PROTOCOL TITLE Simplified Lung Ultrasound protocol for detection of Pneumonia

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LIST OF ABBREVIATIONS AND RELEVANT DEFINITIONS

AE	**Adverse Event**
AUC	**Area under the curve**
AMC	**Amsterdam Medical Center**
BLUE	**Bedside Lung Ultrasound in Emergency**
CCMO	**Central Committee on Research Involving Human Subjects; in Dutch: Centrale Commissie Mensgebonden Onderzoek**
CXR	**Chest X-ray**
CT	**Computed Tomography**
DSMB	**Data Safety Monitoring Board**
ED	**Emergency Department**
GCP	**Good Clinical Practice**
GDPR	**General Data Protection Regulation; in Dutch: Algemene Verordening Gegevensbescherming (AVG)**
ICU	**Intensive Care Unit**
IMDD	**Investigational Medical Device Dossier**
LUS	**Lung ultrasound**
METC	**Medical research ethics committee (MREC); in Dutch: medisch-ethische toetsingscommissie (METC)**
NPV	**Negative predictive value**
PPV	**Positive predictive value**
Review Committee	**Medical research ethics committee (MREC) or CCMO**
ROC	**Receiver Operating Characteristic**
(S)AE	**(Serious) Adverse Event**
Sponsor	**The sponsor is the party that commissions the organisation or performance of the research, for example a pharmaceutical company, academic hospital, scientific organisation or investigator. A party that provides funding for a study but does not commission it is not regarded as the sponsor, but referred to as a subsidising party.**
STARD	**Standards for reporting of diagnostic accuracy**
UAVG	**Dutch Act on Implementation of the General Data Protection Regulation; in Dutch: Uitvoeringswet AVG**
WMO	**Medical Research Involving Human Subjects Act; in Dutch: Wet Medisch-wetenschappelijk Onderzoek met Mensen**

SUMMARY

Rationale: Pneumonia is a common and serious disease that requires early and accurate diagnosis. Lung ultrasound (LUS) is a safe, inexpensive, and reliable method to identify pneumonia at the bedside. The current standard method, the six-point Bedside Lung Ultrasound in Emergency (BLUE) protocol, requires experience to correctly locate and interpret fixed scanning points, limiting its broader use. A simplified sweep-based method, using continuous probe movements over the chest, may reduce operator dependency while maintaining diagnostic accuracy.

Objective: The primary objective is to compare the diagnostic accuracy of the simplified sweep-based protocol with the standard BLUE protocol for identifying pneumonia. Secondary objectives are to assess (1) agreement in LUS A, B, C and E- patterns between both methods, (2) examination time and feasibility of the simplified method, (3) AI development to detect pneumonia via LUS A, B, C and E- patterns, and (4) To compare the diagnostic accuracy of both the simplified sweep-based protocol and the validated BLUE protocol with chest X-ray (CXR) and/or gold standard computed tomography (CT) in diagnosing pneumonia.

Hypothesis: The simplified sweep-based method provides diagnostic accuracy comparable to the standard six-point BLUE protocol for detecting abnormalities consistent with pneumonia.

Study design: this is a single-centre, prospective, observational study conducted at Amsterdam UMC, location Amsterdam Medical Centre (AMC). Adult patients (≥18 years) admitted to the emergency department (ED) or intensive care unit (ICU) with respiratory insufficiency and/or suspected pneumonia will be included. Only awake, non-sedated patients who can sit or be positioned semi-upright, allowing posterior lung scanning, are eligible.

Intervention (if applicable): No intervention or investigational product is used.

Main study parameters/endpoints: The primary study parameter is the diagnostic accuracy (sensitivity, specificity, positive and negative predictive values) of the sweep-based method compared to the standard BLUE protocol.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Patients will experience no risk from participation in the study but will

also not benefit. However, participation may indirectly contribute to improved diagnostic efficiency and accessibility of LUS for future patients.

1. INTRODUCTION AND RATIONALE

Pneumonia is the leading cause of infectious mortality worldwide, causing over 2.5 million deaths in 2019 (1). In Europe, it accounts for 3.3 million cases, nearly 1 million hospitalizations, and 200,000 ICU admissions annually (2). In the Netherlands, it is the most common infectious cause of ICU admission, with about 5,000 cases per year and a mortality rate of 30-40% (3). Accurate and timely diagnosis is critical, yet the current diagnostic standard relies heavily on CXR or CT. These modalities are often difficult to perform in critically ill patients and therefore often delay diagnosis. Moreover, they may be unavailable or impractical in many settings, such as the ED, general practices, or low- and middle-income countries (LMIC) (4).

Lung ultrasound (LUS) has emerged as a safe, rapid, and radiation-free alternative that can be performed at the bedside at comparable performance as CXR (5-9) but its use is limited by operator dependency and the need for specific expertise (10). Using the validated Bedside Lung Ultrasound in Emergency (BLUE) protocol, LUS is accurate in detecting lung abnormalities across a variety of clinical settings (11-14). However, interpretation varies significantly between operators, particularly among non-experts, which reduces reliability and limits scalability (10). Several studies highlight that diagnostic performance decreases with less experienced users, particularly in non-hospital settings (9, 15). A simplified acquisition approach may therefore improve accessibility and standardization of LUS.

Preliminary work suggests that continuous “sweep” techniques, where the probe is moved in a controlled longitudinal motion over each chest region, can capture the same diagnostic information as a point-by-point approach (16, 17). However, these simplified acquisition methods have not yet been clinically compared to the BLUE protocol.

This study aims to address this knowledge gap by directly comparing two acquisition methods: the standard 6-point BLUE protocol and a simplified long-axis sweep protocol. The results will determine whether the simplified method can provide equivalent diagnostic information while reducing the level of expertise required to obtain reliable LUS images.

The study focuses on adult ICU and ED patients with respiratory insufficiency or suspected pneumonia. This population represents the main clinical setting in which LUS is already applied and where simplified methods could offer the greatest benefit. In these patients, CXR

and CT are often difficult to perform, and the diversity of lung pathology provides a robust context for protocol comparison. No minors or incapacitated adults will be included.

2. OBJECTIVES

Primary Objective:

- To compare the diagnostic accuracy of the simplified sweep-based protocol with the validated BLUE protocol for identifying pneumonia

Secondary Objective(s):

- To compare the agreement in LUS ‘ABCE’ patterns identified between the sweep-based and the BLUE protocols
- To measure examination time and feasibility of the simplified method
- To develop AI that automatically detects pneumonia based on LUS A, B, C and E-patterns
- To compare the diagnostic accuracy of both the simplified sweep-based protocol and the validated BLUE protocol with CXR and/or gold standard CT in diagnosing pneumonia

3. STUDY DESIGN

This is a single-center, prospective, observational cohort study conducted at Amsterdam UMC, location AMC. Each participant will undergo two additional LUS examinations during a single session: the standard 6-point BLUE protocol, and a simplified 4-sweeps protocol. Both examinations will be performed consecutively using CE-marked handheld ultrasound devices alongside standard care. The total duration per participant is approximately 10-20 minutes. There will be no follow-up visits.

The study is observational and non-interventional: no investigational product is administered, and no deviation from routine clinical management occurs. A within-subject design was chosen to enable direct comparison of both acquisition methods under identical clinical conditions. The total recruitment and data collection period is expected to last approximately 12 months, followed by data analysis and reporting. We intend to include 88 patients.

We use the BLUE protocol as the reference standard. It has been developed in the ED and validated in the ICU with the standardised LUS scores we also intend to use (A, B, C, E profiles) (11-14, 18). It has a diagnostic accuracy of 90,5% for diagnosing lung oedema, pneumonia, COPD/asthma, pulmonary embolism, pneumothorax (13, 19). A recent meta-analysis for using LUS in the diagnosis of adult pneumonia found a pooled sensitivity, specificity and positive predictive value (PPV) of 92% (95% CI: 91–93%), 94% (95% CI: 94 to 95%) and 93% (95% CI: 89 to 96%), respectively (20). In this meta-analysis, multiple LUS protocols were included and pneumonia was defined using clinical signs and symptoms plus either CXR or chest CT as the reference test.

LUS, specifically when applying the BLUE protocol, outperforms CXR in the diagnosis of pneumonia (12, 21). When chest CT is used as the reference standard for pneumonia diagnosis, LUS (using the BLUE protocol) demonstrates high diagnostic performance, with a sensitivity >0.88, specificity >0.83 and overall accuracy >0.88 (12, 22). For this reason, the BLUE protocol was considered an acceptable reference standard for the diagnosis of pneumonia in the present study. Moreover, the BLUE protocol is particularly useful as reference to the new sweep protocol since they can both be performed at the bed side and in the same session, limiting influence of diagnosis by change over time. In contrast, chest CT is less readily available, not routinely performed in all patients, and often conducted at a different time point, which may introduce bias.

No single reference test for the diagnosis of pneumonia is without limitations. LUS is a good alternative that can be performed at the bed side, but assess only a limited number of predefined lung regions, which may result in missed pneumonia findings due to incomplete

visualization of the lungs. Therefore, a secondary objective is to compare the pneumonia diagnosis based on gold standards CXR and/or CT with the diagnosis based on both LUS protocols.

4. STUDY POPULATION

4.1 Population (base)

Participants will be recruited from adult patients (≥18 years) admitted to the ICU or ED of Amsterdam UMC, location AMC, with respiratory insufficiency and/or suspected pneumonia. The source population is sufficient to achieve the planned sample size within the estimated 12-month recruitment period. The study will include awake, non-sedated patients who can sit or be positioned semi-upright to allow posterior lung scanning. Both male and female patients will be included without restriction on ethnic background. The expected prevalence of pneumonia in this population is approximately 50% based on clinical experience in this setting, since patients are selected on having respiratory symptoms by the referring clinician.

4.2 Inclusion criteria

To be eligible, participants must meet all of the following criteria:

- Age ≥18 years.
- Admitted to the ICU or ED at Amsterdam UMC, location AMC.
- Clinical suspicion of pneumonia and/or presence of respiratory insufficiency.
- Patients who can be scanned in the upright position.
- Written informed consent provided by the patient.

4.3 Exclusion criteria

A potential participant who meets any of the following criteria will be excluded from participation in this study:

- Factors that make LUS unusable, such as major thoracic injury, subcutaneous emphysema, chronic pulmonary effusions, major chest wall abnormalities.

4.4 Sample size calculation

The sample size is based on the primary objective: to determine the diagnostic accuracy (sensitivity and specificity) of a simplified lung ultrasound sweep method compared with the standard BLUE protocol for diagnosing pneumonia in adults with suspected pneumonia.

Based on an expected sensitivity and specificity of 90% and a pneumonia prevalence of 50%, the required sample size was calculated to be 88 participants, according to Table 2 of the work from MA Bujang (23). The calculation follows a 95% confidence level (α = 0.05) and a precision of ±10% for both sensitivity and specificity. This sample size provides sufficient power (>80%) to obtain reliable estimates of sensitivity, specificity, predictive values, and likelihood ratios within clinically relevant margins.

We must ensure that we have at least 44 cases or controls. The required sample size will be adjusted if the prevalence differs from the assumed 50%.

The high diagnostic accuracy of LUS for pneumonia when using the BLUE protocol, demonstrated by its strong sensitivity and specificity compared with the gold standard chest CT (12, 22), indicates that the risk of misclassification is minimal. Given this strong diagnostic performance, additional corrective statistics to address limitations of the BLUE protocol were not considered necessary in the present study.

The expected sensitivity and specificity of 90% were chosen based on clinical relevance and previous studies on LUS for the diagnosis of pneumonia (20), more extensively described in paragraph 3. To minimize the risk of mislabelling, operators will have the opportunity to discuss LUS findings with experienced experts. The new, simplified sweep protocol is therefore required to achieve at least comparable diagnostic accuracy to demonstrate its suitability for clinical use.

5. METHODS

5.1 Study parameters/endpoints

5.1.1 Main study parameter/endpoint

The primary endpoint of this study is the sensitivity and specificity of the simplified sweep-based LUS method for diagnosing pneumonia, compared with the validated BLUE protocol as the reference test.

5.1.2 Secondary study parameters/endpoints (if applicable)

- Sensitivity and specificity of agreement in LUS A, B, C and E patterns from the sweep-based protocol and standard 6-point BLUE protocol
- Examination time of the simplified sweep-based method compared with the BLUE protocol.
- Sensitivity, specificity and AUC for the development and evaluation of an AI model for automatic detection of pneumonia based on the A, B, C and E-patterns in LUS.
- Sensitivity, specificity and accuracy of pneumonia diagnosis of both the simplified sweep-based protocol and the validated BLUE protocol compared with CXR and/or gold standard CT

5.1.3 Other study parameters (if applicable)

Not applicable

5.2 Randomisation, blinding and treatment allocation

Not applicable

5.3 Study procedures

All the procedures of this study have been used in standard clinical care in the Netherlands. All participants will undergo standard diagnostic and therapeutic procedures as determined by their treating physician. These procedures are part of routine clinical care and are not influenced by study participation. No part of clinical management, diagnostics, or therapy will be altered or postponed due to study participation. In addition to standard care, each participant will undergo two LUS examinations performed at the bedside:

1. The standard 6-point BLUE protocol
2. A simplified 4-sweep long-axis protocol

Ultrasound examination 1 (BLUE protocol): six thoracic regions (upper/lower anterior, upper/lower lateral) are scanned according to the standardized BLUE protocol (figure 1). Each region is recorded as a cine loop and stored. Total duration: approximately 5-10 minutes. This procedure is part of standard care, and patients may therefore have already undergone it. However, for research purposes, the researcher will always perform the procedure again.

Ultrasound examination 2 (“Sweep” protocol): Four continuous sweeps over predefined anterior, lateral, and posterior regions are performed (figure 2). Total duration: approximately 5-10 minutes.

Both scans are performed consecutively during a single session using CE-marked portable ultrasound device. The total additional time burden per participant is approximately 10-20 minutes. This includes both scans, so each protocol takes approximately 5-10 minutes. The sweep protocol is performed for research purposes only. Results of the BLUE protocol performed by the researcher will be discussed with the treating team.

After acquisition, ultrasound clips are transferred via a cable connection to a secure hospital research server. The ICU has computers without OneView (“self-managed computers”) that allow data to be transferred to the secured G: server via a cable connection. Data quality is verified and, if necessary, a re-scan may be performed if necessary/feasible. Clips are later annotated by one or more independent reviewers who identify lung patterns (A-, B-, C-, E). Labels will be assigned based on five clinically relevant LUS patterns (7): A-pattern (normal), B1-pattern (≥3 B-lines), B2-pattern (confluent B-lines), C-pattern (consolidation), and E-pattern (effusion). An “A-pattern” is defined as repeating horizontal lines parallel to the pleural line (score 0). A “B1-pattern” is defined as three or more vertical, separated B-lines starting from the pleural line and reaching the bottom of the screen (score 1). A “B2-pattern” is defined as numerous confluent vertical B-lines covering more than 50% of the screen (score 2). A “C-pattern” is defined as a hypo-echoic structure with a diameter of at least 2 cm (score 3). An “E-pattern” is defined as pleural effusion.

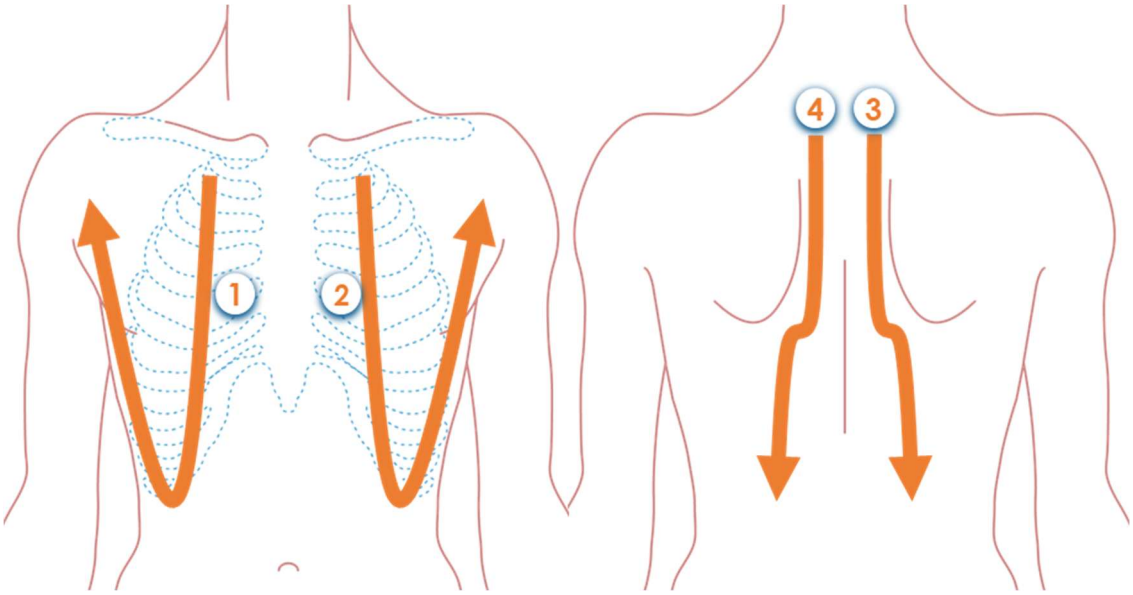

Figure 1: Four lung sweep acquisition protocol. Sweep 1 and 2 capture the ventral and mid-axillary points typically used for a 6-point Blue protocol. Sweep 3 and 4 are added to provide additional information on dorsal abnormalities, which are easier to obtain in ambulatory patients who can sit up.

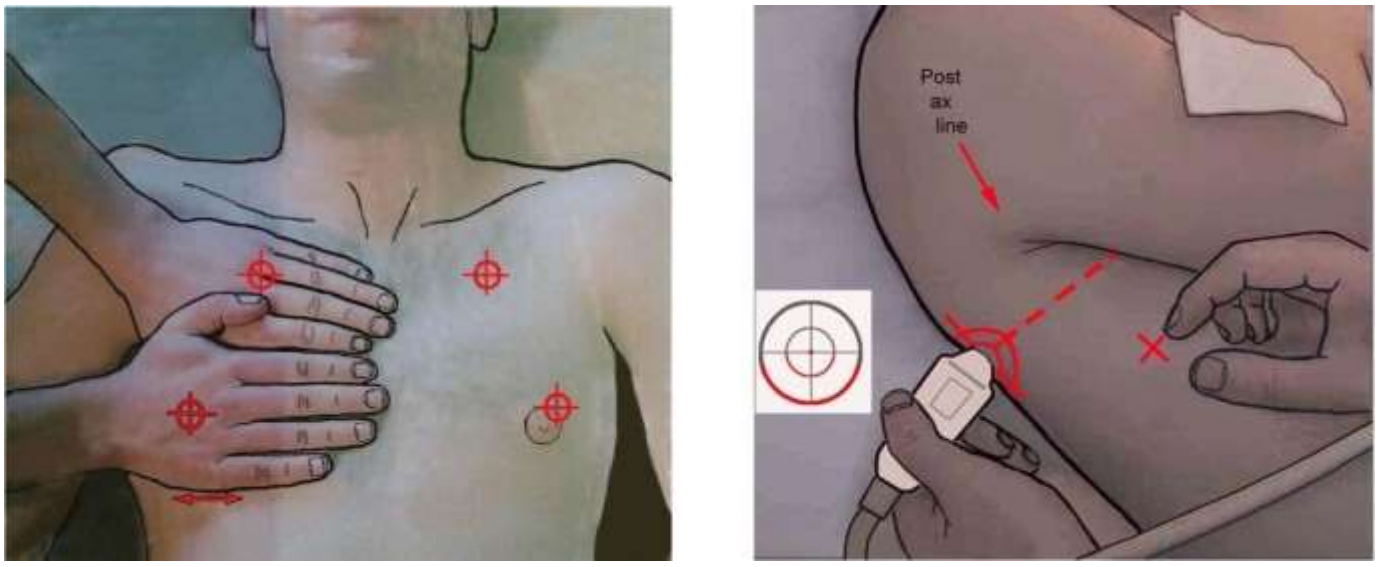

Figure 2: Areas of investigation and BLUE-points: With two patient-sized hands (thumbs excluded), the upper hand touching the clavicle define three points: upper-BLUE (centre of the upper hand), lower-BLUE (centre of the lower palm), and PLAPS-point (intersection of a horizontal through the lower-BLUE point with the posterior axillary line). Left: upper- and lower-BLUE points. Right: PLAPS point.

Table 1 summarizes the study phases, procedures, and timeline. Note that the order of LUS exams 1 and 2 will be randomized to avoid bias.

Table 1: study procedure timeline

Study Phase	Procedure	Responsible Person	Timing	Duration
Screening	Eligibility check	Treating physician	Before consent	5-10 min
Consent	Written informed consent	Researcher	Before scanning	5-15 min
LUS Exam 1	Either BLUE protocol (6 zones) or sweep protocol (4 sweeps)	Researcher	T0	5-10 min
LUS Exam 2	Either BLUE protocol (6 zones) or sweep protocol (4 sweeps)	Researcher	Immediately after	5-10 min
Storage	Pseudonymization & upload	Researcher	Post-scan	5-10 min
Expert Labeling	Pattern annotation	LUS experts / Researcher	Batch (weekly)	5 min per protocol

5.4 Withdrawal of individual research participants

Participants can leave the study at any time for any reason without any consequences if they wish to do so.

5.4.1 Specific criteria for withdrawal (if applicable)

Not applicable

5.5 Replacement of individual research participants after withdrawal

Participants who withdraw consent will not be replaced. Data collected up to withdrawal may be used in anonymized form unless the participant requests full deletion.

5.6 Follow-up of research participants withdrawn from treatment

Subjects withdrawn from this study will not be contacted further, neither other ways of follow up will take place.

5.7 Premature termination of the study

Because of the non-invasive nature of this study, no predetermined termination criteria are established.

6. SAFETY REPORTING

6.1 Temporary halt for reasons of research participant safety

In accordance to section 10, subsection 4, of the WMO, the sponsor will suspend the study if there is sufficient ground that continuation of the study will jeopardise participant health or safety. The sponsor will notify the review committee without undue delay of a temporary halt including the reason for such an action. The study will be suspended pending a further positive decision by the review committee. The investigator will take care that all participants are kept informed.

6.2 AEs, SAEs

6.2.1 Adverse events (AEs)

Adverse events are defined as any undesirable experience occurring to a subject during the study. The prospective observational study design together with non-invasive and non-interventional study procedures make the likelihood of study related adverse advents very low. Therefore, no adverse events are expected and will not be recorded, reported, nor followed until they have abated.

6.2.2 Serious adverse events (SAEs)

A serious adverse event is any untoward medical occurrence or effect that

- results in death;
- is life threatening (at the time of the event);
- requires hospitalisation or prolongation of existing inpatients' hospitalisation;
- results in persistent or significant disability or incapacity;
- is a congenital anomaly or birth defect; or
- any other important medical event that did not result in any of the outcomes listed above due to medical or surgical intervention but could have been based upon appropriate judgement by the investigator.

We ask to waive the obligation of reporting all above listed SAEs. The study population is prone to complications related to recent ICU-admission and medical events. As mentioned before, the study does not contain invasive procedures nor interventions, and therefore the likelihood of study related serious adverse events is close to zero.

7. STATISTICAL ANALYSIS

All analyses will be performed using descriptive and inferential statistical methods appropriate for diagnostic accuracy studies. Statistical uncertainty will be expressed as 95% confidence intervals, and a p-value < 0.05 will be considered statistically significant.

Data will be summarized based on the type of data: continuous variables (e.g., acquisition time) are presented as means with standard deviations in case of a normal distribution or medians with interquartile ranges (25th and 75th percentile) in case of a non-normal distribution. Differences in normally distributed variables between paired measurements are tested with paired t-test, and in non-normally distributed variables with the Wilcoxon signed-rank test. Categorical variables (labels A/B/C/E) are presented as number and percentage. Paired categorical outcomes will be analysed using McNemar's test or agreement statistics such as Cohens κ, as appropriate. Dataset composition will be reported, including the number of participants, total scans, number of clips per protocol (BLUE vs. sweep), and per-zone completeness.

7.1 Primary study parameter(s)

The primary objective is to compare the diagnostic accuracy of the simplified four-sweep protocol (index test) with the validated BLUE protocol six-point scan (reference test) for identifying pneumonia. Diagnostic-level performance will be assessed using confusion matrices, from which sensitivity, specificity, PPV, negative predictive value (NPV), and likelihood ratios will be calculated. We will compare diagnostic classification using McNemar's test. Overall diagnostic discrimination will be summarized using the area under the Receiver Operating Characteristic (ROC) curve (AUC). All analyses will be reported based on STARD guidelines.

7.2 Secondary study parameter(s)

The secondary parameters will be analysed as follows:

- To compare the pattern-level agreement on patient level per protocol (agreement of A-, B-, C-, and E-patterns) by using (weighted) Cohen's κ coefficients and confusion matrices.
- To measure examination duration of each protocol, comparing them by using paired t-tests or Wilcoxon signed-rank tests, depending on normality.
- To develop AI trained on both protocols, to detect A, B, C and E-patterns and diagnose pneumonia based on these patterns using the BLUE protocol decision tree,

which will be measured by confusion matrices, accuracy, AUC, F1, precision, sensitivity (per protocol).
- To compare agreement in pneumonia diagnosis in both the simplified sweep-based protocol and the validated BLUE protocol with CXR and/or gold standard CT, describing sensitivity, specificity and accuracy from confusion matrices and using McNemar's test

7.3 Other study parameters

Information collected from patient file if available:

- General information: age, sex, length, weight, symptoms, use of antibiotics, use of oxygen, blood cultures
- Imaging: results of CT and CXR imaging if available as part of regular patient care
- Outcomes: total hospital stay, duration of ICU/ED admission, hospital mortality

Age, sex, length, weight, and symptoms describe the patient population. Oxygen use, antibiotic treatment, hospital mortality and length of stay provide insights into disease severity. CT is the most accurate for pneumonia diagnosis, while CXR is commonly used as the gold standard, both offering a foundation for comparison with LUS results. The blood cultures, location (ICU/ED) helps highlight diagnostic differences based on the clinical setting.

8. ETHICAL CONSIDERATIONS

8.1 Regulation statement

This study will be conducted according to the principles of the Declaration of Helsinki (as approved on the 75th WMA General Assembly, Helsinki, Finland, October 2024, retrieved on January 5th 2026 via: https://www.wma.net/policies-post/wma-declaration-of-helsinki/, and in accordance with the Medical Research involving Human Subjects Act (WMO) and other guidelines, regulations and Acts.

8.2 Recruitment and consent

The selection of potential participants is performed by the attending physician based on the predefined inclusion and exclusion criteria. The attending physician first assesses whether a patient is eligible for participation and subsequently requests permission to allow the researcher to approach the patient. After this permission is granted, the researcher approaches the patient to provide information about the study and discuss participation. This procedure is applied to patients in both the ED and ICU. Patients will be approached in person by a member of the research team trained in the consent procedure. They will receive both verbal and written information about the study, including its purpose, procedures, risks, and their rights as participants. Patients will be given sufficient time to read the information letter and ask questions before making a decision. If needed, they may discuss participation with family or their treating physician. Written informed consent will be obtained before any study-specific procedure is performed. Participation is entirely voluntary, and refusal or withdrawal at any time will have no consequences for the patient's clinical care.

8.3 Objection by minors or incapacitated research participants

This study will not include minors or legally incapacitated adults. Therefore, no code of conduct for minors or incapacitated adults applies.

8.4 Benefits and risks assessment, group relatedness

Patients will experience no risk from participation in the study but will also not benefit.

8.5 Compensation for injury

We ask to waive the need for liability insurance, because the likelihood of AEs and SAEs are close to zero. Participants are not at risk at any time point throughout the study.

8.6 Incentives

Not applicable.

9. ADMINISTRATIVE ASPECTS, MONITORING AND PUBLICATION

9.1 Handling and storage of data and documents

Patient identity is coded via a random identifier. The subject identification code list is held at the site of patient inclusion by the principal investigator or the study coordinator in a secure place. The subject identification code list will never be shared with any other party. Encoded data will be stored for 15 years at the research department of the Amsterdam UMC.

A data sharing agreement will be made with the study collaborator. The collaboration with DelftAI is established due to their knowledge and resources in AI development and their expertise in product development. The pseudonymized collected LUS imaging will be used to train and validate AI models at the secure servers hosted at DelftAI, with the goal of developing an algorithm capable of automatically detecting pneumonia on LUS. To ensure that all participants are aware of this, this will be added to the informed consent form. Only coded (pseudonymized) data will be transferred. The key linking codes to personal identifiers will remain securely stored at Amsterdam UMC and will not be shared. We will ask informed consent from the patient regarding data sharing with Delft AI B.V. for development of AI algorithms serving the basis of the development of a commercial product.

The transfer will take place via a secure, encrypted channel, and data processing agreements are in place between Amsterdam UMC and DelftAI, ensuring compliance with the General Data Protection Regulation (GDPR / AVG) and Good Clinical Practice (GCP).

DelftAI will use the data exclusively for algorithm training, validation, and performance evaluation. The company will not have access to any identifying or clinical metadata beyond what is necessary for these purposes.

To ensure data security and patient privacy, only coded ultrasound cine loops will be stored on the smartphone or tablet after image acquisition. The smartphone will be provided by DelftAI and is intended solely for research purposes, not for personal use. Ultrasound data will be transferred directly from the mobile device to a locally managed and secure folder on the G: drive via a physical cable connection, without being stored on a local PC. The ICU has computers without OneView (“self-managed computers”) that allow data to be transferred to the secured G: server via a cable connection. Wireless data transfer, cloud-based storage, or automatic synchronization with external servers will not be used on the mobile device. All ultrasound data will be stored on hospital-owned, access-restricted systems. Only authorized members of the research team will have access to the data. Patient data, and the key linking study codes to patient identifiers will be stored separately in a secure location.

9.2 Monitoring and Quality Assurance

Monitoring will be performed before the start of the study and is focused on the completeness of the trial master file.

9.3 Amendments

Amendments are changes made to the research after a favourable opinion by the review committee has been given. All amendments will be notified to the review committee that gave a favourable opinion. Non-substantial amendments will not be notified to the review committee, but will be recorded and filed by the sponsor.

9.4 Annual progress report

The sponsor/investigator will submit a summary of the progress of the trial to the review committee once a year. Information will be provided on the date of inclusion of the first participant, numbers of participants included and numbers of participants that have completed the trial, serious adverse events, other problems, and amendments.

9.5 Temporary halt and (prematurely) end of study report

The investigator/sponsor will notify the review committee of the end of the study within a period of 8 weeks. The end of the study is defined as the last patient's last visit.

The sponsor will notify the review committee immediately of a temporary halt of the study, including the reason of such an action.

In case the study is ended prematurely, the sponsor will notify the review committee within 15 days, including the reasons for the premature termination.
Within one year after the end of the study, the investigator/sponsor will submit a final study report with the results of the study, including any publications/abstracts of the study, to the review committee.

9.6 Public disclosure and publication policy

The results of this study will be disclosed unreservedly and published in a peer reviewed medical journal. The study collaborator will be given the opportunity to review any intended publication or presentation prior to submission, in order to identify confidential information or potential intellectual property. Publication shall not be prohibited or unreasonably delayed by the study collaborator.

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