MEASUREMENT OF ROUNDED OPACITIES IN THE LUNG OF X-RAY IMAGES TOWARDS QUANTITATIVE DIAGNOSIS OF PNEUMOCONIOSIS

J. TORIWAKI* • X. Chen* • J. Hasegawa†

*Department of Information Engineering, Faculty of Engineering, Nagoya University Nagoya, Japan
†Department of Liberal Arts, Chukyo University, Toyota, Japan

INTRODUCTION

From a clinical and occupational health viewpoint, the classification of pneumoconiosis films is of primary importance. The category of profusion used for recording the severity of the pneumoconiosis is based on assessment of the concentration of opacities by comparison with standard pneumoconiosis films whose profusions are given by a four-point scale: categories 0, 1, 2 and 3.[1] However, in practical radiographical diagnosis, objective reading is very difficult even to the experienced readers. It is a fact that there is considerable variation in reading the same film, not only by different readers, but also by the same reader at different times. Therefore, it has been strongly desired to develop an automated measurement method for quantitative diagnosis of pneumoconiosis X-ray films.

In most of previous studies on automated classification of pneumoconiosis films, the approach is to examine some kinds of texture features measured from X-ray images by regarding the opacity distribution as a texture pattern.[2-6] In such approach, however, it is difficult to avoid the influence of rib images and vessel shadows in chest X-ray images, and impossible to introduce necessary diagnosing experiences of medical experts into computer diagnosis process.

Since the advent of the more sophisticated digitization system in recent years which can provide high-resolution digital images, it has been possible to directly detect some kinds of very detailed objects in a chest X-ray film by computer, such as blood vessels, cancer lesions and pneumoconiosis small opacities. In this paper a new method for automated classification of pneumoconiosis chest X-ray films is presented, in which individual small rounded opacities are recognized, and the measured density of them is used as a classification feature. In experiments using ILO standard pneumoconiosis films, it is shown that density values of the small rounded opacities detected by this method are approximately proportional to the categories of profusion of pneumoconiosis. Moreover, the individual opacities detected by our system are compared with those by experienced radiologists to evaluate accuracy in opacity recognition. From the result, we see that not only the density values will be available as one of the effective features for computer diagnosis of pneumoconiosis, but also the detected small rounded opacities may be provided to the readers as reference data, and they are useful in training readers of pneumoconiosis films.

OUTLINE OF THE PROCEDURE

The processing procedure consists of the following three steps. First, the small rounded opacities in an input image are enhanced by a linear filter with a weight function designed based on a model of the small rounded opacity, then candidates of the opacities are obtained as a connected component pattern by thresholding the filtered image. Second, components due to shadows of ribs and vessels are removed by using a shape feature of a connected component to detect only objects suspected to be caused by the small rounded opacities. Third, the film is categorized according to the opacity density which is given by the ratio of the area or the number of the extracted opacities to the area of the lung region.

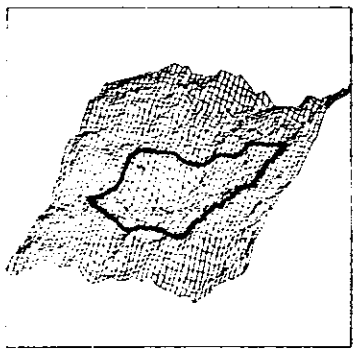
DETAILS OF THE PROCEDURE

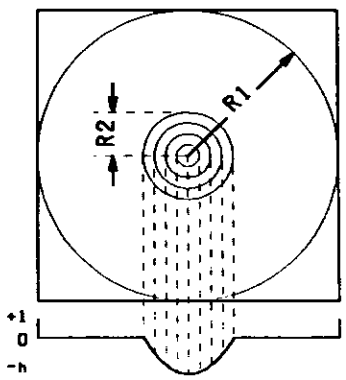
Extraction of Opacity Candidates

Uniform weighted smoothing is used to suppress the random noise which is introduced in the processes of image generation and image digitization. Namely, it gives each point the average gray level of its neighboring points and the point itself.

The small rounded opacities are appearing or even overlapping with many kinds of other shadows such as ribs and blood vessels in a chest X-ray image. A linear differentiation filter is employed to enhance the opacities, in which a weight function is designed based on the local distribution of gray levels of the opacities. We see that the gray levels at a small rounded opacity in an input image are lower than those of the surrounding background. Each of the opacities is observed as a spot-like object with a circular border, whose gray level distribution inside the border is like a bowl shown in Figure 1(a), although its shape is likely to be more complicated. Therefore, a basic model of the weight function designed here is as shown in Figure 1(b), in which, every point on the circle with the radius R1 has the value 1, points in the central area with the radius R2 have negative values distributing as a bowl, and others are zero. The operation with this mask is a type of the 2nd order differentiation, and can enhance the bodies of the opacities against the background whose brightness may be variant according to the zone of the lung. Figure 1(c) shows a weight function practically used in the experiments.

The candidate regions of the small rounded opacities are ob-





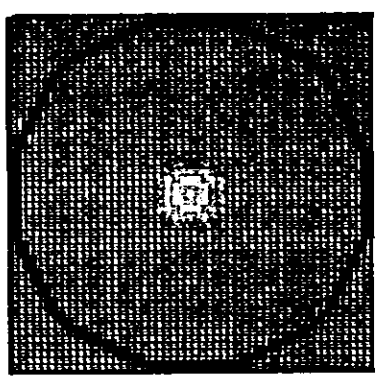


Figure 1. Small rounded opacity and weight function. (a) Local level distribution of an opacity and its neighborhood. (b) Weight function model. (c) Weight function used in the experiments.

tained by clipping the enhanced image with a pre-specified threshold. That is, values of pixels in the filtered image are changed into 0 if they are less than the threshold, then the remaining connected components are regarded as the candidate regions.

Recognition of Opacities

The candidate regions obtained above usually include many components caused by rib images and vessel shadows. Considering that the small rounded opacities should assumedly be isolated and be circular, and that the elongated regions may be generated by rib borders, the opacities can be extracted from the candidate regions by removing those components whose horizontal lengths are longer than a given value.

Furthermore, local maximum points of the enhanced image are detected in each of remaining regions to find the number and the location of the small rounded opacities. The operation is shown by the following equation:

where $\{f_{ij}\}$ and $\{g_{ij}\}$ are the input image (clipped enhanced image) and the output image (maximum point pattern), respectively, and N_{ij} is a local neighborhood region of the point (i,j). When the above operation is done at a considerably smooth area in the enhanced image, the extracted maximum points may construct a connected component by themselves. Every such component is shrunk into a single point.

Density Calculation and Categorization

The 1980 ILO Classification states that classification of a radiograph for profusion of small opacities requires a mental process of integrating profusion over the affected zones.[1] However, in order to classify the pneumoconiosis films automatically, it is necessary to set up some objective measurements for evaluating the profusion of pneumoconiosis films. Here, a density of opacities is used as the measurement, which is defined as the ratio of the area or the number of the extracted opacities to the entire observed area in the lung region. The area of opacities is calculated by the total number of pixels of the opacities recognized from the candidate regions, while the number of opacities is specified as the number of the maximum points. The observed area is the area of processed lung region after removing the area of the components caused by rib borders. Finally, the chest X-rays are categorized according to the density values.

EXPERIMENTAL RESULTS AND DISCUSSION

Eleven chest X-ray images selected from a set of international standard pneumoconiosis radiographs which was accompanied with the 1980 ILO Classification were used in

the experiments. They include nine pneumoconiosis films containing three categories (1, 2 and 3) of each of three sizes (p, q, and r) and two films with category 0. Each film was digitized into 3300×3400 pixels with 12 bits of gray level. Some of them are shown in Figure 2.

Since profusion relates better than size to indices of exposure within any one occupational group,[1] a family of the linear filters matched to the size of small rounded opacities were employed in the enhancement step. The value of the parameters (R1, R2) in the enhancement filter are (2, 10), (3, 20) and (4, 25) for the size p, q, and r, respectively. An example of candidate regions extracted from a film (category 3, size r) is shown in Figure 3. The opacities recognized from it are shown in Figure 4, while the maximum points detected from its enhanced image are shown in Figure 5, where gray values of the enhanced image are drawn in terms of contour lines and the location of each maximum point is represented by a circle with the radius proportional to the corresponding maximum value of the enhanced image. Figure 6 shows those maximum points superimposed by the circles on the corresponding original image. The opacity densities (vertical axis) calculated from each category of films (horizontal axis) are shown in Figure 7. From the results, it is known that the difference of the density between the category 3 and the category 2, or between the category 2 and the category 1 is relatively large, while it is difficult to distinguish the category 1 and category 0 decisively. A reason of this difficulty is that as the size (or the number) of the opacities become smaller, the extraction results will be more likely to be influenced by the blood vessel shadows.

In order to evaluate the accuracy of small rounded opacities detected by computer, they were compared with the opacities traced by experienced radiologists. The following procedure was employed in this tracing experiment. First an image to be

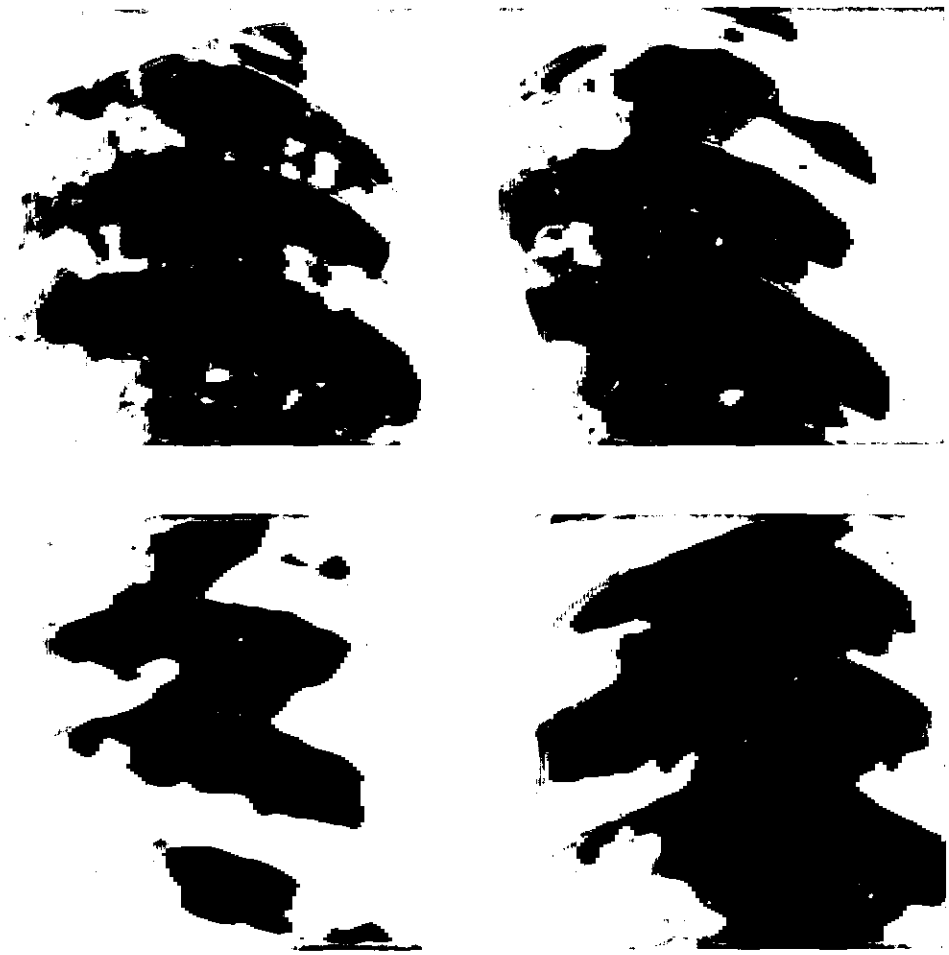


Figure 2. Examples of images used in the experiments cut from a set of international standard films by ILO. (a) (3/3,r/r). (b) (2/2,r/r). (c) (1/1,r/r). (d) normal.

traced is displayed on a high-resolution screen. Then, radiologists trace the small rounded opacities within the area specified by the same radiologists by using an interactive input device. On the screen, the traced opacities and the observed area are displayed by spots at the central position of them and a closed curve, respectively. Meanwhile, the location information of them is stored in the memory and used in the comparison. In Figure 8, each opacity traced by a radiologist is represented by a spot, and that extracted by computer is shown by a circle on the original image. Both results were compared only in the inter-rib regions of the image. Summary of the result is given in Figure 9.

Figure 3. An example of extracted candidate regions of the small rounded pneumoconiosis opacities. (category 3, size r)

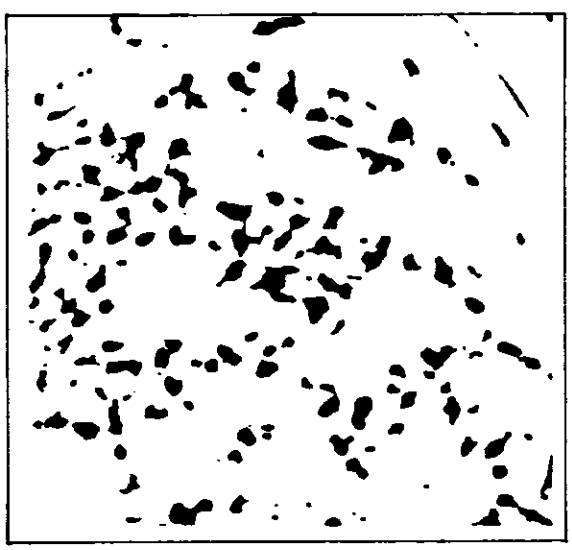


Figure 4. Extracted small rounded pneumoconiosis opacities.

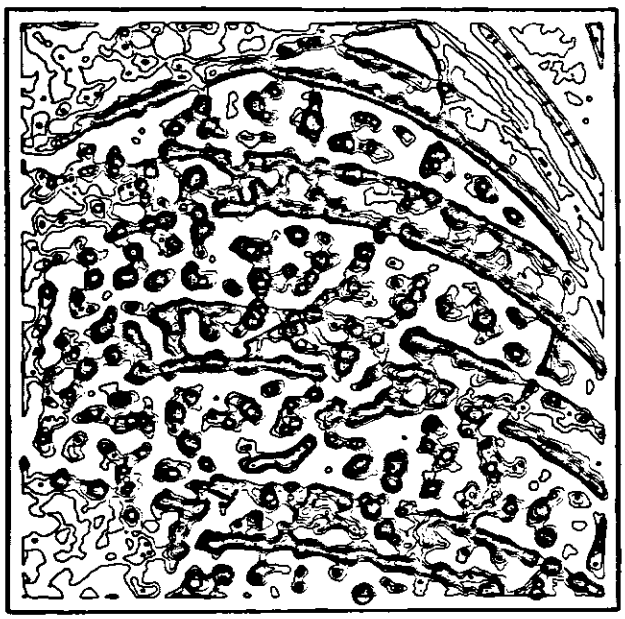


Figure 5. Maximum points of the enhanced image extracted from each of small rounded opacities.

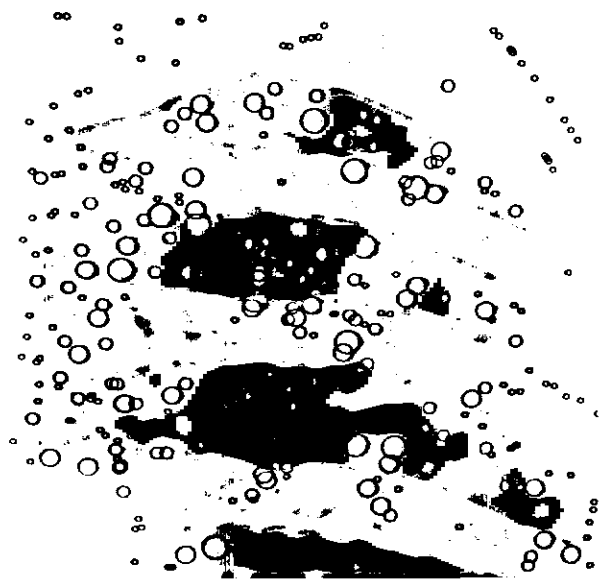
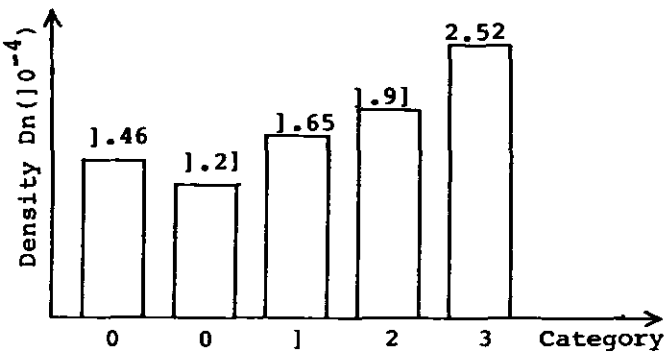


Figure 6. Extracted maximum points superimposed on original image.



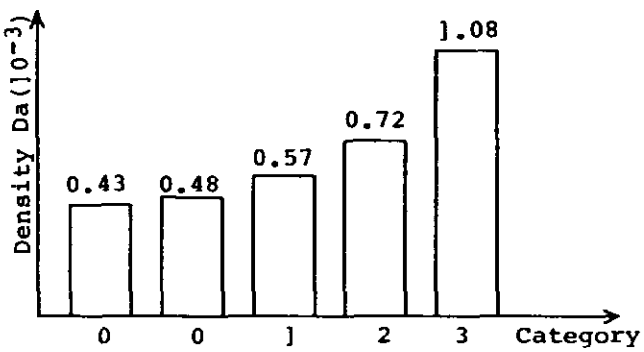


Figure 7. Density of opacities calculated from ILO standard films. (a) Area density. (b) Number density. (size r)

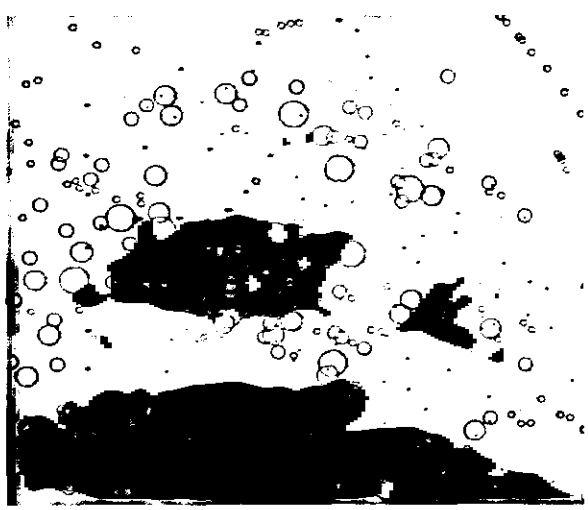


Figure 8. An example of small rounded opacities extracted by an experienced radiologist, and those by computer in the same original image. (category r, size r)

The extraction procedure of small rounded opacities described in this paper was also applied to the pneumoconiosis images obtained by the Fuji computed radiography system. Figure 10 shows both results by computer and radiologists on the original image, and the notation is the same as that used in Figure 8. The results showed that the procedure was also effective to computed radiography image.

CONCLUSION

A method to detect pneumoconiosis small rounded opacities and to evaluate their densities was proposed for automatic categorization of the profusion. It was shown by experiments using ILO standard pneumoconiosis films and the computed

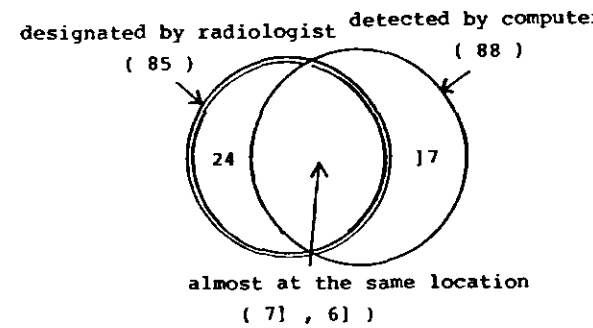


Figure 9. Result of comparison between the opacities extracted by experienced radiologist, and those by computer (Figure 8).

Figure 10. An example of small rounded opacities extracted by experienced radiologists, and those by computer on a film obtained by the Fuji computed radiography system. (category 3, size q)

radiography images that the opacity density measured by the proposed procedure was approximately proportional to the categories of profusion of pneumoconiosis. To improve the system performance, it is necessary to develop a procedure to recognize blood vessel shadows more correctly.

REFERENCES

1. International Labour Office: *Guideline for the Use of ILO International Classification of Radiographs of Pneumoconiosis*. Revised Edition (1980).
2. Kruger, R.P., Thompson, W.B. and Turner, A.F.: Computer Diagnosis of Pneumoconiosis. *IEEE Trans. on Syst., Man, and Cybern.* SMC-4:40-49 (1974).
3. Hall, E.L., Crawford, W.O. and Roberts, F.E.: Computer Classification of Pneumoconiosis from Radiographs of Coal Workers. *IEEE Trans. on Biomed. Eng.* BME-22:618-527 (1975).
4. Jagoe, J.R. and Paton, K.A.: Measurement of Pneumoconiosis by Computer. *IEEE Trans. on Comput.* C-25:95-97 (1976).
5. Stark, H. and Lee, D.: An Optical Digital Approach to Coal Workers' Pneumoconiosis. *IEEE Trans. on Syst. Man. and Cybern.* SMC-6:788-793 (1976).
6. Kobatake, R. and Takatani, O.: Computer Diagnosis of Pneumoconiosis from Radiographs. *Jap. J. of Med. Electro. and Biolog. Eng.* 20:23-29 (1982). (in Japanese)
7. Chen, X. Hasegawa, J. and Toriwaki, J.: Quantitative Diagnosis of Pneumoconiosis Based on Recognition of Small Rounded Opacities in Chest Radiographs. *Rep. of Technical Group on Pattern Recognition and Understanding, IEICE, Japan,* PRU87-9:25-32 (1987). (in Japanese)

This work was supported in part by Grant-in-Aid for Scientific Research (No. 62460125), Ministry of Education of Japan Grant-in-Aid for Cancer Research (62-42), Ministry of Health and Welfare of Japan and the Committee for Quantitative X-Ray Diagnosis of Pneumoconiosis.

ACKNOWLEDGEMENT: The authors are grateful to Doctor Y. Hosoda of Radiation Effects Research Foundation, and members of the Committee for Quantitative X-Ray Diagnosis of Pneumoconiosis for their cooperation and advice.

COST EFFECTIVENESS OF PRE-EMPLOYMENT PULMONARY FUNCTION SCREENING IN NEW HIRE FOR ELECTRONIC ASSEMBLY LINE WORK

R. THAN MYINT,* M.D.,D.I.H. • Shoib Myint,† B.S.

*Assistant Clinical Professor Occupational Medicine, Department of Comprehensive Medicine
University of South Florida, Tampa, Florida
Consultant, Occupational Medicine and Industrial Toxicology
Occupational Medicine and Industrial Health Services, Tampa, Florida
†Post-Graduate Studies, Columbia University, New York, New York, USA

Approximately 179,400 production workers were employed in the United States in facilities that manufacture electronic components and accessories. (SIC 3672-3678).[1]

In the electronic component manufacturing industry, a wide variety of processed material are used. Mixed chemicals exposure and the by-products and synergistic actions effect biologically. Simultaneous exposure to more than one toxic agent such as III Trichloroethane, Acetone, Methylethylketone, Freon, Methylene Chloride, Lead, Flux, Tin, Thalate Esters, Epoxy Resins, Alcohol. These chemicals were used by assembly workers in different departments, like soldering, rework, touch up, plating, conforma coating, potting.

Not many in literature, but few authors, investigators postulate that the Small Airway Diseases (SAD) represents significant airway obstruction in peripheral bronchioles and as such may present an early manifestation of chronic obstructive lung disease, when it may be amenable to treatment.

Myint and Myint[2] postulated that the early findings of FEF_{25-75} impairment with mixed chemicals exposures in electronic industries.

Wright and Colleagues[4] stated that inflammatory process in small airway lining thus reduction in FEF_{25-75} volumes.

In this paper, the author discusses the findings of 275 new applicants' Pulmonary Function Tests (PFT) who were hired for electronic assembly work. Morbidity data on small airway diseases, obstructive lung diseases were analyzed. In addition, the results of visual acquity examination as to perform government contract, applicant must meet government visual standard in near, distant, depth, color and field of vision.

MATERIAL AND METHOD

During the early part of 1987, pre-employment physical examinations were done by certified occupational health physician. Besides hands-on physical, pulmonary function tests were performed by qualified and trained technician and used Jones Pulmonar II in standing position with good effort and cooperation. The standard criteria of the American Thoraxic Society 1979 was used. Results obtained were FVC, FEV_1, FEF_{25-75} and FEV_1/FVC ratio. Predicted values of Knudson were preferred. Due consideration was given to ethnic factor calculation. Seventy-five percent of the predicted value readings was taken as the normal range. The values were corrected to BTPS. The best of at least three spirograms was chosen.

The vision test was performed by Titmus vision, color test was performed by Ishihara plate, field of vision test.

RESULTS

Among 275 applicants, the majority of them were between the age group of 19–39. Non-cigarette smokers were also majority as shown in Table I, 61.81% non-smokers and 38.18% were smokers. Also Table I analyzed number of smokers and non-smokers in each group.

Table II shows abnormal pulmonary function performances: Among 170 of non-smokers 18% had small airway impairment; this could probably be from previous impairment.

Job exposure to mixed chemicals, smokers have higher incident of small airway impairment 33.33%. There were 14 mild and moderate chronic obstructive lung diseases and eight of them were disqualified for assembly work.

Figure 1 illustrates the normal pulmonary function tests (PFT). Higher numbers were observed in younger age group 19–39. As the age gets older with longer exposure history PFT abnormal findings were characteristic.

As the government contract, minimum visual acquity is 20/40 with no defect in color, depth and field of vision using the Titmus Machine. Interestingly, many applicants were not aware of their defective vision. The abnormal vision test was done with and without glasses. Author is concerned about chronic toxic solvent exposure effecting color and field of vision with toxic chemicals which have been reported in United States and European literature. Table III shows the younger age group as having high prevalence of defective distant vision, where other age group has both near and distant vision defect.

DISCUSSION

There is scarcity in literature about cost-effectiveness of Pre-employment Pulmonary Function Tests (PFT).

Table I

Pulmonary Function Testing in Different Age Groups in Pre-employment Screening of Electronic Assembly Workers, Tampa, Florida

AGE GROUP	NON CIGARETTE SMOKERS		CIGARETTE SMOKERS	
19 - 29 91	55	60%	36	39.56%
30 - 39 98	68	69.38%	30	30.61%
40 - 49 54	25	46.38%	29	53.70%
50+ 32	22	68.75%	10	31.25%

Table II

Prevalent of Abnormal Pulmonary Function Performances in Cigarette Smokers and Non Smokers in Pre-employment Screening of Electrnic Assembly Workers, Tampa, Florida

AGE GROUP	FEF25-75		FVC		FEV1/FVC RATIO		PREVIOUS HISTORY OF EXPOSURE TO MIXED CHEMICAL SOLVENTS & SPRAY PAINTS	
NON SMOKERS 170 61.81%	32	18%	6	3.5%	4	2.3%		
SMOKERS 105 38.18%	35	33.33%	8	7.61%	14	13.33%	TOTAL 70	41.17%
TOTAL 275	67	24.36%	14	5.09%	18	6.54%		

As mentioned in literature, small airway disease is an early indication of mixed chemical exposure; the pre-employment PFT screening is constantly worth considering.

At present litigation scenario many legal battles have been lost because claimants suffer from hypersensitivity pneumonitis due to chemical exposure. Also, claimant has been awarded because of small airway impairment because of working on assembly line in electronic industry.

High stake workers compensation expenses have been paid on Permanent Partial Disability due to Chemical Induced Lung Diseases.

Recent study indicated small airway is a sensitive parameter in early detection of expiratory airflow obstruction. Potential high risk employees could be considered for early treatment and job placement.

It is a good documentation of previous existing condition of PFT abnormal findings. As we commonly see in workers compensation scenario, "I never had my lung test abnormal, I have worked with these chemicals and nobody told me about it." The disadvantage factor is under Workers Compensation Law aggravation from present job exposure become compensable and the present employer is liable.

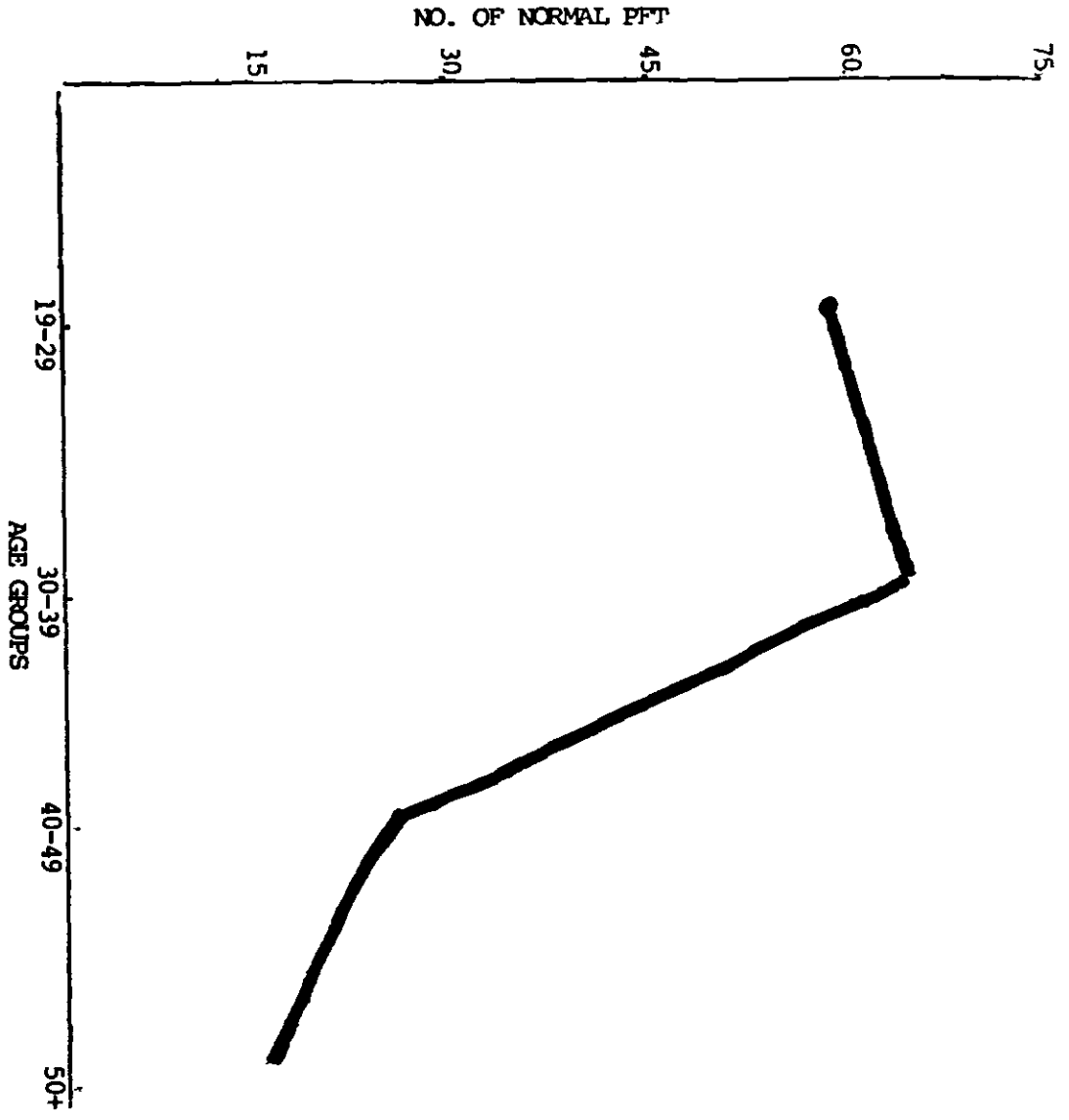


Figure 1. Normal PFT decline with age.

Table III

Visual Defects in 275 Applicants' Physical for Electronic Assembly Plants, Tampa, Florida

AGE	TITMUS VISION TESTS - ABNORMAL		ISHIHARA COLOR VISION	FIELD OF VISION
	NEAR	DISTANT		
19 - 29 91	8	20	1	0
30 - 39 98	16	21	2	3
40 - 49 54	22	21	1	1
50+ 36	17	15	1	3

However, early sign of sensitivity, early sign of bronchitis with baseline PFT value from pre-employment is surely valuable in decisionmaking for the betterment of employer, employee and workers compensation carrier.

Many adverse effects from chemical exposure and cigarette smoking have been reported. If baseline PFT results are available, further education to employee and proper job placement could prevent many problems in the future.

This study is a signal parameter involved therefore future epidemiologic studies can be undertaken with a large population.

REFERENCES

1. Cosio, M., Ghezzo, H., Hogg, J., et al: "The Relationship Between Structural Changes In Small Airway and Pulmonary Function Tests," *N. Engl. J. Med.* 298:1277-81 (1978).
2. Myint, R.T., Myint, S., "Early Small Airway Impairment In Electronic Assembly Workers Exposed To Mixed Chemicals," *Am. Coll. Tox.* 5:6,607 (1986)
3. Wegman, D.H., Peters, J.M., Boundy, M.G., Smith, T.J., "Evaluation Of Respiratory Effects In Miners and Millers Exposed To Talc Free Of Asbestos and Silica," *Brit. J I M* 39:233-8 (1982)
4. Wright, J.L., Lawson, L.M., Pare, P.D., Kennedy, S., Wiggs, B., Hogg, J.C., "The Detection Of Small Airway Disease," *Am. Rev. Respir. Dis.* 129:989-999 (1984).

ACKNOWLEDGEMENT: Both authors express their appreciation to Mrs. Dixie Martinez for her assistance in the preparation of the manuscript.

UTILITY OF QUANTITATED SPUTUM CYTOLOGY TO DETECT THE EFFECTS OF EXPOSURE IN SMOKERS AND NONSMOKERS

TINA J. ROBY,* M.S., CT (ASCP) (IAC) • Gary E. Swan,† Ph.D. • G. Berry Schumann,‡ M.D. • Louis C. Enkema, Jr.,* M.D.

*CytoSciences, Inc. 1601 Saratoga/Sunnyvale Rd. Cupertino, CA 95014, USA
†Health Sciences Program SRI International Menlo Park, CA, USA
‡CytoPathology Division University of Utah Health Services Center Salt Lake City, UT, USA

INTRODUCTION

The primary goal of health monitoring in the workplace is to detect early environmentally induced damage to the body and thus prevent disease. The largest problem in monitoring the pulmonary health of any individual when attempting to prevent the development of lung cancer or obstructive lung disease is the complicating effects of cigarette smoking. Researchers have provided insight into the additive or synergistic effect of tobacco smoke with certain environmental and occupational pollutants, such as asbestos, etc.[9] Although risk ratios for the development of lung cancer due to this synergism have been derived, a standardized methodology to discriminate the toxic effect of the exposure from that of cigarette smoking has yet to be developed.

Traditional testing methodologies have focused on the detection of advanced or end stage disease. Chest radiography is unable to detect the early developmental stages of lung cancer. With rare exception, bronchoscopic and cytologic techniques have focused on the presence or absence of malignancy. Pulmonary function tests become definitively abnormal only after widespread structural damage in the bronchial airways. The limitations of these current approaches are obvious. Too often a lesion, once detected, is largely irreversible and frequently carries with it a poor prognosis.

A quantitative cytologic method has been developed to analyze material from the lungs utilizing sputum analysis. This method provides useful information about early airway damage, hopefully while simple intervention and subsequent reversibility of the damage may still be possible. Our goal is also to provide a test which is inexpensive, non-invasive, objective, reliable, sensitive and accurate to individually evaluate and monitor cellular damage due to inhaled toxins.

Several researchers have provided a rationale for a more detailed and comprehensive study of cytologic components that have been associated with bronchial irritation. Mylius observed that pulmonary macrophages increase in individuals exposed to industrial air pollution.[4] The results from Madison's, et al. study on coke oven workers suggested that early states which precede lung cancer and bronchitis may share common features. Their research found that reactive bronchial epithelial cells and metaplasia were potent predictors of an abnormal FEV_1/FVC.[3] Earlier work by Frost suggested that individuals in high risk industries showed higher incidence of atypical (at least mild dysplasia) cytologic findings in sputa than did individuals in low risk industries. Frost also suggested that the key defense mechanisms of respiratory macrophages, the mucociliary blanket and tracheobronchial epithelium could be effectively monitored.[2]

The objective of this pilot study was to determine whether the effects of occupational exposure are observable in both nonsmokers and smokers and whether these effects could be discriminated from the effects of cigarette smoking. We also studied whether there was a measurable additive or synergistic effect in the group of smokers who also had exposure to occupational toxins.

MATERIALS AND METHODS

Four groups (smokers, exposed and nonexposed; nonsmokers, exposed and nonexposed) of approximately 25 individuals who matched the following criteria were randomly selected from a pool of over 1800 subjects: males of approximately the same age with adequate and satisfactory sputum results; two occupational groups with similar self-reported exposures (asbestos, arsenic, beryllium, inhalants by urban firefighters); and two cigarette smoking groups with similar smoking histories. The selection process yielded 25 nonexposed/nonsmokers, 21 nonexposed/smokers, 24 exposed/nonsmokers and 25 exposed/smokers. We were unable to determine the length, duration and dose of the occupational exposure.

A three-day pooled, spontaneously produced sputum specimen was collected into 23 mls. of Saccomanno's fixative (50% ethanol, 2% polyethylene glycol and rifampin). The samples were processed using the blending methodology according to the Saccomanno technique and stained with a modified Papanicolaou stain.

The microscopic examination of the slides consisted of counting the following eight entities: alveolar macrophages, pigmented macrophages, neutrophils, mucus, mucous spirals, columnar, metaplastic and dysplasia cells. The counts were expressed as a number or amount of that component per slide or 40X field. The amount per slide or 40X field

was then translated via an established algorithm into an ordinal scale with a range of 0 through 10. Zero represented no evidence of that particular entity being present, while 10 represented the maximum amount of any entity being present on the slide.

Two components, although quantitative, were more descriptive in nature. Pigmented macrophages were assessed based on density of coloration and amount and size of particulate matter being present. Mucus was assessed by the thickness, character and pattern. Dysplasia (atypical metaplasia) was assessed using well described morphological parameters.

Although not part of the main analysis, benign bronchial hyperplasia (BH), reactive bronchial lining cells (RBLC), and elevated levels of eosinophils (>10% of the white cell population) were noted if present on each case.

STATISTICAL METHODS

The data array for each cytologic component in this study was viewed as constituting a 2 × 2 analysis of variance with smoking (yes or no) and exposure (yes or no) as the main effects. Because a goal of the study was to identify significant smoker × exposure interactions, an interaction term was modeled in the analysis of variance as well. The general linear model procedure (PROC GLM, SAS® Institute was used to identify significant overall effects; main effects for smoking and exposure, and the interaction effect were tested against Type III sums of squares.[7] A separate general linear model was constructed and tested for each of the eight cytologic components. Because this study was exploratory in nature and limited in sample size, our approach was to analyze each component separately.

For those models demonstrating an overall significant F test, subsequent tests comparing mean scores of nonexposed to exposed subjects, within smokers and nonsmokers were conducted. Tukey's (1952, 1953) procedure was used to control the maximum experimental error rate for multiple comparisons.[6] Differences between means for each component were compared against the minimum significant difference computed by the Tukey procedure at an overall alpha=0.05 level.

RESULTS

Table I shows the age and smoking history for each of the four groups. All groups were equivalent with respect to both age and smoking history. Table II lists the nature of the occupational exposures for the exposed nonsmoking group and the exposed smoking group. The range of exposures in each group was similar.

Overall Models

Tables III and IV show, respectively, the mean values and standard deviations for each component in each group, and the F values resulting from the analyses of variance. Table IV reveals significant overall models for all components except for dysplasia. Corresponding R2 values indicate that these models account for between 19% (spirals) and 53% (pigmented macrophages) of the variability in the cytologic components.

Smoking Main Effects

Present smokers had consistently and significantly higher mean levels on seven out of the eight components (dysplasia being the exception) compared to nonsmokers.

Exposure Main Effects

Exposure status was associated with smaller differences but there were significant effects for pigmented macrophages, neutrophils, mucus, and columnar cells. Individuals reporting exposure had the following mean values compared to those reporting nonexposure: pigmented macrophages (5.6 vs. 5.0) neutrophils (5.7 vs. 4.9), mucus (4.7 vs. 3.7) and columnar cells (4.6 vs. 3.2).

Smoking * Exposure Interactions

Significant interactions emerged for spirals and columnar cells. Marginally significant associations were observed for mucus and metaplasia. Subsequent tests reveal that for three of the four components, the significant interaction term is due entirely to the relationship of exposure to the various components in nonsmokers. Compared to nonexposed nonsmokers, exposed nonsmokers had significantly higher levels for mucus ($t=2.65$, 47df, $p<0.05$), columnar cells

Table I
Age and Smoking History of Sample Populations

	Average Age	s.d.	PackYears	s.d.
NonSmoker/No Exposure	42.5	15.8	--	--
Smoker/No Exposure	41.6	10.2	36.1	15.8
NonSmoker/Exposed	40.7	12.3	--	--
Smoker/Exposed	43.3	9.2	36.0	23.5

s.d. = standard deviation

Table II
Nature of Occupational Exposures

	Nonsmokers (n=21)	Smokers (n=25)
Asbestos	14	11
Arsenic	2	1
Beryllium	2	3
Coal	2	0
CO2	0	1
Diesel Fuel	0	1
Dust (logging)	1	1
Fiberglass	0	1
Insulation	0	1
Smoke (chemical fires)	2	2
Smoke (other fires)	1	0
Welding	0	3

($t=3.69$, 34 df, $p<0.05$), and metaplasia ($t=2.35$, 47 df, $p<0.05$). For the fourth component, spirals, there was the possibility of a crossover interaction which, upon subsequent testing, did not yield significant differences for exposure either within smokers or nonsmokers. While a significant interaction term did not emerge in the analysis of variance for neutrophils, we did observe exposed nonsmokers to have higher mean levels than did nonexposed nonsmokers ($t=2.83$, 47 df, $p<0.05$)

DISCUSSION

We have shown significant cytologic differences between nonsmokers and smokers.[8] These results also indicate that quantitative sputum cytology is capable of detecting measurable differences in subpopulations of nonsmokers with and without exposure to occupational irritants. Of particular note was the elevation of neutrophils, mucus, columnar and metaplastic cells in the exposed nonsmoker group. These data provide evidence that early indications of bronchial irritation due to inhalation of environmental toxins can be monitored. The prognostic ability of these changes to determine the risk of lung disease with continued exposure needs further exploration.

Although there were not statistically significant differences among the smokers with and without exposures in our study, there were more cases showing elevated levels of eosinophils and bronchial hyperplasia in the exposed smoker group (20% and 12%, respectively), as compared to the nonexposed smoker group (8% and 0%, respectively) Table V shows the results of these additional cytologic observations across the four groups. The nonsmoker/exposed group had higher levels of all three entities than any other group (eosinophils—25%; RBLC—12.5%; and BBH—12.5%). One explanation of these elevations might be the presence of an allergic or asthmatic response to the environmental toxin.

Our results indicate that there is no significant synergistic effect in the presence of both cigarette smoking and exposure to an occupational irritant. Although Mylius found that the number of pulmonary macrophages increased with exposure to industrial air pollution and that there appeared to be a synergistic effect of occupational pollution and smoking, our data are not necessarily contradictory.[4] Explanations may be that: a) in the presence of cigarette smoking, there is a ceiling effect resulting from the tobacco smoke which may mask any effect from the exposure for some period of time; b) small sample size; or c) the fact that the exposure variable relied upon self-report. Another important factor to be considered is that the exact nature, length of time of the exposure, or amount of exposure was not fully known in our study. A larger, more controlled study needs to be initiated which would present a clearer and more objective analysis of this phenomena.

Industry, workers, their unions, the insurance industry, the courts, and the medical profession have concern about the identification and nature of respiratory hazards in industry; progress in early diagnosis, prevention and medical intervention of occupationally induced respiratory disease; understanding of the pathogenesis of respiratory disorders and progress in worker protection from respiratory hazards. In most settings and in many individuals, it is difficult to sort out to what extent cigarette smoking has contributed to respiratory disease as compared to the effect of occupational toxins. Traditional methodologies to measure and/or separate the effects of cigarette smoke have shown disappointing and inconsistent results. The effects of industrial toxins to the nonsmoking individual is less difficult to assess since the complicating effects of tobacco smoke are not present. There is however, difficulty in detecting the earliest stages of disease with current testing methodologies which make sense and are cost effective in the workplace.

Table III
Means and Standard Deviations of Cytologic Components

	NonSmoker No Exposure (n=25)	NonSmoker Exposure (n=24)	Smoker No Exposure (n=21)	Smoker Exposure (n=25)
Macrophages	4.4	4.9	6.3	6.6
s.d.	(1.2)	(1.5)	(1.3)	(1.2)
Pigmented Macrophages	4.0	4.4	6.2	6.7
s.d.	(0.8)	(1.3)	(1.0)	(1.3)
Neutrophils	4.1	5.3	5.9	6.0
s.d.	(1.2)	(1.7)	(1.3)	(1.8)
Mucus	2.4	3.8	5.4	5.5
s.d.	(1.8)	(2.0)	(1.4)	(1.6)
Mucous Spirals	0.0	0.2	1.6	0.7
s.d.	(0.0)	(0.5)	(2.5)	(1.1)
Columnar Cells	1.1	4.0	5.5	5.1
s.d.	(1.7)	(3.4)	(1.9)	(2.5)
Metaplastic Cells	1.3	2.8	4.7	4.3
s.d.	(1.8)	(2.4)	(2.6)	(2.6)
Dysplastic Cells	0.2	0.0	0.4	0.3
s.d.	(0.8)	(0.0)	(1.1)	(1.1)

Although sputum cytology has become a medically accepted diagnostic procedure for lung cancer, it has not been accepted as a screening methodology for high risk individuals since the actual incidence of lung cancer is low and the prognosis is not believed to be influenced by screening.[5] The picture would change if newer diagnostic techniques allow for the identification of premalignant changes in the bronchial airways. Treatment modalities such as vitamin (beta carotene) therapy along with smoking cessation are being tested with the hope of eradicating early disease, thus changing the natural course of lung cancer.

Recently Frost stated that sputum cytology may have its greatest value to both the worker and employer in its potential to monitor individual responses to harmful exposures before the development of disease.[1] Despite the results in our smoking subjects, there is clear indication that quantitative sputum cytology provides a noninvasive tool which is capable of showing change in the bronchial airways of individuals in varying environments. Our preliminary results suggest that this testing methodology may be valuable in monitoring individual cellular response to toxic occupational exposure before the onset of serious lung disease. Clearly, further study is required to assess the importance of these preliminary findings.

REFERENCES

1. Frost, J.K. et al: Sputum Cytopathology: Use and Potential in Monitoring the Workplace Environment by Screening for Biological Effects of Exposure. *Journal of Occupational Medicine*. 28:692-703 (1986).
2. Frost, J.K. et al: Pulmonary Cytologic Alterations in Toxic Environmental Inhalation: *Human Pathology* 1:521-536 (1973).
3. Madison, R., Afifi, A.A., Mittman, C.: Respiratory Impairment in Coke Oven Workers: Relationship to Work Exposure and Bronchial Inflammation Detected by Sputum Cytology. *J. Chron. Dis.* 37:167-176 (1984).
4. Mylius, E.A., Gullvag, B.: Alveolar Macrophage Count as an Indicator of Lung Reaction to Industrial Air Pollution. *Acta Cytologica* 30:157-162 (1986).
5. National Cancer Institute (NCI): *Atlas of Early Lung Cancer*. Igaku-Shoin, New York (1983).

Table IV

F-Statistics to Text the Effect of Smoking, Exposure and Their Interaction on Different Cytologic Component Ratings

Effect	Cytologic Component: Macrophages	Pigmented Macrophages	Neutrophils	Mucus	Mucous Spirals	Columnar Cells	Metaplastic Cells	Dysplastic Cells
Smoking	48.2***a	96.9***	16.9***	45.4***	15.7***	30.2***	25.2***	2.5
Exposure	2.0	3.4*	4.7**	5.0**	2.1	5.8**	1.2	0.8
Smoking X Exposure	0.2	0.1	2.5	3.4*	4.2**	10.3***	3.3*	0.0
Overall Model								
F	17.20***	34.30***	8.30***	18.40***	6.90***	15.70***	10.00***	1.00
R2	0.36	0.53	0.21	0.38	0.19	0.34	0.25	0.03

a Numeric value is the F-value computed under the general linear model. F tests for individual effects are tested with 1 and 91 df; those for the overall model are tested with 3 and 91 df.

* p<0.10
** p<0.05
*** p<0.01

Table V

Cytologic Observation of Eosinophils, Reactive Bronchial Lining Cells and Benign Bronchial Hyperplasia

	Nonsmoker/ No Exposure (n=25)		Nonsmoker/ Exposure (n=24)		Smoker/ No Exposure (n=21)		Smoker/ Exposure (n=25)	
	Number	%	Number	%	Number	%	Number	%
Eosinophils*	3	12.0	6	25.0	2	9.5	5	20.0
Reactive Bronchial Lining Cells	0	—	3	12.5	0	—	0	—
Benign Bronchial Hyperplasia	0	—	3	12.5	0	—	3	12.0

*Eosinophils were considered elevated at >10% of the white cell population.

6. *SAS® System for Linear Models*, pp. 55, 61. SAS Institute, Inc. Cary, NC (1986).
7. *SAS® User's Guide: Statistics*, 5th Edition. SAS Institute, Inc. Cary, NC (1985).
8. Schumann, G.B., Swan, G., Roby, T., Sorensen, K., Enkema, L.C., Jr.: Unpublished Data. University of Utah Health Sciences Center, Salt Lake City, UT (1988).
9. Selikoff, I.J., Hammond, E.C., Churg, J.: Asbestos Exposure, Smoking and Neoplasia. *JAMA* 204:104-110 (1968).

ACKNOWLEDGEMENTS: The authors thank Christine Sutcliffe for the manuscript preparation and Robert Curtis, Patricia Jeys and Gayle Hubbard for their assistance in the production and arrangement of the graphics used for presentation.

EFFECT OF COAL DUST ON MUCIN PRODUCTION BY THE RAT TRACHEA

V. P. BHAVANANDAN

Department of Biological Chemistry, The M.S. Hershey Medical Center
The Pennsylvania State University, Hershey, PA 17033

ABSTRACT

The mucus secreted in the respiratory tract provides the first barrier against inhaled particulate and gaseous toxicants. Trachea removed from pathogen-free rats were maintained as organ cultures and used to study the effects of coal dust exposure on the synthesis of mucin. The high molecular weight isotopically labeled (^{3}H-glucosamine, ^{14}C-leucine or ^{35}S-sulfate) mucin could be purified by gel filtration, treatment with testicular hyaluronidase, ion exchange chromatography, delipidation and CsBr density gradient centrifugation. To examine effect of coal dust on mucin production, groups of explant cultures were exposed to media containing coal dust at 100 μg per ml every 2 days for 2 weeks while control cultures were treated with media without dust. Analysis of the spent culture media showed that treatment with dust markedly decreased the production of non-dialysable glycoproteins as well as hyaluronidase-resistant acid-precipitable fraction consisting mainly of mucin. Since the synthesis of protein was not affected to the same extent the decrease in mucin production is not entirely due to cell death. In separate experiments rats were subjected to *in vivo* coal dust exposure in inhalation chambers and tracheae of these and control rats were removed for explant cultures. The incorporation of precursor isotopes into mucin by these explant cultures are being examined.
(Supported by U.S. Bureau of Mines through the Generic Mineral Technology Center for Respirable Dust under grant G1135142, project 4210).

No Paper provided.

CORRELATION BETWEEN GRADE OF COAL WORKERS' PNEUMOCONIOSIS AT AUTOPSY WITH ANTEMORTEM X-RAY CLASSIFICATION

F. H. Y. GREEN • V. Vallyathan • R. Althouse • W. Laqueur

University of Calgary, Health Sciences Center, Alberta, Canada and
National Institute for Occupational Safety and Health, Division of Respiratory Disease Studies, Morgantown, WV 26505, USA

ABSTRACT

British studies have shown a good correlation between radiological category of CWP and severity of pneumoconiosis and lung dust burden at autopsy. Other studies have shown that irregular opacities correlate with interstitial fibrosis and also with severity of post-mortem emphysema. The purpose of this study was to investigate the relationships between the type and severity of CWP post-mortem with category of pneumoconiosis on the radiograph. In addition, we investigated the effects of emphysema, interstitial fibrosis, film quality and lung dust burden on X-ray category. The population studied was 700 miners from Beckley, West Virginia, autopsied between 1960 and 1972. X-rays taken within five years prior to death were obtained on 450 cases. All X-rays were reviewed by 3 NIOSH certified B readers. Whole lung sections from inflated lungs were available on all cases. These were reviewed and graded using NIOSH/CAP criteria. The extent and severity of emphysema was graded according to the method of Thurlbeck. Pathologist and radiologist reader variability was found to be acceptable. Results of these studies confirmed the British findings that there is a good correlation between pneumoconiosis and radiographic category and that the higher the grade of pneumoconiosis the better the correlation. In addition, we found that irregular opacities correlated with the degree of interstitial fibrosis and emphysema. Our study also demonstrated that radiology is less sensitive than pathology in detecting mild forms of CWP.

No Paper provided.