

**Table S1.** The current study situation on micro bubbles test.

| Author                                | Amir and Knio et al.                      | Corradi et al.                    | Cortellaro et al.                   | Duran-Gehring et al. | Gidaro et al.   | Iacobone et al.   |
|---------------------------------------|---|-----------------------------------|-------------------------------------|----------------------|---|---|
| <b>Year, country</b>                  | 2017, United States                       | 2022, Italy                       | 2014, Italy                         | 2014, United States  | 2021, Italy   | 2020, Italy   |
| <b>Patients (catheters, n)</b>        | 137 (137)                                 | 111 (111)                         | 71 (71)                             | 46 (46)              | 125 (125)   | 42 (42)   |
| <b>Setting</b>                        | OR (80%), ICU (20%)                       | OR (100%)                         | ED (100%)                           | ED (100%)            | -   | ICU, Vascular Access Unit   |
| <b>Catheter insertion site (%)</b>    | RIJV: 89.7, LIJV: 5.1, RSV: 0.7, LSV: 4.4 | IJV: 100                          | RIJV: 62, LIJV: 24, RSV: 10, LSV: 4 | IJV: 91, SV: 9       | Basilic vein: 63, brachial vein: 35, cephalic vein: 2 | IJV: 73.8, basilic vein: 14.3, axillary vein: 7.1, brachial vein: 4.8                     |
| <b>TTE views</b>                      | Subcostal, apical                         | Subcostal, apical                 | Subcostal, apical                   | Subxiphoid           | Subcostal, apical                                     | Subcostal, apical   |
| <b>Misplaced catheters (TTE, %)</b>   | 2.4 (3/124)                               | 32 (36/111)                       | 4.2 (3/71)                          | 6.5 (3/46)           | -   | all: 4.8 (2/42), CICC: 6.3 (2/34)   |
| <b>Lung US views</b>                  | All intercostal spaces on MCL             | Not applied                       | Not applied                         | Anterior chest       | Not applied   | On PSL and laterally to the AAL in 3rd to 5th intercostal space                           |
| <b>Pneumothorax rate (Lung US, %)</b> | 0 (123/123)                               | -                                 | -                                   | 4.4 (2/46)           | -   | 0   |
| <b>Comparative method</b>             | CXR                                       | TEE (and CXR)                     | CXR                                 | CXR                  | CXR   | CXR   |
| <b>Misplaced catheters (CXR, %)</b>   | 0.7 (1/137)                               | 11 (12/111), TEE: 33 (37/111)     | 8.5 (6/71)                          | 6.5 (3/46)           | -   | all: 4.8 (2/42), CICC: 6.3 (2/34)   |
| <b>Pneumothorax rate (CXR, %)</b>     | 0 (0/137)                                 | -                                 | -                                   | 4.4 (2/46)           | -   | -   |
| <b>Push to bubbles time (s)</b>       | -   | -                                 | -                                   | -                    | Overall: 2.3 ± 0.8                                    | Positive RASS: 0.89 ± 0.33 (CICC), 1.1 ± 0.20 (PICC)<br>Negative RASS: 3.65 ± 2.00 (CICC) |
| <b>Sensitivity, specificity (%)</b>   | -   | Subcostal: 97, 90; apical: 22, 94 | 33, 98                              | 100, 100             | -   | 100, 100  |
| <b>PPV, NPV (%)</b>                   | -   | Subcostal: 83, 98; apical: 66, 70 | 67, 94                              | 100, 100             | -   | 100, 100  |

|                    |   |   |   |   |  |                 |
|--------------------|---|---|---|---|--|-----------------|
| <b>Annotations</b> | Combination of RASS and use of US to locate guidewire | - | - | - | Despite using peripheral catheters in no central position<br>29.5% had MBT ≤ 2.0 s | 32 CICC, 8 PICC |
|--------------------|---|---|---|---|--|-----------------|

| Author                                | Korsten et al.                     | Meggiolaro et al.  | Vezzani et al.  | Weekes et al.  | Weekes et al.  | Wen et al.      |
|---------------------------------------|------------------------------------|--|---|--|--|-----------------|
| <b>Year, country</b>                  | 2018, Germany                      | 2015, Italy  | 2010, Italy   | 2015, United States  | 2014, United States  | 2014, Germany   |
| <b>Patients (catheters, n)</b>        | 100 (100)                          | 105 (105)  | 99 (99)   | 151 (151)  | 142 (135, 152)   | 202 (219)       |
| <b>Setting</b>                        | ICU, IMC                           | OR (100%)  | ICU   | ED (89%), ICU (11%)  | ED, ICU  | Dialysis Center |
| <b>Catheter insertion site (%)</b>    | RIJV: 53, LIJV: 41, RSV: 2, LSV: 4 | RIJV: 66, LIJV: 9, RSV: 18, LSV: 7   | IJV: 23, SV: 77   | RIJV: 69.5, LIJV: 21.1, RSV: 5.3, LSV: 4.0                             | IJV: 79, SV: 21  | IJV: 100        |
| <b>TTE views</b>                      | Subcostal, apical                  | Subcostal, apical  | Subcostal   | Subcostal, apical  | Subcostal, apical  | Subxiphoid      |
| <b>Misplaced catheters (TTE, %)</b>   | 17 (17/100)                        | 6 (7/105, performing qualitative MBT), 8.6 (9/105, performing usual TTE and vascular US)     | 29.3 (29/99)  | 2.0 (3/135)  | 2.2 (3/135)  | 0.9 (2/219)     |
| <b>Lung US views</b>                  | Not applied                        | Longitudinal and transversal scanning of both hemithoraces                                   | On PSL and laterally to the AAL in 3rd to 5th intercostal space | Anterior chest (on MCL at right hemithorax, on AAL at left hemithorax) | Not applied  | Not applied     |
| <b>Pneumothorax rate (Lung US, %)</b> | -                                  | 0  | 4 (4/99)  | 0  | -  | -               |
| <b>Comparative method</b>             | CXR                                | CXR  | CXR   | CXR  | CXR  | CXR             |
| <b>Misplaced catheters (CXR, %)</b>   | 12 (12/100)                        | 13 (14/105)  | 28.3 (28/99)  | 2.7 (4/135)  | 3 (4/135)  | 0.9 (2/219)     |
| <b>Pneumothorax rate (CXR, %)</b>     | 1 (1/100)                          | 0  | 2 (2/99)  | 0  | 1.5 (2/136)  | 0               |
| <b>Push to bubbles time (s)</b>       | -                                  | Overall: 0.18 [0.13-0.32]<br>Positive RASS: 0.17 [0.12-0.23]<br>Negative RASS: 1.4 [0.7-2.2] | -   | -  | Overall: 1.1 ( $\pm$ 0.3)<br>Negative RASS: 5.0 ( $\pm$ 1.7) | -               |
| <b>Sensitivity, specificity (%)</b>   | 100, 94                            | 50, 100 (performing qualitative MBT); 64, 100 (performing                                    | 96, 93  | 75, 100  | 75, 100  | 100, 100        |

|              |         |  |  |         |         |          |
|--------------|---------|--|--|---------|---------|----------|
|              |         | usual TTE and vascular US)   |  |         |         |          |
| PPV, NPV (%) | 70, 100 | 100, 93 (performing qualitative MBT); 100, 95 (performing usual TTE and vascular US) | -  | 100, 99 | 100, 99 | 100, 100 |
| Annotations  | -       | Elaborate protocol with electrical measuring device and scanning of image frames     | Combined MBT and vascular US of IJV and SV | -       | -       | -        |

Annotations: AAL: anterior axillary line, CICC: centrally inserted central catheter, CVC: central venous catheter, CXR: Chest X-ray, ED: Emergency Department, ICU: Intensive care unit, IJV: Internal jugular vein, IMC: Intermediate care unit, LIJV: left internal jugular vein, LSV: left subclavian vein, MBT: micro bubbles time, MCL: midclavicular line, NPV: negative predictive value, OR: operating room, PICC: peripherally inserted central catheter, PPV: positive predictive value, PSL: parasternal line, RASS: rapid atrial swirl sign, RIJV: right internal jugular vein, RSV: right subclavian vein, SV: subclavian vein, TEE: transoesophageal echocardiography, TTE: transthoracic echocardiography, US: ultrasound.