However, therapeutic findings from other studies indicate that the decline in lung function continues to take place between courses but can be diminished by the intensive use of nebulised antibiotics and steroids.[9 18 20] The major side effects of the intensive use of antibiotics in cystic fibrosis are the development of resistance, allergy to β-lactam antibiotics, possible ototoxicity and renal toxicity caused by aminoglycosides (although this has not yet been a significant problem), cost, and compliance of patients, as also reported by Elborn *et al*.[13] New efficient anti-pseudomonas antibiotics and new treatment strategies are therefore needed for patients with cystic fibrosis.[21–24]

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1 Lawson D. Bacteriology of the respiratory tract in cystic fibrosis: a hypothesis. In: Watte PJ, ed. *The control of chemotherapy. 6.* Edinburgh & London: Livingstone, 1970: 69–77.
2 Nicas TI, Iglewski BH. The contribution of exoproducts to virulence of *Pseudomonas aeruginosa*. *Can J Microbiol* 1985;**31**:387–92.
3 Petersen NT, Høiby N, Mordhorst C-H, *et al*. Respiratory infections in cystic fibrosis caused by virus, chlamydia and mycoplasma: possible synergism with *Pseudomonas aeruginosa*. *Acta Pædiatr Scand* 1981;**70**:623–8.
4 Marks MI. Antibiotic therapy for bronchopulmonary infections in cystic fibrosis. The American approach. In: Høiby N, Pedersen SS, Shand GH, Döring G, Holder IA, eds. *Pseudomonas aeruginosa infection*. Basel: Karger, 1989: 229–36.
5 Høiby N. *Pseudomonas aeruginosa* infection in cystic fibrosis. Diagnostic and prognostic significance of *Pseudomonas aeruginosa* precipitins determined by means of crossed immunoelectrophoresis. A survey. *Acta Pathol Microbiol Scand Section C* 1977;**262**(Suppl):3–96.
6 Schiøtz PO. Local humoral immunity and immune reactions in the lungs of patients with cystic fibrosis. *Acta Pathol Microbiol Scand Section C* 1981;**276**(Suppl):3–25.
7 Goldstein W, Döring G. Lysosomal enzymes from polymorphonuclear leukocytes and proteinase inhibitors in patients with cystic fibrosis. *Am Rev Respir Dis* 1986;**134**:49–56.
8 Schiøtz PO, Jørgensen M, Færø O, *et al*. A longitudinal study of immune complex activity and inflammatory response in sputum sol-phase of CF patients: influence of local steroid treatment. *Acta Pædiatr Scand* 1983;**72**: 283–7.
9 Bisgaard H, Pedersen SS, Nielsen KG, *et al*. Controlled trial of inhaled budesonide in patients with cystic fibrosis and chronic bronchopulmonary *Pseudomonas aeruginosa* infection. *Am J Respir Crit Care Med* 1997;**156**: 1190–6.
10 Szaff M, Høiby N, Flensborg EW. Frequent antibiotic therapy improves survival of cystic fibrosis patients with chronic *Pseudomonas aeruginosa* infection. *Acta Pædiatr Scand* 1983;**72**:651–7.
11 Pedersen SS, Jensen T, Høiby N, *et al*. Management of *Pseudomonas aeruginosa* lung infection in Danish cystic fibrosis patients. *Acta Pædiatr Scand* 1987;**76**:955–61.
12 Frederiksen B, Lanng S, Koch C, *et al*. Improved survival in the Danish cystic fibrosis centre: results of aggressive treatment. *Pediatr Pulmonol* 1996; **21**:153–8.
13 Elborn JS, Prescott RJ, Stack BHR, *et al*. Elective versus symptomatic antibiotic treatment in cystic fibrosis patients with chronic *Pseudomonas* infection of the lungs. *Thorax* 2000;**55**:355–8.
14 Møller N-E, Høiby N. Antibiotic treatment of chronic *Pseudomonas aeruginosa* infection in cystic fibrosis patients. *Scand J Infect Dis Suppl* 1981;**24**:87–91.
15 Ciofu O, Giwercman B, Pedersen SS, *et al*. Development of antibiotic resistance in *Pseudomonas aeruginosa* during two decades of antipseudomonal treatment at the Danish CF center. *Acta Pathol Microbiol Immunol Scand* 1994;**102**:674–80.
16 Regelmann WE, Elliott GR, Warwick WJ, *et al*. Reduction of sputum *Pseudomonas aeruginosa* density by antibiotics improves lung function in cystic fibrosis more than do bronchodilators and chest physiotherapy alone. *Am Rev Respir Dis* 1990;**141**:914–21.
17 Meyer KC, Lewandoski JR, Zimmerman JJ, *et al*. Human neutrophil elastase and elastase/alpha$_1$-antiprotease complex in cystic fibrosis: comparison with interstitial lung disease and evaluation of the effect of intravenously administered antibiotic therapy. *Am Rev Respir Dis* 1991;**144**:580–5.
18 Jensen T, Pedersen SS, Garne S, *et al*. Colistin inhalation therapy in cystic fibrosis patients with chronic *Pseudomonas aeruginosa* lung infection. *J Antimicrob Chemother* 1987;**19**:831–8.
19 Ramsey BW, Pepe MS, Quan JM, *et al*. Intermittent administration of inhaled tobramycin in patients with cystic fibrosis. *N Engl J Med* 1999;**340**: 23–30.
20 Quan J, Vaciljev M, Schaeffler B, *et al*. Treatment for exacerbations only does not arrest progressive lung function decline in cystic fibrosis. In: Heijerman HGM, Van der Laag, eds. *23rd European Cystic Fibrosis Conference*. The Hague: Elsevier, 1999: S84 (abstract 238).
21 Hancock REW. Host defense (cationic) peptides: what is their future clinical potential? *Drugs* 1999;**57**:469–73.
22 Kobayashi H. Airway biofilm disease: its clinical manifestation and therapeutic possibilities of macrolides. *J Infect Chemother* 1995;**1**:1–15.
23 Konstan MW, Byard PJ, Hoppel CL, *et al*. Effect of high-dose ibuprofen in patients with cystic fibrosis. *N Engl J Med* 1995;**332**:848–54.
24 McElvaney NG, Hubbard RC, Birrer P, *et al*. Aerosol alpha$_1$-antitrypsin treatment for cystic fibrosis. *Lancet* 1991;**337**:392–4.

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# Diagnosis of lung cancer: FOB before CT or CT before FOB?

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Any patient presenting to a respiratory physician with a possible diagnosis of lung cancer requires a rapid and accurate histological diagnosis, together with enough staging information to enable a correct management plan to be arranged. Standards for these processes have been suggested.[1] In practice it is incumbent upon physicians to assess each case and to determine the optimum combination of sampling and imaging tests that will be likely to achieve a firm diagnosis and staging at the minimum inconvenience to his or her patients, and with a minimum of delay which is known to be very distressing to them.[2]

Since the advent of fibreoptic bronchoscopy (FOB) in 1974, and with its current very wide availability, most physicians would consider this as their first investigation after a clinical assessment and plain radiology. Selection would be influenced by the latter, so that lesions clearly falling into the category of small solitary pulmonary nodules would be far more likely to be investigated by computed tomographic (CT) scanning and fine needle aspiration biopsy (FNA). For lesions of less than 2 cm in diameter FNA is superior to bronchoscopy even if imaging is used to guide the transbronchial biopsy or transbronchial needle aspiration.[3 4]

The probability that a lesion, thought by a physician to be accessible to bronchoscopy, can actually be diagnosed in this way is not easy to ascertain. However, a recent UK multicentre prospective study of 1660 consecutive cases investigated by FOB because of a prior likelihood of lung cancer showed that a definite tumour was seen in 57%.[5] In a further 20% the appearances were very suggestive of a tumour. Thus, overall, one in five of these tests was negative. The proportion with a positive histological examination at bronchoscopy is likely to have been between 75% (diagnosis within seven days of bronchoscopy) and 85% (diagnosis up to 14 days). Only one in eight patients (15%) had had a prior CT scan, and whether or not this guided the bronchoscopist at all is not known.

This large study with a sensitivity for bronchoscopy of about 77% and a definite histological diagnosis rate of

about 75% or better seems to suggest that the traditional way of assessing lung cancer should continue to be by bronchoscopy first, followed by a CT scan when indicated. However, a paper in this issue of *Thorax* by Laroche *et al*[6] from the Oncology Unit at Papworth suggests strongly that, where the facilities and organisation exist, there may be advantages in reversing this sequence at no greater cost and with a reduction in the number of invasive tests needed to make a firm histological diagnosis. This possibility has been suggested in several retrospective series[7–9] but theirs is the first prospective study.

The authors studied a consecutive series of 171 patients thought on the basis of their basic examination and/or plain radiographs to have a high probability of tumour accessible to bronchoscopy. They showed that a prior spiral CT scan in the randomly allocated "test" population prevented any further tests in six of 90 patients (7%), increased the diagnostic yield of subsequent bronchoscopy to 75% (compared with 54% in the control group in whom bronchoscopy was performed before the result of the spiral CT scan was known), and increased the percentage of patients diagnosed after a single invasive test from 55% to 76%. If the diagnosis was eventually confirmed as lung cancer, 89% of patients were correctly sampled and diagnosed when bronchoscopy was done in the knowledge of the scan result compared with 71% when bronchoscopy was performed before the CT scan. The additional cost of performing spiral CT scans on each patient (given as £121 or US$195) was offset by the need for fewer other invasive tests as a result of the information available from the CT scan, even though they were more expensive—for example, the cost of an FOB was given as £387 (US$620) per case.

The important question then for all cancer units is whether this evidence is good enough to justify a change in routine practice and also whether it is generally practicable to do so.

The technical advances in fibreoptic bronchoscopes since 1974 have been essentially to reduce their diameter, increase their flexibility, and improve their angle of vision and optics. It is unlikely, however, that further changes will alter the performance of these instruments significantly. The application of fluorescence bronchoscopy is still a research tool for early diagnosis. Additional techniques such as perbronchoscopic needle biopsy have been studied intensively but are still not in widespread use because they are technically difficult and have not been shown conclusively to increase the sensitivity of the test, as surgeons still rightly prefer to stage patients preoperatively by mediastinal sampling.[10 11]

By contrast, there have been definite and continuing advances in imaging technology. The time taken to scan patients has reduced, and reconstruction technology has changed in a number of ways. Although conventional scanners are being replaced by spiral/helical scanners, not all of these machines have the same reconstruction ability. This has led to the use of various scanning protocols, although all the recommended techniques involve thinner sections through the main airways. Most units use 5 mm collimation rather than the 3 mm collimation used in the study by Laroche *et al*. The thinner section protocols allow the bronchial anatomy to be visualised very well and this is most vividly demonstrated when the reconstructions allow "virtual bronchoscopy".

The practical issues for most units will inevitably be whether the putative cancer workload could be reorganised to allow same day CT scans and bronchoscopic examinations with no loss of CT or bronchoscopy "slots". There is some preliminary evidence that this can be organised with benefit, even when the referral rate is fairly low—for example, 54 patients in 31 weeks in the study by Williams *et al*.[12] Many units in the UK, and possibly in other countries, do have very busy scanning departments where 2–3 week delays in staging CT scans are not uncommon.[13] The introduction of helical scanners could change this picture because of their greater throughput, but new techniques such as scanning for pulmonary emboli add more cases to the overall CT workload. Yet most patients with lung cancer do have a CT scan, so the challenge of providing early CT scanning is one of organisation.

A second general point, not specifically considered in the paper by Laroche *et al*, is whether CT scanning is better than bronchoscopy in the further investigation of a patient with significant unexplained haemoptysis and a normal examination and radiograph. The evidence here is more clear cut; several series, admittedly retrospective,[14 15] have suggested that CT scanning is more sensitive than routine bronchoscopy for these patients, although at present many patients are referred from primary care specifically for bronchoscopy. Prior CT scanning should aid the bronchoscopist, particularly in the less straightforward case, but it will not completely obviate the need for bronchoscopy as studies have shown that endobronchial disease is missed by spiral CT scanning. This concerns not only in situ disease but includes endobronchial lesions, particularly in subsegmental airways.

The study by Laroche *et al* is important because it shows once again the advantage of assessing and managing patients with cancer in a multidisciplinary way. Although confirmation of these results is necessary, it is highly likely that patients referred to a chest physician with a clinical suspicion of cancer and a compatible radiograph will, in due course, proceed with an initial spiral CT scan before routine bronchoscopic examination. As the paper by Laroche *et al* has shown, a number of these patients will be fully diagnosed by the imaging investigation and the success rate of bronchoscopy may be improved in the others.

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1 Standing Medical Advisory Committee Management of Lung Cancer. *Current clinical practices*. London: Department of Health, 1994.
2 Ubhi SS, Shaw P, Wright S, *et al*. Anxiety in patients with symptomatic breast disease: effects of immediate versus delayed communication of results. *Ann R Coll Surg Engl* 1996;**78**:466–9.
3 Shure D, Fedullo PF. Transbronchial needle aspiration of peripheral masses. *Am Rev Respir Dis* 1983;**128**:1090–2.
4 Shiner RJ, Rosenman J, Katz I, *et al*. Bronchoscopic evaluation of peripheral lung tumours. *Thorax* 1998;**43**:887–9.
5 Clinical Effectiveness and Evaluation Unit of the Royal College of Physicians of London. *Lung cancer audit*. London: Royal College of Physicians, 1999.
6 Laroche C, Fairbairn I, Moss H, *et al*. Role of computed tomographic scanning of the thorax prior to bronchoscopy in the investigation of suspected lung cancer. *Thorax* 2000;**55**:359–63.
7 Mayer B, Ingrisch H, Haussinger K, *et al*. Tumors of the bronchi: the role of evaluation with CT. *Radiology* 1989;**172**:647–52.
8 Aristizabal JF, Randall K, Nath H. Can chest CT decrease the use of preoperative bronchoscopy in the evaluation of suspected bronchogenic carcinoma? *Chest* 1998;**113**:1244–9.
9 Naiditch DP, Funt S, Ettenger NA, *et al*. Hemoptysis: CT-bronchoscopic correlations in 58 cases. *Radiology* 1990;**177**:357–62.
10 Lamb S, MacAuley CE. Endoscopic localisation of pre-neoplastic lung lesions. In: Martinet Y, Hirsch FR, Martinet N, Vignaud J-M, Mulshine JI, eds. *Clinical and biological basis of lung cancer prevention*. Berlin: Birkhauser Verlag, 1998: 231–8.
11 Vansteenkiste J, Lacquet LM, Demedts M, *et al*. Transcarinal needle aspiration biopsy in the staging of lung cancer. *Eur Respir J* 1994;**7**:265–8.
12 Williams TJ, Clearkin RJ, Walter DF, *et al*. A "one stop" CT/bronchoscopy clinic for patients with suspected lung cancer: a district general hospital experience. *Thorax* 1999;**54**(Suppl 3):A34.
13 Standards of Care Committee, British Thoracic Society. *Survey of facilities available to chest physicians for the diagnosis and management of lung cancer*. London: British Thoracic Society, 1996.
14 Set PAK, Flower SDR, Smith JE, *et al*. Hemoptysis: comparative study of the role of CT and fibreoptic bronchoscopy. *Radiology* 1993;**189**:677–80.
15 McGuinness G, Beacher JR, Harkin TJ, *et al*. Hemoptysis: prospective high-resolution CT/bronchoscopic correlation. *Chest* 1994;**105**:1155–62.