed by IBM Corp., Released 2016. IBM SPSS Statistics for Windows, Version 24.0, Armonk, NY: IBM Corp.

### Results

One hundred thirty-two MCs were inserted during the study. MBT was not feasible in 7 (5%) patients with low quality of echocardiographic images. These patients had a significantly higher BMI ( $31 \pm 7,7$ ;  $p=0.02$ ). Subcostal view was available in 114 (91.2%) patients, the remaining 11 (8.8%) patients were examined through apical four-chamber view. The characteristics of the whole population are presented in Table 1, Group 1. Mean MBT in the whole population was  $2.3 \pm 0.8$  s (Table 1). Intra patient variability for MTB was  $0.24 \pm 0.12$  s. In the whole population we identified 41 (29.5%) catheters which had a MBT  $\leq 2.0$  s (Figure 3, red columns).

**Table 1.** Group 1 represents all MCs, Group 2 represents MCs with CXR available.

	Group 1	Group 2	p-Value
<b>General characteristics</b>			
MCs (n)	125	45	—
Age (mean ± SD)	72.2 ± 15.0	74.6 ± 13.7	0.31
Sex = F (%)	49.6	42.2	0.51
BMI (mean ± SD)	25.0 ± 6.7	24.9 ± 6.5	—
<b>Indication</b>			
Antibiotic (%)	55	56	—
DIVA (%)	20	16	—
PTN (%)	17	20	—
Other (%)	8	8	—
<b>Catheter characteristics</b>			
Insertion point-RA distance (cm, mean ± SD)	35.5 ± 4.5	35.7 ± 5.0	—
RX distance (cm, mean ± SD)	—	19.9 ± 4	—
Arm = right (%)	73	73	—
Basilic vein (%)	63	69	—
Brachial vein (%)	35	31	—
Cephalic vein (%)	2	0	—
Vein diameter (mean ± SD)	5.1 ± 1.0	5.1 ± 0.9	—
MBT (mean ± SD)	2.3 ± 0.8	2.0 ± 0.5	0.58
Dwell time (mean ± SD)	16.7 ± 12.3	20.1 ± 12.4	0.11
<b>Reason for removal</b>			
End of therapy (%)	75	77	—
Death (%)	10	16	—
Self-removal (%)	6	0	—
CVC insertion (%)	4	7	—
CRT (n)	5	0	—
Other (%)	5	0	—
<b>Coagulation</b>			
History of DVT (%)	10	9	—
Presence of at least 1 DVT risk factor (%)	82	87	0.51
No therapy (%)	46	40	0.46
Heparin profilaxis (%)	31	29	—
Anticoagulated (%)	23	31	0.30

**Figure 3.** Distribution of the measured microbubbles times. Red columns represent MCs with a MBT < 2s.

Forty-five patients (Table 1, Group 2) perform a chest X-Ray after catheter implantation. No statistical differences were found between this subgroup and the whole

population. The diameter of cannulated vein was unrelated to MBT ( $p=0.84$ ;  $p=0.82$ ) in both Logistic regression model used. The first Logistic regression model assessed a significant correlation among radiographic distance between tip of MC and RA ( $p<0.001$ ), BMI ( $p=0.03$ ), and MBT.  $R_{\text{multiple}}$  of logistic regression model was 0.66. Also in the second logistic regression model a significant correlation between distance from the catheter's insertion point to the RA ( $p<0.001$ ), BMI ( $p=0.03$ ), and MBT was found.  $R_{\text{multiple}}$  of logistic regression model was 0.63.

## Discussion

Feasibility of MBT technique in peripheral catheters is high, only in 5% of patients MBT wasn't performed due to low quality of echocardiographic images. Our experience confirm the previous papers published using central tip catheters,<sup>3-5,12,13</sup> where MBT was performed in all enrolled patients.

In the majority of patients MBT could be measured from a subcostal view which requires a short-term training.

MBT could theoretically be useful for an indirect tip location of the Midline catheter. This is confirmed by the same finding in both logistic regression model, performed using either radiological distance and anthropometric distance. Previous studies showed that MTB is a reliable tool for tip location in central venous catheters. A recent study<sup>14</sup> demonstrated that intraprocedural ultrasound-guided tip location in MCs is feasible in localizing MC's tip inside the axillary vein, about 3 cm distal to the axillary-subclavian transition (Pinch off area) or inside the subclavian vein. Our study was conducted before this paper, so we couldn't compare results of MBT to intraprocedural ultrasound-guided tip location of MCs.

When the microbubbles test is applied to central catheters a 2 s cutoff is used to verify if the tip is correctly located<sup>12</sup> (RA—superior vena cava junction). Because of the length of the MCs used in our study (20 cm) and the point of insertion (middle third of the arm) none of our catheters reached a central position. Nevertheless 41 (29.4%) of the microbubbles times we measured were <2s, implying that 2 s is not a suitable cutoff to confirm the tip of a catheter has reached an acceptable central position. Such finding agrees with Meggiolaro et al.<sup>13</sup> that suggests 500 ms as a cutoff for central venous catheters (CVCs); even though sensitivity and specificity of this cutoff are ideal (100%–99%), the measurement of such a small interval of time requires an appropriate device.

Our study has several limitations.

Firstly, the radiological distance was available only in 36.6% of the whole population. Moreover, the radiological measurements can slightly change according to the patient's position (sitting, supine) and patient's arms in relation to the radiological machine (parallax effect).

Furthermore, in our study MBT was recorded by operator while no machine was used thus explaining the high inpatient variability of measurements ( $0.24 \pm 0.12$  s).

## Conclusions

CEUS is a safe, cost-effective, and feasible technique which can potentially be useful for tip location of Midline catheters.

In accordance to another study which applied the microbubbles test to CVCs in a strict way,<sup>13</sup> we found 2 s is not an accurate cutoff to confirm the tip of a CVC has reached a central position.

## Declaration of conflicting interests

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## ORCID iD

Antonio Gidaro  <https://orcid.org/0000-0002-5379-1091>

## Data availability statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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