Eur Respir J 2007; 29: 78–84
DOI: 10.1183/09031936.00073606

Chest CT screening of asbestos-exposed workers: lung lesions and incidental findings

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ABSTRACT: **The objective of the present study is to determine the feasibility of chest computed tomography (CT) in screening for lung cancer among asbestos-exposed workers.**

In total, 633 workers were included in the present study and were examined with chest radiography and high-resolution CT (HRCT). A total of 180 current and ex-smokers (cessation within the previous 10 yrs) were also screened with spiral CT. Noncalcified lung nodules were considered positive findings. The incidental CT findings not related to asbestos exposure were registered and further examined when needed.

Noncalcified lung nodules were detected in 86 workers. Five histologically confirmed lung cancers were found. Only one of the five cancers was also detected by plain chest radiography and three were from the group of patients with a pre-estimated lower cancer probability. Two lung cancers were stage Ia and were radically operated. In total, 277 individuals presented 343 incidental findings of which 46 required further examination. Four of these were regarded as clinically important.

In conclusion, computed tomography and high-resolution computed tomography proved to be superior to plain radiography in detecting lung cancer in asbestos-exposed workers with many confounding chest findings. The numerous incidental findings are a major concern for future screenings, which should be considered for asbestos-exposed ex-smokers and current smokers.

KEYWORDS: **Asbestos, computed tomography, incidental findings, lung cancer, occupational exposure**

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Received:
June 05 2006
Accepted after revision:
October 07 2006

Asbestos exposure induces a variety of benign and malignant pleural and lung diseases. Lung cancer is the most common asbestos-induced neoplasm. Its risk is associated with the intensity and duration of the exposure and the occurrence of asbestosis [1–3]. Cigarette smoking and exposure to asbestos interact in a strong synergistic fashion [4, 5]. The prognosis of lung cancer is poor: the 5-yr survival rate is 10% in Finland and it has not improved over time [6]. One of the reasons for the poor prognosis is the late diagnosis, when the tumour is already locally disseminated or metastatic. At an early stage, when the cancer is surgically resectable, the 5-yr survival rate ranges 55-72% [7] and even 76% survivorship has been reported [8].

The development of computed tomography (CT) has improved the sensitivity and specificity of imaging. Asbestos-related parenchymal and pleural changes can be detected with high-resolution CT (HRCT) more sensitively than with chest radiography [9, 10]. Spiral CT is capable of finding small lung nodules and, thus, lung cancer in an earlier and more curable stage [11–13]. In addition, it can detect more such nodules than radiography [11, 12]. CT has also proved to be sensitive when used to examine asbestos-exposed workers with confusing lung and pleural pathology [14]. It also detects other diseases in the examined area [13, 15].

The objectives of the present project were: 1) to employ HRCT as the imaging method for pulmonary and pleural diseases possibly present in Finnish workers exposed to asbestos; and 2) to assess the feasibility of lung cancer screening with spiral CT among asbestos-exposed workers classified as current or ex-smokers (cessation within the previous 10 yrs). This latter part of the study focused on lung nodules and malignant lung tumours. Incidental findings were also considered in detail.

STUDY POPULATION AND METHODS

Study design

The present study was a cross-sectional baseline screening study for lung cancer among

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European Respiratory Journal
Print ISSN 0903-1936
Online ISSN 1399-3003

asbestos-exposed workers. In addition to benign and malignant lung lesions, incidental findings were noted and their relevance evaluated. The present study was carried out in 2003 and 2004. The asbestos-exposed workers were imaged with HRCT to find occupational lung and pleural diseases. A total of 180 current or ex-smokers (cessation within the previous 10 yrs), were also screened with unenhanced low-dose spiral CT to detect lung cancer (CT/HRCT group). Spiral CT was scheduled for this group due to the higher risk of lung cancer based on the cumulative effect of asbestos exposure and cigarette smoking. In order to avoid the unnecessary radiation exposure, the estimated lower-risk group was not screened with spiral CT (HRCT only group). Smokers of >70 yrs of age and those presumed not to be operable were excluded from the spiral imaging [16].

Study population

The study population consisted of three groups. The first group included the workers who participated in the asbestos screening programme of the Finnish Institute of Occupational Health (FIOH) in 1990–1992 due to their occupational exposure and had no diagnosed asbestos disease at that time [17, 18]. From all those screened, the present authors selected individuals who were heavily exposed (exposure index >70) [1] and who lived in three geographic areas (Helsinki, Tampere, Turku and their surroundings). The remaining two groups were formed by workers with asbestosis and workers with asbestos-related pleural findings who visited clinics of occupational medicine in Helsinki and Tampere for a clinical follow-up and were willing to participate in the study.

All the participants gave their written informed consent and the study protocol was accepted by the local ethics committee.

METHODS

Posterioanterior chest radiographs were taken in each centre (Helsinki, Tampere and Turku). CT of the chest was performed with three different scanners: two single slice scanners (Siemens Somatom Balance; Siemens Medical, Erlangen, Germany; and Siemens Somatom Plus 4; Siemens Medical) in Helsinki and Tampere and one multislice scanner (GE Lightspeed 16 Advantage; GE Healthcare, Milwaukee, WI, USA) in Turku. HRCT images were obtained during a full inspiration in a prone position. The slice thickness was 1–1.25 mm and the slices were taken at 3-cm intervals from the lung apex to the costophrenic angle. The imaging parameters were 130–140 kV and 100–111 mA. The images were reconstructed with the use of a high spatial reconstruction algorithm and were printed as hard copies at window settings (depending on the centre) appropriate for viewing the lung parenchyma and soft tissues. Spiral CT images were exposed in a supine position and at full inspiration. The slice thickness was 10 mm with a 15–20 mm table feed (110–120 kV, 36–110 mA). The images were reconstructed as 10-mm slices.

As a routine clinical procedure, the chest radiographs were interpreted by a single reader (T. Vehmas in Helsinki, R. Järvenpää in Tampere) separately from the CT image analysis. Attention was paid to possible lung shadows suggestive of a tumour. The HRCT images were analysed and findings were recorded by two radiologists in consensus (T. Vehmas and T. Autti read the Helsinki images, and R. Järvenpää and T. Vierikko read the Tampere and Turku images). The readers were aware that the participants had been exposed to asbestos but they were blinded as to their medical data.

The presence, number and size of the lung nodules were recorded. Where there was a benign-type calcification, or fat in the nodule, and the nodule was <20 mm in diameter, it was considered benign [11, 19]. A finding suspicious of lung cancer was a lung nodule that did not match these criteria and that had appeared or increased in size since the previous examination. A suspicious lesion was immediately re-examined with the use of thinner slices (3 mm).

Noncalcified lung nodules were examined further according to a modification of the protocol used in the Early Lung Cancer Action Project (ELCAP) study [11]. When the nodule was ⩽5 mm in diameter it was re-examined with spiral CT after 6 months and again after 12 months. The growth of these nodules was noted according to both visual assessment and measurement on screen. The slice thicknesses and imaging parameters were individually selected in these cases. For nodules 6-10 mm in diameter, the protocol recommended a biopsy thoracoscopically or with CT guidance. Alternatively, the nodule was re-examined after 3 months and, when needed, it was then treated in a similar manner to that previously described. When nodules were ⩾11 mm in diameter, a biopsy was recommended. All previous chest radiographs and CT images were reviewed when available.

All incidental CT findings were also registered. The radiologist informed the clinicians, who decided whether additional examinations were needed. Expert meetings were also used to solve problematic cases.

RESULTS

A total of 633 (83.5%) of the invited 758 workers attended the imaging study (627 males, six females, mean age 64.5 yrs (range 45.3–86.9 yrs)). In total, 372 workers were studied in Helsinki, 182 in Tampere and 79 in Turku.

A total of 566 (89.8%) were construction workers, of which 264 (41.8%) were plumbers and the rest industrial, real estate and cleaning workers. The mean duration of asbestos exposure was 19.2 yrs (0.5–45.5 yrs). There were 124 (19.9%) current smokers, 361 (58.0%) ex-smokers, 137 (22.0 %) never-smokers and 11 cases lacking data of smoking. The mean number of smoked pack-yrs was 17.2 and the median was 18.8 pack-yrs (0–129 pack-yrs) for the whole group.

Noncalcified lung nodules were found in the CT (HRCT or spiral CT) scans of 86 (14%; 95% binomial confidence interval (CI) 11–17%) of the participants. Nodules were found in 45 of the CT/HRCT group (both HRCT and spiral CT scans were performed) and in 41 of the HRCT only group (only HRCT scans were undertaken). Of these 86 workers, 56 had a single pulmonary nodule, 18 had two nodules and 12 had three or more nodules.

According to the imaging protocol, 61 individuals with nodules were followed with CT. Within 1 yr, 38 of them had one follow-up CT scan, 16 had two CT scans and seven had three. For 17 individuals, nodules of a similar size and location were also apparent in old CT scans; thus, those seen in the current scans were evidently benign and needed no additional

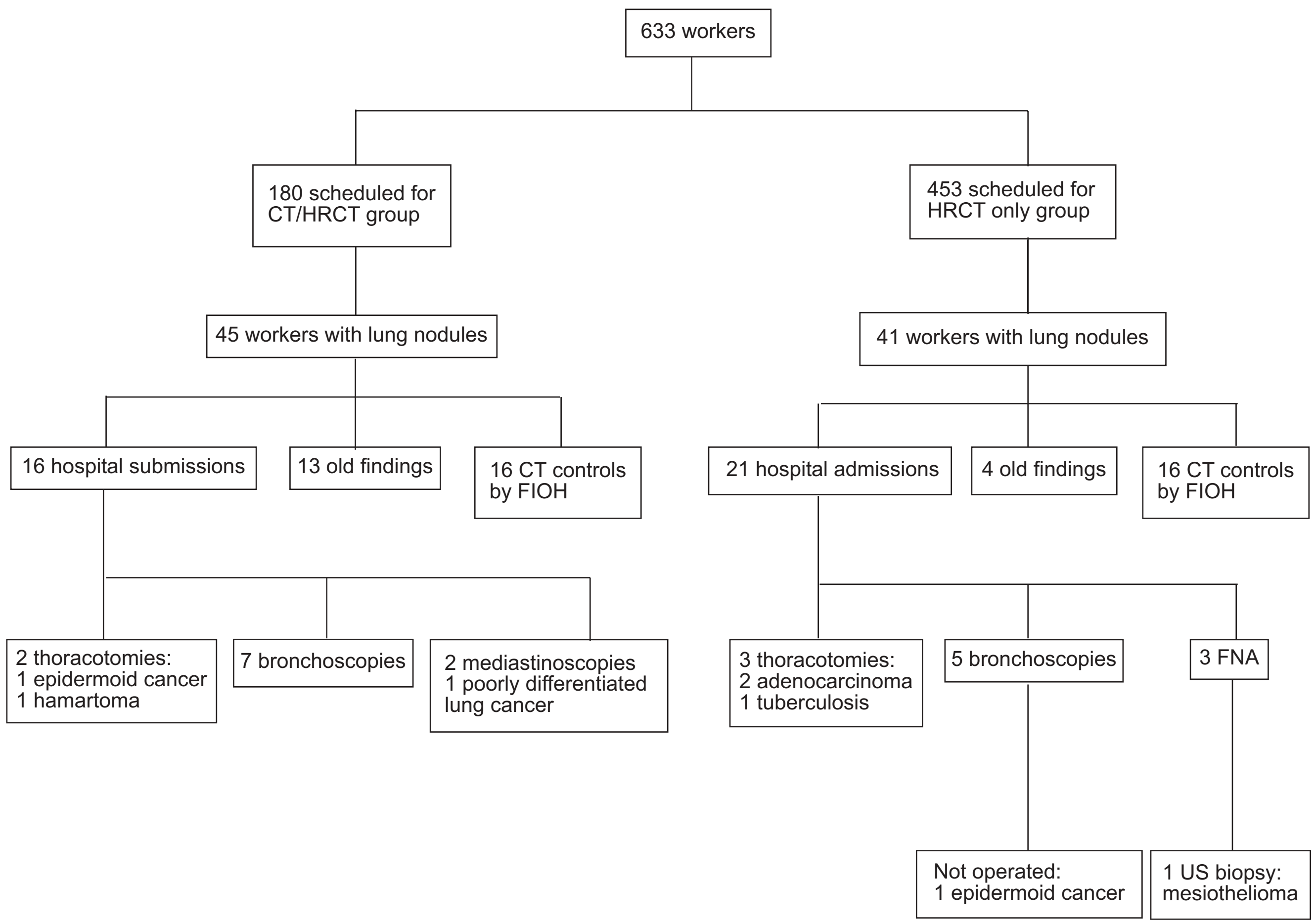

FIGURE 1. Nodules requiring additional examination. CT: computed tomography; HRCT: high-resolution CT; FIOH: Finnish Institute of Occupational Health; FNA: fine-needle aspiration.

attention. A total of 37 workers were admitted directly to the hospital for examination due to lung nodules (fig. 1). The final decision on how to proceed with the nodules was individually decided by the referring physician. There were three CT-guided transthoracic fine needle aspirations for lung nodules and one biopsy of a pleural lesion guided by ultrasound. Two mediastinoscopies and 12 bronchoscopies were performed as further investigations. Some of the repeated CT examinations were performed after hospital admission when other diagnostic examinations were unfeasible.

Five lung cancers were confirmed histologically (0.8%; Poisson CI 1.62–11.67; table 1). There was also one highly suspicious case for lung cancer, but due to poor lung function the patient was inoperable and biopsy was not possible either due to thick pleural plaques between the lesion and the intended puncture site. The histologically confirmed cancers included two adenocarcinomas, two squamous cell cancers and one poorly differentiated lung carcinoma. Two were stage Ia and three were stage IIIb. One patient was initially thought to have a stage Ia cancer but at time of surgery it was discovered to be stage IIIb. Three out of five cancers were found in the HRCT-only group and one of them was a curatively operative stage Ia tumour. The chest radiography found only one cancer. All the lung cancers were found in patients who were current or ex-smokers and no lung cancers were found in nonsmokers.

In addition, one pleural mesothelioma was found. This was regarded as an occupational disease, bringing the total number of verified malignancies to six (1.0%; Poisson CI 2.20–13.06). This patient received chemotherapy. Four thoracotomies were performed, which revealed no malignancy. Two benign lung nodules were operated on: one was a 1.7-cm tuberculotic nodule and the other was a hamartoma. Two patients with suspicious pleural nodules and effusions underwent thoracotomy but the histopathological diagnosis was fibrosis.

No incidental malignancies were found. Among the 633 screened individuals, 343 incidental lesions were detected in 277 cases (44%; 95% Binomial CI 40–48%). Most of these were coronary calcifications, cysts, or benign parenchymal scars or calcifications. Only the most evident coronary calcifications were recorded. In total, 46 of the 343 lesions (13%; 10–17%) presented by 42 individuals were examined further and 33 workers were submitted directly to hospital (fig. 2). Some of the incidental findings were examined further with imaging methods (ultrasound, CT, magnetic resonance imaging), while some needed more invasive examinations (mediastino-, broncho-, thoracoscopy, biopsies). Seventeen thoracic findings (pleural effusions, mediastinal lymph nodes, tracheal nodule, *etc.*) required further examination and they all proved to be benign. Four of the further evaluated 29 abdominal findings were considered clinically significant (an adenoma producing

TABLE 1 Characteristics of patients with lung cancer

Characteristics	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age yrs	66	67	68	73	65
Asbestos exposure index	104.8	43.5	47.0	73.4	24.5
Smoking status	Current smoker	Ex-smoker#	Ex-smoker#	Ex-smoker#	Current smoker
Smoking, pack-yrs	43.0	10.0	10.0	28.9	13.3
Scheduled spiral CT	Yes	No	No	No	Yes
Tumour visible in chest radiography	No	Yes	No	No	No
Histology	Squamous cell cancer	Adeno-carcinoma	Adeno-carcinoma	Squamous cell cancer	Poorly differentiated lung cancer
Tumour stage	Ia	IIIb	Ia	IIIb	IIIb
Therapy	Operation, curative	Operation, noncurative	Operation, curative	Chemo-therapy	Chemotherapy
Histology obtained in	Operation	Operation	Operation	Bronchoscopy	Bronchoscopy and mediastinoscopy
Pleural plaques	Yes	Yes	Yes	Yes	Yes
Asbestosis	Yes	No	No	Yes	No

CT: computed tomography. #: smoking cessation within the previous 10 yrs.

aldosteron, trombocytopenia detected in a person with splenomegalia, cirrhosis of the liver causing ascites and ascites due to heart failure). Most of the findings that led to additional examinations proved to be benign lesions, such as cysts or adrenal incidentalomas. One liver biopsy was performed for multiple haemangiomas.

DISCUSSION

Spiral CT and even HRCT detected more lung nodules and lung cancer in asbestos-exposed workers than chest radiography [11, 12]. Numerous incidental findings not associated with the occupational exposure were also noted. A total of 633 asbestos-exposed workers were imaged with HRCT and 180 of them were also imaged with spiral CT. Noncalcified lung nodules were found in 86 (14%) individuals. Five verified lung cancers were found. Two of the lung cancers were in stage Ia and were curatively operated on. The present authors found 343 incidental findings and 46 of them needed additional examination. Four of these were judged to be clinically important.

Periodical health examinations of asbestos-exposed workers are mandatory in Finland [18]. The participants in the present study were asbestosis patients and asbestos-exposed workers with or without pleural plaques. Pleural plaques and calcifications make the analysis of the lung parenchyma difficult with the use of conventional chest radiography. Spiral CT has proved to be valuable in detecting focal masses that may be obscured by pleural or parenchymal fibrosis [20], as in four of the present cancer patients. In the current study, HRCT detected lesions in 41 workers, who were primarily not imaged with spiral CT. Three of these were lung cancers and one was a mesothelioma. REMY-JARDIN *et al.* [21] examined asbestos-exposed workers with HRCT and spiral CT in the same session. They reported that spiral CT depicted lung nodules in 17 individuals that were otherwise missed in HRCT examinations. Asbestos-associated lung parenchymal diseases are increasingly imaged with HRCT, but when the target of screening is primarily lung cancer HRCT should not replace spiral CT.

The present authors found noncalcified nodules in 14% of the participants. In previous studies [11, 13, 14, 15, 22], noncalcified lung nodules have been found in 18.4–51% of the study population. The range of the number of lung nodules found is wide and may partly be due to the different prevalences of granulomatous infections [13]. In addition, the variability in imaging techniques may explain the difference, as the studies that used a smaller collimation of $\leqslant 5$ mm, reported the highest rate of noncalcified nodules [13, 22]. The present authors found fewer noncalcified nodules than others and probably the major reason for this was that not all the participants of the present series were studied with spiral CT.

The present authors found lung cancer in 0.8% of the participants. Interestingly, the lung cancer detection rate differs considerably between the referred studies: 0.46–2.7% [11, 13, 14, 15, 22]. This is thought to be due to differences in the smoking habits, age and possibly occupational exposure of the populations. The median pack-yrs in four studies [11, 13, 15, 22] was 45, while the smoking history in the present study was considerably lower (median 18.8 pack-yrs). It was surprising that, in spite of both asbestos exposure and smoking among the participants in the present series, no more cases of cancers were detected. The present cancer detection rate was, however, quite comparable with the values presented in most of the articles. It seems that the low risk due to limited tobacco smoking was compensated with an increased risk from asbestos exposure. It is also possible that false-negative cancers occurred due to gaps between slices while screening of the HRCT-only group.

In the year 2000, an international specialist group presented recommendations for the CT screening of asbestos-exposed workers [23]. It concluded that spiral CT has great potential in the screening for lung cancer of well-defined high-risk groups. No practical recommendation was given for such screening but

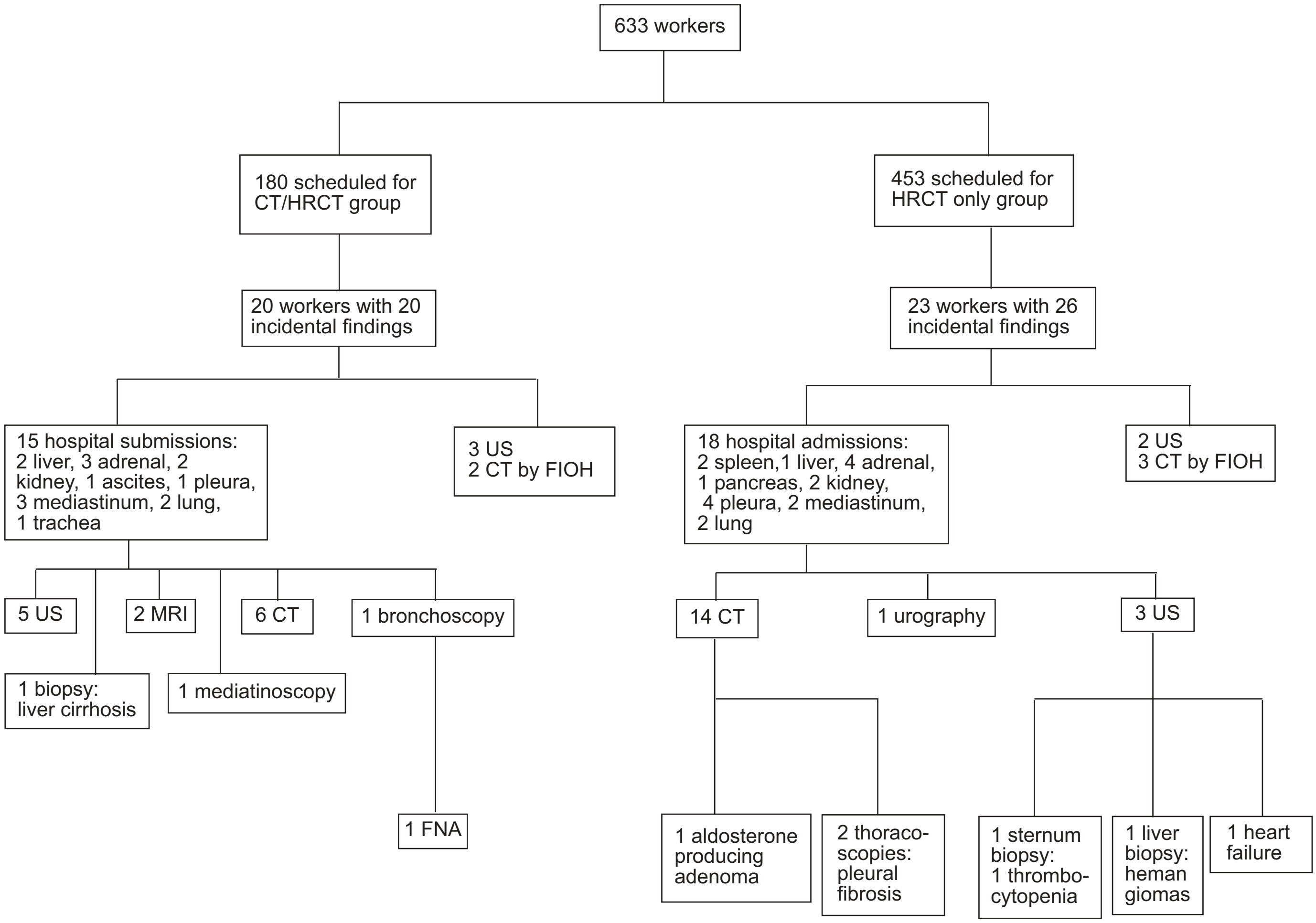

FIGURE 2. Incidental findings requiring additional examination. CT: computed tomography; HRCT: high-resolution CT; US: ultrasound; FIOH: Finnish Institute of Occupational Health; MRI: magnetic resonance imaging; FNA: fine-needle aspiration.

systematic screening projects were suggested. The present authors tried to study the value of both spiral CT and HRCT in lung cancer screening of asbestos-exposed workers, as there are no previous studies concerning the matter. Only the high-risk workers were included in the spiral CT group due to radiation exposure concerns. The groups turned out not to be optimal due to the presence of more cancer cases in the low-risk group. The smoking history criteria (current active smoker or ex-smoker with cessation within the previous 10 yrs) used as part of the current protocol may have been too strict for current or former workers with asbestos exposure.

There were no statistical differences between the five cancer patients and the rest of the screened individuals with respect to the mean age, asbestos exposure index or smoking habits (one-way ANOVA; table 2). The only difference between the groups was that all the participants with a detected lung malignancy had smoked, while no lung cancer cases were detected among nonsmokers. In order to determine the benefit of CT in lung cancer screening, further randomised controlled trials are needed with an adequate follow-up of all participants. Such trials are now underway [24, 25] and the results may provide more information of the feasibility of the screening. If screening for lung cancer is effective, then all the asbestos-exposed workers classified as smokers should be included in the screening group.

Lung cancer screening with low-dose CT has been shown to detect numerous indeterminate lung nodules [11–15, 22], of which the vast majority are benign and therefore make cancer detection difficult. The diagnostic work-up should find small lung cancers as early as possible and unnecessary surgery of benign nodules should be avoided. However, no standard approach for the diagnostic work-up currently exists. In most screening studies, the assessment of growth rate has been the main technique applied [11, 12, 14, 15, 22]. HENSCHKE [26] reported that, in ELCAP studies, 94% of the recommended biopsies resulted in a diagnosis of malignancy and no lobectomies were performed for benign disease. In other lung cancer screening studies [13, 15, 22] this kind of result has been difficult to achieve. In the present study, three lung biopsies for nodules were performed and none of them proved to be malignant, while two benign nodules were operated on.

The present authors detected incidental findings in 44% of the participants. Additional examinations were needed for 7.3% of those screened and clinically important findings were regarded to exist for 0.6%. MACREDMOND *et al.* [15] reported incidental findings in 61.5% and significant findings in 49.2%

TABLE 2 Asbestos exposure index, mean age and pack-yrs for the five lung cancer patients *versus* the rest of the participants

	Subjects n	Mean±SD	Range
Asbestos exposure index			
Other participants	609	79.6±46.3	9.0–268.0
Lung-cancer patients	5	58.6±31.1	24.5–104.8
Age yrs			
Other participants	627	64.5±6.81	45.3–86.9
Lung-cancer patients	5	68.1±3.1	65.5–73.4
Pack-yrs			
Other participants	460	22.7±17.3	0.5–129.0
Lung-cancer patients	5	21.0±14.6	10.0–43.0

The asbestos-exposure index is defined as the cumulative exposure index for the work career until the screening visit. This is calculated summing up the asbestos working years weighted by the respective estimated exposure levels [1].

of their lung cancer screening population, while SWENSEN *et al.* [13] detected significant findings in 14% and incidental malignancy in 7.9%. No incidental malignancies were found in the present study. The definition of the incidental findings and their significance varied (table 3). Such findings may save additional lives but they can also lead to a series of unnecessary examinations, as in the present study, in which most of such findings proved to be benign. Conversely, the value of some incidental findings, such as coronary calcifications, as risk factors is not yet fully known.

After screening examinations many participants need follow-up CT scans or other examinations for noncalcified lung nodules or incidental findings. This necessity not only adds to the cost of the screening but may also increase anxiety and feelings of sickness among participants [27, 28]. These psychological factors seem to have gained little attention in the literature.

In lung cancer screening, attention should also be paid to the radiation dose. With spiral CT, the present authors used similar or a slightly higher mA value (36–110) than the latest screening programmes (40–50 mA) [10–12]. In low-dose CT the effective dose range is 0.3–0.65 mSv [13, 29], while with conventional CT the range is 3–27 mSv [29]. A screen-detected lung nodule may lead to one or more additional diagnostic CT examinations and thus increase the dose. According to BRENNER [30], a mortality benefit of >5% would be needed to outweigh the potential radiation risks of annual CT screening.

TABLE 3 Incidental findings reported in three studies screening for lung cancer

Finding	SWENSEN *et al.* [13][#]	MACREDMOND *et al.* [15][¶]	Present study[+]	Present study[§]
Emphysema		130 (29)		
Bronchiectasis	11 (0.7)	44 (9.8)		
Arterial calcification	1 (0.1)	64 (14.3)	138 (21.8)	
Other lung pathology	2 (0.1)	17 (3.8)	33 (5)	4 (0.6)
Pleural effusion/plaque/nodule	4 (0.3)	4 (0.9)	6 (1)	5 (0.8)
Goiter/thyroid nodule		9 (2)	4 (0.6)	
Aortic aneurysm	51 (3.4)	1 (0.2)	1 (0.2)	
Bronchial/tracheal pathology	9 (0.6)		2 (0.3)	2 (0.3)
Pericardial effusion	9 (0.6)			
Atrial myxoma	1 (0.1)			
Breast finding	17 (1.1)		2 (0.3)	
Breast cancer	3 (0.2)			
Mediastinal lymphadenopathy			6 (1)	6 (1)
Ascites			2 (0.3)	2 (0.3)
Renal cell cancer	4 (0.3)			
Benign/indeterminate hepatobiliary/renal/ spleen disease	57 (3.8)	41 (9.1)	97 (15.3)	16 (2.5)
Adrenal pathology	36 (2.4)[ƒ]		13 (2)	9 (1.4)
Pancreas			1 (0.2)	1 (0.2)
Gastric/ esophageal pathology	2 (0.1)	4 (0.9)	17 (2.7)	
Spine metastasis	1 (0.1)			
Lymphoma	2 (0.1)			
Active endometriosis		1 (0.2)		
Soft tissue nodule/calcification			19 (3)	1 (0.2)
Diaphragm eventration			2 (0.3)	
Total	210	315	343	46

Data are presented as n (%), unless otherwise stated. This value indicates the amount of individual abnormalities observed and the proportion this represents over the total study population. #: significant findings for 1,520 participants; ¶: all findings for 449 participants; +: all findings for 633 participants; §: additional examined findings; ƒ: one pheochromocytoma.

Conclusion

In conclusion, spiral computed tomography screening and, in some cases, high-resolution computed tomography seem to be sensitive in revealing malignant tumours in asbestos-exposed individuals despite an abundant pleural and pulmonary pathology. The problems of screening include the optimal selection of the target group, the large number of benign lesions both in the lungs and elsewhere and iatrogenic hazards, such as radiation exposure and unnecessary investigations caused by irrelevant findings. Screening for lung cancer among the present asbestos-exposed group yielded roughly a similar amount of cancer cases than previous baseline screening trials, in which the participants had no significant asbestos exposure but usually a heavier smoking history.

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