PRACTICAL Platform Trial

Manual of Operating Procedures for Bedside Monitoring Techniques Relevant to Respiratory Physiology

DIAPHRAGM ULTRASOUND

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Abbreviations

Tdi ……………………………………………………………… Diaphragm thickness (synonymous with Tdi,ee)
Tdi,ee ………………………………………………………… Diaphragm thickness measured at end expiration
Tdi,pi ……………………………………………………….. Diaphragm thickness measured at peak inspiration
TFdi ……………………………………………………….. Diaphragm thickening fraction, computed as below
TFdi,max …………………………… Diaphragm thickening fraction during a maximal inspiratory effort

Key Equations

TFdi (%) = [(Tdi,pi – Tdi,ee) / Tdi,ee] X 100

Diaphragm Thickness and Thickening fraction

Diaphragm structure and function can be assessed noninvasively at the bedside using ultrasound. Changes in diaphragm thickness over time can be used to evaluate the negative impacts of mechanical ventilation including the effects of over-assistance myotrauma (atrophy; decreasing end-expiratory thickness over time) and under-assistance myotrauma (possibly causing inflammation, edema; possibly associated with increasing end-expiratory thickness over time). These changes are correlated with adverse clinical outcomes in previous studies. Diaphragm thickening fraction either at rest during tidal breathing or during a maximal inspiratory effort allow assessment of diaphragm activity and function.

Required equipment

Ultrasound machine with a high frequency (10-15 MHz) linear array transducer (usually called “vascular” or “linear” probe).

How to image and record

a. IDENTIFYING THE DIAPHRAGM
    i. The patient should be in a semi-recumbent position (30-45 degrees) on his/her back.
    ii. Place the probe at the zone of apposition; along the right 8th - 10th intercostal space between the mid and anterior axillary line. The lung shadow should not enter the ultrasound field during inspiration.
    iii. Ensure the probe is angled in the sagittal plane so that it is situated entirely between the ribs and there is no rib artefact in the image.
    iv. Look for the two bright, white, and parallel lines of the pleural and peritoneal membranes (seen in Figure 1). The relatively hypoechoic costal diaphragm can be visualized between these lines.
    v. Mark the location of the probe on the patient’s body with an ink marker to ensure measurement of the exact same portion of the diaphragm over time.
    vi. A similar procedure may be used to visualize the left hemidiaphragm; the left side is often more difficult to visualize and measurement precision is much lower.

b. ACQUIRING IMAGES
    i. Once ready to record, place the ultrasound in M-mode. A single vertical scan line will appear. Place the line between the section where the pleural and peritoneal lines are clearest.
    ii. Run the M-mode over 2-3 full cycles of inspiration and expiration (change sweep speed as needed) and then freeze the image.

c. MEASUREMENTS
    i. Diaphragm thickness (Tdi) and tidal thickening fraction (TFdi):
        1. The goal of measuring diaphragm thickness at end expiration (Tdi,ee) is to assess diaphragm muscle mass.

2. The goal of measuring diaphragm thickening fraction during tidal breathing (TFdi) is to assess whether and how much the diaphragm is contracting.
3. Measurements are to be taken at end-expiration, where the diaphragm at its thinnest (diaphragm thickness, Tdi,ee) and at peak inspiration where thickest (Tdi,pi).
4. If the patient does not appear to be breathing, and no or minimal diaphragm thickening is evident during inspiration, Tdi,pi is measured at a location representative of diaphragm thickness during the inspiratory phase (in this case, it will be approximately the same as Tdi,ee) e.g. Figure 2. In the absence of diaphragm contractility or thickening, the inspiratory phase can be recognized by the transient change in hepatic echotexture during inspiration in the lower portion of the M mode image ("seashore" picture)
5. TFdi for each breath is computed as (Tdi,pi – Tdi,ee)/Tdi,ee x 100%.
6. Use the calipers to measure the thickness of the diaphragm internal to the hyperechoic pleural and peritoneal membranes (as per Figures 1 and 2). Note it is important to place the calipers directly above or below one another so that there is no time difference between the markers which may artificially increase the distance.
7. Measure the pair of values for Tdi,ee and Tdi,pi for the **SAME** breath. Measure at least two pairs on separate breaths in the same M-mode image (see Figures 1 and 2).
8. Then, acquire a second M-mode image and measure two pairs of Tdi,ee and Tdi,pi again.
9. Consequently you will have 4 measurements of Tdi,ee and 4 paired measurements to which calculate TFdi.
10. If the values from the second M mode image are not within 10% of the first image, repeat the M mode image acquisition until you obtain two images with a set of values within 10% of each other.

ii. Maximal diaphragm thickening fraction (TFdi,max):
1. The goal of measuring TFdi,max is to assess the maximum ability of the diaphragm to contract and shorten (visualized as muscular thickening in the zone of apposition).
2. Measurements are obtained as above, but during maximal volitional inspiratory efforts by the patient and with only one inspiratory effort recorded per image (see Figure 3).
3. To ensure adequate respiratory drive for maximal volitional effort for maximal diaphragm thickening assessment, measure airway occlusion pressure ($P_{0.1}$) on the ventilator; it should be at least 2 cm H_2O to

proceed. If it is less than 2 cm H_2O, consider having sedation or ventilatory support reduced to increase respiratory drive.

4. Once respiratory drive is adequate, ventilatory support should be temporarily reduced to a minimum level (PSV 0 cm H_2O, PEEP 0 cm H_2O; higher levels of PEEP may be maintained if needed for gas exchange).
5. Patients should be coached to make maximal volitional inspiratory efforts against a non-occluded airway (i.e., inspiratory capacity maneuver), and TFdi should be measured during these efforts.
6. If the patient is unable to follow commands to make maximal inspiratory efforts, a transient airway occlusion maneuver (the so-called Marini maneuver) can be applied for up to 20 seconds to stimulate increased respiratory effort. The occlusion is then released. TFdi,max is measured **AFTER** releasing the occlusion while the patient's respiratory effort remains elevated.
7. The measurement procedure can be repeated until the examiner is confident of an acceptable maximal volitional effort; the **HIGHEST** value of TFdi,max should be taken as the final measurement.

How to analyze

- Diaphragm thickness, Tdi, is the thickness at end expiration when the diaphragm is at its thinnest (measured as Tdi,ee).
- TFdi is measured using Tdi,ee and Tdi,pi and expressed as a percentage. It is calculated as:

$$TFdi\ (\%) = [(Tdi,pi - Tdi,ee) / Tdi,ee] \times 100$$

- A total of 4 values of Tdi,ee are averaged (2 measurements from each of 2 separate images) to obtain the estimate of Tdi,ee.
- TFdi is calculated separately for each of the 4 breaths (2 breaths from each of 2 separate images) and averaged to obtain the estimate of TFdi.

CRF data points to be obtained from the signal analysis

- Tdi,ee and tidal TFdi:
  i. All 4 measurements of pairs of Tdi,ee and Tdi,pi (express in mm, to one decimal place) of right hemidiaphragm (2 measurements each from 2 images) will be entered in the CRF.
  ii. TFdi can be automatically computed from these data points (minimizing need for bedside computations).
- Maximal TFdi:

i. The measurements of Tdi,ee and Tdi,pi during maximal inspiratory efforts giving the highest value for TFdi,max will be entered in the CRF.

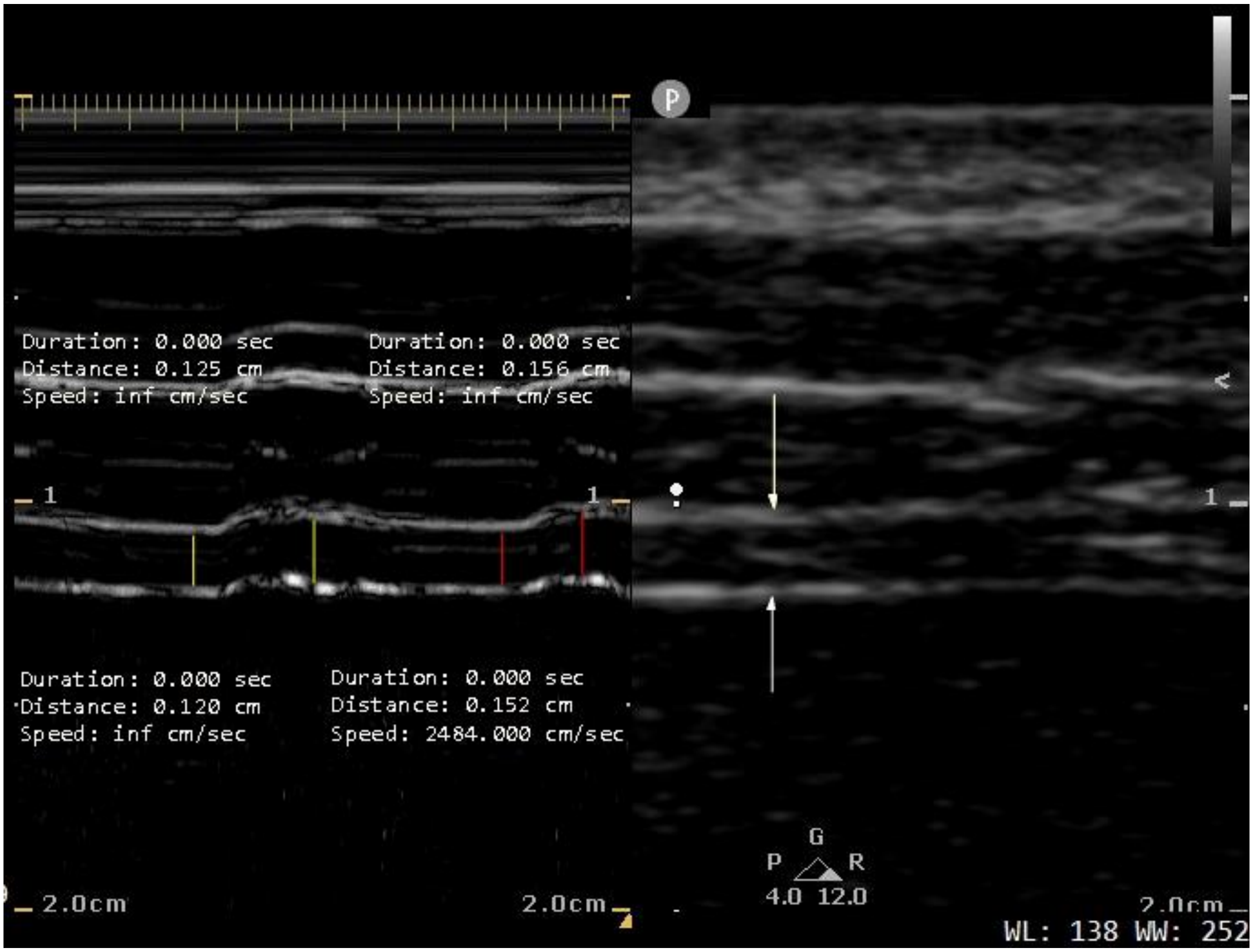

Figure 1: Ultrasound diaphragm thickness and thickening during tidal breathing. In the B mode image (right) the white arrows demonstrate the hyperechoic pleural and peritoneal membranes, the white dot places the vertical marker for M mode. In the M mode image (left), yellow lines measure Tdi,ee and Tdi,pi (left to right) of the first breath and red lines that of the second breath. Tdi (Tdi,ee) measures 1.2 and 1.3 mm, and TFdi 25% and 27% respectively.

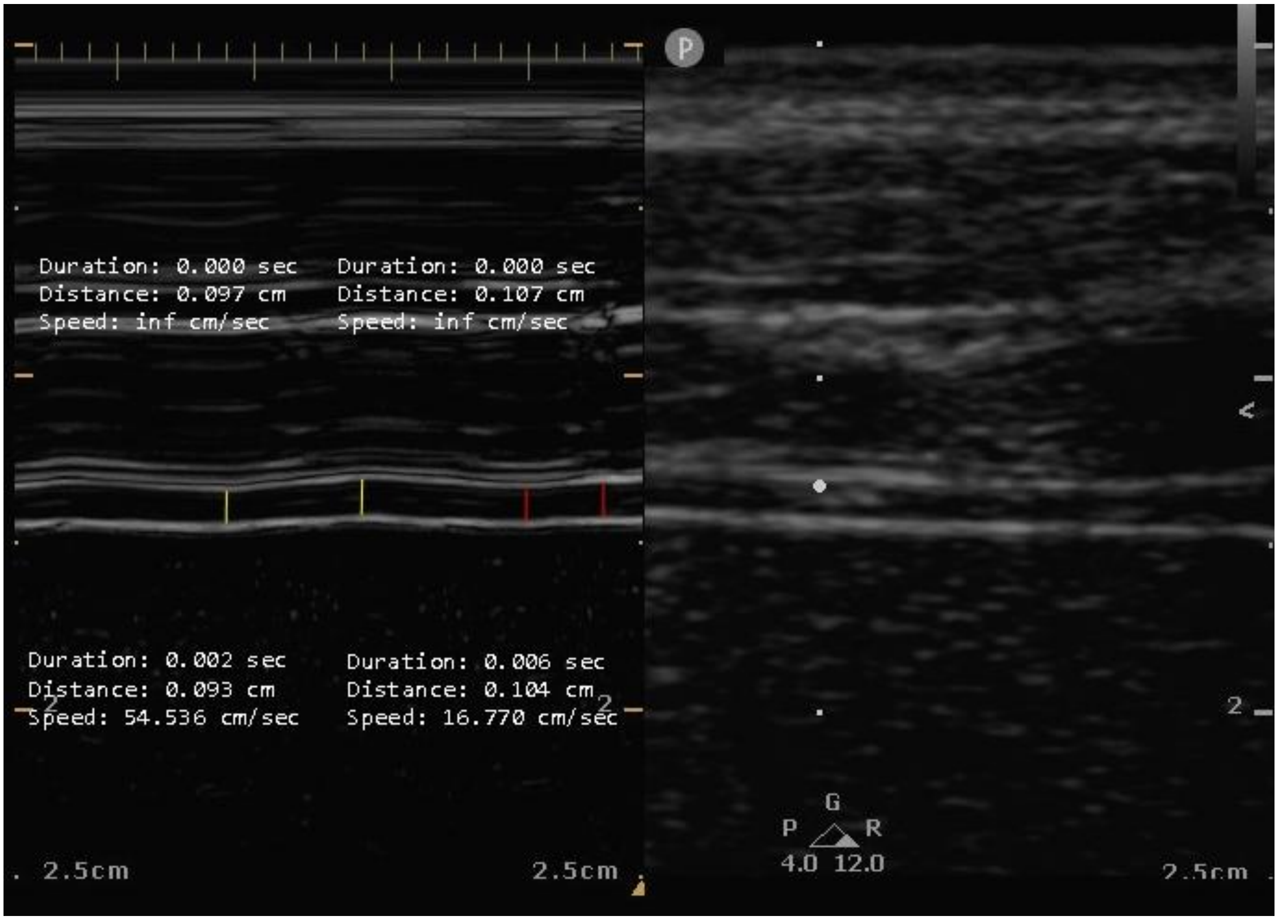

Figure 2: Ultrasound diaphragm thickness and thickening measured in the presence of minimal diaphragmatic contraction. B mode image is on the right and M mode on the left, with sweep speed adjusted to ensure two breaths are included. In absence of clear peak inspiratory thickness, timing of inspiratory effort is determined clinically at the bedside. TFdi here is calculated as 11% but would be averaged over a further two breaths (total four breaths captured in two images).

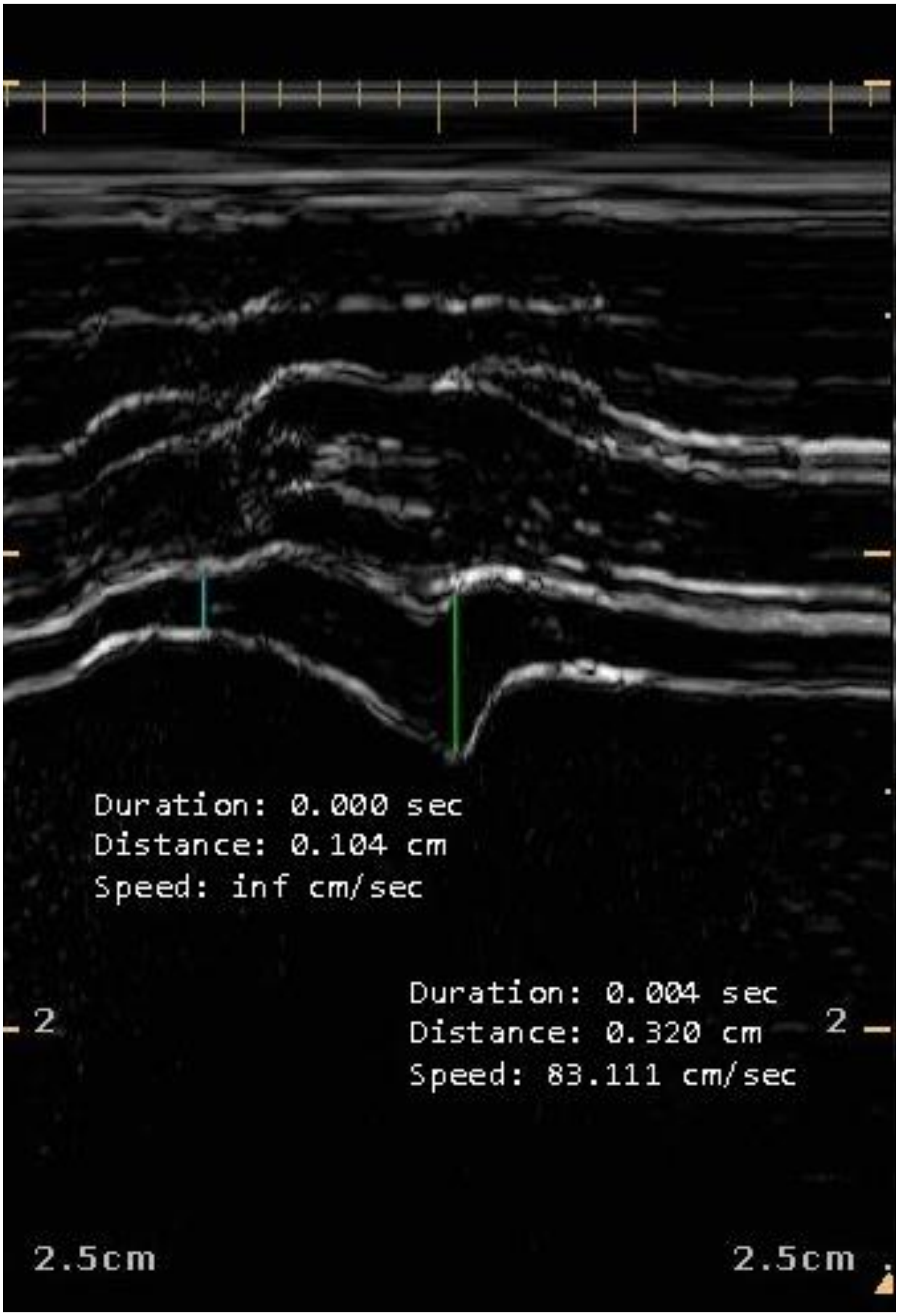

Figure 3: Maximal inspiratory thickening fraction measured with the patient on no inspiratory support (coached volitional maximal inspiratory effort; or following Marini mauver if noncompliant and P0.1 >2 cm. H_2O). Measurement of maximal inspiratory thickening fraction (TFdi,max) in M mode is calculated here as 208%. When the magnitude of volitional effort is in question, multiple attempts may be made to measure maximal thickening. The largest value of maximal TFdi obtained from all these attempts would be recorded as the maximal thickening fraction.

Diaphragm Excursion

Effective diaphragm contractions generate inspiratory flow and volume by lowering the dome of the diaphragm and elevating the lower rib cage. The degree of diaphragm descent caused by diaphragm contraction can be measured using ultrasound. The distance the dome descends is not just dependent on diaphragmatic force generation however but is also impacted by end-expiratory lung volume and lung mechanics. Reduced diaphragm excursion can predict diaphragm dysfunction and an increased duration of mechanical ventilation and hospitalization. Paradoxical diaphragm motion (negative excursion) can be observed in severe diaphragm dysfunction, large pleural effusions, or phrenic nerve injury.

Required equipment

Ultrasound machine with a 2-5 MHz phased array ("abdominal") ultrasound probe.

How to record

a. IDENTIFYING THE DIAPHRAGM

   i. The patient should be in a semi-recumbent position (30-45 degrees) on his/her back. Patients should be spontaneously ventilating **WITHOUT** any inspiratory assistance from the ventilator (i.e., performed on T-piece or CPAP without pressure support). If ventilatory assistance is not removed, then excursion may be attributable to ventilator support rather than diaphragmatic contraction, rendering the measurement invalid.

   ii. Place the probe placed below the subcostal margin in the midclavicular line. The probe should be kept perpendicular to the dome of the diaphragm in all planes to avoid inaccuracies from off-axis imaging.

   iii. The hyperechoic pleural/peritoneal membranes that envelop the diaphragm provide highly visible structures to measure descent on M mode.

   iv. If a single hemidiaphragm is being assessed, the right side should be measured. If both hemidiaphragms are being measured (right and left) the measurements should be labelled accordingly.

b. ACQUIRING IMAGES

   i. Once ready to record, place the ultrasound in M-mode. A single vertical scan line will appear. Place the line between the section where the diaphragm lines are the clearest ensuring this is perpendicular to the muscle to avoid measurement error by off-axis imaging.

   ii. Run the M-mode over ideally at least 3 full cycles of inspiration and expiration (to ensure full excursion captured; change sweep speed as needed) and then freeze the image.

   iii. Excursion may be measured during tidal inspiration or during a maximal inspiratory effort.

   iv. Note that the airway should not be occluded during excursion measurements, as occlusion will limit diaphragmatic motion.

c. <u>MEASUREMENTS</u>
   i. Use the calipers to measure the height from end-expiration to peak inspiration (peak to trough or highest and lowest points), as shown in Figure 4.
   ii. It is important to consider the direction of movement (paradoxical movement can occur with phrenic nerve injury, large pleural effusions and severe diaphragm dysfunction).
      i. With normal diaphragm activity the diaphragm will move toward the probe during inspiration.
      ii. With paradoxical motion, the diaphragm dome will move away from the probe during inspiration.
      iii. If the movement is paradoxical, then excursion must be recorded as a negative value. The peak and trough from the same breath should be used to compute excursion.
   iii. Motion of the dome of the diaphragm toward the ultrasound probe during inspiration (i.e. a descending diaphragm) is taken as a positive number. Motion of the dome away from the ultrasound probe during inspiration (paradoxical motion) is taken as a negative number.

How to analyze

Once confirmed, vertical distance is measured in cm for each breath. There is no further processing required.

CRF data points to be obtained from the signal analysis

Three measurements of diaphragm excursion (express in cm, to one decimal place) of right +/- left hemidiaphragm, during tidal +/- maximal inspiratory, as specified by the protocol. As previously mentioned for tidal excursion these should be within 10%, with the average taken as the true value.

For maximal excursion, the largest positive value (or if no positive values, the least negative value) should be taken as the true value.

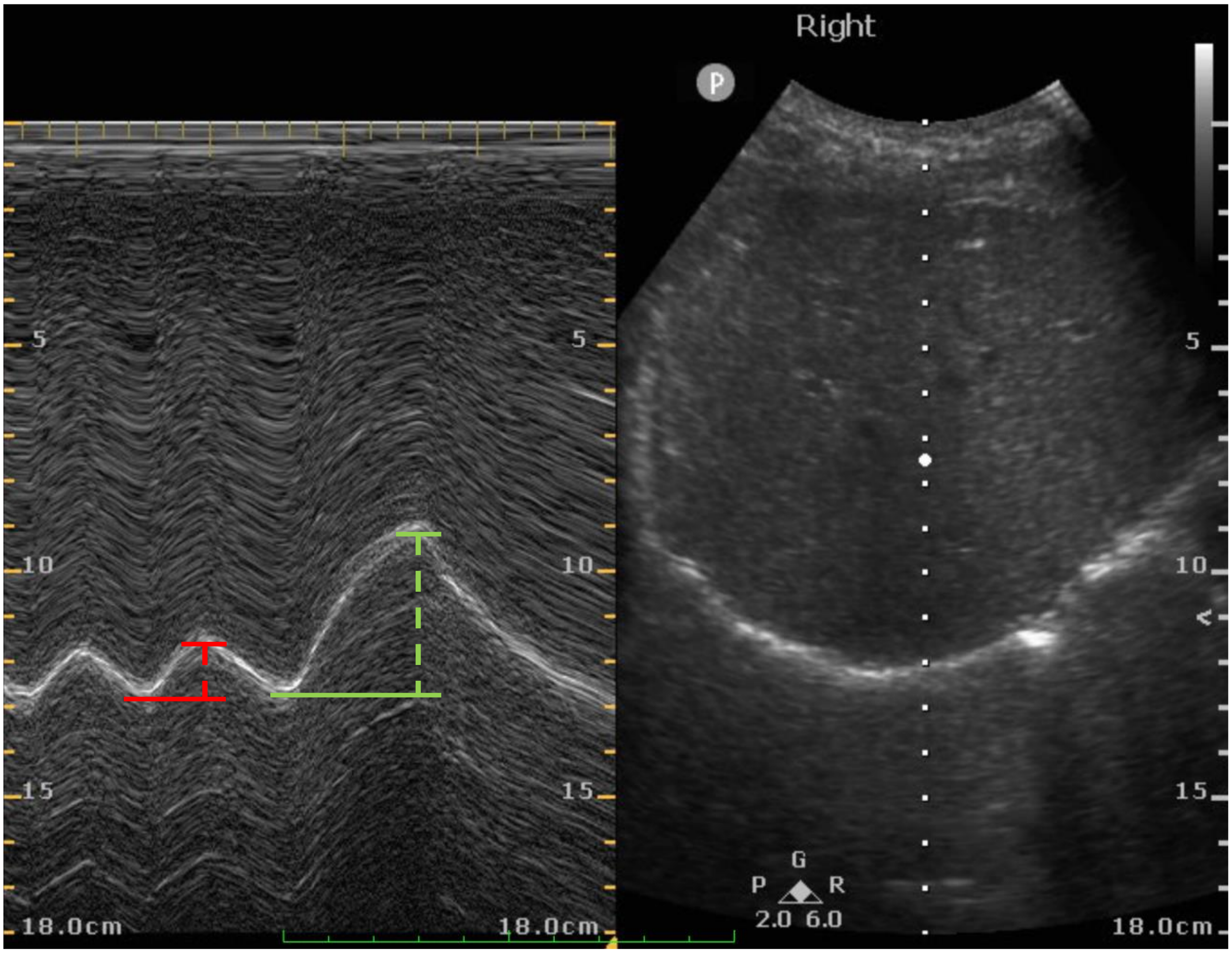

Figure 4: Tidal (red) and maximal (green) diaphragm excursion (right image B mode, left image M mode). The direction of movement of the dome of the diaphragm is descent (movement towards the probe; seen as movement 'upwards' on the image) during inspiration which is assessed clinically at the bedside. This is in keeping with positive diaphragm excursion and as such given a positive value. Here excursion distance (vertical height, not slope distance) is +1.8 cm and +3.4cm respectively.