Simultaneous Assessment of Airway Instability and Respiratory Dynamics with Low-Dose 4D-CT in Chronic Obstructive Pulmonary Disease: A Technical Note

Mark O. Wielpütz^{a, b} Ralf Eberhardt^{b, c} Michael Puderbach^{b, d, e}
Oliver Weinheimer^{a, b} Hans-Ulrich Kauczor^{a, b} Claus P. Heussel^{a, b, d}

^aDepartment of Diagnostic and Interventional Radiology, University Hospital of Heidelberg, ^bTranslational Lung Research Center (TLRC-H), Member of the German Center for Lung Research (DZL), ^cDepartment of Pulmonology and ^dDepartment of Diagnostic and Interventional Radiology with Nuclear Medicine, Thoraxklinik at University of Heidelberg, and ^eDepartment of Radiology, German Cancer Research Center (DKFZ), Heidelberg, Germany

Key Words

Chronic obstructive pulmonary disease · Tracheobronchial obstruction · Tracheomalacia

Abstract

Background: Advanced-stage chronic obstructive pulmonary disease (COPD) is associated with severely altered respiratory dynamics. Dynamic airway instability is usually diagnosed by invasive bronchoscopy. Cine-computed tomography (CT) may be used alternatively, but is limited to predefined anatomical positions. Also, a paradoxical diaphragmatic motion has been described in patients with emphysema. **Objectives:** As the airways and chest wall show inherently high contrast to airway lumen and lung tissue, low-dose CT acquisitions potentially suffice for depicting tracheobronchial and chest wall motion. Therefore, we propose low-dose dynamic respiratory-gated multidetector CT (4D-CT) of the whole chest as a new method to assess respiratory dynamics. **Methods:** 4D-CT was performed in 3 patients (52, 62 and 76 years old) with suspected tracheal instability due to COPD or tracheal stenosis at minimal pitch (0.09°) and radiation exposure (1.4–1.9 mSv) during regular tidal breathing registered by a belt system. Image reconstruction

involved a raw data-based iterative algorithm (1.5-mm slice thickness, 1.0-mm z-axis increment, 5% respiratory increment), resulting in a stack of 6,700 images, which were evaluated with a 4D-viewing tool. **Results:** An excessive dynamic collapse of the trachea in combination with tracheobronchomalacia (TBM) of the main-stem and segmental bronchi, and a paradoxical diaphragmatic motion were demonstrated in 1 case. Moreover, we detected a saber-sheath trachea and main-stem TBM in another case. The third case showed a fixed tracheal stenosis. **Conclusions:** 4D-CT provides unprecedented z-axis coverage and time-resolved volumetric datasets of the whole chest. Airway instability, stenosis and paradoxical diaphragmatic motion may be assessed simultaneously, preceding interventions such as airway stabilization or lung volume reduction.

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Introduction

Chronic obstructive pulmonary disease (COPD) has emerged to become one of the leading causes of morbidity and mortality worldwide. Respiratory dynamics in COPD may be severely impaired in advanced disease, which is a result of different patho-mechanisms [1–3]. It

has long been demonstrated that a chronic, progressive inflammation throughout the tracheobronchial tree may lead to malacia of cartilaginous airways, resulting in a collapse during the respiratory cycle, which often remains undiagnosed when employing pulmonary function testing only [3–5]. The diagnosis of tracheobronchomalacia (TBM) is traditionally made by invasive flexible bronchoscopy, and TBM has been reported in up to 44% of patients with chronic bronchitis [4]. TBM has to be differentiated from excessive dynamic airway collapse (EDAC), which is characterized mainly by a bowing of the posterior membranous part of the trachea [5]. Importantly, bronchoscopic examination and severity estimation is not standardized and is highly user-dependent. Also, an irregular and asynchronous movement of the chest wall and diaphragm has been demonstrated in advanced COPD, which is thought to result from emphysema. It is characterized by a paradoxical ventro-cranial displacement of the anterior parts of the diaphragm in inspiration, which can be observed by imaging only [6].

Thus, TBM has subsequently been assessed by paired inspiratory-expiratory computed tomography (CT) scans and dynamic cine-CT. These allow the quantification of the transverse luminal area, and a reduction to less than 50% has been defined as a diagnostic criterion [5, 7]. However, both techniques are either limited by the inherently static approach (glottis closed) or the short z-axis coverage, respectively.

The high contrast of airspace on the one side versus the airway and chest wall on the other allows for a dramatic reduction of the radiation dose necessary to depict dynamic airway collapse and chest wall motion in diagnostic quality. Moreover, iterative reconstruction algorithms now allow a further reduction of radiation dose while maintaining an acceptable contrast-to-noise ratio [8, 9]. The present report seeks to explain the feasibility, technical aspects and limitations of low-dose dynamic respiratory-gated multidetector CT (3D+t CT or 4D-CT) of the whole chest to simultaneously assess respiratory dynamics regarding: (1) instability of the airway tree and (2) diaphragmatic and chest wall motion in COPD.

Materials and Methods

Patient Data

Three COPD patients were evaluated by 4D-CT who, besides centrilobular emphysema, suffered from severe obstructive symptoms that did not respond to conservative treatment. The first was a 62-year-old patient suffering from end-stage COPD who had accumulated 30 pack years. He had also been recently diagnosed with

obstructive sleep apnea syndrome. Forced expiratory volume in 1 s (FEV₁) was 1.1 liters (40% predicted) and residual volume was 4.9 liters (198% predicted). The second was a 76-year-old male with end-stage COPD after smoking 30 pack years and thus receiving long-term oxygen therapy. His FEV₁ was 0.7 liters (27%) and residual volume was 5.9 liters (224%). The third patient was a 52-year-old male with suspected tracheal stenosis due to long-term ventilation after trauma 20 years ago. Before referral for surgery, 4D-CT was performed for surgery planning, detection of additional instability of the stenotic segment and investigation of the airways distal to the stenosis, which could not be examined by endoscopy since the stenosis could not be passed by the endoscope.

4D Multidetector CT Acquisition

The CT examination was clinically indicated for the evaluation of dynamic airway instability, and our patients initially received an instructed training over 5 min after being transferred onto the CT table in a supine position. After enough time to rest, the patients were asked to breathe calmly at a constant tidal volume and convenient respiratory rate. Respiratory movements were recorded by the respiration belt system provided by the CT manufacturer. Non-contrast-enhanced 4D-CT (Somatom Definition AS64®, Siemens Medical Solutions, Forchheim, Germany) was initiated with a dose-modulated protocol (CARE dose4D®) at the lowest possible pitch of 0.09 (head first and supine) and minimal exposure parameters, i.e. at a tube voltage of 80 kV and reference current-time-product of 10 mAs, and thin collimation of 16 × 1.2 mm. The scan duration was approximately 90 s.

Image Reconstruction and Evaluation

Reconstruction was performed with a slice thickness of 1.5 mm at 1.0-mm increments employing a raw data-based iterative reconstruction algorithm (SAFIRE® ‘strength’ 3, Siemens Medical Solutions) in a medium soft kernel (I40f). The full respiratory cycle was divided into steps each 5% wide, resulting in 21 separately reconstructed volumetric datasets. Each of these datasets represents a freeze frame of the whole chest at one point of the respiratory cycle. The system is able to compensate for minor variations in respiratory pace and depth. If the respiratory movements are not detected correctly by the system or if the registration curve shows single irregular movements, for example cough, the registration may be manipulated manually and steps with irregular movements may be removed before image reconstruction, in order to avoid motion artifacts (online suppl. fig. 1; for all online suppl. material, see www.karger.com/doi/10.1159/000357448). All 21 datasets per patient may each be reviewed separately for airway collapse. However, this is relatively cumbersome and the stack of 6,700 images cannot be handled easily with standard PACS solutions. Therefore, 4D viewing tools such as the ‘CT Cardiac Function’ provided with Syngo.Via® (Siemens Medical Solutions) are recommended and were used for image analysis. Video examples are provided with the online supplementary material.

Results

Feasibility

All three examinations had diagnostic quality with regard to the airways and chest wall, with acceptable image

Fig. 1. Multiplanar reconstructions of the trachea of the first patient in the axial (a, d), sagittal (b, e) and coronal plane (c, f), each oriented at the long axis of the trachea, showing the maximum (a–c) and minimum (d–f) lumen. The patient demonstrated excessive dynamic airway collapse during tidal breathing at the lev-

el of the aortic arch, mainly through a bowing of the posterior membranous part. This collapse occurred with the beginning of the expiratory phase. Lung and trachea volume were each quantified in every respiratory phase with in-house scientific software (YACTA; g).

noise even at the lung apex and base. Motion artifacts resulted mainly during the quick early inspiratory and expiratory phase, and were most emphasized in the lung base near the diaphragm, but were only mild altogether and did not impair diagnostic value. The resulting overall radiation dose equaled to a volume CT dose index of 3.1, 3.0 and 2.9 mGy, respectively, and a dose-length-product of 101, 135 and 110 mGy·cm, or approximately 1.4, 1.9 and 1.5 mSv.

Dynamic Airway Collapse

The first patient showed a dynamic expiratory collapse of the trachea at the level of the aortic arch, which was characterized mainly by a bowing of the posterior membrane (EDAC; fig. 1; online suppl. video 1). Below the tracheal bifurcation, respiratory displacement of the airways in the direction of the z-axis hampers diagnosis on axial images. Therefore, dynamic multiplanar reformats (MPR) oriented at the long axis of the respective airways were performed. Both main bronchi and the intermediate bronchus collapsed to less than 50% of the cross-sectional lumen area on multiple levels (fig. 2; online suppl. video 2, 3). Moreover, a collapse was found for multiple intrapulmonary airways (fig. 3).

Paradoxical Diaphragmatic Motion

For the first patient, emphysema quantification based on a previously performed full-dose MDCT revealed a relative low attenuation area below the threshold of –950 Hounsfield units of 16% of the entire lung (in-house scientific software YACTA [10, 11]). Diaphragmatic motion was analyzed in coronal and angulated sagittal MPR. Both hemi-diaphragms showed a paradoxical motion during tidal breathing, with a ventro-cranial displacement of the anterior parts during early inspiration (fig. 4; online suppl. video 4). Also, during early expiration, a subtle paradoxical outward movement of the chest wall could be appreciated.

Saber-Sheath Trachea

The second patient presented with a narrowing of the transverse diameter of the trachea resulting in a saber-sheath deformation. Although axial reconstructions suggested a dynamic collapse of the trachea, MPR showed that this was solely related to a z-axis movement during respiration (fig. 5; online suppl. video 5). However, this patient showed a dynamic collapse of the main-stem and intermediate bronchi similar to the first case.

Fig. 2. Multiplanar reconstructions of the right main and intermediate bronchus of the first patient in the axial (**a, d**), sagittal (**b, e**) and coronal orientation (**c, f**) with respect to its long axis, showing the maximum (**a–c**) and minimum (**d–f**) lumen during tidal breathing. A diffuse collapse to less than 50% of the cross-sectional area was found.

Fig. 3. Reconstruction of a segmental bronchus of the right inferior lobe for the first patient orthogonal to its long axis, showing its maximum (**a**) and minimum (**b**) lumen during the normal respiratory cycle, corrected for z-axis movement. A similar collapse could be observed for multiple intrapulmonary airways.

Tracheal Stenosis

The third patient showed a fixed tracheal stenosis distal to the glottis at the entry into the thoracic cavity. The subsequent trachea, main-stem and segmental bronchi did not suffer from stenosis or from a dynamic lumen collapse (fig. 6; online suppl. video 6).

Discussion

We demonstrated 3 cases with different entities of acquired tracheal disease: a combination of EDAC and dynamic TBM of subsequent airways related to COPD, fixed

saber-sheath trachea and dynamic TBM of the main-stem bronchi related to COPD, and postintubation fixed tracheal stenosis. All findings could be confirmed by flexible bronchoscopy, which is currently the standard of reference. Airway collapse contributes to morbidity of COPD patients and appropriate treatment may significantly alleviate symptoms [12]. The individual clinical relevance, however, remains largely unclear [13], which in part may be due to insufficiently standardized diagnostic tools. Endoscopic techniques are possibly influencing the extent of collapsibility and are inherently limited to the inner view of the lumen, and thus cannot depict the influence of extraluminal factors such as goiter or the aortic arch upon the tracheal collapsibility. Also, absolute quantification of length and extent of a collapse and stenosis is impossible using endoscopy, and exact localization with respect to anatomy of the airway tree and neighboring organs for surgery planning is limited.

Cine-CT without table feed (2D+t CT) during respiration has been described as having an equal diagnostic impact as bronchoscopy for tracheal instability, and should be preferred to static paired inspiratory/expiratory acquisitions [14–17], but has only very limited z-axis coverage. Importantly, the site of suspected collapse must be defined before commencing the scan. However, not only the trachea, but also the remaining tracheobronchial tree may be diffusely and unpredictably affected by instability and/or stenosis in COPD. Moreover, small-volume acquisitions, especially of the intrapulmonary airways, are often hampered by a respiratory movement of the airways in the direction of the z-axis, and the non-perpendicular

Fig. 4. Multiplanar reconstructions of the whole chest of the first patient in the coronal (**a, d**) and sagittal orientation through the right (**b, e**) and left (**c, f**) diaphragmatic dome for the end-inspiratory (**a–c**) and end-expiratory (**d–f**) phase during tidal breathing. A paradoxical diaphragmatic movement was evident on both sides, characterized by a ventro-cranial movement of the anterior parts of the diaphragm in inspiration (white arrows).

Fig. 5. Multiplanar reconstructions of the trachea of the second patient in the axial (**a, d**), sagittal (**b, e**) and coronal plane (**c, f**), each oriented at the long axis of the trachea, at end-inspiration (**a–c**) and end-expiration (**d–f**). The trachea showed a saber-sheath deformation and narrowing of the lumen but no dynamic collapse. An apparent dynamic instability as suggested by the axial view was due to z-axis movement.

course of the airways with regard to the image plane complicates quantification of the transverse area, such as demonstrated by our second case.

4D-CT as a new method combines the diagnostic capabilities of a dynamic time-resolved cross-sectional image

acquisition with all the postprocessing potential of a high-resolution volumetric dataset. This may only be harvested by viewing tools that can process extensive 4D data and allow for an objective quantification of airway collapsibility and lung volume. Thus, it may prove to have diagnostic

Fig. 6. Multiplanar reconstructions of the trachea of the third patient in the axial (**a**, **d**), sagittal (**b**, **e**) and coronal plane (**c**, **f**), each oriented at the long axis of the trachea, at end-inspiration (**a–c**) and end-expiration (**d–f**). The trachea showed a stenosis distal to the glottis. We did not observe a dynamic instability of the stenosis or the subsequent airway tree.

potential superior to bronchoscopy or cine-CT regarding airway instability. The alterations of diaphragmatic and chest wall motion as demonstrated in our first case have been assessed previously with dynamic magnetic resonance imaging only, but not with CT [18]. Respiratory dynamics including diaphragmatic motion could be new valuable parameters in planning and follow-up of lung volume reduction procedures [18–21]. Because of these advantages, 4D-CT has the potential to supplement bronchoscopy for the assessment of COPD patients, if no other indications than airway instability are present. Also, if bronchoscopy is technically limited, as in our third case, 4D-CT should be considered. Thus, it may reduce procedural morbidity and reduce costs related to bronchoscopy.

The low radiation dose applied with 4D-CT is comparable to combined static inspiratory-expiratory chest CT as it is currently being recommended in the routine work-up of COPD patients and has been used in previous studies [5, 22]. The limited prognosis of patients with advanced COPD on the one hand, and the additional diagnostic information on the other, have to be considered in this context as well. If radiation exposure is a concern, such as in young patients, magnetic resonance imaging may be considered as an alternative, albeit at the cost of spatial resolution [22].

A limitation, however, is that a diagnostic evaluation of the lung parenchyma regarding subtle changes is not pos-

sible with the 4D-CT datasets because of high noise. Moreover, forced breathing maneuvers (i.e. cough) are impossible with the current setup because temporal resolution is limited and regular breathing maneuvers are necessary. A pitch of 0.09 means, in turn, that one point of the lung is scanned for a maximum of 5.5 s [$19.2 \text{ mm (detector width)}/3.5 \text{ mm/s (table speed)}$], not taking respiratory displacement into account. At a respiration rate of 12/min the duration of one respiratory cycle averages 5 s. If the respiratory rate is lower than 12/min, e.g. with a long expiratory rest, gaps of missing image information will result.

In conclusion, 4D-CT of the whole chest is feasible at low-dose with the current state-of-the-art scanner technique, and we propose respiratory gated 4D-CT as a new non-invasive method to comprehensively assess respiratory dynamics. It may have a valuable diagnostic impact in phenotyping advanced COPD, and consecutively in planning and monitoring interventional therapy such as airway stabilization or lung volume reduction.

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