

Ultrasound Detection of Pneumothorax

*Development of a porcine pneumothorax model
to assess and teach
lung ultrasound diagnostics.*

Nils Petter Oveland



Dissertation for the degree of philosophiae doctor (PhD)

University of Bergen, Norway

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*In memory of my father,
who taught me the value of hard work.*

Scientific environment

This thesis is the result of collaboration between the Norwegian Air Ambulance Foundation and Aarhus University/Aarhus University Hospital in Denmark. During the five-year research period, I also worked part-time at the Department of Anesthesiology and Intensive Care, Stavanger University Hospital. The study was also affiliated with the Department of Clinical Medicine at the University of Bergen, Norway.



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carefully listened to my ideas about prehospital ultrasound, and he has done nothing but believe in me since. Without his continued work and effort, there would not have been a Department of Research and Development at the Norwegian Air Ambulance Foundation. For providing me with this great opportunity, I can only hope to repay him with good research results.

I did not previously believe in fate, but this changed in 2008. My summer substitute at the air ambulance base in Stavanger was professor **Erik Sloth**, and he convinced me to embrace point-of-care ultrasonography and showed me how use mobile ultrasound machines at the patient's bedside to diagnose life-threatening conditions. He developed and began to use the Focus Assessed Transthoracic Echocardiography (FATE) protocol as early as 1989, which makes him one of the great pioneers of ultrasound in critical care. Furthermore, he agreed to become my co-supervisor for this project and taught me everything I know about heart and lung ultrasound. Throughout this project, I have enjoyed his good mood, thoughtful remarks and constant eagerness to improve and implement point-of-care ultrasound applications. Today, I can honestly say that I believe in FATE! Another great mentor and friend of mine is **Lars Knudsen**; his practical skills were crucial when we developed the porcine model and conducted our experiments, and he is always there for me when I need support.

The best thing about ultrasonography scanning is the ability to look inside of patients, rather than only being able to inspect, feel or auscultate for existing pathology. To express my thankfulness to the supervisors who have enlightened me, I quote Sir Isaac Newton: "If I have seen further, it is by standing on the shoulders of giants". In my opinion, my supervisors are all visionaries that not only think great thoughts but also act upon them. I will try to follow in your footsteps.

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List of publications

I

- Oveland NP, Sloth E, Andersen G, Lossius HM. A porcine pneumothorax model for teaching ultrasound diagnostics. *Academic Emergency Medicine* 2012; 19(5): 586-92.

II

- Oveland NP, Søreide E, Lossius HM, Johannessen F, Wemmelund KB, Aagaard R, Sloth E. The intrapleural volume threshold for ultrasound detection of pneumothoraces: an experimental study on porcine models. *Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine* March 2013 1; 21(1):11. In electronic format. (doi: 10.1186/1757-7241-21-11)

III

- Oveland NP, Lossius HM, Wemmelund K, Stokkeland PJ, Knudsen L, Sloth E. Using thoracic ultrasonography to accurately assess pneumothorax progression during positive pressure ventilation: a comparison with CT scanning. *Chest* 2013; 143(2): 415-22.

IV

- Oveland NP, Lossius HM, Aagaard R, Connolly J, Sloth E, Knudsen L. Animal laboratory training improves lung ultrasound proficiency and speed. *The Journal of Emergency Medicine* September 2013; 45(3): e71-e78. In electronic format. (<http://dx.doi.org/10.1016/j.jemermed.2013.03.029>)

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Abbreviations

ACCP	American College of Chest Physicians
ALT	Animal Laboratory Training
ATLS	Advanced Trauma Life Support
BTS	British Thoracic Society
CI	Confidence Interval
COPD	Chronic Obstructive Pulmonary Disease
CT	Computed Tomography
CXR	Chest X-Ray
FATE	Focus Assessed Transthoracic Echocardiography
GEE	Generalized Estimating Equations
IQR	Inter-quartile range
NASA	National Aeronautics and Space Administration
PTX	Pneumothorax
S-LP	Sternum-Lung Point
US	Ultrasound/Ultrasonography
WINFOCUS	World Interactive Network Focused on Critical Ultrasound

Abstract

Background

Pneumothorax (PTX) is common after blunt chest injury, and failure to diagnose and rapidly treat an enlarging PTX may cause patient death. The anteroposterior supine chest x-ray (CXR) is the least sensitive of all plain radiographic techniques for detecting PTX. Occult (i.e., if missed on CXR) PTX may subsequently be found by computed tomography (CT) scans, but both of these diagnostic tools are not readily available for the patient. Furthermore, other problems associated with these techniques include the radiation hazard, the time delay after ordering, and obtaining the specialized radiologist's dictation of the CXR and CT results. Contrary, lung ultrasonography (US) is a harmless point-of-care examination to accurately diagnose PTX. The debate is whether lung US should replace CXR as the preferred diagnostic study of injured patients with suspected PTX. This study sought to answer the following remaining questions:

Research questions

- Does lung US perform better than supine CXR and does it have the potential to diagnose even small amounts of intrapleural air?
- Could lung US be used to assess PTX progression during positive pressure ventilation?
- What is the optimal training method to accurately perform these lung US examinations?

We studied experimentally induced PTX in porcine models to answer these questions.

Methods

We validated our model by defining the PTX topography (i.e., the distribution of air within the chest) in the pigs using CT, to find similarities to PTXs in supine trauma patients (paper I: methodological article). Experimentally induced PTX was created by insufflation of air through unilateral or bilateral chest tubes. The size was modified

through incremental injections or the withdrawal of air followed by diagnostic testing using lung US, CXR or CT. This model was used in the following three sub-studies: in paper II to define the volume threshold of intrapleural air when PTXs are accurately diagnosed with lung US and CXR; in paper III to determine whether US can assess PTX progression during positive pressure ventilation; and in paper IV to evaluate whether training in an animal laboratory could improve diagnostic competency and speed of lung US detection of PTX among novices (medical students).

Results

In all of the porcine models, the distribution of intrathoracic air (predominantly in the anterior, medial and basal locations) resembled the PTX topography observed in studies of trauma patients. Lung US could diagnose very small PTXs with intrapleural air volumes as low as 10 mL (mean threshold volume of 18 mL). In addition, lung US was as accurate as CT in assessing the extent of PTXs during positive pressure ventilation when marking the lung points on the chest (i.e., the edge of the PTX where the lung is still in contact with the interior chest wall). As part of a laboratory-training program, scanning porcine PTX models improved lung US skills, increased confidence in making the diagnosis and reduced the scanning time per lung.

Conclusion

Lung US is a safe and very accurate diagnostic tool that can be used to diagnose small-sized PTXs otherwise undetectable on supine CXRs. Lung US can also assess PTX progression, known to be an independent factor of a patient's later need for chest tube insertion. This is potentially helpful in real clinical settings, as it may enable clinicians to use US to make treatment decisions. With the appropriate training, all clinicians can perform lung US examinations to detect PTXs, which suggests that this approach should be used as a valuable adjunctive to the clinical examination of patients with blunt chest trauma.

1. Introduction

1.1 Selection of topic

The thesis titled “Ultrasound detection of pneumothorax” was inspired from two self-experienced encounters with chest trauma patients. The clinical scenarios are retold in second-person grammar (i.e., you) to clarify the selection of the topic and the basic research questions.

Clinical scenarios

#1. You are an air ambulance doctor on call at a level-2 trauma center. During your shift, you are dispatched to a hunting accident where a 14-year-old boy has been shot in the chest and face. When you arrive at the scene 15 minutes later, the patient is lying on his back on the ground complaining of general chest pain and facial discomfort around his right eye. The clinical examination including auscultation shows no respiratory and circulatory instability, but the chest and face have multiple gunshot wounds from the metal pellets. On the way to the hospital, you perform an in-flight ultrasound (US) examination, which shows no sign of blood in the pericardium, abdomen or thorax. However, you suspect a small pneumothorax (PTX) in the left lung apex because the normal sliding movement between the two pleura layers is absent and the tip of lung reappears on the US screen with each breath (**Figure 1A**). Although these US signs of abnormal lung sliding and visible lung point are subtle, your suspicion is passed on to the trauma surgeon in the emergency department. The supine chest x-ray (CXR) shows the metal pellets but no PTX (**Figure 1B**). Subsequent computed tomography (CT) scans confirm the chest injury caused by the gunshot: a small 5 mm-thick apical PTX (**Figure 1C**). No chest tube is inserted, and the patient is brought to the operating room and intubated prior to eye surgery. After a review of the US, CXR and CT images, you question whether lung US would perform better than supine CXR, as this approach may be capable of diagnosing even small amounts of intrapleural air.

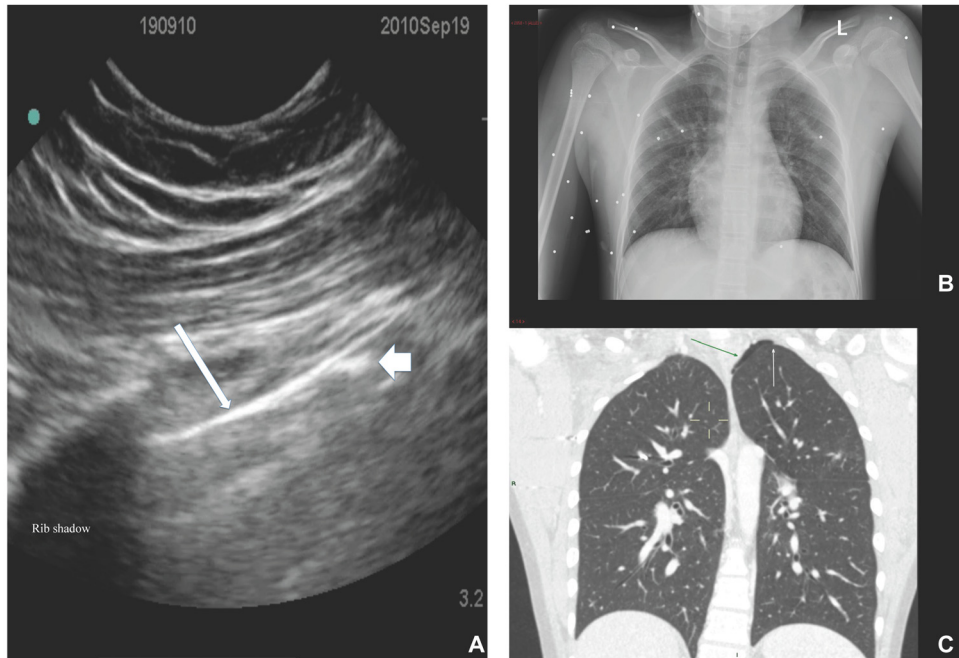


Figure 1. Case scenario. (A) Ultrasound image of a miniscule apical pneumothorax caused by penetrating trauma. The tip of the lung (thick arrow) has detached from the hyper-echoic pleural line (thin arrow) as air interposes the parietal and visceral pleural layers (i.e., the definition of a PTX). This lung point moves to and fro along the pleural line, in a manner synchronous with respiration (visible only on video clips). **(B)** Chest x-ray showing the multiple metal pellets from the gunshot. The pneumothorax is not visible. **(C)** Computed tomography confirming the small amount of intrapleural air displayed as a black pocket in the left lung apex (green arrow). The white arrow shows the lung point. (Photo: Nils Petter Oveland)

#2. You are dispatched to a motorcycle accident, where a 55-year-old male biker has gone off the road and hit a tree at high speed. When you arrive, the paramedics have placed the patient on a backboard, secured his neck with a collar and given him high-flow oxygen through a mask. He is anxious and complains of chest pain and dyspnea. The clinical examination shows no chest instability, but the respiratory rate is clearly elevated (40 breaths/minute) with symmetric breath sounds. The peripheral pulses are present; the heart rate is 136 beats/minute with no signs of external bleeding or long-

bone fractures. You perform a rapid sequence intubation, initiate positive pressure ventilation using a portable respirator and transport the patient via helicopter to a level-2 trauma center 15 minutes away. The trauma team there is notified. The initial assessment and supine CXR obtained in the emergency department do not show any thoracic injuries. The CT scan detects unstable L2 and C7 vertebral-body fractures, multiple small rib fractures, a sternum fracture and bilateral small PTXs in the anterior chest. The surgeon on call wants the patient transferred by helicopter to a level-1 trauma center 70 minutes away because the vertebral fractures are unstable. You express concern for having a patient in a helicopter with bilateral PTXs undergoing positive pressure ventilation and advocate for the insertion of chest tubes, but the surgeon disagrees. Because lung auscultation in-flight is impossible due to noise, you use the portable US machine to repeatedly scan the anterior chest of the patient every 10 minutes. The PTX is outlined on the patient's chest with a pen by marking the US sign "lung point" (i.e., the edge of the PTX where the lung is still in contact with the interior chest wall). The patient is transported to the level-1 trauma center without any progression of the PTX on either side. You question how accurate US is in identifying the lung point compared to CT and whether lung US could be used to assess PTX progression in chest trauma patients during positive pressure ventilation. Later, when you talk to your colleagues, they find this case report interesting but question the necessary training requirements for accurately performing such lung US examinations.

To address these research questions, we performed four sub-studies, in which we compared lung US to CXR and CT. We used an experimental study design in porcine models because we wanted to gradually increase and decrease the PTX size through injections and the withdrawal of air from the pleural cavity. Moreover, the design and radiation exposure required to obtain CXR and CT images precludes the use of real patients. Our results showed that lung US could detect even small-sized PTXs undiagnosed by CXRs, and may be used to follow the progression of PTX size during positive pressure ventilation. In addition, lung US can accurately be performed with the appropriate training. We believe our study supports the use of lung US as an important adjuvant to the clinical examination and continuous assessment of chest trauma patients.

1.2 Traumatic pneumothorax

1.2.1 Thoracic trauma

Trauma is one of the leading causes of death worldwide (5.1 million deaths in 2010) and can be characterized as a global epidemic because it accounts for one in every 10 deaths [1]. Patients with multiple blunt injuries are far more common in civilian practice, but both penetrating and blunt trauma present significant challenges to national health care systems and necessitate a policy action to prevent them [2]. Chest injury is the direct cause of death in 25% of blunt trauma victims and a contributing factor in up to another 50% of trauma deaths [3], which can be explained by the large number of motor vehicle crashes and falls [1, 4]. One serious consequence of chest trauma is PTX, a potential life-threatening condition that sometimes requires immediate treatment to prevent patient death [5]. Chapter one elucidates the basic clinical and diagnostic aspects of traumatic PTX.

1.2.2 Cardiothoracic anatomy

The thoracic cage is a bony structure that connects the posterior vertebral column and anterior sternum via the osteocartilaginous ribs. The thorax contains the heart, lungs, great vessels and esophagus (**Figure 2**) and is demarcated by the diaphragm inferiorly and structures of the neck and lung apices superiorly. The aorta, pulmonary artery, pulmonary veins and vena cava occupy the mediastinum, where they connect to the base of the heart. The heart is contained within the fibrous pericardium, and its apex projects into the left thoracic cavity [6]. In the right and left hemithorax, the pleural sac surrounds each lung; the parietal layer forms the external wall, and the visceral layer encloses the lung parenchyma. During ventilation, the visceral pleura is brought into contact with the parietal pleura, thereby reducing the pleural cavity to a closed, separate space. This space normally contains only a capillary layer of serous fluid that lubricates the apposed surfaces and reduces friction between the parietal and visceral pleura [7]. The dynamic to and fro sliding motion between the layers during respiration is the basis of lung US detection of PTX [8].

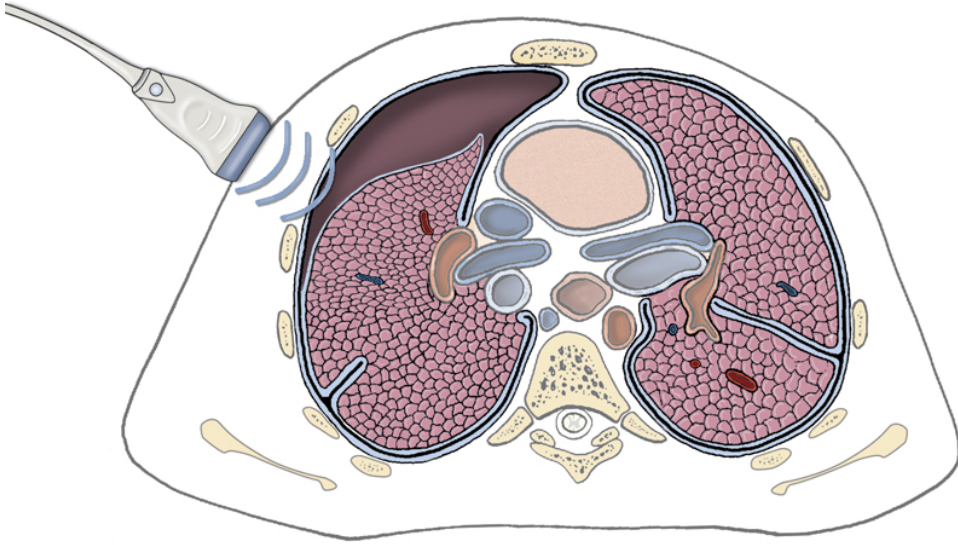


Figure 2. *Pneumothorax* is caused by one of the following mechanisms: air leaking from the airways (proximal or distal conduits) or the alveolar space; air communication between the pleural space and atmosphere; or presence of gas-producing organisms within the pleura. (Illustration: Kari M. Toverud [certified medical illustrator]) This figure was reprinted with permission from ACCP (paper III).

1.2.3 Definition

Pneumothorax is a common clinical condition where air is present in the pleural space (**Figure 2**). When air separates the parietal and visceral pleural layers, the negative intrapleural pressure that keeps the lungs distended is disrupted, leading to a collapse of the elastic lung parenchyma and expansion of the thoracic cage [9].

1.2.4 Classification

There are different classification categories for PTX (**Table 1**). According to etiology, PTXs are classified as either spontaneous or traumatic. A PTX is classified as primary spontaneous if no obvious precipitating factor is present and as secondary spontaneous if the patient has an underlying disease (e.g., COPD, cystic fibrosis). Traumatic PTX is either iatrogenic (i.e., caused by transthoracic or transbronchial biopsies, central

venous catheterizations, pleural biopsy, thoracentesis) or non-iatrogenic following blunt or penetrating chest injuries [9]. PTXs can have a wide continuum of severity, ranging from simple asymptomatic PTX caused by disruption of the pleura space to tension PTX associated with increased intrathoracic pressure [6]. The increasing use of CT to investigate thoraco-abdominal trauma allows for a more precise and three-dimensional evaluation of the thorax. Intrapleural air not seen on supine CXRs is often seen on CT, and this entity is defined as occult PTX (**Figure 3**) [10].

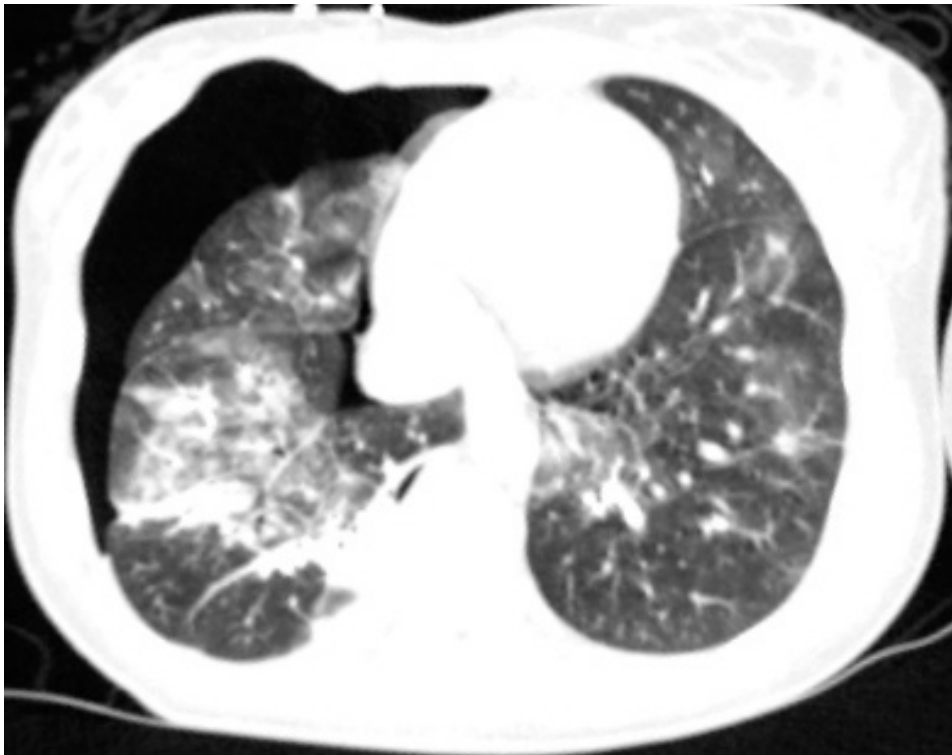


Figure 3. *Occult pneumothorax* after blunt chest trauma. The large amount of intrapleural air anterior to the right lung was not visible on the supine CXR but was subsequently diagnosed on the CT scan images. (Photo: Nils Petter Oveland)

Table 1. Classification of pneumothorax

Etiology	Spontaneous	<p>Primary: no underlying disease</p> <p>Secondary: associated underlying disease</p> <p>Catamenial: in menstruation due to thoracic endometriosis</p>
	Traumatic	<p>Iatrogenic: secondary to medical procedures or positive pressure ventilation</p> <p>Non-iatrogenic: secondary to blunt or penetrating chest trauma</p>
Radiological appearance	Overt	PTX diagnosed by physical examination or as seen on supine CXR
	Occult	PTX neither diagnosed by physical examination nor seen on supine CXR
Clinical severity	Simple	PTX with non-tension physiology
	Tension	PTX with tension physiology resulting in cardiopulmonary collapse (hypotension and hypoxemia)

Abbreviations: CXR: Chest x-ray; PTX: pneumothorax

1.2.5 Epidemiology

In addition to rib fractures and pulmonary contusions, PTXs are the most common chest injuries found in patients with blunt trauma [11, 12]. In a population-based study from Italy, PTX was present in one in every five severely traumatized patients (i.e., a incidence of 81 per one million citizens per year) [5]. These results are consistent with a study of chest injuries from the regional trauma center in Trondheim, Norway, where the most common thoracic injury was rib fracture (55%), and the most common internal thoracic injury was PTX (24%) [13]. A high incidence of extrathoracic injuries, such as head trauma and musculoskeletal injuries, in the extremities has also been associated with major blunt trauma [6, 13], and only the minority of patients with PTX (5%) have isolated chest injuries [3]. Furthermore, PTXs are associated with greater on-scene physiological instability (i.e., low blood pressure and low oxygen saturation) compared to other chest injuries of similar severity [5]. These findings draw attention to the association between PTX and tension physiology, as well as the potential benefits of decompression procedures.

1.2.6 Tension pneumothorax

If air is allowed to enter (from the lung or through the chest wall) but not exit the pleural space via a “one-way valve”-like opening, a tension PTX will quickly develop. The increasing pressure deranges the cardiorespiratory capacity of the patient and makes this an insidious and life-threatening event. This condition is most often seen in the prehospital, emergency department, trauma unit and critical care settings [14]. The instability of trauma patients with PTX [5] may be explained by the progressive accumulation of air within the pleural space, which exerts mechanical pressure on internal structures. The affected lung may then collapse, with a possible shift of the organs to the contralateral thoracic side. Such a mediastinal shift severely impairs the circulation by pinching the central venous return to the heart (**Figure 4**) and reduces ventilation by compressing the remaining lung. Furthermore, the resulting hypotension and hypoxemia can lead to cardiac arrest, at which point diagnostic and treatment delays are highly lethal [6, 14, 15]. Thus, PTXs are a notable cause of preventable

death (i.e., in approximately 16% of prehospital trauma cases) [5, 16, 17] where simple field-friendly interventions may be lifesaving [18].

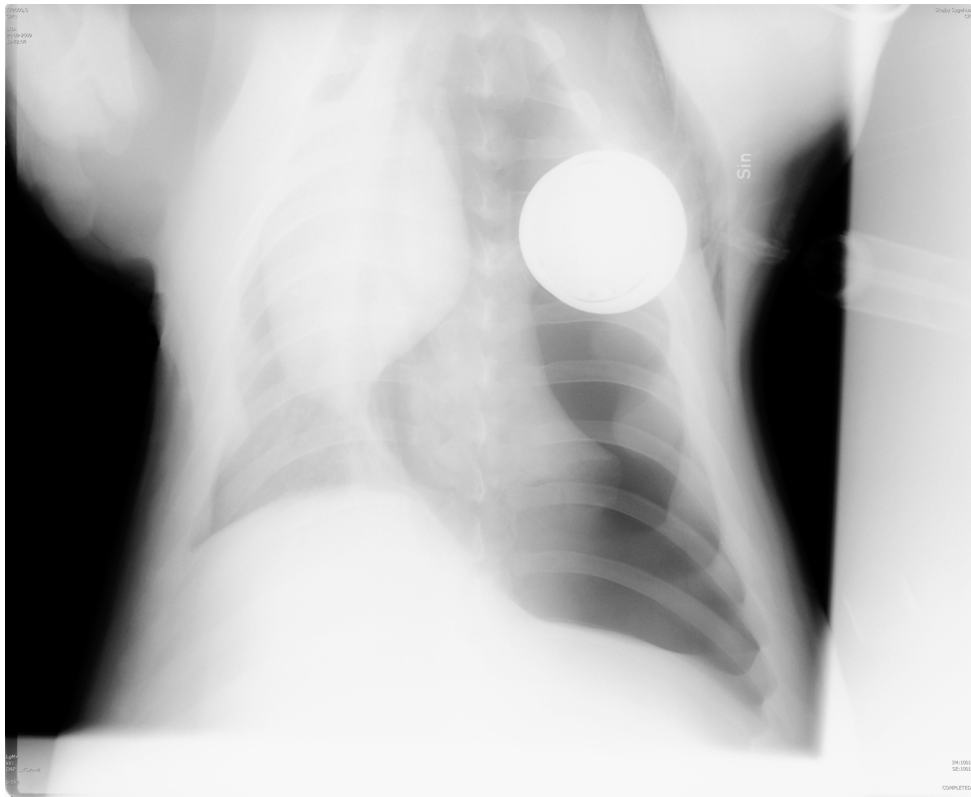


Figure 4. Tension pneumothorax on the left side in a porcine model. The expanding intrapleural air mass pushes the heart over the midline into the contralateral right hemithorax, impairing the lung capacity. The large vessels and right heart chambers are mechanically compressed, which causes cardiovascular collapse due to occlusion of the venous return to the heart and a dramatic drop in cardiac output. (Photo: Nils Petter Oveland)

1.2.7 Treatment

The treatment strategy for traumatic PTX has historically consisted of decompression procedures to release the intrathoracic air, either with a needle or a larger bore chest tube. A clinical suspicion of tension PTX mandates immediate decompression and

should not be delayed by radiological confirmation [6]. The needle thoracostomy is a temporary maneuver that may convert tension PTX to simple PTX [19], and a chest tube connected to a water-sealed suction system can be used to re-expand the lung and definitively close the air leak [6, 18]. The traditional management for PTX cases identified by physical examination or CXR (i.e., overt PTX) has consisted of chest tube insertion, based on the argument that a PTX can evolve into a tension PTX [10, 20]. This argument has been more strongly emphasized for patients undergoing positive pressure ventilation, as reflected in all versions, including the latest 8th edition, of Advanced Trauma Life Support (ATLS) for doctors (the Student Course Manual). These recommendations have stated that neither general anesthesia nor mechanical ventilation should be administered to a patient with PTX until a chest tube is in place [21]. The liberal use of “whole-body” CT scanning of blunt trauma patients has resulted in increased numbers of occult PTXs (i.e., approximately five percent of all trauma registry patients [22]) that would otherwise have gone undiagnosed. The management of occult PTX is controversial, and it is unclear whether these patients require the same treatment as patients with overt PTX [12, 22-25]. In a retrospective study, 65% of injured patients with overt PTXs were drained, compared to only 31% of patients with occult PTXs, and the same diversity was observed in a cohort of mechanically ventilated patients (95% of overt PTXs and 76% of occult PTX received tube thoracostomy [24, 26]). Similar differences in clinical practice have also been seen in other studies [25, 27] and are difficult to explain when considering that both overt and occult PTXs are similar in regard to size and distribution of intrathoracic air [23]. This two-sidedness is also apparent in the latest trauma textbooks; for example, the 8th edition ATLS manual advocates that pleural decompression is standard care [21], while the 2012 book “Trauma” by Mattox, Moore and Feliciano introduces the more prudent practice of simply observing asymptomatic occult PTX cases even if the patients require operation for other injuries or positive pressure ventilation [28]. In general, it seems that small- to moderate-sized occult PTXs in spontaneously breathing patients can safely be observed [10, 29], but prospectively collected data from randomized controlled trials are needed to assess whether cohorts of patients receiving mechanical ventilation can avoid tube thoracostomy [22]. This is important because

unnecessary insertions of chest drains are dangerous and incur a 22% risk of major complications (e.g., pain, intercostal artery bleeding, intra-parenchymal lung injuries, tube misplacement and infections such as empyema and wound infections [30]). The outcome data for management of occult PTX cases obtained from four prospective studies identified in a Medline search are shown in **Table 2**. The studies arrived at somewhat different conclusions, but only one supported tube thoracostomy for all patients on positive pressure ventilation [31]. The two other prospective randomized trials [32, 33] did not report significant outcome differences between patients who were observed and those who received chest tubes. Furthermore, the prospective, observational, multicenter study from 2011 [12] did not randomize trauma patients to receive drainage or observation but rather specifically followed the observation group. The successfully observed patients and those who failed observation (i.e., initially observed but later in need of chest tube) were compared, and an observational strategy for occult PTXs was found to be safe, although a multivariate analysis identified respiratory distress and progression of PTX size (i.e., occult PTX subsequently identified on follow-up CXR) as independent factors associated with observational failure [12]. Recent literature reviews of both retrospective [22] and prospective studies [20] have failed to provide sufficient evidence that clinicians can safely omit tube thoracostomy in mechanically ventilated patients with occult PTXs, which is likely due to the small sample sizes in published studies or the lack of adequate statistical power to identify differences between treatment and observation groups. The OPTICC trial, a large multicenter, randomized, controlled phase III trial, is currently recruiting patients in Canada and aims to be completed by 2015 (**Table 2**). Hopefully, the results from this study will define the optimal management of occult PTX [33]. In addition, several non-clinical factors may influence treatment decisions, and the diagnostic strategies (CXR, CT, lung US or close clinical examination) that are most appropriate for subsequent observation of occult PTXs remain unknown [22]. Regardless of the method used, all occult PTXs should receive a chest drain if close observation is not possible (e.g., patients in the operating room covered with drapes and patients inside of helicopters where there are limited monitoring opportunities and air pressure changes).

Table 2. Outcome data for the management of occult pneumothoraces (PTXs)

Reference	Design	Patients; no. and type of trauma	Intervention / Comparisons	Outcome; no. of patients	Recommendations
Anderson et al. (1993) [31]	Prospective, randomized	40, blunt and penetrating trauma; 27 on positive pressure ventilation.	Observation vs. Tube thoracostomy	8 out of 21 observed patients had progression of their occult PTX, with 3 developing tension PTX.	A chest tube is required for ventilated patients.
Brasel et al. (1999) [32]	Prospective, randomized	39, blunt trauma; 18 on positive pressure ventilation.	Observation vs. Tube thoracostomy	3 out of 21 observed patients had progression of their occult PTX, and 2 of them received chest tubes.	Observation is safe.
Ouellet et al. (2009) [33]	Prospective, randomized	22, blunt trauma; all on positive pressure ventilation or en route to surgery.	Observation vs. Pleural drainage (tube thoracostomy or other pleural catheters)	4 out of 13 observed patients had progression of their occult PTX and non-urgently received chest tubes.	No differences in morbidity between the observation and treatment group. This OPTICC trial pilot proved safe and feasible ^{a)}
Moore et al. (2011) [12]	Prospective, observational, multicenter	569, blunt trauma; 448 (79%) were observed; 73 on positive pressure ventilation.	Successfully observed patients vs. Failed observation (i.e., subsequently required a chest tube)	27 out of 448 failed observation and required tube thoracostomy for occult PTX progression.	Most occult PTXs can safely be observed, but respiratory distress and PTX progression is independently associated with observation failure.

^{a)}The on-going OPTICC trial aims to randomize 430 mechanically ventilated patients with occult pneumothorax to either observation or insertion of chest tubes.

1.2.8 Chapter summary

Pneumothorax, which is common after blunt thoracic trauma, is associated with on-scene patient instability. Severe hypotension and hypoxemia in a patient with suspected PTX could be caused by increased intrathoracic pressure (i.e., tension PTX) and should expedite chest decompression procedures (e.g., needle decompression or tube thoracostomy). Undiagnosed patients that don't receive treatment might die. Pneumothoraxes that initially are missed on CXRs (i.e., occult PTXs) are more likely to be managed without insertion of chest tubes. However, also small- and medium-sized PTXs may expand and become a concern for positive pressure ventilated patients. Such a progression strongly suggests that an observation-only strategy should be terminated. In fact, PTX progression holds a 70-fold increased risk for requiring chest tube insertion. Thus, a reliable, easy, and repeatable diagnostic method to monitor any on-going expansion of intrapleural air is needed.

1.3 Diagnostic evaluation of pneumothorax

1.3.1 Physical examination

The treatment of seriously injured patients requires a rapid assessment of their injuries to provide life-preserving therapy. The physical examination is, and has always been, a pre-requisite for the medical management of trauma patients [34]. In time-critical situations, a systematic approach is desirable; in the ATLS Students Course Manual, such an approach is termed the primary survey and constitutes the ABCDEs of trauma care (i.e., Airway with spine control, Breathing and ventilation, Circulation with hemorrhage control, Disability/neurologic status and Exposure/Environment control). The physical examination of the chest includes inspection (looking for signs of injury, symmetry of the thorax and abnormal breathing movements, distended neck veins), palpation (searching for subcutaneous emphysema, localized chest pain, crepitation, instability of the thorax and tracheal deviation), percussion (tympani or dullness) and finally auscultation (presence of breathing sounds and lateralization) [18]. Clinically, a PTX is characterized by mild

to severe signs and symptoms of chest pain (due to rib fractures), dyspnea, tachypnea, cyanosis, tachycardia, hypotension, contralateral tracheal deviation and ipsilateral lung hyper-resonance with diminished or absent breathing sounds (**Figure 5**) [6]. The chest examination represents a collection of separate diagnostic tests, where some have been proven to correlate well with pathological findings and can be useful for treatment decision-making (e.g., performing pleural decompression, correct triage and transport to appropriate trauma centers) [18]. To palpate for subcutaneous emphysema, crepitation from rib fractures, pain and thoracic cage instability combined with measurements of pulse rate, blood pressure and arterial oxygen saturation measurements are helpful [5, 35]. In particular, subcutaneous emphysema is a strong clinical predictor for concurrent PTX, although this sign is often absent despite injury (i.e., not found in 85% of patients with an actual PTX [26]). Various percussion techniques have also been used to diagnose PTXs in mechanically ventilated patients in the intensive care unit [36]. The most reliable part of the physical examination is the auscultation of the lungs because the clinical suspicion of PTX is reinforced by diminished or absent breath sounds on the affected side [35, 37]. The diagnostic accuracy further improves if the patient complains of respiratory distress and presents an increased respiratory rate [18]; however, auscultation often is difficult due to environmental noise (e.g., during air transport or in the emergency department [38]) and because unequal breath sounds can be caused by either air (PTX) or blood (hemothorax) within the pleural cavity. Moreover, the physical examination can be misleading, and diagnoses solely based on auscultation fail to detect up to 20-30% of PTXs [3, 39]. Although some large PTXs can be identified [39], others may be overlooked but can become clinically relevant [10, 24]. Furthermore, the fact that a high incidence of extrathoracic injuries is associated with blunt trauma makes the diagnosis of PTX even more challenging. Therefore, diagnostic adjuncts are needed as an extension of the physical examination.

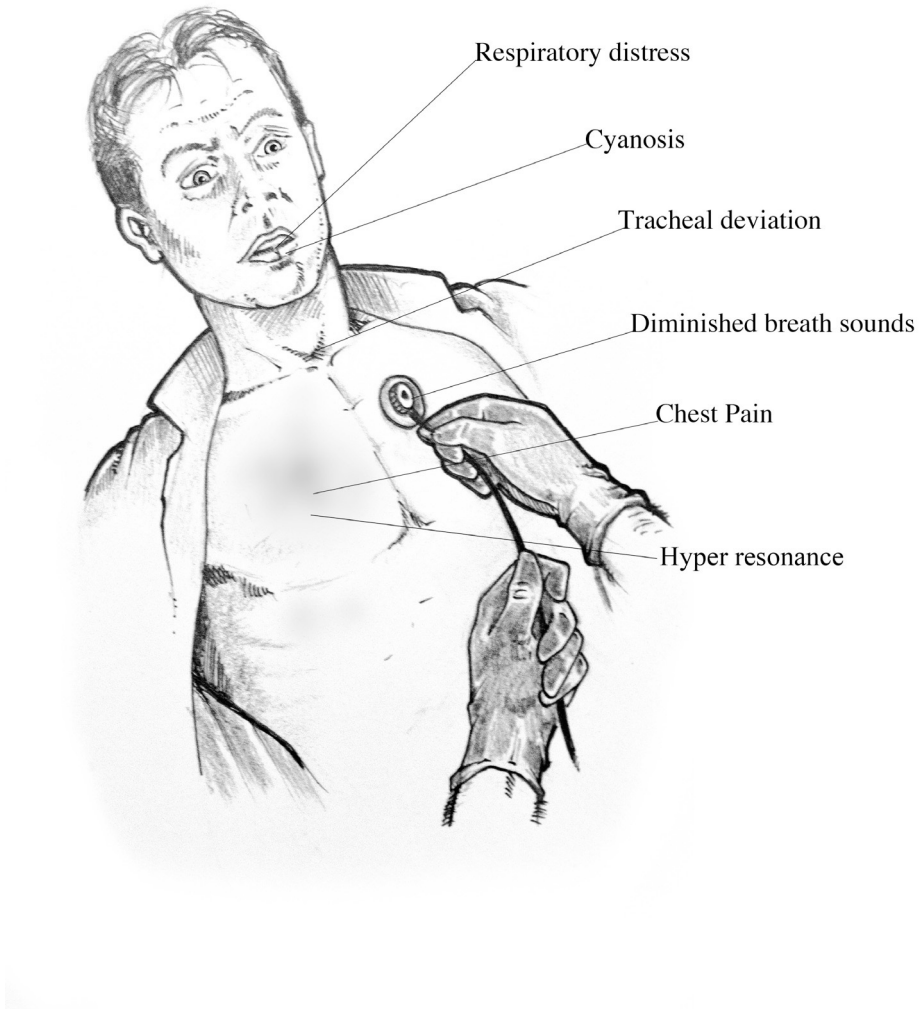


Figure 5. Clinical manifestations of pneumothorax. (Illustration: Kim Söderstrøm [medical illustrator])

1.3.2 Release of air

In some trauma patients, the expedited insertion of chest tubes is necessary. If there is release of air, a characteristic hiss can be heard and used to confirm the correct diagnosis of PTX. However, this invasive procedure is only to be used in

physiological non-permissive patients who are too unstable to await further diagnostic imaging.

1.3.3 Chest x-ray

The portable anteroposterior CXR is routinely obtained as the first radiograph in most trauma patients, and through the use of modern digital machines, these pictures are readily available for the medical team [34]. However, both lung fields must be examined carefully for the presence of PTX signs, as defined in **Figure 6** [40]. Subcutaneous air in the soft tissue should not be overlooked because this is a pathognomonic sign of lung and airway leakage [26]. Injured patients are often confined to the supine position (strapped to backboards) for neuro-axial protection, and the location of a PTX within the chest is directly associated with the force of gravity, the elastic recoil of the lung and the attachment of the lung to the hilar structures. The intrapleural air therefore collects anteromedially in the least-dependent pleural space [41, 42]. Air trapped anterior and medial to the lung is particularly difficult to detect and quantify on supine CXRs, and even large air pockets may be overlooked at hospitalization (**Figure 3**) [23]. In one large prospective observational study of multiply injured patients, the incidence of these occult PTXs was 76% when the supine CXR was interpreted by the trauma team in the emergency department [26]. Most studies refer to board-certified radiologist dictations when reporting the proportion of PTXs that are occult (30% to 55% [24, 25, 27, 43, 44]), although the time required to request and obtain the result of a CXR can be as long as 20 minutes [45]. Therefore, it is the initial interpretations made by the trauma team, and not the delayed dictations by the radiologist, that results in treatment decisions. The conventional supine anteroposterior CXR remains the most available, but least sensitive, of all plain radiographic techniques for diagnosing PTX [23].

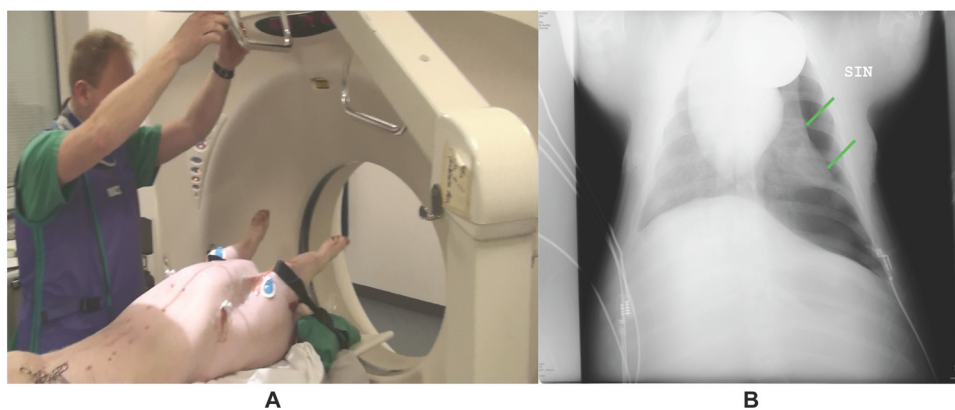


Figure 6. Anteroposterior chest x-ray taken in the supine position of the porcine model. **A)** The radiographic field was adjusted to cover the thorax from the apex to the base. **B)** Classic appearance of left-sided pneumothorax with a readily apparent visceral pleural line (green arrows), depressed diaphragm and the deep sulcus sign (i.e., enlargement of the costophrenic angle). (Photo: Nils Petter Oveland)

1.3.4 Computed tomography

A modern-generation CT scanner is an extremely valuable diagnostic tool with a high sensitivity for blunt aortic injury, great vessel injury, thoracic fractures, pulmonary contusions, hemothorax and PTX. From a multi-slice CT scan of the chest, coronal (**Figure 1**), sagittal and transverse (**Figures 2 and 3**) reconstructions of the thorax are possible, and CT imaging can therefore detect all types of PTX and provide a precise evaluation of intrapleural air [2, 34]. In fact, the awareness of occult PTXs began when intrapleural air was incidentally detected on the upper and lower parts of abdominal and head CT scans, respectively [46, 47]. At present, CT imaging is the reference diagnostic standard to safely rule out or diagnose PTX [34], although it remains disputed which patients should receive thoracic CT after blunt trauma. The value of diagnosing all occult thoracic injuries via a “whole-body” trauma scan is uncertain because few of these additional abnormalities have demonstrated clinical importance [48]. Thus, the pendulum may have swung too far, and an emergent CT scan of the chest after obtaining a negative CXR should not be routinely performed because this type of examination comes with a substantial cost. The radiation hazard

[49-51] is eminent, and the need for patient transportation to the radiology department and the time required to obtain such images can result in delayed diagnosis [45]. Indeed, timing is often critical for physiological non-permissive trauma patients because CT scanning prolongs the time to lifesaving resuscitation (hence, the expression “tunnel of death”).

1.3.5 Chapter summary

Physicians are challenged with a diagnostic dilemma when encountering trauma patients because a physical examination combined an anteroposterior supine CXR is insufficient to diagnose a PTX. Emergent CT scans of the chest can detect all PTXs but have disadvantages, such as exposure to radiation. In addition, in settings such as prehospital, battlefield and remote areas, the clinicians do not have access to these diagnostic modalities. Thus, an accurate mobile method for diagnosing PTXs is needed. Lung US meets these requirements and can be performed in almost any clinical setting. It is a non-invasive, radiation-free, rapid and repeatable bedside diagnostic test that has been shown to be more sensitive than and equally specific as supine CXR.

1.4 Lung ultrasonography

1.4.1 History of the use of ultrasound in medicine

Acoustics is the science of mechanical waves and dates back to Pythagoras, who in the 6th century BC wrote about the mathematical properties of stringed instruments [52]. Sound is a sequence of pressure waves that propagates through a solid, liquid or gas medium and has frequencies from approximately 20 to 20000 hertz (i.e., the range perceptible to the human ear) [53]. Ultrasound is the term used for pressure waves whose frequencies exceed the upper hearing limit, and these types of pressure waves are utilized in multiple industrial applications for detection and cleaning and to take measurements [54]. In addition, US is a medical imaging modality that provides immense diagnostic capabilities and facilitates invasive procedures requiring precision. Both of these uses have contributed to patient care for more than 60 years

[55]. The history of the use of US in medicine and biology follows the related developments in physics, technology and the construction of the needed equipment. A brief summary of key achievements follows [54, 55]:

1794- The Italian biologist Lazzaro Spallanzani demonstrates echolocation in bats.

1842- The Doppler effect (i.e., the change in pitch when the source of vibrations is moving toward or away from the observer) is described by the Austrian physicist Christian Doppler.

1880- The brothers Pierre and Jacques Curie discover the piezoelectric effect in certain crystals (i.e., the conversion of electrical impulses into US waves and vice versa), a fundamental component of today's US probes.

1915- After the Titanic tragedy (1912), the French physicist Paul Langevin makes the first piezoelectric echo probe in an effort to detect icebergs and submarines (used during World War I).

1940s- US energy is applied to the human body for medical purposes (e.g., Dr. Karl Dussvik (Austria) detects brain tumors, Dr. George Ludwig (USA) diagnoses gallstones, and Dr. John Wild (UK) assesses the thickness of bowel tissue).

1952- Douglas Howry and Joseph Holmes construct the first brightness (B-mode) instrument that produces good two-dimensional images at the University of Colorado, USA.

1953- The Swedish cardiologist Inge Edler and the physicist Carl Hellmuth Hertz measure heart activity.

1958- The first reports of the use of US in obstetrics and gynecology come from Glasgow, Scotland, by Professor Ian Donald. His paper "Investigation of Abdominal Masses by Pulsed Ultrasound" (Lancet) is one of the most important papers ever published in the field of diagnostic medical imaging and changed the paradigm of obstetric measurements of fetal growth and development.

1960s- Initially, the image quality from US machines was poor, but the 1960s saw the beginning of dedicated inventors, companies and organizations that through development and research advanced the technology and medical use of US. The innovations, including real-time imaging, Doppler-US, all-digital systems and three-dimension/four-dimension imaging, are too numerous to list.

The diffusion of US use through medical specialties follows a timeline from the innovators (e.g., cardiology and obstetrics/gynecology) to the early adopters (e.g., radiology and surgery), the early majority (e.g., critical care, emergency medicine and psychiatry), the late majority (e.g., anesthesiology, internal medicine and pediatrics) and the laggards (e.g., general practitioners and prehospital emergency medicine). Over the past two decades, the development of compact battery-powered US machines that produce high-quality images has facilitated the growth of point-of-care US (i.e., US performed and interpreted by the clinician at the bedside) [56]. This concept is based on focused (“limited” or “goal directed”) examinations to efficiently diagnose or rule out life-threatening conditions. Two examples are the Focused Assessment with Sonography for Trauma [57, 58] and the Focus Assessed Transthoracic Echocardiography protocols [59]. The latter was developed in 1989 by one of the pioneers of point-of-care US, Professor Erik Sloth from Denmark, and has been used since that time. Another pioneer was Dr. Daniel A. Lichtenstein, a French intensivist, who developed lung US protocols for patients with acute respiratory failure [60] and introduced the idea of “whole body US in the critical ill” [61]. Later, others followed with great textbooks on emergency and critical care US [62-64].

The history of lung US started, in a manner similar to our use of US on pigs, when a veterinarian detected a PTX in a horse in 1986 [65]. This discovery was then reproduced in humans shortly thereafter [66, 67], but there was little practical use of US for the diagnosis of PTX before Lichtenstein et al. published three cornerstone articles on dynamic and static US signs in the lung in the 1990s [68-70], preceding today’s algorithms[8, 71]. In the last decade, many well-performed retrospective reviews and a number of prospective studies have shown that US performs better than CXRs [72], and the World Interactive Network Focused on Critical Ultrasound

(WINFOCUS)'s International Liaison Committee on Lung Ultrasound (ILC-LUS) recently published the first international evidence-based recommendations for point-of-care lung US [73].

Two-thirds of the world's population has no access to imaging technologies. The paradox is that 80-90% of all diagnostic problems potentially could be solved by basic x-ray and US examinations [74]. Until now, the physical examination of critically ill patients has had some advantages over the use of more sophisticated technologies. Physical examination is less expensive and, unlike procedures based on high-tech diagnostic tools, can be performed anywhere. The introduction of point-of-care US has definitively changed these terms. Ultrasound is possibly the most versatile diagnostic tool in modern medicine because it enables physicians to look inside the body in a non-invasive manner and because it is the most cost effective and widely available of all imaging modalities. Therefore, the use of US should be regarded as an important adjunct to clinical examinations.

1.4.2 Principles of ultrasound imaging

An understanding of the physical properties of US is not indispensable for the sonographer, but to become versed in the language of US, it is favorable to review some of the basics of wave physics that apply to mechanical waves. The following is a brief overview of what is covered in US textbooks [61-64].

1.4.2.1 Definitions and formulas

Ultrasound is a mechanical wave that affects the medium (e.g., human tissue) that it penetrates. The medium will have areas in which particles are packed together or scattered, and the difference in density can be graphically displayed as a sine curve, as shown in **Figure 7**.

The *amplitude* is the strength of the US echo (measured in decibels) and describes the maximum difference in pressure between the areas with packed and scattered particles (**Figure 7**).

The **wavelength** (λ) is the distance between two areas with maximally packed particles and represents the distance that the wave travels in a single cycle (**Figure 7**).

The **frequency** (f) is the number of wavelengths that pass a point per second and is measured in hertz. The frequency correlates directly with the axial resolution and inversely with penetration.

The **velocity** (c) is the speed of the wave and equals the product of the frequency and the wavelength (**Figure 7**). The velocity is constant in soft tissues at approximately 1540 meters per second.

$$c = f \times \lambda$$

Attenuation is the progressive weakening of the US wave in a medium as the wave's energy is reflected or changed into other forms (e.g., heat). Several factors determine the rate of energy loss, such as the density of the medium, the number of interfaces encountered and the wavelength (**Figure 8**).

The **resolution** of an US system refers to its ability to discriminate two nearby objects, both axially (i.e., objects that lie on top of each other) and laterally (i.e., objects that lie side by side). A low frequency results in a lower resolution and greater penetration. A high frequency results in a higher resolution and less penetration.

Reflection is the redirection of part of the US beam back to its source (the US probe), as shown in **Figure 7**.

Refraction is the redirection of part of the US beam as it crosses a boundary between different tissues.

Scattering occurs when small objects (e.g., red blood cells or air particles) reflect the US beam in scattered directions.

Absorption is the containment of US energy within a tissue.

Acoustic impedance is the property of a tissue that determines how much of the US wave is reflected or transmitted to deeper structures. At a constant velocity, the acoustic impedance is approximately a function of the tissue density.

Acoustic power is the amount of energy leaving the US probe.

1.4.2.2 Image acquisition

An image is created by producing an US wave, receiving the reflected echoes from the different tissues within the body and interpreting those echoes. The three steps are illustrated and elaborated in **Figures 7 and 8**.

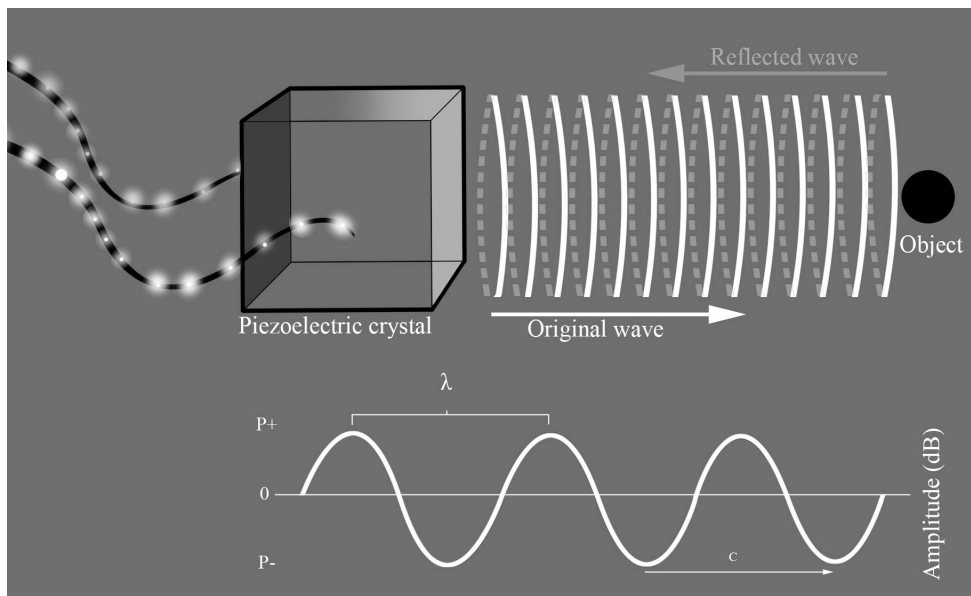


Figure 7. The transmission and reception of sound waves are based on the piezoelectric effect to form diagnostic US images. When a series of electrical impulses are applied to the crystal, it vibrates and generates a wave front. It is this original wave front that is the US beam emitted by the transducer/probe. Similarly, the US machine detects objects within the US beam when the reflected waves strike the crystal and generate minute electrical charges. The strength or amplitude of the US wave is proportional to the strength of the electrical charge, and the frequency (i.e., the number of wavelengths [λ] per second) is determined by the thickness of the

piezoelectric crystal. By using different crystals and designs, US probes can be engineered to have unique characteristics (e.g., linear probes, curvilinear abdominal probes and phased-array cardiac probes). (Illustration: Kim Söderström [medical illustrator])

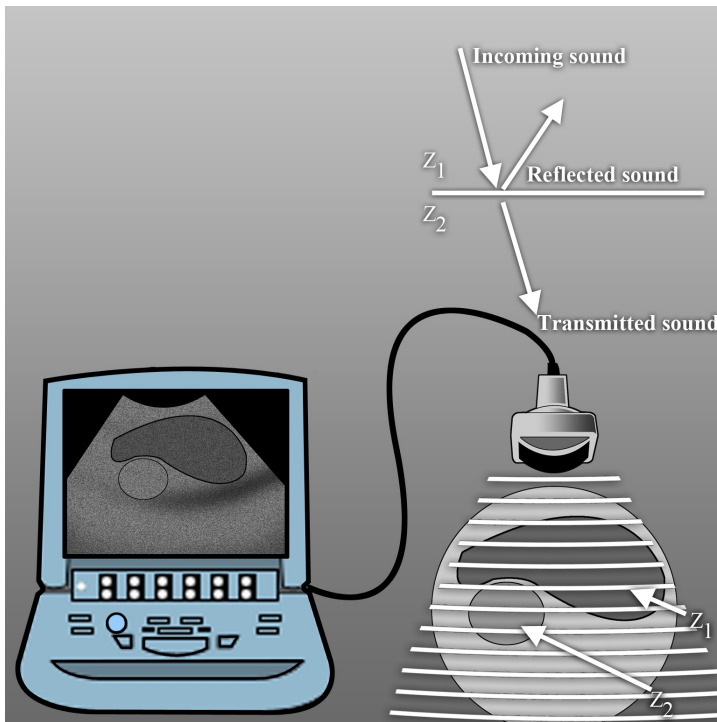


Figure 8. An ultrasound (US) image is constructed from echoes returning from structures within the body. With two-dimensional US, the waves are subsequently emitted in different directions to form a sector. The computer within the US machine determines the depth from which the returning echoes have come by measuring the time between the transmission and reception of the pulsed wave signals. Because the speed of sound in tissues averages a constant 1540 meters per second (i.e., with the exception of waves in bone and air-filled parenchyma) and because the computer knows the length of time that has elapsed, the image representing the echo can be placed at the proper depth on the US screen. The echoes from each reflection point

can be located as a pixel and together form an image on the screen. Ultrasound energy is reflected from interfaces between tissues (Z_1 and Z_2). When the difference in density or acoustic impedance between two tissues is greater (e.g., when one tissue is bone or a gallstone), more energy is reflected, and the image appears bright (known as hyper-echoic). Areas that do not produce echoes (e.g., fluid) are black (known as anechoic) on the screen, and the “grayscale” of US corresponds to tissues with intermediate echoes. (Illustration: Kim Söderström [medical illustrator])

1.4.2.3 Adjusting the image

The sonographer should always optimize the image to increase the chance of diagnosing pathologies. The picture quality of the object on the screen can be adjusted through several parameters on the US machine:

The *focus* allows the operator to narrow the US beam and thereby increase the spatial resolution. As it leaves the probe, the beam generally thickens, but this thickening can often be controlled to some degree by creating focal zones within the beam. The depth of the focal zone can be adjusted and is often indicated on the side of the screen as a pointer.

The *depth* is another important parameter that can be controlled by the sonographer and is often displayed as a centimeter scale on the screen. The tissue or object of interest should be included on the screen by adjusting the image depth.

The *gain* adjusts the intensity of the returned echoes. Due to the attenuation of the US energy, echoes returning from deeper reflectors are weaker. The US machine can amplify these echoes in a process called time gain compensation. Increasing and decreasing the gain cause the US field to brighten and darken, respectively. Some US machines allow the gain to be adjusted at various depths.

1.4.2.4 Scanning modes

There are a variety of display modes used in diagnostic US:

B-mode (brightness mode) is the normal two-dimensional imaging mode and represents width and depth. Each pixel or dot on the screen is coded on a “grayscale” based on the amplitude of the returning wave.

M-mode (motion mode) is when the width of the US beam is substituted for time, meaning that the vertical axis represents depth and the horizontal axis represents time. On the vertical axis (i.e., the M-line), the US machine depicts the motion of the tissue/structures as the time axis progresses.

D-mode (Doppler mode) imaging is based on frequency shifts caused by the movement of the reflector. The Doppler effect is best illustrated by the increase and then decrease in pitch as a moving object (e.g., an ambulance with siren) moves toward or away from an observer. This frequency shift can be displayed on the US screen as a color change (color Doppler) or as audible or graphical peaks (spectral Doppler).

1.4.2.5 Effects and artifacts

The presence of image artifacts is important to recognize as such artifacts can sometimes lead to misinterpretation or help the sonographer to differentiate between diagnoses (e.g., lung US detection of PTX). Some of the basic artifacts are described below:

An **acoustic mirror or shadow** forms when most or all of the US energy is reflected at a tissue interface (i.e., the interface between two tissues with a large difference in density) and nothing passes through. In this situation, an acoustic black shadow extends from the strong reflector to the edge of the screen (e.g., a rib shadow).

Reverberation occurs when the US beam “bounces” between reflective structures (e.g., the two pleural layers of the lung). The US machine misinterprets the reflected signals coming back from the tissue and creates echoic phantoms on the screen (e.g., the A- and B-lines observed when examining the lungs).

Mirror images, a type of reverberation artifact, are also generated based on the false assumption by the US machine that an echo returns to the transducer after a single reflection. If the primary beam encounters a strong reflector first and then hits the “back side” of a structure and is reflected back to the strong reflector before traveling back to the transducer, the display shows a false duplicated mirror image deeper than the strong reflector.

Enhancement occurs when a portion of the waves travel unobstructed through an anechoic structure (e.g., a cystic structure, fluid or a vessel) and return with greater energy than the portion of the US beam that must pass through more dense tissue. The tissues posterior to the low-attenuation structure appear artificially bright compared with their surroundings.

Refraction or a change in the direction of the US beam occurs when the waves cross a boundary between tissues with different propagation speeds. Objects in the path of the reflected (or angled) portion of the beam will be displaced because the computer inside the US machine assumes that the beam travels in a straight path.

Side lobes are low-energy, off-axis beams that are generated by some piezoelectric crystals, and echoes from strong reflectors in their paths will be picked up by the transducer and displayed as having originating from within the main beam.

The **beam width** of the primary US beam is roughly the same width as the transducer. The beam is narrowed at the focal zone and then widens again distally. All echoes from strong reflectors in the widened beam beyond the margin of the transducer will be misplaced and appear within the narrow imaging plane on the screen.

1.4.3 Ultrasound diagnosis of pneumothorax

The use of lung US to identify PTXs has rapidly spread since this technique was first described in veterinarian practice in 1986 [65]. The paradox is that US imaging poorly visualizes the lung parenchyma. Therefore, the conceptual basis for the US diagnosis of PTX is dynamic signs that originate from the pleural line (i.e., the adjacent two visceral and parietal pleural layers). It is sufficient to combine

movements and sonographic artifacts from the pleural line and study them in B-mode and M-mode to rapidly rule out or confirm PTX within minutes. The primary dynamic features are the lung sliding sign [68], B-line reverberation artifacts [69] and the pathognomonic lung point sign [70], all of which are synchronous with respiration, and finally lung pulsation [75] transmitted from heartbeats. The lung US detection of PTX may appear complex due to the need to recognize or exclude these four signs, but the use of a step-by-step approach (**Figure 9**) and a flow-chart for decision making (**Figure 10**) makes the procedure straightforward.

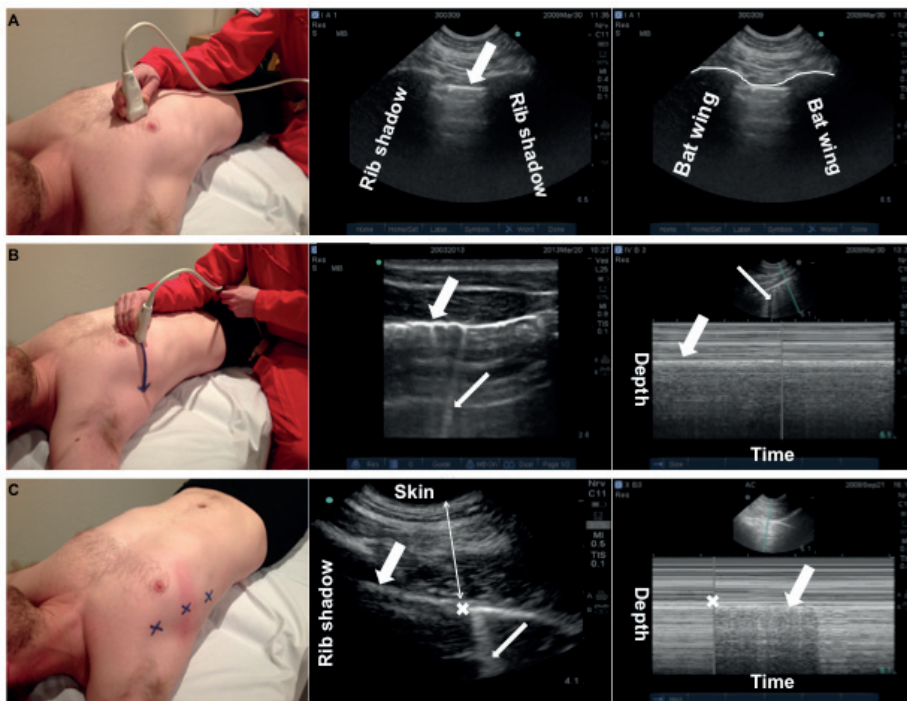


Figure 9. Step-by-step diagnostic approach for the ultrasound (US) detection of pneumothorax (PTX). The wide arrows indicate the pleural line, the thin arrows mark B-lines, and the crosses mark the lung points. **A)** When examining a supine patient, the US scanning should always start in the anterior-inferior chest area (i.e., at the third-fourth intercostal space) between the sternum and the mid-clavicle line (i.e.,

an area close to the mammilla). If there is a PTX, the intrapleural air will move and reside in front of the lung and can easily be detected by a US probe placed adjacent. The initial plane of the probe is longitudinal to visualize two ribs and identify the echogenic pleural line passing between and under the ribs. The image of two rib shadows connected by this pleural line resembles the wingspread of a bat, hence the term “bat sign.” Beginning each lung US procedure by identifying the “bat sign” is important because doing so immediately targets the parietal and visceral pleura, where all the dynamic movements and artifacts originate. **B)** The next step is to slightly rotate the probe so that it is aligned with the intercostal space. This plane is an oblique plane that gives an extended view of the pleural line without interfering rib shadows because the axis is alongside the intercostals. The scanning then follows the curve of the lateral and inferior chest (i.e., the direction indicated by the arrow drawn on the chest), and at any level, the US operator carefully evaluates the images for signs of dynamic “to and fro” horizontal movements at the pleural line (lung sliding) and vertical reverberation artifacts (i.e., echogenic B-lines that extends from the parietal pleura to the end of the screen). Lung sliding and/or B-lines rule out PTX, whereas both signs are absent if the pleural layers are separated by air (i.e., PTX ruled in). Sometimes it is necessary to use M-mode scanning to make the correct diagnosis. If lung sliding is present, the US image has a granular appearance under the pleural line (resembling sand) and horizontal lines above the pleural line (resembling the horizon), and therefore, this type of image is called the seashore pattern. Straight horizontal lines (i.e., a stratosphere pattern) throughout the image indicate the lack of sliding and a possible PTX. **C)** When lung sliding is absent in the anterior chest, the progressive movement of the probe toward the lateral-inferior chest is useful to look for the area where the collapsed lung still adheres to the inside of the chest wall, as shown earlier in **Figure 2**. This location is called the “lung point” and corresponds to the place where lung sliding and/or B-lines intermittently appear during respiration (best illustrated in video clips). When this point is located just beneath the US probe, two distinct patterns are observed on the screen: one corresponding to normal lung sliding where the pleural layers are attached and one without sliding where the layers are separated by air (PTX). In M-mode, this point

appears as a change from the seashore pattern to the stratosphere pattern. The detection of the lung point is 100% pathognomonic for PTX and is useful to evaluate the extension of the PTX. Several intercostal spaces are often scanned on each side of the chest by repeating the procedure (i.e., steps A-C) to confirm the diagnosis of PTX. The cutaneous projections of the observed lung points (white two-sided arrow) can be marked by a pen-cross on the chest to make a topographic map of the lateral extension of the intrapleural air present inside the chest. (Photo: Nils Petter Oveland)

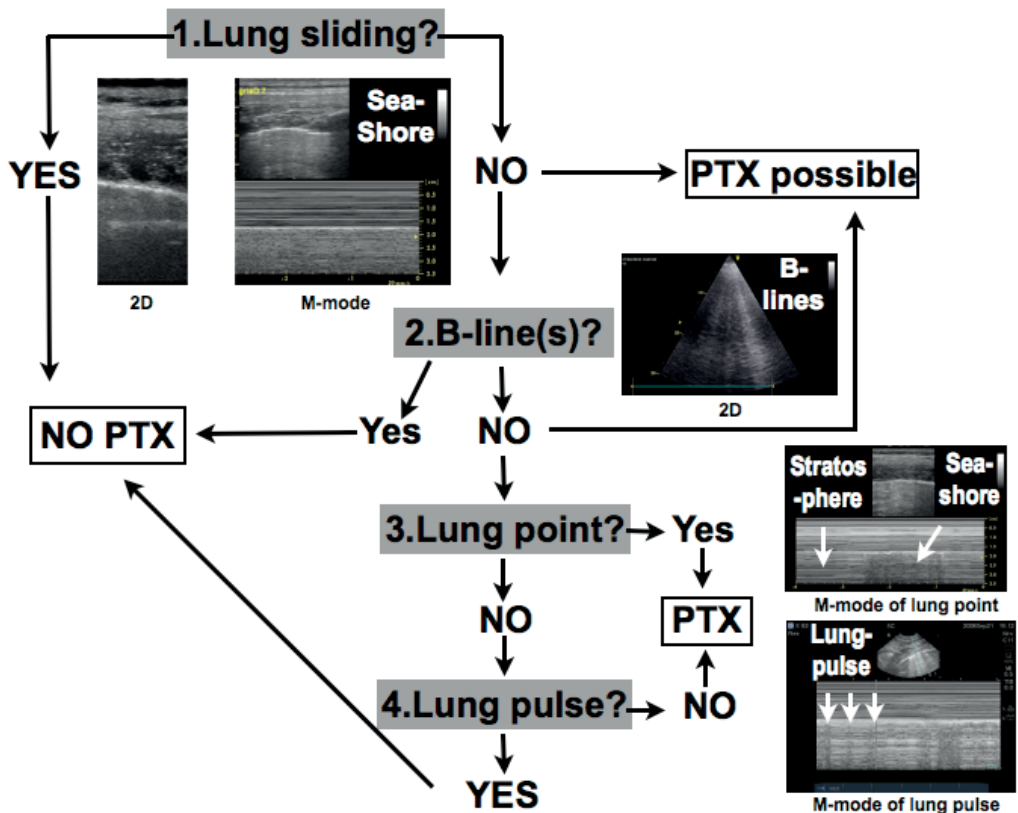


Figure 10. Diagnostic decision making using a flow-chart to distinguish pneumothorax (PTX) and normal lungs. 1) The first sign to be checked is lung sliding, which excludes PTX, but a lack of sliding may be due to other medical conditions involving pleural adhesions that result in motionless pleura (e.g., pleurisy, massive pneumonia, complete atelectasis, fibrosis, severe asthma, emphysema, one-lung intubation, esophageal intubation, ++). In chest trauma cases, the absence of

lung sliding is more likely to indicate a PTX. **2)** The visualization of even one isolated B-line demonstrates the adherence of the visceral pleura to the parietal pleura (i.e., PTX discounted). An US scan of a PTX lacks B-lines but can have horizontal echogenic A-lines that run parallel to the pleural line (i.e., artifacts that appear under the pleural line at a depth determined by the distance from the skin to the parietal pleural layer). The absence of B-lines (i.e., the A-line sign) has 100% sensitivity but only 60% specificity (in itself not enough for PTXs to safely be ruled in). **3)** In contrast to the other US signs, the lung point confirms the diagnosis of PTX and is pathognomonic for the presence of air within the pleural cavity. Unfortunately, not all patients present this sign. One explanation for this absence with large PTXs is the complete retraction of the lung with the elimination of lung sliding in the anterior, lateral and posterior locations on the chest, and thus, no lung point can be visualized. Furthermore, pleural adhesions, as mentioned above, may cause motionless pleura and thereby limit the likelihood of obtaining this sign. However, the detection of the lung point is important to confirm a PTX and evaluate its size. **4)** The last sign is useful in the absence of lung sliding and is often observed in patients with consolidated motionless lungs and apnea syndromes. The transmission of heartbeats through the lung parenchyma generates a pulsating vertical movement of the pleural line called the “lung pulse sign”, which, similar to lung sliding, rules out PTX. When combined, these four signs accurately rule in or rule out PTX in trauma and critically ill patients. The test characteristics for the sonographic diagnosis of PTX are elaborated in section 1.4.4. (Illustration: Erik Sloth)

1.4.4 Diagnostic accuracy of lung ultrasonography for the detection of a pneumothorax

Whether lung US is a better diagnostic strategy than supine CXR in injured patients with a suspected PTX is debated. The British Thoracic Society (BTS) maintains their position of caution regarding the use of US for the detection and management of PTX because there is no evidence of improved patient outcomes [76]. The WINFOCUS organization argues that US is more sensitive for diagnosing PTX and is therefore an improvement on the current standard practice [73]. The latter statement is based on

the initial publications on this diagnostic technique and the later prospective studies comparing lung US to supine CXR and CT. In the last two years, reviews of the literature have been published, and a consensus has been reached by experts, resulting in the first international guidelines for point-of-care lung US. The body of literature that supports the use of lung US for the diagnosis of PTX is increasing, and an illustrative selection is presented in **Table 3** [43, 45, 68-70, 73, 77-83].

Table 3. A historical selection of articles that support the use of lung ultrasound scanning for the diagnosis of pneumothorax (index test)

Reference	Design/Type of publication	Patients/lungs with PTX/included studies	US signs	Ref. test	Sens	Spec
Lichtenstein et al. (1995) [68]	NR	ICU: 43 lungs with PTX. 68 normal lungs.	LS	CXR, CT	95.3	91.1
Lichtenstein et al. (1999) [69]	Prospective observational study	ICU: 41 lungs with PTX. 146 normal lungs.	LS, B-lines	CXR, CT	100.0	96.5
Lichtenstein et al. (2000) [70]	Prospective observational study	ICU: 66 lungs with PTX. 233 normal lungs.	LP	CXR, CT	66.0	100.0
Dulchavsky et al. (2001) [77]	Prospective observational study	382 trauma patients: 39 lungs with PTX.	LS, B-lines	CXR	94.9	100.0
Rowan et al. (2002) [78]	Prospective observational study	27 trauma patients: 11 lungs with PTX.	LS, B-lines	CT	100.0	94.0
Blaivas et al. (2005) [79]	Prospective observational study	176 trauma patients: 53 lungs with PTX.	LS	CT, ROA	98.1	99.2
Soldati et al. (2006) [80]	Prospective observational study	186 trauma patients: 56 lungs with PTX.	LS, B-lines, LP	CXR, CT	98.2	100.0
Zhang et al. (2006) [45]	Prospective observational study	135 trauma patients: 29 lungs with PTX.	LS, B-lines, LP	CT, ROA	86.2	97.2
Soldati et al. (2008) [43]	Prospective observational study	109 trauma patients: 25 lungs with PTX.	LS, B-lines, LP	CT	92.0	99.4
Wilkerson et al. (2010) [81]	Evidence-based review	4 prospective observational studies	LS, B-lines, LP	CT, ROA	NA	NA
Ding et al. (2011) [82]	Meta-analysis	20 English-language studies; 14 pros., 4 NR and 2 retrospec.	LS, B-lines, LP	CT, ROA	88.0	99.0
Alrajhi et al. (2012) [83]	Systematic review and meta-analysis	8 English-language prospective studies	LS, B-lines	CT, ROA	90.9	98.2
Volpicelli et al. (2012) [73]	Conference reports and expert panel.	Consensus meetings of 28 experts. Evidence-based guidelines for lung US extracted from 320 references.	NA	NA	NA	NA

Abbreviations: CT: Computed tomography; CXR: Chest x-ray; PTX: Pneumothorax; US: Ultrasonography; LS: Lung sliding; LP: Lung point; Sens: Sensitivity (%); Spec: Specificity (%); ICU: Intensive care unit; ROA: Release of air; NA: Not applicable; NR: Not reported.

1.4.5 Chapter summary

Pneumothorax is difficult to diagnose after blunt trauma and if overlooked may cause adverse effects, especially if the patient is positive pressure ventilated. The anteroposterior supine CXR is the least sensitive of all plain radiographic techniques to detect PTXs, whereas all occult PTXs may be found on CT scans. The problems are that neither of these diagnostic tools is readily available for the patients and that both are associated with radiation hazards. Lung US has several advantages: it is a point-of-care examination that can be easily performed at bedside, it is harmless, and it can accurately diagnose PTX. However, before the widespread use of lung US to assess patients with blunt chest trauma is advocated, several questions must be answered. Lung US is more sensitive than and equally specific as CXR, but it is not known whether small PTXs may fail to be detected and if lung US can be used to assess PTX progression during positive pressure ventilation. In addition, the accuracy of this diagnostic test is highly operator dependent. Before every physician is encouraged to use lung scanning, it is necessary to show that beginners can learn the necessary skills. Therefore, alternative training methods must be explored and tested. We answered these research questions by studying experimentally induced PTXs in a porcine model.

2. Aim of the study

The aim of this study was to develop a porcine PTX model for assessing and teaching lung US diagnostics. We wanted to determine if the pleural insufflation of air into a live anesthetized pig truly imitates a PTX in an injured patient and if we could determine the minimum threshold volume of air needed for PTXs to accurately be detected by lung US and CXR. In addition, we increased and decreased the PTX size in our model to determine if lung US could be used to monitor PTX progression during mechanical ventilation. Finally, we used our porcine PTX model in an educational program to test whether medical students without any prior scanning experience could improve their diagnostic proficiencies and speeds for the lung US detection of PTX after supervised training in an animal facility.

3. Materials and methods

3.1 Animal model

3.1.1 Research animals

The experimental studies were performed at the animal research laboratory at Aarhus University Hospital Skejby. The vivarium is owned and run by the Institute of Clinical Medicine, Aarhus University, Denmark. The research animals, young female domestic pigs (Danish land race) weighing 46.5 – 61.0 kg, were bred at a local farm and transported to the hospital the same day as the experiment. Before transport, the animals were given an intramuscular tranquilizer, and they were sedated, anesthetized and intubated at the research lab. The basic measurements were performed at the vivarium, and the CT imaging was performed at the Radiology Department. All studies used live anesthetized pigs with a unilateral or bilateral pleural cavity catheter(s). In the studies described in papers I and II, lung US, CXR and CT imaging were performed on the same twenty pigs. In the study described in paper III, repeated CT and lung US measurements were performed on three pigs. The last study (described in paper IV) used 11 pigs for the animal laboratory training and examinations. A total number of 34 research animals were used to complete these studies.

3.1.2 Animal preparation and anesthesia

The animal preparation and anesthesia protocols are described in detail in paper I. In brief, the pigs were anesthetized, intubated and fixated in the supine position on the operating table or CT table. A small thoracotomy was performed at the crossing of the fifth to seventh intercostals with the anterior axillary line, and a three-way stopcock catheter (BD Connecta, BD Medical, Franklin Lakes, NJ, USA) was inserted into the pleural space. The catheter was then anchored to the surrounding muscle and fascia. Excessive air introduced while inserting the catheter was withdrawn using a 10 mL syringe. A stationary respirator (paper II and IV) (GE S5 Advance

Carestation™, Datex-Ohmeda, GE Healthcare, London, UK) or transport respirator (paper I and III) (Oxylog 3000, Dräger Medical, Lübeck, Germany) was adjusted to a tidal volume of 11 to 15 mL/kg, a respiratory rate of 10 to 12 breaths/minute, a positive end-expiratory pressure of 2 to 4 cm H₂O and an inspiratory oxygen fraction of 30%. The end-tidal carbon dioxide level was kept within the normal range (4.0 to 6.5 kPa). All animals were monitored by electrocardiography, and their core temperatures, invasive arterial blood pressures, oxygen saturations and end-tidal carbon dioxide levels were recorded. At the conclusion of the data collection period, each animal was euthanized with an injection of pentobarbital.

3.1.3 Ethical considerations

Qualified and experienced animal caretaker personnel monitored the health of the animals during the study period. The experiments complied with the guidelines for animal experimental studies issued by the Danish Inspectorate for Animal Experimentation under the Danish Ministry of Justice, which also approved the study. The study adhered to the principles in the Guide for the Care and Use of Laboratory Animals [84].

3.2 Diagnostic tests

The diagnostic tests are described in detail in paper I-IV. In brief:

CXR: Supine anteroposterior CXRs were taken of each animal using a portable x-ray machine (Siemens Mobilett II, Siemens, Munich, Germany). An x-ray plate (Eastman Kodak, Rochester, NY) was placed underneath the thorax. The x-ray tube of the machine was placed one meter above the sternum. The radiographic field was adjusted and focused to include the thorax from the apex to the base (**Figure 6**). The radiograph was taken using standard imaging output adjustments (117 kV / 1.25 mA), developed and digitally stored. All the pictures were given encrypted names and presented to a senior radiologist in a sequence determined by a randomization procedure that assigned numbers to the pictures. The radiologist had to identify the presence or absence of a right- or left-sided PTX in each CXR. He was told that the

pigs could have a unilateral PTX, bilateral PTXs or two normal lungs. Additionally, the chest drains that we used were radiologically transparent to conceal any diagnostic information. The radiological definition of PTX was a readily apparent visceral pleural line without distal lung markings (**Figure 6**) [40]. The CXRs were viewed using a DICOM viewer (Phillips R 2.6, Philips Medical Systems, Amsterdam, the Netherlands), and the PTX diagnoses were scored on a five-point Likert scale (1 = definitely absent, 2 = most likely absent, 3 = possibly present, 4 = most likely present and 5 = definitely present), with a score of four or five being considered positive for PTX [85].

CT: Non-contrast enhanced-CT images were obtained using a multi-slice CT scanner (Philips MX 8000 quad; Philips Medical Systems, Best, The Netherlands) with the following parameters: 120 kV, 120-150 mA, standard filter, 6.5 mm-slice thickness, 3.2 mm-slice increments and a 310 to 360 mm field of view. A complete thoracic CT scan from the apex to the base of the lungs during an inspiratory hold was performed. The digital DICOM format pictures were stored and transferred to an archiving workstation. To optimize intrapleural air detection, the window width was adjusted to 1500 Hounsfield units and the window level to -500 Hounsfield units.

US: Transthoracic lung US was performed in three studies (described in papers II-IV) using the maneuvers and diagnostic algorithm described in **Figures 9 and 10**. In the studies described in papers II and III, anesthesiologists with moderate experience (i.e., less than one year of clinical practice with lung US) performed the scanning, whereas US novices (i.e., twenty medical students) were examined in the study described in paper IV. The two devices used were an M-Turbo (Sonosite Inc, Bothell, WA) with one of three different transducers (i.e., a 13-6 MHz linear probe, a 15-6 MHz linear probe or a 8-5 MHz micro-convex probe) and a Vivid Q (GE Healthcare, Horten, Norway) with a 12 L-RS 13-6 MHz linear array transducer.

3.3 Study design

We designed four sub-studies to address the aims of our thesis:

3.3.1 Paper 1

A unilateral catheter was inserted into the pleural cavity of each of 20 pigs, and 500 ml of air was insufflated.

Objective: To define the intrathoracic distribution of air using the reference imaging standard (CT) to determine if the pleural insufflation of air into a live anesthetized pig truly imitates a PTX in an injured patient.

Measurements: After a complete thoracic CT scan, the anterior, lateral, medial, basal, apical and posterior components of the PTXs were compared. The amount of air in each location was quantified by measuring the distance from the lung margin to the chest wall. A supine anteroposterior chest radiograph (CXR) was taken for each pig and interpreted by a senior radiologist. The goals were to describe the PTX topography in the pigs and analyze amount of air in each anatomic location by measuring the maximum vertical distance from the lung edge to the chest wall. In addition, the number of occult PTXs in the 20 pigs was determined by comparing results of each CXR to the corresponding CT image.

3.3.2 Paper 2

Air was insufflated into a unilateral pleural catheter in seven incremental steps (10, 25, 50, 100, 200, 350 and 500 mL) in 20 intubated pigs.

Objective: To determine the volume threshold of intrapleural air at which PTXs can be accurately diagnosed with lung US and to compare this volume with that for CXR.

Measurements: Each injection of air was followed by a diagnostic evaluation with US and a supine anteroposterior CXR. The sonographers continued the US scanning until the PTXs could be ruled in based on the pathognomonic US “lung point” sign. The corresponding threshold volume was noted. A senior radiologist interpreted the

CXR images. The primary goal was to determine the mean threshold volume in milliliters at which the PTXs became detectable using US imaging. Second, the sensitivities of both lung US and CXR for diagnosing PTXs with increasing volumes of insufflated air were calculated by dividing the number of true-positive test results by the actual number of PTXs in the pigs.

3.3.3 Paper 3

Air was introduced and withdrawn in incremental steps (50, 100, 150, 200, 300, 400, 500, 600, 500 and 200 mL) into five hemithoraces in three intubated porcine models.

Objective: To determine the accuracy of US imaging for delineating the PTX extensions and to compare the CT and US assessments of PTX progression during positive pressure ventilation in mechanically ventilated pigs.

Measurements: The lung point was identified on US imaging, marked with subcutaneous needles and referenced against the lateral limit of the intrapleural air space identified on the CT. The distance from the sternum to the lung point (S-LP) was measured on the CT scans and correlated with the insufflated air volume. The outcome measures were determining the difference in the lung point designations between CT and US and analyzing the effects of PTX volume, increasing/decreasing PTX size, thoracic laterality, and chest levels on the S-LP distance.

3.3.4 Paper 4

Twenty medical students without US experience attended a one-day course. Didactic, practical and experimental lectures covered the basics of US physics, US machine knobology and lung US techniques, followed by hands-on training on healthy individuals and porcine PTX models to demonstrate normal and pathognomonic lung US signs.

Objective: To test whether animal laboratory training (ALT) improves the diagnostic competency and speed of PTX detection with US among novices.

Measurements: Each student's diagnostic skill level was tested via three subsequent

examinations (day 1, day 2 and a 6-month follow-up) using experimentally induced PTXs in porcine models. The outcome measures were sensitivity and specificity for the US detection of PTX, self-reported diagnostic confidence and scan time.

3.4 Statistical methods

All statistical computations were performed using SPSS V.18.0 (IBM SPSS, Armonk, NY, USA) and an online calculator (<http://vassarstats.net>; Vassar College, Poughkeepsie, NY, USA).

3.4.1 Descriptive statistics

Descriptive statistics is a numerical summary of a collection of data. The measurements and analyses of the central tendency of the data material were presented as the mean, standard deviation, standard error, inter-quartile range (IQR) and range. When applicable, some continuous variables were expressed as absolute values (paper II) and tested for normality (paper I) using the Shapiro-Wilk test. The data were graphically illustrated as vertical box plots (paper I and IV). The box indicates the interquartile range; the horizontal line in the box, the median; and the “whiskers” of the box, the outer boundaries, which are called Tukey’s hinges. Values more than three IQRs from the end of a box are labeled as extreme and denoted with an asterisk (*). Values more than 1.5 IQRs but less than 3 IQRs from the end of the box are labeled as outliers (o).

3.4.2 Performance characteristics of diagnostic tests

The usefulness of a diagnostic test is the degree to which it adds information beyond that otherwise available and whether this new information changes the management of the patient. The main outcome in papers II to IV is the accuracy of lung US, CXR and CT for the detection of experimentally induced PTXs in a porcine model. The qualities that indicate diagnostic accuracy are sensitivity and specificity with 95% confidence intervals (CI). These measures are calculated using 2×2 tables of frequencies, as illustrated in **Table 4**. The 95% CIs for the proportions were

calculated according to the efficient-score method (i.e., corrected for continuity) [86]. Sensitivity is the test's ability to identify the disease, and specificity is the test's ability to identify patients without disease. The diagnostic accuracy is the proportion of correct results among the total number of tests.

Table 4. Calculations for the characteristics of diagnostic tests

Actual condition of the population			
Test result	Patients with disease	Patients without disease	Totals
Positive	a	b	a+b
	(true-positives)	(false-positives)	
Negative	c	d	c+d
	(false-negatives)	(true negatives)	
Totals	a+c	b+d	a+b+c+d

Prevalence = proportion of population affected by the disease = $(a+c)/(a+b+c+d)$

Sensitivity = proportion of true positives = $a/(a+c)$

Specificity = proportion of true negatives = $d/(b+d)$

Diagnostic accuracy = proportion of correct results = $(a+d)/(a+b+c+d)$

The limits of agreement (Bland-Altman) method [87, 88] was used for the paired measurements (from readers one and two) of the lung point localization divergence (ΔLP us-ct) in paper III. This approach plots the difference between the paired measurements on the Y-axis and the average of the two measurements on the X-axis, and a high agreement is indicated by a difference that stays close to zero over the full range of the measurements.

3.4.3 Multiple linear regression analysis

In paper III, repeated measurements of the S-LP distance were performed. Within-models experiments are very effective because each porcine model is its own “control” and reduces the individual variation. The disadvantages are a possible “carry-over” effect, spontaneous changes in the animal over time and the exclusion of statistical methods that require independence between measurements. A mixed linear model regression was therefore used to analyze the effects of PTX volume, increasing/decreasing PTX size, thoracic laterality and chest levels (explanatory variables) on the S-LP distance (response variable). The interdependencies between the measurements in the porcine model were modeled by a compound correlation structure (an autoregressive structure gave similar results) [89], and P-values ≤ 0.05 were regarded as significant. The aim of regression analysis is to predict or estimate the value of the response variable from the known values of one or more explanatory variables. Multiple linear regression is used when there is one continuous response (e.g., the S-LP distance) variable and two or more continuous (e.g., PTX volume in mL) or categorical (e.g., increasing/decreasing PTX size, thoracic laterality and chest levels) explanatory variables.

3.4.4 Generalized estimating equations (GEE)

In paper IV, the same medical student examined eight different porcine models with both normal lungs and PTX. The interdependencies between measurements exclude “standard” statistical methods. Analyzing data in a regression analysis without taking this clustering of data into account may lead to smaller standard errors and narrower confidence intervals, with the corresponding p-values being too small. A generalized estimating equation (GEE) analysis was therefore used to test the dependency of the number of correct student answers (PTX yes/no) on the timeline (i.e., first examination: day 1; second examination: day 2; final examination: 6-months follow-up) to illustrate a positive learning outcome. Similar timeline assays were performed for the self-reported confidence level and scan time, and $p \leq 0.05$ was regarded as significant. The data were analyzed with an unstructured correlation structure, which

was the best suited method because of the short time period between the initial two examinations followed by a pause of six months before the final exam. The GEE model adjusts for clustering, corrects the parameter estimates and standard errors, and provides estimated marginal means of parameters and confidence intervals when applicable.

4. Results

4.1 Paper I

Insufflation of air into the pleural cavity of porcine models resembles the PTX topography to be expected in supine trauma patients with the air positioned anterior to the lung (i.e., between the lung and anterior chest wall). The senior radiologist described all the PTXs from CT scans (i.e., from 20 porcine models) and found the intrathoracic anatomic location of the air to be anterior (100%), lateral (95%), medial (80%), basal (60%), apical (45%) and posterior (15%). Most of the insufflated air was found in the anterior, medial and basal recesses where the rim of air around the lung (i.e., the mean vertical lung edge-chest wall distance) was greater than 20 mm. In the supine position, one-third of the PTXs remained occult on the CXRs (i.e., a sensitivity for diagnosing PTX of 66.7%).

4.2 Paper II

Lung US can diagnose very small PTXs with intrapleural air volumes as low as 10 mL (mean threshold volume of 18 mL). In the 20 porcine models, 65% of the PTXs were already diagnosed at 10 mL; 25%, at 25 mL; and the last 10%, at 50 mL of air. For lung US, the sensitivity of diagnosing PTX as a function of volume showed a steep increase from 65% to 90% and 100% as the intrapleural air volume increased from 10 mL to 25 mL and 50 mL, respectively. Supine CXRs had a more gradual increase in sensitivity that leveled off at volumes ≥ 350 mL and ended at 67% for the maximum air volume of 500 mL, leaving one-third of the PTXs undiagnosed. These results indicate that lung US outperform supine CXR and is significantly more reliable in the detection of small- and medium-sized PTXs. An intrapleural air volume ≥ 50 mL was sufficient for US imaging to identify all PTXs in our porcine models, but CXR missed 80% at that volume.

4.3 Paper III

Lung US is as accurate as CT in assessing the extension of PTXs in a positive pressure ventilated porcine model when marking the lung points on the chest. We designated 131 lung points and found an overall mean difference of only 6.8 mm (standard deviation 7.1 mm and range 0.0-29.3 mm) between US and CT.

Furthermore, there was a high level of agreement in the paired lung point measurements between two readers, as shown by a Bland-Altman plot. The mixed multiple linear regression analysis from the CT scans found a linear relationship between PTX volume and the lateral position of the lung point during mechanical ventilation. The correlation was significant ($p < 0.001$) for both thoracic sides, but the mean S-LP distance increased by 4 mm in the right lung and by 11 mm in the left lung when we increased the PTX volume by 100 mL. This result implies that the lung point moves in a progressive arc from the anterior to the lateral and posterior aspects of the chest wall as the PTXs expand.

4.4 Paper IV

As part of a laboratory-training program, scanning porcine PTX models improves lung US skills, increases confidence in making the diagnosis and reduces the scanning time per lung among novices. Twenty medical students completed the ALT program and the two initial examinations on eight pig models, and depending on availability, 11 of the 20 students attended the 6-month follow-up examination on one pig model. The students had no previous experience in performing lung US to diagnose PTX. In the first hands-on examination, 160 lung US examinations were performed, and 139 lungs (86.9%) were correctly diagnosed, resulting in 10 false positives and 11 false negatives. In the second examination, 159 of 160 (99.4%) diagnostic answers were correct, with one false positive. The sensitivity increased from 81.7% to 100.0%, and the specificity increased from 90.0% to 98.9%. The medical students had no deterioration of their skills when the dependency of the correct answers was tested on the timeline (first examination: day 1; second examination: day 2; final examination: 6-month follow-up), with $p = 0.018$.

Furthermore, the mean self-reported confidence levels (scale 1 to 10) with the standard error of the mean were 7.8 ± 0.4 , 8.8 ± 0.4 and 9.0 ± 0.4 for the three examinations. A 1-minute drop to a final scan time of less than three minutes per lung occurred between the initial two examinations, with a slight increase six months later.

5. Discussion

5.1 General discussion

This thesis shows that the insufflation of air into the pleural cavity of porcine models resembles the PTX topography to be expected in supine trauma patients. Using these models, we found that US can diagnose small amounts of intrapleural air and accurately assess the progression of PTXs during positive pressure ventilation. As part of a laboratory-training program, scanning porcine PTX models improves lung US skills, increases confidence in making the diagnosis and reduces the scanning time per lung among novices.

Paper I demonstrates that the experimentally induced PTXs in porcine models have a predominant anterior distribution, with most of the air found in anterior, medial and basal recesses. In the supine position, almost no air escapes behind the lungs. As expected in supine trauma patients, the intrapleural air, if free to move, resides in the same areas in front of, medial to and basal to the lung parenchyma. This outcome seems logical because the PTX distribution in humans is determined by gravity, the elasticity of the lung tissue and the hilar hinge mechanism through which the lungs attach to the main vascular and bronchial structures in the mediastinum [23, 41]. The close similarities between human and porcine PTX topography suggest that pigs have a similar distribution pattern. The anterior air is particularly difficult to detect and quantify on supine CXRs because the lungs are pushed against the spine, where the air is undetectable by anteroposterior-directed x-ray beams (**Figures 2 and 3**). Multiple studies [23, 45, 47, 79] and systematic reviews [10, 22, 81] all showed high proportions of occult PTXs, ranging from 25% to 75% of the cases. The sensitivity of CXR for detecting PTXs in our porcine models was 66.7%, leaving one-third of the PTXs unrecognized after the insertion of 500 mL of air. This miss-rate is similar to the results from radiographic studies of blunt trauma patients and comparable with the threshold of intrapleural air (400 mL) required in supine human cadavers for CXRs to successfully detect PTX [85, 90]. The anterior topography seems to be a disadvantage for the standard chest radiographs but is the conceptual basis for the

increased diagnostic sensitivity of lung US. The anterior chest is the first lung area to be examined in the extended focused assessment with sonography for trauma protocol [57, 58]. This part of the chest is always readily accessible in the supine position, even in challenging environments, such as inside ambulance cars and helicopters [91, 92]. After chest trauma, a US probe placed closed to the patient's sternum would very likely be positioned over an area with PTX. The PTX topography found in our pigs, therefore, makes them ideal training- and research models for the US diagnostics of PTX.

Porcine anatomy is not identical to human anatomy, but their metabolic, respiratory and cardiovascular systems are similar to those of humans [93-95]. Pigs have, therefore, been used in biomedical research for many years [96, 97]. Experimental studies of PTX were conducted in the 1990s using injections of air into both animal [15] and cadaver chests [85]. The National Aeronautics and Space Administration (NASA) later refined the method of using pigs when they assessed the magnitude of PTXs under microgravity conditions using lung US [98-100]. Today, point-of-care US examinations are the only practical diagnostic tool used in space. In addition, porcine models have been used for training purposes by the military [101] and medical schools [102]. However, none of these studies evaluated their models with the reference standard CT. Paper I is the first methodological article to use CT to demonstrate the similarities between experimentally induced PTXs in pigs and the PTXs expected in trauma patients. We found this validation to be important before using these models in our US educational and research projects (Paper II-IV).

Paper II demonstrates that US can diagnose very small PTXs. The mean threshold volume of 18 mL to detect PTXs is exceptionally low and approximates what is possible to detect using CT imaging. The sensitivity of the US detection of PTXs increased from 65% to 90% and 100% as the intrapleural air volume increased from 10 mL to 25 mL and 50 mL, at which point 80 % of the PTXs were missed on the CXRs. This result is not surprising and shows that supine CXR is the least sensitive diagnostic technique for demonstrating PTXs in porcine models compared with lung US. Our study contributes some new aspects to the ongoing scientific debate

regarding whether US should replace CXR as the initial diagnostic test after blunt chest trauma [72]. There is diversity in the current guidelines. The BTS feels that the utility of lung US for diagnosing PTXs is limited in hospital practice due to the ready availability of CXRs and the lack of prospective studies that demonstrate improved outcomes and management changes after lung scanning [76]. They refer to one post-intervention study of 29 patients with PTXs after lung biopsies that showed a lower sensitivity for lung US than CT scans [103]. They caution that small PTXs may fail to be detected by lung US, but they do acknowledge that diagnosing even small PTXs, especially during positive pressure ventilation, may be relevant for treatment or observational strategies [72]. WINFOCUS's International Liaison Committee on lung US consists of experts in pleural and lung US and has used the GRADE criteria and RAND methodologies to develop evidence-based recommendations and consensus statements [104]. In their guidelines, lung US, and not CXR, is the preferred diagnostic test in the initial evaluation of critically ill or injured patients with suspected PTXs [73]. However, lung US has some pitfalls, and its use requires properly trained sonographers [72]. In the guidelines, there was no consensus and weak evidence supporting bedside lung US as a useful tool to differentiate between small and large PTXs. Paper II is the first to present the exact volume threshold of the US detection of PTXs based not only on the obliteration of normal lung sliding between the pleural layers but also the identification of the "lung point", which is the only PTX-specific US sign [70]. Our results show that US outperforms supine CXR and is much more reliable in the detection of small- and medium-sized PTXs, suggesting that lung US may be a helpful adjunctive to use in blunt chest trauma patients with suspected PTXs.

Paper III shows that there is a linear relationship between the volume of a PTX and the lateral position of the lung point inside the chest during mechanical ventilation and that US imaging is as accurate as CT for localizing these lung points. The results are clinically relevant and may enable clinicians to use US to accurately follow the progression of PTXs during positive pressure ventilation. Considering the volume of a PTX appears rational before making treatment decisions because the size may be

linked to the amount and mechanism of air leakage. Different calculation methods have been developed to evaluate the extent of PTXs. The plain CXR is a poor method for quantifying size as it usually produces underestimations [105, 106] because air volume is difficult to assess from two-dimensional images. The attempts are based on the assumption that the lungs and the hemithoraces have the shape of a cube. Thus, the volume of a PTX approximates the ratio of the cube of the lung diameter to the hemithorax diameter [107]. If the distance from the lung to the chest wall is 1 cm on the CXR, the PTX occupies approximately 27% of the hemithorax volume (e.g., if the lung is 9 cm in diameter and the hemithorax is 10 cm, then $[10^3 - 9^3]/10^3 = 27\%$). Similarly, a 2 cm PTX occupies 49% of the hemithorax. The BTS's guidelines, therefore, divide PTXs into "small" or "large" if the rim of air is < 2 cm or > 2 cm, respectively. If the proximity of the lung edge to the chest wall exceeds 2 cm, aspirating with a needle may be advisable because there is a low risk of complications [107]. Estimating the PTX volume more accurately requires CT imaging. The first linear size (thickness)-based method was established by Wolfman et al. [108], who classified PTXs as miniscule, anterior or anterolateral based on the size and location of the intrapleural air (i.e., miniscule PTXs were defined as thin collections of air up to 1 cm in anteroposterior thickness, observed on no more than four contiguous images; anterior PTXs as collections of pleural air > 1 cm that does not extend laterally to the midcoronal line; and anterolateral PTXs as collections of air extending posteriorly beyond the midcoronal line). A more cumbersome system was presented by de Moya et al. [25], who measured the largest air collection along a line perpendicular to the chest wall or mediastinum and combined this line with an evaluation of whether the PTX crossed the transhilar axial plane. The relationship of the PTX to the pulmonary hilum was later excluded because it did not offer any information in addition to the thickness measurements alone [12]. A great limitation to both of these methods is that the cephalic-caudal extents of the PTXs remains unclear. Furthermore, Wolfman et al. [108] only used abdominal CT scans, which preclude the determination of any PTXs in the superior thoracic cavity. This issue was corrected by De Moya et al. [25], who only used thoracic CT scans. However, to precisely assess the volume of a PTX, performing computer-aided volumetry

measurements is necessary. This image analysis tool, also known as computerized volumetry, calculates the volume of the air within the pleural space from multiple consecutive CT images using automated algorithms [109]. The more known parallel example is the computerized volumetry of tumors, which provides a reliable and objective estimate of tumor size that agrees well with the clinical outcome [110, 111]. The same methodology provides a sophisticated method to accurately evaluate PTX size but requires severely injured patients to be transported to the CT room, is time-consuming and delays the diagnosis and possibly the treatment actions. More importantly, radiation is a risk of cancer, especially in children and young adults [51]. Some CT-classification systems have been tested [112], and some await prospective validation; however, no consensus on the clinical utility of these PTX scoring systems has yet been established [12]. Thus, an easier method for assessing PTX size and progression is needed. Lung US can be performed at the bedside without the need for patient transport or radiation exposure [45, 71]. However, similar to the other diagnostic methods, there is little consensus that lung US compares well with CT in the assessment of PTX extension, and weak evidence exists that US is useful for differentiating between small and large PTXs using the detection of the lung point [73]. The results in favor of [43, 45] or opposed to [79, 113] using lung point localization to grade PTX size are mixed. Blaivas et al. [79] argued that differentiating between medium- and large-sized PTXs is difficult, as indicated by a weak correlation between increasing PTX volumes and the lateral position of the lung point on the CT scans. In their study, no statistical analysis or references support this statement, with the only support provided by the author's comments on three CT images. Soldati et al. [43] found an opposite result with a mean difference between the US and CT lung points of only 19 mm and concluded that lung US can be used to characterize PTX size and extension with an accuracy close to that of CT imaging. Their measurements are solid but cannot be extrapolated to mechanically ventilated patients, who were excluded in their study. Paper III is the first to demonstrate that lung US is comparable with CT for localizing lung points, even with models that are positive pressure ventilated. The linear response of the S-LP distance to the PTX volume also implies that the lung point moves in a progressive arc from the anterior

to the lateral and posterior aspects of the chest wall as the PTXs expand and that the lung point movement can be used to accurately assess PTX size over time (**Figure 9**).

Paper IV shows that novices can learn how to diagnose PTXs using lung US. By incorporating our porcine PTX models in an 8-hour ALT program, medical students who are inexperienced in lung US improved their diagnostic skills, self-confidence and efficacy in making the correct diagnosis, with no deterioration six months later. One method for learning lung US is to scan real trauma patients, which might be appropriate for skilled emergency physicians familiar with the environment in the emergency department [114]; however, other methods may be necessary to obtain an acceptable skill level among novices before using this technique in real clinical settings. A cadaver model that is randomized for tracheal or esophageal intubation could be used to study the presence or absence of the lung sliding sign [115], but this sign is more easily demonstrated with a simple experimental model that uses two intravenous pressure bags submerged in water [116]. Cadavers are ideal anatomical models [85] but are less accessible and offer no physical properties, such as heartbeats, respiration and hemorrhage. Viewing instructional videotapes may improve PTX image recognition [117, 118], but technical skills are not developed without hands-on training. Courses describing the technique through theoretical lectures and real-time scanning of mock volunteers do enhance the standard of the lung US detection of PTXs [114, 119, 120]. However, healthy volunteers do not have any pathology. In the last decade, the special field of medical simulation has emerged, using computer-operated mannequins [121-123] as pathological models to facilitate the training of both diagnostic and treatment algorithms. A Medline inquiry (terms; Pneumothorax AND Ultrasound AND [Simulators OR Mannequins]) provided no results addressing mannequins used for lung US practice to detect PTXs. Anesthetized pigs are vastly different from these other educational models because the participants diagnose an actual PTX in a breathing animal. This experience is particularly important because the diagnosis relies on dynamic signs that occur at the pleural line synchronous with respiration (**Figures 9 and 10**). Two animal studies using experimentally induced PTXs in porcine models have reported deviant results

after teaching lung US skills to beginners. The sensitivity and specificity of lung US scanning for PTX ranged from 73% to 95% and from 84% to 100%, respectively [101, 102]. The participants only received short 10- to 60-minute introductory lectures before performing a limited number of lung US examinations (i.e., 44 and 96 in total, respectively). Many emergency US educational programs have focused on the number of examinations required to become skilled. The guidelines from the American College of Emergency Physicians suggest that trainees should perform between 25 to 50 examinations, whereas the European Federation of Societies for Ultrasound in Medicine and Biology recommend a minimum of 200 examinations to achieve a basic level 1 in lung US [124, 125]. In our ALT program, we adopted a non-numerical model that focuses on a competency-based checklist evaluation of each student. Using these checklists, the students had to demonstrate competency in each educational step (i.e., theoretical understanding of basic US physics and US signs, normal lung US scanning technique and, finally, PTX recognition) before being allowed to continue their training. Paper IV shows a positive learning outcome among medical students undergoing training in an animal laboratory. The sensitivity for the US detection of PTX increased from 81.7% to 100.0%, and the specificity increased from 90.0% to 98.9%. To our knowledge, our study is the first to demonstrate that US technical skills do not deteriorate when tested six months later, which should reassure the skeptics that everyone with the appropriate training could learn lung US to accurately diagnose a PTX.

5.2 Limitations

Studying the complexities of lung US is difficult, particularly in time-critical, irreproducible and unstable trauma patient situations. Therefore, alternative PTX models must be explored and tested. In surgical specialties, animal laboratories have successfully been used for research purposes under close supervision in a controlled environment [93]. However, the results from any animal experiment cannot automatically be extrapolated to human subjects and must always be interpreted with caution. In this thesis, there are certain limitations. First, the porcine anatomy is different to that of trauma patients. The thorax is more cone-shaped, with a very

small and steeply angled apical area. The lungs are composed of apical, middle, and diaphragmatic lobes, with an accessory lobe to the right. The intralobular fissure is incomplete between the left apical and middle lobes. The trachea extends from C4/C5 to T5, where it bifurcates into the bronchi. At T3, it provides a bronchus to the apical lobe of the right lung [94]. These anatomical differences could have affected the distribution of insufflated air in our models. The cone-shaped chest allows for air to collect more easily on the outside of the lung, accounting for the increased proportion of lateral PTXs (95%) found in our models. In addition, less air was found around the top of the lungs because of the distinct shape of the porcine apical thorax. Therefore, the students were asked to scan the anterior and lateral aspects of each lung and avoid the apex, which was found to be unsuitable for US scanning. Second, the insertion of the chest tubes may have introduced small amounts of air into the pleural cavity. This excessive air was withdrawn using a syringe, but some residual air may have been added to the insufflated air volumes specified in the study protocol. Third, the positive pressure ventilation in our intubated models could potentially impact the size and progression of the PTXs. However, in humans, both the PTX size and the intrathoracic distribution of air in an intubated cohort have been reported to be similar to those in a non-intubated cohort [23], suggesting that PTX topography is not greatly affected by positive pressure ventilation. Lastly, our study design precluded the sonographers and radiologist from being completely blinded to the diagnosis they were evaluating (i.e., they knew it was a PTX) and, sometimes, to the thoracic side where the air was insufflated. This aspect could have affected the lung US and CXR results compared with blinded examinations. We also know that lung US is a very operator dependent examination and that the reproducibility of our results is more uncertain in more inexperienced hands and in real clinical settings.

These limitations are important, but we believe that our model is appropriate and that the four sub-studies address our research questions in a clinically meaningful way. In fact, the methods we used and the radiation hazard posed by serial CXR and CT scans, precludes using this experimental approach in human subjects.

5.3 Perspectives and future research

Scientific and technical developments will continually advance the special field of medical US. Since the beginning of my Ph.D. project in 2009, several important papers, guidelines and reviews on lung US have been published. Three reviews and meta-analyses concluded that bedside US performed by clinicians is a more sensitive screening test than supine anteroposterior CXR for the detection of PTXs in adult patients with blunt chest trauma [81-83]. In the international guidelines for lung US from 2012, there is strong consensus and evidence that lung US should be used in clinical settings when PTXs are included in the differential diagnosis. At this point, there are insufficient data to suggest that bedside US examinations should completely replace the supine CXR in the initial management of trauma patients [81]. One possible reason is that the diagnostic accuracy of any US procedure is dependent on the skill of the operator. Ding et al. [82] retrieved 20 English-language articles in which the pooled sensitivity and specificity were 88% and 99%, respectively, for the lung US detection of PTXs and 52% and 100%, respectively, for CXR. However, when they analyzed US performed by clinicians other than radiologists, the areas under the ROC curves showed no significant differences between US and CXR [82]. Although there is strong consensus, the level of evidence is low for lung US being a better initial study to diagnose PTXs in critically ill and injured patients with suspected PTX [73]. The cautions from the BTS may, therefore, be justified, as none of the prospective studies have demonstrated improved outcomes and management changes using US instead of CXR [76]. This thesis does not give answer to this clinical uncertainty but does show that CXRs are undoubtedly unreliable in diagnosing small and even moderate- to large-sized PTXs in porcine models. In contrast, the performance of lung US scanning for even small to miniscule PTXs is excellent and superior to that of CXR. Upcoming studies should determine how the implementation of lung US in emergency care settings could alter management strategies to improve patient outcome. In addition, the dependence between the diagnostic accuracy of lung US and the operator's experience necessitates studies that describe the optimal training required to accurately perform these examinations [81,

82]. Our ALT program, which uses competency-based checklists, provides novices with a high level of long-term diagnostic proficiency and speed for diagnosing PTXs. However, the time, venue and cost required to provide ALT are considerable, and when combined with ethical considerations, alternatives to using animals for medical training should always be sought. Further research should determine the best hands-on educational model for developing US skills, i.e., whether this should involve performing a set number of examinations, a competency-based curriculum, or some combination of the two. Another remaining question is how to best manage and monitor occult PTXs. The hypothesis is that an identifiable cohort of positive pressure ventilated patients can safely be observed without the insertion of chest tubes. The factors that predict the failure of this observational strategy (i.e., the subsequent need for a chest tube) have been identified. Positive pressure ventilated patients have a tripled risk, and those with respiratory distress are six times more likely to fail observation. In addition, the patients with a progression of their PTX (i.e., occult PTXs found on follow-up CXR) are 70 times more likely to undergo a tube thoracostomy [12]. Because this invasive procedure is associated with a 22% risk of major complications [30], unnecessary chest tubes should always be avoided. We believe the most important contribution of this thesis is the evidence that lung US can be used to accurately follow the progression of PTXs during positive pressure ventilation. If a decision is made to observe mechanically ventilated trauma patients with occult PTXs, we propose repeated lung US examinations to assess any PTX progression. Although the OPTICC trial is set to determine the treatment strategy of occult PTXs in general [33], future research should try to find any relationship between the cutaneous projections of the lung points marked with US and the best treatment options.

The goal of any diagnostic test or treatment is to affect some predefined outcome. The most important one is often the increased survival of the patients. The Utstein Formula stipulates that survival can be enhanced through better medical science, educational efficiency and local implementation. These factors interact in such a way that they can be regarded as multiplicands [126]. Lung US for diagnosing PTXs

depends not only on published papers showing its superiority to supine CXR but also on the quality of the education given to treating clinicians and the validity of the evidence-based guidelines. We had this perspective in mind when conducting our four sub-studies. Papers II and III add new knowledge to the field of lung US, and paper I and IV discuss the educational aspects. Thus, the only aspect missing from the Utstein formula is implementation. We have therefore started to use the ALT program in our US courses for air ambulance physicians in Scandinavia, held biannually in the city of Stavanger, since 2011. In our future research, we will use the knowledge and experience from this thesis and our courses to identify how point-of-care US examinations could improve patient outcomes.

6. Conclusion

Now we return to the clinical scenarios where we questioned first whether lung US performs better than supine CXR and has the potential to diagnose even small amounts of intrapleural air and, secondly, the accuracy of US in identifying the lung points compared with CT scans and whether lung US could be used to assess PTX progression in positive pressure ventilated chest trauma patients. We conclude, after reviewing the results in this thesis, that lung US has the capacity to detect even small PTXs. By adding this diagnostic tool to the clinical examination of chest trauma patients, clinicians may diagnose PTXs that otherwise would be missed on supine CXRs. Furthermore, lung point movement is a predictor of PTX progression that can be evaluated and marked by repeated lung US examinations. This feature may increase the safety of monitoring occult PTXs at the bedside, thereby avoiding complications from unnecessary chest tubes and prolonged hospitalization. Finally, to our skeptical colleagues, lung US is a basic technique to exclude or diagnose PTXs that is easily learned by novices.

7. References

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8. Papers I-IV

EDUCATIONAL ADVANCE

A Porcine Pneumothorax Model for Teaching Ultrasound Diagnostics

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Abstract

Objectives: Ultrasound (US) is a sensitive diagnostic tool for detecting pneumothorax (PTX), but methods are needed to optimally teach this technique outside of direct patient care. In training and research settings, porcine PTX models are sometimes used, but the description of the PTX topography in these models is lacking. The study purpose was to define the distribution of air using the reference imaging standard computed tomography (CT), to see if pleural insufflation of air into a live anaesthetized pig truly imitates a PTX in an injured patient.

Methods: A unilateral catheter was inserted into one pleural cavity of each of 20 pigs, and 500 mL of air was insufflated. After a complete thoracic CT scan, the anterior, lateral, medial, basal, apical, and posterior components of the PTXs were compared. The amount of air in each location was quantified by measuring the distance from the lung edge to the chest wall (LE-CW). A supine anteroposterior chest radiograph (CXR) was taken from each model and interpreted by a senior radiologist, and the image results were compared to CT.

Results: All 20 hemithoraces with PTX were correctly identified by CT, while six remained occult after interpreting the CXRs. The PTXs were anterior (100%), lateral (95%), medial (80%), basal (60%), apical (45%), and posterior (15%). The major proportion of the insufflated 500-mL volume was found in the anterior, medial, and basal recesses.

Conclusions: The authors found the distribution of the intrathoracic air to be similar between a porcine model and that to be expected in human trauma patients, all having predominantly anterior PTX topographies. In a training facility, the model is easy to set up and can be scanned by the participants multiple times. To acquire the necessary skills to perform thoracic US examinations for PTX, the porcine models could be useful.

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Pneumothorax (PTX) is common after blunt chest injury.^{1,2} Failure to diagnose and rapidly treat an enlarging PTX may cause patient death.³ The advancements in imaging technology have led to an increased emphasis on thoracic ultrasound (US), found to be more sensitive than and as specific as supine anteroposterior chest radiographs (CXRs) in diagnosing traumatic PTX.^{4–6} Computed tomography (CT) is the diagnostic reference standard, but the need to transfer the patients to the radiology department may result in delayed diagnosis and treatment.^{7,8}

The necessary training requirements to accurately perform thoracic US examinations have never been elaborated.⁹ Especially in time-critical, irreproducible, and unstable trauma patient situations, teaching the complexity of thoracic US is difficult; therefore, experimental PTX models are necessary. A model must be able to demonstrate four dynamic US signs: the lung sliding, the B-lines, the lung point, and the lung pulse, all originating from the pleural interface.¹⁰ The technical skills to operate the US machine, visualize the pleu-

ral line, and systematically search for the US lung signs to diagnose a PTX are important. Cadavers have been used for this purpose because they are ideal anatomical models, but a major drawback is the absence of any heartbeat. This reduces the realism of the US scans, especially since the lung pulse sign is caused by transmission of heart beats through the lung parenchyma. At best, a cadaver model randomized to tracheal or esophageal intubation could be used to study the presence or absence of the lung sliding sign.^{11,12} The same can be achieved with a simpler experimental model using two intravenous pressure bags submerged in water,¹³ but none of these models actually look at a real PTX. In medical simulation, computer-operated manikins¹⁴⁻¹⁶ are used as pathologic models to facilitate training of both diagnostic and treatment algorithms. A Medline and Embase literature search (terms: pneumothorax and ultrasound and [simulators or manikins]) gave no results regarding the use of manikins with PTX for US skill training.

Live anesthetized pigs with induced PTXs do not have the shortcomings seen in the other models. Their respiratory and cardiovascular systems are very much like the human systems, making these animals an important resource in biomedical research.^{17,18} What is missing is a description of the PTX topography in this model. Two recent studies used pigs to teach their participants thoracic US, but none evaluated their experimentally induced PTX against other imaging capacities such as CXR or CT.^{19,20} In supine human trauma and critically ill patients, the topography of PTX is known.^{21,22} The intrathoracic distribution of air in porcine PTX models should be studied before these models are accepted into US educational programs and curriculums.

In this study, we examined an experimental porcine model meant for US diagnostic training and research. The purpose was to describe the PTX topography in these models using the reference imaging standard CT, to see if pleural insufflation of air into a live anesthetized pig truly imitates a PTX in an injured patient.

METHODS

Study Design

This was a laboratory study of PTX in a porcine model. Qualified and experienced animal caretaker personnel monitored the health of the animals during the study period. The experiments complied with the guidelines for animal experimental studies issued by The Danish Inspectorate for Animal Experimentation under the Danish Ministry of Justice, which also approved the study, and adhered to the principles in the National Institutes of Health Guide for Care and Use of Laboratory Animals.²³

Animal Model

A total of 20 female Danish landrace pigs (mean \pm SD body weight = 54.1 \pm 4.9 kg) were used in this study. To create an experimental PTX, air was injected into the pleural space and was followed by a diagnostic evaluation with an anteroposterior CXR and a thoracic CT scan. The volumes of porcine and human lungs are comparable, with a total lung capacity of 55 mL/kg.^{18,24} Five-hundred milliliters of injected air (9.3 mL/kg) make

up one-sixth of the estimated mean total lung capacity of 3,000 mL and was chosen to create a PTX without a total lung collapse and pressure physiology (i.e., tension PTX). Furthermore, 500 mL of air will obliterate the lung sliding sign in a porcine model of this size (i.e., 4.3 mL/kg is sufficient),¹⁹ which is important if the model is to be used for US training. To determine which side received the PTX (right vs. left), coded envelopes were randomly drawn. The result was that eight pigs had a right PTX and 12 had a left PTX; none had a bilateral PTX.

Study Protocol

Each animal was sedated, anesthetized, and intubated at the animal research laboratory. The anesthesia was maintained with a continuous infusion of fentanyl and propofol. A transport respirator (Oxylog 3000, Dräger Medical, Lübeck, Germany) was used and adjusted to a tidal volume of 11 to 15 mL/kg, a respiratory rate of 10 to 12 breaths/min, a positive end expiratory pressure of 2 to 4 cm H₂O, and an inspiratory oxygen fraction of 30%, to keep the end-tidal carbon dioxide level within the normal range (4 to 6.5 KPa). All animals were monitored with electrocardiogram, core temperature, invasive arterial blood pressure, oxygen saturation, and end-tidal carbon dioxide level. The hair on the animals' chests was removed using an electrical shaver, and a 10-cm three-way stopcock catheter (BD Connecta, BD Medical, Franklin Lakes, NJ) was inserted into the pleural space through a small thoracotomy at the crossing of the fifth to seventh intercostals and anterior axillary line (Figure 1). This catheter was chosen because it was invisible on the CXRs. The surgical incision was closed by subcutaneous and cutaneous stitches. The PTX in each pig was created by 10 consecutive insufflations of air over 1 minute using a 50-mL syringe (Omnifix, B. Braun Medical, Melsungen, Germany) connected to the catheter. The three-way stopcock catheter was closed after each injection so no air escaped and the syringe refilled with air. At the radiology department, the animals were fixed in the supine position on a CT table. At the conclusion of data collection, each animal was euthanized with an injection of phenobarbital.



Figure 1. Porcine model with the catheter entering the pleural space.

Diagnostic Tests

A supine anteroposterior CXR was obtained from each animal using a portable x-ray machine (Siemens Mobillett II, Siemens, Munich, Germany). An x-ray plate (Eastman Kodak, Rochester, NY) was placed underneath the thorax. The x-ray tube of the machine was brought into position 1 meter above the sternum. The radiographic field was adjusted and focused to include the thorax from the apex to the base. The radiograph was taken using standard imaging output adjustments (117 kV/1.25 mA), developed, and digitally stored. A senior radiologist, unaware of the CT image results, was asked to determine the presence or absence of a PTX in each CXR. The radiologist was preinformed that the radiographs could be normal or have a PTX in the left, right, or both hemithoraces. The CXRs were given encrypted names and presented to the radiologist in a randomized sequence by drawing a number and assigning it to each radiograph. The radiologic definition of PTX used was a readily apparent visceral pleural line without distal lung markings (Figure 2).²⁵ The radiographs were viewed using a DICOM viewer (Philips R 2.6, Philips Medical Systems, Amsterdam, the Netherlands), and the PTX diagnoses were scored on a five-point scale (1 = definitely absent, 2 = probably absent, 3 = possibly present, 4 = probably present, and 5 = definitely present).²⁶ When calculating the sensitivity and specificity, the five-point scale was dichotomized with a score of 4 or 5 being considered positive for PTX.

To define the intrathoracic location of the air, a non-contrast-enhanced CT scan was performed using a multislice CT scanner (Philips MX 8000 quad, Philips Medical Systems, Best, the Netherlands) with the following parameters: 120 kV, 120 to 150 mA, standard filter,

6.5-mm slice thickness, 3.2-mm slice increment, and 310- to 360-mm field of view. A complete thoracic CT was obtained from the apex to the base during a short time period with inspiratory hold. The pictures were digitally stored and transferred to a picture archiving workstation. The window width was adjusted to 1500 Hounsfield units, and the window level to -500 Hounsfield units, to optimize the detection of the intrathoracic air. A second senior radiologist then analyzed and described the PTX topography according to the anterior, lateral, medial, basal, apical, or posterior position of the air relative to the lung parenchyma. As a semi-quantitative measurement of the amount of air in each of these anatomic locations, the same radiologist measured the distance from the lung edge to the chest wall (LE-CW; Figure 3). This method is derived from an objective scoring system for occult PTXs, measuring the largest dimension of the largest air collection along a line perpendicular to the chest wall.²⁷ A mean size of >7 mm is a potential factor associated with failure of observation and need of chest drain.²⁸ Furthermore, the British Thoracic Society guidelines divides the size of a PTX into "small" or "large" depending on the presence of a visible rim of air less <20 mm or ≥ 20 mm between the lung margin and chest wall on an anteroposterior CXR.²⁹ One measurement from each of the six anatomic positions was performed in each animal. The measurement was done at the CT slice level where the LE-CW distance was at its maximum, as estimated by the radiologist. Some locations did not contain any air and the distance was set to zero. The radiologist also went through the consecutive CT slices from each pig to assess any displacement of the mediastinal structures.

Data Analysis

The continuous variable LE-CW distance was measured in millimeters. The mean distance with standard deviation (SD) per anatomic location (anterior, lateral, medial, basal, apical, posterior) was calculated based on the measurements from all of the 20 animals. The data were found to be normally distributed after performing the Shapiro-Wilk test ($p \geq 0.05$ in all six anatomic positions). The statistical power was low because of the small number of measurements (i.e., only three in the posterior position). The median, 25th percentile, 75th percentile, and interquartile ranges (IQRs) were therefore also reported. Furthermore, the number of occult PTXs in the 20 animals was determined comparing the result of each CXR to the reference standard CT. The CXR and CT data were incorporated into 2×2 frequency tables and the sensitivity, specificity, and their 95% confidence intervals (CI) were calculated.³⁰ All the statistical calculations were performed using SPSS V 18.0 (IBM SPSS, Armonk, NY) and VasserStats (<http://faculty.vassar.edu/lowry/VassarStats.html>; Vassar College, Poughkeepsie, NY).

RESULTS

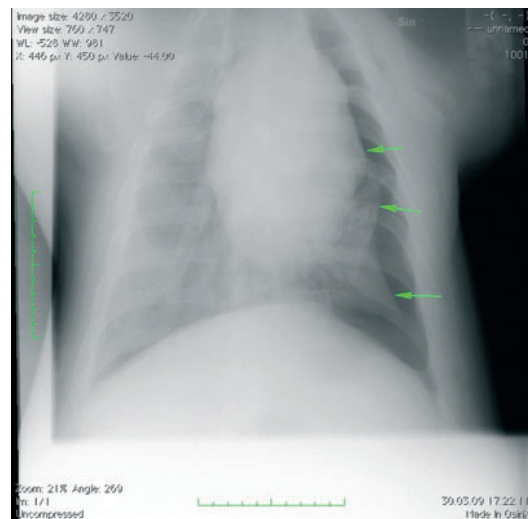


Figure 2. Supine anteroposterior CXR from the porcine model showing a left-sided PTX with readily apparent visceral pleural line without distal lung markings (arrows). CXR = chest radiograph; PTX = pneumothorax.

A total of 20 supine anteroposterior CXRs were obtained, but because two radiographs appeared blank after development, 18 valid hemithoraces with PTX, and

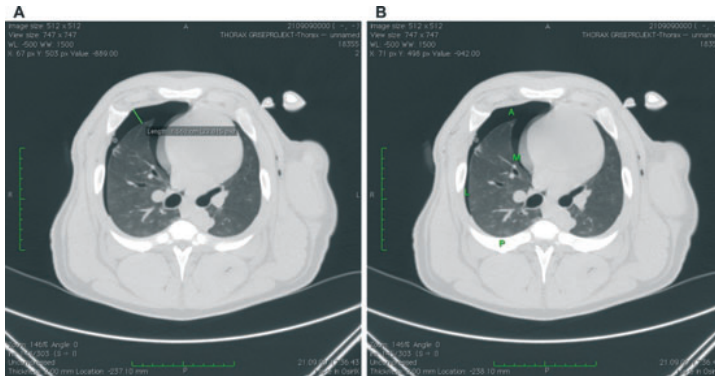


Figure 3. CT scan of a PTX, (A) Measurement of the LE-CW distance. (B) Intrathoracic distribution of the PTX. Air is in the anterior, medial, and lateral locations with no air posterior to the lung parenchyma. CT = computed tomography; LE-CW = lung edge–chest wall; PTX = pneumothorax.

18 without were included. The radiologist correctly identified 12 hemithoraces (66.7%) with PTX, while six (33.3%) were falsely considered to be negative. The sensitivity of the supine anteroposterior CXR for detecting these PTXs was 66.7%, and the specificity was 83.3% (Table 1).

The CT scans correctly identified all 20 hemithoraces with PTX and had no false positives, giving a sensitivity and specificity of 100% (Table 1). The intrathoracic anatomical locations of the air were anterior (100%), lateral

(95%), medial (80%), basal (60%), apical (45%), and posterior (15%; Table 2). The amount of air in these locations varied between each porcine model. The rim of air was large (i.e., a mean LE-CW distance ≥ 20 mm) in the anterior, basal, and medial parts of the pleural space, indicating a larger volume of air there compared to the smaller rim of air (i.e., a mean LE-CW distance < 20 mm) found in the lateral and apical locations, with almost no air behind the lung parenchyma (Table 2 and Figure 4). The 500 mL of insufflated air

Table 1
Sensitivity and Specificity of CXR and CT

Study	TP	FP	TN	FN	<i>n</i> *	<i>n</i> †	<i>n</i> ‡	Sensitivity, %	95% CI	Specificity, %	95% CI
CT	20	0	20	0	40	0	40	100.0	80.0–100.0	100.0	80.0–100.0
CXR	12	3	15	6	36	4	40	66.7	41.2–85.6	83.3	57.7–95.6

CI = binomial confidence interval, calculated by use of normal approximation interval.³⁰

CT = computed tomography; CXR = chest radiography; FN = false negative; FP = false positive; TN = true negative; TP = true positive.

**n* = valid hemithoraces.

†*n* = missing hemithoraces.

‡*n* = total hemithoraces.

Table 2
Distribution of Intrathoracic Air in a Porcine Model

Anatomic Location	Porcine PTX Distribution, <i>n</i> (%)		LE-CW Distance (mm)						
			Mean	SD	SE mean	Median	25th percentile	75th percentile	IQR
Apical	9	45	13.9	10.0	3.3	12.0	7.0	14.0	7.0
Basal	12	60	29.5	11.0	3.2	29.0	21.5	39.5	18.0
Lateral	19	95	14.2	6.5	1.5	13.0	10.0	19.0	9.0
Medial	16	80	20.6	9.0	2.3	19.5	15.0	29.0	14.0
Anterior	20	100	69.1	27.5	6.1	76.5	54.5	86.0	31.5
Posterior	3	15	7.0	2.6	1.5	6.0	*	*	*

IQR = interquartile range between the 25th and 75th percentile; *n* = numbers of hemithoraces with air in the corresponding anatomical location; PTX = pneumothorax; SD = standard deviation; SE mean = standard error of mean.

*25th percentile, 75th percentile, and IQR not calculated because of too few measurements.

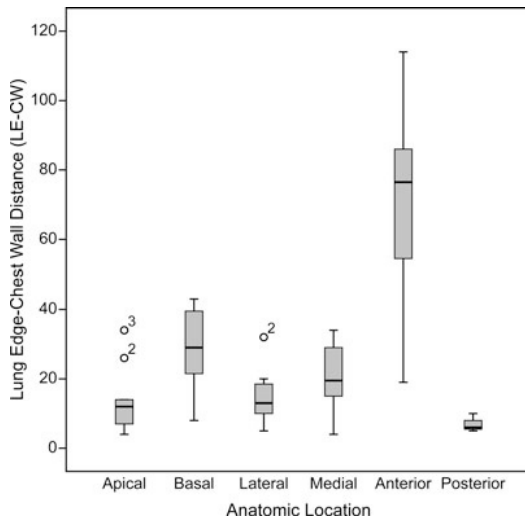


Figure 4. Box plot of the distance in the six anatomical positions. The bolded line inside the box represents the median value while the lower and upper limits of the box are the 25th and 75th percentiles. The vertical lines extend to the maximum and minimum values. The points above the box in the apical and lateral location are outliers and the numbers indicate the corresponding measurement. LE-CW = lung edge–chest wall.

caused moderate displacement of the mediastinal structures in 55%, minor displacement in 30%, and none in 15% of the animals.

DISCUSSION

Our study confirms that in a supine porcine model, all of the experimentally induced PTXs resulted in air distribution in the anterior location. We also found that the air is common in the medial (80%) and basal pleural spaces (60%), with little or no air escaping behind the lung. This is similar to what would be expected in a supine patient with no pleural adhesions or interfering thoracic injuries, where the intrathoracic air collects in the least-dependent anteromedial space and seldom in the posterior recess.^{21,31} The same distribution of air was found in nearly all of our models, confirming a close similarity between human and porcine PTX topography. The porcine lung has two lobes on the left side and four lobes on the right side,¹⁸ but this minor anatomic difference from human lungs did not alter the distribution. In humans the location of the intrathoracic air is directly associated with the force of gravity, the elastic recoil of the lung and chest wall, and the attachment of the lung to the hilar structures.^{31,32} This seems also to be true in a supine porcine model, since the air, if free to move, collects in the same anatomical positions. Among the distribution differences are an increased proportion of lateral PTXs in the models (95%). This effect may be explained by the more cone-shaped porcine thorax, which more easily allows the air to collect on the outside of the lung. The small

and distinct shape of the porcine apical thorax could also explain why less air was found there. Despite some differences, the deviation from human trauma patients is arguably minor when analyzing the amount of air in each anatomical location. Most of the insufflated air is found in the anterior, medial, and basal recesses in our models (Figure 4), the same locations where air most commonly collects in humans.³¹

In the supine position, the anteroposterior CXR of the pigs failed to detect one-third of the PTXs, again comparable to radiographic studies of chest trauma patients.^{4,33} All of these occult PTXs were subsequently found on the CT scans. Although air in the anteromedial location is difficult to detect and quantify on a supine anteroposterior CXR, the anterior chest is one of the positions to be scanned with US in the extended focused assessment with sonography for trauma (e-FAST) protocol.⁶ The predominantly anterior PTX topography found in our models therefore makes this an ideal training model for US diagnosis of PTX. This is because an US probe placed on the anterior chest would likely be positioned over an area with the PTX.

The other advantages with porcine PTX models are that they can be used for multiple scans and are fairly easy to set up in a training facility. The model is universal and can be used by various medical specialties, all of whom may benefit from training before using thoracic US to detect PTX in trauma patients. The minimum number of thoracic US examinations necessary to achieve competency in this field is unknown,⁹ but the guidelines from the American College of Emergency Physicians suggest that trainees should perform between 25 to 50 examinations.³⁴ In the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) guidelines, a minimum of 200 examinations are recommended to achieve a skill level 1 in thoracic US, encompassing multiple pathologic conditions such as pleural effusions, pericardial effusions, chest wall and lung diseases, and PTX.³⁵ Several of these pathologic conditions could be induced in the same porcine model.^{36,37} US used on experimental models could supplement theoretical lectures and scanning of normal human subjects to acquire these necessary skills.

In the global perspective, two-thirds of the world's population has no access to imaging technologies, while basic x-ray and US examinations potentially could solve up to 80% to 90% of all diagnostic problems.³⁸ The importance of implementing US and developing effective curricula to teach health care providers how to use this technology could have wide-ranging implications. This could justify the future use porcine PTX models designed for US training and research.

LIMITATIONS

This study has certain limitations. First, the porcine anatomy is not identical to that of humans; the thorax is more cone-shaped and this affects the intrathoracic distribution of air. The miss rate of PTX on the CXRs could be in part affected by this difference, but no previous studies on pigs discussing this exist. Furthermore, the radiologist was not blinded to the study

purpose and was specifically told to look for PTXs in the pictures. This could improve the CXR diagnostic accuracy results, but the sensitivity and specificity were not higher than human radiographic studies. Second, the small thoracotomy may have introduced small amounts of air into the pleural cavity, thereby making the actual intrathoracic volume higher than the insufflated 500 mL of air.

A third point deserves to be underlined. Our porcine models were intubated and mechanically ventilated, which could affect the size and evolution of the PTX. However, in humans both the PTX size and the intrathoracic distribution of air in an intubated cohort have been reported to be similar to those of a nonintubated cohort,²¹ suggesting that PTX topography is not greatly affected by applying positive pressure ventilation. The use of our porcine models for US training should therefore be generalizable to human trauma patients, intubated or not. Last, the PTXs were not created in the normal pathophysiologic manner, but rather by insufflating air through an artificially placed tube. The placement of the catheter was not random, but at the same position of the chest in each animal. This may have affected the intrathoracic distribution of air, but did not result in any major differences in PTX topography compared to humans. The use of a different insufflation technique may not give the same result.

CONCLUSIONS

We provide a detailed description of a porcine pneumothorax model that was easy to create with air distribution that closely mimics human pneumothorax and should be considered as a useful tool to teach ultrasound diagnostics. Additional studies on the use of US with this model are under way.

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ORIGINAL RESEARCH

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The intrapleural volume threshold for ultrasound detection of pneumothoraces: An experimental study on porcine models

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Abstract

Background: Small pneumothoraces (PTXs) may not impart an immediate threat to trauma patients after chest injuries. However, the amount of pleural air may increase and become a concern for patients who require positive pressure ventilation or air ambulance transport. Lung ultrasonography (US) is a reliable tool in finding intrapleural air, but the performance characteristics regarding the detection of small PTXs need to be defined. The study aimed to define the volume threshold of intrapleural air when PTXs are accurately diagnosed with US and compare this volume with that for chest x-ray (CXR).

Methods: Air was insufflated into a unilateral pleural catheter in seven incremental steps (10, 25, 50, 100, 200, 350 and 500 mL) in 20 intubated porcine models, followed by a diagnostic evaluation with US and a supine anteroposterior CXR. The sonographers continued the US scanning until the PTXs could be ruled in, based on the pathognomonic US "lung point" sign. The corresponding threshold volume was noted. A senior radiologist interpreted the CXR images.

Results: The mean threshold volume to confirm the diagnosis of PTX using US was 18 mL (standard deviation of 13 mL). Sixty-five percent of the PTXs were already diagnosed at 10 mL of intrapleural air; 25% at 25 mL; and the last 10%, at 50 mL. At an air volume of 50 mL, the radiologist only identified four out of 20 PTXs in the CXR pictures; i.e., a sensitivity of 20% (95% CI: 7%, 44%). The sensitivity of CXR increased as a function of volume but leveled off at 67%, leaving one-third (1/3) of the PTXs unidentified after 500 mL of insufflated air.

Conclusion: Lung US is very accurate in diagnosing even small amounts of intrapleural air and should be performed by clinicians treating chest trauma patients when PTX is among the differential diagnoses.

Keywords: (MeSH terms): Pneumothorax, Ultrasonography, Chest x-ray, Computed tomography, Pleura and (models animal)

Background

Pneumothorax (PTX), defined as the presence of air in the pleural space [1], is a dynamic condition with a wide continuum of severity. Tension PTXs can occur when air is allowed to enter the pleural space from the lung parenchyma, mediastinum or through the chest wall

without exiting. The increased pressure may quickly lead to a collapse of the lung and cardiovascular compromise [2]. Failure to diagnose and treat this condition may cause patient death [3]. Smaller PTXs are often more subtle and may be managed without insertion of chest tubes [4,5]. Still, they may expand and become of concern in patients who require positive pressure ventilation [6] or are subject to air ambulance transportation with limited monitoring capacity and air pressure changes [7]. Progression of a PTX is a strong individual predictor for failure when using an observational strategy, with a

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70-fold increased risk for needing a tube thoracostomy [6]. As a notable cause of preventable death [8], a prompt and accurate test to detect PTX is warranted [9]. The diagnostic challenge is that the physical examination of the patient, including auscultation, is often insufficient [4,10] and that supine anteroposterior chest x-rays (CXR) frequently fail to detect any intrapleural air [11,12]. These occult PTXs may subsequently be found on computed tomography scans, but the involved time delay and radiation hazard are potential limitations [13,14]. Lung ultrasonography (US) is a non-invasive, non-radiating, rapid and repeatable bedside diagnostic test for detecting PTX that has been shown to be more sensitive and equally specific as supine CXR [15]. We know that US is highly accurate at detecting any progression of PTX size [16], but we lack a clear understanding of the exact amount of intrapleural air needed for US imaging of PTXs to be successful. The aim of our study was to define the threshold volume at which we could diagnose PTXs with US and to compare this to CXR.

Materials and methods

Study design and setting

This was a laboratory study using a porcine PTX model [16,17] at the vivarium at the Institute of Clinical Medicine, Aarhus University, Denmark. Qualified and experienced animal caretaker personnel monitored the health of the animals during the study period. The experiments complied with the guidelines for animal experimental studies issued by the Danish Inspectorate for Animal Experimentation under the Danish Ministry of Justice, which also approved the study. The study adhered to the principles in the Guide for the Care and Use of Laboratory Animals [18]. Twenty pigs with a mean body weight of 54.1 kg (standard deviation of 4.9 kg) were used. To create an experimental PTX in each porcine model, air was introduced through a small chest tube and the intrapleural volume was gradually increased through seven incremental series of insufflation, followed by a diagnostic evaluation with US and a supine anteroposterior CXR. By drawing envelopes with a right or left code, eight pigs were randomized to have a chest drain on the right thoracic side; and 12, the left side. No pigs had bilateral PTX.

Animal model

The preparation of the porcine PTX model has been described in detail in previous studies [16,17]. In brief, the pigs were anesthetized, intubated and fixated in the supine position on the operating table. A small thoracotomy was performed at the crossing of the fifth to seventh intercostals with the anterior axillary line, and a three-way stopcock catheter (BD Connecta, BD Medical, Franklin Lakes, NJ, USA) was inserted into the pleural

space (Figure 1). The catheter was then anchored to the surrounding muscle and fascia. Excessive air introduced by the catheter placement was withdrawn using a 10 mL syringe. To control that the pleural space was empty, the study supervisor scanned the thorax for presence of intrapleural air. The respirator (GE S5 Advance Carestation™, Datex-Ohmeda, GE Healthcare, London, UK) was adjusted to a tidal volume of 11 to 15 mL/kg, a respiratory rate of 10 to 12 breaths/minute, a positive end expiratory pressure of two to four cm H₂O and an inspiratory oxygen fraction of 30%. The end-tidal carbon dioxide level was kept within the normal range (4.0 to 6.5 kPa). All animals were monitored by electrocardiography, and their core temperatures, invasive arterial blood pressures, oxygen saturations and end-tidal carbon dioxide levels were trended. At the conclusion of data collection, each animal was euthanized with an injection of pentobarbital.

Diagnostic tests

Examinations with lung US and supine anteroposterior CXR were performed to exclude any lung pathology after the catheter insertion and again after each of the seven consecutive series of air insufflations (10, 25, 50, 100, 200, 350 and 500 mL of air).

US

Two anesthesiologists with moderate experience (i.e. less than one year of clinical practice with lung US) performed the US scanning of the 20 lungs in each volume series (n = 7) with a set time limit of three minutes per lung. The first sonographer scanned the first 12 porcine models using a M-Turbo (SonoSite Inc., Bothell, WA, USA) with a C11 micro convex 8–5 MHz



Figure 1 Ultrasound scanning of the porcine pneumothorax model. The catheter enters the pleural space and is used for incremental air insufflations.

broadband array transducer (SonoSite Inc.) and the second sonographer the last eight models using Vivid Q (GE Healthcare, Horten, Norway) with a 12 L-RS multifrequency 6–13 MHz linear array transducer (GE Healthcare, Horten, Norway). The study design precluded the sonographers from being blinded to the thoracic side with the chest drain, but the diagnostic criteria of PTX were very strict based on the demonstration of the dynamic US sign “lung point” [19] in both brightness mode and time-motion mode. The scanning followed a stepwise technique to identify specific US signs as illustrated in Figure 2 and further embellished here: 1) The bat sign: On a longitudinal scan at the anterior chest two ribs with the pleural line in-between are identified. 2) Detection of lung sliding and/or B-lines: The probe is rotated approximately 90 degrees to align in the intercostal space and then gradually moved towards the lateral-posterior parts of the chest. The aim is to detect the presence or absence of horizontal movements of the pleural layers, called lung sliding and/or vertical B-lines (i.e. reverberation artifact originating from the pleural line). Lung sliding and/or B-lines rule out PTX, while both signs are absent if the pleural layers are separated by air. 3) Sea shore sign in time-motion mode: When lung sliding is present the US image has a granular appearance under the pleural line (resembling sand) and horizontal lines above the pleural line (resembling the horizon). 4) Stratosphere sign in time motion-mode: Straight horizontal lines throughout the image indicate abolished lung sliding. 5) Lung point indicating PTX: The boarder between the intrapleural air and the part of the lung still in contact with the interior chest wall is called the lung point. It appears on the US screen as two distinct sonographic patterns of lung sliding and no-lung sliding that interchange synchronous with respiration,

and can be displayed in both brightness and time-motion mode.

Once the sonographers confirmed the diagnosis of PTX, the scanning ceased and the corresponding intrapleural threshold volume was noted.

CXR

The CXRs were given encrypted names and presented to a senior radiologist in a sequence determined by a randomization procedure that assigned numbers to the pictures. The radiologist had to determine the presence or absence of a PTX on the right and left thoracic sides in each CXR (Figure 3). He was told that the porcine models could have a unilateral PTX, bilateral PTXs or even two normal lungs; additionally, the chest drains that we used were radiologically transparent to conceal any diagnostic information. The radiological definition of PTX is illustrated in Figure 4 [20]. The CXRs were viewed using a DICOM viewer (Phillips R 2.6, Philips Medical Systems, Amsterdam, the Netherlands), and the PTX diagnoses were scored on a five-point Likert scale (1 = definitely absent, 2 = probably absent, 3 = possibly present, 4 = probably present and 5 = definitely present), with a score of four or five being considered positive for PTX [21].

Data analysis

The main outcome measure in this study was to define the threshold at which PTXs become detectable using US imaging. The mean threshold volumes for the 20 pigs were presented as absolute and mean values (mL) with standard deviations. Furthermore, we calculated the sensitivity of both CXR and US for diagnosing PTX at increasing volumes of insufflated air by dividing the

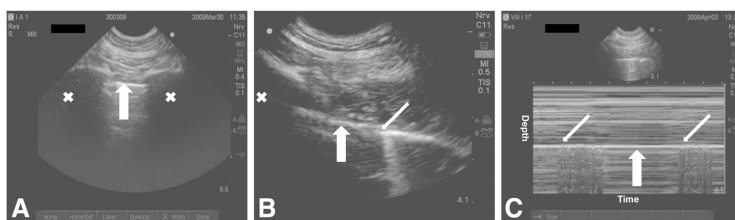
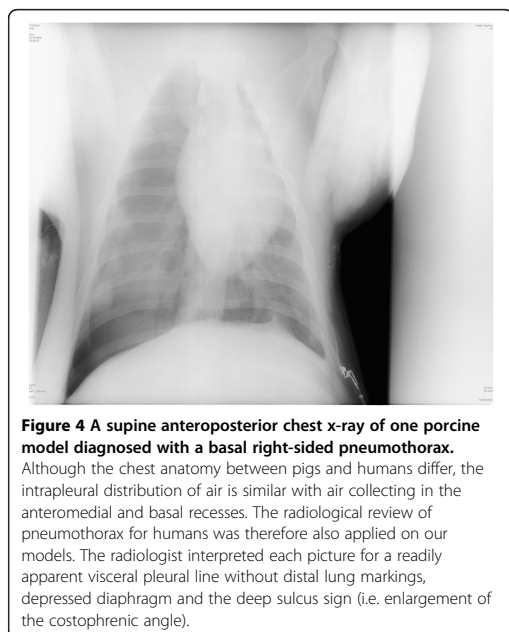
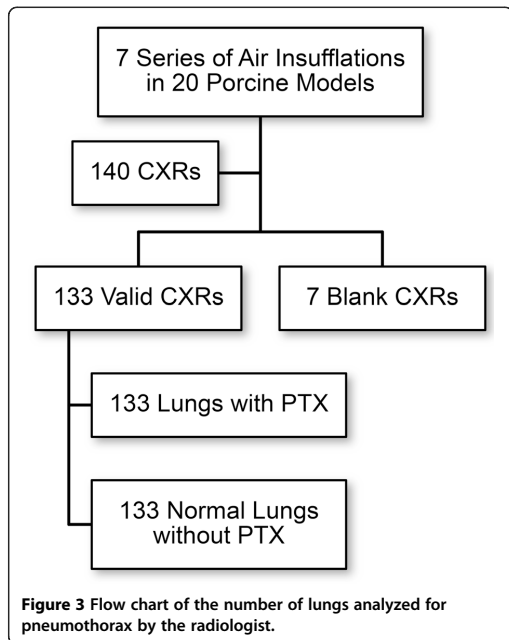


Figure 2 Ultrasound detection of pneumothorax. Symbols: Wide arrow, pleural line; thin arrow, lung point; X, rib shadow. **A**) The pleural line between two ribs is identified close to the sternum. **B**) The probe is rotated to align in the intercostal space and then gradually moved towards the lateral-posterior area of the chest, always following the pleural line. The aim is to detect “to and fro” horizontal movement at the pleural line, which is called lung sliding, excluding air between the pleural layers (visible only on video clips). Even with a pneumothorax present, the lung is still in contact with the interior chest wall. This contact point is called the “lung point” and moves in and out of the ultrasound screen alongside the pleural line, synchronous with respiration (visible only on video clips). The lung point is 100% pathognomonic for pneumothorax. **C**) In time-motion mode, the lung point appears as two distinct sonographic patterns; one pattern is suggestive of normal lung sliding (seashore pattern) and is interposed by horizontal lines (stratosphere pattern) that are seen when intrapleural air is present.



number of true positives found by the diagnostic tests with the actual number of PTXs in the porcine models. An online calculator was used to calculate the confidence intervals (<http://vassarstats.net>; Vassar College, Poughkeepsie, NY, USA), and the other analyses were performed using SPSS V.18.0 (IBM SPSS, Armonk, NY, USA).

Results

The total mean threshold volume to confirm the diagnosis of PTX in 20 porcine models using US was 18 mL (standard deviation [SD] of 13 mL). The sonographers detected 13 PTXs (65%) at an intrapleural volume of only 10 mL; an additional five PTXs (25%) were detected at 25 mL, and the last two PTXs (10%) were identified at 50 mL. The characteristics and threshold volumes of the individual animals are illustrated in Table 1. The absolute difference in mean threshold volume between the sonographer using the microconvex probe and the sonographer using the linear probe was 8 mL (i.e. a mean threshold detection volume of 15 mL [SD 12 mL] and 23 mL [SD 13 mL] respectively). The sensitivity of US detection of PTX increased from 65% to 90% and 100% as the intrapleural air volume increased from 10 mL to 25 mL and 50 mL, respectively (Table 2). At an air volume of 50 mL, the sonographers diagnosed all PTXs, while the radiologist only identified four out of 20 PTXs on the CXR pictures; i.e., a sensitivity of 20% (95% CI: 7%, 44%). As shown in Figure 5, the sensitivity of CXR as a function of volume gradually increased. However, the sensitivity leveled off at volumes ≥ 350 mL and was 67% at the maximum volume of 500 mL (95% CI: 41%, 86%), leaving one-third (1/3) of the PTXs unidentified. The diagnostic performance of supine anteroposterior CXR in diagnosing PTX is summarized in Table 3.

Discussion

This animal study demonstrates that US has the capacity to diagnose very small PTXs. The mean threshold volume of 18 mL of intrapleural air is exceptionally low and approximates what is possible to detect using the reference standard computed tomography. Furthermore, the results confirm that supine anteroposterior CXR is a poor diagnostic technique to detect air within the chest cavity in pigs. Similarly, radiographic studies using human cadavers in the supine position have demonstrated that up to 400 mL of air in the pleural space is required to detect PTXs [22]. In our study, even 500 mL of air was insufficient, as the radiologist only diagnosed 12 out of 18 (67%) of these large PTXs. Other studies using US on porcine models with PTX show that an average of 4 mL/kg [23] or 50 mL [24] was required to obliterate the normal sliding between the pleural layers. Our study is the first to present the exact volume threshold of US

Table 1 Threshold volume of intrapleural air for ultrasound confirmation of pneumothorax in 20 porcine models

Pig	Weight (Kg)	Catheter level (Costa)	Thoracic side (Pneumothorax)	Threshold volume (mL) ^a
1	61.0	3-4	Left	10
2	58.5	3-4	Left	10
3	55.5	5-6	Right	25
4	58.3	4-5	Left	10
5	58.0	5-6	Right	10
6	58.0	5-6	Left	10
7	58.0	4-5	Left	10
8	59.5	4-5	Left	10
9	58.0	5-6	Right	10
10	61.0	5-6	Left	10
11	46.5	5-6	Right	10
12	50.3	5-6	Right	50
13	52.4	6-7	Right	25
14	49.6	5-6	Left	25
15	48.6	5-6	Left	10
16	50.0	6-7	Left	50
17	52.0	5-6	Left	25
18	50.0	5-6	Right	10
19	46.4	6-7	Left	10
20	50.1	6-7	Right	25

^a The insufflated air volume at which the sonographer diagnosed pneumothorax by identifying the specific ultrasound “lung point” sign.

detection of PTX based on not only obliteration of normal lung sliding between the pleural layers but also identification of the “lung point”: the only PTX-specific US sign [19].

Competing concerns, such as spinal injury, hemodynamic compromise and the need for clinical interventions, often confine trauma patients to the supine position, where the intrapleural air collects anteromedially to the lung parenchyma. Air in this location is particularly difficult to detect and quantify in supine CXR [25]. In all of the porcine models, the sonographers observed that small PTXs resided close to the sternum on the anterior chest. This is the first lung area to be examined in the eFAST protocol [26], which may explain the increased sensitivity of US to

Table 2 The sensitivity of ultrasound detection of pneumothorax at different intrapleural air volumes

PTX volume	TP	n	Sensitivity (%)	95% CI
10 mL	13	20	65	(41, 84)
25 mL	18	20	90	(67, 98)
50 mL	20	20	100	(80, 100)

Abbreviations: PTX, pneumothorax; TP, true positive; n, number of lungs with PTX.

diagnose PTXs that are otherwise undetected on CXRs. Still, there is a scientific debate regarding whether US should replace CXR [27]. The British Thoracic Society maintains their caution to use US in the detection and management of PTXs, reflected in the last 2010 British Thoracic Society guidelines on pleural procedures and thoracic US [28]. The World Interactive Network Focused on Critical Ultrasound and the International Liaison Committee on Lung Ultrasound have expressed their concern in their comments to the guidelines [27]; in March 2012, they published the first international evidence-based recommendations for point-of-care lung US [29]. In the paper, US is presented as the preferred diagnostic test in the initial evaluation of critically ill or injured patients with suspected PTX. This conflict between the guidelines calls for further research. The British Thoracic Society made a statement that “if the PTX is so small as to be undetectable on CXR, then it is unlikely to require intervention and use of US will not have changed the management” [27], which may be valid for spontaneously breathing patients but not in patients receiving positive pressure ventilation. Detecting even small amounts of air is highly relevant, as mechanical ventilation triples the risk of observation failure and the need for a chest tube [6]. The British Thoracic Society acknowledges this clinical challenge [27] but questions whether small PTXs may fail to be detected by US [30]. Our study strengthens the evidence to the contrary, demonstrating that US could be the preferred method for diagnosing these miniscule PTXs. The results indicate that US outperform supine CXR and are significantly more reliable in the detection of small- and medium-sized PTXs. This finding is evident when comparing sensitivities between the two diagnostic tests from the first three volume series (10 mL, 25 mL and 50 mL), where a PTX volume of 50 mL was enough for US imaging to identify all PTXs in porcine models but CXR missed 80%.

Porcine anatomy is not identical to human anatomy; however, their respiratory and cardiovascular systems are similar [31,32]. Therefore, before commencing this study, we validated and tested our experimental porcine model against computed tomography and noted that the PTX topography was similar to what is expected in human trauma patients. Furthermore, our studies also revealed that the PTX volume could easily be altered through insufflation and deflation [16,17]. In fact, the design of this study, with incremental injections of air combined with the radiation hazard posed by serial CXR or computed tomography scans, precludes using this experimental approach in human subjects. However, there are limitations. First, the thoracotomies may have introduced small amounts of air into the pleural cavities when the catheters were introduced. This excessive air was withdrawn using a syringe, but some residual air may have been added to the insufflated air volumes

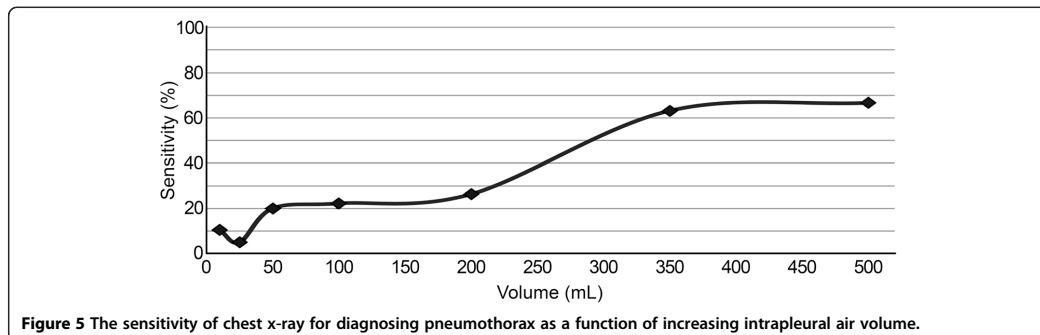


Figure 5 The sensitivity of chest x-ray for diagnosing pneumothorax as a function of increasing intrapleural air volume.

specified in the study protocol. The results reported in this study (i.e. the mean volume threshold in mL) may be too low because of this. Second, lung US is a very operator-dependent examination, and the sonographers had up to one-year experience; the reproducibility of the threshold volume is uncertain in more inexperienced hands and real clinical settings. Third, two ultrasound devices and probes (i.e. one microconvex and one linear) were used, with potentially different characteristics and ability to detect PTX. The sub-analysis based on the probes showed an absolute difference in threshold detection volume of only 8 mL, not found to be clinical relevant. Multiple transducers can be used to detect PTX, and the two probes used to scan in this study proved satisfactory. Finally, unlike the radiologist, the sonographers were not blinded to the thoracic side with the chest drain. This aspect of the procedure could have affected the US scan results and resulted in a lower threshold volume necessary to confirm the PTX diagnosis compared to blinded examinations. Still, in this study the diagnostic criteria for PTX was based on identification of the pathognomonic lung point sign in both brightness and time-motion mode. We believe the clear difference in accuracy between lung US and

supine CXR in detecting intrapleural air that was determined in our study is not readily explained by this limitation.

Conclusions

The mean threshold volume to confirm the diagnosis of PTX using lung US in a porcine model was only 18 mL, a result previously unreported. At 50 mL of intrapleural air, all PTXs were diagnosed using US while supine CXRs missed 80%. Therefore, lung US is a safe and accurate diagnostic test to diagnose even small PTXs that are otherwise undetectable and should be performed by clinicians treating chest trauma patients as an important adjunct to the clinical assessment.

Abbreviations

CXR: Chest x-ray; PTX: Pneumothorax; SD: Standard deviation; US: Ultrasound.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

NPO, MD – Literature Search, Study Design, Data Collection, Data Interpretation, Writing, Critical Review of the manuscript, ES, MD, PhD – Data Analysis, Data Interpretation, Writing, Critical Review of the manuscript, HML, MD, PhD – Study Design, Writing, Critical Review of the manuscript, FJ, MD – Data Interpretation, Writing, Critical Review of the manuscript, KW, cand.med – Study Design, Data Analysis, Data Interpretation, Writing, Critical Review of the manuscript, RA, MD - Study Design, Data Analysis, Data Interpretation, Writing, Critical Review of the manuscript, ES, MD, PhD, DMsc – Literature Search, Study Design, Data Collection, Data Analysis, Data Interpretation, Writing, Critical Review of the manuscript. All authors read and approved the final manuscript.

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Table 3 The sensitivity of anteroposterior supine chest x-ray in diagnosing pneumothorax at different intrapleural air volumes

PTX volume	TP	n ^a	Sensitivity (%)	95% CI
10 mL	2	19	11	(2, 35)
25 mL	1	20	5	(0, 27)
50 mL	4	20	20	(7, 44)
100 mL	4	18	22	(7, 48)
200 mL	5	19	26	(10, 51)
350 mL	12	19	63	(39, 83)
500 mL	12	18	67	(41, 86)

Abbreviations: PTX, pneumothorax; TP, true positive; n, number of lungs with PTX.

^a Due to some blank chest x-ray pictures, the "n" values differ in the volume series.

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Using Thoracic Ultrasonography to Accurately Assess Pneumothorax Progression During Positive Pressure Ventilation

A Comparison With CT Scanning

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Background: Although thoracic ultrasonography accurately determines the size and extent of occult pneumothoraces (PTXs) in spontaneously breathing patients, there is uncertainty about patients receiving positive pressure ventilation. We compared the lung point (ie, the area where the collapsed lung still adheres to the inside of the chest wall) using the two modalities ultrasonography and CT scanning to determine whether ultrasonography can be used reliably to assess PTX progression in a positive-pressure-ventilated porcine model.

Methods: Air was introduced in incremental steps into five hemithoraces in three intubated porcine models. The lung point was identified on ultrasound imaging and referenced against the lateral limit of the intrapleural air space identified on the CT scans. The distance from the sternum to the lung point (S-LP) was measured on the CT scans and correlated to the insufflated air volume.

Results: The mean total difference between the 131 ultrasound and CT scan lung points was 6.8 mm (SD, 7.1 mm; range, 0.0-29.3 mm). A mixed-model regression analysis showed a linear relationship between the S-LP distances and the PTX volume ($P < .001$).

Conclusions: In an experimental porcine model, we found a linear relation between the PTX size and the lateral position of the lung point. The accuracy of thoracic ultrasonography for identifying the lung point (and, thus, the PTX extent) was comparable to that of CT imaging. These clinically relevant results suggest that ultrasonography may be safe and accurate in monitoring PTX progression during positive pressure ventilation. *CHEST 2013; 143(2):415-422*

Abbreviations: CXR = chest radiograph; PTX = pneumothorax; S-LP = sternum-lung point

Physical examination, including lung auscultation, is insufficient for diagnosing a pneumothorax (PTX) in blunt trauma victims.^{1,2} The most common adjunct

used to evaluate a PTX is the plain chest radiograph (CXR) but this modality has a low sensitivity for detecting intrapleural air in patients with trauma, who are typically confined in the supine position for spinal immobilization.^{3,4} As a consequence, more than

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one-half of all traumatic PTXs are found only by a CT chest scan,⁵ which is the gold standard diagnostic test for a PTX.^{4,6} Clinically silent and radiographically undetected PTXs that are subsequently identified on CT scans are defined as occult PTXs.⁷⁻⁹ Once an occult PTX is identified, it must be decided whether to undertake tube thoracostomy or to simply observe the patient.¹⁰ Inserting a chest tube, which many believe is the only safe and appropriate PTX treatment,⁷ is associated with a 22% risk of major complications.¹¹ Observation without chest drainage, considered sufficient in spontaneously breathing patients,¹² carries a risk of PTX progression during positive pressure ventilation. Occult PTXs can evolve into tension PTXs,⁷ at which point diagnostic and treatment delays are highly lethal.¹³ Thus, a reliable, easy, and repeatable method for monitoring PTXs is needed. Ultrasonography meets all these requirements and can be performed in almost any clinical setting.¹⁴ The first international evidence-based set of recommendations for lung ultrasonography, published in March 2012,¹⁵ contains no expert consensus on how ultrasonography compares with CT scanning for assessing PTX extensions. Further research is necessary.¹⁵ We aimed to determine the accuracy of ultrasound imaging for delineating PTX extensions and to compare ultrasonography and CT scan assessment of PTX progression during positive pressure ventilation in mechanically ventilated pigs.

MATERIALS AND METHODS

This was a laboratory study of a PTX in a porcine model. Qualified and experienced animal caretaker personnel monitored the health of the animals during the study period. The experiments complied with the guidelines for animal experimental studies issued by the Danish Inspectorate for Animal Experimentation under the Danish Ministry of Justice, which also approved the study. The study adhered to the principles in the *Guide for the Care and Use of Laboratory Animals*.¹⁶

Animal Model

Three female Danish Landrace pigs (mean \pm SD body weight = 56.0 \pm 2.0 kg) were used (supplied from a local farm owned by Aarhus University). The animals were anesthetized with a combination of fentanyl, ketamine, and propofol; intubated; and positive pressure ventilated using a transport respirator (Oxylog 3000; Dräger) set to a tidal volume of 750 mL, a respiratory rate of 15 breaths/min, a positive end-expiratory pressure of 2 to 4 cm H₂O, and an FIO₂ of 30%. The end-tidal CO₂ level was kept within the normal range (4.0-6.5 kPa). All the animals were monitored by ECG, and their core temperatures, invasive arterial BPs, oxygen saturations, and end-tidal CO₂ levels were trended. In the radiology department, the animals were fixed in the supine position on a CT scan table. A three-way stopcock catheter (BD Connecta; Becton, Dickinson and Company) was inserted into the pleural space through a small thoracotomy at the intersection of the fifth to the seventh intercostal space and the anterior axillary line (Fig 1). The catheter was then anchored to the surrounding muscle and fascia. Bilateral (n = 2) and unilateral (n = 1) PTXs were induced by incrementally injecting and withdrawing air



FIGURE 1. Chest of a porcine model with intrapleural catheter and needles.

from the pleural cavity using a 50-mL syringe (Omnifix, 50 mL; B. Braun Medical Inc) connected to the catheter. At the conclusion of the data collection, the animals were killed with an injection of pentobarbital.

Diagnostic Tests

Diagnostic ultrasound and CT scan thoracic evaluations were performed at 10 different PTX volumes. The PTX volumes were: 50, 100, 150, 200, 300, 400, 500, 600, 500, and 200 mL.

Ultrasonography: The ultrasound scans were performed by two experienced anesthesiologists using a Vivid Q ultrasound machine (General Electric Company) with a 12L-RS multifrequency 6-13 MHz linear array transducer (General Electric Company). To map the PTX topography, the pleural line between two ribs close to the sternum was identified. The probe was rotated to align with the intercostal space and was then gradually moved toward the lateral-inferior area of the chest. This maneuver was conducted to locate the point on the chest adjacent to the collapsed lung on the interior chest wall, which was defined as the “lung point.”¹⁷ The lung point corresponds to the lateral edge of the PTX.¹⁸ Subcutaneous needles that were easily visualized on the subsequent CT scan were placed during inspiration to designate the cutaneous projection of the lung points and the lateral limit of the intrapleural air collection. The number of needles used varied from two (for smaller PTXs) to four (for larger PTXs). The diagnostic algorithm for ultrasound identification of the lung point is illustrated in Figures 1 to 3.

CT Imaging: To define the extension of the intrapleural air collection, a non-contrast-enhanced CT scan was performed using a multislice CT scanner (Philips MX 8000 quad, Koninklijke Philips Electronics N.V.) with the following parameters: 120 kV, 120 to 150 mA, standard filter, 6.5-mm slice thickness, 3.2-mm slice increments, and a 310- to 360-mm field of view. A complete thoracic CT scan was obtained from the apex to the base during a short inspiratory hold period. The Digital Imaging and Communications in Medicine format pictures were stored and transferred to an archiving workstation. To optimize intrapleural air detection, the window width was adjusted to 1,500 Hounsfield units and the window level to -500 Hounsfield units.

Data Analysis

The accuracy of the ultrasound imaging for delineating the PTX extension was determined by measuring the distance from

Sonographic signs of pneumothorax (PTX)

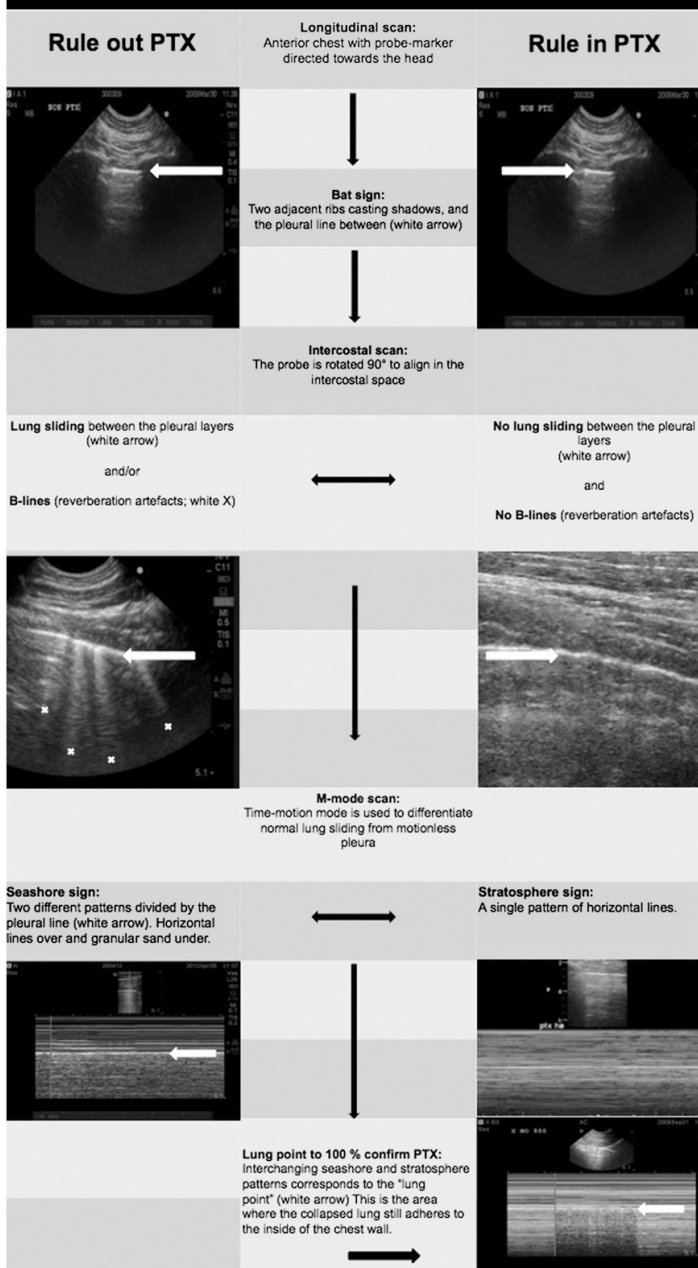


FIGURE 2. Flowchart suggesting the correct sequence for ultrasound identification of the lung point. The lung point is localized at the interface between two distinct sonographic patterns that are synchronous with respiration: one with no lung sliding (the "stratosphere sign" in M-mode) and the other with normal lung sliding (the "seashore sign" in M-mode) illustrated in the lower right corner. Demonstration of normal lung sliding is only possible on video clips.

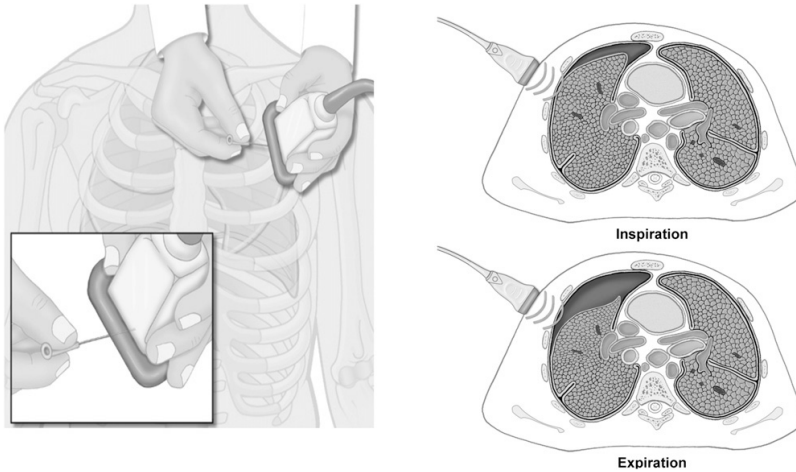


FIGURE 3. Lung points were located at the chest adjacent to the collapsed lung on the interior chest wall and aligned in the center of the ultrasound probe during inspiration. Needles were inserted to mark its cutaneous projection on the chest wall. (Illustrations: Kari M. Toverud [certified medical illustrator].)

the cutaneous needle tip to the lateral limit of the intrapleural air layer on the CT scan (Fig 4A). The difference in the lung point designations (Δ LP ultrasound-CT scan) was measured at three areas on the chest (the anterior chest between costae 1 and 5, the lateral chest between costae 5 and 8, and the posterior chest between costae 8 and 12), and the measurements were expressed as absolute and mean values (millimeters) with SDs and ranges. To reduce possible sources of bias, two readers performed all the measurements in random order, and the degree of agreement between their separate readings was analyzed using a Bland-Altman plot. A straight line from the central part of the sternum to the lung point (the S-LP distance) at two preset chest levels on the CT scans (the high level between costae 2 and 3 and the medium level between costae 5 and 6) was drawn to evaluate the

relation between lung point location and PTX size (Fig 4B). A mixed linear model regression was used to analyze the effects of PTX volume, increasing/decreasing PTX size, thoracic laterality, and chest levels on the S-LP distance. The interdependencies between the measurements in the porcine model were modeled by a compound (or autoregressive) correlation structure.¹⁹ All the statistical calculations were performed using SPSS 18.0 (IBM).

RESULTS

A total of 131 lung points were identified. The overall mean difference between the two modalities

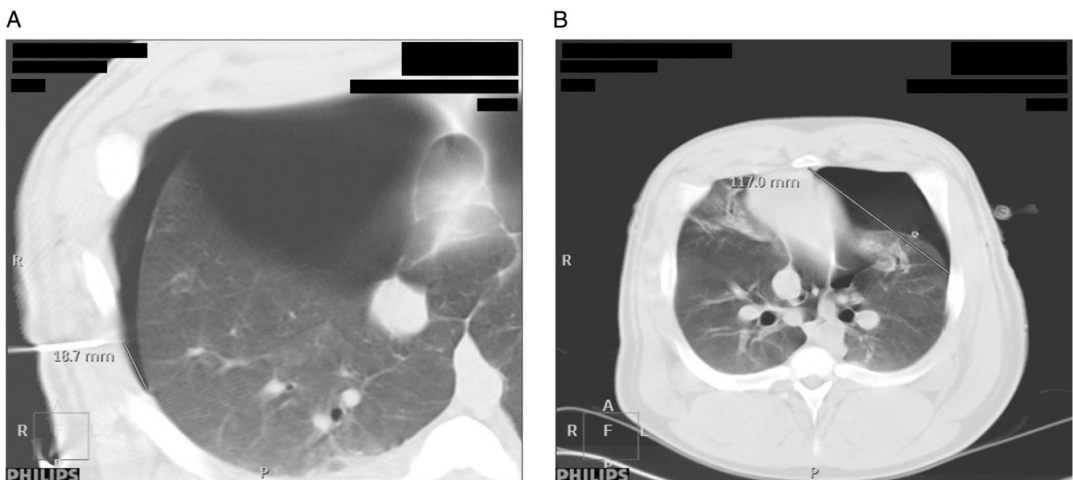


FIGURE 4. A, Difference in lung point localization was determined by comparing the ultrasound-placed needles with the extension of the PTX on the CT scans. B, The sternum-lung point (S-LP) distance. The lung is increasingly separated from the chest wall as the PTX expands, leading to lateralization of the lung point and increased S-LP distance. See Figure 2 legend for expansion of other abbreviations.

ultrasonography and CT imaging was 6.8 ± 7.1 mm, with colocation in the anterior, lateral, and posterior chest regions of 6.8 ± 8.6 mm, 6.4 ± 6.1 mm, and 7.3 ± 6.4 mm, respectively. The mean variance between the ultrasound and CT scan measurements of the lateral PTX limits was 0.0 to 29.3 mm (Table 1). Furthermore, there was a high level of agreement in the lung point measurements between readers one and two, as illustrated in the Bland-Altman plot (Fig 5). The 95% limits of agreement interval was -12.0 to 13.9 .²⁰

The mixed-model regression analysis revealed a linear relationship between the S-LP distance and the PTX volume ($P < .001$). The strength of the relation between the S-LP distance and the PTX volume differed between the left and right lungs ($P = .001$), but this divergence decreased at larger PTX volumes (Fig 6). When the PTX volume increased by 100 mL, the mean S-LP distance increased by 4 mm ($P < .001$) in the right lung and by 11 mm in the left ($P < .001$) (95% CIs, 0.01-0.07 and 0.08-0.13,²⁰ respectively). The effect of PTX volume on the S-LP distance did not vary with the chest level ($P = .746$), illustrated in Figure 6 by the parallel curves between the high and medium levels on both the right and left sides. With increasing PTX volumes, the lung point moved laterally and then medially with the subsequent withdrawal of air. Insufflation and deflation had the same absolute effect on the change in the S-LP distance ($P = .904$). The results of the mixed linear model analysis are summarized in Table 2.

DISCUSSION

Our study demonstrates that there is a linear relationship between PTX volume and the lateral position of the lung point during mechanical ventilation, and that ultrasound imaging is as accurate as CT imaging for localizing lung points. These findings are clinically relevant and may enable physicians to use ultrasonography to accurately follow the progression of PTXs during positive pressure ventilation.

Table 1—Difference in Lung Point Localization Between the Two Diagnostic Modalities Ultrasonography and CT Scanning

Measurements	Reader	No.	Mean, mm	SD, mm	Range, mm
Total	I	131	6.8	7.1	0.0-29.3
	II	131	8.1	7.5	0.0-29.4
Anterior chest	I	44	6.8	8.6	0.0-29.3
	II	38	7.1	7.8	0.0-27.2
Lateral chest	I	44	6.4	6.1	0.0-20.3
	II	45	8.6	8.2	0.0-28.5
Posterior chest	I	43	7.3	6.4	0.0-24.3
	II	48	8.4	6.6	0.0-29.4

Although it may seem reasonable to consider the size of the PTX when making procedural decisions, a newly published large prospective observational study found PTX size not to be an independent predictor of observation failure (defined as the subsequent need for a chest drain) in patients with blunt trauma. The most striking findings were that the patients whose occult PTXs expanded were > 70 times more likely to require chest tube drainage and that mechanical ventilation tripled this risk.²¹ This study used CXR imaging to assess the PTX progression, despite its being a poor method for detecting PTXs and one that underestimates the size.^{12,22} Two CT scan-based PTX classification systems, a linear size (thickness)-based algorithm^{23,24} and computer-aided volumetric measurements,²⁵ have been suggested as potential guides for making treatment decisions, but no consensus on the clinical usefulness of these PTX scoring systems has been established.²¹

The conceptual basis for using bedside thoracic ultrasound imaging in patients with occult PTX is that any PTX size progression should be detected early and treated promptly, without the need for patient transport or radiation exposure.^{26,27} There is little consensus on using lung point localization to grade PTX progression¹⁵ because the results in favor^{18,27} or opposed to using ultrasound imaging for this purpose^{14,28} are mixed. Blaivas et al¹⁴ argued that it is difficult to differentiate between medium- and large-sized PTXs, as evidenced by the weak correlation between increasing PTX volumes and the lateral position of the lung point on CT scans. They offered no statistical analysis or references to support this statement, only commenting on three CT images in the article. Soldati et al¹⁸ found a mean difference of 19 mm between ultrasound and CT scan lung points and they concluded that lung ultrasonography can be used to characterize PTX size and extension with an accuracy that approaches the reference standard. They excluded patients with occult PTX who needed mechanical ventilation because these patients often have more extensive and clinically significant PTXs. These assumptions may be invalid, because the occult PTX size and severity distributions in positive-pressure-ventilated patients are similar to nonintubated patients,⁵ and because clinically significant PTXs are equally frequent in both these patient groups.¹⁰

The remaining questions are whether an identifiable cohort of patients who are mechanically ventilated with occult PTX can be safely observed without undergoing tube thoracostomy,²⁹ and how these patients should be monitored. The first question remains controversial, pending completion of prospective randomized trials, whereas the second is addressed in this experimental study. Our results (a mean difference between the ultrasound and CT scan locations of only 6.8 mm)

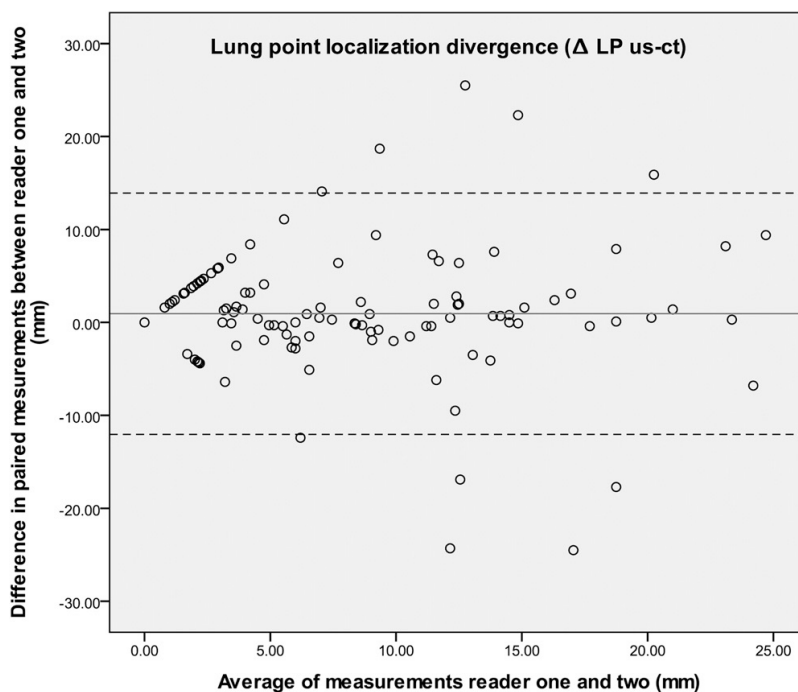


FIGURE 5. Bland-Altman plot of the paired measurements from the two readers. The high degree of agreement is indicated by a difference in measurements (the *y*-axis) that remains close to zero over the full measurement range (the *x*-axis). LP = lung point; us = ultrasound.

demonstrate that ultrasonography is comparable to CT imaging for localizing the lung point during positive pressure ventilation in a porcine model. The linear response of the S-LP distance to the PTX volume implies that the lung point moves in a progressive arc from the anterior to the lateral and to the posterior aspect of the chest wall as the PTXs expand. This progression was assessed at two different chest levels and was independent of whether the PTX was increasing or decreasing in size (Fig 6, Table 2).

Porcine anatomy is not identical to human anatomy, but the respiratory and cardiovascular systems are similar; therefore, pigs are an important animal model in biomedical research.^{30,31} Before commencing this study, we validated our PTX model using the reference standard CT scan and found equal distribution of intrapleural air as in supine patients with trauma.³² This study also revealed that the PTX volume and lung point position could easily be altered through insufflation and deflation. We performed all our measurements at the CT scan laboratory, which reduced the risk of any PTX progression occurring between the ultrasound and the CT scans. Soldati et al¹⁸ allowed up to 1 h to elapse between their tests, whereas all our measurements were performed during an inspiratory hold and within minutes of each other.

Unfortunately, the current study design, combined with the radiation hazard posed by serial CT scans, precludes using this experimental approach in human subjects.

We do recognize some limitations. First, one pig had a small amount of pleural fluid in the basal part of the right hemithorax that could have affected the localization of the lung point. Second, the thoracotomies may have introduced small amounts of air into the pleural cavities when the catheters were introduced, thereby increasing the actual PTX volume beyond the insufflated air volumes specified in the study protocol. Although excessive air was withdrawn using a 10-mL syringe before starting the air injections, it is possible that some air remained in the pleural cavity. This residual air may explain the differences in the mean S-LP distances of the right and left hemithoraces with equal PTX volumes (Fig 6). Another explanation for this finding may be the anatomic asymmetry of the thorax, with the presence of the heart in the left hemithorax affecting the air distribution. Finally, a large PTX can eliminate the lung point sign completely because the lung totally collapses and loses contact with the interior wall of the chest cavity. These patients often experience respiratory distress due to diminished lung capacity

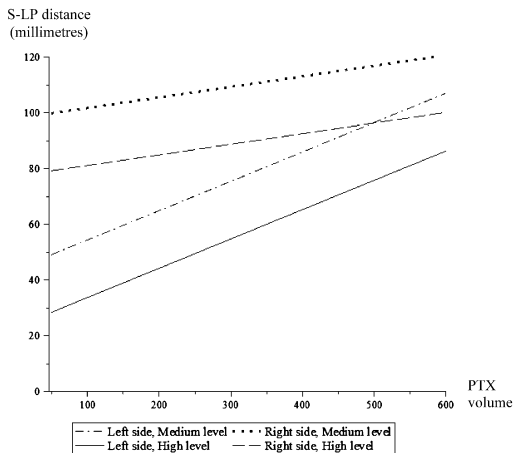


FIGURE 6. Graph illustrating the mixed linear model of the S-LP relative to the PTX volume. See Figure 2 and 4 legends for expansion of abbreviations.

and cardiovascular compromise due to tension PTXs.^{13,33} A tension PTX is diagnosed clinically and requires immediate needle decompression without the diagnostic delay associated with CXR or ultrasound imaging.¹

CONCLUSIONS

We have demonstrated that lung point movement is an indicator of PTX progression during positive pressure ventilation that can be evaluated as accurately by ultrasonography as by CT scanning. This

Table 2—Mixed Linear Model Analysis of the Sternum to Lung Point Distance Relative to the Pneumothorax Volume on the Thoracic Insufflation Side and Chest Level

Variable	Coefficient		F Test
	Estimate	95% CI	P Value
Intercept, mm	43.7	16.0 to 71.3	.010
Side ^a			
R	54.0	39.5 to 68.5	<.001
L	0.0	Reference	...
Level ^b			
High	-20.6	-27.7 to -13.4	<.001
Medium	0.0	Reference	...
Volume, mL	0.11	0.08 to 0.13	<.001
Thoracic side	-0.067	-0.11 to -0.03	.001
(R) × volume			
Thoracic side	0.000	Reference	...
(L) × volume			

L = left; R = right.

^aRight and left thoracic sides; the left is the reference.

^bChest level; high is between costae 2 and 3; medium is between costae 5 and 6 (reference).

finding may open up new possibilities for monitoring PTX development at the bedside. If a decision is made to observe patients who are mechanically ventilated with trauma and occult PTXs, we propose using serial thoracic ultrasound imaging to assess any PTX progression, which is known to be the strongest predictor of a patient's need for chest tube insertion. Further research should focus on the relationship between the cutaneous projections of the lung point and the optimal treatment options.

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Dr Oveland: contributed to the concept and design; analysis and interpretation of the data; acquisition of the ultrasound and CT imaging data; and the drafting, writing, review, revision, and approval of the manuscript.

Dr Lossius: contributed to the concept and design; analysis and interpretation of the data; and the writing, review, and approval of the manuscript.

Dr Wennelund: contributed to the concept and design, analysis and interpretation of the data, and review of the manuscript.

Dr Stokkeland: contributed to the concept and design, analysis and interpretation of the data, and review of the manuscript.

Dr Knudsen: contributed to the concept and design; analysis and interpretation of the data; acquisition of the ultrasound and CT imaging data; and the writing, review, revision, and approval of the manuscript.

Dr Sloth: contributed to the concept and design; analysis and interpretation of the data; acquisition of the ultrasound and CT imaging data; and the drafting, writing, review, and approval of the manuscript.

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Ultrasound in Emergency Medicine

ANIMAL LABORATORY TRAINING IMPROVES LUNG ULTRASOUND PROFICIENCY AND SPEED

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Abstract—Background: Although lung ultrasound (US) is accurate in diagnosing pneumothorax (PTX), the training requirements and methods necessary to perform US examinations must be defined. **Objective:** Our aim was to test whether animal laboratory training (ALT) improves the diagnostic competency and speed of PTX detection with US. **Methods:** Twenty medical students without lung US experience attended a 1-day course. Didactic, practical, and experimental lectures covered the basics of US physics, US machines, and lung US, followed by hands-on training to demonstrate the signs of normal lung sliding and PTX. Each student's diagnostic skill level was tested with three subsequent examinations (at day 1, day 2, and 6-month follow-up) using experimentally induced PTX in porcine models. The outcome measures were sensitivity and specificity for US detection of PTX, self-reported diagnostic confidence, and scan time. **Results:** The students improved their skills between the initial two examinations: sensitivity increased from 81.7% (range 69.1%–90.1%) to 100.0% (range 94.3%–100.0%) and specificity increased from 90.0% (range 82.0%–94.8%) to 98.9% (range 92.3%–100.0%); with no deterioration 6 months later. There was a significant learning curve in choosing the correct answers ($p = 0.018$), a 1-point increase in the self-reported diagnostic confidence (7.8–8.8 on a 10-point scale; $p < 0.05$), and a 1-min reduction in the mean scan time per lung ($p < 0.05$). **Conclusions:** Without previous experience and after

undergoing training in an animal laboratory, medical students improved their diagnostic proficiency and speed for PTX detection with US. Lung US is a basic technique that can be used by novices to accurately diagnose PTX. © 2013 Elsevier Inc.

Keywords—lung ultrasound; animal laboratory training; pneumothorax

INTRODUCTION

Lung ultrasonography (US) is an accurate, rapid, and repeatable bedside diagnostic test for detecting pneumothorax (PTX). A recent meta-analysis indicated that bedside lung US had higher sensitivity and similar specificity compared with supine chest x-ray study (1). In March 2012, the first international evidence-based recommendations suggested that lung US should be used in clinical settings when PTX is in the differential diagnoses (2). There are numerous possible advantages of lung US, including minimizing patient exposure to radiation, delaying or even avoiding transportation to the Radiology Department, and guiding potential life-saving therapies (i.e., pleural drainage or closer patient observation without chest tubes) (3). The potential

disadvantage is that US accuracy in diagnosing PTX is highly dependent on operator skill and weak expert consensus is that lung US is a basic technique with a possible learning curve (1,2). Today, there is uncertainty about the optimal methods of lung US training and the number of examinations that are necessary to demonstrate competency (4). Teaching the complexities of lung US is difficult, particularly in time-critical, irreproducible, and unstable trauma-patient situations. Therefore, alternative training methods must be explored and tested. In surgical specialties, animal laboratories have successfully been used to teach surgical procedures under close supervision in a controlled environment, thereby enhancing attending residents' technical skills (5,6). We investigated whether animal laboratory training (ALT) produced similar outcomes for emergency diagnostic procedures. The aim of this study was to test whether medical students, without any prior scanning experience, could improve their diagnostic proficiencies and speeds for US detection of PTX after supervised training in an animal facility.

METHODS

The ALT program was conducted in the vivarium at the Institute of Clinical Medicine, Aarhus University Hospital, Skejby, Denmark. Qualified, experienced animal caretaker personnel monitored animal health during the study period. The experiments complied with the guidelines for animal experimental studies that are issued by the Danish Inspectorate for Animal Experimentation under the Danish Ministry of Justice, which approved the study; the study also adhered to the principles in the Guide for Care and Use of Laboratory Animals (7).

Recruitment of Participants

First-year to graduate-year medical students ($n = 20$) at Aarhus University were recruited for the initial ALT program and two examinations on eight porcine models. Student demographics (i.e., age, sex, and years of medical training) and previous US experience were recorded. Each student signed a consent form with a statement of confidentiality, which was intended to inform them of their rights, obligations, and a promise of secrecy not to collaborate or reveal their own results to their fellow students. At the 6-month follow-up examination, only 11 of the initial 20 participants were able to attend due to conflicting time schedules with lectures at the University. The dropout was random (i.e., not controlled by the project manager) and based on the students' availability. The follow-up examination included only one pig because of a limited time slot of 2 h at the laboratory facility to complete the studies.

Table 1. Learning Objectives for Lung Ultrasound Education

<p>1. Basic US physics Piezoelectric crystals to generate US images The US wave (frequency, length and speed) Wave reflection and absorption Wave frequency vs. depth trade-off US transmission in different tissues/medium Artifacts</p> <p>2. US machines (knobology) Power on/off Changing probes Ergonomics Probe orientation (left/right/up/down/rotation/tilt) Depth Gain Focus Freeze Save Brightness mode (B-mode) Motion mode (M-mode)</p>	<p>3. Normal lung US Basic chest wall and lung anatomy Identification of the pleural line Lung sliding in B-mode Lung sliding in M-mode B-lines (reverberation artifacts) Diaphragm (right and left side)</p> <p>4. Pneumothorax No lung sliding in B-mode No lung sliding in M-mode No B-lines (reverberation artifacts) The lung point in B- and M-mode</p>
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US = ultrasound.

Competency-based checklist: The students had to demonstrate competency in each step (one to four) before being allowed to continue their training. The terms used are described in detail in Figure 1.

Faculty

The faculty included anesthesiologists ($n = 4$) and an Emergency Physician ($n = 1$). Faculty members contributed with lectures and supervised hands-on training sessions and student examinations.

Animal Model

Eleven Danish female landrace pigs (mean \pm standard deviation body weight 56.1 ± 1.8 kg) were used in this animal study. The porcine PTX model for teaching US diagnostics has been described in detail previously (8). Briefly, the pigs were anesthetized, intubated, and fixated in the supine position on the operating table. A small thoracotomy was performed at the crossing of the fifth to seventh intercostal and at the anterior axillary line; a three-way stopcock catheter (BD Connecta, BD Medical, Franklin Lakes, NJ) was inserted into the pleural space. To obliterate normal lung sliding between the pleural layers, approximately 200 mL of air ($4-5$ mL/kg) was insufflated. The faculty then verified the presence of intrapleural air using US and monitored the PTX between

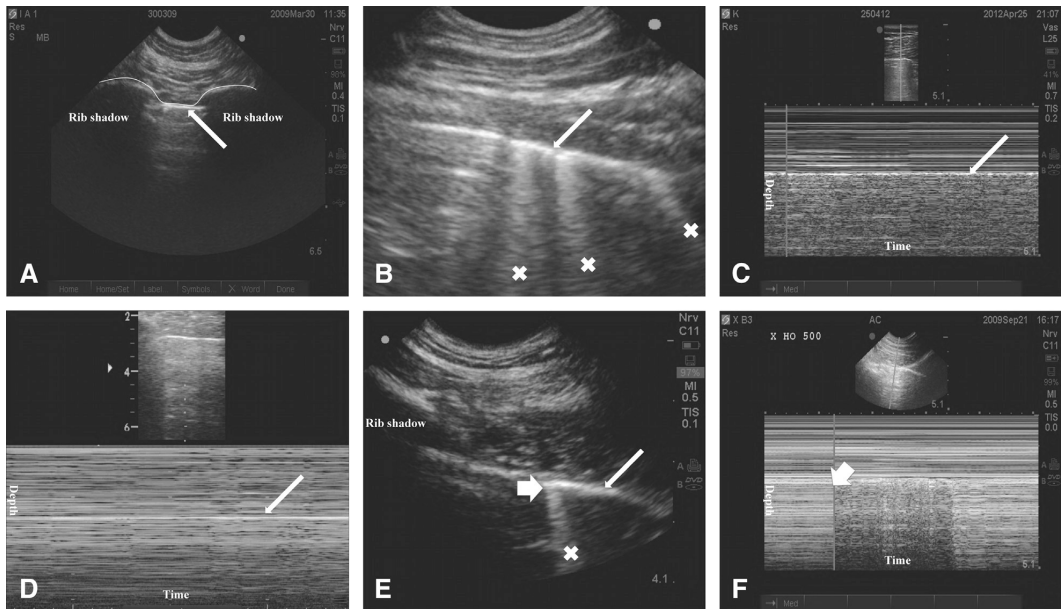


Figure 1. Algorithm to diagnose a pneumothorax (PTX). Throughout the figure, thin arrows point at the pleural line and X marks artifacts extending from the pleural line to the bottom of the screen, called B-lines. Thick arrows indicate the lung points. (A) The bat sign: On a longitudinal scan at the anterior chest, two ribs with the pleural line in-between are identified (this image resembles a bat, as shown by the thin white line). (B) Detection of lung sliding or B-lines: This image is obtained by rotating the probe approximately 90 degrees to align in the intercostal space and then gradually moved toward the lateral-posterior parts of the chest. The aim is to detect the presence or absence of horizontal movements of the pleural layers, called lung sliding (visible only on video clips) or B-lines. Lung sliding or B-lines rule out PTX, and both signs are absent if the pleural layers are separated by air. (C) Seashore sign: Time motion-mode from image B. When lung sliding is present, the image has a granular appearance under the pleural line (resembling sand) and horizontal lines above the pleural line (resembling the horizon). (D) Stratosphere sign: Abolished lung sliding can also be visualized in time motion-mode. Notice here the straight horizontal lines throughout the image in contrast to image (C). (E) Lung point: The border between the intrapleural air and the part of the lung still in contact with the interior chest wall is called the lung point (thick arrow). It appears on the screen as two distinct sonographic patterns that interchange synchronous with respiration (visible only on video clips). Identification of the lung point is 100% specific for PTX. (F) Lung point in time motion-mode: The interface between the seashore and stratosphere pattern is the lung point (thick arrow).

examinations. On a few occasions, it was necessary to insufflate 50 mL of air to keep the PTX at its original size. At the opposite side of each animal's chest, a sham operation was performed using an identical catheter placed subcutaneously without entering the pleural cavity. At the conclusion of data collection, each animal was euthanized with an injection of pentobarbital.

Training Program

The 8-h educational program consisted of didactic, practical, and experimental sessions. Phase one (2 h) comprised lectures covering basic US physics, knobology of the US apparatus, and normal lung US signs. In phase two (2 h), the lungs of healthy volunteers were scanned. Phase three (4 h) consisted of scanning experimentally induced PTXs in two porcine models. During this session, the faculty emphasized the difference between normal and pathognomonic lung US signs. The faculty followed

a competency-based procedure using learning objective checklists to ensure that each student demonstrated an acceptable skill level before being allowed to enter the next educational step (Table 1).

Lung US

The students performed all US scans using M-Turbo machines (Sonosite Inc, Bothell, WA) with one of two multifrequency (13-6 MHz or 15-6 MHz) linear array transducers (Sonosite Inc), and they followed a standardized lung scanning technique, which is illustrated in Figure 1.

Examination

The participants were given written multiple-choice questions ($n = 34$) covering US physics ($n = 10$), recognition of US pictures ($n = 17$), and video clips ($n = 7$). Two

Table 2. Baseline Characteristics of the Medical Students

	Examinations One and Two	6-Month Follow-Up Examination
Age (years), mean \pm SD	23.1 \pm 2.7	22.3 \pm 2.5
Male, n (%)	7/20 (35.0)	4/11 (36.4)
Female, n (%)	13/20 (65.0)	7/11 (63.6)
No. of completed semesters,* mean \pm SD	4.8 \pm 3.2	5.1 \pm 3.2
Previously observed US examinations, n (%)	3/20 (15.0)	NA
Previously performed US examinations, n (%)	3/20 (15.0)	NA
Lung US experience in detecting PTX, n (%)	0/20 (0.0)	NA
Use of lung US since the ALT program, n (%)	NA	1/11 (9.1)

ALT = animal laboratory training; NA = not applicable; PTX = pneumothorax; SD = standard deviation; US = ultrasound.

* Out of 12 possible semesters at the medical school.

scanning examinations followed the ALT program, and the 6-month follow-up examination ended the study.

First examination. PTXs were introduced in three of eight lungs (right side, $n = 2$ and left side, $n = 1$); one pig had two normal lungs, and none had bilateral PTX. Coded envelopes were randomly drawn to determine which side received the PTX (right vs. left). The students were instructed to randomly scan the eight lungs; the random order was determined by choosing a numbered card (one to eight) that corresponded to each lung. The participants did not know whether to expect that each pig would have unilateral or bilateral PTX, or two normal lungs. After each lung scan, the students were asked to diagnose the lung as normal or PTX and to score their confidence level about the diagnosis on a scale from 1 (not sure at all) to 10 (absolutely sure). The scanning time was measured from skin contact (of the probe) to the final diagnosis given by the participant. Faculty members were present at the examination, however, they did not provide instructions.

Faculty feedback and second examination. Before the second examination, the faculty provided 10-min summary lectures to each student, emphasizing the impor-

tance of using the lung US scanning algorithm systematically. In the second examination, PTXs were introduced in four of the eight lungs (right side, $n = 3$ and left side, $n = 1$), and none of the pigs had bilateral PTX; otherwise, this examination was identical to the first examination.

6-Month follow-up examination. At the 6-month follow-up examination, a final survey was given to the medical students to determine the number of lung US scans they had performed clinically since the ALT program. The examination was identical to the previous two examinations, except that one pig was prepared with one normal lung (left side) and one PTX (right side). The students did not receive any training before the final testing.

Data Analysis

Student performance was assessed through theoretical multiple-choice questions and hands-on practical examinations. The confidence level, scan time, and multiple-choice scores were presented as mean \pm standard deviation. The diagnostic skills in detecting PTX using lung US were analyzed using 2×2 frequency tables, and sensitivity, specificity, and 95% confidence intervals were calculated (9). Because not all participants completed the 6-month follow-up examination, a subanalysis was done to visualize possible differences in diagnostic skills in the follow-up group of 11 participants and the nine participants' dropout group. The diagnostic accuracy (i.e., the percentage of all correct answers) after the initial examinations (day 1 and day 2) was therefore calculated for the two groups separately. In addition, a generalized estimating equation analysis with an unstructured correlation structure tested the dependency of the number of correct student answers (PTX yes/no) on the timeline (i.e., first examination, day 1 \rightarrow second examination, day 2 \rightarrow final examination, 6 months) to illustrate the learning curves. Similar timeline assays were performed for the confidence level and scan time, and $p < 0.05$ was regarded as significant. All of the statistical calculations were performed using SPSS V.18.0 (IBM SPSS, Armonk, NY) and VasserStats (<http://vassarstats.net>; Vasser College, Poughkeepsie, NY).

Table 3. Sensitivity and Specificity of Pneumothorax Detection with Ultrasound

Examination	TP	FP	TN	FN	n*	Sensitivity (%)	95% CI	Specificity (%)	95% CI
Day 1	49	10	90	11	160	81.7	69.1–90.1	90.0	82.0–94.8
Day 2	80	1	79	0	160	100.0	94.3–100.0	98.9	92.3–100.0
6 months	11	0	11	0	22	100.0	81.5–100.0	100.0	81.5–100.0

CI = confidence interval; FN = false negative; FP = false positive; TN = true negative; TP = true positive.

* Number of lung ultrasound examinations.

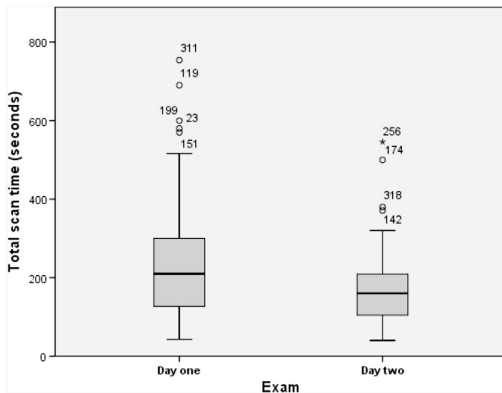


Figure 2. Box plot of the scan time (seconds) per lung on examination days 1 and 2. The box indicates the interquartile range, the horizontal line in the box, the median; and the “whiskers” of the box are outer boundaries called Tukey’s hinges. The points above the boxes are outliers marked by numbers that indicate the corresponding measurement.

RESULTS

Participants

Twenty medical students completed the laboratory training and the two subsequent examinations; depending on availability, 11 of the 20 students attended the 6-month follow-up examination. Table 2 shows the students’ demographics, including their baseline characteristics and previous US training.

Written Test Scores

The mean test scores for the multiple-choice questions were 31.0 ± 2.7 of 34 points (91.1% correct). The scores for the US physics questions, the picture test, and the video-clip test were 8.4 ± 1.4 (of 10), 16.0 ± 1.3 (of 17), and 6.6 ± 0.5 (of 7), respectively.

Sensitivity and Specificity for PTX Detection

In the first examination, 160 US examinations were performed and 139 lungs (86.9%) were correctly diagnosed, resulting in 10 false positives and 11 false negatives. The medical students detected 90 of 100 normal lungs and 49 of the 60 PTXs, for a sensitivity score of 81.7% and a specificity score of 90.0%; the 95% confidence intervals were (69.1–90.1) and (82.0–94.8), respectively. In the second examination, 159 of 160 (99.4%) diagnostic answers were correct, with one false positive. The sensitivity was 100.0% and specificity was 98.9%; the 95% confidence intervals were (94.3–100.0) and (92.3–100.0), re-

spectively. The subanalysis of diagnostic accuracy in the 6-month follow-up group ($n = 11$) and dropout group ($n = 9$) was 94.3% and 91.6%, with 95% confidence intervals of (90.0–98.7) and (85.9–97.4), respectively.

In the 6 months between the laboratory training and the follow-up examination, one student had performed lung US for approximately 1 h on a fellow student (Table 2). The participants that did return for testing interpreted all the 22 US examinations correctly (i.e., 11 normal lungs and 11 PTXs), resulting in 100.0% sensitivity and specificity scores and confidence interval of (81.5–100.0).

The medical students had no deterioration in sensitivity and specificity between the three examinations when the dependency of the correct answers was tested on the timeline (first examination day 1 → second examination day 2 → final examination 6 months), with $p = 0.018$. The diagnostic scores for the three time periods are summarized in Table 3.

Confidence Level

Mean confidence levels (using a 1 to 10 scale) were 7.8 ± 1.9 , 8.8 ± 1.6 , and 9.0 ± 1.3 for the three examinations. The increase in self-reported confidence from the first to the final examination (i.e., 6-month time span) was significant ($p = 0.006$).

Scan Time

Mean scan time per lung was 230 ± 134 s and 168 ± 82 s at the first and second examinations, respectively, and it increased 6 months later to 222 ± 80 s. Examination times decreased significantly between the initial examinations (i.e., a 1-min drop; $p < 0.05$), resulting in scan times of <3 min per lung (illustrated by the box-plot in Figure 2).

DISCUSSION

Our study shows that ALT significantly improved the diagnostic proficiency and speed for PTX detection with US in a group of medical students who had no prior scanning experience of the lungs. Animal laboratories provide a realistic simulation environment in which students are able to repeatedly perform diagnostic procedures on living tissue. This experience is particularly important for lung US because PTX diagnosis relies on dynamic signs that occur at the pleural line simultaneously with respiration (Figure 1). Many emergency US educational programs have focused on the number of examinations required for skill acquisition. In our training, however, we adopted a non-numerical model that focuses on a competency-based checklist evaluation of each student (10,11). This model yielded a written test score of 9 (of

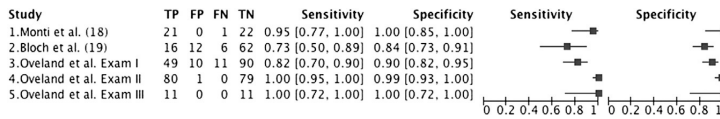


Figure 3. Forest plot comparing the sensitivity and specificity of lung ultrasound detection of pneumothorax in studies using porcine models. FN = false negative; FP = false positive; TN = true negative; TP = true positive.

10) correct answers, improved the students' diagnostic capabilities and technical skills, and increased their diagnostic self-confidence. In addition, we provide the first evidence that students who receive ALT sustain improvement in their diagnostic competency, shown by the lack of deterioration in sensitivity and specificity between the assessments. The reduction in the mean scan time per lung is also suggestive of a learning outcome among the students.

One method for learning lung US is to scan trauma patients, however, other ways might be necessary to obtain an acceptable skill level before use in real clinical settings. Cadavers have been used for training purposes because they are ideal anatomical models, although the realism of the US scans is low, particularly because of the lack of heartbeats and normal respiration. At best, a cadaver model that is randomized for tracheal or esophageal intubation could be used to study the presence or absence of the lung sliding sign (12). The same result can be achieved with a simpler experimental model that uses two intravenous pressure bags submerged in water (13). Brief training modules that use instructional videotapes improve PTX image recognition, however, technical skills are not developed without hands-on training (14,15). Scanning healthy volunteers combined with a theoretical understanding of image interpretation enhances the standard for lung US detection of PTX (16,17). However, anesthetized pigs are vastly different from these other educational models because the participants are diagnosing an actual PTX in a breathing animal. Other studies using experimentally induced PTXs in porcine models have reported deviant results ranging in sensitivity from 73% to 95%, with specificity ranges from 84% to 100%. The participants in these studies received short 10 to 60-min introductory lectures before performing lung US examinations (i.e., 44 and 96 in total) (18,19). In addition, their laboratory training focused on the lung sliding and B-lines, only allowing PTX to be safely ruled out (20,21). In contrast, our 8-h ALT program emphasized the importance of the lung point, a pathognomonic US sign for PTX when found (22). The combination of competency-based checklist evaluations for each student and a much larger number of practice examinations (i.e., 342 in total) could explain the higher sensitivity and specificity for US detection of

PTX that was found in our study. A forest plot compares our results with the other porcine PTX model trials (Figure 3).

The time, venue, and cost required to provide ALT is considerable and, when combined with ethical considerations, alternatives to using animals for medical training should always be sought. In medical simulations, plastic mannequins are used as pathological models to facilitate the training of both diagnostic and treatment algorithms (23–25). These models will always lack certain physical properties of living tissue, including hemorrhage, a beating heart, and breathing lungs. These shortcomings are diminished by the introduction of computer-based simulation, a promising technology that has enormous educational potential for teaching procedures. Still, Medline and Embase literature searches (terms: *pneumothorax* AND *ultrasound* AND [*simulators* OR *mannequins*]) returned no results of studies using computer-operated mannequins for lung US skill training.

Limitations

The porcine anatomy is not identical to that of humans, however, their respiratory and cardiovascular systems are similar (26,27). When validated against computed tomography, our porcine PTX model had the same distribution of intrapleural air that can be expected in supine trauma patients (8). However, we do recognize some limitations. The apex of the chest is cone shaped and unsuitable for US scanning. Therefore, the students were asked to scan the anterior and lateral aspects of each lung and avoid the apex. In addition, only 11 of the original group of 20 medical students could attend the last examination 6 months after the training. This leaves the possibility that the returning participants could have had better diagnostic skills after the initial training and examinations, but the subanalysis only showed a very small difference of 2.7 percentage points (i.e., 94.3% minus 91.6%) in diagnostic accuracy between the two groups (i.e. follow-up and dropout). Still, the 100% diagnostic accuracy found on the 6-month follow-up examination might be lower in a more comprehensive study, where more US examinations are performed on more than one pig.

CONCLUSIONS

This study provides evidence that novices can learn how to diagnose PTX using lung US. Training in an animal facility imparts a high level of long-term diagnostic proficiency and speed for diagnosing PTX. Additional research should reveal the best hands-on educational model for developing US skills, whether this should involve performing a set number of examinations, a competence-based curriculum, or some combination of the two.

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ARTICLE SUMMARY

1. Why is this topic important?

Pneumothorax is common after significant blunt chest trauma and failure to diagnose and treat this condition can cause patient death. Lung ultrasound detects nearly all pneumothoraxes and the training requirements and methods necessary to perform these examinations must be defined.

2. What does this study attempt to show?

We test whether animal laboratory training is associated with sustained improvement in the diagnostic competency and speed of pneumothorax detection with ultrasound.

3. What are the key findings?

Animal laboratory training imparts a high level of long-term diagnostic proficiency for ultrasound detection of pneumothorax. The students' scan time per lung decreased by >1 min after the training.

4. How is patient care impacted?

Adding lung ultrasound to the physicians' armamentarium could improve the diagnostic accuracy for detection of pneumothorax and result in more prompt and correct patient care.