



## Cardiothoracic Imaging

## To investigate dose reduction and comparability of standard dose CT vs Ultra low dose CT in evaluating pulmonary emphysema

Ciara O'Brien<sup>a,\*</sup>, Hong Kuan Kok<sup>a</sup>, Brendan Kelly<sup>a</sup>, Kanako Kumamaru<sup>b</sup>, Abhilash Sahadevan<sup>c</sup>, Stephen Lane<sup>c</sup>, Orla Buckley<sup>a</sup>

<sup>a</sup> Departments of Radiology, Tallaght Hospital, Dublin, Ireland

<sup>b</sup> Department of Radiology, Brigham and Women's Hospital, Boston, MA, USA

<sup>c</sup> Respiratory Medicine, Tallaght Hospital, Dublin, Ireland

## ARTICLE INFO

## Keywords:

Emphysema

COPD

Computed tomography (CT)

Dose reduction

Iterative reconstruction

## ABSTRACT

**Objectives:** The aim of this study was to investigate the extent of dose reduction and comparability of standard dose CT vs Ultra low dose CT in evaluating pulmonary emphysema.

**Methods:** Forty-nine patients with emphysema were recruited from a tertiary referral respiratory clinic. Each patient had a non-contrast Standard Dose (SD) and Ultra Low Dose (ULD) thoracic CT. The images were reconstructed using contemporary iterative reconstruction with a standard lung kernel. Lung volumes and emphysema severity was calculated using a commercially available automated densitometry segmentation package. The effective dose was calculated for both CT protocols.

**Results:** Automated densitometry calculated the total lung volume and percentage lung area of emphysema. The findings were highly comparable between ULD and SD protocols. A strong correlation was seen between ULD and SD images in measurement of total lung volume ( $R = 0.925$ ,  $p < 0.001$ ) and percentage lung involvement by densitometry ( $R = 0.940$ ,  $p < 0.001$ ). There is a 95% dose reduction with the ULD protocol, the mean effective dose is  $0.12 \pm 0.09$  mSv versus  $2.33 \pm 1.54$  mSv for the SD protocol.

**Conclusions:** ULD thoracic CT is a comparable protocol for the assessment of emphysema severity relative to standard dose CT. ULD CT is performed at a 95% dose reduction compared to SD CT.

## 1. Introduction

Emphysema, both in isolation and as a part of Chronic Obstructive Pulmonary Disease (COPD), is a major global health problem with an overall estimated worldwide prevalence of 7.6% [1]. Early diagnosis can facilitate identification of the disease phenotype and severity guiding treatment and management [2]. Diagnosis currently is spirometry based. There tends to be a big discordance between symptoms, spirometry and CT morphology of emphysema. GOLD staging is the classic method of defining disease severity, however; patients with the same GOLD stage may have differing disease phenotypes and therefore require more alternative treatment. Radiology provides a clear and detailed account of the phenotype and severity of disease and therefore in conjunction with spirometry is optimal for the quantification and description of the COPD. CT is non-invasive and provides detailed evaluation of the morphology of the emphysema and its distribution. CT can also detect other causes for symptoms such as; shortness of breath, cough or haemoptysis. In our CT protocol we included

calculations of densitometry and lung volumes, contributing added value to the evaluation of symptoms and treatment planning. Most patients benefit from medical therapy such as; bronchodilators, glucocorticoids and antibiotics for acute exacerbations while a smaller subgroup will benefit from more invasive lung volume reduction procedures [3]. CT guides cardiothoracic planning in this latter group.

This study demonstrates the added value of CT in the assessment of COPD and employs an ULD technique comparable to that of a combined dose from a PA and Lateral chest radiograph.

## 2. Materials and methods

## 2.1. Study design

We conducted a prospective single-arm study to compare Ultra low dose (ULD) and standard dose (SD) thoracic CT in the assessment of emphysema. Patients had a SD CT immediately followed by a ULD CT on separate breath holds. The patient demographics including BMI were

\* Corresponding author at: Tallaght Hospital, Dublin 24, Ireland.

E-mail address: [ciara.obrien@uhn.ca](mailto:ciara.obrien@uhn.ca) (C. O'Brien).

<https://doi.org/10.1016/j.clinimag.2018.10.012>

Received 5 June 2018; Received in revised form 11 October 2018; Accepted 12 October 2018

0899-7071/© 2018 Elsevier Inc. All rights reserved.

**Table 1**  
Patient demographics including smoking history, GOLD stage, exacerbations and BMI.

| No | Age | Gender | Pack years | No. of annual exacerbations | GOLD stage | BMI  |
|----|-----|--------|------------|-----------------------------|------------|------|
| 1  | 62  | F      | 20         | 2                           | C          | 22   |
| 2  | 84  | F      | 40         | 1                           | A          | 24.9 |
| 3  | 62  | F      | 45         | 1                           | A          | 21.4 |
| 4  | 64  | M      | 100        | 2                           | D          | 23.9 |
| 5  | 75  | F      | 30         | 3                           | D          | 28.4 |
| 6  | 47  | F      | 30         | 1                           | B          | 31   |
| 8  | 73  | F      | 50         | 2                           | C          | 28.2 |
| 9  | 66  | F      | 15         | 0                           | A          | 29.6 |
| 10 | 70  | F      | 0          | 4                           | C          | 28.1 |
| 11 | 80  | F      | 30         | 2                           | D          | 24.3 |
| 12 | 56  | M      | 50         | 0                           | A          | 34.6 |
| 13 | 57  | F      | 40         | 2                           | C          | 27.8 |
| 14 | 65  | F      | 0          | 0                           | A          | 21.2 |
| 15 | 82  | M      | 50         | 2                           | D          | 27.7 |
| 17 | 59  | M      | 60         | 3                           | C          | 28.2 |
| 19 | 70  | M      | 40         | 1                           | A          | 30.7 |
| 22 | 70  | M      | 15         | 2                           | C          | 22.1 |
| 23 | 61  | M      | 0          | 0                           | A          | 40.5 |
| 24 | 71  | M      | 50         | 1                           | A          | 23.5 |
| 25 | 72  | M      | 2          | 6                           | D          | 26.8 |
| 26 | 64  | F      | 55         | 0                           | B          | 44.1 |
| 27 | 59  | M      | 35         | 4                           | D          | 30.5 |
| 28 | 63  | F      | 80         | 2                           | D          | 61   |
| 29 | 61  | M      | 40         | 2                           | D          | 30.1 |
| 30 | 57  | M      | 40         | 4                           | D          | 23   |
| 31 | 77  | M      | 60         | 0                           | A          | 29.1 |
| 32 | 64  | F      | 20         | 3                           | C          | 32   |
| 33 | 75  | M      | 60         | 3                           | D          | 30   |
| 34 | 46  | M      | 35         | 3                           | D          | 29   |
| 35 | 75  | F      | 75         | 1                           | B          | 32   |
| 36 | 69  | M      | 50         | 3                           | D          | 30.9 |
| 37 | 68  | M      | 40         | 1                           | A          | 24.2 |
| 38 | 74  | F      | 30         | 0                           | B          | 26.8 |
| 39 | 63  | M      | 40         | 1                           | A          | 30.8 |
| 39 | 61  | F      | 40         | 3                           | D          | 32.9 |
| 41 | 66  | M      | 100        | 0                           | D          | 24.1 |
| 43 | 70  | M      | 60         | 3                           | C          | 30.9 |
| 44 | 49  | M      | 30         | 4                           | D          | 24   |
| 45 | 58  | F      | 40         | 6                           | D          | 24.2 |
| 48 | 54  | M      | 50         | 0                           | A          | 33.9 |
| 49 | 53  | M      | 40         | 0                           | A          | 18.7 |
| 50 | 76  | F      | 5          | 1                           | A          | 18.7 |

documented for each participant. The study was approved by the institutional review board and all patients gave informed consent. The study and manuscript were prepared using the STARD checklist [4].

## 2.2. Participants

Patients with a diagnosis of COPD were recruited from the respiratory medicine service in a tertiary referral university teaching hospital between September 2013 and June 2014 and underwent consecutive SD and ULD thoracic CT studies. Patients were eligible for inclusion if their age was > 20 years and if they had a diagnosis of COPD made by a respiratory physician. Exclusion criteria included previous lobectomy or pneumonectomy, new or known diagnosis of lung cancer, pneumonia and acute respiratory tract infection treated with antibiotics within the preceding 8 weeks of study recruitment. Pertinent demographics were recorded including smoking history, functional status and physiologic measurements of lung function were performed in a dedicated pulmonary laboratory. Fifty patients were prospectively recruited to the study, one subject was excluded following recruitment due to a new diagnosis of lung carcinoma made on the initial standard dose CT. Patient demographics are outlined in Table 1.

## 2.3. CT acquisition protocol

Patients were scanned on a multidetector CT system (Aquilion PRIME, Toshiba, Tokyo, Japan) using non-contrast SD and ULD scan protocols. Scans were obtained from the lung apex to the costophrenic angles in full inspiration. Patients were coached to perform similar inspiratory effort for both scan acquisitions. ULD acquisition was performed immediately following the SD acquisition on a separate breath-hold. The SD protocol used a tube potential of 120 kVp and with tube current modulation based on automated exposure control, pitch of 1.38, rotation time of 500 ms and an  $80 \times 0.5$  mm detector configuration with images reconstructed in 1 mm slice thickness. The ULD protocol used a tube potential of 120 kVp, tube current of 10 mA without dose modulation and pitch of 1.38 (yielding an effective output of 3 mAs), rotation time of 350 ms and an  $80 \times 0.5$  mm detector configuration with images reconstructed in 1 mm slice thickness volume. Both protocols were reconstructed with a standard FC54 lung kernel and a fourth generation adaptive iterative dose reduction using three dimensional processing technique (AIDR 3D, Toshiba) [5].

## 2.4. Measurements of emphysema severity

All studies were analysed by a subspecialty trained cardiothoracic radiologist with ten year experience who was blinded to clinical information. Both sets of CT studies were reviewed on a dedicated reporting workstation using commercially available proprietary lung analysis software (Lung Analysis V4.73, Toshiba) on diagnostic reporting monitors (Radforce, Eizo and Coronis Fusion 6MP LED, Barco). Fixed image window settings with a width of 1200 and level of  $-500$  were applied for image review (Fig. 1). Automated computerised densitometry assessment was performed by segmentation of the acquired volumetric data by analysing pulmonary contours and diseased segments based on CT attenuation values. The severity of emphysema was quantified by the low attenuation area percentage (LAA %). Hounsfield Units (HU) of  $-940$  was the baseline threshold used. This was chosen over the  $-950$  in other recent papers as this was our software manufacturers recommendation. We then performed additional assessments at  $-920$  and  $-960$  to determine if changing the threshold caused a significant difference in stratification by ULD versus SD. Visual maps indicating distribution of emphysema and calculated parameters including total lung volumes and percentage disease involvement were derived (Fig. 2). Emphysema severity by densitometry was further stratified based on the LAA involved into three groups – mild (< 10% lung area), moderate (10–20%) and severe (> 20%).

## 2.5. Dose estimation

Dose-length product measurements (DLP, mGy-cm) were recorded by the scanner following completion of all studies based on CT dose index volumes (CTDIvol). Dose estimates (E, in milliSievert (mSv)) were calculated using an ICRP chest conversion factor ( $E = DLP \times 0.014$ ) [6].

## 2.6. Statistical analysis

Mean scores for disease severity were calculated for automated emphysema scoring. Continuous data were expressed as mean  $\pm$  standard deviation where appropriate. Normality tests were initially performed using the Shapiro-Wilk test. Continuous data were subsequently analysed using one-way repeated-measures analysis of variance and paired *t*-tests. Between group correlation was performed using linear regression analysis and the intraclass correlation coefficient (ICC) using a two-way random effects model. The mean measurement bias was compared using Bland-Altman analysis.

The agreement of the severity category between two protocols was assessed by the kappa statistic.

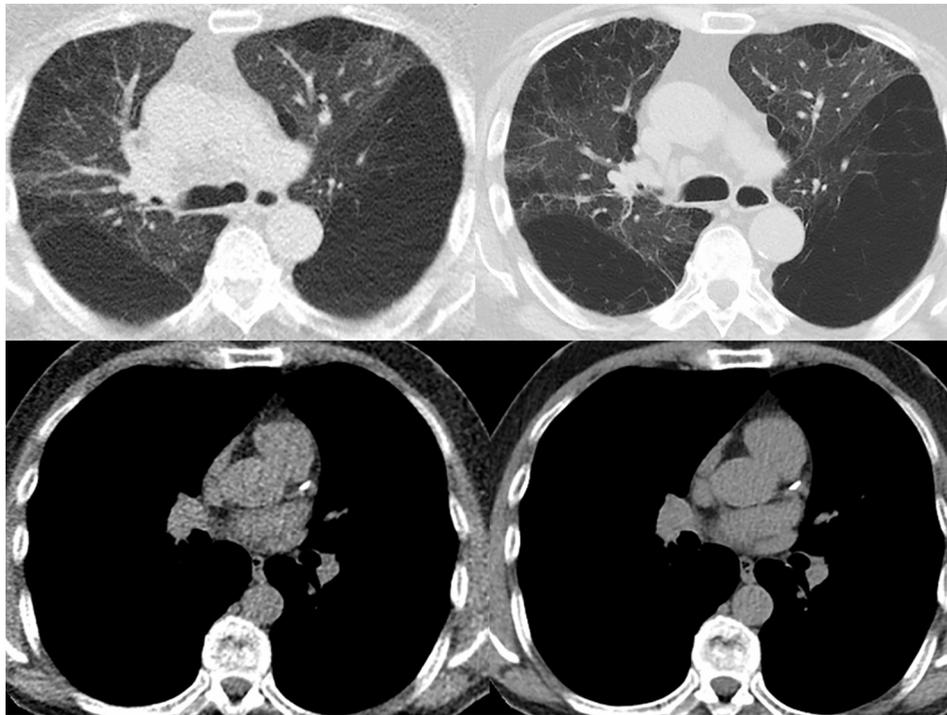


Fig. 1. Image example of an ULD CT versus a STD CT on lung and mediastinal windows.

As sensitivity analyses, we changed the threshold to define the low attenuation from  $-940$  HU to  $-920$  HU and  $-960$  HU, and performed the same analyses regarding LAA% to confirm if the main results were robust. Statistical analysis was performed in SPSS 16.0 (SPSS, Chicago, IL). A  $p$ -value of  $\leq 0.05$  was taken to represent statistical significance.

We also evaluated the effect of patient's BMI on the lung volume and the low attenuation area. The absolute percent difference in the lung volume and the absolute difference in LAA% between protocols were correlated with BMI by using Spearman's rank correlation coefficient.

### 3. Results

Forty-nine patients were enrolled into the study between September 2013 and June 2014. The mean age of our cohort was 64.7 (range 46–82) years and included 26 male and 23 female subjects. Mean

Table 2

Comparison between the SD and ULD CT protocol for the assessment of emphysema severity based on lung volume, automated threshold based segmentation of emphysema involvement and effective dose.

|  | SD          | ULD         |                 |
|--|-------------|-------------|-----------------|
| Total lung volumes (ml)                                | 5444 ± 1640 | 5569 ± 1613 | $p = 0.17$      |
| Emphysema severity by automated threshold segmentation |             |             |                 |
| Mean % lung area ± SD                                  | 21.4 ± 10.9 | 23.0 ± 9.8  | $p = 0.089$     |
| Mild (< 10%), $N$                                      | 9           | 4           | $\kappa = 0.63$ |
| Moderate (10–20%), $N$                                 | 13          | 13          |                 |
| Severe (> 20%), $N$                                    | 27          | 32          |                 |
| Effective dose (mSv)                                   | 2.33 ± 1.54 | 0.12 ± 0.09 | $p < 0.001$     |

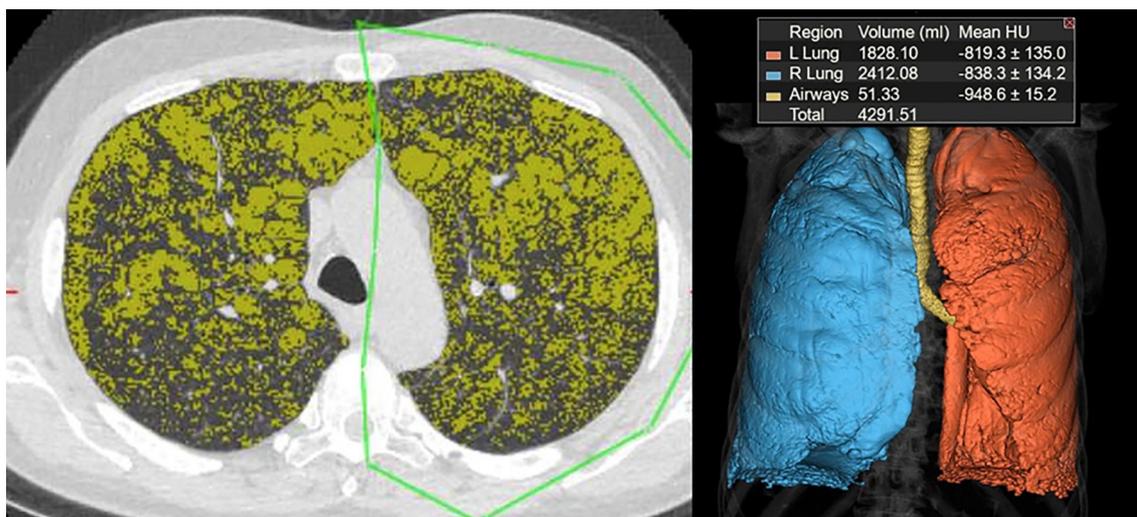


Fig. 2. Image example of the visual maps which indicate the distribution of emphysema and the calculated parameters including total lung volumes and percentage of disease involvement.

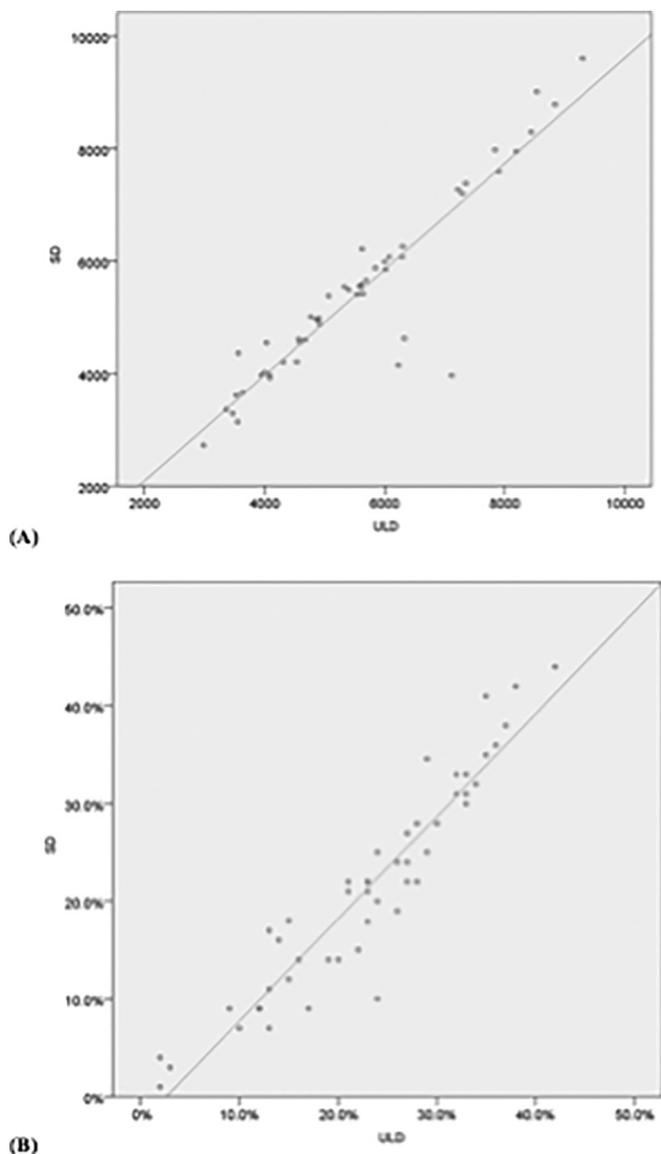


Fig. 3. Graph demonstrating strong and significant correlations between both SD and ULD protocols for both lung volume and LAA%.

smoking history was  $46.4 \pm 24.8$  pack years with an average of  $2.9 \pm 1.8$  acute exacerbations per year, see Table 1.

### 3.1. Comparison of ULD and SD acquisition

Table 2 shows the results comparing SD and ULD CT protocol for the assessment of emphysema severity based on total lung volume and automated threshold segmentation of LAA% involved by emphysema. There was no significant difference in mean lung volume. The agreement of the severity classification between SD and ULD was moderate ( $\kappa = 0.63$ ). However, overall mean LAA% was higher in the ULD compared to the SD acquisition protocol and more patients were classified into severe category when using the ULD protocol.

Using the SD protocol study as a reference standard, there were strong and significant correlations between both SD and ULD protocols, as shown in Fig. 3, for both lung volume ( $R = 0.925$ ,  $ICC = 0.924$ ,  $p$ -values  $< 0.001$ ) and LAA% ( $R = 0.940$ ,  $ICC = 0.926$ ,  $p$ -values  $< 0.001$ ).

Changing the threshold to define the low attenuation from  $-940$  HU to  $-920$  HU and  $-960$  HU had no significant impact on results with equivalent R ICC and  $p$  values.

The BMI was available for 40 of the 49 patients (mean  $28.8 \pm 7.4$ ). The BMI moderately correlated with the difference in the lung volume between protocols ( $\sigma = 0.44$ ,  $p = 0.004$ ). The findings related to BMI in this study are likely due to the cohort of patients recruited as they mostly had moderate to severe emphysema. The BMI is thought to have a greater impact on the ULD protocol results in patients with mild emphysema.

### 3.2. Radiation dose comparison between ULD and SD acquisition

There was a substantial dose saving with the ULD protocol with a mean effective dose of  $0.12 \pm 0.09$  mSv versus  $2.33 \pm 1.54$  mSv with the SD protocol ( $p < 0.001$ ). This represents a 95% decrease in absolute dose reduction over the standard CT thorax protocol.

## 4. Discussion

Emphysema remains one of the most prevalent smoking related lung diseases and accounts for a significant burden to healthcare systems globally. Description of the disease phenotype is an important factor in determining suitability for lung volume reduction surgeries. CT provides information on the multifactorial components of COPD including emphysema, air trapping and bronchial wall thickening. Measurement of emphysema severity using CT densitometry techniques have been established in the literature [7–9]. More recently, Ultra low dose techniques have been developed allowing thoracic CTs to be acquired in the sub-millisievert (mSv) range [10–12]. However, such techniques have not been widely applied to the assessment of emphysema severity by CT lung densitometry. In the current study ULD CT was compared to SD examinations performed on the same cohort. This methodology has been applied previously in similar research [10–12].

The advancements in multi detector CT technology over the past decade including high efficiency detectors, increased z-axis detector coverage, rapid tube rotation times, contemporary iterative reconstruction techniques and refinements in scan protocols have resulted in a major reduction in radiation dose to patients undergoing CT examinations [5,10,11,13]. With the ULD CT protocol utilised in our study combining a low mAs setting with AIDR3D iterative reconstruction, we have demonstrated that accurate measurements of lung volume and emphysema severity by automated densitometry can be achieved for the approximate equivalent dose of a combined posterior-anterior and lateral chest radiograph [14]. Our data support and complement related research in the field [15].

Due to the high intrinsic image contrast in pulmonary tissue, low mAs can be used with a fixed kVp and overall image quality can be relatively preserved. In our study, it was possible to reduce the tube current-time product to a fixed 3 mAs compared to approximately 40 mAs employed in low dose CT protocols from lung cancer screening studies [1,13]. When combined with a contemporary iterative reconstruction technique such as AIDR3D, the image quality in the ULD scan protocol was sufficient for accurate assessment of emphysema severity. Advanced iterative reconstructions allow improved signal to noise ratio, maintaining a diagnostic image quality, even at very low mAs compared to earlier generation iterative or filtered back projection techniques. There was a non-significant trend to overestimate mild emphysema severity on ULD images. Indeed 5 patients were upgraded from mild to moderate and from moderate to severe when moving from SD to ULD. If this was due to under-sampling (i.e. a type II error), it may have potential implications for the use of ULD for screening as it could upgrade some normal patients to mild disease. Further research is needed in the quest for an accepted threshold, which may cast additional light on the sensitivity and specificity of ULD compared to SD. No significant difference was seen for total lung volume estimation between both scan protocols.

It is acknowledged that patients with mild emphysema benefit from early detection and therapeutic intervention compared to those with

moderate-severe emphysema. Wang et al. studied a patient cohort where 4 of 60 patients had more than subtle emphysema [15] in comparison our case mix had more patients with moderate to severe emphysema which we believe is more reflective of this clinically important population. In practice, the ULD technique may be better utilised in the subtle-mild subgroup of patients with COPD.

CT densitometry has the ability to characterise emphysema predominant COPD as opposed to airway predominant or mixed disease. The good correlation of results from SD and ULD CT for assessment of emphysema suggests this protocol may have a role in the early detection of emphysema. We used a threshold segmentation value of  $-940$  HU to define low attenuation areas of emphysema, as this was the recommended default threshold by the manufacturer. In addition, to perform further sensitivity analyses the images were assessed using thresholds of  $-920$  and  $-960$  HU. Our aim was not to decide on an optimum cut off threshold for detecting emphysema but rather to compare two CT acquisition protocols at a fixed threshold. Indeed, the ideal CT threshold has not been established with different authors suggesting threshold values ranging from  $-910$  to  $-970$  HU [16–19].

The average BMI calculated for our population was  $28 \text{ kg/m}^2$ . The BMI was moderately correlated with the difference in the lung volume between protocols ( $\sigma = 0.44$ ,  $p = 0.004$ ), while the large difference in LAA% was not associated with higher BMI. The less than expected impact of body mass index on the correlation is likely secondary to the mean severity of disease in the region of 21–23% (SD-ULD) unlike the cohort in the Wang et al. study [15]. In the moderate-severe category the impact of photon starvation would be less than in patients with subtle or mild disease. The correlation of BMI and LAA% at SD and ULD was tested at the three thresholds without significant impact on the result.

#### 4.1. Study limitations

The automated densitometry was performed by one chest radiologist. While inter and intra observer agreement is well established in ULDCT techniques [10–12] repeated analysis by multiple radiologists may be helpful. These potential concerns are further mitigated by the automation of volume estimation process [15,16].

The ULD scans were acquired and analysed on a scanner from a single manufacturer and differing image quality results have been reported with different imaging protocols/reconstruction techniques from differing manufacturers [5,10,11,20]. Lee et al. described limitations in the assessment of emphysema with a ULD protocol utilising a tube current of 80 kVp and a sinogram-affirmed iterative reconstruction technique (SAFIRE), particularly in the upper lobes where assessment was limited by beam-hardening artefacts resulting from the shoulders [10]. Neroladaki et al. also previously reported difficulty characterising emphysema in their study which was based on a ULD protocol utilising a 100 kVp tube voltage and a model based iterative reconstruction (MBIR) [11]. We did not find this to be a problem with our ULD scan protocol which is based on a tube voltage of 120 kVp.

Our study, unlike other papers [21], did not include any normal controls which limits interpretation of results, especially when potentially attempting to generalise results to a screening population. While this limitation in study design lowers the level of evidence associated with the study, the results and potential patient benefits therein, contribute to the growing evidence base in favour of ULD techniques. As stated 5 patients were upgraded from mild to moderate and from moderate to severe when moving from SD to ULD which may be due to Type II error. A larger sample size may have mitigated against this. There are however potential benefits to over estimation when considering potential screening applications. Furthermore, especially when considering potential screening applications of the ULD technique, ULD decreases evaluation of soft tissues due to noise, which could limit the utility of the technique. Finally, in more subtle disease the higher BMI would have greater effect due to photon starvation potentially masking

subtle disease.

## 5. Conclusion

Our results demonstrate acceptable correlation between ULD and SD thoracic CT for assessment of lung volume and densitometry. Thus stratification of emphysema severity can be performed for the equivalent dose of a PA and lateral chest radiograph.

## Disclosures

This project was funded by a research grant of 25,000 euro which was awarded by the Meath Foundation a charitable foundation at Tallaght Hospital Dublin.

The funding was used to purchase the densitometry software from Toshiba Medical Systems.

Dr Orla Buckley was an invited speaker at the Toshiba Lunch time Symposium ESTI Amsterdam 2014.

No conflict of interests are associated with this original scientific work.

## References

- [1] Halbert RJ, Natoli JL, Gano A, Badamgarav E, Buist AS, Mannino DM. Global burden of COPD: systematic review and meta-analysis. *Eur Respir J* 2006 Sep;28(3):523–32.
- [2] Mannino DM, Buist AS. Global burden of COPD: risk factors, prevalence, and future trends. *Lancet* 2007 Sep 1;370(9589):765–73.
- [3] Agusti A. The path to personalised medicine in COPD. *Thorax* 2014 Sep;69(9):857–64. BMJ Publishing Group Ltd.
- [4] Bossuyt PM, Reitsma JB, Bruns DE, Gatsonis CA, Glasziou PP, Irwig L, et al. STARD 2015: an updated list of essential items for reporting diagnostic accuracy studies. *Radiology* 2015 Dec;277(3):826–32. Radiological Society of North America.
- [5] Yamashiro T, Miyara T, Honda O, Kamiya H, Murata K, Ohno Y, et al. Adaptive iterative dose reduction using three dimensional processing (AIDR3D) improves chest CT image quality and reduces radiation exposure. *Int J Radiat Oncol Biol Phys* 2014;98(3):e105735.
- [6] Deak PD, Smal Y, Kalender WA. Multisection CT protocols: sex- and age-specific conversion factors used to determine effective dose from dose-length product. *Radiology* 2010 Oct;257(1):158–66. Radiological Society of North America, Inc.
- [7] Cavigli E, Camiciottoli G, Diciotti S, Orlandi I, Spinelli C, Meoni E, et al. Whole-lung densitometry versus visual assessment of emphysema. *Eur Radiol* 2009 Jul;19(7):1686–92.
- [8] Gevenois PA, De Vuyst P, Sy M, Scillia P, Chaminade L, de Maertelaer V, et al. Pulmonary emphysema: quantitative CT during expiration. *Radiology* 1996 Jun;199(3):825–9.
- [9] Nishimura K, Murata K, Yamagishi M, Itoh H, Ikeda A, Tsukino M, et al. Comparison of different computed tomography scanning methods for quantifying emphysema. *J Thorac Imaging* 1998 Jul;13(3):193–8.
- [10] Lee SW, Kim Y, Shim SS, Lee JK, Lee SJ, Ryu YJ, et al. Image quality assessment of ultra low-dose chest CT using sinogram-affirmed iterative reconstruction. *Eur Radiol* 2014 Apr;24(4):817–26. (Springer Berlin Heidelberg).
- [11] Neroladaki A, Botsikas D, Boudabbous S, Becker CD, Montet X. Computed tomography of the chest with model-based iterative reconstruction using a radiation exposure similar to chest X-ray examination: preliminary observations. *Eur Radiol* 2013 Feb;23(2):360–6. Springer-Verlag.
- [12] Ju YH, Lee G, Lee JW, Hong SB, Suh YJ, Jeong YJ. Ultra-low-dose lung screening CT with model-based iterative reconstruction: an assessment of image quality and lesion conspicuity. *Acta Radiol* 2017 Aug 8;21:028418511772609.
- [13] Prasad SR, Wittram C, Shepard J-A, McLeod T, Rhea J. Standard-dose and 50%-reduced-dose chest CT: comparing the effect on image quality. *Am J Roentgenol* 2002 Aug;179(2):461–5. American Roentgen Ray Society.
- [14] Mettler FA, Huda W, Yoshizumi TT, Mahesh M. Effective doses in radiology and diagnostic nuclear medicine: a catalog. *Radiology* 2008 Jul;248(1):254–63.
- [15] Wang R, Sui X, Schoepf UJ, Song W, Xue H, Jin Z, et al. Ultralow-radiation-dose chest CT: accuracy for lung densitometry and emphysema detection. *AJR Am J Roentgenol* 2015 Apr;204(4):743–9. American Roentgen Ray Society.
- [16] Wang Z, Gu S, Leader JK, Kundu S, Tedrow JR, Sciruba FC, et al. Optimal threshold in CT quantification of emphysema. *Eur Radiol* 2013 Apr;23(4):975–84. Springer-Verlag.
- [17] Gevenois PA, de Maertelaer V, De Vuyst P, Zanen J, Yernault JC. Comparison of computed density and macroscopic morphometry in pulmonary emphysema. *Am J Respir Crit Care Med* 1995 Aug;152(2):653–7. American Public Health Association.
- [18] Gevenois PA, De Vuyst P, de Maertelaer V, Zanen J, Jacobovitz D, Cosio MG, et al. Comparison of computed density and microscopic morphometry in pulmonary emphysema. *Am J Respir Crit Care Med* 1996 Jul;154(1):187–92. American Public Health Association.
- [19] Madani A, Zanen J, de Maertelaer V, Gevenois PA. Pulmonary emphysema: objective quantification at multi-detector row CT—comparison with macroscopic and microscopic morphometry. *Radiology* 2006 Mar;238(3):1036–43.
- [20] Yuan R, Mayo JR, Hogg JC, Paré PD, McWilliams AM, Lam S, et al. The effects of radiation dose and CT manufacturer on measurements of lung densitometry. *Chest* 2007 Aug;132(2):617–23.
- [21] Messerli M, Ottlinger T, Warschkow R, Leschka S, Alkadhi H, Wildermuth S, et al. Emphysema quantification and lung volumetry in chest X-ray equivalent ultralow dose CT—individual comparison with standard dose CT. *Eur J Radiol* 2017 Jun 1;91:1–9.