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Original Article

## Lung Segmentation by Cascade Registration

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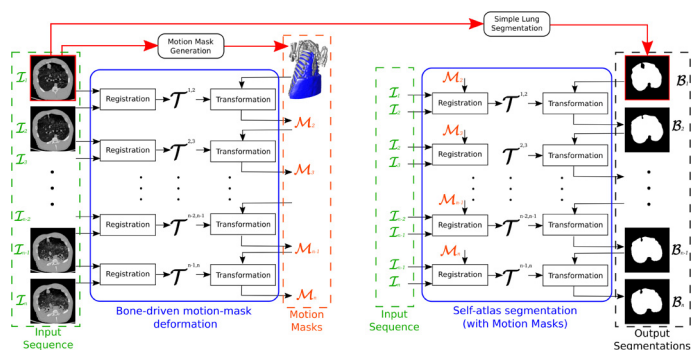
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### Graphical abstract



### Abstract

**Objectives:** The aim of this work is to delineate the lungs in three-dimensional image sequences of the same subject, with decreasing inhomogeneous contrasts, and to assess the applicability of the method to quantify the aeration in subjects diagnosed with acute respiratory distress syndrome (ARDS).

**Methods:** Assuming that the first, and most-contrasted, image of the sequence can be successfully segmented by an existing method, we propose to align the remaining images with the first one, using a cascade of successive registrations, and then to deform the initial segmentation, using a cascade of transformations. Because the lungs slide against the rib cage, the registration requires the use of motion masks that separate the moving organs from less moving ones. Nevertheless, while such masks can be relatively easily obtained in well-contrasted images, obtaining them in images locally lacking contrast is challenging. Our main contribution is the method proposed to generate appropriate motion masks for the entire image sequence despite the decreasing contrasts. This method also uses the principle of cascade registrations and transformations starting from an initial mask obtained in the most-contrasted image of the sequence.

**Material:** The entire segmentation method was applied to CT images of 16 piglets with induced ARDS, 20 through 35 images per piglet, acquired at varying mechanical-ventilation conditions.

**Results:** The processing time was less than 15 minutes/image, on average. Dice similarity index with an independent standard was of 0.963 globally, but clearly worse overlap was locally measured in the bottom-most region of the lungs (average Dice of 0.810), where the largest displacements and contrast variations were observed.

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**Conclusions:** The proposed method allows lung segmentation despite the loss of contrast, and can be used to quantify the lung aeration in subjects with ARDS. An improvement in the bottom-most region may be foreseen by combining gray-level based registration and anatomical-landmark matching.

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**Keywords:** ARDS; Computed Tomography; Segmentation; Image Registration; Cascade

## 1. Introduction

Acute respiratory distress syndrome (ARDS) presents a high mortality rate, estimated around 40% [1,2] and slightly decreasing over the past two decades [3] in intensive care units. ARDS may be the consequence of various pulmonary aggressions, e.g., bacteriological or chemical, such as pneumonia, chemical product aspiration, or extrapulmonary sepsis, and its main clinical manifestations are alveolar collapse, pulmonary oedema, and hypoxemia. During its treatment, the patient's breathing process is generally supported by mechanical ventilation, which uses a positive end-expiratory pressure (PEEP) in order to achieve alveolar recruitment, i.e., reopening collapsed alveoli and maintaining them opened. Although various ventilation protocols have been proposed and probed to reduce the mortality rate, mechanical ventilation should be adapted to each particular case, otherwise it may deteriorate the state of the patient [4]. Indeed, the principal ventilator settings, namely PEEP and tidal volume ( $V_t$ ), must be determined as a trade-off between maximizing the recruitment and oxygenation, and minimizing the ventilator-induced lung injury (VILI), which may occur due to over-distention of already opened alveoli and/or to periodic opening/closing of insufficiently recruited alveoli. In order to evaluate the state of the lungs, namely quantify the recruited as well as over-aerated pulmonary parenchyma, and assess the response of the lungs to mechanical ventilation, computed tomography (CT) images may be acquired and analyzed. Indeed, CT numbers are directly related to the quantity of air in each voxel of the pulmonary parenchyma [5]. Nevertheless, to quantify the aeration, the lungs must be previously delineated in each CT volume, which is a tedious and error-prone task if performed manually.

The objective of this work is to automate the segmentation of the lungs from CT-volume series, i.e., from three-dimensional (3D) images corresponding to the same subject diagnosed with ARDS, where each volume is acquired at different ventilation settings. Lung segmentation in CT images has been exhaustively studied for various applications, e.g., related to lung cancer and chronic obstructive pulmonary disease (COPD), where the parenchyma is well-contrasted with respect to the surrounding tissues, and opaque regions – if any – are focal. The methods devised for these applications will be referred to as “conventional” (see Section 2.1). Segmenting CT images of subjects with ARDS is much more challenging due to contrast loss resulting from large opaque regions (Fig. 1) that may vary in shape and size, depending on the ventilation settings. We propose a method based on 3D image registration, assuming that the series of CT images to be segmented contains one image

(say  $\mathcal{I}_1$ , typically acquired at inspiration with highest PEEP) that can be segmented using a conventional method (with interactive correction if necessary). The segmentation of the remaining images is obtained by deforming the lungs segmented in  $\mathcal{I}_1$ , according to transformations estimated in a cascade-registration process.

## 2. Related work

In this section, first, we present conventional, as well as advanced, approaches for lung segmentation (subsection 2.1) with a focus on work dealing with ARDS or similar images. Then, we describe state-of-the-art methods for lung registration (subsection 2.2).

### 2.1. Lung segmentation

In the literature, “lung segmentation” commonly refers to the delineation of the region wrapped by the pleura, which encompasses lung parenchyma together with pulmonary bronchi, vessels, and nerves. Lung segmentation in CT has many applications as a pre-processing step, e.g., to delimit the region of interest in applications such as airway segmentation [6], pulmonary vessel segmentation [7–9], and nodule detection [10–14]. In most of these applications the images present high contrast between lungs (low attenuation) and surrounding tissue (high attenuation). Conventional methods exploit these characteristics and use thresholding or region growing, together with mathematical-morphology operations to segment the lungs. The most used and cited conventional method was proposed in [15].

More sophisticated lung segmentation methods are needed to deal with large high-density regions appearing inside the lung in diseases and syndromes such as interstitial lung disease, fibrosis, atelectasis, and ARDS. In the interstitial lung disease, texture information may be used [16] to differentiate between surrounding tissues and pathological lung regions not reached by a conventional algorithm. An atlas approach was also proposed [17] to segment lungs with large dense pathological regions: first, lungs were manually segmented in a set of images referred to as atlas; then, to segment a new image, all the atlas images were registered to the new image; subsequently, transformations thus obtained were used to deform the lung masks from atlas images onto the new image, and the final result was deduced from these deformed masks by using a voting strategy. Applied to two ARDS cases, this method obtained a relatively low overlap (Jaccard index 0.58) against an independent standard. Nevertheless, [18] proposed a hybrid

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