Paper II

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High resolution CT in cystic fibrosis—the contribution of expiratory scans

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Abstract

Introduction: The use of high-resolution computed tomography (HRCT) is well accepted as an accurate method for evaluation of lung parenchyma in cystic fibrosis (CF). Several scoring methods exist and, in common, all are based on HRCT findings during inspiration alone. *Objective:* To examine whether expiratory HRCT scans could add information about the degree of mosaic perfusion in patients with CF. *Methods and patients:* Pulmonary HRCT was performed in 17 CF patients (median age of 12 years) with 1-mm thin sections and 10-mm intervals during inspiration, followed by 1-mm thin sections with 20-mm intervals during expiration. HRCT was scored by using a modified Bhalla method. *Results:* The mean HRCT score was 8.2. Out of 17 patients, 11 (65%) demonstrated a pathological mosaic perfusion in expiration, while only three patients showed mosaic perfusion in inspiration. The degree of expiratory mosaic perfusion was graded as severe in nine patients and moderate in two patients. There was a significant correlation between our modified HRCT score and lung function, as measured by forced expiratory volume in 1 s (FEV1% predicted, $P < 0.01$). *Conclusion:* Mosaic perfusion in expiration was a common pathological HRCT finding in our study group. The clinical significance of this finding needs further evaluation.

Keywords: X-ray computed HRCT; Cystic fibrosis; Bronchiectasis

1. Introduction

Because >90% of all deaths in cystic fibrosis (CF) patients are related to pulmonary disease, early detection of lung parenchymal damage is a major cornerstone in managing CF. Pulmonary high-resolution computed tomography (HRCT) visualize the airway involvement characteristically of this disease, i.e. bronchiectasis, peribronchial thickening, mucous plugging, cystic or bullous lung lesions, collapse and consolidation. Different systematic CT scoring systems have been proposed to classify these findings, of which Bhalla's is the most commonly used [1]. His system does not take the degree of mosaic perfusion into consideration, as has been proposed by Helbich et al. [2].

We wanted to examine whether and to what extent expiratory HRCT scans could add information about the degree of mosaic perfusion in patients with CF. Next, we wanted to correlate our modified scoring system with pulmonary function measured as forced expiratory volume in 1 s (FEV1).

2. Methods and patients

Haukeland University Hospital serves as a regional centre for CF patients in Western Norway. Our study included 17 patients from our cohort of patients with CF (nine males and eight females; age range: 6–34 years; median age: 12 years). The diagnosis was based on the findings of elevated sweat chloride concentrations and typical clinical manifestations in all patients. Seven patients (41%) were found to be homozygous for the dF508 mutation, while the remaining ten patients had either two other mutations (one patient) or one detectable mutation (three patients) or no mutation (six patients). All patients had received conventional therapy

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Table 1
General patient data, mean values ± S.D.

	$N = 17$
Age (years)	13.6 ± 7.2 (6–34)
Sex ratio (f/m)	8/9
Chloride sweat in mmol/l	100 ± 20 (62–129)
Body mass index, kg/m^2	17.4 ± 3.1 (12.6–25.8)
Shwachman–Kulczycki score	76 ± 14.7 (45–93)
FVC–forced vital capacity in percent of predicted	95.1 ± 19.6 (54–126)
FEV1–forced expiratory volume in one second in percent of predicted	82.9 ± 20 (37–112)

Ranges in parentheses.

for CF for at least 6 months and they were in a clinically stable condition.

Our cohort of patients with CF consisted of 29 patients > 5 years. In three patients, HRCT scans were only performed in inspiration, one patient was coughing constantly and HRCT scans of eight patients were unfortunately not accessible for evaluation.

Data were collected between February 1999 and August 2000 (Table 1). The regional ethical committee approved our study protocol and informed consent was obtained from patients and/or their families.

Our patients attended the outpatient department every second and third month, or more often when needed. All patients have been treated with standard therapy regime for CF, 15 out of 17 patients (88%) received pancreatic enzyme supplementation. Five patients had chronic lung infection with *Pseudomonas aeruginosa* and they were given 12-day courses of intravenous antibiotic treatment every third month.

Clinical status was evaluated by a Shwachman–Kulczycki score [3]. Standard spirometry was assessed by Sensor Medics Vmax (CA, USA) equipment.

High-resolution CT was performed with a Hi Speed CT (General Electric Medical, WI, USA) using a slice thickness of 1- and 10-mm intervals during inspiration, followed by 1-mm scans at 20-mm intervals during expiration (level and width settings of approximately −600/1500). All CT scans were evaluated by one of us (KR) and the findings were classified according to Bhalla's scoring system (Table 2a).

In addition, the presence and degree of mosaic perfusion in inspiration was evaluated according to Helbich et al. (Table 2b).

Finally, we evaluated the presence and degree of mosaic perfusion in expiration (Table 2c). Our modified scorings system thus includes 11 items and the maximum score is 29.

Table 2
(a) HRCT scoring system for cystic fibrosis according to Bhalla [1]; (b) Hebich's modification of the Bhallas scoring system; adding evaluation of inspiratory mosaic perfusion; (c) Our modification of Bhallas scoring system, adding evaluation of both inspiratory and expiratory mosaic perfusion

Category	0	1	2	3
(a)				
Severity of bronchiectasis	Absent	Mild (luminal diameter slightly greater than diameter of adjacent vessel)	Moderate (luminal diameter two to three times the diameter of the vessel)	Severe (luminal diameter more than three times the diameter of the vessel)
Severity of peribronchial wall thickening	Absent	Mild (thickening less or equal to diameter of adjacent vessel)	Moderate (thickening greater than and up to twice the diameter of adjacent vessel)	Severe (thickening more than two times the diameter of adjacent vessel)
Extent of bronchiectasis*	Absent	1–5	6–9	> 9
Extent of mucous plugging*	Absent	1–5	6–9	> 9
Extent of sacculations and abscesses*	Absent	1–5	6–9	> 9
Generations of bronchial divisions involved (bronchiectasis or plugging)	Absent	Up to the fourth generation	Up to the fifth generation	Up to the sixth generation and distal
Severity of bullae	Absent	Unilateral (≤ 4)	Bilateral (≤ 4)	> 4
Severity of emphysema*	Absent	1–5	> 5	
Severity of collapse or consolidation	Absent	Subsegmental	Segmental or lobar	
(b)				
Severity of mosaic perfusion in inspiration*	Absent	1–5	> 5	
(c)				
Severity of mosaic perfusion in inspiration*	Absent	1–5	> 5	
Severity of mosaic perfusion in expiration*	Absent	1–5	> 5	

* Numbers are the number of bronchopulmonary segments.

Data analysis was performed using a commercially available software package (SPSS). Descriptive statistics included mean, minimum and maximum values, S.D. and median. The association between HRCT score and FEV1 (% predicted) was assessed by the Pearson correlation coefficient. P values are two-tailed and $P < 0.05$ was considered significant.

3. Results

The mean HRCT score was 8.2 ($\pm$6.1), ranging from 1 to 21 (median 8). Eleven out of 17 patients (65%) demonstrated expiratory mosaic perfusion. Two of these showed expiratory mosaic perfusion in one to five bronchopulmonary segments and nine patients in more than five segments (Table 3).

Only three of these 11 patients (27%) showed mosaic perfusion in inspiration (Fig. 1(a, b), Fig. 2(a, b)). The findings were concordant in two of the patients and different in one patient, who showed a higher degree of mosaic perfusion in expiration. One patient had a completely normal HRCT scan and received a score of zero.

There was a significant negative correlation between our modified HRCT score and FEV1 (% predicted) at the 0.01 level, $r = -0.778$ (Fig. 3).

The following findings are exclusively based on inspiratory HRCT findings: Bronchiectasis was the most frequent finding and occurred in 13 of 17 patients (77%). The bronchiectasis was graded as mild in eight and moderate in five patients. Peribronchial thickening was present in 12 patients (71%) and graded as mild in all these patients. Mucous plugging was present in ten patients (59%), six of whom had mucous plugging in one and five bronchopulmonary segments, one patient had mucous plugging in six and nine segments and three patients in more than nine segments. Moreover, we detected consolidations in eight patients, sacculations in five patients, mosaic perfusion in inspiration in three patients and bullae in one patient. None had abscesses or emphysema.

4. Discussion

Mosaic perfusion is considered to be one of the first signs of small airway disease and it is related to regional constrictive bronchiolitis, a common sign in CF [2,4,5]. Investigation of this area by pulmonary function tests is difficult to perform, especially in young patients. The earliest macroscopic findings in the lungs of infants dying of CF are considered to be mucous plugging of the bronchi and bronchioles [6]. It is reasonable to believe that mosaic perfusion, which only occurs during expiration, represents a lower degree of pathology than mosaic perfusion seen in both in- and expiration.

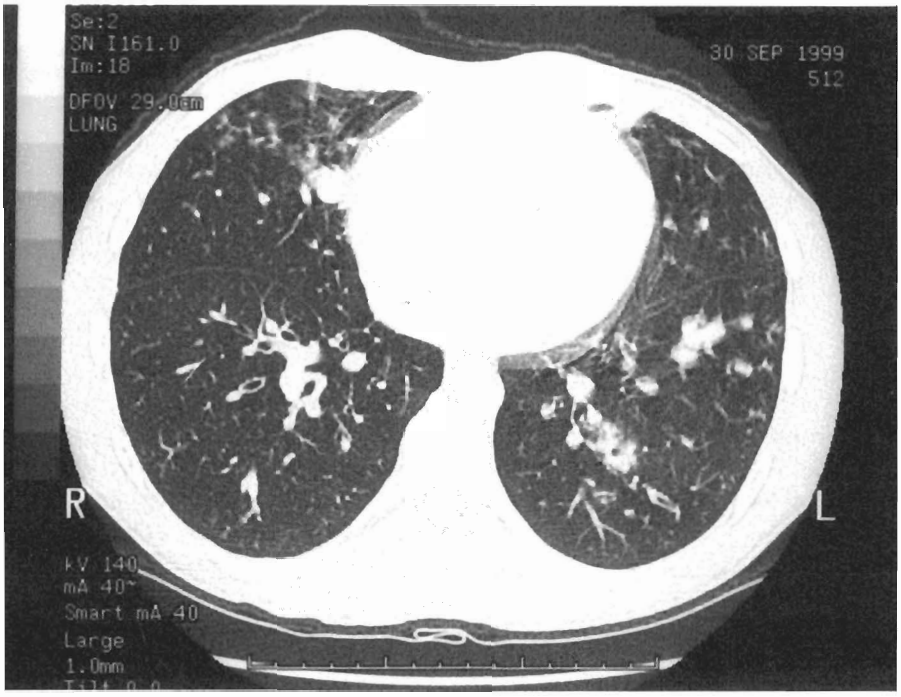
Nine of 11 patients had expiratory mosaic perfusion in more than five bronchopulmonary segments, which is maximum score for this item. The latter expresses the extent of lung pathology, which is clearly demonstrated in expiration. 53% of our CF patients (9/17) had severe mosaic perfusion in expiration. In eight of these patients, no concomitant inspiratory mosaic perfusion could be found.

Scoring of pulmonary HRCT in CF is based on several different methods [1,7,8]. Evaluating findings in inspiration alone is common to these methods. Stan-

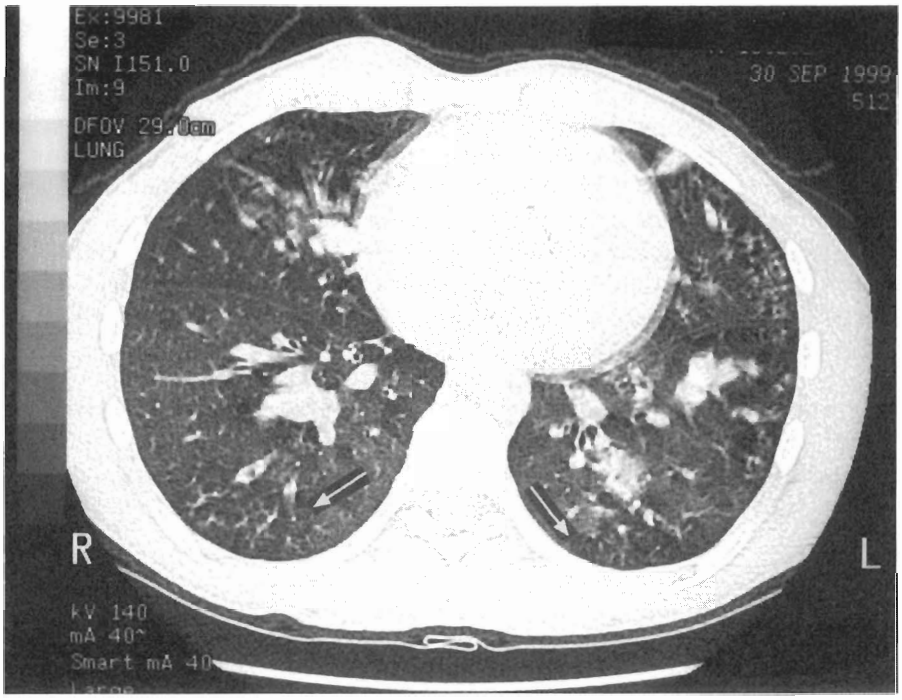
Table 3
Individual patient data of 17 patients listed as HRCT score, mosaic perfusion in expiration and mosaic perfusion in inspiration, lung function measured as FEV1, Shwachman–Kulczycki (SK) score and age

HRCT score	Mosaic perfusion in expiration*	Mosaic perfusion in inspiration*	FEV1% of predicted	SK score	Age (years)
0	0	0	91	85	7
1	0	0	98	90	13
1	0	0	112	93	13
2	1	0	85	91	8
5	2	0	95	77	10
5	0	0	101	86	13
5	2	0	91	90	21
7	2	1	99	83	6
8	1	0	78	76	8
8	0	0	82	81	9
9	0	0	74	67	12
10	2	0	109	84	17
11	2	0	69	73	17
12	2	0	73	49	8
17	2	2	55	65	12
17	2	0	37	57	23
21	2	2	61	45	34

* 0, Absent; 1, affection of one to five bronchopulmonary segments; 2, affection of more than five bronchopulmonary segments.



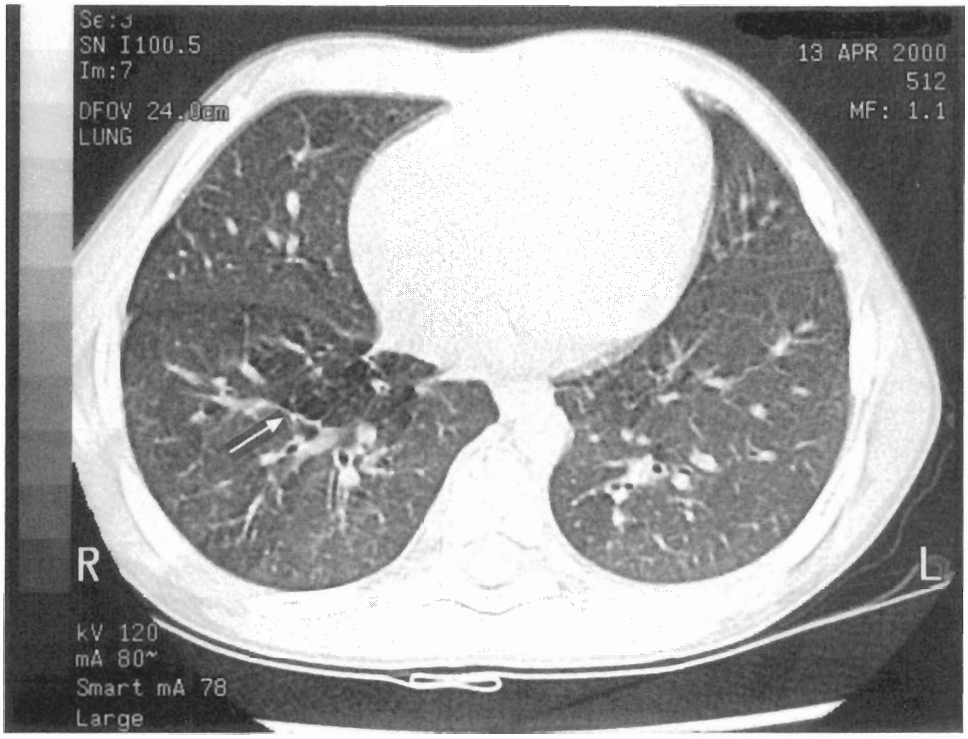
(a)



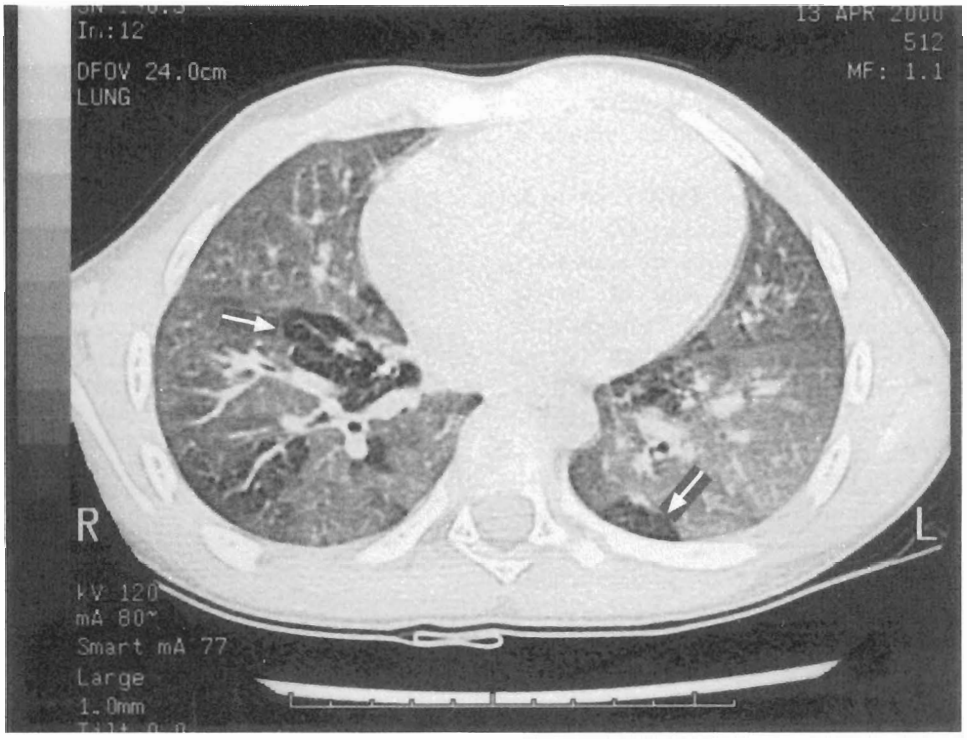
(b)

Fig. 1. (a, b) HRCT scan through the lung basis of a 17-year-old patient in inspiration (a) and in expiration (b) demonstrating mosaic perfusion in both lower lobes during expiration only (b, arrows). In addition, there are bronchiectasis, mucous plugging and consolidation.

dardized evaluation of HRCT findings in expiration has not been performed as a routine in CF patients. Interestingly, we showed that almost two-thirds of our CF patients demonstrated pathological HRCT findings in terms of mosaic perfusion in expiration. Expiratory mosaic perfusion is by this the third most frequent



(a)



(b)

Fig. 2. (a, b) HRCT scan through the lung basis of a 7-year-old patient in inspiration (a, thin arrow) and expiration (b, thick arrows), demonstrating mosaic perfusion in both lower lobes during in- and expiration. In addition, there are bronchiectasis and mucous plugging.

individual CT abnormality in our study population, ranging after bronchiectasis and peribronchial thickening.

Robertson et al. were the first investigators to concentrate on both inspiratory and expiratory HRCT scans in CF patients [9]. They invented a promising

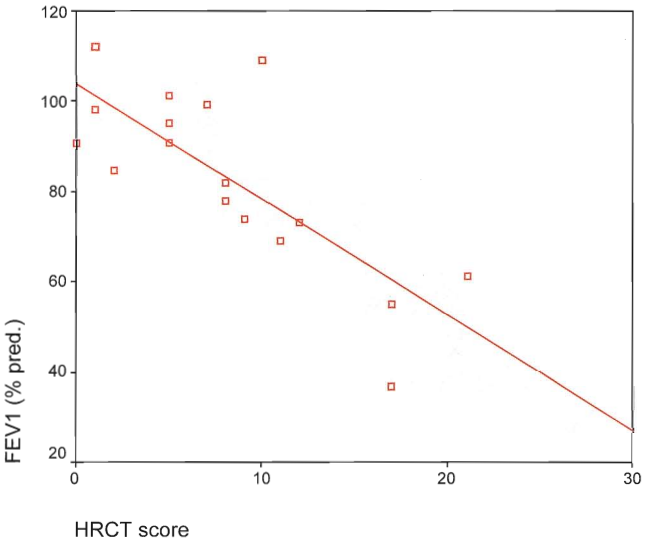


Fig. 3. Correlation between forced expiratory volume in 1 s (FEV1, % predicted) and our modified HRCT score ($r = -0.778$, $P < 0.01$). The graph reflects a regression line.

technique to evaluate findings at definite lung volumes (spirometry-triggered HRCT). In the context of notable changes during therapy for pulmonary exacerbation, they suggest a novel scoring method ('reversible and irreversible' components). Mucous plugging improved significantly after treatment, while air trapping, bronchiectasis and bronchial wall thickening did not. Regions of air trapping and mosaic attenuation were better delineated by expiratory scans near residual volume in all patients.

Arakawa et al. studied expiratory HRCT scans in patients with diffuse lung disease including CF [10]. A total of 45 patients showed air trapping on expiratory scans and 36 had some type of lung or airway abnormality visible on inspiratory scans. Nine patients (five with bronchiolitis obliterans, three with asthma bronchiale, one with chronic bronchitis) had air trapping on expiratory scans, but complete normal HRCT findings during inspiration. Parallel to our findings, all CF patients with air trapping on expiratory scans had lung or airway abnormality visible on inspiratory scans at the same time.

Our modified scoring system correlates significantly with lung function as measured by FEV1. This negative correlation is in accordance with previously reported findings based on the original scoring system [1,11].

Further investigations are needed to determine whether the finding of mosaic perfusion in expiration is of value for the clinical management of patients with CF.

Acknowledgements

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