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The utility of dynamic chest radiography in patients with asthma, COPD, COVID-19 and ILD: A pilot study

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ABSTRACT

Introduction and Objectives: Assessment of breathlessness requires a combination of imaging and lung function testing. Dynamic digital radiography (DDR) of the thorax is an imaging technique that allows physiological and anatomical information to be gathered at the time of chest X-ray and has the potential to significantly streamline diagnostic pathways. The aims of this study were to investigate the acceptability of DDR to patients and explore the correlation between DDR-derived measurements with lung volumes measured using full pulmonary function tests (PFT).

Materials and Methods: We conducted a single-centre, prospective, pilot study of patients with confirmed asthma, chronic obstructive pulmonary disease (COPD), interstitial lung disease (ILD) or post-COVID-19 infection. Participants underwent DDR and paired PFT between March 2021 and August 2022. Dynamic digital radiography acceptability was measured using a 10-cm visual analogue scale (VAS). Point estimates and exact confidence intervals were used to evaluate participant preference. Digital dynamic radiography would be considered acceptable if the lower bound of the 95% confidence interval (exact) is greater than 50%. Pearson correlation (r) was used to explore associations between DDR measurements and PFT parameters.

Results: 40 participants (asthma, $n = 11$; COPD, $n = 9$; ILD, $n = 11$; post-COVID, $n = 9$) had DDR with adequate image acquisition and PFT. Mean age of participants was 63.38 years (standard deviation 14.89) and 63% were male (25/40). The lower 95% confidence interval threshold for VAS acceptability was 92% for all groups combined and considered acceptable. The projected lung area at end inspiration (PLA_{insp}) closely correlated with total lung capacity across all disease cohorts ($r = 0.80$, $p < 0.001$) and projected lung area at end expiration (PLA_{exp}) was strongly correlated with residual volume in airways disease (COPD: $r = 0.87$, $p = 0.003$; asthma: $r = 0.85$, $p = 0.002$).

Conclusion: Dynamic digital radiography is an acceptable investigation for respiratory patients. DDR-derived measurements correlate with lung volumes obtained from PFTs. Larger studies are required to validate DDR as a possible method to identify and monitor air trapping in airways disease, allowing early detection and assessment of treatment effectiveness.

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KEYWORDS

Dynamic digital radiography; pulmonary function test; air trapping; novel biomarker; asthma

SUMMARY

Assessment of breathlessness requires a combination of imaging and lung function testing. Dynamic digital radiography (DDR) of the thorax is an imaging technique that allows physiological and anatomical information to be gathered at the time of chest X-ray and has the potential to significantly streamline diagnostic pathways. The aims of this study were to investigate the acceptability of DDR to respiratory patients and explore the correlation between DDR-derived measurements with lung volumes measured using full pulmonary function tests (PFT).

Our pilot study results demonstrate DDR is an acceptable investigation for patients with asthma, chronic obstructive pulmonary disease (COPD), interstitial lung disease (ILD) and post-COVID-19 infection (lower 95% confidence interval for visual analogue score acceptability was 92% for all groups combined). Furthermore, DDR-derived measurements correlate with lung volumes obtained

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from pulmonary function tests. The projected lung area at end inspiration on DDR (PLA_{insp})closely correlated with total lung capacity across all disease cohorts ($r = 0.80$,$p < 0.0001$) and projected lung area at end expiration (PLA_{exp}) was correlated with residual volume in airways disease (COPD: $r = 0.87$, $p = 0.003$; asthma: $r = 0.85$, $p = 0.002$).

Dynamic digital radiography may be an acceptable and simple method to identify and monitor air trapping and may facilitate earlier detection of airways disease.

Introduction

Early detection of chronic respiratory disease is necessary to improve patient outcomes.[1–4] Current diagnostic pathways utilising traditional methods of assessing breathlessness, including, pulmonary function testing (PFT) and imaging, such as chest X-ray (CXR) or computed tomography (CT) have notable limitations that contribute to delayed diagnosis. PFT is time-consuming, requires specialist respiratory physiologist supervision,[5] can be difficult for patients to perform and can have limited acceptability.[6] Therefore, despite the availability of PFT, it is often underused.[1,4] Furthermore, a normal CXR is unable to exclude underlying pathology, and more detailed cross-sectional imaging often requires significant exposure to ionising radiation.

Given these limitations, diagnosis is often delayed, reducing opportunities for early intervention. A simple test that can identify differences in breathing patterns associated with common respiratory conditions is desirable. Such a test would allow for focused follow-up investigations or negate the need for further investigations entirely and has the potential to streamline diagnostic pathways for breathlessness in the future.

Dynamic digital radiography (DDR) is a thoracic imaging modality in which sequential chest radiographs with high temporal and spatial resolution are taken throughout the respiratory cycle, providing physiological and anatomical data.[7] Dynamic digital radiography involves lower radiation exposure than CT scanning,[8] and takes little more time than a standard CXR.[9] Dynamic digital radiography provides a wealth of information about pulmonary function throughout the respiratory and cardiac cycles, including diaphragm movement,[10–16] changes in visible lung area,[15–20] and changes in X-ray translucency, which can be used to construct display maps indicative of perfusion[21–24] and ventilation[7,9,25–28] without the need for contrast agents.

Current evidence suggests there is a correlation between DDR-derived projected lung area at full inspiration (PLA_{insp}) and forced vital capacity (FVC) measured on spirometry in healthy individuals[20] and those with respiratory disease.[15–20] Furthermore, there is evidence that differences in DDR-derived measurements may be used to differentiate patients with obstructive and restrictive lung disease.[18] Further correlations between DDR-derived values and PFT in patients with respiratory disease are required to validate DDR's use in a clinical setting.

We conducted an observational pilot study to evaluate patient acceptability of DDR and investigate the correlation between DDR-derived measurements and pulmonary function test parameters in patients with a range of respiratory diseases (including asthma, chronic obstructive pulmonary disease (COPD), interstitial lung disease (ILD) and post COVID-19 infection).

Methods

Our prospective observational, single-centre study was approved by the Health Research Authority (West Midlands – Black Country Research Ethics Committee panel reference 20/WM/0032) and registered on the International Standard Randomised Controlled Trial Number (ISRCTN) database (ISRCTN14507847). Informed consent was obtained from all participants.

Study participants

Between March 2021 and August 2022, adult (≥18-years-old) patients attending Liverpool University Hospitals NHS Foundation Trust outpatient respiratory clinics with a clinically confirmed diagnosis of asthma, COPD, ILD, or post-COVID-19 infection who had completed or were due to complete PFT within 6 months were invited to participate.

All participants had a classical history, examination, and diagnostic testing of their respective disease group. Specifically, for the asthma group, bronchodilator reversibility, FEV_1 variability, or previous positive bronchial challenge test was considered diagnostic. For the COPD group, an FEV_1/FVC ratio less than 0.7 was considered characteristic. For ILD participants, a high-resolution CT (HRCT) with findings in keeping with ILD were necessary for inclusion, and for the COVID-19 group, a serologically confirmed diagnosis and CXR or CT changes in keeping with COVID-19 were required. Participants in the COVID-19 group were at least 12 weeks post recovery from the infection.

Patients with an acute exacerbation of respiratory illness, pregnancy, exposure to radiation (defined as more than 0.4 millisievert, mSv) for research purposes over the past 12 months, or more than one clinically significant respiratory condition were excluded. Urinary pregnancy testing was obtained from all women of child-bearing potential and local COVID-19 protocols were followed throughout image acquisition.

Study procedures

Standing postero-anterior (PA) and lateral DDR images were acquired using a dynamic radiography system (Konica Minolta Inc., Tokyo, Japan), comprising an AeroDR HD high sensitivity flat panel detector (Konica Minolta, Inc.) and a pulsed X-ray generator (DHF-155HII with Cineradiography option, Hitachi Medical Corporation, Tokyo, Japan).

All subjects were imaged in the standing position and using a 'deep breathing' protocol: participants were instructed to breathe normally for several tidal breaths before taking one forced deep breath to maximal inspiration then followed by full expiration. A graphical representation of the breathing protocol during image acquisition can be found in Figure 1. To minimise radiation exposure, all participants had a trial run of the breathing exercises immediately prior to image acquisition and a single attempt was made to capture satisfactory images.

The dynamic image data, captured at 15 frames per second (fps) for PA exposures and 6 fps for lateral exposures, were synchronised with the pulsed X-ray. The exposure time was approximately 10–15 s (s) depending on participant time to complete the breathing protocol. The entrance surface dose for dynamic digital radiography was approximately 0.3–1.0 milligray (mGy). The total radiation dose each participant

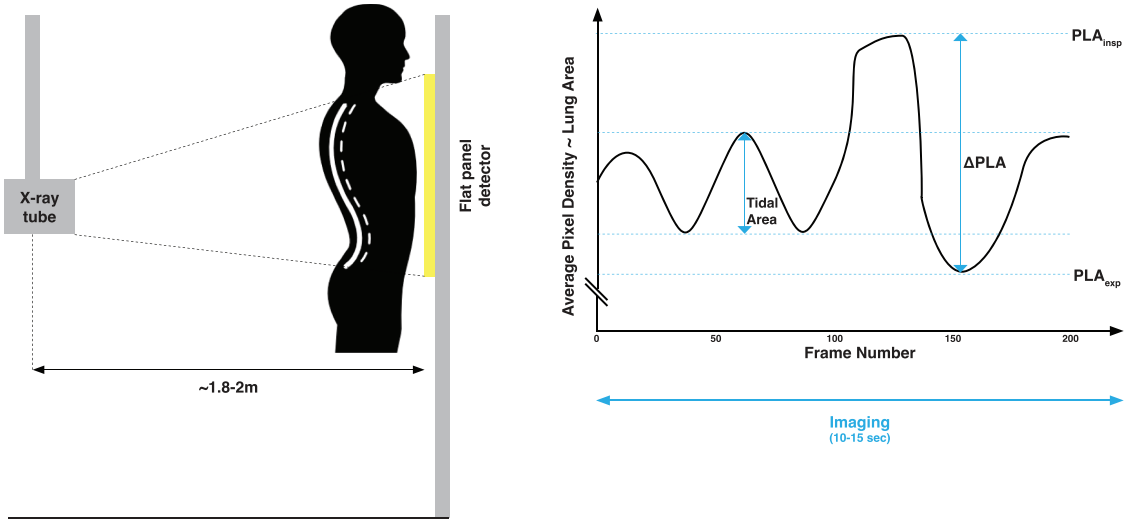

Figure 1. 'Deep breathing' protocol image acquisition.

received was 0.7 mSv, which is equivalent to approximately 12 weeks' additional exposure to background radiation. The exposure conditions are included in appendix 1.

Following DDR, participants were asked to assess the acceptability of the test and associated breathing manoeuvres by marking a cross on a 10 cm visual analogue score (VAS), with a range from 0, indicating "bad" to 10, indicating "good".

Image analysis

Anonymised imaging data acquired during DDR were analysed using proprietary software (Konica Minolta, Inc.), which calculated DDR-derived parameters automatically. Projected lung area (PLA) was generated through automatic tracing of lung borders, taking into account the left heart border, and can be charted throughout the respiratory cycle. Calculations at maximal inspiration (PLA_{insp}), at one second of expiration (PLA_{exp1}), maximal expiration (PLA_{exp}) and the difference between maximum and minimum PLA (ΔPLA) were made. Combined lung areas were calculated from PA exposures by summing the right and left projected lung areas using the DDR software. An example of PLA calculation at PLA_{insp} and PLA_{exp} using the proprietary software is shown in Figure 2. Automated mid-point hemi-diaphragm tracking calculated average diaphragm speed and diaphragm speed at 1 s of expiration. Images were independently reviewed by respiratory physicians (RR in-training with 5 years of experience and FF in-training with 4 years of experience) for accuracy and tracking errors were manually corrected. Demographic and clinical characteristics, including forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), TLC (total lung capacity) and RV (residual volume), were manually extracted from electronic patient records and the most recent pulmonary function test by study physicians (RR, FF and AN, in-training 4 years of experience).

Statistical analysis

As this was a pilot study, no formal sample size calculation was performed. Statistical analysis was performed with SAS (version 9.4) by RM with 28 years of experience. For our primary analysis, point estimates and 95% confidence intervals for the proportion of participants that describe the experience of undergoing DDR as acceptable (>5/10 on VAS) were calculated. Dynamic digital radiography would be considered acceptable if the lower bound of the 95% confidence interval (exact) is greater than 50%. A Pearson correlation (r) between the DDR-derived measurements and PFT parameters was calculated for all participants and disease groups. A p value of <0.05 was considered significant.

Results

In total, 49 participants underwent DDR, of whom 40 were included in the final analysis. Reason for exclusion is outlined in Figure 3. For the 40 participants included, the mean age was 63.38 years

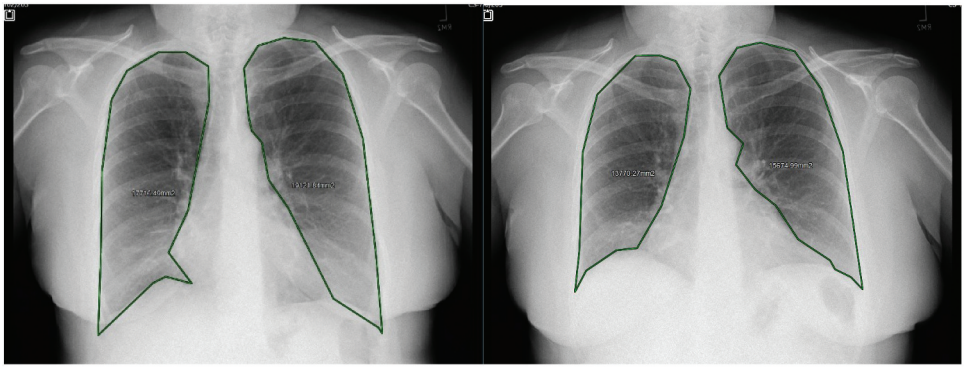

Figure 2. Example of PLA_{insp} (maximum lung area) and PLA_{exp} (minimum lung area) calculation using proprietary software.

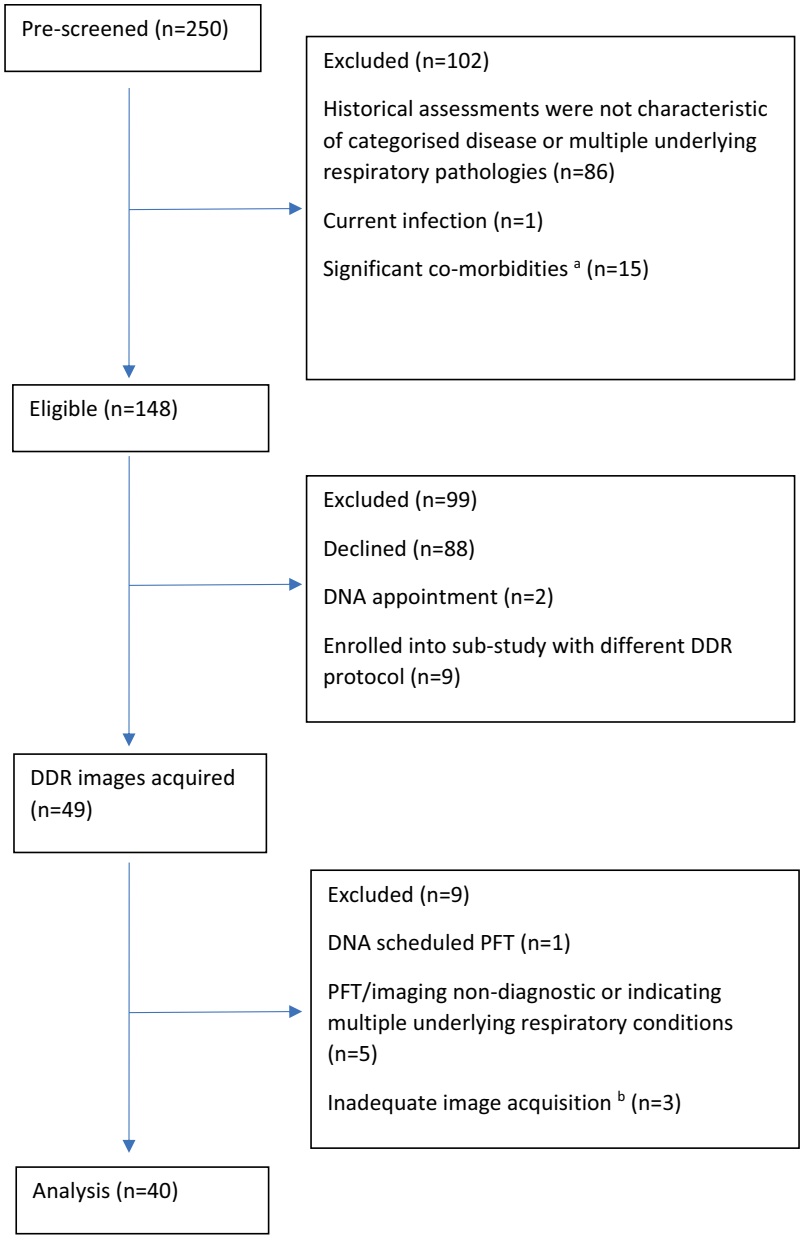

Figure 3. Flowchart of study recruitment process. DDR, Dynamic digital radiography; DNA, did not attend; n, number; PFT, pulmonary function test [a]At the investigators discretion, taking into consideration national and local COVID-19 rules and guidelines. [b]Incomplete lung field capture during maximal inspiration or inadequate penetration on lateral views

(standard deviation 14.89) and 63% were male (25/40). Participant characteristics are further described in Table 1.

Acceptability VAS score

Overall, participants felt that dynamic digital radiography of the chest was an acceptable test with a lower 95% confidence interval threshold of 92% for all groups combined. Table 2 summarises the VAS score by disease group.

Table 1. Summary of demographic and clinic characteristics, by disease group.

		Overall ($N = 40$)	COPD ($N = 9$)	Asthma ($N = 11$)	ILD ($N = 11$)	COVID-19 ($N = 9$)
Age, μ (SD), years		63.38 (14.89)	65.85 (11.58)	56.68 (13.85)	73.05 (14.47)	57.30 (14.51)
Sex	Male	25 (63)	4 (44)	5 (45)	10 (91)	6 (67)
N(%)	Female	15 (38) *	5 (56)	6 (55)	1 (9)	3 (33)
BMI, μ (SD), Kg/m^2		31.89 (6.21)	28.60 (1.89)	34.95 (6.64)	27.90 (2.82)	36.30 (6.71)
Cardiac Disease[a] N(%)		17 (43)	3 (33)	3 (27)	7 (64)	4 (44)
Smoking history	Current Smoker	6 (15)	5 (56)	1 (9)	0 (0)	0 (0)
N(%)	Ex-Smoker	13 (33)	4 (44)	2 (18)	5 (45)	2 (22)
	Never Smoked	21 (53)*	0 (0)	8 (73)	6 (55)	7 (78)

μ, Mean; %, percentage; BMI, Body Mass Index; COPD, Chronic Obstructive Pulmonary Disease; ILD, Interstitial Lung Disease; N, number; SD, Standard Deviation.
*Percentages do not add up to 100 due to rounding.
[a]Cardiac Disease defined as a history of ischaemic heart disease, atrial fibrillation or other clinically significant cardiac arrhythmia, heart failure and/or hypertension.

Table 2. Summary of VAS score for the acceptability of DDR.

	Number (N)	Number of Responders N (%)	95% Confidence Interval (%)
Combined	40	40 (100)	92, 100
COPD	9	9 (100)	66, 100
Asthma	11	11 (100)	72, 100
ILD	11	11 (100)	72, 100
Post-COVID-19	9	9 (100)	66, 100

%, percent; COPD, Chronic Obstructive Pulmonary Disease; ILD, Interstitial Lung Disease; N, number; SD, Standard Deviation.

Correlation between PA ddr-derived measurements and PFT parameters

There was a strong and positive correlation between combined right and left lung PLA_{insp} with TLC ($r = 0.80$, $p < 0.001$). The correlation was greatest in COPD ($r = 0.94$, $p < 0.001$), post-COVID ($r = 0.89$, $p = 0.003$) and asthma groups ($r = 0.76$, $p = 0.01$) and least in the ILD participants ($r = 0.48$, $p = 0.16$). There was also a moderate and positive correlation between PLA_{insp} and FVC across all groups ($r = 0.56$, $p < 0.001$).

There was a moderate and positive overall correlation between PLA_{exp} and RV ($r = 0.64$, $p < 0.001$),) with the strongest correlation observed in airways disease (COPD: $r = 0.87$, $p = 0.003$; asthma: $r = 0.85$, $p = 0.002$) and no correlation in those with ILD ($r = -0.05$, $p = 0.90$). There was a weak correlation between ΔPLA and FEV_1 ($r = 0.30$, $p = 0.06$). Table 3 summarises the correlation between DDR-derived measurements and PFT parameters.

Table 3. Summary of the correlations between ddr-derived measurements from a PA view and PFT parameters.

DDR Measurement	PFT Parameter	DDR Measurement	Pearson Correlation (p value)
PLA_{insp}	TLC	Overall	0.80 (<0.001)
		COPD	0.94 (<0.001)
		Asthma	0.76 (0.01)
		ILD	0.48 (0.16)
		Post-COVID-19	0.89 (0.003)
PLA_{insp}	FVC	Overall	0.56 (<0.001)
		COPD	0.73 (0.02)
		Asthma	0.52 (0.10)
		ILD	0.47 (0.14)
		Post-COVID-19	0.82 (0.007)
PLA_{exp}	RV	Overall	0.64 (<0.001)
		COPD	0.87 (0.003)
		Asthma	0.85 (0.002)
		ILD	−0.05 (0.90)
		Post-COVID-19	0.66 (0.08)
PLA_{exp1}	FEV_1	Overall	0.12 (0.41)
Average diaphragm speed in first second of expiration	FEV_1	Overall	0.18 (0.23)
ΔPLA	FEV_1	Overall	0.30 (0.06)

COPD, chronic obstructive pulmonary disease; DDR, dynamic digital radiography, FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; ILD, interstitial lung disease; PA, postero-anterior X-ray view; PFT, pulmonary function test; PLA_{exp}, projected lung area at end expiration; PLA_{exp1}, projected lung area at 1 second of expiration; PLA_{insp}, projected lung area at end inspiration; ΔPLA, Difference between PLA_{insp} (maximal PLA) and PLA_{exp} (minimum PLA); RV, residual volume; TLC, total lung capacity.

Comparison between DDR measurements from lateral and PA images

Lateral- and PA-derived PLA_{insp} both correlated with TLC to a similar degree (lateral $r = 0.70$, PA $r = 0.80$). PLA_{exp} correlated with RV on both lateral and PA projection images in asthma (lateral $r = 0.91$, PA $r = 0.85$) and COPD (lateral $r = 0.96$, PA $r = 0.87$). Table 4 compares the correlations between key DDR-derived measurements and associated PFT parameters using lateral and PA X-ray views.

Discussion

Pulmonary function tests can be difficult for both staff and patients to perform. They require patient coordination, specialist physiologist supervision and have limited acceptability among patients with advanced respiratory disease.[5,6] A simple method to monitor lung volumes is desirable for early disease detection and evaluation of treatment efficacy. Our pilot study demonstrates DDR is an acceptable investigation for patients with a range of respiratory diseases. We were able to deploy a reproducible image capture protocol and obtain DDR derived parameters across a range of respiratory conditions. Although 3 out of the 49 (6%) participants were excluded from the final analysis as we were unable to obtain DDR-derived measurements from a single attempt at image capture, this investigation failure rate is substantially lower than estimates for inadequate PFT.[29]

We observed a strong and positive correlation between PLA_{insp} on PA DDR and TLC ($r = 0.80$, $p < 0.001$) across a range of disease groups. This is in keeping with previously established findings in patients with cystic fibrosis,[30] as well as findings from static chest radiographs,[31] and complements the strong correlation between FVC and PLA_{insp} found in numerous other studies.[15–20] Similarly, PLA_{exp} on PA projection was strongly and positively correlated with RV in airways disease (COPD: $r = 0.87$, $p = 0.003$; asthma: $r = 0.85$, $p = 0.002$), which may reflect underlying air trapping. Again, this complements existing research demonstrating PLA_{exp} correlates with RV in patients with respiratory pathology.[30]

Notably, PA DDR is simple for both staff and patients to perform. PLA_{exp} obtained from a PA projection was equally positively correlated with RV when compared with lateral views in airways disease (asthma: lateral $r = 0.91$, PA $r = 0.85$; COPD: lateral $r = 0.96$, PA $r = 0.87$) and raises the prospect of an easily measurable DDR biomarker for air trapping. Air trapping is a pathological feature of both COPD and asthma and is closely associated with exacerbation risk and symptom burden,[32,33] as well as mortality in COPD.[34] Easily monitoring air trapping will allow early assessment of treatment efficacy and enhance tailoring of management plans for patients with chronic airways disease.

The strong correlations between PLA_{insp} and PLA_{exp} and TLC and RV, respectively, contrasted with the lack of any correlations between DDR-derived measurements and FEV_1 ($r = 0.12$, $p = 0.41$). Previous studies have demonstrated an inconsistent relationship between FEV_1 and DDR parameters, however, a lack of correlation in this study may reflect the small sample size.[17–19]

Within our study, correlation between DDR-derived measurements and PFT results was noticeably weaker in participants with ILD, which is in contrast to findings from Ueyama et al. who found DDR parameters correlated closely with PFT measurements, including FVC.[17] Given ILD is an umbrella term for

Table 4. Difference between DDR measurements derived from lateral projection compared with PA projection radiograph.

DDR Measurement	PFT Parameter	Group	Lateral DDR Combined Left and Right Pearson correlation (p value)	PA DDR Combined Left and Right Pearson correlation (p value)
PLA_{insp}	TLC	Overall	0.70 (<0.001)	0.80 (<0.001)
		COPD	0.82 (0.006)	0.94 (<0.001)
		Post-COVID-19	0.27 (0.53)	0.89 (0.003)
		ILD	0.26 (0.49)	0.48 (0.16)
		Asthma	0.91 (<0.001)	0.76 (0.01)
PLA_{exp}	RV	Overall	0.86 (<0.001)	0.64 (<0.001)
		COPD	0.96 (<0.001)	0.87 (0.003)
		Post-COVID-19	0.58 (0.18)	0.66 (0.08)
		ILD	0.26 (0.50)	−0.05 (0.90)
		Asthma	0.91 (<0.001)	0.85 (0.002)

COPD, chronic obstructive pulmonary disease; DDR, dynamic digital radiography; ILD, interstitial lung disease; PA, postero-anterior X-ray view; PFT, pulmonary function test; PLA_{exp}, projected lung area at end expiration; PLA_{insp}, projected lung area at end inspiration; RV, residual volume; TLC, total lung capacity.

a diverse group of respiratory conditions affecting the lung parenchyma, this negative finding may be due to heterogeneity within our participant cohort and could have influenced combined group correlations. Similarly, weaker correlations could also represent differences in image acquisition, with lower X-ray exposure in our study contributing to increased difficulty of automated lung edge-detection software in participants with parenchymal disease with increased opacification on radiographic imaging. Patients with parenchymal disease may require higher acquisition exposures (such as those used by Ueyama et al.) and further research is necessary to understand the optimum X-ray conditions in this patient group.

This study provides further evidence supporting the correlation between DDR-derived measurements, RV, and TLC in participants with a range of different respiratory diseases and suggests potential avenues for future research, including the role of this technology as a potential biomarker to easily monitor air trapping in patients with obstructive airways disease. It is also the first study to directly assess patient acceptability of DDR, which is key to future use.

The study was limited by its small sample size and was not powered to detect differences in PLAs between disease groups or correlations between DDR-derived measurements and PFT parameters. Similarly, while every effort was made to ensure participants were characteristic of their disease groups, there was likely substantial heterogeneity in ILD and post-COVID-19 cohorts, which may influence combined group correlations. Furthermore, although DDR was considered acceptable in the patient cohort studied, the delivery of the 'deep breathing' protocol may limit the use of this technology in patients who have difficulties receiving or understanding verbal information.

Larger studies are required to validate DDR and understand the utility of this technology as a possible method of assessing and monitoring air trapping in airways disease and explore the optimum X-ray exposures in patients with ILD.

Conclusion

Dynamic digital radiography is an acceptable investigation for patients with common respiratory disease, although our study population was limited to patients who were able to receive and understand verbal breathing instructions. Despite a small sample size, DDR-derived end-inspiratory PLA is closely and positively correlated with TLC, and end-expiratory PLA is positively correlated with RV in patients with airways disease. This correlation was not observed in patients with ILD, and this patient cohort may require higher X-ray exposures than those with airways disease. Larger studies are required to explore and validate the role of DDR as a potentially simple method to measure lung volumes, allowing earlier detection and monitoring of treatment effectiveness in airways disease.

Disclosure statement

Authors F Fyles and TS FitzMaurice report support for educational conference travel from Konica Minolta, Inc. R Bedi has previously provided consulting services to PHC Corporation of North America, RebrAIn, SAS, in HEART, Inc. and Konica Minolta, Inc. R Bedi is a current full-time employee of New Erie Scientific, LLC. TS FitzMaurice reports honoraria for the presentation of educational material from Konica Minolta Healthcare, Inc, outside of the submitted work. H Burhan reports speaking: AstraZeneca, Chiesi, GSK, Sanofi, Regenron. Advisory Boards: AstraZeneca, GSK, Novartis, Sanofi, Regeneron. Conference Attendance: Sanofi, Regeneron, AstraZeneca, GSK, Chiesi. Educational and Service Improvement Grants: NHSE (Accelerated Uptake Programme), NIHR North West Coast Clinical Research Network, AstraZeneca, GSK, Chiesi. None of the other authors declare any competing interests.

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Appendix

Appendix1 [Supplementary information]: Dynamic digital radiography exposures

Tube voltage 100 kilovoltage (kV); tube current, 50 milliampere (mA); duration of pulsed X-ray, 3.2 millisecond (ms); source-to-image distance, 2 metres (m); additional filter, 0.5 mm aluminium (Al) + 0.1 mm copper (Cu). The additional filter was used to reduce the low-energy component (soft X-rays). The pixel size was 388 micrometre (μm) × 388 μm, the matrix size was 1024 × 768, and the overall image area was 40 centimetre (cm) × 30 cm. The grey-level range of the images was 16384 (14 bits), and the signal intensity was proportional to the incident exposure of the X-ray detector.