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Computed tomography based estimates of regional gas and tissue volume of the lung in supine subjects with chronic airflow limitation or fibrosing alveolitis

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ABSTRACT Twelve patients with chronic airflow limitation and 12 patients with a histological diagnosis of fibrosing alveolitis were studied. The calculated mean (SD) tissue volume of a single lung at total lung capacity was 467 (91) ml in the patients with alveolitis, which was 43% (14%) more than predicted for healthy people of the same age, sex, and height. The tissue volume of a single lung at total lung capacity was 436 (82) ml in the patients with chronic airflow limitation, which was 26% (21%) more than predicted. At residual volumes the tissue contents of the fibrotic and the obstructed lungs changed very little (to 407 (84) ml and 433 (84) ml respectively). This allowed tissue volume to be used as a marker of position within the lung, to match inspiratory and expiratory slices and to calculate regional ventilation. In both groups local ventilation was diminished and more variable than in healthy lungs—that is, in the mid 70% of lung volume the local residual volume to total gas volume ratios (RV/TGV) were 32% (10%) in the fibrotic group and 66% (14%) in the group with chronic airflow limitation, compared with 23% (5%) in healthy subjects. As expected, the fibrotic lungs were much denser (0·246 (0·036) g/ml) and the lungs with chronic airflow obstruction were less dense (0·114 (0·026) g/ml) than were healthy lungs (0·126 (0·017) g/ml).

We have previously shown that computed tomography could measure the total gas and tissue volumes and the regional vital capacities and residual volumes of the lungs in healthy men.[1] The aim of the present study was to discover how well computed tomography could recover the same volumes in patients with lung disease.

Methods

We studied 12 patients with chronic airflow limitation and 12 patients with fibrosing alveolitis. They were chosen from larger groups of patients with probable emphysema or fibrosis in whom computed tomography had been performed for clinical reasons. Their scans, which were stored on magnetic tape, were selected for more detailed study retrospectively, on the basis of clinical, radiographic, functional, and (in the case of fibrosing alveolitis) histological confirmation of the diagnosis.

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The 12 patients with chronic airflow limitation were all referred for assessment of emphysema or for evaluation of bullous lung disease that was shown to be generalised emphysema.[2] All 12 had presented with complaints of breathlessness and poor exercise tolerance; three had α_1 antitrypsin deficiency. All admitted to cough and sputum production on direct questioning, and had chronic bronchitis, as defined by the Medical Research Council criteria.[3] Anthropometric, functional, and clinical data on these patients are given in tables 1 and 2. On the basis of this evidence and the radiological details of their computed tomography scans we concluded that these patients had chronic bronchitis and emphysema. This point is examined further below.

Each patient was asked to breathe in to total lung capacity, signal and hold that position for five seconds while an inspiratory scan was taken. They were also asked to breathe out to residual volume, signal and hold that position while an expiratory scan was taken. Their lungs were studied in this fashion from apex to base at constant intervals of between 10–15 mm.

The scans were examined on a display console, with

Table 1 *Details and lung function of 12 patients with chronic airflow limitation*

Subject No (sex)	Age (y)	Height (cm)	Lung function (% predicted)						Duration of symptoms (y)
			FEV_1	FVC	TLC	RV	TLCO	KCO	
1 (M)	35	179	17	35	121	327	44	78	5
2 (M)	43	170	104	136	133	132	55	58	5
3 (F)	43	161	26	92	149	265	23	25	7
4 (M)	53	177	24	57	119	243	28	51	8
5 (M)	54	184	36	70	141	269	61	83	7
6 (M)	56	187	33	55	114	186	29	44	6
7 (M)	62	196*	26	73	127	122	28	37	10
8 (F)	68	165	26	69	122	222	28	38	5
9 (M)	70	166	26	75	141	243	31	43	6
10 (M)	70	178	36	92	123	178	45	51	7
11 (M)	71	168	26	56	120	193	40	73	6
12 (F)	75	163	25	40	134	259	36	50	5
Mean	58	173	34	71	129	220	37	53	6
SD	13	10	23	27	11	60	12	18	2

*Span.
FVC—forced vital capacity; TLC—total lung capacity; RV—residual volume; TLCO—transfer factor; KCO—transfer coefficient.

an organ identification subroutine that outlines the boundary of any contiguous region having radiographic densities within a nominated range. We chose the lower density limit of −999 Hounsfield units, which excludes any tissue volume element (of 1 × 1 × 10 to 15 mm) containing more than 99·9% air. The upper density limit was −300 Hounsfield units, which excludes any volume element containing more than 70·3% of soft tissue as opposed to air (soft tissues other than fat generally have radiographic densities close to +40 Hounsfield units). This boundary outlines the pleural surface of the lung, allowing for the partial volume effect at its curved surfaces; but it also excludes large vessels radiating from the hilum for variable distance into the lung. Direct measurements of the diameters of included and excluded vessels, made with a pair of screen cursors, showed that the boundary excludes any blood vessels with diameters above 5 mm.

Once the outlines had been obtained in this way, they were adjusted manually to include any pathological air spaces within the lung that had been excluded by the −999 HU limit, and to include any subpleural fibrosis that had been excluded by the −300 HU limit. When the outlines had been redrawn in this way, the volume and mean radiographic density of the lung slice were calculated, an arbitrary region of interest subroutine being used. Radiographic densities were then converted to physical densities, on the assumption of a linear relationship (justified previously[1]), and tissue weight was calculated by multiplying lung slice volume by lung slice density. Tissue volume was derived from tissue weight, on the assumption that air free lung tissue has a specific gravity of 1·04. The reproducibility of this technique was checked by applying it on 10 occasions to one

Table 2 *Details and lung function of 12 patients with fibrosing alveolitis*

Subject No (sex)	Age (y)	Height (cm)	Lung function (% predicted)						Duration of symptoms (months)
			FEV_1	FVC	TLC	RV	TLCO	KCO	
1 (F)	21	161	66	60	56	59	26	31	17
2 (M)	35	178	49	48	35	45	31	84	12
3 (F)	39	166	70	67	64	69	30	52	24
4 (M)	45	170	57	63	69	71	43	79	20
5 (F)	52	150	73	75	66	57	56	97	23
6 (M)	52	180	71	77	75	71	37	59	36
7 (M)	59	183	58	45	30	54	19	48	32
8 (F)	62	175	77	62	61	66	35	72	19
9 (M)	63	165	77	63	58	40	34	73	40
10 (M)	65	171	23	76	64	41	40	74	33
11 (M)	66	178	85	77	63	42	31	54	40
12 (M)	69	176	88	64	55	49	34	69	27
Mean	52	171	66	65	58	55	35	66	27
SD	15	9	17	11	13	12	9	18	9

FVC—forced vital capacity; TLC—total lung capacity; RV—residual volume; TLCO—transfer factor; KCO—transfer coefficient.

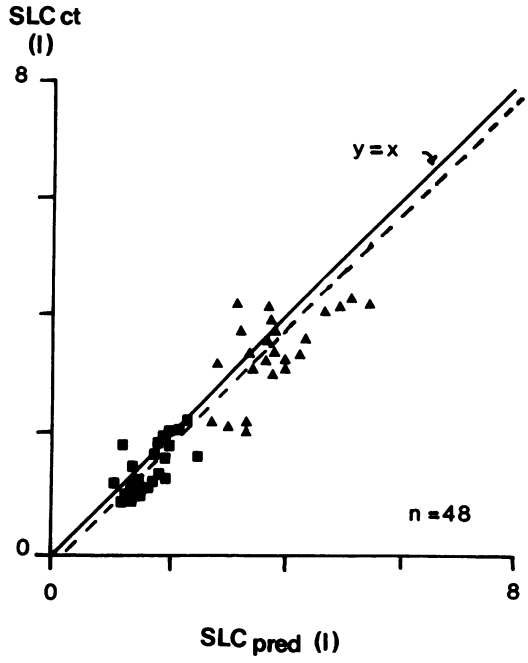

Fig 1 *Comparison of computed tomography and whole body plethysmographic estimates of single lung capacity (SLC) in 12 subjects with fibrosing alveolitis (squares) and in 12 with chronic airflow limitation (triangles). SLC predicted represents 47·5% of the plethysmographic measure of total lung capacity apportioned to the left lung and the remainder to the right lung.*[8] *The mean (SD) error in SLCct was 370 (381) ml. The dashed line represents the SLCct corrected for the known reduction in SLC in the supine posture.*[7]

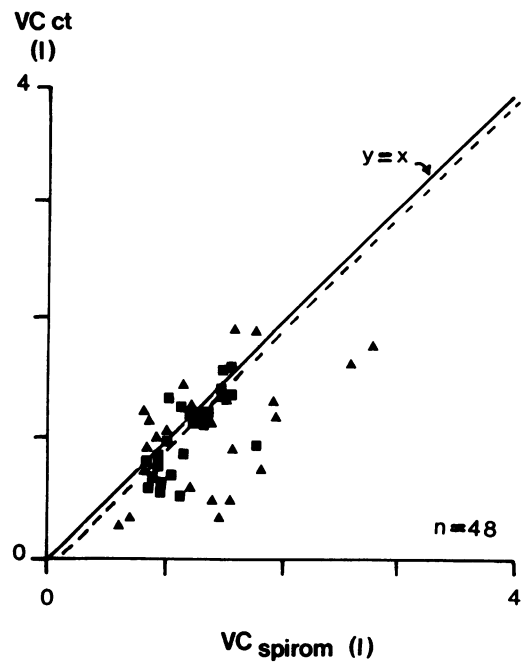

Fig 2 *Comparison of computed tomography and spirometric estimates of single lung vital capacity (VC) in 12 subjects with fibrosing alveolitis (squares) and 12 with chronic airflow limitation (triangles). In each case 47·5% of the spirometric measurement of whole lung vital capacity was apportioned to the left lung and the remainder to the right lung.*[8] *The mean (SD) error in VCct was 257 (406) ml. The dashed line represents the SLC ct corrected for the known reduction in VC in the supine posture.*

slice of a lung with chronic airflow limitation and on 10 occasions to one slice of fibrotic lung. The measurements of lung slice volume and lung slice weight were reproduced within ±0·5% on each occasion.

Values for each slice were summed to obtain the total gas capacity, residual volume, and tissue content of each right or left lung. Predictions of the tissue contents of the lungs were derived from the patient's age, sex, and height (which predict total lung capacity—that is, gas alone) by multiplying by 0·114; this is taken from Weibel's morphometric study,[4 5] for reasons stated in our previous paper[1] that are discussed in more detail later. Predictions of gaseous lung volumes were taken from Cotes[6] and modified by recent findings on 165 healthy individuals aged 30–58 years in this laboratory (which raise predictions of total lung capacity by 5% and of forced expired volume and forced vital capacity by 10%, and reduce predicted carbon monoxide transfer factor (TLCO) by 7%[7]).

Results

Computed tomography based estimates of the vital capacity and total capacity of each right or left lung are compared with the spirometric and plethysmographic estimates in figures 1 and 2, on the assumption that 52·5% of the volumes derived from two lungs can be attributed to the right lung.[8] The mean (SD) computed tomography based estimate of the individual total lung capacities (gas) was 370 (381) ml (n = 48) smaller than the plethysmographic estimate (fig 1). The systematic difference of 370 ml is partly due to the reduction in single lung capacity of about 250 ml that occurs in the supine posture.[9]

The mean (SD) computed tomography based estimate of the vital capacities of individual lungs was 257 (406) ml (n = 48) smaller than the spirometric measurements (fig 2). This average difference of 257 ml is some 100 ml greater than the fall in single lung vital capacity seen when healthy people or patients

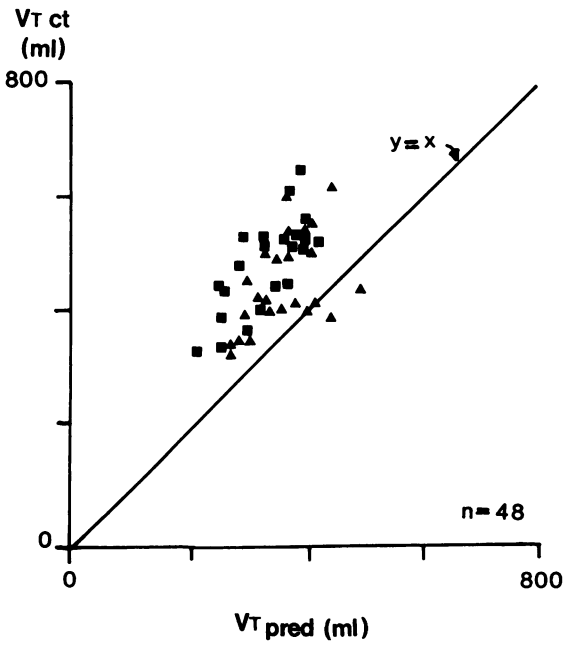

Fig 3 *Comparison of computed tomography based estimates (VTct) and predictions of single lung tissue volume based on predicted TLC[6] in 12 subjects with fibrosing alveolitis (squares) and in 12 with chronic airflow limitation (triangles). In each case 47·5% of the total lung capacity was apportioned to the left lung and the remainder to the right.[8] These volumes were then multiplied by Weibel's estimate of lung density at TLC (0·114: ref 4) to obtain the plethysmographic prediction of single lung tissue volume (VT pred). The mean (SD) increased in VTct over predicted values was 139 (52) ml for subjects with fibrosis and 92 (72) ml for subjects with chronic airflow limitation.*

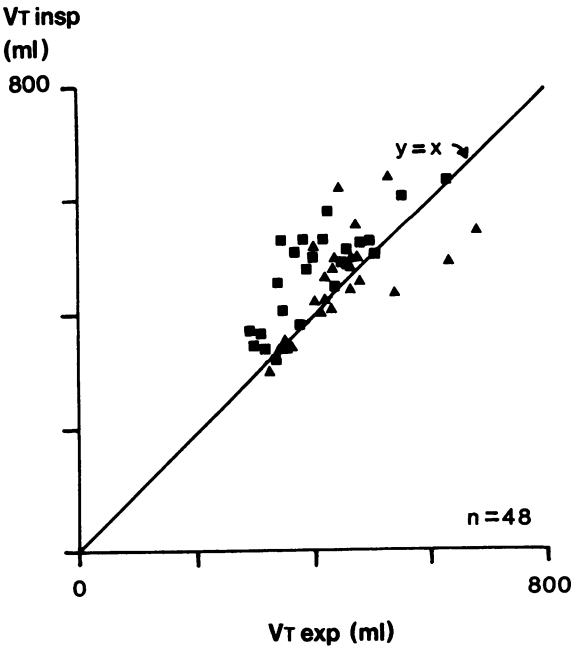

Fig 4 *A comparison of single lung tissue volume at total lung capacity (VT insp) and at residual volume (VTexp) in 12 subjects with fibrosing alveolitis (squares) and in 12 with chronic airflow limitation (triangles). The mean (SD) error in VTinsp was 38 (51) ml.*

with restrictive or obstructive lung disease lie down.[9 10]

We presume that before the patients acquired their disease they would have had total lung capacities (gas) that would on average correspond to those predicted from their age, sex, and height. Our best estimate of the tissue content that their lungs would have contained in the absence of disease is the predicted total lung capacity multiplied by the factor of 0·114 that we derived from Weibel's data (see below). Comparison of the computed tomography based estimates of tissue content with such predictions suggested that the individual lungs of the patients with chronic airflow limitation contained 92 (SD 72) ml (n = 24) of excess tissue. This is equivalent to a mean increase of 26% (21%). Computed tomography estimates of the tissue content in individual fibrotic lungs suggested an excess tissue content of 139 (52) ml (n = 24), equivalent to an increase of 43% (14%) (fig 3).

There was good agreement between the tissue contents of each lung at total lung capacity and residual volume (fig 4). The volume at full inspiration exceeded that on full expiration by an average of 38 (51) ml, which is equivalent to an increase of 9% (14%). This conservation of tissue volume allowed us to match inspiratory and expiratory scans and so calculate regional vital capacities. To do this we had to match each actual inspiratory scan with a theoretical expiratory scan whose properties were predicted from the characteristics of the neighbouring pair of actual expiratory scans. This interpolative procedure can be applied only when slice volumes and tissue contents are distributed in a mathematically continuous rather than an erratic fashion. To check that this assumption was valid in diseased lungs with obvious regional variations in structure, we compared the characteristics of each slice with those predicted by interpolation from the properties of its actual neighbours. These comparisons are shown in figures 5 and 6, which indicate that there are no abrupt changes in lung properties on this scale of sampling (10–15 mm intervals). There is very good interpolation of slice area and therefore volume. There is also good interpolation of lung density and therefore tissue content in the mid 95% of the lung; but considerable errors

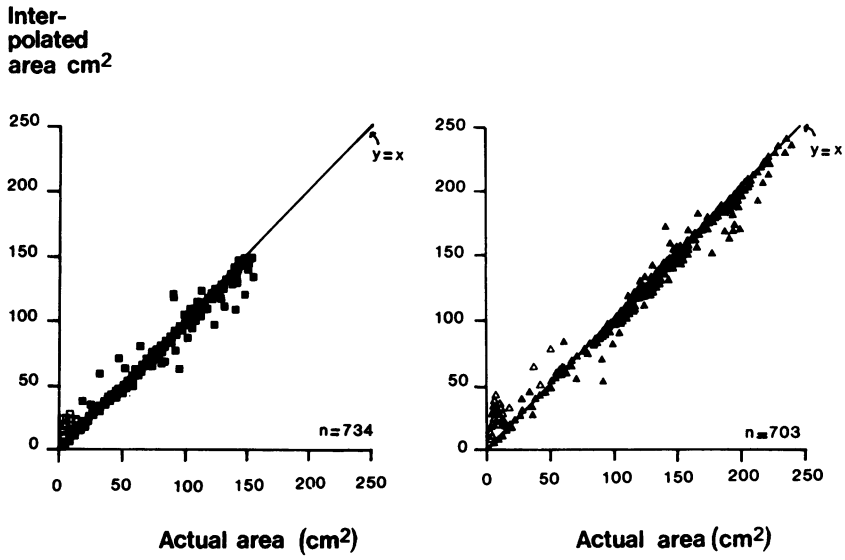

Fig 5 *A comparison of actual and interpolated estimates of the area of computed tomography slices of single lungs in (left hand panel) 12 subjects with fibrosing alveolitis (squares) and in (right hand panel) 12 subjects with chronic airflow limitation (triangles). In practice, departures from the line of identity will on average be four times less than those shown here. Open squares and open triangles indicate slices, of very small volume, at the extreme apex or base of the lung. Closed squares and triangles indicate slices in the mid 95% of the lung.*

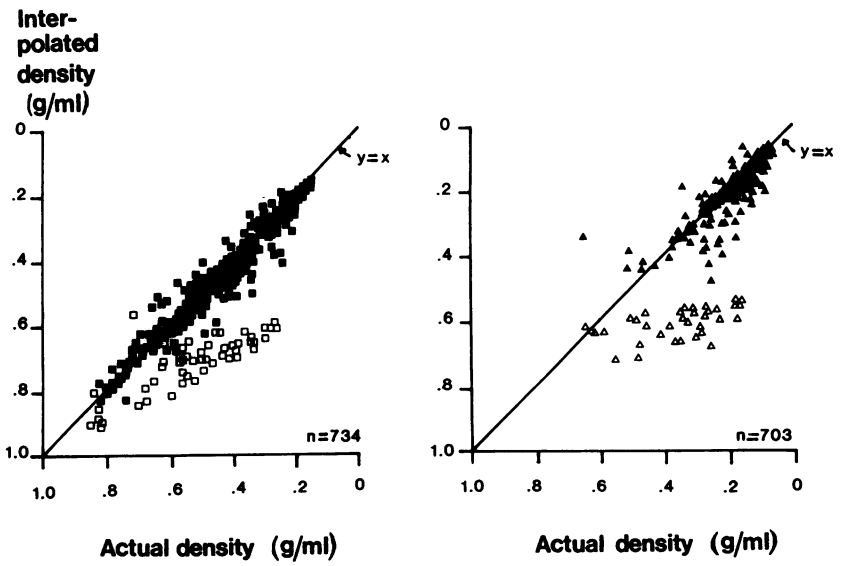

Fig 6 *Comparison of actual and interpolated estimates of the density of computed tomography slices of single lungs (left) in 12 subjects with fibrosing alveolotis (squares) and (right) in 12 subjects with chronic airflow limitation (triangles). In practice, the departure from the line of identity will on average be four times less than those shown here. Open squares and open triangles indicate slices, of very small volume, at the extreme apex or base of the lung. Closed squares and triangles indicate slices in the mid 95% of the lung.*

Table 3 *Residual volume to total lung (gas) volume ratios (as percentages) for 12 patients with fibrosis and 12 with chronic airflow limitation*

Fibrosis			*Chronic airflow limitation*		
Subject No	*Mean*	*SD (within subjects)*	*Subject No*	*Mean*	*SD (within subjects)*
1	23·7	5·3	1	59·9	17·3
2	22·5	4·5	2	48·0	12·3
3	32·1	6·1	3	65·1	10·7
4	34·1	9·2	4	84·2	7·8
5	26·9	5·2	5	70·5	12·6
6	30·9	6·9	6	66·2	11·1
7	29·4	4·0	7	83·2	11·4
8	54·9	8·3	8	55·7	12·3
9	42·0	6·1	9	53·8	8·9
10	32·9	8·6	10	57·8	11·1
11	28·8	6·9	11	54·3	19·5
12	22·5	3·5	12	87·3	7·4
Mean	31·7	6·2		65·5	11·9
SD	9·2			13·2	

Table 4 *Tissue volume to total lung volume (gas and tissue) ratios (as percentages) for 12 patients with fibrosis and 12 with chronic airflow limitation*

Fibrosis			*Chronic airflow limitation*		
Subject No	*Mean*	*SD (within subjects)*	*Subject No*	*Mean*	*SD (within subjects)*
1	24·4	9·6	1	9·4	6·0
2	23·9	9·6	2	12·5	5·5
3	21·9	6·1	3	12·9	7·5
4	28·7	11·4	4	10·6	2·4
5	22·8	7·0	5	7·9	3·2
6	23·9	7·6	6	11·5	2·2
7	21·8	5·8	7	9·3	1·7
8	28·0	7·2	8	10·2	2·4
9	24·6	6·8	9	10·2	4·4
10	32·9	7·7	10	8·4	2·1
11	25·6	12·0	11	8·4	4·5
12	25·3	4·1	12	14·1	4·8
Mean	25·3	7·9		10·5	3·9
SD	3·2			1·2	

occur in the small volumes of lung at the extreme apices and costophrenic margins, where partial volume artefacts are greatest.

In the lungs of healthy supine men the residual volume to total gas volume ratio of each scan slice of lung averaged 23% (SD 5%).[1] In the patients they were higher and more variable, averaging 32% (9%) in the patients with fibrosis and 66% (13%) in those with chronic airflow limitation in the mid 70% of lung volume (table 3). In healthy subjects the distribution of tissue volume is very uniform at about 12% (2%) of total lung volume in the mid 70% of total lung volume.[1] In the patients with fibrosis the tissue volume was higher, averaging 25% (3%) of total volume, and in patients with chronic airflow limitation the corresponding average was 11% (1%) (table 4).

Discussion

Several features of these results suggest that the computed tomography techniques for determining regional gas and tissue volumes can be applied to diseased lungs. These are the agreement between computed tomography based and whole body plethysmographic estimates of total lung capacity; the agreement between computed tomography based and spirometric estimates of vital capacity; the agreement between inspiratory and expiratory tissue contents; and the agreement between actual and interpolated values of area and slice density.

The finding of apparent increases in lung tissue content in both conditions rests on the accuracy of our predictions of normal values. The figure we used comes from a morphometric study by Weibel,[4 5] and is the only one we know that allows us to distinguish and subtract the weight of the main bronchi and all blood vessels greater than 5 mm in diameter, which are automatically excluded from computed tomography estimates of lung weight by boundary selection. The figure did also provide a good prediction of com-

puted tomography estimates of normal lung weight, the computed tomography estimate exceeding the predicted value by an average of 31 (SD 70) ml, equivalent to an excess of 6% (18%).[1] There is also agreement with independent estimates of lung weight by Pierce *et al*[11] and Armstrong *et al*,[12] who used the difference between radiographic and gas dilution lung volumes as a measure of tissue volume. In these studies mean lung weight was estimated to 720 (SD 37) and 843 (110) g respectively. In both cases the estimates were made in the upright position, at total lung capacity and functional residual capacity respectively. Rhodes *et al*,[13] using positron emission tomography, measured lung density during quiet breathing, close to functional residual capacity. They found it to be 0·29 (0·08) g/ml (including the vascular component) and 0·12–0·16 g/ml for extravascular lung density. In a 6 litre lung this would give lung weights of 870 and 470 ml respectively.

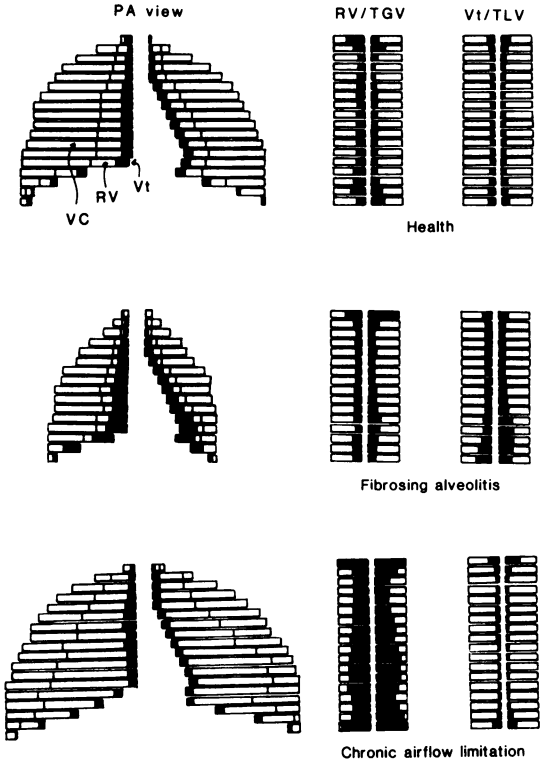

Fig 7 *Graphical presentation of regional information obtained from computed tomographs at total lung capacity and residual volume in one healthy man (top) one subject with fibrosing alveolitis (centre), and one subject with chronic airflow limitation (bottom). Each slice represents an equal percentage of the total height of the lung. The diagram on the left shows for each slice of lung, local tissue volume (VT), indicated by the shaded bar; residual volume (RV), indicated by the smaller unshaded bar; total gas volume (TGV) given by the combined length of the two unshaded bars; and total lung volume (TLV) given by the combined length of all three bars. These characteristics are shown, as proportions of total gaseous volume (TGV) or total volume (gas and tissue, TLV) in the sets of bar charts on the right.*

The finding of an apparent increase of 43% (SD 14%) in the tissue content of fibrotic lungs accords well with other evidence on the characteristics of fibrosing alveolitis.[14–17] In the reviews cited there was a constant finding of increased material of a cellular, fibrotic, or mixed nature. Our previous study suggested that computed tomography could determine changes in lung tissue content of the order of ±5 ml, which is about 1/28th of the average volume of excess material found in fibrotic lungs. This suggests that some computed tomography measure of tissue content might be of value in assessing the severity, progress, or response to treatment of the disease.

The finding of a smaller but substantial increase—of 26% (SD 21%)—in the tissue content of lungs with chronic airflow limitation was not expected. Fletcher *et al*[18] and Burrows *et al*[19] have described radiographic and functional criteria for the diagnosis of emphysema in life, including a grossly elevated increased TLC (greater than 120% predicted) and a reduced TLCO (less than 52% and 55% predicted respectively). Eleven of our 12 subjects with chronic airflow limitation had a TLC greater than 120% predicted and one had a TLC of 114% predicted. In 11 of the 12 the TLCO was less than 55% predicted. The computed tomography appearances in each case were those of emphysema.[20] On this basis we believe that all the subjects had emphysema. The image we had of this condition was of a lung made lightweight and overblown by the destruction of alveoli. In these lungs the density was low because of distension (0·114 0·026) g/ml, compared with 0·126 (0·017) g/ml in healthy men), but the total tissue content was raised. This excess material could be inflammatory as all the subjects had a long smoking history and coincident chronic bronchitis.[3] The only reference we have been able to find on the tissue content of emphysematous lung supports the idea that it is not associated with a loss of lung weight.[21]

The technique described here enables areas of raised or diminished tissue content or air trapping to be quantified on a firmer basis than previously from computed tomography scans, and is complementary to the statistical approach described by Hayhurst *et al*.[22] It provides quantitative measurements of regional function that might help in the preoperative assessment of patients due to have total or partial lung resection. For this purpose we need to present the information in a way that can be appreciated easily, and we have chosen the solution illustrated in

figure 7, which compares the findings in a normal subject with the findings in one of the patients with fibrosing alveolitis and one of the patients with chronic airflow limitation. In principle, the graphical display can be superimposed on a conventional posteroanterior chest film. It is, however, essential to note that the graph is constructed from data obtained in a supine patient whereas most posteroanterior views are taken with the patient standing or sitting up.

We suggest that the data reported here support the use of computed tomography to study regional function in the diseased lung.

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