... IS NOT REDUCED IN INTERLEUKIN-12 KNOCK-OUT MICE
LM Pfeiffer, DR Hemenway, M Rincon Univ. Vermont, Burlington, VT
... is manifested by accumulations of macrophages and lymphocytes followed
RATIONALE: An inhalation model of silicosis in mice showed increased
... interferon-γ (IFN-γ) mRNA, localization of IFN-γ mRNA in lung lesions,
... numbers of lung lymphocytes producing IFN-γ protein. IFN-γ knock-out
... less silicosis than wild-type (WT) mice. Interleukin-12 (IL-12) secreted
... macrophages is believed to be a primary cytokine stimulus for IFN-γ
... IL-12 is produced as a heterodimer (p70) from p35 and p40 gene sub-units.
... tured that IL-12 might be the primary signal responsible for IFN-γ up-
... and an essential early response element in silicosis. **METHODS:** We exposed
... and IL-12 p40 subunit gene-deleted (IL-12-KO) mice to an aerosol of
... silica (60 mg/m3) or sham-air for 5 hr/d for 12 days, and examined the mice
... and 126 days. **RESULTS:** WT mice developed progressive silicosis as
... lung pathology, increased lung wet weight, and accumulation of lung total
... IL-12 KO mice showed silicosis pathology and total lung collagen which were
... from the WT mice. Commercial ribonuclease protection assay (Pharmingen)
... increased abundance of IL-12 p40 mRNA in lung tissue from WT mice exposed
... time points, while expression of IL-12 p35 was not changed. IL-12 KO
... no p40 mRNA and minimal p35 mRNA. IFN-γ mRNA was increased
... both WT and IL-12 KO mice exposed to silica. **CONCLUSIONS:** IL-12
... to be a critical pathway cytokine in producing the pathological responses or
... characteristic of silicosis. More research is needed to determine the factors
... IFN-γ production and inflammation in silicosis.

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A SURVEY OF SILICOSIS AMONG EMPLOYEES AT HIGH RISK
SITES IN VIETNAM. N Arnaiz, S Chai, N Toan, M Kiefer, J Kaufman, L
... part. Occupational and Environmental Medicine Program, University of
... Seattle, WA, USA. NIOEH, Ministry of Health, Hanoi, Vietnam.
... TION Vietnam is a rapidly industrializing country with many workers
... heavy industry and infrastructure development. Few resources are
... towards occupational health hazard identification and control. It is suspected
... silicosis disease burden is present in the Vietnamese work force. This risk
... undertaken in order to estimate the prevalence of silicosis among workers
... high levels of respirable dust in several Vietnamese provinces.
... US Occupational medicine physicians in Vietnam identified worksites with
... respirable dust and likely substantial crystalline silica exposure by per-
... industrial hygiene walk-through assessments. They conducted a risk survey for
... convenience samples of workers thought to be at high risk for silicosis
... administering questionnaires and performing chest radiographs (CXR). The CXR
... interpreted according to the International Labor Organization classification
... pneumoconiosis. Quadrant films were used as profusion score standards.
... 176 CXR of workers from 10 provinces in Vietnam were reviewed. The
... of the subjects was 39 years (range 19-63); the mean years in trade was 15.8
... abnormal CXR consistent with silicosis were found in 5.55% of the subjects
... category >0, rounded opacities. Total years in trade was correlated with an
... CXR (Spearman's R=.058, p=.049) but not age (Spearman's R=.044,
... industries with evidence of silicosis include building materials production,
... mining, tool manufacturing, and chemical fertilizer production.
... CONCLUSIONS Silicosis is present among workers with high levels of dust exposure
... Basic hazard control measures should be implemented in workplaces with
... respirable dust. A more focused study should be undertaken that
... the measurement of respirable silica levels with detailed occupational and
... histories and CXR to identify specific worksites for higher levels of hazard
... medical surveillance.
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ASBESTOS INDUCED A549 CELL MITOCHONDRIAL DYSFUNCTION
... CYTOCHROME C RELEASE AND CASPASE 9 ACTIVATION.
... Chandel N, Weitzman SA, Kamp DW. Division of Pulmonary & Critical
... Chicago - Lakeside and Northwestern Univ. Medical School, Chicago, IL.
... asbestos-induced alveolar epithelial cell (AEC) apoptosis due to iron-induced free
... are implicated in causing lung toxicity. We showed that the mitochondrial death
... may mediate AEC apoptosis since amosite asbestos (ASB) reduces
... mitochondrial membrane potential (Δψm) as assessed by a fluorometric technique and
... Bcl-xi overexpression were protective. To determine whether inert
... glass beads [GB] or titanium dioxide [TiO2]) decrease Δψm, we exposed
... GB, TiO2, or ASB (25 μg/cm²) for 24h. We found that ASB, but not GB
... induced Δψm. Further evidence implicating the mitochondria is that asbestos
... cytochrome c release from the mitochondria to the cytoplasm as assessed by
... as well as by immunofluorescent microscopy. Also, ASB activated caspase 9
... normal death pathway) as assessed by an ELISA and phytic acid (PA), an iron
... sodium benzoate (NB), a hydroxyl radical scavenger, were protective
... asbestos induced negligible caspase 8 activation (death receptor pathway). We
... that asbestos, but not inert particulates, reduce A549 cell Δψm resulting in
... cytochrome c release and caspase 9 activation. These data firmly support the hypothesis
... of asbestos-induced mitochondrial dysfunction as well as iron-derived free radicals in the
... of asbestos-induced AEC pulmonary toxicity.

Cell Caspase 9 Activity (% Change from control; RU/μg protein / 24 h)

	ASB (25 μg/cm²)	ASB+PA (500 μM)	ASB+NB (1 mM)
...	80±14 (6)*	1±1 (6)†	1±1 (6) †

... ± SEM (n); p < 0.05 vs. control; † p < .05 vs. ASB. NA (not assessed)
Veterans Affairs Merit Review (DK) and RO1 GM60472-02 (NC).
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ACUTE AND CHRONIC FIBROPROLIFERATIVE LESIONS INDUCED BY ASBESTOS IN TRANSGENIC MICE OVEREXPRESSING PDGF-B
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Platelet-derived growth factor (PDGF) isoforms and PDGF receptor-α are upregulated in fibroproliferative lesions in response to asbestos exposure. To examine the functional role of PDGF in asbestos-induced lung disease, we have evaluated the impact of PDGF-B overexpression in the lung on the development of pulmonary fibrosis induced by asbestos inhalation. Transgenic mice expressing PDGF-B from the surfactant protein C promoter and nontransgenic mice on a C57BL/6 background were exposed to aerosolized chrysotile fibers once a week for 5 hr for 5 weeks (average of 12.2±0.3 mg/m³) or 8 weeks (average of 11.2 ± 0.6mg/m³). Lungs from mice exposed to asbestos for 5 weeks were analyzed 48 hr and 8 weeks after the last exposure. Fibrotic lesions at alveolar duct bifurcations were more pronounced as judged by histological scoring in transgenic mice compared with nontransgenic mice 48 hr after exposure. Lung hydroxyproline content was increased in transgenic and nontransgenic mice compared with unexposed mice 48 hr after exposure. Eight weeks after exposure, lung hydroxyproline content in SPC-PDGFB mice was still elevated compared with unexposed mice, but in nontransgenic mice it had returned to normal levels. Mice exposed to asbestos for 8 weeks were examined histologically 10 months after the end of exposure. Both SPC-PDGFB and nontransgenic mice developed diffuse pulmonary fibrosis concentrated in the alveolar ducts. No difference in the severity or distribution of lesions was observed between transgenic and nontransgenic mice. These results indicate that a limited exposure (8 times) to chrysotile aerosol can produce long lasting fibrotic lesions. Overexpression of PDGF-B stimulates the initial development of asbestos-induced lesions and also inhibits their resolution in early stages, but does not affect the chronic progression of asbestos-induced fibrosis.

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Title: TEXTURE ANALYSIS OF OPACITY PROFUSION IN CHEST RADIOGRAPHS OF MINERS WITH PNEUMOCONIOSIS
P. Soliz[1], C. Pattichis[2], M. Pattichis[2], D. James[2,3], L. Ketai[2]; [1]Kestrel Corporation and [2]Univ. of New Mexico, Albuquerque; [3]Miners Colfax Medical Center, Raton, NM, USA
Rationale: Individuals who have been exposed through their occupations to high levels of dust, asbestos, or other particulates are at risk for interstitial lung diseases such as pneumoconiosis. These individuals must have periodic examinations including chest radiographs to monitor for signs of the opacities associated with pneumoconiosis. The International Labor Organization (ILO) has established a protocol to score the degree of profusion, size, and shape of opacities. *Aim:* This research assessed texture analysis techniques for quantitatively characterizing the nature of the opacities as presented through ribs and parenchyma. *Methods:* Radiographs were of coal-mine or silica dust exposed miners participating in a health screening program. A total of 252 regions of interest (ROIs) (166, 49, 21, 16 and 9 with profusions of category (shape and size) 0, 1(q), 1(r), 2(q) and 2(r) respectively) were identified from 80 digitized chest radiographs by two B-readers. Fifty-eight different texture features were computed. *Results and Conclusions:* The non-parametric Wilcoxon rank sum test was carried out to compare the different profusion categories versus that of profusion 0. Results showed that significant differences exist (at a=0.05) between 0 vs 1(q), 0 vs 1(r), 0 vs 2(q) and 0 vs 2(r) for 44, 17, 46 and 6 features respectively. For each group, the median and the spread of the data (difference between the 75th and 25th percentile) for a few features are given.

ROI feature	Prof. 0	Prof. 1(q)	Prof. 1(r)	Prof. 2(q)	Prof. 2(r)
Median	170 {159}	245 {275}	268 {219}	200 {135}	212 {98}
Entropy	.436{.253}	.579{.312}	.660{.348}	.560 {.087}	.554{.128}
Contrast	49 {90}	105 {238}	162 {250}	85 {152}	91 {103}

In conclusion, texture features provide statistically useful information for the characterization of profusion categories in interstitial lung diseases.
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PREVALENCE OF RADIOLOGIC PNEUMOCONIOSIS IN ACTIVE UKRAINIAN COAL MINERS
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School of Public Health, University Of Illinois, Division of Pulmonary and Critical Care Medicine, Cook County Hospital and Rush University, Chicago, Illinois and the Institute of Occupational Health, Kiev, Ukraine
Introduction: Coal mine dust levels in Ukrainian coal mines have been reported to be more than 10 times the level in US coal mines. The prevalence of radiologic pneumoconiosis among coal miners in Ukraine has not been well studied due to lack of resources for full format frontal chest radiographs and certified B-readers equipped with the ILO standard films for the International Classification of Pneumoconiosis. This abstract reports the first results of standardized examinations of a random sample drawn from a cohort of 7000 coal miners from Donetsk, Ukraine. **Methods:** Standard frontal CXRs were obtained on 500 randomly selected underground miners with at least 5 years of experience. B-readings of CXRs were performed on each film by two NIOSH certified B-readers. **Results:** 268 CXRs were available for review.

	Quality 1 or 2	Category 0/1	Category 1/0	Category 1/1
Reader A	92%	9%	7%	0.7%
Reader B	91%	8%	3%	0.7%

No cases of complicated pneumoconiosis were found. Less than 1% of cases had pleural disease. **Conclusion:** Rates of pneumoconiosis were found to be 1.32 to 2.75 times the levels (2.8%) found in the most recent US miners in the Mine Safety and Health Administration's coal worker's chest x-ray surveillance program. This may be an underestimate of the true prevalence in Ukrainian coal miners due to a significant healthy worker effect.
This abstract is funded by NIOSH Grant T42/CCT510424-07

A529

Title: Computer-Assisted Chest Radiograph Reader   *2 00 22 995*
Investigator: Peter Soliz, Ph.D.
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City & State: Albuquerque, NM
Telephone: (505) 345-2327
Award Number: 1 R43 OH003595-01
Start & End Date: 9/30/1998–3/31/1999
Total Project Cost: $99,320
Program Area: Not NORA
Key Words:

Abstract:
To reduce inter- and intra-reader variability in diagnosing chest radiographs, a neural network-based computer-aided diagnostic system was developed and tested. The results of an experiment with 124 digitized chest radiographs, demonstrated high degrees of sensitivity and specificity in classifying chest radiographs. The use of a computer-assisted chest radiograph reader eliminated the inconsistencies in the human readers. The Computer-assisted Chest Radiograph Reader System (CARRS) applies recognized principles in the psychophysics of human vision, incorporates neural network-based image analysis and integrates these with a graphical user interface. Advances in digital image processing, and classification techniques have made CARRS feasible for meeting screening, research and development, and clinical requirements.

Through the adoption of the International Labor Organization (ILO) classification procedures, it had been hoped that reader variation in the classification of parenchymal abnormalities could be minimized. The ILO classification of the pneumoconioses is based on a structured procedure for detecting and characterizing patterns on chest radiographs. Numerous studies have shown, however, that inter- and intra-observer variability of radiograph readings by trained medical personnel has persisted.

The methodology was implemented through the following tasks: 1) From a data base of several thousand patients, a set of 205 chest radiographs were manually graded by two pulmonologists; 124 of the films were then digitized at 12-bit high spatial resolution. 2) Textural features were calculated using high order statistical techniques. The features were classified by the pulmonologists to "train a neural network to extract classification rules chest radiographs based on the ILO methodology. 3) The neural network classification from the graded system was tested using 65 chest radiographs.

For 5-10 areas selected by the pulmonologist on the chest radiograph, a feature vector composed of image characteristics such as density distribution, entropy, fractal dimension, opacity counts, shape, etc. was calculated. This feature vector characterized numerically the areas used by the pulmonologist to grade the radiograph. The neural network trained on the same regions used by the pulmonologist, and through a quantitative feature vector, "learned" the characteristics of each ILO classification.

The laterally-primed adaptive resonance theory (LAPART) neural network was selected. LAPART presents the results of the training in human interpretable "rules." LAPART trains in a single pass ("fast") making it attractive for a clinical setting. To demonstrate that calculated characteristics of chest radiographs could be used to train the LAPART to classify the radiographs using objective and quantitative parameters, a pilot study was conducted. 32 statistical features from 124 digitized chest radiographs were calculated. Statistical parameters were selected based on their contribution to the separation of classes. The parameters included entropy, contrast, fractal dimension, and co-occurrence statistics. The computational efficiency of LAPART was demonstrated in this experiment. LAPART was trained on a Pentium 200. Training time for 10 experiments, where the training and testing radiographs were randomly selected, averaged 15 seconds per experiment.

In conclusion these experiments showed that LAPART is a worthy candidate for basing a semi-automatic chest radiograph classification system. The experiments demonstrated that CARRS has low classification variability and has a significantly high accuracy. The results of each of the 10 experiments showed that the LAPART neural network algorithm could be trained to "learn" the extent of the "hypercubes" which represented each of the six classifications in 32-dimensional space. LAPART classification accuracy averaged 98 %. "Truth" was determined by the two radiologists.

Publications
No publications to date.

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ABSTRACTS

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