**Atelectasis** describes small areas of collapsed lung. Atelectasis and collapse both describe the same pathophysiology, though atelectasis tends to be used to describe small areas of lung that are not fully expanded, whereas collapse tends to be used to describe larger more confluent areas.

**Lung atelectasis** (plural: atelectases) refers to the collapse or incomplete expansion of pulmonary parenchyma.

#### **Terminology**

Atelectasis may be used synonymously with collapse, but some authors reserve the term "atelectasis" for partial collapse, not inclusive of total atelectasis of the affected part of the lung or whole lung collapse.

#### **Pathology**

Atelectasis is a radiopathological sign that can be categorized in many ways. Each approach aims to help identify possible underlying causes together with other accompanying radiological and clinical findings.

Atelectasis can be subcategorised based on the underlying mechanism, as follows:

#### • <u>resorptive (obstructive) atelectasis</u>

- o occurs as a result of complete obstruction of an airway
- no new air can enter the portion of the lung distal to the obstruction, and any air that is already there is eventually absorbed into the pulmonary capillary system, leaving a collapsed section of the affected lung
- because the visceral and parietal pleura do not separate in resorptive atelectasis, traction is created, and if the loss of volume is considerable, mobile thoracic structures may be pulled toward the side of volume loss ("mediastinal shift")
- potential causes of resorptive atelectasis include obstructing neoplasms, <u>mucus</u> <u>plugging</u> in asthmatics or critically ill patients and <u>foreign body aspiration</u>
- o resorptive atelectasis of an entire lung ("collapsed lung") can result from complete obstruction of the right or left main bronchus

# • passive (relaxation) atelectasis

- occurs when contact between the parietal and visceral pleura is disrupted with loss of normal negative pressure and the lung relaxes due to natural elastic recoil
- the three most common specific etiologies of passive atelectasis are <u>pleural</u> <u>effusion</u>, <u>pneumothorax</u> and diaphragmatic abnormality

# • compressive atelectasis

occurs as a result of any thoracic space-occupying lesion (e.g. large pneumothorax)
 compressing the lung and forcing air out of the alveoli

# • <u>cicatrisation atelectasis</u>

o occurs as a result of scarring or fibrosis that reduces lung expansion

 common etiologies include granulomatous disease, necrotizing pneumonia and radiation fibrosis

# • adhesive atelectasis

- o occurs from surfactant deficiency <sup>2</sup>
- depending on etiology, this deficiency may either be diffuse throughout the lungs or localized
- gravity dependant atelectasis (dependent atelectasis)
  - o in the most dependent portions of the lungs due to the weight of the lungs
- osteophyte-induced adjacent pulmonary atelectasis and fibrosis

Atelectasis can also be subcategorised by morphology:

- <u>linear (a.k.a. plate, band, discoid) atelectasis</u>: a minimal degree of collapse as seen in patients who are not taking deep breaths ("splinting"), such as postoperative patients or patients with rib fracture or pleuritic chest pain; this is very common
- round atelectasis: classically associated with asbestos exposure

Lastly atelectasis can be described according to anatomical extent:

- lung atelectasis: complete collapse of one lung
- <u>lobar atelectasis</u>: collapse of one or more lobes of a lung.
- segmental atelectasis: collapse of one or more individual pulmonary segments
- <u>subsegmental atelectasis</u>: collapse of a portion of a pulmonary segment

# **Radiographic features**

Vary depending on the underlying mechanism and type of atelectasis

## Plain radiograph / CT

#### **Direct signs of atelectasis**

- displacement of interlobar fissures
- crowding together of pulmonary vessels
- crowded <u>air bronchograms</u> (does not apply to all types of atelectasis; can be seen in subsegmental atelectasis due to small peripheral bronchi obstruction, usually by secretions; if the cause of the atelectasis is central bronchial obstruction, there will usually be no air bronchograms)

# Indirect signs of atelectasis

- pulmonary opacification
- shifting granuloma (or any other previously documented lesion, used as a reference for comparison)
- <u>compensatory hyperexpansion</u> of the surrounding or contralateral lung

- displacement of the heart, mediastinum, trachea, hilum
- <u>elevation of the diaphragm</u>
- propinquity of the ribs

# Resorptive (obstructive) atelectasis

- increased density (opacity) of the atelectatic portion of lung
- displacement of the fissures toward the area of atelectasis
- upward displacement of hemidiaphragm ipsilateral to the side of atelectasis
- crowding of pulmonary vessels and bronchi in region of atelectasis
- +/- compensatory overinflation of unaffected lung
- +/- displacement of thoracic structures (if atelectasis is substantial)

# Linear (plate, discoid, subsegmental) atelectasis

 relatively thin, linear densities in the lung bases oriented parallel to the diaphragm (known as <u>Fleischner lines</u>)

#### **Ultrasound**

The sonographic morphology of atelectatic lung may resemble hepatic parenchyma, often referred to as "tissue-like" or "hepatized" in appearance. Distinguishing features of atelectasis by etiology may appear as follows:

- compressive atelectasis is most often visualized in the costophrenic recess bordered by a disproportionately large pleural effusion
  - o low-level, homogenous echogenicity with few to no air bronchograms
  - o margins are usually regular with a triangular shape <sup>10</sup>
  - o a shred sign may be present at the transition to aerated lung
- obstructive atelectasis
  - o early static air bronchograms due to distal air trapping
  - $\circ$  as the air is resorbed, bronchi may fill with fluid resulting in anechoic, tubular structures known as <u>fluid bronchograms</u> <sup>11</sup>
  - o may be differentiated from blood vessels with <u>color flow Doppler</u>

# СТ

Air bronchograms indicate patency of the proximal airways and the airways will be crowded indicating volume loss. If air bronchograms are absent suspect an obstructing lesion or mucoid impaction. In this latter case, bronchoscopy may be helpful.

Following IV contrast medium, atelectatic lung enhances more than skeletal muscle 12.

These features of volume loss and marked enhancement together with the absence of fever help to distinguish atelectasis from pneumonic consolidation.

**Resorptive** or **obstructive atelectasis** is a form of <u>lung collapse</u> that is due to obstruction of the airways supplying a lung segment or lobe. It is a term used to distinguish atelectasis identified on imaging based on the underlying pathophysiology to guide diagnosis.

#### **Clinical presentation**

The presentation of patients with atelectasis depends on the underlying cause. However, breathlessness is common if there is significant lung collapse and infective symptoms can be present if there is co-existing sepsis.

# **Pathology**

As the name implies, in this form of atelectasis there is partial or complete bronchial obstruction which leads to poor ventilation of the airways supplied. As ventilation between the distal airspaces and the trachea is disrupted the residual air in the affected lung is resorbed by the circulating blood at a rate greater than it is replaced by fresh ventilated air. This causes volume loss in the affected lung. Volume loss may be minimal in distal airways obstruction due to the presence of collateral ventilation via the pores of Kohn.

The rate at which atelectasis progresses depends on whether there is obstruction of a lobar or segmental bronchus. Lobar obstruction manifests as <u>lobar atelectasis</u>. In <u>segmental atelectasis</u>, there is often a degree of collateral ventilation from adjacent lung segments which causes a slightly distinct radiographic presentation. The speed of collapse is quicker if the patient is being given 100% oxygen <sup>3</sup>.

Collapse occurs quickly if the obstruction is due to a luminal lesion that can act as a one-way valve.

Eventually, there can be sequestration of local lung secretions over time and areas of significant atelectasis are prone to become infected. Hence, this type of collapse is frequently seen with coexisting consolidation.

#### **Etiology**

The causes of resorption (obstructive) at electasis can be thought of in terms of where the obstructing lesion is arising from with respect to the bronchial lumen:

#### extraluminal

- neoplasm
- lymphadenopathy

#### bronchial

- fibrotic stricture
- <u>neoplasm</u>
- spontaneous rupture <sup>4</sup>

# luminal

- mucus plugging
  - <u>asthma</u>
  - pneumonia

- postoperative
- post anesthetic
- o pus
  - bacterial pneumonia
- o blood
  - post-traumatic lung injury
- o foreign body
- endobronchial intubation

# **Radiographic features**

## Plain radiograph / CT

The imaging features of atelectasis are similar on plain radiographs and CT with more detail being available on the CT:

- increased density at the site of atelectasis
- loss of normal thoracic silhouettes (<u>silhouette sign</u>)
- displacement of the fissures toward the area of atelectasis
- upward displacement of ipsilateral hemidiaphragm
- crowding of pulmonary vessels and bronchi affected area
- compensatory hyperinflation of the unaffected lung
- mediastinal shift
  - o ipsilateral tracheal deviation
  - o ipsilateral shift of the heart

If volume loss is minimal and there is consolidation present, then the term **drowned lung** can be used to indicate transudate replacing the air in the collapsing lung. The transudate is rapidly cleared when the obstruction is removed, as is commonly seen in postoperative patients with mucus plugging.

#### Ultrasound

As a consequence of the cessation of ventilation, <u>lung sliding</u> is immediately abolished. In contrast to a <u>pneumothorax</u>, another cause of <u>absent lung sliding</u>, the presence of a <u>lung pulse</u> implies that the visceral and parietal pleura are still in apposition. As alveolar gas is absorbed, the lung parenchyma may assume a tissue-like echogenicity, with the following internal features <sup>9</sup>:

- <u>air bronchograms</u>
  - unlike dynamic air bronchograms (present in e.g. pneumonia) these lentiform, branching echogenicities do not move with respiration <sup>8</sup>
  - o referred to as static air bronchograms

- fluid bronchograms <sup>7</sup>
  - o tubular hypoechoic structures lacking vascular flow on color Doppler

**Passive atelectasis**, also known as **relaxation atelectasis** is due to elastic recoil of the lung when normal negative pleural pressure is reduced or lost due to a pleural collection such as a <u>pneumothorax</u> or <u>pleural effusion</u>.

## **Clinical presentation**

The clinical presentation would depend on the extent of atelectasis and how quickly it develops. Small and gradually developing areas of atelectasis may be asymptomatic or present as a non-productive cough. Larger areas that develop more quickly can present with hypoxia, <u>respiratory failure</u>, cough, and/or <u>pleuritic chest pain</u> <sup>6</sup>.

Physical examination of the <u>lungs</u> may reveal a diminished movement of the affected area, dullness on percussion decreased or absent breath sounds, and ipsilateral tracheal deviation <sup>6</sup>.

## **Pathology**

With a loss of the negative intrapleural pressure there is equalization of intrapleural and intraalveolar pressures and the lung is said to "relax" due to its normal elastic recoil resulting in lung volume loss <sup>5</sup>. In the case of diaphragmatic abnormalities, there is a reduction in downward force to fully expand the lungs resulting in passive atelectasis <sup>5</sup>.

#### **Etiology**

Causes of passive atelectasis may be grouped into three main categories 5:

- simple pneumothorax
- diaphragmatic abnormalities
  - o diaphragmatic hernia
  - o <u>diaphragmatic paralysis</u>
  - o <u>diaphragmatic eventration</u>
- conditions of hypoventilation
  - o pleural effusion or empyema
  - hemothorax
  - pleural tumor
  - chest wall mass

#### Radiographic features

## Plain radiograph

There may not be a significant increase in density from the atelectasis, as perfusion of the affected lung also decreases <sup>ref</sup>.

CT

- atelectatic lung may demonstrate marked enhancement, greater than that of skeletal muscle (see case 2)
- the presence of air bronchograms helps to exclude airway obstruction as a cause
- as gases are the main constituent of normal lung, loss of aeration can cause profound collapse

**Compressive atelectasis** refers to a form of <u>lung atelectasis</u> due to compression by a space-occupying process.

Some authors describe it as a subtype of <u>passive (relaxation) atelectasis</u> where the reduction in lung volume is greater than its normal relaxed state <sup>1</sup>. Whereas others describe it as the intrapulmonary counterpart of passive (relaxation) atelectasis due to an intrapulmonary mass lesion <sup>4</sup>.

# **Pathology**

# **Etiology**

- extrapulmonary
  - o <u>pleural effusion</u>
  - o <u>empyema</u>
  - o <u>hemothorax</u>
  - o <u>pneumothorax</u>
  - o pleural tumor
  - o chest wall mass lesion
- intrapulmonary
  - o <u>lung cancer</u>
  - o bullous disease
- abdominal distension
  - o large intra-abdominal tumors
  - o <u>hepatosplenomegaly</u>
  - massive <u>ascites</u>
  - pregnancy
  - o morbid obesity

**Cicatrisation atelectasis** is a form of <u>lung atelectasis</u> which occurs as a result of scarring or <u>fibrosis</u> that reduces lung expansion. Cicatrisation atelectasis is classic in tuberculosis. The term is closely related to cicatrisation collapse when an entire lobe is collapsed from the same process.

## **Etiology**

• granulomatous disease especially <u>tuberculosis</u>

- <u>necrotizing pneumonia</u>
- <u>radiation fibrosis</u>
- <u>silicosis</u>
- scleroderma
- <u>idiopathic pulmonary fibrosis</u>

**Adhesive atelectasis** refers to the specific form of <u>lung atelectasis</u> that occurs due to the decrease or absence of pulmonary surfactant produced by type II pneumocytes. Without sufficient surfactant the alveoli collapse due to increased surface tension. It is most commonly seen in neonates with respiratory distress syndrome.

## Etiology

## Diffuse surfactant deficiency

- respiratory distress syndrome (RDS) of the newborn (surfactant deficiency disorder)
- ARDS
- smoke inhalation
- hypoxemia
- prolonged shallow breaths
- uremia
- post operative i.e. cardiac bypass surgery

#### Localized surfactant deficiency

- <u>pulmonary embolism</u>
- <u>pulmonary hemorrhage</u>
- <u>acute radiation pneumonitis</u>
- pneumonia

**Gravity-dependent atelectasis** refers to a form of <u>lung atelectasis</u> that occurs in the dependent portions of the <u>lungs</u>.

# **Pathology**

Gravity-dependent atelectasis occurs due to a combination of reduced alveolar volume and increased perfusion. Due to gravity, it usually has a dependent and subpleural distribution. It is very commonly seen in the posterior lung bases on CT, particularly in elderly individuals.

In normal lung, gravity gradients exist in end-inspiration between the <u>apex</u> and <u>lung base</u> of 4:1 in the erect patient and between the anterior and posterior lung of 2.5:1 in the supine patient <sup>1</sup>. These gradients increase in the presence of lung disease that increases the weight of the lung causing atelectasis.

# **Pathology**

## **Etiology**

- bedridden patients
- patients with prolonged shallow breathing
- impaired mucociliary clearance
- <u>pneumonia</u>
- pulmonary edema

# **Differential diagnosis**

- early interstitial lung disease: prone CT chest can usually differentiate <sup>2</sup>
- Osteophyte-induced adjacent pulmonary atelectasis and fibrosis are typically seen as
  focal pulmonary interstitial opacities adjacent to thoracic spinal <u>osteophytes</u>. They are a
  relatively common finding in thoracic CT imaging.

# Epidemiology

They are more common in older individuals.

# Pathology

• They are thought to represent a variable combination of <u>compressive</u> atelectasis ± fibrosis (focal pulmonary fibrosis).

# Location

- They are typically seen involving the <u>medial basal segment of the right lower</u> <u>lobe</u> and <u>posterior segment of the left lower lobe</u> where osteophytes are more commonly located.
- Some studies have suggested that the likelihood of lung fibrosis is commensurate with the size of the osteophyte<sup>3</sup>. Subpleural fat is considered a protective measure against osteophyte-induced lung fibrosis.

# Treatment and prognosis

• Most are not thought to be of clinical significance, generally do not appear to progress, and are not considered a pre-clinical form of more extensive <u>fibrosing lung disease</u> <sup>2</sup>.

**Linear atelectasis** (plural: atelectases), and also known as **discoid**, **plate** or **band atelectasis**, refers to a focal area of <u>subsegmental atelectasis</u> that has a linear shape. Linear atelectasis may appear to be horizontal, oblique or perpendicular and is very common. It usually occurs as a consequence of subsegmental bronchial obstruction and can resolve as quickly as it occurs.

#### **Terminology**

Depending on its shape, linear atelectasis is also known as plate, discoid or band atelectasis (and historically as Fleischner lines on chest radiographs, but not on CT).

# Subsegmental vs linear atelectasis

There is confusion about the use of the terms "subsegmental atelectasis" and "linear atelectasis" (and their synonyms). From an academic point of view, the term linear atelectasis is reserved for atelectasis which appears primarily in the lung bases and is secondary to hypoventilation. Conversely, subsegmental atelectasis includes both linear atelectases and all other forms of atelectasis that do not involve a whole bronchopulmonary segment. In other words, every linear atelectasis is a subsegmental atelectasis, but not every subsegmental atelectasis is a linear atelectasis.

# **Pathology**

## **Etiology**

- hypoventilatory change in patients who are not taking deep breaths ("splinting")
  - o postoperative status
  - o chest wall trauma such as rib fracture
  - o pleuritic chest disease
- <u>pulmonary embolism</u>
- pneumonia
- <u>aspiration</u>
- bronchogenic carcinoma

# History and etymology

Fleischner lines were named after <u>Felix Fleischner</u> (1893-1969), an Austrian-American radiologist, who first described them in 1938.

**Round atelectasis**, also known as **rounded atelectasis**, **folded lung** or **Blesovsky syndrome**, is an unusual type of <u>lung atelectasis</u> where there is infolding of a redundant pleura. The way the lung collapses can at times give a false mass-like appearance.

## **Epidemiology**

#### **Associations**

Round atelectasis may be associated with:

- <u>asbestos lung exposure</u> <sup>3</sup>: most commonly
- therapeutic pneumothorax in the treatment of <u>tuberculosis</u> <sup>1</sup>
- congestive heart failure <sup>2</sup>
- hepatic hydrothorax <sup>17</sup>
- end stage renal disease <sup>17</sup>
- pulmonary infarction<sup>2</sup>
- post-infectious pleural inflammation / parapneumonic effusion

# **Pathology**

Two theories have been put forward. The second theory is more favored while the multifactorial etiology suggests both mechanisms probably operate in different patients:

- Hanke and Kretzschmar
  - o underlying pleural effusion causes local atelectasis in the adjacent lung
  - o a cleft or infolding of the <u>visceral pleura</u> will then form if the rate of pleural fluid formation exceeds alveolar air absorption

- this then causes the lung to tilt on the cleft
- o the lung then curls on itself in a concentric fashion
- fibrous adhesions suspending the atelectatic segment (and usually tilt the lung cranially) develop
- as the effusion resorbs, the aerated lung fills in the space between the area of round atelectasis
- organization of the fibrinous exudate and fibrous contraction lead to additional lung parenchymal distortion
- Schneider et al. (expanded on by Dernevik and colleagues)
  - o a local <u>pleuritis</u> caused by irritants such as asbestos
  - in the event of a benign <u>asbestos-related pleural effusion</u>, the pleura contracts and thickens with shrinkage of the underlying lung, and atelectasis develops in a round configuration

#### **Etiology**

- exposure to mineral dust: <u>asbestosis</u>, <u>pneumoconiosis</u> <sup>13</sup>
- exudative pleuritis: tuberculosis, hemothorax <sup>13</sup>
- less commonly seen in <u>histoplasmosis</u>, <u>legionella</u>, <u>end-stage renal disease</u> <sup>13</sup>
- sarcoidosis <sup>13</sup>

# Location

There may be a predilection towards the lower lobes <sup>4</sup>.

# **Radiographic features**

#### CT

- round or oval in shape
- almost always seen adjacent to a pleural surface
- there is associated adjacent pleural abnormality, e.g. pleural thickening or pleural effusion
- comet tail sign <sup>2</sup>: produced by the pulling of bronchovascular bundles giving the shape of a comet tail
- crow feet sign
- as it represents collapsed lung, it commonly demonstrates a typical parenchymal enhancement
- posterior lower lobes are most commonly involved and, sometimes, bilateral or symmetrical <sup>14</sup>

Rounded atelectasis can occasionally increase in size on serial scans <sup>6,7</sup>.

#### **Nuclear medicine**

#### **FDG-PET**

- not metabolically active
- may play a role in differentiating from malignancy when there are few or atypical features on chest radiographs and CT<sup>9</sup>

# **Diagnosis**

All five of the following findings must be present to diagnose round atelectasis:

- 1) Adjacent pleura must be abnormal.
- 2) Opacity must be peripheral and in contact with the pleura.
- 3) Opacity must be round or elliptical.
- 4) Volume loss must be present in the affected lobe.
- 5) Pulmonary vessels and bronchi leading into the opacity must be curved this is the comet tail sign<sup>15</sup>.

**Lobar collapse** refers to the collapse of an entire lobe of the lung. As such it is a subtype of <u>atelectasis</u> (collapse is not entirely synonymous with atelectasis, which is a more generic term for 'incomplete expansion'). Individual lobes of the lung may collapse due to obstruction of the supplying bronchus.

# **Pathology**

Most often collapse of most or all of a lobe is secondary to bronchial obstruction causing <u>resorptive</u> atelectasis.

# **Etiology**

- luminal
  - o aspirated foreign material
  - mucus plugging
  - o endobronchial mass
  - o <u>misplaced endotracheal tube</u>
- mural
  - <u>lung cancer</u>
- extrinsic
  - o compression by adjacent mass

#### Radiographic features

There are several classical rules that a lobar collapse follows 9:

- bowing or displacement of a fissure/s occurs towards the collapsing lobe
- a significant amount of volume loss is required to cause <u>air space opacification</u>

- the collapsed lobe is triangular or pyramidal in shape, with the apex pointing to the hilum
- the collapsed lung peripherally maintains contact with the costal parietal pleura, except:
  - o in RML collapse where the lobe collapses adjacent to the mediastinum
  - o in the presence of pleural effusion
  - o in the presence of pneumothorax

Several factors may influence the typical appearance of lobar collapse, including pre-existing lung disease, amount of volume loss, concomitant consolidation, pleural effusion or the presence of pneumothorax.

#### Plain radiograph

Generally, there is pulmonary air space opacification but the appearance on chest x-ray varies according to the lobe involved and are discussed separately:

- right upper lobe collapse
- right middle lobe collapse
- <u>right lower lobe collapse</u>
- left upper lobe collapse
- left lower lobe collapse

Some features, however, are generic markers of volume loss and are helpful in directing one's attention to the collapse, as well as enabling distinction from opacification of the lobe without collapse (i.e. consolidation e.g. <u>lobar pneumonia</u>). These features include <sup>5,9</sup>:

- direct signs
  - o displacement of fissures
  - o crowding of pulmonary vessels
- indirect signs
  - o elevation of the ipsilateral hemidiaphragm
  - crowding of the ipsilateral ribs
  - o shift of the mediastinum towards the side of atelectasis
  - compensatory hyperinflation of normal lobes
  - hilar displacement towards the collapse
  - o shifting granuloma sign

#### CT

Lobar collapse is usually trivially easy to identify on CT, but identification of the cause is not always easy, as the collapsed lung can make identification of an obstructing lesion difficult. The density of the collapsed lobe is high post contrast administration.

**Segmental atelectasis** (plural: atelectases) refers to collapse of one or several segments of a lung lobe. It is a morphological subtype of <u>lung atelectasis</u>. It is better appreciated on CT and Its radiographic appearance can range from being a thin linear to a wedge-shaped opacity that does not abut an interlobar fissure. **Subsegmental atelectasis** (plural: atelectases) is a descriptive term for the mildest form of lung atelectasis, involving less than one bronchopulmonary segment.

#### **Terminology**

The term subsegmental atelectasis includes any loss of lung volume so small that it does not cause indirect signs of volume loss (as might be seen with larger atelectases). A subtype of subsegmental atelectasis is <u>linear atelectasis</u> (also known as discoid or plate-like atelectasis, and historically as Fleischner lines on <u>chest radiographs</u>).

#### Subsegmental vs linear atelectasis

There is confusion about the use of the terms "subsegmental atelectasis" and "linear atelectasis" (and their synonyms). From an academic point of view, the term linear atelectasis is reserved for atelectasis which appears primarily in the lung bases and is secondary to hypoventilation. Conversely, subsegmental atelectasis includes both linear atelectases and all other forms of atelectasis that do not involve a whole <a href="mailto:bronchopulmonary segment">bronchopulmonary segment</a>. In other words, every linear atelectasis is subsegmental atelectasis, but not every subsegmental atelectasis is linear atelectasis.

# **Pathology**

## **Etiology**

Many subsegmental atelectases are secondary to airway obstruction of a small segment of the lung, either from benign (<u>mucus plug</u>, airway inflammation) or malignant causes (<u>endobronchial tumor</u>).

Linear atelectasis is usually due to a lack of adequate inspiration, and not due to any underlying airway obstruction. They are most commonly seen in post-surgical patients or those with <u>abdominal</u> pain, and may also be observed in the morbidly obese or immobile patients.

#### Radiographic features

# Plain radiograph/CT

By definition, subsegmental atelectasis (regardless of its etiology) does not produce volume loss and subsequent shifting of mobile thoracic structures, and in most cases lacks clinical relevance and does not need to be reported.

Linear atelectases may result in minor linear densities of varying thickness usually parallel to the diaphragm, most commonly at the lung bases or less mobile regions of the lungs (e.g. lingula).

Other subsegmental atelectases present as linear or wedge-shaped densities and can affect any lung lobe. Unlike linear atelectases, subsegmental atelectases due to obstructive causes usually adopt a radial distribution rather than a horizontal one, as they are secondary to airway obstruction rather than parenchymal compression (as occurs in hypoventilation). Therefore, they follow the distribution of the bronchial and bronchiolar tree.

## **Differential diagnosis**

- small <u>linear scars</u>: can mimic this pattern and tends not to resolve on serial imaging
- <u>subpleural lines</u>: commonly in <u>asbestosis</u>

#### **Summary**

# epidemiology

varies widely depending on the underlying cause

## presentation

 usually breathlessness, but can be asymptomatic and presentation also depends very much on the underlying cause

## pathophysiology

- o caused by:
  - adjacent compression
    - e.g. a lung tumor, dilated aorta, large osteophyte
  - passive atelectasis
    - when the lung relaxes away from the parietal pleural surface, e.g. pleural effusion, pneumothorax
  - dependent atelectasis
    - in the posterior portions of the lung due to patients not fully expanding their lungs while lying for long periods

#### role of imaging

- confirm atelectasis
  - differentiate from air-space opacification
- help to determine the cause (may need CT)

## treatment

- management of the underlying cause
- deeper breathing if the cause is due to hypoventilation

#### Radiographic features

## Chest x-ray

Atelectasis is usually seen on chest x-rays as small volume linear shadows, usually peripherally or at the lung bases. The underlying cause (such as a lung tumor or pleural effusion) may also be visible. Lobar collapse will have a more typical and appearance based on the lobe involved, whereas atelectasis can be more eccentric in position and appearance.

# **CT** chest

CT allows a more accurate depiction of the involved lung. The dependent lung can be affected by subsegmental collapse just because of lying down (particularly if the patient has been supine for a long period of time, or they are under general anesthesia). This part of the lung is easier to visualize because it is hidden behind the diaphragm on a frontal chest x-ray

CT is often helpful to determine the cause or confirm that there is no proximal obstruction, though most cases of atelectasis are diagnosed and managed without CT investigation.

#### Case 1

## **Post-operative Atelectasis**

#### Clinical:

**History** – This 50 year old female was two days post-operative from a colostomy. She presented with a fever, cough, and fatigue.

Symptoms - Mild cough.

**Physical** – The lungs were clear on auscultation. Poor inspiration was noted due to abdominal discomfort.

**Laboratory** – Her white blood cell count was mildy elevated.

#### DDx:

**Atelectasis** 

Pneumonia

#### **Imaging Recommendation**

Chest X-ray

**ODIN Link Linear Atelectasis** 

## **Imaging Assessment**

#### Findings:

There were bands of linear opacity in both lower lungs. No evidence of any air bronchograms. Mild eventration of the right diaphragm was seen. No masses or adenopathy.

## Interpretation:

Bilateral lung, linear atelectasis.

# Diagnosis:

Plate or band-like atelectasis.

#### Discussion:

#### **Definition of Atelectasis:**

Atelectasis is diminished inflation of all, or part of, the lung. The synonym "collapse" is often used interchangeably with atelectasis, particularly when it is severe or accompanied by an obvious increase in lung opacity.

On x-rays and CT scans, reduced volume is seen, accompanied by increased opacity (chest radiograph) or attenuation (CT scan) in the affected part of the lung. Atelectasis is often associated with abnormal displacement of fissures, bronchi, vessels, diaphragm, heart, or mediastinum. The

distribution can be subsegmental, segmental, or lobar. Subsegmental atelectasis is often qualified by descriptors such as linear, discoid, or platelike.

# The different types of atelectasis are:

**Passive** – Another entity occupies the space usually occupied by lung, most often pleural fluid, but masses i.e. lung, or pleural, can enlarge and cause compression of the adjacent lung. Pneumothorax can also lead to passive atelectasis as the air in the pleural space causes the underlying lung to partially collapse.

**Resorptive** – An obstruction (intraluminal or extraluminal) prevents the normal ingress and egress of air. The gas in the aerated lung (bronchi, respiratory bronchioles, alveoli) downstream of the obstruction is resorbed/absorbed. This can be seen with endobronchial malignancies, mucous plugs in the bronchi, or extrinsic masses compressing airways leading to bronchial obstruction.

Also, inability to fully inflate the lungs i.e. splinting of the chest due to pain, and prolonged bed rest. may lead to linear bands of resorptive atelectasis.

**Cicatrizing** (/'sikə,trīz/) — Abnormal lung elasticity prevents the lung from expanding completely. This is often encountered after radiation therapy to the lung or as the result of a fibrosing infection such as tuberculosis.

# X-ray findings may include:

- Atelectasis is often opaque lung associated with the diminished volume of air containing lung.
- Atelectasis can occur in a subsegmental (linear), segmental, or lobar distribution.
- The appearance of the diminished lung volume depends upon the type of atelectasis.

#### Case 2

# **Post Intubation Atelectasis**

#### Clinical:

**History** – This 3 year old male presented with severe asthma and required endotracheal intubation.

**Symptoms** – None – intubated, sedated, and paralyzed.

**Physical** – No breath sounds in the left hemi-thorax or upper right lung.

**Laboratory** – Non-contributory.

DDx:

Atelectasis

Collapse

Pneumonia

**Imaging Recommendation** 

Chest X-ray

**Imaging Assessment** 

# Findings:

The left lung is totally opacified as is the right upper lobe. The endotracheal tube is in the right main bronchus quite distal in location. Note how the cardiac shadow was not seen in the right hemithorax as the central mediastinal structures have all shifted to the left due to the total atelectasis of the left lung.

#### Interpretation:

Total, resorptive, atelectasis with obstruction of the bronchi supplying both lobes of the left lung and the right upper lobe by the endotracheal tube.

#### Diagnosis:

Misplaced endotracheal tube leading to resorptive (obstructive) atelectasis.

#### Case 3

#### Pleural effusions, Passive atelectasis

#### Clinical:

**History** – This 42 year old male had severe gallstone pancreatits. He presented with severe shortness of breath and abdominal pain.

**Symptoms** – Severe shortness of breath with increased work of breathing and anxiety due to breathlessness.

**Physical** – Diminished breath sounds in both hemi-thoraces. Decreased volume in both lungs.

**Laboratory** – Non-contributory.

#### DDx:

**Atelectasis** 

Collapse

Pneumonia

Pleural effusions

# **Imaging Recommendation**

Chest X-ray

Passive Atelectasis – Ultrasound, large pleural effusion with atelectasis

# **Imaging**

# **Findings CXR**:

The volume of the aerated lungs is very diminished. There were large, bilateral pleural effusions.

# Interpretation:

Basilar atelectasis due to large bilateral pleural effusions.

#### **Findings US:**

The basilar lung is an echogenic collapsed, triangular structure. The collapsed lung is basically suspended in the pleural fluid. There is a large, anechoic region surrounding the collapsed lung.

## Diagnosis:

Passive atelectasis due to large, bilateral, pleural effusions.

#### Abstract

Atelectasis is the loss of volume caused by decreasing gas in a specific area of the lung. It occurs when the lung sacs (alveoli) do not fully inflate, resulting in a lack of oxygen to the blood, tissues, organs, and fill with alveolar fluid. It can be caused by pressure outside of your lung, an obstruction, poor airflow, or scarring. It is critical to diagnose this lung condition as soon as possible. Chest X-rays are the most commonly utilized diagnostic tool for this condition. Examining chest X-rays, however, is difficult even for a professional radiologist. There is a need to improve diagnosis accuracy. As a result, this study proposes a novel detection and classification approach for rapid diagnosis of atelectasis utilizing patient chest X-ray data. To diagnose atelectasis from chest X-ray images, we used state-ofthe-art models like VGG19, Inception, and a deep learning method (CNN). This study presents an effective method for categorizing chest X-ray images as normal or atelectasis-infected. This study offers a convolutional neural network (CNN) method to aid medical experts in identifying atelectasis disease. The anisotropic diffusion filtering (ADF) approach was used to improve image edge preservation, reduce noise, and contrast limited adaptive histogram equalization (CLAHE) for improving the contrast of low-intensity images. After evaluating the CNN model, it achieved 99.88 % training accuracy, 99 % validation accuracy, and 99 % test accuracy. In this study, CNN achieved a result that outperformed state-of-the-art models (VGG19 and Inception). As a result of the findings, deep features provided consistent and reliable features for detecting atelectasis. Therefore, the suggested method expedites atelectasis diagnosis and radiologists' screening of atelectasis patients.

# 1. Introduction

Atelectasis occurs when the lung sacs (alveoli) do not fully inflate, resulting in a lack of oxygen to the blood, tissues, and organs. It can be caused by pressure outside of your lung, an obstruction, poor <u>airflow</u>, or scarring [1]. If there isn't enough air going in to expand your alveoli, or if there is too much pressure pushing on them, they can collapse (atelectasis). Atelectasis can affect a single lung or the entire lung. If a significant portion of your lung is compromised, your blood may not receive enough oxygen, which can lead to health problems [2].

If you have atelectasis, you will feel as if you are not getting enough air. Coughing, chest pain, a rapid heart rate, bluish skin or lips, and other symptoms may occur [3]. The following are the most common causes of atelectasis. Blockage of one of the tubes (bronchi) that branch out from the trachea (windpipe) and lead to lung tissue, as well as conditions that reduce deep breathing or impair a person's capacity to cough [4]. The blockage could be caused by something inside the bronchus, such as a mucus plug, a tumor, or an inhaled foreign object (such as a pill, food, or toy). Alternatively, something pressing from the outside, such as a tumor or an enlarged lymph node, may block the bronchus [4]. Another of the most common causes of atelectasis is surgery. When anesthesia is used to keep you asleep during surgery, you do not breathe deeply enough to fill your lungs or cough to clear mucus from your lungs. This can result in obstructions or a shortage of oxygen to the alveoli, resulting in resorptive atelectasis (Fig. 1) [2].

#### 2. Download: Download full-size image

## Fig. 1. Shows normal and collapsed lung (alveoli) [2].

The importance of early identification of atelectasis disorders is more significant than ever. Atelectasis is the partial or total collapse of a lung or a lung lobe. Early detection of this illness can enhance patient outcomes and reduce the risk of consequences. Early detection allows for rapid medical care, which may include bronchial hygiene techniques, breathing exercises, or the use of positive <u>airway pressure</u> devices. These treatments are intended to re-expand collapsed lung tissue and improve <u>respiratory function</u>.

There are various methods for detecting atelectasis early on. Chest X-rays, which can reveal irregularities in lung tissue, are a common method [4,5]. Healthcare practitioners can spot any indicators of atelectasis and take suitable steps by reviewing the X-ray images [6]. This approach allows for early detection and intervention, which can improve patient outcomes significantly before the condition needs surgery.

Artificial neural networks (ANN) and machine learning (ML) approaches are currently being widely used [7]. These techniques are used to examine vast amounts of data from experiments, simulations, and field observations. Overall, the application of ML approaches improves the accuracy and efficiency of data analysis [8]. Further research and exploration of these methodologies are expected to result in major advances in the diagnosis of atelectasis. Machine learning is a subset of artificial intelligence (AI), has grown in importance in the field of medical imaging, particularly for the detection and diagnosis of lung diseases like atelectasis. Its significance is to improve the accuracy and efficiency of diagnostic operations by evaluating images from X-rays for subtle patterns and abnormalities [6]. In this case, machine learning can efficiently learn from large X-ray image datasets, identify key features, and make predictions based on these patterns, aiding in the early diagnosis of atelectasis, thereby enhancing the efficiency of medical diagnosis [9]. Deep learning techniques, such as artificial neural networks, are being developed to identify regions of interest and classify images based on atelectasis presence, with recent advancements integrating attention mechanisms. Deep learning advances have recently played an important role in the biomedical industry [10]. Among the deep learning techniques, Convolutional neural networks (CNNs) have showed considerable promise in image classification and segmentation and have thus been widely accepted by the research community [11]. Deep learning and computer vision techniques used in biomedical image detection have proven to be very useful in providing a quick and accurate diagnosis of disease that matches the accuracy of a reliable <u>radiologist</u> [12].

In this work, CNN, pre-trained CNN models VGG19 and Inception with sigmoid classifier were utilized to determine atelectasis. Furthermore, contrast limited adaptive histogram equalization (CLAHE) was used for improving the contrast of low-intensity images, and an anisotropic diffusion filtering (ADF) technique was applied to eliminate multiplicative speckle noise from the X-ray images. The following are noted as this paper main contributions:

• >

CNN model was developed for better identification of atelectasis disease.

• >

ADF image filtering algorithms was the most suitable filtering algorithm for medical image.

• >

CNN features achieved high training, validation, and testing accuracy of 99.88 %, 99 %, and 99 %, respectively.

The following sections comprise the research paper: Section <u>1</u> presents the topic and discusses its significance. Section <u>2</u> delves into tasks relating to our model. Section <u>3</u> describes the paper's methodology, including the architecture of a basic CNN model and the specific models provided in this paper. This section also goes over the dataset that was used to train and evaluate the six models. Section <u>4</u> displays the outcomes of each model, Section <u>5 Experimental results</u>, <u>6 Discussion</u> displays the results of each model's and discussion respectively, and Section <u>7</u> concludes the research study. Section <u>8</u> contains a list of references.

#### 2. Related works

This section examines related papers dealing with <u>atelectasis</u> diagnosis. Automated illness diagnosis technologies are being developed to alleviate the burden of diagnostic testing in hospitals. Most of these strategies also aid in treatment and decision-making. In the literature, numerous <u>deep learning algorithms</u> for detecting atelectasis from chest X-rays using benchmark and clinically obtained pictures are being examined.

Deep Convolutional Neural Networks were utilized by Rahib et al. [6] to detect chest diseases. The CNN is trained using 70 % of the available data from the 120,120 different 12 classes, with the remaining 30 % used for testing. Backpropagation neural networks (BPNNs) with supervised learning and competitive neural networks (CpNNs) with unsupervised learning were also built for comparison purposes by the authors with 1000 images. The accuracy of the CNN, BPNN2, and CpNN2 models is 92.4 %, 80.04 %, and 89.57 %, respectively.

Bharati et al. [13] demonstrate Hybrid deep learning for diagnosing lung illnesses from X-ray images. The authors use various sorts of existing deep learning approaches, such as convolutional neural network, vanilla neural network, visual geometry group based neural network (VGG), and capsule network, to predict lung illness from 14 categories. They present a new hybrid deep learning framework that integrates VGG, data augmentation, and spatial transformer networks (STN) with CNN. The hybrid CNN and VGG networks, as well as the modified capsule network, achieved accuracy rates of 67.8 %, 69 %, 69.5 %, and 63.8 %, respectively.

Zeng et al. [14] reported a deep learning technique to the identification of atelectasis and attic retraction pocket in <u>otitis media with effusion</u> using otoscopic images. A deep learning model for recognizing atelectasis and attic retraction pocket was developed and validated using 6393 otitis media with effusion (OME) otoscopic images from three sites, but there is inconsistent illumination of the otoscopes. On the <u>test dataset</u>, the cardiologists' diagnostic performance model produces the following results: 90.9 % specificity, 84.2 % sensitivity, 88.9 % negative predictive value, and 87.0 % positive predictive value.

External validation based on <u>transfer learning</u> is proposed by Huang et al. [9] for diagnosing atelectasis using portable chest X-rays. Using <u>natural language processing</u> tags, 14 categories were extracted from the intensive care chest X-ray medical information market database, 45,808 frontal chest radiographs were labeled "atelectasis," and 75,455 chest radiographs were labeled "no finding." This retrospective investigation retrieved 300 X-ray pictures labeled "atelectasis" and "normal" for use as an external dataset in this experiment. The AUC, sensitivity, specificity, and accuracy values were 88.57, 75.10, 88.30, and 81.70 %, respectively. The resulting AUC, sensitivity, specificity, and accuracy were 98.39, 70.70, 100, and 86.90 %, respectively, when compared to the external validation set.

Problem of statement: The statement emphasizes the importance of chest X-ray image analysis in diagnosing at electasis. The previous investigations used a limited number of at electasis chest X-ray images to investigate at electasis with regards to different lung disease classifications. However, this approach led to inappropriate detection and disparities in the classification of at electasis. They highlight the significance of chest X-ray analysis as a dependable tool for clinicians and radiographers [15,16]. However, the previously described works encountered various difficulties that impacted the precision of the detection results. These difficulties include an issue with class imbalance, a lack of image processing techniques such as noise reduction, managing low-intensity images, and a lack of critical information collected from the images. As a result, in order to produce relevant and trustworthy classification results, our study emphasizes the importance of removing noise from X-ray image datasets before using them for model construction and classification. To overcome these limitations, this work proposes using a variety of image preprocessing methods to improve the accuracy of at electasis diagnosis. These methods include noise removal, low-intensity image management, and feature extraction with CNN, VGG19, and Inception.

#### 3. Methodology

#### 3.1. Data collection

A dataset was generated from 5000 original images, of which 2500 were normal [17] and 2500 were atelectasis infected, gathered from the online repositories [18]. To balance the dataset for binary classification, 2500 normal X-ray images and 2500 atelectasis were taken from the repository. Overall, the final dataset used for the classification job is a subset of the original dataset that includes 2500 positive image samples (labeled with 'Atelectasis') and 2500 negative image samples (labeled with 'No Findings or normal'). After the images were preprocessed, they were merged and split into training and testing sets through a five-fold cross-validation process. The complete image data collection was correctly split into 70 % training, 10 % validation, and 20 % testing sets.

# 3.2. Preprocessing

Next to the acquisition of the image data, the original three-channel images were downsized from  $1024 \times 1024$  to  $224 \times 224$  pixels to minimize computation and for faster processing [19]. All the next steps have been applied to these reduced images. We chose the Bicubic interpolation technique over the others since it produces a better result [20]. We used gamma correction, an image enhancement technique that preserves a picture's mean brightness while producing natural-looking photos by choosing an appropriate gamma value (see Fig. 2).

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Fig. 2. Shows the normal image is on the left, and the contrast limited adaptive histogram equalization image is on the right.

#### 3.3. Contrast enhancement

The contrast of low-intensity images was improved using contrast limited adaptive histogram equalization (CLAHE) [21]. Edge detection was used to improve image look by improving contrast and visibility of objects of interest. In regular histogram equalization, the image's global contrast is employed. As the histogram extends and is not restricted to a certain spot, this results in areas that are excessively bright or too dark. As a result, contrast limiting is utilized to maintain a specified

amount of contrast. <u>Bilinear interpolation</u> is employed between tile borders [22]. CLAHE equalization was performed on the acquired images with a sample shown in <u>Fig. 2</u>.

# 3.4. Anisotropic diffusion filter

Due to the fact that our data was generated from chest X-ray images received from repositories, there is some noise in the images owing to the X-ray process. This noise has the potential to affect the accuracy or <u>dependability</u> of any data-based study or findings. However, in order to draw more meaningful inferences from the data, it is necessary to reduce and adjust for noise. Anisotropic diffusion filter (ADF) is a commonly used technique in medical <u>image processing</u>. This kind of <u>image filtering</u> aims to improve the image's edges and lessen noise. It works by selectively smoothing sections of an image while maintaining edges and boundaries, using diffusion exclusively in low-gradient regions and limiting diffusion in high-gradient areas. This aids in the preservation of edge sharpness and clarity. ADF also minimizes noise by smoothing out small-scale changes in pixel intensity, producing a cleaner, less <u>noisy image</u>. ADF improves <u>image quality</u> by keeping critical information like edges while limiting noise influence by combining these processes [23]. In medical imaging, where images are frequently noisy and contain complex features, this technique is especially helpful. Anisotropic diffusion filters can aid in enhancing the precision of diagnosis and image analysis in the medical field. ADF are generally effective tools for raising the diagnostic utility and quality of medical images [24].

#### 3.5. Proposed system architecture

A proposed method system architecture for atelectasis disease classification is depicted in Fig. 3. The process involves several steps, including image preprocessing, for improving the contrast of low-intensity images, noise removal, feature extraction, and classification. Firstly, image preprocessing entails resizing and normalizing images to a standard size. Secondly, contrast limited adaptive histogram equalization (CLAHE) was used for improving the contrast of low intensity images. Thirdly, ADF filtering technique is used to eliminate noise and image augmentation is used to enhance images. Fourthly, feature learning is achieved by extracting feature vectors from chest X-ray images using CNN, VGG19, and Inception, methods. In this method, relevant information from the chest X-ray is extracted and described in the image's nature, such as region part, edge part, and so on. As input, those extracted features are provided into the classification model in order to train it. Finally, we are classifying the image into predefined class (Normal or Atelectasis) using sigmoid.

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- Fig. 3. Proposed model system architecture.
- 3.6. Feature extraction

# 3.6.1. Convolutional neural network

Convolutional Neural Networks (CNN) are a type of <u>deep neural network</u> that analyzes visual imagery. As shown in <u>Fig. 4</u>, it consists of multiple hidden layers in addition to an input and output layer [25]. The fundamental advantage of CNN over other neural networks is that it recognizes crucial features efficiently and effectively without any human supervision [26]. To categorize an object, our CNN models are used to train and validate each input image of the dataset, which passes through a succession of layers with filters consisting of kernels, pooling, fully connected layers, and even

apply <u>activation function</u>. We also used Adam as an optimizer and the Rectified Linear Unit (ReLU) as an activation function in this work. Because average pooling smooths down the image, making it difficult to distinguish sharp features, max pooling, which addresses the maximum output within a rectangular neighborhood, was chosen as the pooling layer for this inquiry. Following the use of the pooling layer in our model, we used a flatten layer to flatten the entire network. The last <u>convolutional layer's</u> output is flattened and fed into a dense layer with 256 neurons. This is then fed into a layer that is activated by the <u>sigmoid function</u>. Since our classification is binary, the output is in terms of normal or atelectasis infected, we employed the sigmoid activation function at the deep learning network's final layer.

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- Fig. 4. Basic neural network learning layer diagram.

#### 3.6.2. Transfer learning

In addition to CNN, we used pre-trained models such as VGG19 and Inception. <u>Transfer</u> <u>learning</u> allows the model to save the original parameter values of a previously trained model in order to produce an effective score without using a large amount of processing power [27]. The use of hyper parameters allows the deep learning model to achieve significant outcomes during the training phase [28]. Choosing the exact settings can cause a significant difference at first, making hyper parameter tweaking a required task (<u>Table 1</u>) [29].

Table 1. CNN model hyper parameters and their values.

Hyper Parameter	Value
Kernel size	3 × 3 for all layers
Padding	Same
Optimizer	Adam
Pooling	Max pooling (2)
Activation function	ReLU, Sigmoid
Learning rate	0.001
Epoch	50
Batch size	64
Iteration	57

Hyper Parameter	Value
Dropout	0.25, 0.3

#### 4. Evaluation techniques

All the models were tested on the <u>test dataset</u> after the completion of the training phase. Their performance was validated using the accuracy, recall, precision, and F1 score. With the help of the <u>confusion matrix</u>, the number of true positives, true negatives, false positives, and false negatives could be calculated, which further helped in checking the efficacy of the model. The following formulae tells how to calculate the above different metrics:(1)Accuracy=TP+TNTP+FP+FN+TN(2)Precision=TPTP+FP(3)Recall=TPTP+FN(4)F1Score=2\*(Rec all\*Precision)Recall+Precision

Here, true positive (TP), true negative (TN), false positive (FP) and false negative (FN) were used to denote number of atelectasis images identified as atelectasis, number of normal images identified as normal, number of normal images incorrectly identified as atelectasis images and number of atelectasis images incorrectly identified as normal, respectively.

# 5. Experimental results

We ran four distinct experiments to evaluate the model in this study, which we are going to discuss in the following section. Overall, our method offers a solid and efficient methodology for image categorization problems. For our investigations, we use a Google compute engine instance called Google Colab. These resources enabled efficient and effective deep learning experimentation.

# 5.1. CNN feature extraction before image preprocessing

The first model performance was assessed without the use of any contrast enhancement or <u>image</u> <u>noise</u> removal techniques. The results showed that training accuracy was 99.83 % and validation accuracy was 97.75 %. However, after examining the validation accuracy displayed in <u>Fig. 5</u>, it became clear that the model was overfitting. This conclusion was strengthened by the fact that the validation loss was significantly greater than the training loss. However, there is significant overfitting because the discrepancy between training and validation accuracy is quite considerable. The graphs in <u>Fig. 5</u>, demonstrate a gradual increase in both training and validation accuracy, though there is a considerable difference between them. Similarly, as seen in <u>Fig. 6</u>, the training and validation losses showed a constant decrease trend.

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Fig. 5. Training and validation accuracy of CNN model before image preprocessing.

- 1. Download: Download high-res image (213KB)
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- Fig. 6. Training and validation loss of CNN model before image preprocessing.

# 5.2. CNN feature extraction after image preprocessing

In experiment 2, the model was trained using the contrast of low-intensity images using CLAHE (total 5000 images) and filtered images with the best filtering mechanism called anisotropic diffusion filter (ADF) that is specially designed for medical images. This finding demonstrates that CLAHE and image filtering is important in improving the model performance. The results showed that training accuracy was 99.88 % and validation accuracy was 99.00 %. The number of epoch's increases as training and testing accuracy improves, while training and validation loss decreases, as indicated by the training and validation loss curves in Fig. 7, Fig. 8. The lower the loss, the better the model's recognition outcomes. Overfitting was avoided since the training and validation curves were so closely related. The accuracy and losses for training and validation follow a linear pattern, indicating the network was adequately trained and capable of making accurate predictions. In general, when compared to other experiments, this CNN model is substantially more accurate.

- 1. <u>Download: Download high-res image (194KB)</u>
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- Fig. 7. Training and validation accuracy of CNN model after image preprocessing.
  - 1. Download: Download high-res image (207KB)
  - 2. <u>Download: Download full-size image</u>
- Fig. 8. Training and validation loss of CNN model after image preprocessing.
- 5.3. VGG19 feature extraction after image preprocessing

VGG reduce the size of the activation maps by half, it also demonstrated that a few small  $3 \times 3$  convolution filters it makes the improvement over <u>AlexNet</u> by replacing a single  $7 \times 7$  or even  $11 \times 11a$  large kernel sized filters, achieve better performance while reducing the computation cost [30]. VGG applies classification block is used, consisting of two dense layers of 4096 neurons each, and the last layer, which is the output layer, of 1000 neurons. The 16 and 19 refer to the number of weighted layers that each network has convolutional and dense layers and pooling layers are not counted [31]. Our VGG19 model has shown impressive results, achieving a training accuracy of 99.69 % and a validation accuracy of 99.25 %. The <u>graphical representations</u> of model accuracy and model loss VGG19 are given in <u>Fig. 9</u>, <u>Fig. 10</u>, respectively. These show the variation in training and validation accuracies and losses from epoch to epoch, and the graph is straight up.

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- Fig. 9. Training and validation accuracy of VGG19 model after image preprocessing.
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- Fig. 10. Training and validation loss of VGG19 model after image preprocessing.
- 5.4. Inception feature extraction after image preprocessing

The larger the deep learning model, the more susceptible it is to overfitting, and increasing the number of parameters necessitates an increase in computational resources. These issues are solved in the Inception model, allowing the depth and width of the deep learning model to be increased while keeping the computational cost constant [26]. This model introduces a sparsely linked network design. Convolutions are computed one by one,  $3 \times 3$ , and  $5 \times 5$ , and an <u>auxiliary</u> classifier is utilized as a regularizer in the design [32]. Our Inception model has shown impressive results, achieving a training accuracy of 100 % and a validation accuracy of 98.75 %. As shown in <u>Fig. 11</u>, there were some fluctuations in the accuracy curves during the early epochs, but they finally stabilized and advanced linearly towards the end of the training. From <u>Fig. 12</u>, we clearly see that the result of the training loss curves is closely tracking the validation loss curves.

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- Fig. 11. Training and validation accuracy of VGG19 model after image preprocessing.
  - 1. Download: Download high-res image (196KB)
  - 2. Download: Download full-size image
- Fig. 12. Training and validation loss of VGG19 model after image preprocessing.

According to the CNN model after image preprocessing <u>confusion matrix</u>, which is shown in <u>Fig. 13</u> (CNN after image preprocessing) of the 500 atelectasis positive patients have been identified properly using our suggested model from the chest X-ray images. Only 4 out of 500 patients who tested as positive for atelectasis were mistakenly labeled as atelectasis negative. Similar to this, 494 of 500 normal individuals have received the proper diagnosis based on their chest X-ray images. Only 6 patients have ever been misdiagnosed as having atelectasis (see Fig. 13).

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Fig. 13. Depicts the confusion matrix of 1000 testing images, which represents 20 % of the total 5000 images of each suggested model. The remaining 80 %, which amounts to 4000 images, are designated for training and validation purposes.

#### 6. Discussion

Our suggested strategy for detecting and diagnosing atelectasis disease was rigorously tested utilizing X-ray images and performance evaluation criteria. We used CNN from Neural Networks, and VGG19 and Inception from pre-trained models to extract features, and sigmoid classifier. As we have seen in the below in <u>Table 2</u>, and <u>Fig. 14</u> above the training, validation, and testing performance and of the model for atelectasis disease recognition. The first and second models were trained using the

original data without increasing the contrast of low-intensity CLAHE and without adding an anisotropic diffusion filter to remove noise. In the other studies, we applied image enhancement to improve low-intensity contrast and noise filtering, which achieves higher accuracy than the original data set result. This study employs X-ray images to do binary classification between atelectasis and healthy patients using CNN and pre-trained approaches. The CNN model outperformed the existing state-of-the-art (VGG19 and Inception). Our study findings indicate that the atelectasis diagnosis model has surpassed previous studies in terms of accuracy and run time, as illustrated in Table 2. This improvement is crucial since it improves both the precision of diagnosis and the speed with which the model performs. This suggests that our study makes a major contribution to enhancing the accuracy of atelectasis diagnosis, perhaps leading to better patient outcomes. The proposed CNNs have shown a significant increase in both capacity and efficiency for detecting atelectasis in real-world clinical scenarios. This advancement has the potential to greatly improve diagnostic capabilities and patient outcomes in the field of respiratory medicine. Artificial intelligence experts predict that AI will become a regular part of radiologists' everyday routines, resulting in more efficient and accurate work. With Al-based computers performing typical reading tasks like quantification and segmentation, radiologists may focus on more value-added activities. This includes integrating patients' clinical and imaging information, engaging in professional relationships, improving visibility to patients, and playing an important role in integrated clinical teams to improve patient care. Implementing these modern technology will not only increase diagnosis accuracy but will also reduce workflow in radiology departments, eventually benefiting both healthcare professionals and patients. As shown in Table 2, the suggested at electasis diagnosis model has a training run time of nearly 2 min and a testing run time of 1 s. This indicates that the proposed study will help improve the accuracy and speed of atelectasis detection in real world clinical settings. The model's efficient run time is a critical aspect in its practicality and usability in clinical settings. The suggested methodology offers a cost effective solution for atelectasis diagnosis by minimizing the time necessary for both training and testing. This is especially useful in real world clinical situations where prompt and accurate diagnosis is critical for providing timely patient care. The combination of improved accuracy and reduced run time establishes our proposed atelectasis detection model as a relevant and cost effective tool for real world clinical applications. As a result, our proposed model is both cost effective and useful for usage in real world clinical areas, and ultimately contributing to better patient care (see <u>Table 3</u>).

Table 2. Shows the summary model's performance in training, validation and testing, as well as precision, recall, F1-score, training and testing time.

Models	Class	Precision (%)	Recall (%)	F1- score (%)	Training Accuracy (%)	Validation Accuracy (%)	Test Accuracy (%)	Training time (minutes)	Testing time (minutes
CNN before image	Normal	97	100	99	99.83	97.75	98.50	0:02:25	1s, 20 m
preprocessing	Atelectasis	100	97	98					
CNN after image	Normal	99	99	99	99.88	99.00	99.00	0:02:25	1s, 14 m
preprocessing	Atelectasis	99	99	99					

Models	Class	Precision (%)	Recall (%)	F1- score (%)	Training Accuracy (%)	Validation Accuracy (%)	Test Accuracy (%)	Training time (minutes)	Testing time (minutes
VGG19	Normal	98	99	99	99.69	99.25	98.79	0:02:19	1s, 17 m
	Atelectasis	99	98	99					
Inception	Normal	99	99	99	100	98.75	98.79	0:14:28	4s, 72 m
	Atelectasis	99	99	99					

Table 3. Shows a comparison among existing methods in the atelectasis detection.

Authors	Technique	Image no.	Recall (%)	Precision (%)	F1-score (%)	Overall Accuracy (%)
Rahib et al.	CNN, BPNN, CpNN	120,120	-	-	_	92.4
Bharati et al. [13]	CNN, VGG	120,120	62	68	-	
Zeng et al. [14]	Deep Learning	6393	93	84	_	89
Huang et al. [ <u>9]</u>	ResNet50	60,000	75.1	88.3	_	81.7
Our model	CNN, VGG19, Inception	5000	99	99	99	99

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Fig. 14. Presents additional <u>graphical representation</u> of a comparison of the suggested models' experimental results.

#### 7. Conclusion

As a result, it is determined that the deep learning model given above accurately classifies chest X-rays for atelectasis diagnosis. The various preprocessing processes serve to ensure that the performance of convolutional neural networks and <u>deep neural networks</u> is not overfitted, and so the results obtained are always coherent. The proposed model accurately predicts whether a particular chest X-ray sample has atelectasis or is normal. This is extremely beneficial in the medical sector for making an early and precise diagnosis of atelectasis in patients. Early diagnosis is critical in

saving a person's life by guaranteeing effective and timely patient care. The primary goal of this work is to improve medical proficiency in locations where radiotherapists are still few. Our research will aid in the early detection of atelectasis in order to provide better health-care services and avoid negative outcomes such as mortality. We observed the performance of CNN and other pre-trained CNN models and then chose CNN for the feature extraction step after considering the results. The CNN model produced the greatest results across four experiments, with 99.88 % training accuracy, 99 % validation accuracy, and 99 % testing accuracy. In the near future, our research will most likely lead to the development of better algorithms for detecting atelectasis.

#### Abstract

#### Objectives

To investigate the value of spectral-detector <u>computed tomography</u> (SDCT) parameters for the quantitative differentiation between <u>atelectasis</u> and pneumonia on contrast-enhanced chest CT.

#### Material and methods

Sixty-three patients, 22 clinically diagnosed with pneumonia and 41 with atelectasis, underwent contrast-enhanced SDCT scans during the venous phase. CT numbers (Hounsfield Units [HU]) were measured on conventional reconstructions (CON<sub>120kVp</sub>) and the iodine concentration (C<sub>iodine</sub>, [mg/ml]), and effective atomic number (Z<sub>eff</sub>) on spectral reconstructions, using region-of-interest (ROI) analysis. Receiver operating characteristics (ROC) and contrast-to-noise ratios (CNRs) were calculated to assess each reconstruction's potential to differentiate between atelectasis and pneumonia.

#### Results

On contrast-enhanced SDCT, the difference between atelectasis and pneumonia was significant on  $CON_{120kVp}$ ,  $C_{iodine}$ , and  $Z_{eff}$  images (p < 0.001). On  $CON_{120kVp}$  images, a threshold of 81 HU achieved a sensitivity of 93 % and a specificity of 95 % for identifying pneumonia, while  $C_{iodine}$  and  $Z_{eff}$  images reached the same sensitivity but lower specificities of 85 % and 83 %.  $CON_{120kVp}$  images showed significantly higher CNRs between normal lung and atelectasis or pneumonia with 30.63 and 27.69 compared to  $C_{iodine}$  images with 3.54 and 1.27 and  $Z_{eff}$  images with 4.22 and 7.63 (p < 0.001). None of the parameters could differentiate atelectasis and pneumonia without contrast media.

# Conclusions

Contrast-enhanced SDCT can differentiate atelectasis and pneumonia based on the spectral parameters  $C_{\text{iodine}}$ , and  $Z_{\text{eff.}}$  However, they had no added value compared to CT number measurement on  $CON_{120\text{kVp}}$  images. Furthermore, contrast media is still needed for a differentiation based on quantitative SDCT parameters.

#### 1. Introduction

Pulmonary infections are responsible for significant morbidity and mortality worldwide, and clinical symptoms, laboratory tests, and imaging methods are used for diagnosis and therapy control [1, 2]. The ideal reference diagnosis for pneumonia is the detection of pathogenic agents in the <a href="https://linear.com/li

<u>Computed tomography</u> (CT) can provide a regional and morphological description of lung pathologies and should be considered in patients with an unclear clinical condition or inadequate response to pneumonia therapy [2, 3]. Imaging signs of thoracic infection can be useful, sometimes

suggesting a specific diagnosis and often narrowing the differential diagnosis. The consolidated lung is a common imaging sign of pulmonary infection, but it can also reflect atelectasis, a non-infectious lung pathology [4]. Radiological features like volume loss or a positive air bronchogram can help to differentiate pneumonia from atelectasis, but they remain qualitative, non-obligatory observations [4, 5]. In some clinical situations, the diagnosis of pneumonia is not unambiguous, and quantitative CT parameters would be desirable to facilitate a more confident diagnosis. The Hounsfield unit (HU), a relative quantitative measurement of x-ray density, is the most frequently used quantitative CT parameter, but unfortunately, the differences between atelectasis and pneumonia are usually not significant enough to allow a confident diagnosis on non-enhanced images. Here, contrast media administration can help since atelectasis shows a stronger contrast-enhancement than pneumonia [6]. In this context, Edwards *et al.* reported a threshold of 85 HU to diagnose pneumonia which reached a high 97 % sensitivity and 85 % specificity on contrast-enhanced CT pulmonary angiograms [6].

Spectral-detector computed tomography (SDCT) uses an X-ray tube and two different detector layers to selectively absorb different energies from the polychromatic X-ray spectrum [7, 8]. This technical approach allows for the simultaneous measurement of low and high-energy photons at the same spatial and angular location, facilitating dual-energy post-processing in the projection domain, different from other dual-energy techniques [9, 10, 11, 12]. The obtained spectral data set enables the retrospective analysis of the pixel-wise iodine concentration ( $C_{iodine}$ ) and the calculation of the effective atomic number ( $Z_{eff}$ ), reflecting the blood supply and the effective atomic number of inorganic materials. In the literature, SDCT parameters were already used to differentiate lung cancer from inflammatory masses and showed benefits when detecting pulmonary embolism and assessing pleural contrast uptake [13, 14, 15]. Due to the significantly different blood supply of atelectasis and pneumonia, we hypothesized that  $C_{iodine}$  and  $Z_{eff}$  images might have advantages over conventional images since they may offer additional information regarding perfusion properties. Therefore, we conducted this study to investigate if SDCT parameters  $C_{iodine}$  and  $Z_{eff}$  are beneficial compared to CT number quantification on conventional images for distinguishing atelectasis from pneumonia on contrast-enhanced chest CT.

#### 2. Materials and methods

#### 2.1. Patient cohort

This retrospective study was approved by the institutional ethics committee (S-781/2018), and informed consent for data processing was waived. Database research encompassing the years 08/2017 - 06/2020 identified 3167 patients who underwent venous phase contrast-enhanced or non-enhanced chest SDCT. CT acquisitions were serially evaluated for inclusion and exclusion criteria. The inclusion criteria were (1) radiologic feature of the consolidated lung, (2) consolidated lung >1 cm² in size on four continuous slices, (3) age >18, and (4) absence of motion artifacts. The exclusion criteria were (1) tumor (>1 cm²), (2) radiologic features of atypical pneumonia, (3) metastatic lung disease, or (4) previous lung surgery.

CT acquisitions were classified as <u>atelectasis</u> or pneumonia based on the presence of a non-radiologic clinical scoring system adapted from Edwards et al. [6]. Clinical criteria were (1) <u>hypoxia</u>, <u>tachypnea</u>, grunting, chest in drawing and/or crackles on <u>auscultation</u>, (2) blood testing (C-reactive protein (CRP) > 5 mg/l or white blood cell count (WBC) >4–10/ml), (3) antibiotic treatment (Abx.) for pneumonia (aminopenicillin and/or after admission in the hospital with a second- or third-generation cephalosporin) or (4) documentation of pneumonia as a discharge diagnosis or clinical suspicion of pneumonia as an indication for chest CT. One point was given for the

presence of each criterion. Each case was classified as atelectasis if one or less, and as pneumonia if three or more criteria were met. If two criteria were met, patients with an apparent non-pulmonary infection were also classified as atelectasis, and patients with cough and no other apparent non-pulmonary infections were classified as pneumonia (Figure 1).

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Figure 1. Flowchart for patient recruitment. Database research encompassing the years 2017–2020 identified 3167 patients who underwent chest CT. Two hundred twenty-six patients had consolidated lung >1 cm² in size on four continuous slices as an imaging feature. Out of these, 123 patients were excluded due to motion artifacts, tumor >1 cm², radiologic features of atypical pneumonia, metastatic lung disease, or previous lung surgery. The remaining 103 patients were split up in contrast-enhanced and non-contrast CT. Finally, the patients were classified as atelectasis or pneumonia based on clinical criteria.

# 2.2. CT acquisition

All SDCT examinations were performed using a 128-slice dual-layer CT system (IQon; Philips GmbH, Hamburg, Germany). All patients were acquired in <u>supine position</u> during an inspirational breathhold in the craniocaudal direction. The following acquisition parameters were used: collimation  $2 \times 64 \times 0.625$  mm; rotation time 0.33-0.75 s; pitch 0.798-1.014; tube current 120 kVp, dose modulation type: DoseRight 3D-DOM with an Dose Right Index (DRI) of 17 (Philips GmbH, Hamburg, Germany). All images were reconstructed in axial orientation using an image matrix of  $512 \times 512$  with a slice thickness of 1-1,5 mm and an increment of 0.75-3 mm using a dedicated spectral reconstruction algorithm (Spectral, Philips GmbH, Hamburg, Germany) and a fixed kernel (B; Philips GmbH, Hamburg, Germany). Conventional 120 kVp (CON<sub>120kVp</sub>), iodine concentration (C<sub>iodine</sub>), and effective atomic number (Z<sub>eff</sub>) images were reconstructed (<u>Table 1</u>).

Table 1. SDCT acquisition parameters.

Protocol	Collimation (mm)	Image matrix	Pitch	Gantry rotation time (s)	Acquisition time (s)	Tube current (kVp)	Tube current- time product (mAs)	Absolute Min (mAs)	Absolute Max (mAs)
Native chest	2 × 64×0.625	512 × 512	1.014	0.75	7.8	120	47	35	230
Venous chest	2 × 64×0.625	512 × 512	0.984	0.33	3.5	120	93	40	300
Venous body	2 × 64×0.625	512 × 512	0.798	0.5	9.6	120	74	65	300

In all patients who underwent contrast-enhanced CT, the contrast media (350 mg lohexol/ml; AccupaqueTM 350; GE Healthcare GmbH, Solingen, Germany) was injected via an <u>antecubital vein</u> or a <u>central venous catheter</u> using a power injector. Venous phase imaging was triggered by <u>bolus</u> <u>tracking</u> at the level of the truncus pulmonalis with a threshold of 150 HU and a post-threshold-delay

of 35 s. Single bolus contrast-injection was performed for venous chest acquisitions administering 50 ml contrast media followed by a 60 ml saline solution chaser bolus at a 4 ml/s flow rate. Venous body acquisitions used a biphasic contrast-injection protocol consisting of two contrast boli, the first with 50 and the second with 40 ml contrast agent, both followed by a saline solution chaser bolus of 15 and 30 ml, respectively. The interval between both boluses was 30 s, and the flow rate was 3 ml/s. All protocols were slightly adjusted to the patients' body weight.

# 2.3. Image analysis

Two readers with two and seven years of experience in thoracic imaging analyzed the images, using a picture archiving and communication system (PACS) workstation (Centricity, Version 7.0; General Electrics, New York, USA) and a dedicated post-processing software provided by the SDCT manufacturer (IntelliSpace Portal 10; Philips GmbH, Hamburg, Germany). Images were read in a nonrandomized fashion, and the regions of interest (ROIs) were placed in consensus. On conventional images, two standardized oval ROIs of 1 cm<sup>2</sup> and one maximum-sized ROI were placed each in the consolidated lung (pneumonia or atelectasis), the normal lung, and pleural effusion (PE), excluding bronchi and third-order or larger pulmonary vessels. Normal lung regions were chosen by absence of consolidation or ground glass attenuation at the hilum level and at least 1 cm away from the pleura. Singular vessel ROIs were placed in the ascending aorta (AA) and the right pulmonary artery (RPA) at the right proximal pulmonary artery level. ROIs placed on conventional images were automatically transferred to the corresponding position on the iodine concentration (Ciodine) and the effective atomic number (Z<sub>eff</sub>) images. For each ROI, absolute attenuation values in Hounsfield units (HU), iodine concentration (mg/ml) and effective atomic number as well as respective standard deviations (SD) were recorded. Measurements of two ROIs were averaged. According to the definition of van Engen et al., the contrast-to-noise ratio (CNR) between two tissues (1 and 2) was defined as CNR= $|S1-S2|/0.5(\sigma 12+\sigma 22)$  with S being the averaged HU on CON<sub>120kVp</sub>, iodine concentration ( $C_{iodine}$ ) or effective atomic number ( $Z_{eff}$ ) in two homogeneous ROI, and  $\sigma$  being the standard deviation in the same ROIs [16].

#### 2.4. Statistical analysis

All data were recorded in a dedicated spreadsheet (Excel, Microsoft Corp., Redmond, USA), and analyses were performed with SigmaPlot (Systat Software GmbH, Erkrath, Germany) and SPSS (IBM SPSS Statistics 25, New York; USA). All data are given as mean ± standard deviation (SD). Quantitative imaging parameters results were tested for significant differences with the Mann-Whitney Rank Sum Test for non-paired measurements. An additional analysis using the Bonferroni-Holm method for multiple testing was performed, which did not change the number of significant results. Receiver operating characteristic (ROC) analysis was used to evaluate the performance of conventional  $(CON_{120kVp})$ , iodine concentration  $(C_{iodine})$ , and effective atomic number  $(Z_{eff})$  images in discriminating between pneumonia and atelectasis. The overall performance was summarized using the area under the curve (AUC). Thresholds were chosen by maximizing the Youden index (J = sensitivity + specificity -1), which treats sensitivity and specificity as equally important and is not weighted by the pre-test probability [17]. Statistical significance was defined as  $p \le 0.05$ . CNRs of all three quantitative parameters were compared using one-way analysis of variances (ANOVA) for repeated measures, and post-hoc tests with Bonferroni's correction or Dunn's method as appropriate in case of multiple comparisons. In addition, for each data set a feature vector was composed out of the HU, Ciodine and Z<sub>eff</sub> values of the pneumonia, aorta and atelectasis region. Subsequently, principle component analysis (PCA) implemented in the freely available analysis software PAleontological STatistics (PAST) was performed in a 9 dimensional feature space separately for the data sets with and without contrast enhancement [18, 19].

#### 3. Results

#### 3.1. Patient cohort

In total, 103 patients aged  $62.2 \pm 16.6$  years (range: 19–88 years) could be recruited. Sixty-three patients, 22 clinically diagnosed with pneumonia and 41 with atelectasis, underwent contrastenhanced SDCT, and 40 patients, 21 clinically diagnosed with pneumonia, and 19 with atelectasis, underwent non-enhanced chest SDCT. There were no significant differences in age (p = 0.574, p = 0.818) or BMI (p = 0.833; p = 0.483), when comparing both groups (Table 2). In both atelectasis groups, 55 % of cases had less than two clinical criteria, which allowed an exact classification. 42 % of cases fulfilled two clinical criteria, but since all of them had an apparent non-pulmonary infection, they were also classified as atelectasis. In both pneumonia groups, 70 % of cases had more than two clinical criteria and were therefore classified as pneumonia. 30 % of cases fulfilled only two clinical criteria, but most of them had a cough, and no other apparent non-pulmonary infection was found; therefore, they were classified as pneumonia (Table 2).

Table 2. Patient demographics and diagnostic criteria for patients with contrast-enhanced and non-enhanced chest CT.

Patient demographics	Contrast-enhanced			Non-enhanced		
	Atelectasis	Pneumonia	р	Atelectasis	Pneumonia	р
N	41	22	-	19	21	-
Sex (m/f)	20/21	12/10	-	9/10	13/8	-
Age (y)	64.4 ± 15.1	66.8 ± 14.3	0.574	55.5 ± 20.2	59.3 ± 15.5	0.818
BMI (kg/cm²)	27.7 ± 5.4	28.9 ± 8.2	0.833	24.5 ± 4.3	28.4 ± 4.1	0.483
Diagnostic criteria						
Fever and/or cough	2 (5 %)	11 (50 %)	-	7 (37 %)	17 (81 %)	-
Leucocytosis and/or CRP	20 (49 %)	11 (50 %)	-	3 (16 %)	6 (29 %)	-
Abx. treatment	25 (61 %)	21 (95 %)	-	11 (58 %)	18 (86 %)	-
Clinical diagnosis of pneumonia	2 (5 %)	22 (100 %)	-	1 (5 %)	21 (100 %)	-
Nonpulmonary septic foci	27 (66 %)	4 (18 %)	-	13 (68 %)	3 (14 %)	-

Total no. criteria present

Patient demographics	Contrast-er	hanced	Non-enhanced			
	Atelectasis	Pneumonia	р	Atelectasis	Pneumonia	р
0 of 4	12 (29 %)	0 (0 %)	-	7 (37 %)	0 (0 %)	-
1 of 4	11 (27 %)	0 (0 %)	-	3 (16 %)	0 (0 %)	-
2 of 4	18 (39 %)	9 (41 %)	-	9 (47 %)	4 (19 %)	-
3 of 4	0 (0 %)	5 (23 %)	-	0 (0 %)	11 (52 %)	-
4 of 4	0 (0 %)	8 (36 %)	-	0 (0 %)	6 (29 %)	-

<u>Patient characteristics</u> given as median and standard deviation. <u>BMI</u> = body mass index. Distribution of diagnostic criteria with the final clinical diagnosis of atelectasis or pneumonia. Abx indicates antibiotics.

# 3.2. Influence of ROI sizes and contrast-phase on quantitative CT parameters

Quantitative CT parameters were compared between standardized and maximum-sized ROI, and no significant differences were found in the atelectasis or the pneumonia group (p = 0.953, p = 0.683) (Table 3).

Table 3. Influence of ROI sizes on the quantitative CT parameters.

Empty Cell	Atelectasis			Pneumonia			
	standardized	maximum- sized	р	standardized	maximum- sized	р	
Region of intere	st (mm²)						
Normal lung	10 ± 0	46 ± 12	<0.001	10 ± 0	55.51 ± 16.03	<0.001	
Consolidated lung	10 ± 0	19 ± 7	<0.001	10 ± 0	22.01 ± 8.80	<0.001	
Pleural effusion	10 ± 0	32 ± 18	<0.001	10 ± 0	15.87 ± 8.74	<0.001	
CT numbers me	asured on CON	<sub>120kVp</sub> (HU)					
Normal lung	-814 ± 57	-797 ± 47	0.055	-810 ± 65	-816.98 ± 52.30	0.953	
Consolidated lung	105 ± 21	102 ± 21	0.683	60 ± 13	62.23 ± 13.34	0.869	

Empty Cell	Atelectasis			Pneumonia			
	standardized	maximum- sized	р	standardized	maximum- sized	р	
Pleural effusion	9 ± 8	10 ± 11	0.514	6 ± 11	11.94 ± 14.11	0.536	
lodine concentra	ation measure	d on C <sub>iodine</sub> (mg/	/ml)				
Normal lung	0.71 ± 0.39	0.68 ± 0.20	0.468	0.67 ± 0.39	0.70 ± 0.23	0.230	
Consolidated lung	2.65 ± 0.94	2.59 ± 0.92	0.809	1.28 ± 0.39	1.28 ± 0.50	0.824	
Pleural effusion	0.06 ± 0.12	0.09 ± 0.17	0.705	0.09 ± 0.08	0.10 ± 0.12	0.569	
Effective atomic	number meas	ured on Z <sub>eff</sub>					
Normal lung	9.37 ± 0.57	9.52 ± 0.66	0.356	9.36 ± 0.65	9.42 ± 0.60	0.681	
Consolidated lung	8.63 ± 0.39	8.62 ± 0.39	0.937	8.03 ± 0.20	8.03 ± 0.26	0.742	
Pleural effusion	7.19 ± 0.17	7.22 ± 0.21	0.350	7.24 ± 0.16	7.26 ± 0.17	0.878	

Standardized ROI ( $2 \times 1 \text{mm}^2$ ) were compared with ROIs of maximum size. Mean  $\pm$  standard deviation for CT numbers on conventional (CON<sub>120kVp</sub>) images as well as iodine concentration (C<sub>iodine</sub>) and effective atomic number (Z<sub>eff</sub>) on spectral images in the atelectasis and the pneumonia group. Pleural effusion was present in n = 13 patients in the atelectasis, and never in the pneumonia group.

In 63 patients contrast medium was applied intravenously and no significant differences between the atelectasis and pneumonia group were found for volume (ml), duration (sec) and flow rate (ml/s) (p = 0.667, p = 0.527, p = 0.088). ROIs were used to determine the average attenuation in the descending aorta (DA) and the <u>right pulmonary artery</u> (RPA), also showing no significant differences between both groups (p = 0.846, p = 0.941, p = 0.915) (<u>Table 4</u>).

Table 4. Contrast administration protocol and measurements in vessel ROIs on contrast-enhanced chest CT.

Empty Cell	Atelectasis	Pneumonia	р
Contrast administration protocol			
Volume (ml)	86.68 ± 19.19	80.95 ± 22.36	0.667
Duration (s)	28.04 ± 5.85	24.92 ± 5.70	0.527

Empty Cell	Atelectasis	Pneumonia	р
Flow rate (ml/s)	3.10 ± 0.42	3.22 ± 0.43	0.088
CT numbers in vessel ROIs (HU)			
Descending aorta	193 ± 82	197 ± 83	0.846
Right pulmonary artery	179 ± 83	153 ± 21	0.941
Average of DA and RPA	187 ± 83	178 ± 68	0.915

Contrast media volume, application duration, and flow rate are given for the atelectasis and the pneumonia group. Contrast administration data was missing for 12 patients. The CT number values in Hounsfield units on conventional images are given for the descending aorta (DA) and the right pulmonary artery (RPA). Both measurements were also averaged.

3.3. Contrast media is needed for quantitative discrimination between atelectasis and pneumonia

On non-enhanced SDCT, no significant differences were found between the atelectasis and the pneumonia group, neither on  $CON_{120kVp}$  (p = 0.054) nor on  $Z_{eff}$  images (p = 0.563) (Figure 2 and Table 5). The AUCs for non-enhanced images were expectedly small, with the largest AUC 0.68 (0.50–0.86) achieved on  $CON_{120kVp}$  images with a sensitivity of 56 % and specificity of 52 %.  $Z_{eff}$  had an AUC of 0.57 (0.26–0.64) with a slightly higher sensitivity of 61 % and the same specificity.

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Figure 2. Boxplots for quantitative CT measurements. Values are given for the regions of interest on (A, D) conventional (CON<sub>120kVp</sub>), (B) iodine concentration ( $C_{iodine}$ ), and (C, F) effective atomic number ( $Z_{eff}$ ) images for atelectasis and the pneumonia for all patients (N). The cut-off values were calculated using the Youden-Index.

Table 5. Quantitative parameters on non-enhanced chest SDCT.

Empty Cell	Atelectasis	Pneumonia	р				
CT numbers measured on CON <sub>120kVp</sub> (HU)							
Normal lung	-833 ± 58	-835 ± 56	0.789				
Consolidated lung	37 ± 15	26 ± 10	0.054				
Pleural effusion	1 ± 9	-	-				
Effective atomic number measured on Z <sub>eff</sub>							
Normal lung	7.91 ± 0.49	7.65 ± 0.44	0.076				

Empty Cell	Atelectasis	Pneumonia	р
Consolidated lung	7.24 ± 0.20	7.31 ± 0.12	0.563
Pleural effusion	7.10 ± 0.14	-	-

Mean  $\pm$  standard deviation for ROIs on conventional (CON<sub>120kVp</sub>) and effective atomic number (Z<sub>eff</sub>) images are given for the atelectasis and the pneumonia group. Pleural effusion was present in n = 13 patients in the atelectasis, and never in the pneumonia group.

3.4. Quantitative parameters can discriminate atelectasis from pneumonia with contrast media

On contrast-enhanced SDCT, CT numbers of the consolidated lung were significantly higher in the atelectasis group than in the pneumonia group for  $CON_{120kVp}$ , (p < 0.001). Correspondingly,  $C_{iodine}$ , and  $Z_{eff}$  were also significantly higher in the atelectasis group (p < 0.001). We found no significant differences for normal lung or <u>pleural effusion</u> measurements between both groups (Figure 2, Figure 3, and Table 6).

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Figure 3. Conventional, iodine concentration, and effective atomic number images of contrast-enhanced chest CT in three different patients. (A, B, C) Bilateral pleura effusion within adjacent homogenous atelectasis (white arrow) in a 45-year-old woman. (D, E, F) Right-sided <u>lobar pneumonia</u> with a positive air bronchogram a 51-year-old woman. (G, H, I) Bilateral pleural effusion with adjacent atelectasis in a 45-year-old man. On the right side is a focal area with hypoperfusion within the atelectasis (white arrow), which is suspicious for a <u>superinfection</u> of the atelectasis. Quantitative CT parameters are shown for atelectasis (square) and pneumonia (circle).

Table 6. Quantitative parameters on contrast-enhanced chest SDCT.

Empty Cell Atelectasis		р					
CT numbers measured on CON <sub>120kVp</sub> (HU)							
-814 ± 57	-810 ± 65	0.971					
105 ± 21	60 ± 13	<0.001					
9 ± 8	6 ± 11	0.723					
Iodine concentration measured on C <sub>iodine</sub> (mg/ml)							
0.71 ± 0.39	0.67 ± 0.39	0.498					
2.65 ± 0.94	1.28 ± 0.39	<0.001					
0.06 ± 0.12	0.09 ± 0.08	0.077					
	20kVp (HU)  -814 ± 57  105 ± 21  9 ± 8  On C <sub>iodine</sub> (mg/ml)  0.71 ± 0.39  2.65 ± 0.94	$_{20kVp}$ (HU) $_{-814 \pm 57}$ $_{-810 \pm 65}$ $_{105 \pm 21}$ $_{60 \pm 13}$ $_{9 \pm 8}$ $_{6 \pm 11}$ on $_{codine}$ (mg/ml) $_{0.71 \pm 0.39}$ $_{0.67 \pm 0.39}$ $_{2.65 \pm 0.94}$ $_{1.28 \pm 0.39}$					

Empty Cell	Atelectasis	Pneumonia	р			
Effective atomic number measured on Z <sub>eff</sub>						
Normal lung	9.37 ± 0.57	9.36 ± 0.65	0.943			
Consolidated lung	8.63 ± 0.39	8.03 ± 0.20	<0.001			
Pleural effusion	7.19 ± 0.17	7.24 ± 0.16	0.180			

Mean  $\pm$  standard deviation for ROIs on conventional (CON<sub>120kVp</sub>), iodine concentration (C<sub>iodine</sub>), and effective atomic number (Z<sub>eff</sub>) images are given for the atelectasis and the pneumonia group. Pleural effusion was present in n = 29 patients in the atelectasis, and in n = 17 patients in the pneumonia group.

## 3.5. Best contrast-to-noise ratio was achieved on conventional images

On  $CON_{120kVp}$  images, significantly higher CNRs were achieved between normal lung and atelectasis or pneumonia compared to the  $C_{iodine}$  and  $Z_{eff}$  images (p < 0.001). On the  $Z_{eff}$  images, the highest CNRs were found between the aorta, pleural effusion, and atelectasis or pneumonia (p < 0.001) (<u>Table 7</u>).

Table 7. Contrast-to-noise ratios for consolidated lung.

Empty Cell	CON <sub>120kVp</sub>	C <sub>iodine</sub>	Z <sub>eff</sub>	р
Atelectasis				
vs. aorta	4.32	6.91	24.83	<0.001
vs. normal lung	30.63	3.54	4.22	<0.001
vs. pleural effusion	5.21	5.01	23.37	<0.001
Pneumonia				
vs. aorta	7.14	9.79	37.52	<0.001
vs. normal lung	27.69	1.27	7.63	<0.001
vs. pleural effusion	2.98	2.63	7.30	<0.001

Contrast-to-noise ratios between atelectasis or pneumonia and the aorta, normal lung and pleural effusion was calculated using conventional ( $CON_{120kVp}$ ), iodine concentration ( $C_{iodine}$ ), and effective atomic number ( $Z_{eff}$ ) images.

# 3.6. All quantitative parameters showed comparable diagnostic properties

On contrast-enhanced SDCT, the AUC to differentiate atelectasis from pneumonia on  $CON_{120kVp}$  images was 0.98 (CI 0.94–0.99), whereas it was slightly lower for  $C_{iodine}$  and  $Z_{eff}$  images, with

0.94 (CI 0.87–0.99) and 0.93 (CI 0.87–0.99), respectively. On CON<sub>120kVp</sub> images, a threshold of 81 HU achieved a sensitivity of 93 % and specificity of 95 % for identifying pneumonia.  $C_{iodine}$ , and  $Z_{eff}$  images reached comparable sensitivities of 95 % when using a threshold of 1.74 mg/ml and 8.27, but with somewhat lower specificities of 85 % and 83 %, respectively (p < 0.001) (<u>Figure 4</u> and <u>Table 8</u>).

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Figure 4. The area under the curve for diagnosis of pneumonia for quantitative SDCT parameters. Sensitivity and specificity for pneumonia on contrast-enhanced (A) and non-enhanced (B) SDCT for conventional attenuation ( $CON_{120kVp}$ ), iodine concentration ( $C_{iodine}$ ), and effective atomic number ( $Z_{eff}$ ) images.

Table 8. Sensitivity and specificity of quantitative SDCT parameters for discriminating atelectasis from pneumonia.

AUC (95% CI)	Threshold	Sensitivity (%)	Specificity (%)	р			
CT numbers measured on CON <sub>120kVp</sub> (HU)							
0.98 (0.94–0.99)	81	93	95	<0.001			
lodine concentration	n measured on C	iodine (mg/ml)					
0.94 (0.87–0.99)	1.74	85	95	<0.001			
Effective atomic number measured on Z <sub>eff</sub>							
0.93 (0.87–0.99)	8.27	83	95	<0.001			

Sensitivity and specificity as well as area under the curve (AUC) for detecting pneumonia on contrast-enhanced chest SDCT. Thresholds were chosen for conventional (CON $_{120kVp}$ ), iodine concentration (C $_{iodine}$ ), and effective atomic number (Z $_{eff}$ ) images by maximizing the Youden index.

## 3.7. Diagnosis can be based CT on number measurements

The principal component analysis (PCA) showed the highest variance on the CT number axis, whereas the other parameters only showed little variance, implying that the criterion CT number alone is enough to decide between atelectasis and pneumonia (Figure 5).

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Figure 5. The principal component analysis (PCA). (A) PCA biplot shows both the component scores of pneumonia (dots) and atelectasis (squares). (B) Loadings for conventional (CON $_{120kVp}$ , Hounsfield Units [HU]), iodine concentration ( $C_{iodine}$ , [mg/ml]), and effective atomic number ( $Z_{eff}$ ) for lung, the aorta and pneumonia refer to the Component 3 axis. The graph shows, that the differentiation between atelectasis and pneumonia is almost entirely based on the CT number in HU of pneumonia and to a lesser extent of the CT number in HU of the aorta. The other parameters were irrelevant.

#### 4. Discussion

This study investigated the value of SDCT for quantitative differentiation between atelectasis and pneumonia on contrast-enhanced chest CT. We showed that the quantitative parameters  $C_{iodine}$  and  $Z_{eff}$  could distinguish atelectasis and pneumonia but without added value compared to CT number measurements on conventional images. As expected, in a negative control group of 40 non-enhanced CT, none of the quantitative parameters could differentiate atelectasis and pneumonia.

CT imaging plays an important role since radiologic findings are considered in the diagnosis. The consolidated lung is a frequent finding in chest CT, in which the air within the affected airspaces is replaced, increasing the pulmonary attenuation and obscuring the margins of adjacent airways and vessels [4]. The radiologist needs to differentiate infectious consolidations caused by pneumonia from non-infectious consolidations caused by atelectasis. Radiological signs suggesting pulmonary infection are the air bronchogram, a volume increase, vessel or airway crowding, adjacent ground glass, or tree-in-bud opacities [4, 5]. However, although radiologic signs may help to assign consolidations to an infectious or non-infectious cause, they remain qualitative non-obligatory observations. Therefore, the diagnosis might be unsure, for example, in patients with underlying chronic disease such as heart failure and pleural effusion, who frequently have basal atelectasis that cannot be reliably distinguished from parenchymal infection [20]. In these cases, quantitative CT parameters would be desirable to facilitate a more confident diagnosis.

Atelectasis and pneumonia differ in tissue density and contrast enhancement which can be detected by quantitative CT parameters. In pneumonia, the volume of the affected lung tissue increases since the alveolar airspaces are filled with fluid or cells, whereas in atelectasis, the lung volume is reduced by compression, absorption of alveolar air, or impaired <u>pulmonary surfactant</u> production or function [21]. Therefore, the lung tissue density per voxel is higher in atelectasis. The contrast enhancement will be influenced by the number of capillaries per voxel and the complex interaction of pathophysiological mechanisms regulating <u>local perfusion</u>. Atelectasis and pneumonia are causing regional alveolar <u>hypoxia</u> leading to <u>hypoxic pulmonary vasoconstriction</u> and reducing pulmonary perfusion regionally, while active inflammation in pneumonia may increase perfusion [22]. However, the volume effect seems to have a more substantial influence since a higher contrast enhancement can be overserved in atelectasis, represented by higher CT numbers and higher SPCT parameters values.

The CT number is a relative quantitative measurement of x-ray density and the most frequently used quantitative CT parameter. On non-enhanced images, the difference in tissue density alone is usually not significant enough to make a sure distinction between atelectasis and pneumonia, which we confirmed by measuring a non-significant difference of 11°HU (p = 0.054). Edwards et al. reported a threshold of 85 HU with a sensitivity of 90 % and a specificity of 92 % for pneumonia by using their contrast-enhanced pulmonary CT angiogram protocol [6]. In our study, the difference between atelectasis and pneumonia was also significant on CON<sub>120kVp</sub>, achieving a sensitivity of 93 % and specificity of 95 %. However, in our study, the optimal threshold was slightly lower with 81 HU. Nonetheless, we believe that both thresholds are comparable. Edwards et al. reported a median value of 119 HU for atelectasis and 62 HU for pneumonia, whereas we determined means of 105 HU and 60 HU, respectively. They also reported higher averaged CT numbers of 252 HU and 278 HU than ours, with 187 HU and 178 HU for the ROIs placed in the ascending aorta and the right pulmonary artery. The higher HU values reported by Edwards et al. imply higher concentrations of contrast material and can be explained by their triggered arterial phase CT angiogram protocol with a minimal acquisition delay of around 8-10 s [23]. Our study's venous chest and body protocols had longer acquisition delays of 30-45 s depending on the patient's cardiac output. Furthermore, they

administered their contrast material with a higher flow rate of 4–5 ml/s than ours of 1.98–3.92 ml/s. In summary, our data showed that pneumonia could be diagnosed with high sensitivity and specificity on  $CON_{120kVp}$ , which is following the existing literature.

SDCT can provide additional material-nonspecific and material-specific energy-dependent information like iodine concentration ( $C_{\text{iodine}}$ ) and the effective atomic number ( $Z_{\text{eff}}$ ). We assumed that these parameters might offer a better differentiation of atelectasis and pneumonia by depicting microvessel density and blood supply. In this context, significant correlations between iodine uptake and perfusion parameters derived from DECT and first-pass dual-input perfusion computed tomography (DIPCT) have been reported [24]. Furthermore, SDCT parameters were already used to differentiate lung cancer from inflammatory masses and to detect pulmonary embolism and pleural contrast uptake [13, 14, 15]. As expected,  $C_{\text{iodine}}$  and  $Z_{\text{eff}}$  showed significantly higher values in the atelectasis group (p < 0.001), while both parameters showed comparable sensitivities of 95 %, but overall lower specificities of 85 % and 83 %. Therefore, both parameters had no added diagnostic value compared to CT number measurements on conventional images. This conclusion was also strengthened by principal component analysis, which showed that the differentiation between atelectasis and pneumonia could be solely based on CT numbers measurements.

We also investigated whether spectral images have better contrast-to-noise-ratios. The ratio between the contrast of two adjacent structures and the noise level are two major criteria to assess the ability to separate different structures. We calculated the CNR values between the aorta, normal lung, and pleural effusion vs. atelectasis or pneumonia.  $CON_{120kVp}$  images had significantly higher CNRs between consolidated and normal lung than the corresponding  $C_{iodine}$  and  $Z_{eff}$  images (p < 0.001). On spectral images, the noise increases dramatically if the spectral resolution is low [25]. Therefore, the lower CNRs are most likely caused by a higher noise level even though contrast may be enhanced. On  $Z_{eff}$  images, significantly higher CNRs were found between the aorta or pleural effusion and atelectasis or pneumonia (p < 0.001). The reason for this is because blood and pleural effusion consist mostly of inorganic materials, which is reflected by  $Z_{eff}$ . In summary,  $C_{iodine}$  and  $Z_{eff}$  had no benefit compared to  $CON_{120kVp}$  images on non-enhanced chest SDCT with regard to CNR.

There are some technical limitations to our study. First, a validated gold standard is missing, as no histological correlation was performed. Bronchoalveolar lavage or lung biopsy are the reference methods for diagnosing pneumonia but are seldom performed and were not available in a retrospective setting. The clinical criteria we used to assign patients to the pneumonia group have been used slightly modified in other studies [6, 26, 27]. Unfortunately, there were many multimorbid patients in our patient cohort who often had several extrapulmonary infections. A considerable part of the patients had a clinical score of two, which did not clearly assign them to the atelectasis or the pneumonia group. In these cases, individual decisions were made, which was challenging due to the partially overlapping clinical symptoms of atelectasis and pneumonia [28]. Nevertheless, Edwards et al. reported comparable results for CT number measurements on CON<sub>120kVp</sub>, implying that our clinical assignment was adequate enough to allow the assessment of Ciodine and Zeff images. Furthermore, we ignored the intra- and inter-individual differences in iodine distribution, which can be seen as another limitation. In the literature, significant differences in iodine concentrations were reported between sexes and age in different parenchymal organs, influencing the obtained quantitative iodine concentration and the applied iodine thresholds [29]. However, even though comparable effects can be expected in the lungs, we argue that our calculated thresholds are still valid since they are based on averaged values, by which the impact of intra- and inter-individual differences are reduced.

#### 5. Conclusion

We showed that the quantitative parameters  $C_{\text{iodine}}$  and  $Z_{\text{eff}}$  could distinguish at electasis and pneumonia in contrast-enhanced SDCT but without added diagnostic value compared to CT number measurements on conventional images. Thus, in every day routine CT contrast material application can add diagnostic value based on quantitative measurements in cases where radiological and clinical diagnosis both are equivocal.

#### Case Presentation

A 52-year-old man was referred to our hospital for <u>cough</u>, fever, <u>chest pain</u>, and progressive dyspnea. He has worked as a full-time security staff at a community center and was in a normal state of health until 11 months prior to referral when he began experiencing cough, expectoration, a high-grade fever (up to 39.7°C), <u>chills</u>, and left <u>chest pain</u>. He visited the local hospital several times with suspected lung cancer. <u>Bronchoscopy</u> showed chronic inflammatory changes in his bronchi. He was given a course of antibiotics, but his fever had not subsided. The patient had visited a bamboo rat farm and consumed bamboo rat meat one year previously. He had never smoked.

## **Physical Examination Findings**

Several <u>lymph nodes</u> with a maximum diameter of approximately 0.5 cm<sup>2</sup> were palpated in the left cervical region. There was tenderness in the third and fourth anterior ribs on the left side and the <u>manubrium</u>. Breath sounds were diminished markedly in the whole <u>left lung</u>. No other abnormalities were noted, including <u>skin lesions</u>.

### **Diagnostic Studies**

A <u>complete blood count</u> revealed a <u>WBC count</u> of  $19.67 \times 10^9 / L$  with 83.6% <u>neutrophils</u> and hemoglobin at 7.5g / dL. T-cell subset counts were all normal, and <u>HIV antibodies</u> were negative. Acid-fast bacilli, <u>tuberculin test</u>,  $(1-3)-\beta$ -D-glucan, and serum tumor markers were all negative or within normal limits. Blood and <u>sputum cultures</u> were negative for bacteria and fungi.

A chest CT revealed left <u>lung atelectasis</u>, enlarged mediastinal <u>lymph nodes</u>, and a left-sided <u>pleural effusion</u> (<u>Fig 1</u>A, B). A PET-CT scan indicated increased uptake of 18F-fluorodeoxyglucose with a maximum <u>standardized uptake value</u> of 11.4 in the <u>left lung</u> and multiple nodules in both lungs. There was an increase in <u>glucose metabolism</u> in the lymph nodes of the <u>neck</u>, mediastinum, <u>abdominal cavity</u>, and <u>retroperitoneum</u>, and there were multiple <u>osteolytic lesions</u> in the <u>sternum</u> and ribs (<u>Fig 1</u>C).

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Figure 1. A-C, Chest <u>CT scan</u> and PET-CT scans. A and B, Chest CT revealed pleural effusion and <u>atelectasis</u> in the left lung field and pleural effusion in the left <u>thoracic cavity</u>. C, PET-CT imaging revealed increased uptake of 18F-fluorodeoxyglucose with maximum <u>standardized uptake values</u> of 11.4 in left lung field, 11.3 in the lymph nodes, and 7.1 in bone.

<u>Bronchoscopy</u> revealed multiple submucosal nodules in the left principal bronchi (<u>Fig 2</u>A). Pathologic examination revealed congestion and edema in the <u>submucosa</u> with massive infiltration by lymphocytes and a <u>granulomatous lesion</u> (<u>Fig 2</u>B). Culture of the pleural fluid sample indicated a <u>Penicillium</u> species that exhibited temperature-dependent dimorphic growth (<u>Fig 2</u>C). Sausage-

shaped yeast-like cells with septate hyphae (from culture at 25°C) were observed under a microscope (Fig 2D).

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Figure 2. A, Bronchoscopy revealed multiple submucosal nodules in the lower-left principal bronchi. B, The pathologic examination results of bronchoscopy showed congestion and edema in the submucous with massive infiltration by lymphocytes and a granulomatous lesion. C, Fungal culture of pleural fluid during yeast phase at 37°C with no production of red pigment and mycelia obtained at 25°C with the production of red pigment. D, Sausage-shaped yeast-like cells with septate hyphae (from 25°C culture) were observed under the microscope (Medan staining, ×400).

What is the diagnosis?

Diagnosis: Disseminated <u>Talaromyces marneffei</u>

### Discussion

Also called <u>Penicillium marneffei</u>, *T marneffei* is a thermally <u>dimorphic fungus</u> that can cause severe <u>mycosis</u> in <u>immunocompromised patients</u>, such as those with HIV, autoimmune disease, or <u>hematologic malignancy</u> and those who have undergone <u>organ transplantation</u>. However, it rarely is observed in immunocompetent individuals. *T marneffei* infection therefore is considered an <u>opportunistic infection</u>. It is prevalent mainly in Southeast Asia, which includes Thailand, Vietnam, Northeastern India, Southern China, Hong Kong, Taiwan, Laos, Malaysia, Myanmar, and Cambodia.

In China, <u>epidemiologic studies</u> show 87.72% of patients with *T marneffei* infection are HIV positive, and 8.5% are without any documented underlying diseases. Bamboo rats are the natural hosts of *T marneffei*. *T marneffei* is not only isolated from the organs of bamboo rats but also the surrounding environments of their burrow, such as soil. People, especially those with immunodeficiency, who are exposed to environments surrounded with bamboo rats are particularly vulnerable to *T marneffei*. Therefore, a history of residing or traveling in an endemic area and exposure to environments where bamboo rats live may well serve as an important clue/heuristic for a physician to diagnose *T marneffei*.

The pathogenesis of *T marneffei* infection is yet to be fully understood. Inhalation of <u>conidia</u> from the environment is a key pathway to infection. The <u>conidia</u> then proliferate in macrophages and disseminate to other internal organs through the <u>reticuloendothelial system</u>, especially the lungs, bone marrow, bone, skin, lymph nodes, spleen, liver, and reticuloendothelial tissues. The most common symptoms of *T marneffei* infection are fever, <u>cough</u>, <u>skin lesions</u>, <u>generalized</u> <u>lymphadenopathy</u>, and <u>hepatosplenomegaly</u>, along with local abscesses and <u>osteolytic lesions</u>.

The clinical manifestations of *T marneffei* infection are different in HIV-negative and HIV-positive patients. Osteolytic lesions are common in HIV-negative patients, but diagnosis is often delayed and misdiagnosed as malignancy, TB, or histoplasmosis. Osteolytic lesions typically occur at sites of neutrophil accumulation. The accumulation of neutrophils and the release of proteolytic enzymes lead to osseous tissue lysis, liquefaction, and necrosis. In HIV-negative patients, WBC counts, neutrophils, and lymphocytes are increased significantly, and the ratio of CD4+/CD8+ is >0.5. The severity of the disease depends on the host's degree of immunosuppression. The mortality rates for patients not infected with HIV and those who are infected are 27.7% to 29.4% and 20.7%, respectively, which might be related to an initial misdiagnosis in HIV-negative patients who ultimately

were found to have *T marneffei*. Alternatively, the diagnosis may be delayed due to a lack of clinical suspicion.

Microbiologic culture is the gold standard for diagnosing *T marneffei* infection. *T marneffei* is the only known *Penicillium* species that exhibits temperature-dependent dimorphic growth. Yeast-like cells are found in the culture at 37°C. The fungi outside the host cells are elongated, often curved, and sausage-like, and they have clear central septi. At 25°C, the fungus is mycelia-like and produces a characteristic red pigment that diffuses into the culture medium. Secreted enzymes that are expressed by mycelia and yeast are linked to virulence in *T marneffei*.

Fungal culture provides direct and reliable evidence for the diagnosis of *T marneffei*. Clinical specimens that are used commonly for culture include bone marrow aspirate, skin biopsy specimens, lymph node biopsy specimens, blood, sputum specimens, tissue, urine, stool, pleura, cerebrospinal fluid, pleural fluid, ascites, and pericardium. However, a disadvantage of this method is that the culture of fungi generally takes approximately three to four days, which frequently results in the delay of appropriate antifungal therapy. In addition, the sensitivity of fungal culture from blood can be low (76.7%) in HIV-positive patients and is only 47.1% in HIV-negative patients. Currently, there are no reliable commercial kits for rapid testing of *T marneffei*. Nowadays, pathologic diagnosis is of extreme importance in *T marneffei* diagnosis. After being stained with hematoxylin and eosin, periodic acid-Schiff, or Grocott methenamine silver stain, *T marneffei* can be seen in macrophages or histiocytes.

There are three main pathologic changes that occur in tissues that are infected with *T marneffei*: <u>granuloma</u>, purulent inflammation, and reactive necrotizing inflammation. Most HIV-positive patients with *T marneffei* infection show reactive necrotizing inflammatory changes; those with normal immune function show <u>granulomatous</u> lesions and suppurative reactions.

Currently, there is no uniform standard for <u>antifungal</u> treatment of *T marneffei* infection in HIV-negative patients, especially in cases with <u>osteolytic lesions</u>. The drugs most commonly used for <u>antifungal therapy</u> of *T marneffei* are <u>amphotericin B</u>, <u>voriconazole</u>, and <u>itraconazole</u>, which show good therapeutic effects. However, despite prolonged antifungal treatment, most patients, regardless of their HIV status, relapse after several months or years.

## **Clinical Course**

In our case, after the patients had received <u>voriconazole</u> treatment for one month, the results of lung CT (<u>Fig 3</u>A) and <u>bronchoscopy</u> (<u>Fig 3</u>B) showed improvements. Unfortunately, the patient still showed osteolytic lesions (<u>Fig 4</u>A) and systemic <u>lymphadenopathy</u>. New lesions were found in the liver, spleen, and abdominal lymph nodes (<u>Fig 4</u>B, C), and there was still intermittent fever. The patient eventually died after receiving antifungal therapy for four months. This outcome is considered to be related to the delayed diagnosis and treatment that resulted in its systemic spread.

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Figure 3. A-B, Chest CT and submucosal nodules in bronchi of the patient decreased in size after receiving antifungal treatment for one month. A, Chest CT reveals that the pleural effusion and left lung atelectasis had improved. B, Bronchoscopy shows that multiple submucosal nodules in the lower-left principal bronchi were smaller than before.

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Figure 4. A, <u>Bone scan</u> shows abnormally active <u>bone lesions</u> throughout the body. B and C, Abdomen CT reveals new lesions in the liver, spleen, and abdominal lymph nodes (arrows). D, Histopathologic findings of <u>cervical lymph nodes</u> reveal lymphatic sinus dilatation with massive infiltration by neutrophils and granuloma formation in the cortex.

#### Abstract

This article introduces an easy and practical way to help detect lobar atelectasis on frontal chest radiographs. A proposed "V V O I" hand motions method is detailed in this article. This method depends on 4 simple hand motions, which could help detect 4 important direct and indirect corresponding signs of atelectasis. Our aim is to introduce the "V V O I" trick as a memory aid to facilitate detecting difficult cases of lung collapse, particularly for nonradiologists and radiologists in training. The importance of using this method in conjunction with the lateral chest radiograph is emphasized. In addition, several pitfalls in using this method are also explained.

### Résumé

Le présent article présente une méthode simple et pratique de détection des atélectasies intéressant un seul lobe sur les radiographies thoraciques frontales. Il s'agit en fait d'une méthode de mouvements des doigts appelée « V V O I ». Celle-ci consiste en fait en quatre mouvements simples qui permettent de détecter quatre signes directs et indirects importants d'atélectasie. Nous souhaitons introduire la méthode « V V O I » comme aide-mémoire pour faciliter la détection des cas moins évidents d'affaissement des poumons, surtout par des non-radiologues ou des radiologues en formation. L'article souligne l'importance d'accompagner cette méthode d'une radiographie thoracique en incidence latérale. L'article décrit également plusieurs pièges à éviter inhérents à cette méthode.

Atelectasis is a common finding on chest radiographs and may be the only manifestation of a variety of benign and malignant conditions that range from mucus plugging to primary and metastatic endobronchial tumours. Detection of atelectasis, therefore, is important in daily practice. This task, however, is often difficult because the findings may be subtle or atypical [1]. A practical and fun method is presented here to rapidly assess the radiographs for the presence of atelectasis. This memory aid is called the "V V O I" hand motion trick.

Different direct and indirect signs of volume loss have been described in the radiology literature. In addition to an increased density of the airless collapsed lung, these signs are mainly based on the displacement of 4 well-known anatomical landmarks [2], which form the building blocks of the "V V O I" hand motion trick.

The 4 Components of the "V V O I" Hand Motion Trick

### The Hemidiaphragms

The diaphragm is a musculofibrous structure that separates the thorax from the abdomen [3], [4]. On the upright chest radiograph, the dome of the right hemidiaphragm is higher than the left hemidiaphragm in 90% of cases [3], [4], [5]. The difference in height is between 1.5–2.5 cm (about one-half of an intercostal space) [3], [4], [5]. In about 7% of cases, the 2 hemidiaphragms are at the same level [5], and, in about 3% of cases, the left hemidiaphragm is higher (however, the difference usually does not exceed 1–2 cm) [4], [5]. The right hemidiaphragmatic dome usually resides at the level of the fifth-seventh ribs anteriorly [3], [4], [5] and ninth-tenth ribs posteriorly [4].

The first hand motion (Figure 1) depends on the above-mentioned facts. Form a "V" by using the index and middle finger. On a normal chest radiograph, you should be able to position your hand so that the right index finger points to the higher right hemidiaphragm, while the middle finger points to the lower left one. This is the first "V" in the "V V O I" motion. This is coined "the first victory sign."

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Figure 1. "V V O I" hand motion: the first "V." (A) On normal radiographs, using the right hand to form a "V" will result in the index finger pointing to the higher right hemidiaphragm and the middle finger pointing to the lower left hemidiaphragm. (B) Exaggeration of the tilt to the left (clockwise) should raise the possibility of right-sided volume loss. (C) Reversal of the tilt to the right (counter clockwise) might indicate left-sided volume loss.

The way the hand is tilted will determine the side of the volume loss. This is shown in detail in Figure 1. However, a few pitfalls must be kept in mind. First, the diaphragmatic location varies depending on the patient's position and respiration [4]. Second, the diaphragm might be elevated because of subdiaphragmatic (eg, gastric distension) or diaphragmatic (eg, phrenic nerve paralysis) causes [6]. Third, diaphragmatic elevation may not be evident with right middle [4], [7] or mild right upper lobes atelectasis [2], [7].

### The Hila

The hilum is the interconnection between lung and mediastinum. Each hilum contains pulmonary arteries and veins, airways, nerves, lymphatics, lymph nodes, and connective tissues. The pulmonary arteries and veins are the main contributors to the radiographic density of the hilum [3]. On the upright chest radiograph, the left hilum is higher than the right hilum in 97% of the cases [8], usually by about 2.5 cm (about 1 fingerbreadth) [4], [9]. Both hila appear at the same level in the remaining 3% of cases [8]. It is important to note that the right hilum is never higher than the left in normal individuals [8]. Changes in the vertical orientation of the interlobar artery can be a useful hint in evaluating the hilar position [1], [2].

The second hand motion (Figure 2) depends on knowing the normal hilar position. Form a "V" with your right hand in a similar manner to the first "V" motion; however, the hand is tilted the other way, so that the right index finger points to the lower right hilum while the middle finger points to the higher left one. This is coined "the second victory sign." The way the hand tilts with this motion will determine the side of the volume loss, if present. This is explained in Figure 2. In addition, combining the results of the first and second hand motions will give a rough estimation of which lobe of the lung is affected. Again, middle lobe atelectasis can be a deceiving entity on the frontal chest radiograph, because the normal hilar position is usually maintained [7]. Causes other than collapse (eg, adjacent emphysematous bullae) may alter the hilar position.

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Figure 2. "V V O I" hand motion: the second "V." (A) On normal radiographs, the hand-formed "V" is tilted the other way, so that the right index finger points to the lower right hilum and the right middle finger points to the higher left hilum. (B) Reversal of the tilt to the left (clockwise) should raise the possibility of right upper or left lower lobar volume loss. (C) Exaggeration of the tilt to the right (counter clockwise) might indicate left upper or right lower lobar volume loss.

#### The Cardiac Shadow

Although the cardiac shadow generally occupies the central chest portion, about 50%–80% of the heart shadow resides to the left of the midline [4], [9]. This simply means that about two-thirds of the cardiac shadow is located to the left of the midline. This brings us to the "O" in the "V V O I" hand motion trick (Figure 3). Form a circle (an "O") by using the index and thumb fingers, and then place it immediately to the left of the midline. This circle should overlap two-thirds of the heart shadow. For easy remembrance, this hand motion is termed "the perfection sign." Shifts of the cardiac position because of volume loss will alter this sign. The use of this third hand motion is better explained in Figure 3. However, a few considerations should be kept in mind. First, this sign is highly affected by the patient's position. So, assess for rotation before considering this sign pathologic. Second, although this sign is most pronounced with lower lobe atelectasis [2], [7], it is not useful with right middle lobe volume loss [2], [7]. Finally, the position of the heart may be altered by other cardiac and extracardiac causes (eg, cardiac chamber enlargement).

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Figure 3. "V V O I" hand motion: the "O." The hand forms a circle by using the index and thumb fingers. Placing this circle to the left of the midline of a normal and well-positioned chest radiograph should lead to the "O" overlapping about two-thirds of the cardiac shadow. Filling of the "O" by more than two-thirds of the heart shadow suggests left-sided volume loss. Filling of the "O" by less than two-thirds of the heart shadow suggests right-sided volume loss.

## The Minor Fissure

The minor fissure is formed by the apposition of the visceral pleura that separates the right upper and middle lobes. This fissure is frequently undulating and not a straight line. The anterior and lateral portions are lower than the medial and posterior ones [3]. The minor fissure is seen in about 50%—80% of frontal radiographs and is frequently incomplete, with a complete fissure only seen in about 10% of cases [3]. The minor fissure appears as a horizontal thin line, at about the level of the right fourth rib anteriorly [3]. The lateral edge contacts the chest wall at the axillary portion of the sixth rib [9]. On a posteroanterior radiograph, the medial termination of the minor fissure is seen at the lateral margin of the interlobar pulmonary artery. If the minor fissure is projecting medial to this point, then right lower lobe volume loss should be suspected [3].

The fourth hand motion, the "I" in the "V V O I," is based on the above facts (Figure 4). The fourth hand motion is simply performed by pointing to the minor fissure, if seen, by using the index finger and following the fissure along its expected location. This is termed "the number 1 sign." The way to use this motion is shown in Figure 4. Because the minor fissure can be displaced by various nonatelectatic causes, this sign is not to be used alone.

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Figure 4. "V V O I: hand motion: the "I." (A) If the minor fissure is visualized on a normal radiographs, then its course could be followed by using the index finger at its expected location. (B) Depression of the fissure could denote right lower or middle lobe atelectasis. (C) Elevation of the fissure could denote right upper lobe volume loss.

Use of the "V V O I" Hand Motion

As summarized in Figure 5, the "V V O I" hand motion can be used as a swift method for assessing the presence of atelectasis on a chest radiograph. Two practical examples are demonstrated in Figure 6, Figure 7. The aim of introducing this "V V O I" hand motion trick is to facilitate the search for atelectasis on chest radiographs, particularly for nonradiologists and radiologists in training. When using this simple trick, it is important to remember all the pitfalls and limitations that can be associated with such a method. The diagnosis of atelectasis should be followed by a more comprehensive assessment of the lungs by using frontal and, if needed, lateral radiographs. It is also important to use this method in conjunction with other radiographic findings (ie, parenchymal opacity) as well.

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Figure 5. An overall summary of the "V V O I" hand motion trick.

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Figure 6. Example 1 to illustrated the "V V O I" hand motion. (A) A 43-year-old man with chronic cough. (B) The first "V" is slightly rotated clockwise because of right hemidiaphragmatic elevation. (C) The second "V" tilt is obviously reversed because of hilar elevation. (D) The "O" is filled by more than two-thirds of the heart shadow. However, this is because of the patient's rotation (a pitfall to keep in mind). (E) The "I" points to an upward-displaced minor fissure. The constellation of findings points to right upper lobe collapse, which was proven to be caused by bronchostenosis secondary to previous tuberculosis. Note that this finding could be easily missed because of the marked compensatory overinflation of the right middle and lower lobes.

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Figure 7. Example 2 to illustrate the "V V O I" hand motion. (A) A 46-year-old woman with bilateral axillary lymphadenopathy. (B) The first "V" tilt is exaggerated (clockwise rotation). (C) The second "V" tilt is exaggerated (counter clockwise rotation). (D) The "O" is filled by about half of the heart shadow, denoting rightward shift of the cardiac structures. (E) The "I" appears within the normal position. The constellation of findings points to right lower lobe collapse, which was caused by bronchial obstruction by a known lymphomatous mass. The increased right retrocardiac density and the nonvisualization of the interlobar artery are 2 additional important findings.

Foreign body aspiration (FBA) is commonly seen in the age group of 1–3years, is a common cause of morbidity and mortality in children worldwide. They are less commonly seen below one year, hence challenging to manage. Aspiration of organic FB (Foreign body) causes severe airway mucosal inflammation. If not promptly removed, <a href="chronic inflammation">chronic inflammation</a> sets in leading to the development of granulation tissue around it, ultimately presenting as a lung infection and collapse. Author is reporting here two rare cases of acute atelectasis in infants and their management. Introduction

Peanuts are the most common organic <u>foreign bodies aspirated</u> in children presenting with initial choking followed by <u>wheeze</u> or <u>stridor</u>. The Vegetable or organic <u>foreign bodies</u> usually expand and change their consistency in airways due to hygroscopic action and elicit <u>tracheobronchitis</u> leading to diffuse pulmonary reactions, subsequently causing <u>atelectasis</u> of the affected lung even in the <u>absence</u> of primary pulmonary pathology.

Their presentation in infants and management has been rarely been reported.

Case report

#### Case 1

A one-year-old male child born by full term <u>vaginal delivery</u> with birth weight of 2.5 kg to a non-consanguineously married couple. Developed sudden onset of respiratory difficulty following suspicious history of aspiration of a <u>foreign body</u>. <u>Chest radiography</u> and <u>computed tomography of chest</u>; showed total collapse of left lung and hence baby was shifted to our tertiary care <u>paediatric</u> centre on oxygen and was admitted in paediatric <u>intensive care unit</u> (<u>Fig. 1</u>A and B).

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Fig. 1. A-and Fig B- plain <u>computed tomography</u> images axial and coronal sections of <u>thorax</u> showing total left lung collapse. Fig C- bronchoscopic image showing thick secretions at left main bronchus. Fig D-retrieved organic foreign body in pieces from left terminal bronchus. Fig E- completely resolved left atelectasis.

Baby was immediately posted for rigid <u>bronchoscopy</u>, where in a rigid <u>endoscope</u> is passed across the trachea and bronchi per orally under <u>general anaesthesia</u>; revealed thick secretions in the whole of left bronchial tree (<u>Fig. 1</u>C), which were difficult to be sucked out via catheter, hence the foreign body removal forceps was introduced through these thick secretions and tried to loosen the secretions and were therefore be able to be suctioned out. Once the main bronchial and mid bronchial thick secretions were cleared, amid these sections foreign body in tiny pieces were found floating, which were retrieved in pieces along with thick secretions (<u>Fig. 1</u>D). Following this, there was a significant improvement of air entry on left side. Baby was kept on ventilator for 8hours and then weaned off from ventilator, uneventfully over 24hours. Immediate chest radiography revealed improved air entry into left side (<u>Fig. 1</u>E).

#### Case 2

Nine months, previously healthy female baby brought to emergency room with sudden onset of <u>cough</u> and fever since 4days having doubtful history of <u>foreign body aspiration</u>. Baby was requiring continuous oxygen support via nasal prongs and on admission chest radiography revealed left <u>lung atelectasis</u> without mediastinal shift (<u>Fig. 2</u>F). Baby was immediately taken for rigid bronchoscopy and a piece of <u>areca</u> nut 0.5 cm x 0.4 cm lodged in the left <u>main bronchus</u> was retrieved uneventfully along with some thick secretions (<u>Fig. 2</u>G and H). Baby improved clinically following the procedure and hence was discharged after 24hours (<u>Fig. 2</u>I).

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Fig. 2. Fig F-chest radiography showing left lung collapse Fig G- bronchoscopic view of areca nut piece lodged at left main bronchus amid thick secretions. Fig H- retrieved areca nut piece. Fig I- post procedure chest radiography.

## Discussion

Children with FBA present with a sudden onset of choking and coughing to emergency room by parents or caretakers with alleged history of ingesting or playing with foreign body, is enough to

proceed for further investigations like <u>chest radiography</u> and <u>bronchoscopy</u>. Affected side will have decreased breath sounds on <u>auscultation</u>. 1.2

Though the obstructive <a href="mailto:emphysema">emphysema</a> or hyperinflation on the affected side is the most common <a href="mailto:radiological finding">radiological finding</a>, in the presence of atelectasis, foreign body airway (FBA) cannot be ruled out.

Delay in diagnosis and its removal increases the risk for complications like <u>bronchopneumonia</u>, atelectasis, <u>bronchiectasis</u> and <u>lung abscess.1</u>, 2, 3, 4

Rigid bronchoscopy, a rigid <u>endoscope</u> passed across <u>larynx</u> trachea and bronchi via <u>oral cavity</u>, under <u>general anaesthesia</u> in <u>supine position</u> is the gold standard for diagnosis and as well as for therapeutic purposes in foreign body <u>airway management.1</u>, 2, 3, 4

Tissue reaction to the foreign body airway (FBA) in the bronchial tree depends on the nature of the FB, the degree of obstruction, and the duration of its presence. 1, 2, 3, 4

Though the atelectasis may be due to long term or chronic complications of FBA, its presence suddenly or acutely, in infants is rarely reported in the <u>absence</u> of primary lung parenchymal pathology.

The possible aetiology of atelectasis in children and infants may be due to smaller and collapsible airways, more pliant chest walls, and inefficient and ineffective collateral ventilation. Bronchial inflammation due to vegetable FBA produces cellular debris, <u>mucus</u> plugs, and oedema, which promotes the development of atelectasis or acute lung collapse in infants. <sup>1</sup>/<sub>2</sub>, 4, 5

In up to 15 %, lung atelectasis develops distally from the point of obstruction, where in, air gets absorbed, and the affected area of the lung loses volume retracts and collapses. 3, 4, 5

Author is reporting here two infants presenting with sudden onset of respiratory distress requiring continuous oxygen via nasal pongs with chest imaging showing acute left lung collapse with suspicion history of FBA given by parents. Urgent rigid bronchoscopy revealed thick secretions in whole left bronchial tree which was difficult to suck out via suction catheter in the first case. Hence the foreign body removal forceps was introduced through thick secretions and tried to loosen these thick secretions with jaws of forceps, foreign body was noticed amid these thick secretions near terminal bronchus, which was retrieved in pieces (Fig. 1C and D). and a areca nut piece was lodged in the left main bronchus amid thick secretions in second case(Fig. 2F—H). Following the procedure air entry improved on left lung by auscultation as well as radiologically in both babies (Figs. 1E and 2I).

Though the atelectasis may be due to long term complications of FBA, its presence suddenly or acutely in an infant is rarely reported, one case due to a foreign body and another case due to thick secretions behaving like a foreign body in the absence of primary lung parenchymal pathology which is common in adults.

Author is reporting these cases of foreign body aspiration in infants due to their uncommon presentations and importance of prompt as well as urgent intervention, due to their narrower airways, causing high mortality if delayed.

### Conclusion

Presence of a foreign body in acute atelectasis should be ruled out promptly and urgently by rigid bronchoscopy in a tertiary care centre by experienced clinicians having all facilities to avoid morbidity and mortality.

\*Both verbal and written informed consent has been obtained from parents for this case report

### Abstract

### Objectives

This study was aimed at examining the effects of the thoracic block technique on vital signs, <u>arterial blood gases</u>, and <u>lung compliance</u> in children with unilateral <u>atelectasis</u> receiving <u>mechanical ventilation</u>.

## Methods

Forty-four boys and girls with unilateral <u>atelectasis</u> and receiving <u>mechanical ventilation</u>, ranging in age from 4 months to 4 years, were recruited from the Abo El-Reesh <u>Hospital intensive care unit</u> at Cairo University. They were assigned to control and study groups: group A included 22 children receiving <u>chest physical therapy</u>, and group B included 22 children receiving the same chest physical therapy program as well as the thoracic block technique. Electrocardiography, mechanical ventilation, and <u>blood gas analysis</u> were conducted to assess the respiratory and heart rates, dynamic compliance, and <u>arterial blood gases</u>, respectively.

### Results

Respiratory rate and heart rate were significantly lower in the study group than the control group (p=0.03). PaO<sub>2</sub> and SaO<sub>2</sub> increased in both groups, and the increase was more significant (p=0.01 and 0.001, respectively) in group B than group A. A significant decrease in PaCO<sub>2</sub> was observed in both groups, and the decrease was more significant in group B than group A (p=0.02). A significant increase in dynamic lung compliance was observed in both groups, and the increase was more significant in group B than group A (p=0.01).

#### Conclusions

Applying the thoracic block technique rather than chest <u>physical therapy techniques</u> alone in children with <u>atelectasis</u> receiving mechanical ventilation may lead to improvements in arterial blood gases and dynamic lung compliance, and has no negative effects on heart rate and respiratory rate.

## Introduction

Pediatric community-acquired pneumonia is defined as "the appearance of pneumonia <u>signs and symptoms</u> in a previously healthy child as a result of an infection which has been developed outside of the hospital." Pulmonary atelectasis refers to a lung that has partially collapsed or insufficiently expanded. As the atelectasis condition worsens, the blood circulating through the area dissolves the trapped gas in the alveoli, thereby causing <u>hypoxia</u> and <u>pulmonary vasoconstriction</u>. Lung collapse negatively affects <u>lung compliance</u>, <u>pulmonary vascular resistance</u>, and <u>oxygenation</u> status, and the <u>arterial blood gases</u> (ABG) demonstrate arterial <u>hypoxemia</u>. A primary negative predictor of unsuccessful <u>extubation</u> in children overall is the presence of lobar collapse, which impairs gas exchange.

In <u>critical care units</u> and <u>postoperative recovery units</u>, atelectasis is a frequent pulmonary alteration that may indicate that a child requires extra <u>respiratory care</u>, such as oxygen supplementation and <u>artificial ventilation</u>, if the manifestations are severe. Chest <u>physiotherapy</u> (CPT) for those children is a non-invasive therapy that clears the lungs by clearing the airways. Physical therapists use <u>postural drainage</u>, cupping, shaking, and deep respiratory exercises to remove <u>mucus</u>, improve respiration efficiency, and prevent lung collapse.

The thoracic block technique (TBT) is a manual technique that combines non-invasive <u>artificial ventilation</u> (with a mask) or invasive artificial ventilation (with an endotracheal tube) with manual compression of most un-collapsed areas of the lung during exhalation, such that only the atelectic region was free. Re-inflation of the alveoli may increase oxygenation status by decreasing or resolving improper ventilation issues, through alteration of thoracic pressure or proper positioning. The positive pressure from this technique improves the ventilation/perfusion relationship, decreases the <u>work of breathing</u>, increases gas exchange surfaces, encourages reexpansion of already-collapsed alveoli, and decreases <u>intrapulmonary pressure</u>, thereby contributing to greater oxygenation. This non-invasive method is applied through external manual compression on one side of the chest and is a safe technique.

Few studies have focused on the effects of the TBT on atelectasis in children. Previous research conducted by our team<sup>9</sup> has indicated that the TBT increases the percentage of fully improved lobes of atelectatic lungs, according to chest X-rays, thus laying groundwork for investigating the effects of the TBT on more variables affected by atelectasis. Therefore, this study conducted a trial to examine a technique that might effectively reverse the effects of atelectasis in children, thus increasing their rate of recovery and decreasing their mortality rate.

## Materials and Methods

## Study design

This controlled clinical trial enrolled 44 children treated at our intensive care unit (ICU), who were assigned to one of two groups according to closed envelopes. In the control group (group A), 22 children received the CPT program only, whereas in the study group (group B), 22 children received the CPT program and the TBT. G\*POWER statistical software (version 3.1.9.2; Franz Faul, Universitat Kiel, Germany) was used for calculating sample size, on the basis of data on respiratory rates obtained from a pilot study conducted in five children per group. The required sample size was found to be 20 children per group. On the basis of an estimated dropout rate of 10%, this number was increased to 22 children per group. Calculations were based on  $\alpha = 0.05$ , power = 80%, and effect size = 0.92. Post hoc power analysis was conducted and yielded an average power of 85% for the study. The study procedures were explained to the parents, who provided signed consent for participation. The study was registered at clinicaltrials.gov under number NCT05821998.

## **Participants**

As shown in the flowchart (<u>Figure 1</u>), at the beginning of the study, 54 children were recruited, but 10 children did not continue. Four children were excluded for not meeting the inclusion criteria, one child died, and five children were extubated before the second re-evaluation.

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## Figure 1. Flow chart of the study.

Forty-four children (23 boys and 21 girls) were recruited from the Abo El-Reesh Hospital ICU, Cairo University. The children ranged in age from 4 months to 4 years; were diagnosed with <u>community acquired pneumonia</u>; received <u>mechanical ventilation</u>; had unilateral partial to total <u>lung atelectasis</u>, as detected by chest X-ray; and received partial sedation only for ventilator synchronization. Children were excluded from this study if they were medically unstable (e.g., had bradycardia, <u>tachycardia</u>, or tachypnea), or had <u>pneumothorax</u>, <u>rib fracture</u>, or uncontrolled convulsions.

#### Instrumentation

• -

Electrocardiography was used to monitor the heart rate (HR) and respiratory rate (RR).

• -

An <u>ABG</u> analyzer (GEM premier 3000, produced in the United States in 2000) was used for <u>ABG</u> analysis to measure  $PaO_2$ , which provides information on <u>oxygenation</u> status, and  $PaCO_2$  in the blood, which is an indicator of ventilation status and  $SaO_2$ .

• -

A mechanical ventilator (Maquet <u>Critical Care</u> AB, Solna, Sweden) was used to measure dynamic <u>lung</u> <u>compliance</u> (Cdyn). Cdyn represents the difference in volume with respect to the difference in pressure across tidal breath.

**Procedures** 

#### **Evaluation**

1.

Heart rate and respiratory rate: Each child was placed in <u>supine position</u>, with the head of the bed elevated 30°. Electrocardiography leads were positioned on the chest, one near each <u>clavicle</u> and one near the fourth intercostal gap at the left mid-axillary line. HR and RR from the monitor were recorded before the session and 10 minutes after the session had ended, for regular monitoring. Monitoring proceeded to ensure that the child was stable, but only data from the first and last days were statistically analyzed.

2.

**Arterial blood gases:** The obtained samples were placed in the blood gas analyzer to detect PaO<sub>2</sub>, PaCO<sub>2</sub>, and SaO<sub>2</sub>. <u>ABG</u> was measured on the first day before the session and the tenth day after the session.

• 3

**Dynamic lung compliance:** Dynamic lung compliance was measured directly from the ventilator on the first day before the session and the last day after the session.

Intervention

CPT program

<u>Physical therapy</u> started from the second day after ICU admission. Both groups received the CPT program for 30 minutes, in one session daily for 10 days.

1.

**Percussion:** The child was placed in side lying posture and the therapist clapped with his hand (cupped) for 5 minutes on the dorsal, lateral, and frontal regions of the <u>thorax</u> on each side. Percussion applied across bone prominences, the last few ribs, the spine, <u>drainage tubes</u>, the <u>sternum</u>, the abdomen, sutured areas, the kidneys, the liver, or below the rib cage is not advised and was avoided. 11

#### 2.

**Vibration:** The child was placed in a side-lying posture on each side, and in supine position. A mechanical vibrator (Unix UM-30 electronic, Seoul, Korea) was placed on the child's anterior and posterior chest. Another maneuver involved having the child lie supine while receiving manual chest vibration for 5 minutes on the upper, middle, and lower chest zones. 12

#### 3.

Modified <u>postural drainage</u>: The child was placed in one of the following positions for 15 minutes: supine, to drain the anterior basal lobe, with the head raised 15°–30°; side-lying, to drain the medial and lateral basal lobes; or side-lying to prone, to drain the posterior basal lobe. Inverted position was avoided, and the affected lung was uppermost. <sup>13</sup>

# Thoracic block technique

The study group received CPT as well as the TBT. The child's head was raised 30° while lying on the back. The physical therapist placed one hand on the front of the chest and the other hand on the back. Manual compression was applied on one side of the chest as the child exhaled, such that only the atelectasis area, as detected previously by chest X-ray, was left free. Ultra-sonography guidance was not used, and the children received partial sedation only for ventilator synchronization. Depending on the child's response (e.g., crying or remaining still in a calm state, or changes in HR), the procedure was repeated several times consecutively. Compression was maintained for 20 seconds and was followed by a 20-second rest. Each child underwent ten sessions, with one session per day for 10 days. In the presence of <a href="hemodynamic">hemodynamic</a> instability, such as bradycardia (as detected by electrocardiography using electrodes connected during the session) and decreased SpO<sub>2</sub> (detected with a <a href="pulse oximeter">pulse oximeter</a> on the child's finger or toe), the treatment was discontinued.

## Statistics

Descriptive statistics and unpaired t-tests were used for comparison of ages between groups. Shapiro Wilk test was used for determining the normality of the data distribution. To test for homogeneity between groups, Levene's test for homogeneity of variances was used. Unpaired t-test was conducted for comparison of PaO<sub>2</sub>, PaCO<sub>2</sub>, SaO<sub>2</sub>, Cdyn, HR, and RR between groups. Paired t-test was conducted for comparisons before versus after treatment PaO<sub>2</sub>, PaCO<sub>2</sub>, SaO<sub>2</sub>, Cdyn, HR, and RR in each group. For all statistical tests, the level of significance was set at p <0.05. All statistical measures were conducted in Statistical Package for Social Sciences (SPSS) version 25 for Windows.

### Results

No significant differences in demographic data were observed between groups regarding age, weight, height, <u>BMI</u>, and sex (<u>Table 1</u>). For the HR and RR, no significant differences were observed between groups before treatment (p = 0.84 and p = 0.43). Significant increases in HR and RR were observed in the control group after treatment. No significant differences in HR and RR were observed before and after treatment in the study group (<u>Table 2</u>). HR and RR were significantly lower in the study group than the control group after treatment (<u>Table 4</u>).

Table 1. Comparison of participant characteristics between the study and control groups.

Empty Cell	Control group	Study group	MD	t-value	p-value
	Mean ± SD	Mean ± SD			
Age (months)	8.3 ± 3.7	10.2 ± 4.7.	-1.9	1.48	0.13
Weight (kg)	8.29 ± 1.27	8.75 ± 1.49	-0.46	-1.08	0.28
Height (cm)	69.63 ± 4.90	70.93 ± 5.28	-1.3	-0.84	0.40
BMI (kg/m²)	17.11 ± 2.13	17.29 ± 1.48	-0.18	-0.32	0.75
Sex, n (%)					
Girls	10 (45.5%)	11 (50%)		$(\chi^2=0.09)$	0.76
Boys	12 (54.5%)	11 (50%)			

SD, Standard deviation; MD, Mean difference;  $\chi^2$ , Chi squared value; p-value, Probability value.

Table 2. Comparison between pre- and post-treatment mean HR and RR values in the control group and study group.

Item	Pre-treatment	Post- treatment	MD	% change	t- value	p- value	Sig
	X <sup>-</sup> ±SD	X <sup>-</sup> ±SD	_				
HR (beats/min) (control group)	126.55 ± 15.35	139.09 ± 18.38	-12.54	9.91	-2.96	0.007	S
RR (breaths/min) (control group)	32.36 ± 7.08	34.86 ± 5.36	-2.5	7.73	-2.86	0.009	S
HR (beats/min) (study group)	127.5 ± 16.42	128.64 ± 12.3	-1.14	0.89	-0.3	0.76	NS
RR (breaths/min) (study group)	30.63 ± 7.36	31.72 ± 4.36	-1.09	3.56	-0.61	0.54	NS

X<sup>-</sup>: Mean; SD: Standard deviation; MD: Mean difference; t value: Paired t-value; p-value: Probability value; S: Significant.

For blood gases, no statistically significant differences in  $PaO_2$ ,  $PaCO_2$ , and  $SaO_2$  were observed among groups before treatment (p = 0.53, p = 0.52, and p = 0.86, respectively). A significant increase in  $PaO_2$  and  $SaO_2$  after treatment was observed in both the control and study groups (p <0.05);

moreover, a significant decrease in  $PaCO_2$  after treatment was observed in both the control and study groups (p <0.05) (Table 3).

Table 3. Comparison between pre- and post-treatment mean PaO<sub>2</sub>, PaCO<sub>2</sub>, SaO<sub>2</sub>, and Cdyn values in the control group and study group.

Item	Pre- treatment	Post- treatment	MD	% of change	t- value	p- value	Sig
	X <sup>-</sup> ±SD	X <sup>-</sup> ±SD	_				
PaO <sub>2</sub> (mm Hg) (control group)	47.22 ± 6.27	64.59 ± 12.01	-17.37	36.79	-7.12	0.001	S
PaCO <sub>2</sub> (mm Hg) (control group)	49.5 ± 5.72	39.36 ± 6.86	10.14	20.48	4.98	0.001	S
SaO <sub>2</sub> (%) (control group)	78.31 ± 8.69	87 ± 8.36	-8.69	11.10	-3.5	0.002	S
Cdyn (ml/cm H₂O/kg) (control group)	0.78 ± 0.25	1.03 ± 0.26	-0.25	32.05	-4.61	0.001	S
PaO <sub>2</sub> (mm Hg) (study group)	48.36 ± 5.85	72.81 ± 9.02	-24.45	50.56	-11.49	0.001	S
PaCO <sub>2</sub> (mm Hg) (study group)	50.77 ± 7.21	35.22 ± 5.13	15.55	30.63	14.12	0.001	S
SaO <sub>2</sub> (%) (study group)	77.91 ± 7.25	94.81 ± 4.56	-16.9	21.69	-11.83	0.001	S
Cdyn (ml/cm H₂O/kg) (study group)	0.81 ± 0.27	1.24 ± 0.23	-0.43	53.09	-6.95	0.001	S

In addition,  $PaO_2$  and  $SaO_2$  were significantly greater in the study group than the control group after treatment (p <0.05), whereas  $PaCO_2$  was significantly lower in the study group than the control group after treatment (p <0.05) (<u>Table 4</u>).

Table 4. Comparison of post treatment mean HR, RR, PaO<sub>2</sub>, PaCO<sub>2</sub>, SaO<sub>2</sub>, and Cdyn values between the control and study groups.

Empty Cell	Control group	Study group	MD	t- value	p-value	Sig
	X <sup>-</sup> ±SD	X <sup>-</sup> ±SD	_			
HR (beats/min)	139.09 ± 18.38	128.64 ± 12.3	10.45	2.21	0.03	S
RR (breaths/min)	34.86 ± 5.36	31.72 ± 4.36	3.14	2.12	0.03	S
PaO <sub>2</sub> (mm Hg)	64.59 ± 12.01	72.81 ± 9.02	-8.22	-2.56	0.01	S
PaCO <sub>2</sub> (mm Hg)	39.36 ± 6.86	35.22 ± 5.13	4.14	2.26	0.02	S
SaO <sub>2</sub> (%)	87 ± 8.36	94.81 ± 4.56	-7.81	-3.85	0.001	S
Cdyn (ml/cm H₂O/kg)	1.03 ± 0.26	1.24 ± 0.23	-0.21	-2.71	0.01	S

Regarding dynamic lung compliance, no significant difference in Cdyn was observed between groups before treatment (p = 0.74). Cdyn was significantly greater after treatment in the control group (p = 0.001), showing a 32.05% improvement, as well as in the study group (p = 0.001), showing a 53.09% improvement ( $\underline{\text{Table 3}}$ ). Cdyn was significantly greater in the study group than the control group after treatment (p = 0.01) ( $\underline{\text{Table 4}}$ ).

#### Discussion

Untreated atelectasis and decreased <u>mucociliary clearance</u> can prolong mechanical ventilation times and <u>pediatric ICU</u> length of stay. <sup>14</sup> Our results showed statistically significant improvements in ABGs, Cdyn, RR, and HR in favor of the study group receiving the TBT, among children with atelectasis on mechanical ventilation.

Significant changes in HR and RR were observed, and the percentage increase indicated clinical deterioration of children in the control group. The study group showed more significant clinical improvements in HR and RR than the control group.

After CPT, the HR and RR increased, possibly because of the stimulatory effects of percussion and vibration, and a transition in secretion from the central to the peripheral airways, thereby leading to breathing difficulty. These factors contributed to <a href="tachycardia">tachycardia</a> and <a href="tachypnea">tachypnea</a>, which lasted longer than 10 minutes in some patients. After 10 minutes of application of the TBT, the HR and RR didn't change as compared to pre-treatment values, possibly because the TBT had a less stimulating effect than CPT, and the use of a proper time frame for recording allowed the children to become more relaxed and regulate their breathing.

Our results were consistent with those reported by Gomes et al., <sup>15</sup> who have explored the effects of CPT on lung collapse in <u>newborns</u> with invasive mechanical ventilation, and observed increases in HR and RR. Even in healthy individuals, the stimulatory effects of percussion can produce <u>tachycardia</u>, thus causing <u>tachypnea</u> and increasing VO<sub>2</sub> to meet oxygen demand. <sup>16</sup> However, the TBT did not significantly increase the HR or RR, and therefore had no negative effects on vital signs.

The results of our study are in line with those reported by Diniz et al., who have examined the effects of the TBT on children with atelectasis and children without respiratory disease. They have found that the TBT temporarily increased the RR with respect to pre-treatment values, but the RR

returned to baseline values after 10 minutes of treatment. The findings might be explained by children's capacity to adjust the rate of exhalation and the duration of each exhalation while the chest is compressed, thus allowing them to inhale just before reaching the volume of elastic equilibrium. Because of these processes, the respiratory device's passive mechanical features elicited a dynamic increase in RR, and some children screamed during and immediately after the maneuver. Crying might also have increased the RR. After 10 minutes, the children became calm, and the RR returned to resting values.

Regarding ABG, improvements in  $PaO_2$  and  $SaO_2$  were observed in both groups. The study group receiving TBT showed more significant increases in  $PaO_2$  and  $SaO_2$  than the control group. Although a decrease in  $PaCO_2$  in both groups was observed, thus indicating improvement, group B showed a more significant decrease in  $PaCO_2$  than group A, thus indicating clinically greater improvement in oxygenation status.

This finding might be explained by the TBT and the specially designed CPT program being more effective in raising PaO<sub>2</sub>, SaO<sub>2</sub>, and lowering PaCO<sub>2</sub> than the CPT program alone. The use of manual chest compression in addition to positive pressure to raise <u>intrathoracic pressure</u> has been reported to promote atelectatic area reopening and to oxygenate the blood. The TBT improves ABG by making more alveoli available for gas exchange, thus leading to removal of more CO<sub>2</sub> from the blood and better oxygenation.

Our results were consistent with those reported by Kole and Metgud, <sup>17</sup> who have studied the effects of lung squeezing technique and rolling on PaO<sub>2</sub>, SaO<sub>2</sub>, and SpO<sub>2</sub> in preterm neonates with chest problems, and have observed significant improvements in oxygenation status. The studies differed in that Kole and Metgud used a lung squeezing technique in which chest compression was applied to both sides for only 5 seconds and then released for neonates, and explored its effects on ABGs, whereas our study applied the TBT on the healthy side for 20 seconds for older children, and explored its effects on ABGs and other variables.

Our findings were consistent with results reported by El Tohamy et al.,  $^{18}$  who have examined the effects of CPT on ABG in neonates and have reported improvements in PaCO<sub>2</sub>, PaO<sub>2</sub>, and SaO<sub>2</sub> levels in children. In addition, our results agree with those reported by Zeng et al.,  $^{19}$  who have examined pulmonary CPT effects and found increased PaO<sub>2</sub> in the study group, and greater incidence of atelectasis in the control group than the study group. The displacement and <u>evacuation</u> of chest secretions during <u>physical therapy</u> sessions in critically ill children considerably enhances bronchial cleanliness and gas exchange, optimizes the <u>mechanics</u> of <u>breathing</u>, and is reflected in ABG.  $^{20}$ 

Regarding dynamic compliance, improvements were observed in the control and study group, and a higher increase in Cdyn was observed in the study group than the control group. The TBT can prevent or treat improper ventilation conditions with adjustment of the <u>alveolar pressure</u> and proper placement, thereby improving <u>pulmonary perfusion</u> and, in children with atelectasis, positively affecting lung compliance.<sup>6</sup>

Our results were consistent with those reported by Biarzi et al.,<sup>21</sup> who have observed that the manual chest compression approach enhances lung compliance. This increase was explained by the negative pressure caused by manual chest compression, which in turn increased the <u>transpulmonary pressure</u>. This aspect is a key advantage of manual chest compression over mechanical ventilator use to increase <u>tidal volume</u>, because the latter requires increasing inspiratory pressure, which can potentially harm lung tissues through <u>barotrauma</u>.

Our results were also consistent with those of Via et al., <sup>22</sup> who have reported that manual chest compression and decompression increase <u>tidal volume</u> because of the high elastic forces in the thoracic cage, thereby increasing transpulmonary pressure and negative pressure in the <u>pleura</u>, and resulting in a greater pressure difference, and increased flow and inspired tidal volume.

The increase in Cdyn in the current study might be explained by the recovery of a substantial number of atelectatic alveoli, decreased areas of overdistension of healthy lung units, and reversal of non-homogeneous <u>ventilation</u> distribution, as observed in infants with diseases characterized by altered surfactant activity.

# Study strengths

Prior studies have not sufficiently examined the role of the TBT in reversing the effects of atelectasis and enhancing the recovery rate of children receiving mechanical ventilation. Therefore, this study suggests important clinical implications for applying the TBT together with CPT for these children, to improve their blood gases and dynamic lung compliance, and decrease <u>adverse effects</u> on HR and RR.

## Study limitations

Some children screamed during or immediately after the technique. Crying in children may contribute to a substantial increase in RR.

#### Conclusion

Using the TBT with CPT causes greater improvements in ABG values and dynamic lung compliance than designed CPT techniques alone, and has no <u>adverse effects</u> on vital signs (HR and RR) in children with atelectasis who are mechanically ventilated.

# Recommendations

Future studies may examine the effects of the TBT on children receiving <u>CPAP</u> or nasal oxygen support; assess the effects of the TBT on neonates; compare the effects of the TBT and manual hyperinflation on children with atelectasis; investigate the effects of the TBT on weaning time and ICU length of stay; and explore the effects of the TBT on chest expansion.

Children are at higher risk of atelectasis due to their anatomical and physiological particularities. Several physiotherapy techniques are used to treat atelectasis, but only four studies cite methods in pediatric patients undergoing Invasive Mechanical Ventilation (IMV). The objective of this study was to evaluate the Structured Respiratory Physiotherapy Protocol (SRPP) for airway clearance and lung reexpansion for infants on IMV with atelectasis. This is a prospective study including 30 infants (mean ± standard deviation age 8.9 ± 8.0 months; weight 7.5 ± 3.0 kg; BMI 15.8 ± 1.6 kg/cm<sup>2</sup> and IMV duration 7.7 ± 4.3 days). The sample was randomized into a Control Group (CG), which received routine physiotherapy, and an Intervention Group (IG), submitted to SRPP (postural drainage, mechanical thoracic vibration, manual hyperinflation, stretching of the accessory respiratory muscles, and functional positioning). Both groups were evaluated before and after physiotherapy for respiratory effort using the Wood Downes Score (WD) and pulmonary aeration using lung ultrasonography (Lung Ultrasound Score – LUS). The outcome of the intervention was evaluated by the magnitude of the effect by the Hedges' g test [(small (0.2 < Hedges' g < 0.5), moderate (0.5 < Hedges' g < 0.8) and large (Hedges' g > 0.8) effects]. There were large within-group effects on the reduction of WD in the CG after intervention in both the CG (Hedges' g = -1.53) and IG (Hedges' g = -2.2). There was a moderate effect on LUS reduction in the CG (Hedges' g = -0.64) and a large effect on IG (Hedges' g = -1.88). This study has shown that the SRPP appears to be safe and may be effective in improving airway clearance and lung reexpansion in children on IMV with atelectasis. Keywords

**Pediatrics** 

Respiratory physiotherapy

Pulmonary atelectasis

Ultrasound

Mechanical ventilation

Introduction

Developing lungs are predisposed to collapse. At electasis is one of the most frequent pulmonary complications in children undergoing Invasive Mechanical Ventilation (IMV).

Children are at higher risk of atelectasis, owing to both obstruction and dynamic airway collapse, due to their distinct anatomical and physiological features. These predisposing features include smaller diameter, less well-supported airways; flexible/compliant chest walls with relatively less compliant lungs; and limited, developing collateral ventilation channels.<sup>3</sup>

In Pediatric Intensive Care Units (PICUs), more than 20% of patients require IMV.<sup>4</sup> The implementation of protective ventilation strategies with the use of low tidal volumes may, in some cases, contribute to the development of atelectasis secondary to insufficient inflation of the alveolar units.<sup>4</sup>

In addition, infection of the lower respiratory system is one of the leading causes of mortality in children under the age of five. During Lower Respiratory Tract Infections (LRTI), mucociliary clearance may be impaired by increased inflammation and/or overload due to excessive mucus production, with consequent impairment of ciliary function, predisposing these patients to secondary complications such as pulmonary atelectasis.

Lung collapse may cause or exacerbate increased work of breathing, hypoxemia, hypercapnia, and acute respiratory failure (mild, moderate, or severe). Long-term complications of unresolved atelectasis include the development of bronchiectasis and chronic lung disease. Early recognition and management of atelectasis are therefore essential to hasten resolution, avoid adverse short and long-term sequelae, and optimize clinical outcomes such as PICU and hospital length of stay and mortality. And a mortality.

The signs and symptoms of pulmonary atelectasis are often nonspecific, however, the application of imaging technologies has increased diagnostic sensitivity and specificity. Although chest X-Ray is still the gold standard for diagnosing atelectasis, due to its cost and effectiveness, it has significant limitations including patient exposure to ionizing radiation, relatively low sensitivity in detecting inflammatory lung lesions, low negative predictive value, and discrepancies in interpretation among specialists.

In view of the limitations of radiography, the use of Point of Care Lung Ultrasound (POCLUS) has been proposed as an additional tool for identifying and monitoring pulmonary atelectasis in children. Among the advantages are the low associated financial costs; clinical utility of trained healthcare professionals being able to easily and quickly perform the test at the bedside; and avoidance of harmful ionizing radiation, allowing multiple repeated scans if needed to determine progression and/or response to therapy.<sup>12</sup>

The interventions used in the treatment of pulmonary atelectasis in intubated children are limited and, to date, there are no clinical trials that identify the most efficient treatment for the resolution of pulmonary atelectasis in pediatrics and neonatology.<sup>2</sup>

Chest physiotherapy in patients with pulmonary atelectasis is a minimally invasive treatment that aims to maintain or improve airway patency by removing obstructive secretions, reducing airway resistance, promoting gas exchange, and decreasing the work of breathing.<sup>13</sup>

Although respiratory physiotherapy interventions include several techniques for the treatment of atelectasis, there are only four studies 14, 15, 16, 17 that cite different methods of respiratory physiotherapy aimed at resolving atelectasis in pediatric patients on IMV. However, none of them are randomized controlled trials and none use standardized, protocol-driven interventions.

Therefore, the main objective of this study was to develop and analyze the clinical and imaging effects of a Structured Respiratory Physiotherapy Protocol (SRRP) for airway clearance and lung reexpansion in children on IMV diagnosed with unilateral pulmonary atelectasis.

### Materials and methods

Study design and population

This was a prospective randomized controlled clinical trial, registered in the Brazilian Clinical Trials Registry (ReBEC): RBR-106bhfwy, carried out in the PICU of the Menino Jesus Municipal Children's Hospital (HMIMJ), in São Paulo, from October 2020 to March 2022. The study was approved by the Research Ethics Committee of the University of São Paulo School of Medicine (FMUSP) and by the Research Ethics Committee of the HMIMJ (opinion 3,689,413). The study started after its approval.

The study included 30 infants (age: 28 days to 24 months) on IMV for a period greater than or equal to 12 hours through an orotracheal cannula, diagnosed with pulmonary atelectasis by a pediatric intensive care physician through clinical examination and imaging (chest X-Ray and POCLUS), whose legal guardians had authorized the child's participation in the study through the Free and Informed Consent Form (ICF). Exclusion criteria included: patients with bilateral atelectasis; any type of air leak syndrome; pulmonary hemorrhage; presence of diseases presenting with bone fragility; rib cage and/or pulmonary contusions; subcutaneous pacemakers; treatment with anticoagulants for more than 72 continuous hours; hemodynamic instability; thrombocytopenia (platelet count < 50,000); presence of an intercostal chest drain; underlying neuromuscular or cardiac diseases and presence of spinal deformities.

Patients who met the inclusion criteria were electronically randomized (<a href="https://www.random.org/lists/">https://www.random.org/lists/</a>) into two groups: Control Group (CG) and Intervention Group (IG) as described in Fig. 1.

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Fig. 1. Description of patient selection. Note: ICU, Intensive Care Unit; IMV, Invasive Mechanical Ventilation.

The sample size was calculated based on historical audit data from the study site – between August and December 2018, 49 patients underwent tracheal intubation in this PICU, with 13 of these patients developing pulmonary atelectasis. It was therefore estimated that over a period of 12

months, approximately 26–30 patients would develop pulmonary atelectasis. When entered into a power analysis (using the statistical program openepi.com), with equal numbers in the Intervention (IG) and Control (CG) groups, a sample of 30 patients (15 each in IG and CG) yielded a statistical power of 80%, with 20% error.

In order to characterize the sample, the following data were collected from the patient's medical records: age, gender, clinical diagnosis of hospitalization, weight, height, laboratory tests, and the Pediatric Index of Mortality 2 (PIM 2) outcome prediction score.

Data collection was performed by the physical therapist responsible for the study. Upon detecting the presence of atelectasis on the chest X-Ray, the pediatric intensive care physician responsible for the PICU called the physical therapist via cell phone. After the activation, the researcher checked whether the patient met the inclusion criteria of the study. If so, the authorization of the legal guardian was requested to allow the child's participation in the study through the informed consent form. After signing the informed consent form, the patient was electronically randomized into CG or IG.

### Chest X-ray

The baseline anteroposterior radiological images were considered to be free of atelectasis when there was normal pulmonary transparency with free costophrenic sinuses visualized. Lobar or segmental atelectasis was considered when opacification of the lobe or lung segment was present with any of the following concomitant signs: loss of air/gas volume, the most direct sign being the displacement of the interlobar fissure; the deviation of the heart and mediastinum and the elevation of the diaphragm to the same side as atelectasis in extensive collapse.<sup>18</sup>

The Radiological Atelectasis Scoring System was used to score atelectasis observed on lung X-Rays. <sup>19</sup> Each radiograph was scored by the physiotherapist for atelectasis, hyperinflation, and mediastinal displacement. The presence or absence of pulmonary hyperinflation was each marked as one (1) point or zero (0) points, respectively. The presence or absence of a mediastinal deviation was scored as one (1) or zero (0). Atelectasis was scored for each lung lobe. Partial atelectasis of one lung lobe was scored as one (1) point, and complete atelectasis of one lobe was scored as two (2) points. The scores were summed for the chest X-Ray of each patient.

## Point of care lung ultrasound (POCLUS)

Lung ultrasound was performed immediately before initiating interventions (baseline) and repeated 30 minutes after intervention (post-intervention measure). The assessment was performed by the main researcher, a physiotherapist trained and certified to perform lung ultrasound. The POCLUS images were recorded and subsequently analyzed by an independent evaluator blinded to study allocation and patient history. The independent evaluator was a pediatric intensive care physician with ultrasonography certification and extensive clinical experience over more than eight years.

The lung was scanned antero-posteriorly, craniocaudally, transversely, and longitudinally to the costal arches. Initially, POCLUS was performed with the patient in the supine position and subsequently turned laterally to evaluate the posterior pulmonary region.

The ultrasound image was considered unaltered when it showed an association between pleural sliding and the presence of horizontal repeats of the pleural line called "A-lines". A-lines are a type of reflection artifact originating from the pleural line, seen as a series of hyperechoic parallel lines, equidistant from each other, below the pleural line, with spacing equal to the distance between the skin and the pleural line. 12

The main imaging characteristics of atelectasis visualized by ultrasound are loss of aeration generating a visible, hyperechoic parenchymal area, which may present ill-defined and irregular borders; large lung consolidations with static bronchograms; whilst dynamic air bronchogram can rule out atelectasis. Other signs of atelectasis on POCLUS include abnormalities in the pleural line and disappearance of the A-line. The coalescent B-line (or B-pattern) can be interpreted as a higher degree of severity or a state prior to the development of atelectasis, especially if the lesion has a focal location. The B-lines are hyperechoic vertical artifacts originating from the pleural line that extends to the periphery of the lung field and move with the pulmonary sliding. At the point of intersection, the B-lines obliterate the A-lines.

The loss of lung aeration identified at POCLUS was graded using the Lung Ultrasound Score (LUS), validated for this purpose.  $^{24}$  A score of 0 indicates normal aeration i.e., the presence of lung slippage and horizontal A-lines, or less than three vertical B-lines; a score of 1 indicates moderate loss of aeration indicated by the presence of  $\geq$ 3 B-lines, regularly or irregularly spaced, originating from the pleural line or small juxta pleural consolidations; a score of 2 indicates severe loss of aeration, i.e.; the presence of coalescing B-lines in several intercostal spaces, occupying the entire intercostal space; and a score of 3 indicates complete loss of pulmonary aeration, characterized by the presence of tissue echogenicity and static or dynamic air bronchograms, as observed in lung consolidation.

### Monitoring

Patients in both groups had vital sign measurements assessed at baseline (immediately before intervention) and at 10 and 30 minutes after intervention: and underwent three evaluations Heart Rate (HR); Respiratory Rate (RR); body temperature; PA; SpO<sub>2</sub>. Clinical severity was classified according to the Wood-Downes Score (WD)<sup>25</sup> as mild (1 to 3 points), moderate (4 to 7 points) and severe (8 to 14 points) according to the sum of the following items: the presence of wheezing (0 = No; 1 = End of expiration; 2 = Full expiration; 3 = Inhalation and expiration); the presence of chest indrawing (No = 0; Subcostal = 1; Supraclavicular subcostal and nasal flare = 2; supraclavicular, subcostal, intercostal, suprasternal, and nasal flare = 3); total respiratory rate (< 30 breaths per minute = 0; 31–45 = 1; 46–60 = 2; > 60 = 3); heart rate (< 120 beats per minute = 0; > 120 = 1); ventilation and breath sound on auscultation (0 = Good and symmetrical breath sounds; 1 = Regular and symmetrical; 2 = Very decreased breath sounds; 3 = Silent chest and cyanosis (0 = No; 1 = Yes).

During monitoring, the number of aspirations, quantity, and quality of aspirated tracheal secretion were recorded, according to the Suzukava Method:<sup>26</sup> Fluid when the aspiration tube is free of secretions after aspiration, using only vacuum; Moderate, when the aspiration tube presents secretions adhered to the wall of the probe after aspiration but is free after the use of 0.9% saline solution; Thick, when the aspiration probe has secretions adhered to the probe wall even after instillation of 0.9% saline solution.

# Control group

The CG was submitted to routine respiratory physiotherapy care and interventions of the Physical Therapy Service, including manual vibration of the patient's chest wall and Manual Hyperinflation (MH) with a self-inflating bag without control of Peak Inspiratory Pressure (PIP), number of repetitions or established intervals.

The technique of manual vibration in the chest is based on the properties of modifying the consistency of airway mucus. This thixotropic gel, highly viscous under static conditions can become less viscous and is able to flow when shaken. Thus, when applying vibrations to the chest wall, mechanical energy is transmitted to the airways aiding the ciliary beating, thus reducing the viscosity

of bronchial secretions, which can be more easily eliminated by positioning, coughing, or aspiration of the airways. <sup>28</sup>

Manual Hyperinflation (MH) aims to mobilize pulmonary secretions proximally by increasing Peak Expiratory Flow (PEF) and promoting pulmonary re-expansion by increasing pulmonary distension pressure, which favors increased airflow to the poorly ventilated regions through the collateral channels (where present) and by redistributing and renewing surfactant in the alveoli. The technique is performed by applying a series of deep manual insufflations with brief inspiratory pauses, followed by a rapid release of the bag to increase expiratory flow and stimulate coughing.

## Intervention group

The IG was submitted only to the SRPP developed for this study and applied by the main research physiotherapist. The SRPP intervention included modified postural drainage with mechanical chest wall vibration applied using an electronic massage device (Super da G-Life®); MH using a self-inflating bag; stretching of the respiratory muscles; and functional positioning of the patient in bed.

The patient was first positioned with elevation of the head of the bed by 30° in lateral decubitus, so that the atelectatic pulmonary region was non-dependent, maintaining this position during the application of the other interventions.

Mechanical vibration over the chest wall was performed with the use of a massager positioned over the atelectatic region, in the craniocaudal and lateromedial directions, for ten minutes, with a frequency of 50 Hertz (Hz). Manual hyperinflation with a self-inflating bag consisted of slow and deep inflation of the bag, followed by an inspiratory pause of two to three seconds and rapid release after this period with oxygen flow at five liters per minute, with 10 repetitions. To monitor the PIP provided during MH, a Murenas analog manometer was used, not exceeding the PIP of 30 cm  $H_2O$ . No PEEP valve was used.

After performing MH, the patients' accessory respiratory muscles were stretched by the physiotherapist throughout the expiratory phase, bringing the muscle to maximum length, with two sets in 10 consecutive respiratory cycles for each muscle, with a five-second interval between each set.<sup>30</sup> The stretches were performed bilaterally as follows: upper trapezius: with the patient positioned in the dorsal decubitus position, the physiotherapist rested one hand on the occipital region, side flexing the head to the opposite side whilst, with the other hand, moving the ipsilateral shoulder in the craniocaudal direction; sternocleidomastoid: with the patient positioned in the dorsal decubitus position, the physiotherapist passively flexed (away from the muscle to be stretched) and laterally rotated towards the target muscle, by placing one hand in the occipital region and the other on the upper thorax region, displacing in the craniocaudal direction; pectoralis major: with the patient positioned in dorsal decubitus, with the arm to be stretched abducted and externally rotated at the shoulder, with elbow flexion, the physiotherapist applied a passive stretch by applying pressure using one hand on the upper third of the arm and the other on the lateral region of the upper thorax, following the orientation of the muscle fibers; intercostal muscles: with the patient in lateral decubitus with the forearm flexed and the hand resting on the occiput, the physiotherapist supported the patient's arm with one hand while the other was positioned on the lower rib cage during inspiration; the physiotherapist facilitated expansion of the rib cage by moving the patient's arm in the craniocaudal direction and following the expiratory movement without applying pressure (Fig. 2). $\frac{30}{}$ 

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Fig. 2. Positioning for stretching the respiratory muscles: (A) Upper trapezius; (B) Sternocleidomastoid; (C) Pectoralis major and (D) Intercostals. Source: The author (2023).

In both groups, the orotracheal tube was aspirated, when necessary, after the interventions and during the procedures. The quantity and quality of aspirated tracheal secretion were classified using the Suzukava method.<sup>26</sup>

Finally, functional positioning was performed in bed, aiming to favor respiratory mechanics, optimize pulmonary function, and stimulate the child's sensorineural and psychomotor development.

### Interrupt criteria

The criteria for interruption of the protocol were: Heart Rate (HR) greater than 200 beats per minute (bpm); Respiratory Rate (RR) greater than 45 breaths per minute (bpm); Blood Pressure (BP) values above 120/80 millimeters of mercury (mmHg) or less than 80/40 mmHg; Pulse Oxygen Saturation (SpO<sub>2</sub>) less than 88% with the need for increased FiO<sub>2</sub> during the application of the protocol. The presence or absence of signs of respiratory distress (accessory respiratory muscle use, pallor, sweating, and psychomotor agitation) was also considered according to the Wood-Downes Score (WD) used in this study. <sup>26</sup> In the presence of any changes mentioned above, the protocol was interrupted, and the child was placed in bed and kept under monitoring. The patient who needed to interrupt the procedures could be included again in the study six hours after interrupting the first attempt. Daily attempts could be made, within 48 hours of the first attempt, after this period the patient was considered as not benefiting from the study protocol.

## Statistical analysis

Descriptive statistics included measures of central tendency by means ± Standard Deviations (SD), medians and interquartile ranges (IQR 25%–75%), and absolute and relative frequencies.

The Kolmogorov-Smirnov test was used to evaluate the normality of the distribution, and considering that most variables were not normally distributed, between-group analyses were conducted using the non-parametric Wilcoxon/Mann-Whitney tests. Fisher's exact tests were used for comparisons between frequencies. To compare repeated vital sign measurements (before physical therapy, after 10 and 30 minutes), the non-parametric Friedman test was used, with post-hoc analysis using the paired Wilcoxon test (signed rank). Bonferroni correction was used as appropriate.

# Evaluation of the magnitude of the effect (effect size)

The intervention of the study was not compared to a placebo, but to a control group, in which routine physical therapy of the Hospital was performed. Therefore, statistical differences were not expected in the two groups when comparing parameters before and after respiratory therapy, and the only way to evaluate the outcome of the study intervention is through the magnitude of the effect (effect size). The standardized effect magnitude allows researchers to communicate the practical significance of the results, rather than just reporting statistical significance. Cohen's "d" test (Cohens' d) is used to describe the standardized mean difference of an effect. A correction of Cohens' d is Hedges' "g" (Hedges' g), which is unbiased and corrected for small samples (n < 20), and it was this test that the authors used to measure the effect of the intervention on the LUS and Wood Downes scores (paired measures before and after respiratory physiotherapy). The way to interpret the Hedges' g is as suggested by Cohen: small (0.2 < Hedges' g < 0.5), moderate (0.5 < Hedges' g <

0.8), and large (Hedges' g  $\geq$  0.8 effects). These values assume negative values when the effect is reduced, e.g., a reduction in a score; but they can be informed by their absolute values. If the absolute value is greater than one (1), it means that the difference between the means is greater than one SD.

The analyses were performed using R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL <a href="https://www.R-project.org/">https://www.R-project.org/</a>.

#### Results

During the study period, 845 children were admitted to the PICU of the HMIMJ, of which 26% underwent orotracheal intubation and 7% developed pulmonary atelectasis. Of these children, 40 met the inclusion criteria due to atelectasis, 10 patients were excluded (one with scoliosis, two with orotracheal tube displacement, tissue trauma, air leak syndrome (pneumothorax or pneumomediastinum) (Fig. 3).

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Fig. 3. Sample selection flowchart.

The sample of 30 children was randomized into two groups (n = 15 in the CG; n = 15 in the IG). The median (IQR 25%–75%) age of the patients was 7 (2–17) months in the CG and 4 (2–13.5) months in the IG. The groups presented similar characteristics (p > 0.05) in terms of epidemiology and clinical variables (Table 1).

Table 1. Epidemiological characteristics, clinical variables and laboratory tests of the sample according to groups and results of statistical tests.

Variables	Group C	Group Control		Group Intervention		
N	15		15		-	
Female gender, n (%)	6	40	4	26.7	0.6	
Age (months) <sup>a</sup>	7	2.0-17.0	4	2.0-13.5	0.7	
Diagnostics						
Viral bronchiolitis	11	73.3	11	73.3	С	
Pneumonia	-	-	1	6.7	С	
Nephrotic syndrome	_	-	1	6.7	С	
Septic shock	3	20	2	13.3	С	

Variables	Group Control		Group Intervention		p*
N	15		15		_
Wheezing crisis	1	6.7	_	_	С
Weight (Kg) <sup>b</sup>	7.7	3.2	7.4	2.9	0.4
Height (cm) <sup>b</sup>	68.3	12	67	12.6	0.7
BMI (Kg/cm²)b	15.5	1.7	16.2	1.6	0.4
PIM2 <sup>b</sup>	5	7.5	2.1	1.3	0.6
Duration of IMV (days) <sup>a</sup>	7	5.5-8.5	6	4.5-8.5	0.5
ICU length of stay (days) <sup>a</sup>	15	11.0–16.0	12	9.5–18.5	0.4
Hospital length of stay (days) <sup>a</sup>	19	17.0-24.0	21	12.5–24.5	0.6
рН <sup>а</sup>	7.4	0.1	7.4	0.1	0.3
PaO <sub>2</sub> <sup>a</sup>	91.5	40.3	108.7	37.8	0.3
PaCO <sub>2</sub> <sup>a</sup>	46	10.7	46.3	14.1	0.8
HCO <sub>3</sub> <sup>a</sup>	29	7	26.7	5.2	0.2
BEª	3.8	7.3	1.1	4.9	0.1
SaO <sub>2</sub> <sup>a</sup>	93.1	8.3	96.3	4.5	0.5
PaO <sub>2</sub> /FiO <sub>2</sub> <sup>a</sup>	256.9	171.4	299.7	106.6	0.3
Hba	10	1.4	9.7	1.5	0.3
Htª	30.2	4.2	27.6	4.5	0.07
Platelets <sup>a</sup>	326533.3	143116.8	316000	134982	0.6
Lactate <sup>a</sup>	1.8	1.6	1.6	1	0.9
CRP <sup>a</sup>	3.5	2.9	5.7	5.5	0.4
Viral panel					

Variables	Group Control		Group Intervention		p*
N	15		15		-
RSV	9	81.8	8	72.7	С
Bocavirus	2	18.2	_	_	С
Parainfluenza I e II	-	_	1	9.1	С
Metapnemovirus	-	_	1	9.1	С
Seasonal coronavirus	-	_	1	9.1	С

NOTE: <sup>a</sup> Median (IIQ 25%–75%); <sup>b</sup> Mean ± Standard Deviation; <sup>c</sup> Variables with multiple subvariables did not allow generating statistical significance due to the number of cases.

p\*, p-values by the Wilcoxon/Mann-Whitney test or Fisher's exact test, when applicable; N, Absolute number; Kg, Kilogram; cm, Centimeters; BMI, Body Mass Index; PIM2, Pediatric Index of Mortality 2; IMV, Invasive Mechanical Ventilation; ICU, Intensive Care Unit, pH, Hydrogen Potential; PaO<sub>2</sub>, Partial Pressure of Oxygen; PaCO<sub>2</sub>, Partial Pressure of Carbon Dioxide; BE, Base Excess; SaO<sub>2</sub>, Arterial Oxygen Saturation; PaO<sub>2</sub>/FiO<sub>2</sub>, Ratio of Partial Pressure of Oxygen to the fraction of inspired oxygen; Hb, Hemoglobin; Ht, Hematocrit; CRP, C-Reactive Protein; RSV, Respiratory Syncytial Virus.

Laboratory parameters prior to respiratory therapy interventions were statistically similar (p > 0.05), see <u>Table 1</u>. Ventilatory parameters and Radiological Atelectasis Scoring System scores of both groups were similar (p > 0.05), see <u>Table 2</u>. Regarding the variables diagnostics, viral panel, IMV mode, VAP, location of atelectasis, quality and color of secretion, it was not possible to add statistical significance due to the small sample size in the subcategories of each of them.

Table 2. Description of modes, ventilation parameters, incidence of Ventilator-Associated Pneumonia (VAP), Radiological Atelectasis Scoring System score, location of atelectasis and characteristics of tracheal secretion according to groups and results of statistical tests.

Variables	Control	Control group		Intervention group	
IMV mode, n (%)					
PCV (cm H <sub>2</sub> O)	11.0	73.3	10.0	66.6	b
PSV (cm H₂O)	1.0	6.7	1.0	6.7	b
PRVC (cm H <sub>2</sub> O)	-	-	1.0	6.7	b
SIMV (cm H <sub>2</sub> O)	3.0	20.0	3.0	20.0	b

Ventilatory parameters<sup>a</sup>

Variables	Control group		Intervention group		р*
PIP (cm H <sub>2</sub> O)	21.7	3.0	22.1	3.6	0.8
PEEP (cm H <sub>2</sub> O)	7.0	1.0	6.8	0.6	0.7
RR (ipm)	27.3	5.3	25.8	3.8	0.7
IT (s)	0.6	0.1	0.6	0.1	0.7
FiO2 (%)	44.0	18.4	37.8	12.2	0.6
MAP (cm H <sub>2</sub> O)	11.5	2.0	13.0	1.9	0.1
TV (mL)	65.8	36.8	61.3	38.9	0.3
VT (mL/Kg)	6.0	3.0	8.0	2.5	0.9
Intratracheal cuff, n (%)	6.0	40.0	6.0	40.0	b
VAP, n (%)	2.0	13.3	1.0	6.7	b
Radiological score <sup>a</sup>	2.7	0.9	3.1	0.9	0.3
Location of atelectasis <sup>a</sup>					
RUL	9.0	60.0	11.0	73.3	b
RML	4.0	26.7	4.0	26.7	b
Ш	2.0	13.3	_	-	b
Aspirations <sup>a</sup>	1.8	0.8	2.1	0.8	0.4
Quality, n (%)					
Moderate	14.0	93.3	15.0	100.0	b
Thick	1.0	6.7	_	_	b
Colour, n (%)					
Clear	10.0	66.7	10.0	66.7	b
Yellowish	5.0	33.3	5.0	33.3	b

Note: <sup>a</sup> Mean and standard deviation; <sup>b</sup> Variables with multiple subvariables did not allow generating statistical significance due to the number of cases.

p\*, p-values by the Wilcoxon/Mann-Whitney test.

N, Absolute Number; IMV, Invasive Mechanical Ventilation; PCV, Pressure Controlled Ventilation; PSV, Pressure Support Ventilation; PRVC, Pressure-Regulated and Volume-Controlled Ventilation; SIMV, Synchronized Intermittent Mandatory Ventilation; cm H<sub>2</sub>O, Centimeters of Water; PIP, Peak Inspiratory Pressure; PEEP, Positive End-Expiratory Pressure; RR, Respiratory Rate; ipm, Incursions per minute; IT, Inspiratory Time; s, seconds; FiO<sub>2</sub>, Fraction of Inspired Oxygen; MAP, Mean Airway Pressure; TV, Total Volume; mL, Milliliter; VT, Tidal Volume; mL/Kg, Milliliter per kilo; VAP, Ventilator-Associated Pneumonia; Radiological score, Radiological Atelectasis Scoring System; RUL, Right Upper Lobe; RML, Right Middle Lobe; LLL, Left Lower Lobe.

Evaluation of lung ultrasound score (LUS) and Wood-Downes (WD) scores

There was no significant difference in the baseline or post-intervention median (IQ 25%–75%) LUS scores between the control and intervention groups: 2 (1–3) vs. 3 (2–3) (p = 0.21) and 1 (1–2.5) vs. 1 (0.5–2) (p = 0.5) respectively. Similarly, there were no significant between-group differences in the median (IQ 25%–75%) baseline or post-intervention WD scores between CG and IG: 4 (3–5) vs. 4 (3–5) (p = 0.9) and 3 (2–3) vs. 2 (1–2.5) (p = 0.18), respectively.

Significant within-group differences were observed in both CG and IG comparing baseline to post-intervention measures (Table 3). Median (IQR 25%–75%) LUS in the CG and IG changed from 2(1–3) and 3 (2–3) before respiratory physiotherapy to 1 (1–2.5; p = 0.01) and 1 (0.5–2; p < 0.001) after intervention respectively. Median (IQ 25%–75% WD score changed from 4 (3.5–5) and 4 (3–5) to 3(2–3; p < 0.001) and 2 (1–2.5; p < 0.001) postintervention in the control and intervention groups respectively.

Table 3. Description of LUS and Wood-Downes Score comparing groups, moments and results of statistical tests.

Score	Median	P 25	P 75	p*
LUS CG before	2.0	1.0	3.0	0.01
LUS CG after	1.0	1.0	2.5	
LUS IG before	3.0	2.0	3.0	<0.001
LUS IG after	1.0	0.5	2.0	
WD CG before	4.0	3.5	5.0	<0.001
WD CG after	3.0	2.0	3.0	
WD IG before	4.0	3.0	5.0	<0.001

Score	Median	P 25	P 75	p*
WD IG after	2.0	1.0	2.5	

Note: P25, 25<sup>th</sup> percentile; P75, 75<sup>th</sup> percentile.

p\*, p-values by the Wilcoxon/Mann-Whitney test.

LUS, Lung Ultrasound Score; WD, Wood-Downes; CG, Control Group; IG, Intervention Group; Before, Before respiratory physiotherapy; After, After respiratory physiotherapy.

Assessment of the magnitude of the effect

There was a moderate effect on the reduction of the LUS score in the CG after respiratory physiotherapy (Hedges' g = -0.64, 95% CI: -1.35 to 0.08), and a 2.9-fold greater effect on the IG (Hedges' g = -1.88, 95% CI: -1.01 to -2.73), characterizing a large effect on the reduction of this score (Fig. 4).

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Fig. 4. Magnitude of the effect (effect size) of the intervention proposed in the study (GI) on LUS (y axis), compared to the effect of routine physiotherapy (CG), shown by the differences between the medians (green bars) and the values "g" for Hedges.

There was a large effect on the reduction of the WD score in the CG after physical therapy (Hedges' g = -1.53, 95% CI -3.1 to -1.29), and a 1.4-fold greater effect in the IG (Hedges' g = -2.2, 95% CI: -2.32 to -0.71) (Fig. 5).

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Fig. 5. Magnitude of the effect (effect size) of the intervention proposed in the study (GI) on the Wood-Downes score (y-axis), compared to the effect of routine physiotherapy (CG), shown by the differences between the medians (green bars) and by Hedges' "g" values.

Evaluation of effects on physiological parameters

The parameters of heart rate, respiratory rate, temperature,  $SpO_2$ , systolic, mean, and diastolic blood pressure at all measurement points were statistically similar between CG and IG (<u>Table 4</u>).

Table 4. Description of vital signs according to groups and moments and results of statistical tests.

Variables	Group co	Group control		Group intervention	
HR before (bpm)	139.9	26.7	142.7	23.3	0.9
HR 10 min (bpm)	140.9	22	140.5	20.3	0.8

Variables	Group co	ntrol	Group inter	rvention	<b>p</b> *
HR 30 min (bpm)	137.1	23.9	135.9	19.7	0.8
RR before (ipm)	38.3	11.1	37.4	10.2	0.8
RR 10 min (ipm)	36.8	8.5	34.7	7.6	0.7
RR 30 min (ipm)	32.5	7.1	32.3	5.4	0.9
Temp. before (°C)	36.7	0.5	36.6	0.5	0.7
Temp. 10 min (°C)	36.6	0.4	36.6	0.5	0.7
Temp. 30 min (°C)	36.7	0.4	36.6	0.5	0.6
SPO <sub>2</sub> before (%)	95.5	3.4	96.5	4.1	0.4
SPO <sub>2</sub> 10 min (%)	98.2	2.5	98.2	2	0.8
SPO <sub>2</sub> 30 min (%)	97.9	2.4	98.5	2.2	0.5
SBP before (mmHg)	98.1	17.2	104.3	13.1	0.3
SBP 10 min (mmHg)	104.5	17.3	104.1	15.4	0.8
SBP 30 min (mmHg)	99.4	20.5	98.5	16.6	0.6
DBP before (mmHg)	57.1	14.3	59.5	9.6	0.4
DBP 10 min (mmHg)	57.6	12.5	53.7	10.2	0.7
DBP 30 min (mmHg)	55.4	13.5	52.9	11.5	0.7
ABP before (mmHg)	71.5	14.3	75.5	10.1	0.3
ABP 10 min (mmHg)	74.4	13	71.6	12.6	0.6
ABP 30 min (mmHg)	71.2	13.9	68	12.2	0.3

Note: Data are in means and standard deviations.

p\*, p-values according to the non-parametric Friedman test, with post-hoc analysis using the paired Wilcoxon test (signed rank), with Bonferroni correction.

Before, Before respiratory physiotherapy; HR, Heart Rate; min, Minutes; RR, Respiratory Rate; Temp, Body Temperature in degrees Celsius; degrees Celsius; SPO<sub>2</sub>, Peripheral Oxygen Saturation; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; ABP, Average Arterial Pressure.

#### Discussion

The loss of lung volume caused by atelectasis can modify respiratory mechanics and impair gas exchange, which can lead to an increase in IMV time, tracheal extubation failure, increased length of hospital stays, and morbidity and mortality.<sup>32</sup> This study, including children undergoing IMV, evaluated the effectiveness of a Structured Respiratory Physical Therapy Protocol (SRPP) by means of immediate evaluation by pulmonary ultrasonography compared to a control group aimed at airway clearance and pulmonary re-expansion of atelectasis areas.

This is not the first study to report the use of physiotherapist-applied non-invasive interventions to treat pulmonary atelectasis in children on IMV. However, this is the first study to develop and evaluate an SRPP for the resolution of unilateral pulmonary atelectasis in children.

In both intervention and control groups, the most frequent location of pulmonary atelectasis was the right upper lobe, which has been described previously. 15, 16 This finding can be explained anatomically by the fact that the right upper lobe bronchus is at a 90-degree angle from the right main bronchus, limiting secretion drainage. 33

As described in the study by Galvis et al., <sup>14</sup> the factors that may have contributed to the development of atelectasis in these patients in addition to the anatomical and physiological features typical of the pediatric age group include factors related to the health status and critical care modalities. These may include alteration of mucociliary transport, resulting from the artificial airway, mucosal edema and/or excessive mucus production due to trauma associated with repeated suctioning; thickening of mucus caused by the disease process, fluid restriction and diuretic use; accumulation of secretions resulting from inadequate bronchial drainage, particularly in children receiving excessive sedation and neuromuscular blockade; inadequate humidification of inspired gas and incomplete removal of tracheal secretions during tracheal aspiration. <sup>34</sup>

Previous studies 14, 15, 16, 17 on this topic have used chest X-Rays as the primary tool to evaluate the resolution of pulmonary atelectasis and the efficacy of treatments. By offering diagnostic accuracy similar to chest radiography, without exposure to ionizing radiation, POCLUS is a dynamic and agile tool to perform and interpret lung changes, quickly integrating the information into the patient's clinical context. Ultrasound was successfully used in this study to evaluate the outcome of respiratory physiotherapy interventions performed in children on IMV with pulmonary atelectasis, which was detected in the first evaluation by means of radiological imaging, evaluated by the intensive care physician.

Bedside lung ultrasound is a diagnostic tool that has been increasingly used in Intensive Care Units (ICU), because it is a safe test for both the patient and the team, and can be performed frequently at the bedside by adequately trained PICU professionals, including physiotherapists, allowing non-invasive monitoring of progression and response to therapeutic interventions accurately, quickly, safely and dynamically.<sup>35</sup> Although the authors cannot comment on the sensitivity, specificity or reliability of POCLUS in this context, as post-intervention images were not compared with chest X-Ray findings, owing to ethical and resource limitations, and between-rater comparison was not made, previous studies have reported that lung ultrasound is highly reliable both sensitive and specific in identifying and quantifying pathological changes, including atelectasis. 12, 21 Although further

studies are needed, this study supports the feasible and potential utility of using POCLUS to determine short-term responses to chest physiotherapy interventions.

In addition to the evaluation, the LUS<sup>24</sup> was used to quantitatively classify the POCLUS image before and after respiratory physiotherapy interventions in both groups. Adult and neonatal clinical practice experts have suggested that clinical evaluation plus semi-quantification of ultrasound scores can be used as a tool to quantify peripheral lung aeration and clinical severity of the patient.<sup>36</sup> This approach is based on the hypothesis that the lower the peripheral lung expansibility (areas visualized by the POCLUS), the fewer lung areas will be available for gas exchange.<sup>37</sup> Therefore, it is expected that the clinical manifestations of these pulmonary alterations will be more severe.

Faced with this hypothesis, a retrospective study, <sup>37</sup> including 74 children from zero to 12 months of age, diagnosed with bronchiolitis, and admitted to PICUs, developed a simple and rapid score that combines clinical data (presence of wheezing and reduced oral intake) and ultrasound data (involvement of the right posterior upper pulmonary zone) to predict, during the first evaluation, the need for hospitalization in the PICU, as well as the indication of ventilatory support with CPAP (continuous airway pressure).

However, one of the limitations of the study was the absence of patients on IMV.

In the present study, although there were large within-group effect sizes, no significant between-group differences were observed in the clinical (WD)<sup>25</sup> or Ultrasonographic (LUS)<sup>24</sup> scores before versus after respiratory physiotherapy intervention. This suggests that both IG and CG interventions were associated with an improvement in pulmonary imaging (partial or total resolution of pulmonary atelectasis) and in the children's breathing patterns. The magnitude of the treatment effect was, however, greater in the intervention group, suggesting that the protocolized intervention may be more effective at resolving atelectasis in mechanically ventilated children. This requires confirmation in a larger sample study.

The application of mechanical thoracic vibration in the IG may have been one of the factors related to the better findings in the reduction of WD and LUS scores in this group. The natural frequency of ciliary beats in mammals is 13 Hz, an increase in bronchial clearance is observed when vibrations reach frequencies between 11 and 15 Hz. <sup>38</sup> In the range between 20 and 45 Hz, vibration produces relaxation of the respiratory muscles, verified by a decrease in respiratory rate and an increase in tidal volume. <sup>38</sup> The mechanical vibration apparatus used in the study provides a continuous frequency of 50 Hz and, therefore, may have been one of the factors related to the better findings in the intervention group. Bilan et al. <sup>15</sup> used mechanical vibration in some patients in their study for 10 to 20 minutes, and there was no comparison between the interventions or the description of the frequency in Hz used.

Another intervention included in the SRPP, which may have influenced the resolution of pulmonary atelectasis, is the stretching of the accessory respiratory muscles. The stretching of a muscle fiber promotes an increase in the number of sarcomeres in series. The addition of muscle strength due to stretching is possibly due to the better interaction between actin and myosin filaments. Thus, the stretching of the respiratory muscles may have helped in the better performance of the inspiratory and expiratory muscles and increased thoracic expansion and may have contributed to the improvement of respiratory mechanics and to an increase in lung volumes.

Another intervention included in the SRPP, which may have contributed to better results in the intervention group, is manual hyperinflation with a self-inflating bag performed in a standardized manner. Regarding the form of MH application, only one study<sup>17</sup> explained how the intervention was

applied (first, slow insufflation, followed by an inspiratory pause of two to three seconds, followed by rapid pressure release), and was performed in the same way in the present study, with the objective of promoting an increase in Peak Expiratory Flow (PEF), displacing secretion to the central airways and simulating the effect of coughing. As a safety measure to avoid baro and volutrauma, both the present study and the studies by Galvis et al. A Herrada et al. Used a manometer during MH to limit Peak Inspiratory Pressure (PIP) between 30–35 cm H<sub>2</sub>O.

Regarding the safety of the interventions proposed by the SRPP, vital signs are important, as they allow the rapid identification of clinical deterioration of patients before, during, or after physiotherapy interventions.  $^{29}$  In the present study, vital signs in both groups were statistically similar before and after respiratory physiotherapy. It was not necessary to interrupt the interventions in any of the groups, demonstrating that they do not cause risks of clinical deterioration (bradycardia or tachycardia, tachypnea, drop in SpO<sub>2</sub> or changes in blood pressure) to the patients included in the study, being safe in this context. The retrospective study by Herrada et al.  $^{17}$  also reported that the respiratory physiotherapy interventions were well tolerated and that although all patients presented with tachycardia after the interventions, none of them presented with significant hemodynamic consequences that required medical intervention.

Among the limitations of this study are: a) The SRPP was performed only once, and the patient was not followed up after 30 minutes. Therefore, it was not possible to evaluate maintenance of any clinical or ultrasound improvements, nor the impact on meaningful clinical outcomes such as duration of IMV or PICU length of stay; b) The US findings were not compared to chest X-Ray, so you cannot comment on sensitivity or specify or the tool in this context; c) Variables with several subvariables did not allow comparison due to the number of cases; d) Due to COVID-19, one of the PICUs in the institution where the study took place was closed, due to the low demand of pediatric patients during this period, making it possible to reach the planned sample size of the study, but over a longer period of data collection.

There are still challenges to be faced for the implementation of POCLUS in the routine of physical therapists, such as the provision of skills training, mentoring, and support from experienced mentors. It is a tool that can optimize the functional diagnosis made by the physiotherapist, as well as guide the interventions that may be proposed. Further research is needed to identify the impact of the inclusion of ultrasound in the clinical decision-making of physiotherapists.

It is suggested that SRPP be applied to larger samples and with longitudinal follow-up to confirm its benefits in the medium and long term, as well as to compare component interventions to identify which one has the greatest impact on the resolution of pulmonary atelectasis in children on IMV.

# Conclusion

This study has shown that the Structured Respiratory Physical Therapy Protocol appears to be safe and may be effective in improving airway clearance and lung re-expansion in children on IMV with unilateral pulmonary atelectasis.

## Abstract

# Background

Upper-lung field <u>pulmonary fibrosis</u> (upper-PF), radiologically consistent with pleuroparenchymal fibroelastosis (PPFE), was reported to develop in patients with a history of <u>asbestos</u> <u>exposure</u> and <u>tuberculous pleurisy</u>, indicating that chronic <u>pleuritis</u> is correlated with upper-PF

development. Round <u>atelectasis</u> reportedly emerges after chronic <u>pleuritis</u>. This study aimed to clarify the association between round <u>atelectasis</u> and upper-PF.

#### Methods

We examined the radiological reports of all consecutive patients with round atelectasis between 2006 and 2018 and investigated the incidence of upper-PF development.

## Results

Among 85 patients with round atelectasis, 21 patients (24.7%) were confirmed to finally develop upper-PF lesions. Upper-PF was diagnosed after round atelectasis recognition in more than half of the patients (13/21, 61.9%), whereas upper-PF and round atelectasis were simultaneously detected in the remaining 8 patients. At the time of round atelectasis detection, almost all patients (19/21, 90.5%) had diffuse pleural thickening and round atelectasis was commonly observed in non-upper lobes of 19 patients (90.5%). Fourteen patients had round atelectasis in unilateral lung, and the remaining 7 patients had round atelectasis in bilateral lungs. Among all 14 patients with unilateral round atelectasis, upper-PF developed on the same (n = 11) or both sides (n = 3). Thus, upper-PF emerged on the same side where round atelectasis was present (14/14, 100%). The autopsy of one patient revealed a thickened parietal-visceral pleura suggestive of chronic pleuritis. Subpleural fibroelastosis was also observed.

## Conclusions

Upper-PF occasionally develops on the same side of round atelectasis. Upper-PF may develop as a <u>sequela</u> of chronic pleuritis.

## Introduction

Pleuroparenchymal fibroelastosis (PPFE) is a rare form of bilateral idiopathic interstitial pneumonia characterized by pleural-parenchymal involvement [[1], [2], [3], [4]]. In addition, PPFE pathologically corresponds to subpleural atelectasis [1,5]. Recently, upper lung field pulmonary fibrosis (upper-PF) radiologically consistent with PPFE has been reported to develop after lung cancer surgery as a late complication on the operated side [[6], [7], [8]]. Notably, almost all patients who later developed upper-PF had pleural effusion on the operated side [6], and this pleural effusion accompanied pleural thickening, which was suggestive of chronic pleuritis. Another study showed that patients with asbestos exposure or tuberculous pleurisy also developed upper-PF [9]. These results indicate that chronic pleuritis correlates with the development of upper-PF [6,9].

Round atelectasis is the retraction and folding of the lung associated with retractile fibrosis of the visceral pleura [10] and usually develops due to asbestos exposure [11,12]. However, round atelectasis can also develop in conjunction with tuberculosis, parapneumonic effusions, pulmonary embolization, and Dressler's syndrome [13]. These reports indicate that round atelectasis is closely correlated with chronic pleuritis [[11], [12], [13]]. Because the development of both round atelectasis and upper-PF seems to be correlated with chronic pleuritis, patients with round atelectasis may develop upper-PF. To verify this hypothesis, we conducted a retrospective study to assess the incidence of upper-PF throughout the clinical course among patients with round atelectasis.

Effect of ultrasound-guided transversus abdominis plane block in reducing atelectasis after laparoscopic surgery in children: A randomized clinical trial

## Abstract

# Background

Atelectasis is a commonly observed postoperative complication of general anesthesia in children. Pulmonary protective ventilation strategies have been reported to have a beneficial effect on postoperative atelectasis in children. Therefore, the present study aimed to evaluate the efficacy of the ultrasound-guided transversus abdominis plane (TAP) block technique in preventing the incidence of postoperative atelectasis in children.

#### Materials and methods

This study enrolled 100 consecutive children undergoing elective laparoscopic bilateral <a href="https://example.com/hernia-repair">hernia</a> repair and randomly divided them into the control and TAP groups. Conventional lung-protective ventilation was initiated in both groups after the induction of general anesthesia. The children in the TAP group received an ultrasound-guided TAP block with 0.3 mL/kg of 0.5% <a href="mailto:ropivacaine">ropivacaine</a> after the induction of anesthesia.

#### Results

Anesthesia-induced atelectasis was observed in 24% and 84% of patients in the TAP (n = 50) and control (n = 50) groups, respectively, before discharge from the post-anesthetic care unit (T3; PACU) (odds ratio [OR], 0.062; 95% confidence interval [CI], 0.019–0.179; P < 0.001). No significant difference was observed between the control and TAP groups in terms of the lung <u>ultrasonography</u> (LUS) scores 5 min after <u>endotracheal intubation</u> (T1). However, the LUS scores were lower in the TAP group than those in the control group at the end of surgery (T2, P < 0.01) and before discharge from the PACU (T3, P < 0.001). Moreover, the ace, legs, activity, cry and consolability (FLACC) pain scores in the TAP group were lower than those in the control group at each postoperative time point.

# Conclusion

Ultrasound-guided TAP block effectively reduced the incidence of postoperative atelectasis and alleviated pain in children undergoing <u>laparoscopic surgery</u>.

Keywords

Ultrasonography

Nerve block

Pulmonary atelectasis

Postoperative pain

Children

Glossary

ASA

American Society of Anesthesiologists

**CONSORT** 

**Consolidated Standards of Reporting Trials** 

**ERAS** 

# enhanced recovery after surgery

**FLACC** 

face, legs, activity, cry and consolability

HR

heart rate; LUS, Lung ultrasonography

MAP

mean arterial blood pressure

**PACU** 

post-anesthetic care unit

**PPCs** 

postoperative pulmonary complications

TAP

transversus abdominis plane

SpO2

<u>pulse oximetry</u> or pulse <u>oxygen saturation</u>

## 1. Introduction

<u>Inguinal hernia</u> is a common disease observed in the <u>pediatric</u> population. The advances in the field of enhanced <u>postoperative recovery</u> in recent years have led to <u>laparoscopic surgery</u> becoming the treatment of choice for pediatric inguinal hernias. Laparoscopic surgery is associated with several advantages, such as rapid postoperative recovery, minimal bleeding, and light systemic stress response. However, owing to the elevation of the diaphragm [1], the establishment of laparoscopic <u>pneumoperitoneum</u> results in a decrease in the compliance of the respiratory system [2], an increase in the <u>airway resistance</u>, and a decrease in the <u>functional residual capacity</u>. Therefore, anesthesiologists should carefully consider the incidence of perioperative <u>atelectasis</u> in children undergoing laparoscopic surgery.

Atelectasis is a respiratory complication that is commonly observed following general anesthesia. Children are more susceptible to developing respiratory complications, such as atelectasis, after the induction of general anesthesia than adults. This may be attributed to the higher chest wall compliance, higher airway resistance, poorer lung compliance, and lower functional residual capacity observed in children. The formation of atelectasis leads to a gas exchange disorder, which leads to <a href="https://www.hypoxemia">hypoxemia</a> and other postoperative pulmonary complications (PPCs) [3,4]. The incidence of perioperative atelectasis in children has been reported to be as high as 68–100% [5], [6], [7]].

Rapid and accurate diagnosis of atelectasis is essential for improving <u>respiratory function</u> in children and reducing the incidence of perioperative pulmonary complications. Lung <u>ultrasonography</u> (LUS), a convenient and noninvasive imaging modality that does not involve radiation, has become an ideal bedside tool for monitoring the changes in <u>lung ventilation</u> during the <u>perioperative</u> <u>period</u> [[8], [9], [10]].

Several factors influencing the incidence of pulmonary complications, such as atelectasis caused by laparoscopic surgery, are related to general anesthesia [11], CO<sub>2</sub> pneumoperitoneum [12], and postoperative analgesia [13]. The transversus abdominis plane (TAP) block inhibits the afferent nerve fibers between the transversus abdominis and internal oblique muscles, thereby achieving an analgesic effect via the blockade of nerve conduction of the sensory nerves in the anterior abdominal wall. Thus, TAP can be used to achieve postoperative analgesia after abdominal surgery in children [14,15]. Friedrich et al. [16]. reported that the administration of lowdose fentanyl significantly reduced the incidence of postoperative respiratory complications. Based on the findings of the abovementioned studies, it was hypothesized that ultrasound-guided TAP block may provide effective postoperative analgesia and reduce the use of opioids, thereby decreasing the incidence of atelectasis in children. Therefore, this randomized controlled trial aimed to verify the effect of ultrasound-guided TAP block on atelectasis and other outcomes in children undergoing laparoscopic surgery.

#### 2. Methods

# 2.1. Study population

This study was conducted at the Xinhua Hospital affiliated with Shanghai Jiaotong University School of Medicine. The study was approved by the local ethics committee (XHEC-SHDC-2021-102) and registered with the Chinese Clinical Trial Registry (ChiCTR- 2100053928, principal investigator: S.L.; date of registration: December 2, 2021) before commencing patient enrollment. Written informed consent was obtained from the parents or guardians of the participants prior to commencing the trial. The study was conducted in accordance with the Consolidated Standards of Reporting Trials (CONSORT) guidelines.

Children aged 1–6 years with an American Society of Anesthesiologists (ASA) physical status of I or II who underwent laparoscopic bilateral <a href="hernia repair">hernia repair</a> were eligible for inclusion in this study. The exclusion criteria were as follows: a history of chronic or acute pulmonary pathology, contraindication for receiving <a href="hernia">TAP block</a>, uncorrected <a href="congenital heart disease">congenital heart disease</a>, known allergy to <a href="maintenance-american method">amide local anesthetic drugs</a>, and liver and <a href="hidney dysfunction">kidney dysfunction</a>. The exit criterion was the <a href="maintenance-american method">surgical method</a> changing from laparoscopy to <a href="maintenance-american method">laparotomy</a>.

# 2.2. Randomization and blinding

The children were randomly allocated to the TAP block and control groups at a 1:1 ratio using a simple randomization procedure (computerized random number; <a href="https://www.randomizer.org">https://www.randomizer.org</a>) by a researcher who was blinded to the study. The randomization sequence was placed in sealed opaque envelopes, which were opened by an experienced anesthetist who performed the block and <a href="anesthesia induction">anesthesia induction</a>. The anesthetist did not participate in other aspects of the trial. A resident anesthetist blinded to the randomization collected the intraoperative data. An opaque patch was placed on the block site after the surgery such that the physician who performed the ultrasound examination and collected the postoperative data in the PACU was blinded to the group allocation.

# 2.3. Anesthesia and ventilation protocol

Monitoring of the electrocardiogram, blood pressure, and <u>oxygen saturation</u> was initiated when the children entered the operating room. All children underwent standard <u>general anesthesia</u> induction and <u>endotracheal intubation</u> as per the protocol, including 100% pre-oxygenation, <u>intravenous injection</u> of 3 mg/kg of <u>propofol</u> and 1 µg/kg of <u>fentanyl</u>, and <u>neuromuscular blockade</u> with 0.6 mg/kg of <u>rocuronium</u>. The children were intubated using an endotracheal tube with an

appropriately sized cuff after the <u>induction of anesthesia</u>. Ventilation was performed in the volume control mode (GE, Carestation 620, USA). Anesthesia was maintained via the administration of <u>sevoflurane</u> in a mixture of oxygen and air. The <u>tidal volume</u>, positive end-expiratory pressure, and inspired oxygen concentration were set at 8 ml/kg, 5 cm H<sub>2</sub>O, and 40%, respectively. The respiratory rate was adjusted such that end-tidal carbon dioxide was maintained at 35–45 mmHg. Patients who spontaneously breathed room air after <u>extubation</u> were transferred to the PACU in the <u>supine</u> <u>position</u> for 1 h of observation. <u>Pneumoperitoneum</u> was maintained using CO2 at an intraperitoneal pressure of 9 mmHg, and insertion position of the exhaust pipe were the same for all patients.

# 2.4. Lung ultrasonography

LUS was performed at three time points: 5 min after endotracheal intubation (T1), at the end of surgery (T2), and before discharge from the PACU (T3). All LUS evaluations were performed by two anesthesiologists who had performed >50 pulmonary ultrasonographic examinations in the pediatric population using a portable ultrasound device (GE, Versana Active, USA) with an 8–13 MHz linear transducer. The chest was divided into 12 regions by dividing each hemithorax into six regions using three longitudinal (parasternal, anterior axillary, and posterior axillary) and two axial (one above the diaphragm and the other 1 cm above the nipples) lines. These 12 regions were scanned sequentially from right to left, cranial to caudal, and anterior to posterior [10,16]. Monastesse's modified LUS score was used to evaluate the severity of atelectasis [17]. B-lines and juxtapleural consolidation were the most common signs of atelectasis. All cases were assigned a score of 0–3, with each score indicating the following: 0, 0–2 B lines; 1 score,  $\geq$ 3 B lines or  $\geq$ 1 small subpleural consolidation separated by normal pleural lines; 2, multiple coalescent B lines or multiple small subpleural consolidation separated by irregular or thickened pleural lines; and 3, white lung or subpleural consolidation  $>1 \times 2$  cm). Anesthesia-induced atelectasis with a score of  $\geq$ 2 in any area was considered significant [5].

## 2.5. Technique of ultrasound-guided TAP block

An anesthesiologist with experience in pediatric ultrasound-guided nerve blocks performed TAP blocks under general anesthesia using a portable ultrasound device (GE, Versana Active, USA). An 8–13 Hz linear transducer was placed obliquely between the 12th rib and iliac crest and vertically scanned along the midaxillary line to the contralateral abdominal wall to locate the three layers of muscles (external oblique, internal oblique, and transversus abdominis muscles). After disinfection, the needle was inserted into the block site using the in-plane technique under sterile conditions. The needle tip was inserted into the space between the internal oblique and transversus abdominis muscles, and 0.3 ml/kg of 0.5% ropivacaine was injected after ensuring negative aspiration. Fig. 1 depicts an ultrasonographic image showing a hypo-echoic area owing to the diffusion and penetration of the liquid drug. Placebo drugs were not administered to the control group.

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Fig. 1. Ultrasonography of transversus abdominis plane block. (A) pre-injection; **(B)** post-injection. EOM, external oblique muscle; IOM, internal oblique muscle; TAM, transversus abdominis muscle.

A surgical <u>skin incision</u> was made 15 min after the completion of the TAP block. Fentanyl (0.5  $\mu$ g/kg) was administered every 2 min if the heart rate (HR) or <u>mean arterial blood pressure</u> (MAP) increased to >20% of the baseline value after skin incision until these parameters returned to within 20% of the

baseline value. The number of additional doses and frequency of fentanyl administration were recorded for both groups. The face, legs, activity, cry and consolability (FLACC) scale [18] was used to evaluate pain in both groups at the end of the surgery, 1 h postoperatively, and 4 h postoperatively. Fentanyl (0.5  $\mu$ g/kg) was administered as the <u>rescue analgesic</u> if the FLACC score was  $\geq$ 5. Vital signs, such as HR and oxygen saturation. were closely monitored and recorded.

# 2.6. Outcome variables and statistical analyses

The primary outcome measure was the incidence of significant atelectasis at T3. The secondary outcomes included the incidence of significant atelectasis at other predefined time points; pulmonary ultrasound scores at T1, T2, and T3; the FLACC scores at each postoperative time point; intraoperative and postoperative fentanyl supplemental doses; incidence of airway adverse events; and length of hospital stay. The incidence of adverse reactions to the TAP block, including bleeding and bruising at the puncture site and the incidence of postoperative nausea and vomiting, were also recorded.

# 2.7. Sample size

The sample size was calculated based on the data from previous studies. The incidence of atelectasis was reported to be as high as 94% in children undergoing magnetic resonance examination under tracheal intubation under general anesthesia in a previous study [6]. The sensitivity of LUS in the diagnosis of atelectasis is 88% compared with that of magnetic resonance imaging [10]. Children undergoing laparoscopic surgery were included in this study. An increase in the intra-abdominal pressure during pneumoperitoneum aggravates alveolar collapse, thereby increasing the incidence of atelectasis. Therefore, it was assumed that the incidence of atelectasis would be 90% and 60% in the control and TAP groups, respectively. The sample size was calculated to be 40 participants per group using PASS 2008 (version 8.0.16; NCSS Statistical Software, Keysville, Utah, USA), with an  $\alpha$  error of 0.05 and power of 90%. The required sample size was set to 50 individuals per group, considering a 20% attrition rate.

# 2.8. Statistical analysis

Data were analyzed using SPSS Statistics software (version 23.0, IBM, Armonk, NY, USA). The Kolmogorov–Smirnov test was used to evaluate the normality of the data. Continuous data are presented as mean and SD or median and interquartile range. Standard hypothesis tests (two-sided *t*-test or Mann–Whitney *U* test) were used to analyze the baseline characteristics and outcome parameters. Categorical data are presented as n (%) and were analyzed using the chi-squared test or <u>Fisher's exact test</u>. Repeated measures analysis of variance was used to perform intergroup comparisons of repeated measurement data. A P-value of <0.05 was considered statistically significant.

## 3. Results

A total of 100 children were enrolled in this study and randomly allocated to the control (n = 50) and TAP (n = 50) groups (Fig. 2). Table 1 presents the demographic characteristics of the patients. No significant differences were observed between the baseline characteristics of the two groups. The pneumoperitoneum time and ventilation time were similar in both groups.

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Fig. 2. Study flow diagram.

Table 1. Personal characteristics.

Empty Cell	Control group ( n = 50)	TAP group( n = 50)	P- value
Age,mean(SD),y	3.05 (1.14)	3.29 (1.36)	0.342
Sex (female/male)	14/36	20/30	0.146
Height, mean(SD), cm	100.08 (9.28)	99.42 (13.33)	0.775
Weight, mean(SD),kg	14.65(3.13)	14.33 (3.26)	0.616
BMI, mean(SD),kg/m <sup>2</sup>	14.57(2.12)	14.50(2.13)	0.875
ASA physical status, I/II	42/8	40/10	0.572
Capnoperitoneum duration, mean(SD), min	31.04 (3.45)	30.30 (3.32)	0.274
Mechanical ventilation duration, mean(SD), min	45.24 (4.03)	46.32 (4.75)	0.221

Data are presented as mean ± SD or number of patients (%). Chi-square or Fisher' exact tests: Sex; ASA physical status; *U* test: Age, and Capnoperitoneum duration; *t*-test: Height, Weight and Mechanical ventilation duration.

The incidence of significant anesthesia-induced at electasis at T3 in the TAP group was lower than that in the control group (24% vs. 84%; P < 0.001; odds ratio (OR) 0.062; 95% confidence interval (CI): 0.019–0.179). At electasis was observed in 16 and 44 children in the TAP (32%) and control (88%) groups, respectively (OR, 0.066; 95% CI, 0.019–0.198; P < 0.001) at T2 (Table 2). However, no significant differences were observed at T1 (84% vs. 76%; P = 0.454; OR, 0.606; 95% CI, 0.192–1.816).

Table 2. Comparison of intra and postoperative variables between groups.

Empty Cell	Control group ( n = 50)	TAP group ( n = 50)	P-value
Length of hospitalization, mean(SD), days	2.42 (0.65)	2.34 (0.57)	0.507
Minimum SpO₂ in PACU, mean(SD), %	95.26 (2.33)	98.76 (1.30)	< 0.001**
Intraoperative consumption of fentanyl, mean(SD), µg/kg	1.33 (0.24)	1.13 (0.22)	< 0.001**

Empty Cell	Control group ( n = 50)	TAP group( n = 50)	P-value
Consumption of rescue analgesia at t1, mean(SD), μg/kg	0.45 (0.15)	0.08 (0.18)	< 0.001**
Consumption of rescue analgesia at t2, mean(SD), μg/kg	0.08 (0.19)	0	<0.01*
Consumption of rescue analgesia at t3, mean(SD), μg/kg	0.03 (0.12)	0	0.08
The incidence of atelectasis at T1, n(%)	38 (76)	42 (84)	0.227
The incidence of atelectasis at T2, n(%)	44 (88)	16 (32)	< 0.001**
The incidence of atelectasis at T3, n(%)	42 (84)	12 (24)	< 0.001**

All data are presented as mean  $\pm$  SD or number of patients (%). P value was analyzed by Student-t test, Pearson chi-square test or Fisher's exact test. t 1: at the end of the operation; t 2: 1 h after the operation; t 3: 4 h after the operation. T 1: After endotracheal intubation; T 2: At the end of surgery; T 3: Before discharge from PACU. SpO<sub>2</sub>, <u>pulse oximetry</u>. PACU, postanesthesia care unit. \*P < 0.01 vs Control group. \*\*P < 0.001 vs Control group.

The LUS scores of the TAP group were compared with those of the control group at the three time points. The results are summarized in <u>Fig. 3</u>A. The LUS scores of the control group and TAP groups were similar at T1 ( $4.78 \pm 1.68 \ vs. \ 4.84 \pm 1.7$ , P = 0.86). However, the mean LUS score of the control group (8.64) was higher than that of the TAP group ( $8.48 \pm 2.45 \ vs. \ 7.12 \pm 1.65$ , P < 0.01) at T2. The difference between the LUS scores of the two groups became more evident at T3, and the LUS score of the control group was much higher than that of the TAP group ( $6.38 \pm 1.44 \ vs. \ 3.4 \pm 1.07$ , P < 0.001).

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Fig. 3. Box plot for the LUS and FLACC scores during the study. **(A)** A box plot of the LUS scores in each group. Three predefined time points: 5 min after endotracheal intubation (T1); at the end of surgery (T2); before discharge from PACU (T3). **(B)** The FLACC scores are shown as box plots. t1: at the end of the surgery; t2: 1 h after the surgery; t3: 4 h after the surgery. The thick line across the box represents the median, the ends of box represent the 25th and 75th percentiles, and the whiskers represent the range. \*P < 0.01 vs Control group. \*\*P < 0.001 vs Control group.

The FLACC pain scores of the two groups were measured at three time points: at the end of surgery (t1), 1 h postoperatively (t2), and 4 h postoperatively (t3) (Fig. 3B). The FLACC scores in the control group was significantly higher than those in the TAP groups at all time points (6 [6,7] vs. 3 [3,4],

P < 0.001 at t1; 4.5 [4,5] vs. 3 [2,3], P < 0.001 at t2; 4 [3,4] vs. 2 [2,3], P < 0.001 at t3). The intraoperative dose of fentanyl in the TAP group was significantly lower than that in the control group (P < 0.001; Table 2). The difference between the dose of fentanyl administered as an analgesic drug in the control and TAP groups gradually decreased over time. No significant differences were observed between the two groups at t3 (0.45 ± 0.15 μg/kg vs. 0.08 ± 0.18 μg/kg, P < 0.001 at t1; 0.08 ± 0.19 μg/kg vs. 0, P < 0.01 at t2; 0.03 ± 0.12 μg/kg vs. 0, P = 0.08 at t3). No statistically significant differences were observed between the two groups in terms of the length of hospital stay (P = 0.51; Table 2); however, the minimum SpO<sub>2</sub> in the TAP group during the stay in the PACU was higher than that in the control group (98.76 ± 1.3 vs. 95.26 ± 2.33, P < 0.001) when air was inhaled in the recovery room. No complications related to the nerve block were observed in either group.

#### 4. Discussion

This prospective, randomized controlled study revealed that ultrasound-guided TAP block effectively reduced the incidence of atelectasis and LUS scores in children after laparoscopic surgery. This finding indicates that better <u>postoperative analgesia</u> was achieved with a reduced dose of analgesics.

The risk factors for atelectasis in children can be categorized as patient-, anesthesia-, and surgery-related. Anesthesia-related factors mainly include postoperative analgesia and anesthetic drug residue [19]. Previous studies have shown that combined epidural analgesia improves lung function and prevents atelectasis more effectively than opioid analgesia [20,21]. The dose of fentanyl, a commonly used opioid, is associated with the incidence of postoperative atelectasis in a dose-dependent manner [16]. TAP block and epidural analgesia exert comparable analgesic effects after abdominal surgery [22]. Moreover, TAP block also reduces the dosage of fentanyl [23] and the incidence of opioid-related adverse effects on the respiratory system. Thus, it was speculated that the TAP block may reduce the incidence of postoperative atelectasis in children.

TAP block exerts analgesic effects over the skin, muscle, and parietal peritoneum of the anterior abdominal wall by inhibiting the anterior branches of T7-L1 spinal nerves [24]. Fredrickson et al. first reported the use of pediatric TAP block in 2008 and described the successful implementation of this technique in eight children undergoing inguinal hernia repair [25]. Ultrasonography has enabled the visualization of the anatomical structure of the abdominal wall using a high-frequency ultrasound probe. This has aided in improving the success rate and safety of puncture [26]. Ultrasound-guided TAP block has been applied increasingly in the field of pediatrics. Most pediatric studies on the TAP block have reported a reduction in opioid use and the postoperative pain scores, indicating its effectiveness. Sola et al. reported that ultrasound-guided TAP block provided effective postoperative analgesia in >95% of children undergoing hernia repair based on the FLACC score [14]. Carney et al. conducted a randomized, double-blind, placebo-controlled study of 40 children undergoing appendectomy and considered postoperative morphine consumption as the main experimental result. Ultrasound-guided TAP block, performed on the surgical side of the children using 0.3 ml/kg normal saline or 0.75% ropivacaine in their study [27], was found to reduce postoperative opioid consumption in pediatric patients. The FLACC score of the TAP group was lower than that of the control group at t1, t2, and t3 in the present study (P < 0.001). Furthermore, the fentanyl dose was found to be significantly lower in the TAP group than in the control group 1 h postoperatively (P < 0.01). These findings confirm the effectiveness of the TAP block in multimodal analgesia in children.

<u>Computed tomography</u> remains the gold standard for the clinical diagnosis of atelectasis; however, its use is limited owing to radiation exposure, difficulty in transporting the device, and other factors [28]. LUS has gradually become one of the most commonly used methods for the bedside diagnosis

of atelectasis in recent years owing to its advantages of accuracy, safety, and simplicity [10]. LUS can also be used to measure the severity of atelectasis, which could facilitate the formulation of personalized lung recruitment strategies [5,17,29] and the prediction of the incidence of PPCs [30]. The dorsal lung is the most frequent location of atelectasis in children in the supine position, which may be attributed to the influence of gravity [7]. Fig. 4 presents an LUS image depicting the changes in the dorsal lung of children in the two groups at three time points. Atelectasis was observed in >75% of patients after anesthesia-induced endotracheal intubation (76% and 84% in the control and TAP groups, respectively), and no significant difference was observed between the LUS scores of the two groups. This finding is consistent with those of previous studies, which reported that atelectasis caused by general anesthesia occurs within minutes of anesthesia induction [6,7,10]. The incidence of atelectasis increased further in both groups at the end of the surgery, which may be attributed to the establishment of a laparoscopic pneumoperitoneum. Elevation of the diaphragm, increased airway resistance, and decreased lung compliance increase the incidence of atelectasis. However, the LUS score of the control group was higher than that of the TAP group (P < 0.01). The LUS score of the TAP group was significantly lower than that of the control group before discharge from the PACU and the third LUS examination (P < 0.001). The FLACC pain scores of the TAP group were significantly lower than those of the control group at the end of the surgery and 1 h postoperatively (P < 0.001). Moreover, the cumulative consumption of fentanyl in the TAP group was markedly lower than that in the control group 1 h postoperatively (P < 0.01). These results suggest that effective postoperative analgesia was achieved and that the administration of low-dose fentanyl may reduce the severity of postoperative atelectasis.

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Fig. 4. Lung ultrasound images of one representative patient per group. **(A1-A3)** Control group; **(B1-B3)** TAP group. T1: 5 min after endotracheal intubation; T2: At the end of surgery; T3: Before discharge from PACU.

Laparoscopic hernia repair is a simple, fast, less invasive procedure. Moreover, it is associated with fast recovery. Thus, this approach is being used increasingly in the pediatric <u>day surgery</u> room, necessitating better postoperative analgesia and <u>pulmonary function</u> protection strategies. TAP block did not increase the length of hospital stay in the present study (P = 0.507). Moreover, the minimum  $SpO_2$  in the TAP group during the stay in the PACU was higher than that in the control group ( $98.76 \pm 1.3$  vs.  $95.26 \pm 2.33$ , P < 0.001) when entering PACU without oxygen inhalation after surgery. Furthermore, no TAP block—related adverse reactions or complications were observed in the TAP group.

Nevertheless, the present study has some limitations. First, follow-up LUS assessments were not performed after discharge from the <u>PACU room</u>. Consequently, the duration of postoperative atelectasis and its impact on lung function could not be determined. Moreover, the long-term LUS scores of the two groups of children could not be compared. Second, pain assessments were performed only at three time points: at the end of the surgery, 1 h postoperatively, and 4 h postoperatively. No additional pain remedies were administered, and the duration of TAP block analgesia and the presence of rebound pain were not evaluated. Lastly, this study included healthy children aged between 1 and 6 years. Thus, the results cannot be generalized to an older pediatric patient population or children with cardiac or pulmonary conditions. Therefore, further studies with

large sample sizes with different baseline comorbidities must be conducted to validate these findings.

In conclusion, the present study demonstrated that ultrasound-guided TAP block was effective in reducing the incidence of anesthesia-induced atelectasis. Moreover, it facilitated adequate pain control and decreased opioid consumption. Thus, TAP block could be administered as a part of multimodal analgesia after laparoscopic hernia repair to enhance postoperative recovery.

## **Ethics statement**

This study was reviewed and approved by [Ethics Committee of Xinhua Hospital Affiliated to Shanghai Jiaotong University School of Medicine], with the approval number: [XHEC-SHDC-2021-102].

All participants/patients (or their proxies/legal guardians) provided <u>informed consent</u> to participate in the study.

Data availability statement

The original contributions presented in the study are included in the article; further inquiries can be directed to the corresponding author/s.

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CRediT authorship contribution statement

**Siyuan Li:** Writing – original draft, Methodology, Formal analysis, Data curation. **Yan Wang:** Formal analysis, Data curation. **Yunqian Zhang:** Data curation. **Hui Zhang:** Formal analysis, Data curation. **Shenghua Wang:** Writing – original draft, Formal analysis, Data curation. **Ke Ma:** Formal analysis, Data curation. **Lai Jiang:** Supervision, Methodology, Conceptualization. **Yanfei Mao:** Writing – original draft, Methodology, Conceptualization.

The role of lung ultrasound for detecting atelectasis, consolidation, and/or pneumonia in the adult cardiac surgery population: A scoping review of the literature

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Abstract

Objectives

Postoperative pulmonary complications (PPCs) frequently occur after cardiac surgery and may lead to adverse patient outcomes. Traditional diagnostic tools such as auscultation or chest x-ray have

inferior diagnostic accuracy compared to the gold standard (chest computed tomography). Lung ultrasound (LUS) is an emerging area of research combating these issues. However, no review has employed a formal search strategy to examine the role of LUS in identifying the specific PPCs of <u>atelectasis</u>, consolidation, and/or pneumonia or investigated the ability of LUS to predict these complications in this cohort. The objective of this study was to collate and present evidence for the use of LUS in the adult cardiac surgery population to specifically identify <u>atelectasis</u>, consolidation, and/or pneumonia.

#### Review method used

A scoping review of the literature was completed using predefined search terms across six databases which identified 1432 articles. One additional article was included from reviewing reference lists. Six articles met the inclusion criteria, providing sufficient data for the final analysis.

## Data sources

Six databases were searched: MEDLINE, Embase, CINAHL, Scopus, CENTRAL, and PEDro. This review was not registered.

# Review methods

The review followed the PRISMA Extension for Scoping Reviews.

## Results

Several LUS methodologies were reported across studies. Overall, LUS outperformed all other included bedside diagnostic tools, with superior diagnostic accuracy in identifying atelectasis, consolidation, and/or pneumonia. Incidences of PPCs tended to increase with each subsequent timepoint after surgery and were better identified with LUS than all other assessments. A change in diagnosis occurred at a rate of 67% with the inclusion of LUS and <a href="transthoracic echocardiography">transthoracic echocardiography</a> in one study. Pre-established assessment scores were improved by substituting chest x-rays with LUS scans.

# Conclusion

The results of this scoping review support the use of LUS as a diagnostic tool after cardiac surgery; however, they also highlighted a lack of consistent methodologies used. Future research is required to determine the optimal methodology for LUS in diagnosing PPCs in this cohort and to determine whether LUS possesses the ability to predict these complications and guide proactive <u>respiratory supports</u> after <u>extubation</u>.

## Introduction

Open-heart surgery (OHS) is associated with numerous long-term benefits, including a reduction in cardiac-related symptoms, improved quality of life, and improved life expectancy. Whilst demonstrating long-term benefits, this surgery is not without risk, with reported 30-day mortality of 2–3% and 1-year mortality of approximately 6%. Common postsurgical complications include heart rhythm disturbances, delirium, and postoperative pulmonary complications (PPCs). 6,7

Dependent on the definition, the incidences of PPCs in patients undergoing a coronary bypass graft range from 5% to 90% and contribute significantly to increased hospital length of stay, intensive care unit length of stay, and increased morbidity and mortality.[9], [10], [11], [12], [13] For patients undergoing OHS, studies have reported that approximately two-thirds of patients who develop the specific PPC of acute respiratory distress syndrome (ARDS) will die, either within hospital

or within 1-month after discharge. <sup>14</sup> Long-term survival is also affected by PPCs, with postoperative pneumonia approximately halving a patient's 5-year survival after OHS. <sup>15</sup> PPCs also create a major economic burden on the healthcare system with healthcare costs doubling for patients undergoing cardiac surgery who develop ventilator-associated pneumonia. <sup>16</sup> Furthermore, studies have reported that up to 85% of PPCs occur within the first 3 days following a major surgery. <sup>17</sup> However, accurate diagnosis of PPCs in the early postoperative phase remains challenging due to the inferior diagnostic accuracy of traditional tools such as auscultation or chest x-ray (CXR) compared to the gold standard computed tomography (CT), <sup>18,19</sup> which is impractical and uncommonly used after these procedures. Additionally, when CT is used, it exposes patients to significant levels of ionising radiation. <sup>20</sup>

Over the past two decades, lung ultrasound (LUS) has been increasingly used by bedside clinicians in critical care settings as an imaging technique to identify lung pathology and PPCs. 21 LUS has demonstrated excellent diagnostic accuracy for a variety of pulmonary diseases and PPCs including pneumothoraces, pleural effusions, pneumonia, and pulmonary oedema. [22], [23], [24], [25], [26], [27] In addition to the growing use of LUS in the medical profession, this technique is gaining popularity in the field of physiotherapy to improve clinical assessments and guide individualised respiratory care. 28,29 In Australia, physiotherapists are often integrated within hospitals' multiprofessional surgical teams, providing preoperative education, early mobilisation, and respiratory management to prevent PPCs and restore function after surgery. Pulmonary complications predominantly treated by physiotherapists are more accurately diagnosed with LUS than traditional techniques. For example, LUS is more accurate than CXR or auscultation in diagnosing consolidation related to pneumonia<sup>26</sup>,[30], [31], [32] and is more accurate than CXR for detecting atelectasis.[33], [34], [35] However, limited access to LUS and inability to interpret LUS findings have been identified as barriers to uptake by physiotherapists as part of clinical decisionmaking.<sup>36</sup> Improving physiotherapists' access to LUS may allow them to identify PPCs earlier and provide timely, appropriate, and targeted respiratory management.

Emerging research is also investigating the use of LUS as a monitoring and predictive tool via lung aeration scores. For example, a 36-point aeration score has been developed that allocates a score of 0 (normal) to 3 (no aeration) across 12 defined lung zones, with lower scores indicating better aeration.[37], [38], [39] Lung aeration scores have demonstrated promising results in patients weaning from extended mechanical ventilation (>48 h duration), with a score of >17 predictive of postextubation distress.<sup>40</sup> In patients with respiratory failure from coronavirus disease (COVID-19), several studies have demonstrated that higher lung aeration scores strongly correlate with the requirement for invasive mechanical ventilation.[41], [42], [43] Despite the monitoring and predictive use of LUS in other patient cohorts, this has not yet been investigated in the cardiac surgery population.

Two reviews have previously described the broader use of LUS in this population. <sup>44,45</sup> Cantinotti et al. <sup>44</sup> provided an overview of the existing literature for the clinical application of LUS in cardiac surgery for identifying pulmonary complications that included pleural effusion, consolidation, pneumothoraces, diaphragmatic motion anomalies, and pulmonary oedema. Efremov et al. <sup>45</sup> provided a detailed methodology for LUS in the cardiac surgery population and reported the diagnostic and prognostic accuracy of LUS in identifying similar pulmonary complications, with the addition of pulmonary embolism. Both reviews highlighted the frequent occurrence of pulmonary complications following cardiac surgery and emphasised a lack of standardised protocols for LUS assessment to identify these. However, neither review included a formal search strategy to find existing literature examining the use of LUS for identifying PPCs in patients undergoing cardiac surgery. Therefore, by employing a formal search strategy, the aim of this scoping review is to collate

and present evidence for the use of LUS in the adult cardiac surgery population to specifically identify atelectasis, consolidation, and/or pneumonia.

#### Abstract

CT-body divergence limits the accuracy of electromagnetic navigation bronchoscopy(ENB) in peripheral lung lesions diagnosis. Finding one effective and safe method to eliminating CT-body divergence may improve ENB accuracy. Thus, we developed a modified ENB which combining intraprocedural CT guided Navigation with Ventilatory strategy for Atelectasis to eliminate CT-body divergence. We called it inCTNVA-ENB. We present the case of an 80-year-old female with peripheral pulmonary nodule (without bronchial direct connection). She underwent inCTNVA-ENB, and the navigation probe accurately reached 6mm next to the target lesion without complications. The operation time was 42 minutes, and rapid on-site evaluation showed adenocarcinoma cells. CT data revealed the CT-body divergence caused by atelectasis was reduced.

#### 1. Introduction

Electromagnetic navigation bronchoscopy (ENB) is an important tool for the diagnosis and treatment of respiratory diseases, and the accuracy is 70 %–83 % [1]. The presence of CT-body divergence is responsible for the accuracy limitation, which associated with atelectasis and CT data bias [2].

To eliminate CT-body divergence, we firstly proposed a modified ENB strategy, which combining intraprocedural CT guided Navigation with Ventilatory strategy for Atelectasis. And we called it as **in**traprocedural **CT** guided **N**avigation with **V**entilatory strategy for **A**telectasis (inCTNVA). Here, we present a case of inCTNVA-ENB with satisfied result.

## 2. Case presentation

One 80-year-old female visited our center for chest CT revealing pulmonary nodule. CT data showed one  $1.2 \times 0.8$ cm ground glass opacity (GGO) in left upper lobe. Three years ago, this lesion had been discovered by chest CT examination, and she received percutaneous biopsy. But biopsy results indicated benign tumor. The size of lesion increased from  $0.6 \times 0.6$ cm to  $1.2 \times 0.8$ cm (Fig. 1).

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Fig. 1. CT data showed one  $1.2 \times 0.8$ cm ground glass opacity (GGO) in left upper lobe.

She rejected percutaneous biopsy and surgical resection to obtain pathological diagnosis. The patient was healthy before, without any chest trauma or surgery history, no smoking and drinking history. The routine examinations were normal, including coagulation function.

After signing informed consent, the patient underwent inCTNVA-ENB as follows.

- 3. inCTNVA-ENB procedure
  - 1)

Preoxygenation with  $60 \% \ \text{FiO}_2$  to avoid absorbent at lectasis.

2)

After deep general anesthesia and tracheal intubating with 8.5mm endotracheal tube, we implanted the bronchoscope.

• 3)

Keeping Positive End-expiratory Pressure (PEEP) at  $40 \text{cmH}_2\text{O}$  for 40 seconds, and repeated it 4times to reverse intubation induced atelectasis. Then, we set up oxygenation with  $60 \% \text{ FiO}_2$  to ensure blood oxygen saturation >92 %.

4)

To keep breath holding at peak inspiration and minimize the change in lung volume, we manually used the Adjustable Pressure Limiting (APL) valve at the end of inspiration to maintain the circuit pressure at 25cm  $H_2O$  PEEP.

• 5)

Performing CT scan and completed ENB after the navigation paths planning. On the transverse plane, navigation system showed the probe located 0.6cm outside center of target (Fig. 2A and B).

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Fig. 2. A. and B. show the position of ENB probe and targeted lesion(green ball). C. Chest CT showed navigation probe reached 6mm outside target lesion. D.Rapid on-site evaluation showed adenocarcinoma cells. E. Postoperative pathological section showed adenocarcinoma in situ.(For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

• 6)

Performing CT scan again to confirm the location of ENB probe. CT data is consistent with the result in step 5 (<u>Fig. 2</u>C). Then we performed rapid on-site evaluation (ROSE) to obtain pathological diagnosis (<u>Fig. 2</u>D).

It took a total of 42 minutes from step 1 to step 6. And ROSE showed adenocarcinoma. Subsequently, the patient immediately underwent video-assisted thoracoscopy pulmonary wedge resection. The intraoperative rapid frozen section examination and postoperative pathological diagnosis were adenocarcinoma in situ (Fig. 2E).

## 4. Discussion

ENB is a practical tool that combines electromagnetic navigation, virtual bronchoscopy and 3D CT imaging techniques to achieve real-time navigation and precise location of pulmonary lesions. However, this technology is based on static CT data for virtual reconstruction, which may inevitably cause bias in lesions navigation, namely CT-body divergence, one of the main reasons affecting the accuracy of ENB [3].

Atelectasis is one important cause of CT-body divergence, which is related with prolonged intubation, unsatisfactory ventilation protocols, and high ratio of inspired oxygen. Previous studies have shown that atelectasis may presented within 5 minutes after general anesthesia, which is manifested as blurred signals in ultrasound and shift of lesions, affecting the identification of actual location of the

lesions [2]. Therefore, the use of specific ventilation strategy may reduce atelectasis. Salahuddin et al. and Michael A. Pritchett et al. have proposed a series of bundle strategies during anesthesia bronchoscopy to prevent intraprocedural atelectasis [4,5]. However, there have been no studies focusing on the prevention of atelectasis in ENB examination.

In addition, CT data bias is another cause of CT-body divergence. According to literatures, CT data used to plan navigation paths is usually collected several days before surgery, when patient is conscious and in the end deep inspiratory. However, patients are under anesthesia state and mechanical ventilation during ENB, there are differences in the actual lung volume comparing with pre-procedural CT data, which may cause CT-body divergence [1,[3], [4], [5]]. In addition, ENB need to place the bronchoscope into the endotracheal tube, which will inevitably increase the airway resistance, thus changing the anatomical position of the lung and further aggravating the CT-body divergence.

Regarding the above two points, we use CT data obtained after general anesthesia and bronchoscope implantation to plan the navigation path. And we keep pulmonary in a static and expansive state during ENB. At the same time, a special ventilation strategy to prevent atelectasis was combined to reduce the difference between the actual target nodule location and the navigation target.

In this study, to evaluate the impact of the specific ventilatory strategy on CT-body divergence induced by atelectasis, the relative distance of the target lesion between the CT data before ENB and the CT data after anesthesia intubation was calculated. For specific methods, we referred to the research of Chen [6]. This was done by aligning preENB-anesthesia CT scan pairs using the main carina as a common point of translation. Motion in the X direction equated to medial and lateral movement, motion in the Y direction equated to anterior and posterior movement, and motion in the Z direction equated to cranial and caudal movement within each patient. Then 3D points picture was drawn to display the lesion location (Fig. 3, supplementary material). When we applied the specific ventilatory strategy, the atelectasis almost disappeared and the target lesion shifting was significantly reduced.

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Fig. 3. The physical three-dimensional (3-D) motion of lesion by using the main carina as a common point of translation (red, green and blue dots represent the position of target lesion in preENB CT, anesthesia CT and postENB CT respectively), showing the accuracy improvement of inCTNVA-ENB.(For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

To our knowledge, inCTNVA is the first time that applying intraoperative CT data for ENB path planning, which is also the first practical and feasible strategy applying modified ventilatory method for atelectasis avoidance after anesthesia and tracheal intubation to eliminate the CT-body divergence. InCTNVA represents a safe and effective strategy of ENB in the diagnosis and treatment of pulmonary lesions, especially for the peripheral lesions without bronchial direct connection.

Background

<u>Atelectasis</u> negatively influences peripheral <u>bronchoscopy</u>, increasing CT scan-body divergence, obscuring targets, and creating false-positive radial-probe <u>endobronchial ultrasound</u> (RP-EBUS) images.

## **Research Question**

Can a ventilatory strategy reduce the incidence of atelectasis during <u>bronchoscopy</u> under <u>general</u> <u>anesthesia?</u>

# Study Design and Methods

Randomized controlled study (1:1) in which patients undergoing bronchoscopy were randomized to receive standard ventilation (laryngeal mask airway, 100% Fio<sub>2</sub>, zero positive end-expiratory pressure [PEEP]) vs a ventilatory strategy to prevent atelectasis (VESPA) with <u>endotracheal intubation</u> followed by a recruitment maneuver, Fio<sub>2</sub> <u>titration</u> (< 100%), and PEEP of 8 to 10 cm H<sub>2</sub>O. All patients underwent chest CT imaging and a survey for atelectasis with RP-EBUS bilaterally on bronchial segments 6, 9, and 10 after artificial airway insertion (time 1) and 20 to 30 min later (time 2). Chest CT scans were reviewed by a blinded chest radiologist. RP-EBUS images were assessed by three independent, blinded readers. The primary end point was the proportion of patients with any atelectasis (either unilateral or bilateral) at time 2 according to chest CT scan findings.

## Results

Seventy-six patients were analyzed, 38 in each group. The proportion of patients with any atelectasis according to chest CT scan at time 2 was 84.2% (95% CI, 72.6%-95.8%) in the control group and 28.9% (95% CI, 15.4%-45.9%) in the VESPA group (P < .0001). The proportion of patients with bilateral atelectasis at time 2 was 71.1% (95% CI, 56.6%-85.5%) in the control group and 7.9% (95% CI, 1.7%-21.4%) in the VESPA group (P < .0001). At time 2, 3.84  $\pm$  1.67 (mean  $\pm$  SD) bronchial segments in the control group vs 1.21  $\pm$  1.63 in the VESPA group were deemed atelectatic (P < .0001). No differences were found in the rate of complications.