HISTOLOGICAL FINDINGS AND LUNG DUST ANALYSIS AS THE BASIS FOR OCCUPATIONAL DISEASE COMPENSATION IN ASBESTOS-RELATED LUNG CANCER IN GERMANY

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Abstract

Objectives: This study has researched the significance of histologically raised findings and lung dust analyses in the context of claiming the recognition of and thus compensation for an asbestos-associated occupational disease. **Material and Methods:** For this approach, all findings from the German Mesothelioma Register in 2015 that included lung dust analyses were evaluated and were compared with information on asbestos fiber exposure at work based on fiber years, and with the results of radiological findings. **Results:** For 68 insured persons, recognition of an asbestos-induced lung disease according to Section 4104 of the German Ordinance on Occupational Diseases (Berufskrankheitenverordnung – BKV) could be recommended solely on the basis of the histological examinations of lung tissues and complementary lung dust analyses. Neither did the calculation of the cumulative asbestos dust exposure at work yield 25 fiber years, nor could bridge findings (e.g., plaques) be identified. In addition, the autopsies of 12 patients revealed plaques that had not been diagnosed during radiological examinations. These results show that – irrespective of the prescribed working techniques and radiological diagnosis – pathological/anatomical and histological diagnostics are often the only way for the insureds to demonstrate the causal connection between asbestos and their disease. Even after long intervals of up to 40 years post last exposure, the asbestos fibers would still be easily detectable in the lung tissues evaluated. **Conclusions:** Whenever suitable tissue is available, it should be examined for mild asbestosis with the aid of a lung dust analysis. Otherwise there is a risk that an occupational disease is wrongfully rejected. In the context of health insurance, the lung dust analysis and the resulting proof of the presence of asbestosis often constitute one option of providing evidence of an occupational disease. Int J Occup Med Environ Health 2018;31(3):293–305

Key words:
Occupational disease, Lung asbestos fiber burden, Asbestos bodies, Lung cancer, Lung dust analysis, Compensation

INTRODUCTION

Asbestos is a fibrous silicate mineral which owes its notoriety to its wide spectrum of industrial applications. The fiber is distinguished by properties like being imperishable, indestructible, fire-resistant, extremely stable, weatherproof, biopersistent, but resilient and easy to work. On the other hand, the fibers are so tiny that they may enter the lungs as air-borne dust in the inhaled air and then trigger diseases of the lungs [1]. Pleural mesothelioma and plaques are typical asbestos-related diseases. Asbestosis belongs to the pneumoconiosis. The asbestos fibers, when inhaled, induce septal fibrosis of lung tissue leading to tissue scarring. Beyond that, asbestos may also cause cancer of the lung. Mesothelioma may occur with very low asbestos exposure even brief one but it is thought that other cancers and fibrosis require more exposure.

While asbestos was banned in Germany in 1993, it continues to be used worldwide. In addition, asbestos is still present in many buildings [2] and the environment [3]. With the asbestos ban the exposure for insureds has changed dramatically. While historically exposure was high during mining and manufacturing or while dusty sawing, drilling, grinding and installing asbestos containing material, today's exposure is quite low with proper disposal [4–6]. Nevertheless, unless asbestos is being banned around the globe, asbestos diseases are bound to persist [5,7] and people will die [8]. As exposure cessation for insureds dates back up to the 60s the traceability of asbestos fibers in lung tissue after this long latency period is of significance for the diagnosis of asbestosis and occupational compensation.

In principle, recognition as an occupational disease (Berufskrankheit – BK) and thus compensation are granted for asbestosis (BK 4103), lung cancer or laryngeal cancer (BK 4104), and mesothelioma (BK 4105) if they are associated with exposure to asbestos dust in the work environment. However, due to their variate etiology, recognition of lung or laryngeal cancers as occupational diseases under BK 4104 of the Ordinance on Occupational

Diseases (Berufs-Krankheiten-Verordnung – BKV) [9] is possible only if they are:
– related to asbestos pneumoconiosis (asbestosis), or
– related to a pleural disease due to asbestos dust, or
– if evidence is produced for a work-related exposure to a cumulative dose of asbestos fiber dust of at least 25 fiber years (25×10^6 fibers/m$^3 \times$ years).

Hence, apart from an established medical diagnosis of the primary tumor and proof of occupational exposure, at least one bridge finding, complying with current law requirements, needs to be provided as a precondition for recognition.

If a suspected case of an asbestos-associated occupational disease is reported to include evidence of a lung tumor or laryngeal tumor, the accident insurance provider will first obtain a person's work history, based on the Falkenstein Recommendation [10] and the Association of the Scientific Medical Societies in Germany (Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften – AWMF) S2 Guideline on the Medical Appraisal of Asbestos-Associated Diseases [11].

If contact with asbestos in the context of an insured occupation is confirmed, further steps of investigation, that address the required bridge findings, will be introduced. To do so, the entire work life will be analyzed so as to be able to convert the asbestos exposure of an insured person into fiber years. Any available X-ray scans will be evaluated by experienced radiologists for typical asbestos-related changes of the tissue or the pleura, and a high-resolution computer tomography (HR-CT) will be carried out, if required, and will be based on the protocol of the Falkenstein Recommendation [10]. If a patient underwent surgery for lung cancer treatment, this is an opportunity to histologically evaluate the resected tissue for any bridge findings like asbestosis or pleural plaques.

Depending on the overall health or the preferences of the insured, the individual steps of investigation may be initiated concurrently with the aim of accelerating the process. As a rule, however, histological testing of any available tis-

sue samples according to the diagnostic algorithm of the Falkenstein Recommendation [10] will only be initiated if there are no radiological bridge findings [12] and a total of 25 fiber years cannot be ascertained either, i.e., if no other bridge findings exist. If no bridge findings may be confirmed during the life time of an insured person and if this person dies, new investigational opportunities result in the context of an autopsy.

It is important to remember that minimum asbestos-related changes as in grade I asbestosis (minimal asbestosis) cannot be identified radiologically even in high-resolution HR-CT [13] and that small plaques also elude radiological diagnosis quite frequently [14,15]. The extent of plaques is thought to correlate with the asbestos burden in lung tissue [16]. Diagnosing such minimal changes like grade I asbestoses requires pathological/anatomical and histological examinations possibly in connection with lung dust analyses in specifically dedicated and highly experienced laboratories [17].

Objective

This study was designed to investigate the significance of pathological/anatomical and histological examinations of bridge findings in combination with a lung dust analysis for recognition procedures, evaluating current data. To do so the histologically obtained bridge findings were correlated and compared with fiber years and radiological diagnostic outcomes.

MATERIAL AND METHODS

We analyzed 1038 data records of the German Mesothelioma Register which in 2015 had been subjected to pathological, histological, routine evaluation and the dust analysis on the grounds of suspected asbestos-related disease was conducted, too. In 767 cases occupational asbestos exposure was confirmed; calculations of the fiber years by the respective accident insurance providers were available for 512 insured persons; exposure periods were given for 534 data sets. A statement on the plaque status based on radiological diagnostics was comprised in 727 files, and a BK 4103 had already been recognized in 27 cases, without, however, differentiating between lung asbestosis and "pleural asbestosis" (Table 1). There were 851 problems raised, that related to bridge findings in the context of an investigation procedure for BK 4104 (Table 2). All tissue

Table 1. Radiologic findings and exposure data from clinical reports, and exposure evaluation – provided by the insurer – concerning insureds exposed to asbestos as registered by German Mesothelioma Register [23], 2015

Cohort statistics	Insureds (N = 1 038)		Range [years]
	n	%	
Fiber analytics done	1 038	100.0	
electron microscopic fiber analytics	36	3.5	
Plaques status according to radiological/surgical report determined	727[a]	70.0	
Asbestos exposure determined	767	73.9	
duration of exposure	534	51.4	1–52
end of exposure	493	47.5	0–66
Fiber years calculated	512	49.3	0–84[b]
BK 4103* (asbestosis/plaques) recognized	27	2.6	

*According to the BKV (Berufs-Krankheiten-Verordnung – Ordinance on Occupational Diseases) [9].
[a] 170 plaques, 557 no plaques.
[b] In fiber years ($\times10^6$ fibers/m^3×years).

Table 2. Insureds exposed to asbestos examined (including lung dust analysis) and autopsied as registered by German Mesothelioma Register [23], 2015, by disease

Insureds	BK 4103* (asbestosis/plaques)	BK 4104* (lung cancer/ laryngeal cancer)	BK 4105* (mesothelioma)
Examined[a]	109	851	48
Autopsied (out of examined)	51	171	29

* According to the BKV (Berufs-Krankheiten-Verordnung – Ordinance on Occupational Diseases) [9].
[a] Insureds of whom lung tissue was available. If not autopsied, the tissue was from surgery.

samples were collected from the tissue obtained in the surgical resection of the tumor (N = 783) or were removed during autopsy (N = 255). Two samples were obtained on the occasion of exhumations, and one sample was obtained from an explant. None of the tissue samples was collected for the sole purpose of a dust analysis.

Lung dust analysis

The German Mesothelioma Register was assigned to carry out lung dust analyses by accident insurance providers, patients, family members, courts, and for scientific quality assurance or by request of the treating hospital if suitable lung tissue was available, but:

– occupational asbestos exposure could not reliably be confirmed, and occupational disease under BK 4103, BK 4104, BK 4105 or BK 4114 was under consideration,

– pleural/pulmonary bridge findings relating to an occupational disease under BK 4104 could not be obtained radiologically and the question of existing grade I asbestosis had been raised,

– no pleural bridge findings were available and the so-called "technical bridge" of 25 fiber years had not been reached either,

– fibrotic lung changes of varying genesis needed to be discriminated from each other by differential diagnosis.

The lung dust analysis followed an established process [18] using phase contrast light microscopy as described in the AWMF S2 Guideline, Annex 5 [11]. Whenever possible, 4 tissue samples from various sites were investigat-

ed. Following cold incineration of the tissue and enriching inorganic dusts on filters, they were examined under the microscope at ×200 or ×400 magnification using the differential interference contrast (DIC) technique with polarizing imaging. The asbestos fibers, that had been found, were counted, i.e., both the encased fibers, the so-called asbestos bodies, and separately free fibers without encasement were considered in the assessment especially if asbestos body counts were low. In the case of any doubt an electron microscopic examination was done. All statistical analyses were done with the asbestos body count. By this method alone we were able to confirm 10 asbestos bodies/g of wet tissue if the fiber diameter was wider than 0.2 μM. This restriction was due to the upper limit of light microscopic resolution. For the normal population without detectable exposure to asbestos, the reference values of this method are below 23 (9±13) asbestos bodies/g of wet lung tissue [15].

Grade I asbestosis

Diagnosis of grade I asbestosis followed the internationally accepted criteria of the 1997 Helsinki Consensus Conference [19] in its amended version of 2014 [20] which are also the basis for the definition of the German Society of Pathology [21]. As asbestos bodies may be very small, the search for them in specifically stained sections was very intense using up to ×400 magnification. In some cases several sections per tissue samples had to be prepared for histological evaluation.

Electron microscopic examination

If no or remarkably few asbestos bodies were found under the light microscope, but secondary lung changes like fibrosis, inflammation, putrefaction or autolysis were present, the analysis was extended by electron microscopic evaluation according to the current Helsinki Criteria [20]. This method may yet provide evidence of asbestos fibers in lung tissues [22]. Samples of a total of 36 patients were examined under the electron microscope.

RESULTS

The tissue samples were obtained between 1993 and 2015, however, only 21 samples were older than 5 years, 3 samples were older than 10 years and 3 samples were older than 15 years; 84.4% of the samples were collected over the last 3 years (2013–2015). Patients were born between 1923 and 1974; when samples were taken they were 40–92 years old, with the vast majority being 55–80 years of age (Figure 1a). Latest asbestos contact dated back to up to 66 years before, but in isolated cases persisted even at the time of examination because the insured person was working in building refurbishment or waste removal. The mean interval to last asbestos contact was 27 years (Figure 1b). Duration of asbestos exposure ranged from a few months to 52 years; mean duration was found to be 18 years (Figure 1c).

In our collective from 2015 which totaled 1038 cases that were subjected to the lung dust analysis, 609 patients (58.7%) had asbestos body counts of less than 23/g of wet lung tissue; thus no increased asbestos burden could be established as against the non-exposed population and no asbestosis was present. These results corresponded to the prescribed working techniques that could not demonstrate outcomes of 25 fiber years and to radiological diagnostics by which no plaques or fibrosis could be revealed. In addition, no occupational contact with asbestos could be established for 22 patients.

Sixty patients had previously had a tentative diagnosis of asbestosis or "pleural asbestosis" (plaques), for 27 of them
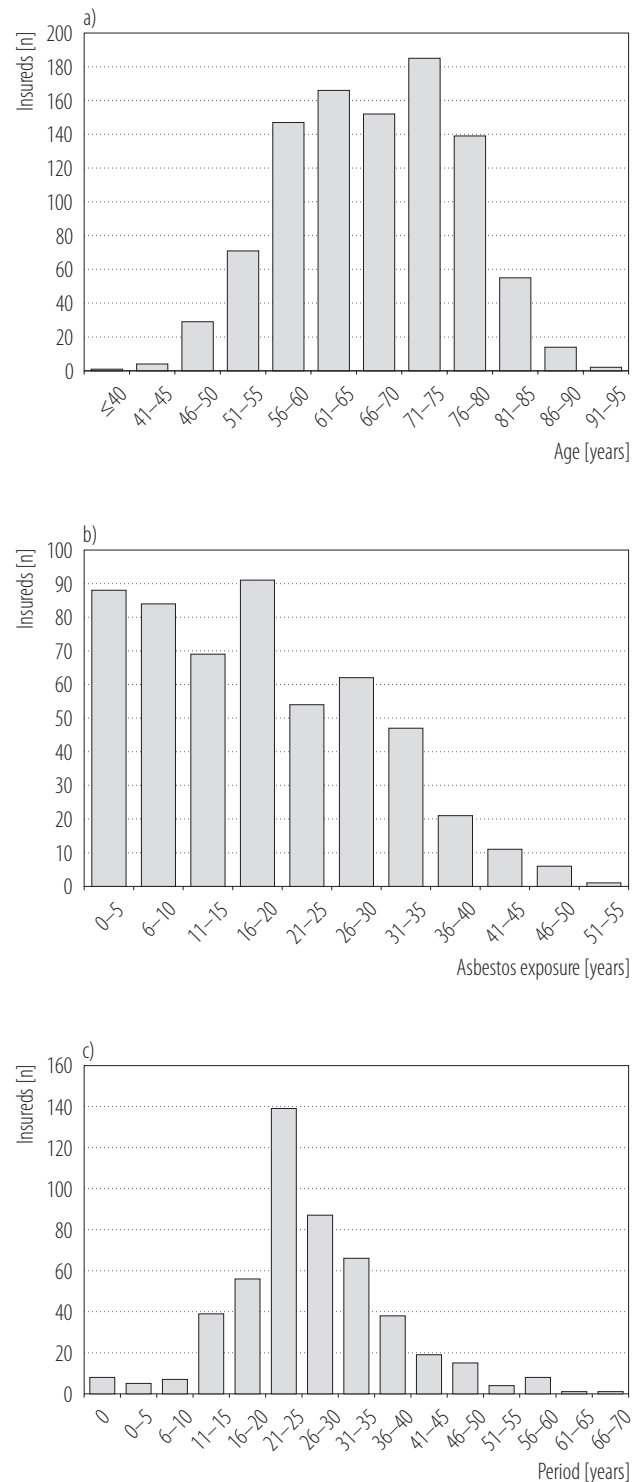

Fig. 1. Cohort statistics of insureds exposed to asbestos: a) age at the time of tissue sampling, b) duration of asbestos exposure, c) time elapsed between last confirmed asbestos contact and the time of tissue sampling

occupational disease under 4103 of the BKV had already been recognized. Histology confirmed the occupational disease in 21 of the cases (77.8%), with asbestosis of the lung and histopathological evidence of asbestos bodies in the lung tissues being established in 15 samples. In 6 cases neither asbestoses nor plaques could be confirmed by histopathological examination. On the other hand, asbestosis and evidence of asbestos bodies in the lung tissue were demonstrable in 7 of the 33 non-recognized cases for BK 4103. In the case of other 2 patients only previously undiagnosed hyaline plaques could be identified, so that an asbestos-related occupational disease could be established in a total of 9 patients (27.3%).

The collective included 31 patients where the clinical diagnosis had indicated a non-specified fibrosis or pleural fibrosis without evidence of any asbestos exposure. Histological evaluation permitted to identify asbestosis or plaques, hence recognition of an occupational disease could be recommended for 8 out of these patients (25.8%).

In addition, histological evidence of asbestosis or plaques could be obtained for 120 insured persons where no suspicion of fibrosis or asbestosis had previously been expressed. All of these 120 diagnoses were first-time diagnoses that only had been made when the German Mesothelioma Register carried out pathological/anatomical evaluations of the cases. Histological proof of a lung asbestosis was successful in the case of 76 patients after a complementary lung dust analysis had been carried out.

Thus, the results of the lung dust analyses provided histological evidence of an existing asbestosis of grade I or higher for 104 patients examined (10%). The maximum concentration of asbestos bodies found was 1 464 000/g of wet lung tissue (1 464 000 asbestos bodies, 372 000 free asbestos fibers). The minimum according to asbestos bodies alone in the collective evaluated was 100 asbestos bodies (in this case additionally 600 free asbestos fibers)/g of wet lung tissue. Taking asbestos bodies and free asbestos fibers into a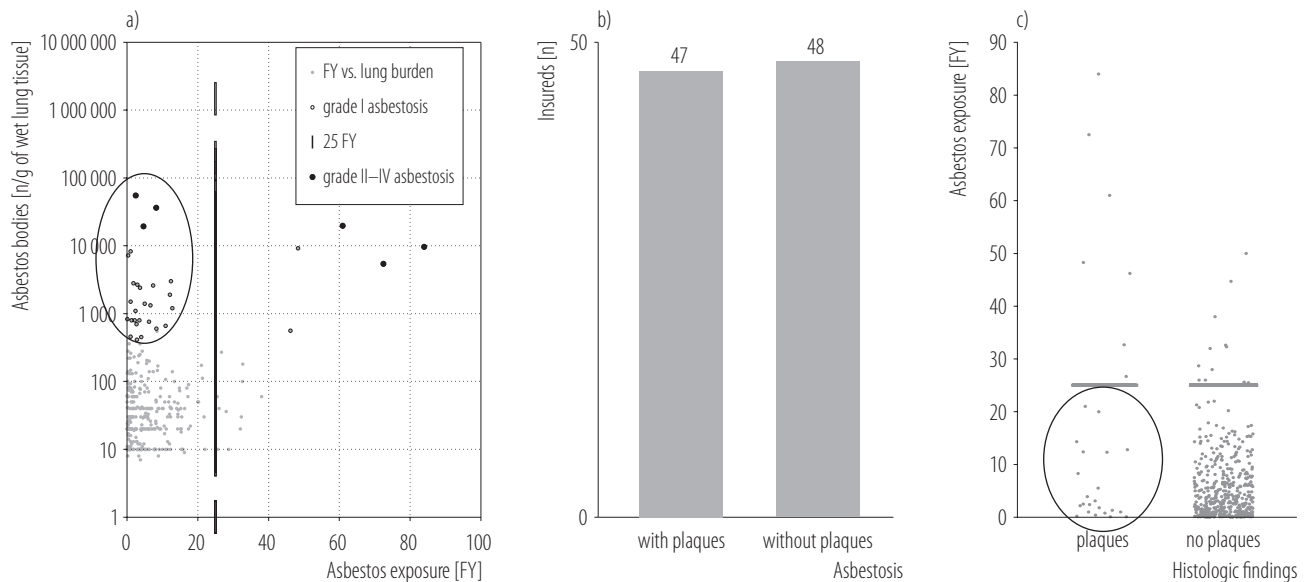ccount, the minimum was 672 (in this case 460 asbestos bodies and including 212 free asbestos fibers)/g of wet lung tissue.

As regards lung and laryngeal cancer cases, 68 (8%) asbestoses of grade I or higher could be confirmed as the sole bridge finding and recognition as occupational disease could be recommended. These bridge findings were only made possible by combining the lung dust analytical examinations and histological lung evaluations using iron staining. Without such complementary examinations an occupational disease under BK 4104 would have been rejected for lack of bridge findings. The German Mesothelioma Register regularly establishes histologically low-grade asbestoses as bridge findings and as a result recommends recognition as occupational disease [23].

The analysis of lung dust fibers relied on quantitation of the current asbestos burden in lung tissue at the time of tissue sampling. Past occupational exposure to asbestos dust was calculated in fiber years by the respective accident insurance provider. The cluster analysis of the scatter plots for asbestos burden of lung tissues against the grade of occupational exposure showed good correlation where the number of fiber years was high (Figure 2a). However, an additional cluster was determined for low asbestos dust exposure in the work environment (meaning exposure that was below the 25 fiber years stipulated by legislation) and for a demonstrably high asbestos burden in the lung tissue of the insured person and histologically verified asbestosis.

In 50.5% of the histologically established asbestoses, it was not possible to diagnose any plaques by pathological/anatomical evaluation (Figure 2b).

A comparison of the plaque status after pathological/anatomical diagnoses with the fiber years determined again shows a group of 22 patients where the calculated exposure was shorter than 25 fiber years, but where plaques were found during autopsy or could be confirmed by pathological/anatomical evaluation (Figure 2c). Hence, recognition as an occupational disease was recommended under patho-

a) The circle indicates histologically established asbestoses as potential bridge findings for BK 4104 (asbestosis according to the BKV (Berufs-Krankheiten-Verordnung – Ordinance on Occupational Diseases [9])) for insureds not attaining 25 fiber years (FY) ($\times 10^6$ fibers/m^3×years).
c) The circle highlights histologically confirmed plaques in insufficient numbers of fiber years.

Fig. 2. Correlation between bridge findings based on required working techniques and histological bridge findings for insureds exposed to asbestos: a) asbestos bodies found in lung tissue vs. the fiber years determined by insurance provider with cluster analysis, b) the histologically confirmed bridge findings asbestosis and plaques as indicator lesions, c) the fiber years calculated in plaques confirmed by histology and during autopsy

logical/anatomical aspects. When including the radiologically confirmed plaques, the total of 53 patients with plaques but an estimated asbestos dust exposure of under 25 fiber years were revealed in the collective examined.

DISCUSSION

The primary focus of pathological routine diagnostics is on changes that adversely impact health, i.e., malignancies, in particular. In this case, asbestos-induced changes are often overlooked or are not identified as such since they are not relevant for a patient's treatment. It is only in the context of an occupational disease under Section 4103 or 4104 of the BKV that demonstrating radiological or histological bridge findings is of significance. Lung tissue changes which often are only minimal and the asbestos bodies embedded in the tissue only may be visualized when using a special staining process for histo-

logical preparation and choosing a higher magnification like ×200 to ×400. Advanced stages of asbestosis like grade II–IV conditions might even be detected under the light microscope. But if this first examination leaves questions unanswered, the lung dust analysis by an experienced reference lab is required [17].

The lung dust analysis is a method that is very helpful for diagnosis because the asbestos bodies may be enriched on a filter to attain the equivalent of about 2000 histologic sections to be evaluated. With the tissue background removed, the filter preparations afford visibility of free fibers when viewed in phase contrast technique; free fibers have no encasement and, therefore, cannot be made visible even when applying iron-staining.

All asbestoses (N = 104) found in the 2015 collective were first-time diagnoses carried out by the German Mesothelioma Register. In all of the 68 cases where asbestosis had

been diagnosed as a bridge finding for BK 4104, recognition as an occupational disease had been recommended and this would not have been possible without the quite demanding lung dust analysis and histological examination applying iron staining. Without the histological add-on investigation recognition as an occupational disease would have been rejected.

According to the Falkenstein Recommendation [10] and the related AWMF Guideline [11] available tissue samples are to be investigated for grade I asbestosis. The stringent implementation of this Recommendation would mean that recognition as an occupational disease cannot be rejected if no such examination has been carried out. Experience gathered by the German Mesothelioma Register shows that the histological examination of available tissue samples sometimes was only requested by the occupational public health and safety professional of a given area, or after a notice of opposition/a law suit had been filed by the insured person or a family member after BK 4104 had been rejected. A reliable diagnosis may be obtained only if existing tissue samples are evaluated for the specific purpose of settling the question of whether there is a grade I asbestosis.

The results obtained in the 2015 collective demonstrate that there is no suitable method beyond histology that is able to replace the histological diagnosis of grade I asbestosis. It is worth noting that there is no limit value to be derived from the prescribed working techniques that would allow to abandon the histological examination of available tissue samples if that limit was undercut. Any occupational exposure always dates back to many years before. At the time of the assessment many companies may no longer exist, there are no contemporary witnesses, or an insured person cannot contribute precise facts because he or she is no longer sure of these facts or, at the time of exposure, was not aware of any contact with asbestos. All patients investigated on insurance, clinical or patients request had a supposed occupational exposure to asbestos. Thus it is more likely that the occupational history

calculated in fiber years has been underestimated than assuming an environmental exposure leading to asbestosis. Lung cancer and fibrosis require more exposure than environmental levels. According to the Helsinki criteria [20] for fiber counts above 100 asbestos bodies/g wet lung tissue (1000 asbestos bodies/g dry weight) an occupational history should be considered. The asbestoses diagnosed in 2015 where fiber years ranged 0.1–12.8, demonstrate the significance that is to be attributed to pathologically/anatomically and histologically obtained bridge findings in recognition procedures for BK 4104 (Figure 2a).

Histologically confirmed plaques or plaques found during autopsy served as bridge findings and resulted in a recommendation of recognition. However, a negative plaques status did not exclude an asbestosis as proven by the results of the analysis under the report that was carried out in 2015 (Figure 2b). It should be mentioned that radiologic data is from clinical routine findings, occupational physicians or experienced radiologist and therefore vary in quality. Positive CT findings are definitive for occupational compensation, available tissue will not be forwarded for histologic examination. For tissue from surgery maybe no biopsy was taken from plaques. The histologic diagnoses including the lung dust fiber analysis in this study were done routinely using a standardized method. We therefore abstained from calculations of sensitivity and specificity of radiologic findings.

Since the end of World War II Germany had seen a continuous rise in the use of asbestos, with its maximum being reached at the end of the seventies. After that the use of asbestos was found to be declining steadily until the ultimate ban of its use in Germany in 1993 [24]. This ultimate ban of asbestos now has been effective in Germany for 23 years; 36 years have passed since the first ban on the use of asbestos became effective in 1979. Nevertheless, asbestos bodies were easily detectable in the lung dust analyses and histological evaluations (Figure 3a). This fact is confirmed by other authors [25–27] and in other studies [28]. Asbestos fibers, including chrysotile/white asbes-
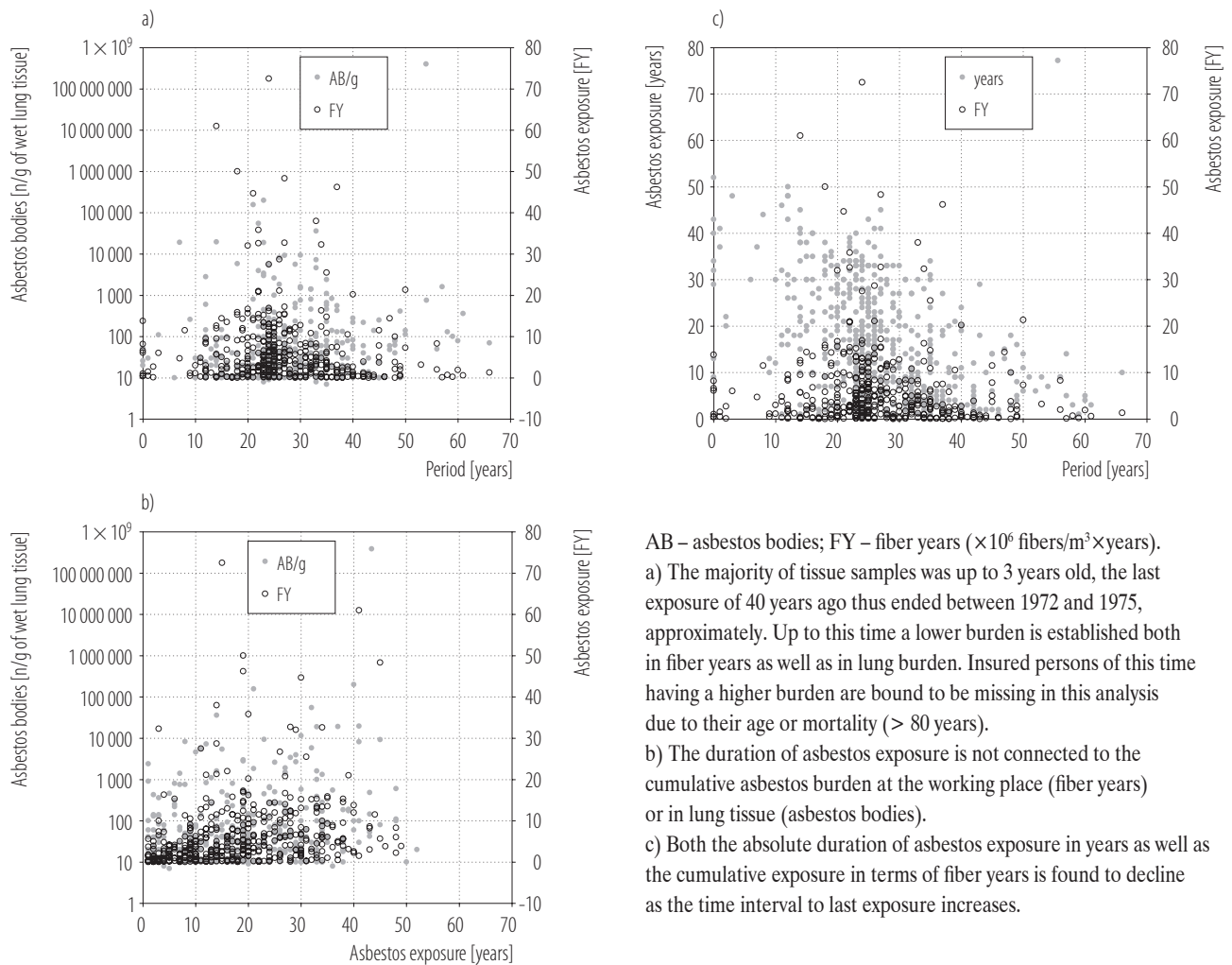
AB – asbestos bodies; FY – fiber years ($\times 10^6$ fibers/m^3 $\times$years).
a) The majority of tissue samples was up to 3 years old, the last exposure of 40 years ago thus ended between 1972 and 1975, approximately. Up to this time a lower burden is established both in fiber years as well as in lung burden. Insured persons of this time having a higher burden are bound to be missing in this analysis due to their age or mortality (> 80 years).
b) The duration of asbestos exposure is not connected to the cumulative asbestos burden at the working place (fiber years) or in lung tissue (asbestos bodies).
c) Both the absolute duration of asbestos exposure in years as well as the cumulative exposure in terms of fiber years is found to decline as the time interval to last exposure increases.

Fig. 3. Correlation analysis: a) asbestos burden in lung tissue of insureds exposed to asbestos and fiber years with period between last confirmed asbestos contact and the time of tissue sampling, b) the asbestos burden in lung tissue and fiber years with the duration of asbestos exposure, c) the period between last confirmed asbestos contact and the time of tissue sampling with the duration of asbestos exposure or cumulative level of the asbestos dust burden

tos which was the main type used in Germany, have a very long half-life in the human lung [29–32].

High asbestos body counts were obtained in lung tissue samples from insureds whose last asbestos exposure dated back to up to 40 years ago (Figure 3a). When exposure to asbestos dust dated back even longer, the insureds in this collective showed a lower asbestos exposure. This applies both to the absolute duration of asbestos exposure in years as well as to the cumulative exposure level calculated in fiber years (Figure 3c). Hence, the asbestos body counts in
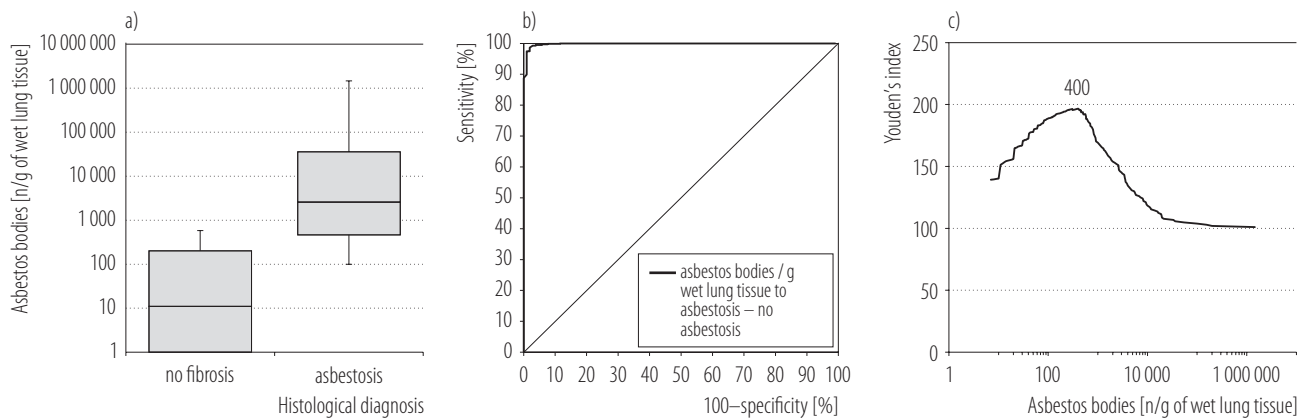
lung tissue are lower in these very old cases of exposure. The simple explanation for this lies in the life expectancy of people in Germany:

For the evaluation of the detectability of high asbestos dust exposure that dates back to over 40 years ago, it would be necessary to examine insureds who already in their young years had carried out highly hazardous work. This may be exemplified by the figures for an insured person who had started hazardous work at the age of 20 and continued this work for 20 years. After another 40 years without any ad-

a) The 95% quantiles are given as boxes and the minimum and maximum are included as error indicators. No meaningful limit value could be derived as the ranges for no fibrosis and asbestosis have an overlap. Results from lung dust analyses always need to be interpreted against the background supplied by histology.

b) The area under curve (AUC) is 0.998, p-value < 0.001.

c) The highest index is at the value of 400 asbestos bodies/g of wet lung tissue. Using this value sensitivity is 98.61% and specificity is 98.08%. Between counts of 100 (100% sensitivity) and 600 (100% specificity) the diagnosis strongly depends on histology. It should be kept in mind, that the diagnosis of asbestosis always needs a defined fibrosis pattern. An asbestos body count alone does not make the diagnosis.

Fig. 4. Statistical analysis: a) asbestos bodies found in the lung dust analysis for insureds exposed to asbestos and with histologically confirmed asbestoses and histologically non-verified asbestoses, b) receiver operator curve (ROC) of the asbestos body count in relation to the histologic diagnosis, c) Youden's index for the ROC analysis

verse exposure this insured person would be 80 years old. According to the German mortality table 2012/2014 the average live expectancy is now below 80 years: it is 78.1 for men and 83.1 for women [33]. Examining the detectability of an asbestos exposure that dates back to 40–60 years ago would thus require an insured person with an asbestos-related disease to reach the age of 80 to 100 years old. The majority of the collective investigated was between 55 and 80 years old (Figure 1a). Therefore, insureds of the older age and very old age with very early exposure to asbestos are missing in this investigation.

A correlation between the factual duration of exposure in years and the actual level of asbestos exposure could not be established for either the asbestos burden in lung tissue or for the calculated fiber years (Figure 3b).

Finally, we investigated whether the results of the lung dust analyses permitted to establish a limit value that in turn would serve as an indicator of the histological results. For this the asbestos body counts obtained in histologically confirmed asbestoses were set off against the figures determined in the lung dust analysis for the samples in which no asbestosis could be identified by histological or radiological methods since there was no fibrosis (Figure 4a). While there was, in fact, a bimodal distribution of the asbestos dust burden in the lung tissue, no limit value could be defined that would have permitted a clear discrimination of the 2 groups because data ranges overlapped. In cases of doubt an electron microscopic analysis has been added.

For scientific purpose we did a receiver operator curve (ROC) analysis (Figure 4b) and calculated sensitivity and specificity for various cut-off values of the asbestos body count in view of the histologic findings. The area under curve (AUC) was 0.998 with a p-value of < 0.001. The highest Youden's index was at the value of 400 asbestos bodies/g of wet lung tissue. Using this value, sensitivity was 98.61% and specificity – 98.08%. Between counts of 100 (100% sensitivity) and 600 (100% specificity) the diagnosis strongly depends on histology. It has to be kept

in mind that according to the Helsinki Criteria [17,19,20] each lab has to define its own reference values as fiber counts vary with the method of counting and tissue preparation. It should be pointed out, that the diagnosis of asbestosis always needs a defined fibrosis pattern. An asbestos body count alone does not make the diagnosis. When there is no fibrosis, asbestosis cannot be diagnosed by the methods of histology.

Conversely, a low number of fibers from the lung dust analysis may be sufficient for the diagnosis of asbestosis, if there is clear confirmation of fibrosis while the general condition of the tissue is poor due to secondary effects like tumorous, autolytic or inflammatory changes. Evaluation of a lung dust analysis does not rely on asbestos body counting alone but also considers free fibers and structures with an unidentifiable central fiber as well as the overall picture the dust burden presents. The overall result of a lung dust analysis should always be interpreted against the background of histological findings and should consider the condition of the tissues analyzed.

Occupational diseases tend to be underreported; this fact cannot be disputed [34,35], and this may be because no report of suspicion has been filled or because investigations have remained incomplete. The results of this study show that pathological/anatomical examinations that are supported by an assessment based on lung dust analyses may lead to the recognition of an occupational disease. If there is suitable lung tissue, all diagnostic means should be exploited and the tissue should be subjected to a lung dust analysis and the subsequent verification of bridge findings. Relying on technical investigations and radiological diagnostics alone carries the risk that a significant part of occupational diseases under Section 4104 of the BKV will remain undetected and thus will not be compensated.

CONCLUSIONS

The prescribed working techniques or radiological parameters are no suitable means of excluding a histological di-agnosis like asbestosis. A grade I asbestosis cannot even be diagnosed and, therefore, cannot be excluded by high-resolution computer tomography (HC-CT).

Even if the original histological assessment did not include findings of an asbestos-related pulmonary fibrotic process, asbestosis may yet be identified if the lung dust analysis is performed as a complementary examination. Even after very long intervals of up to 40 years post last exposure, the asbestos fibers would still be easily detectable in the lung tissues evaluated.

Grade I asbestosis may only be established by histological methods. If suitable lung tissue is available, an occupational disease under Section 4104 cannot be rejected on the grounds that exposure did not total 25 fiber years or that radiological evaluation did not reveal any bridge findings, unless the tissue was specifically subjected to a pathological/anatomical evaluation for asbestosis. The histological verification of asbestosis or plaques – even if found as a result of autopsy – will help many insured persons to find insurance justice.

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