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Worsening respiratory function in mechanically ventilated intensive care patients: Feasibility and value of xenon-enhanced dual energy CT

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ABSTRACT

Objectives: To evaluate the feasibility and incremental diagnostic value of xenon-enhanced dual-energy CT in mechanically ventilated intensive care patients with worsening respiratory function.
Methods: The study was performed in 13 mechanically ventilated patients with severe pulmonary conditions (acute respiratory distress syndrome (ARDS), $n=5$; status post lung transplantation, $n=5$; other, $n=3$) and declining respiratory function. CT scans were performed using a dual-source CT scanner at an expiratory xenon concentration of 30%. Both ventilation images (Xe-DECT) and standard CT images were reconstructed from a single CT scan. Findings were recorded for Xe-DECT and standard CT images separately. Ventilation defects on xenon images were matched to morphological findings on standard CT images and incremental diagnostic information of xenon ventilation images was recorded if present.
Results: Mean xenon consumption was 2.95 l per patient. No adverse events occurred under xenon inhalation. In the visual CT analysis, the Xe-DECT ventilation defects matched with pathologic changes in lung parenchyma seen in the standard CT images in all patients. Xe-DECT provided additional diagnostic findings in 4/13 patients. These included preserved ventilation despite early pneumonia ($n=1$), more confident discrimination between a large bulla and pneumothorax ($n=1$), detection of an airway-to-pneumothorax fistula ($n=1$) and exclusion of a suspected airway-to-mediastinum fistula ($n=1$). In all 4 patients, the additional findings had a substantial impact on patients' management.
Conclusions: Xenon-enhanced DECT is safely feasible and can add relevant diagnostic information in mechanically ventilated intensive care patients with worsening respiratory function.

1. Introduction

Acute respiratory diseases are one of the leading causes of death and morbidity in critical care patients [1,2]. Frequently, an unexplained acute decline in respiratory function can be seen in these patients. In this scenario, chest CT is frequently used to identify potential causes of respiratory dysfunction.

An ideal imaging technique of the lungs should have high spatial resolution, presenting precise morphologic data of lung structures, and provide information about lung function simultaneously. Additionally, the imaging technique should be easy to handle, non-invasive, cost-effective and associated with as minimal radiation exposure as possible. At present, no single imaging modality satisfies all of these criteria. Standard non-contrast chest CT is commonly used to generate cross-sectional high resolution images of lung morphology. For functional imaging of the lungs, e.g. lung ventilation imaging, scintigraphic methods with lower spatial resolution are applied [3,4]. A potentially suitable but not widely used technique that provides information about both lung morphology and regional ventilation is magnetic resonance imaging (MRI) using inhaled, hyperpolarized gases [5,6]. However, MRI is time consuming, technically demanding and hardly applicable in intensive care patients.

Stable, non-radioactive xenon gas is radiopaque, and can therefore be used as a contrast agent to visualize ventilation in CT

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imaging. First attempts in xenon-enhanced pulmonary ventilation CT were made in the 1980s [7]. In recent years, dual-energy CT (DECT) has been introduced into clinical routine. When performed with a dual-source CT scanner, two X-ray tubes are run at different voltages, offering improved discrimination between different materials or tissue and contrast agent [8]. The feasibility of visualizing lung ventilation by xenon-enhanced dual-energy CT (Xe-DECT) has been demonstrated in spontaneously breathing patients [9]. Initial results have also shown the technical feasibility of Xe-DECT in mechanically ventilated patients in combination with iodine-enhanced perfusion mapping [10].

The purpose of this study was to assess the feasibility and safety of xenon-enhanced dual-energy CT in critically ill patients and to assess whether xenon ventilation imaging yields additional diagnostic information as correlated with standard chest CT images alone, derived from the same CT scan.

2. Materials and methods

2.1. Patients

The study was performed in 13 mechanically ventilated and sedated patients. Patients were recruited from an anesthesiological ICU unit, specialized on patients with ARDS and postoperative patients after transplantation or other major surgery. Inclusion criterion for the xenon-DECT was defined as worsening respiratory function as assessed by the referring physician.

The study was performed after ethics committee approval as a prospective, single-center study. All patients or their legal guardians provided written informed consent. As experimental studies yielded contradictory results on xenon action on cerebral blood flow [11,12] patients with known or suspected elevated intracranial pressure were excluded from the study.

2.2. Xenon ventilation

Xenon gas was provided by Air Liquide (Duesseldorf, Germany). After connection to a mechanical ventilator (Tangens 2C ventilator, EKU Elektronik, Leiningen, Germany), respirator settings were individually adjusted to the patients' ventilator settings on the intensive care unit. After ventilation with 100% oxygen to ensure proper denitrogenation (inspiratory oxygen fraction $\geq$ 99%), the automatic xenon dosing mode was started (using the electronically controlled EGAMIX-system of the ventilator), by setting the xenon-target concentration to 50%. CT scanning was performed during the wash-in phase, at an expiratory xenon concentration of about 30%. There were two reasons for choosing the wash-in phase at a xenon concentration of 30% for ventilation images. First, Xenon concentrations below 40% have been shown to be safe in conscious patients [13]. To allow for a potential translation of the protocol to conscious and spontaneously breathing patients, we did not want to exceed this concentration. Second, we postulated that even poorly ventilated lung regions will eventually saturate with xenon after prolonged xenon ventilation. Therefore, we expected an early, wash-in phase image acquisition to provide the best differentiation of pathologic and normal ventilation pattern. Directly after the CT scan, xenon wash-out was started by ventilation with 100% oxygen, until xenon was no longer detectable in the expiration. During the whole CT procedure, heart rate, ECG, arterial blood pressure and oxygen saturation were monitored continuously. Additionally, the ventilator continuously recorded inspiratory and expiratory oxygen, carbon dioxide and xenon fractions as well as airway flows and pressures.

2.3. Image acquisition

In this prospective study, the first 8 patients were examined on a first-generation dual source CT (DSCT) scanner (Somatom Definition DS, Siemens Healthcare, Forchheim, Germany). The following 5 examinations were performed on a second-generation DSCT system (Somatom Definition FLASH, Siemens Healthcare). Scanning was performed at full inspiration. For the first-generation DSCT scanner, acquisition parameters were: tube voltages, 140 and 80 kVp at 30 and 117 effective mAs, with attenuation-based tube current modulation; rotation time, 0.5 s; collimation, 14 mm $\times$ 1.2 mm; pitch, 0.7. For the second-generation DSCT scanner, acquisition parameters were: tube voltages, 140 kVp with a 0.1 mm tin filter and 100 kVp at 165 and 140 effective mAs, with attenuation-based tube current modulation; rotation time, 0.28 s; collimation, 128 mm $\times$ 0.6 mm; pitch, 0.55. The range of all CT scans included the whole lungs from apex to base. The tube currents had been adapted such that the CT dose index was identical at 5.37 mGy for both scanner protocols. Mean examination time was 11.0 s for the 64-slice DSCT protocol and 8.8 s for the 128-slice DSCT protocol.

2.4. Image reconstruction

Based on the acquired data of the dual-energy CT scan, color-coded distribution maps of xenon were generated on a dedicated workstation (Syngo MultiModalityWorkplace, MMWP, Siemens Healthcare, Erlangen, Germany) with specific Dual-Energy post-processing software, approved by the U.S. Food and Drug Administration. This software analyze the density values in the corresponding high and low energy CT datasets using a three-material decomposition algorithm to quantify and visualize the photo effect caused by xenon. Ventilation images were reconstructed with a slab thickness of 3 mm and a D30 reconstruction kernel. Additionally, standard CT images were derived from the CT datasets, reconstructed with a B30 kernel, 3 mm slice thickness and 1.5 mm increment. In order to obtain CT images resembling 120 kVp images of a single energy chest CT, average images were reconstructed with contributions of 70% from the 140 kVp dataset and 30% from the 80 kVp for the first generation scanner and equal contribution from both tubes for the second-generation scanner (spectra Sn140 kVp and 100 kVp). Overlay images were generated from the same data set by superimposing xenon ventilation images on the standard CT images.

2.5. Image analysis

Image reading was performed by two radiologists in consensus with 7 and 3 years' experience in thoracic imaging. Reading of the xenon ventilation maps was performed blinded to the standard chest CT images and ventilation defects and heterogeneities were recorded by lung lobes. Standard chest CT images were then carefully reviewed for any thoracic pathologies and findings of the ventilation maps as compared to the standard CT readings were classified as match (i.e. concordant ventilation defects with pathological findings in the standard CT images) or mismatch (i.e. differing patterns). Finally, ventilation images and standard CT images were viewed side-by-side and additional diagnostic information of the combination compared to findings of standard CT images alone was recorded, if present.

3. Results

3.1. Patient population

The patient population consisted of 13 patients aged 34–76 years (see Table 1). The principal diagnosis was ARDS in 5 patients.