COMPUTER DETERMINATION OF ALVEOLAR NUMBER PER UNIT AREA OF LUNG TISSUE

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ABSTRACT

The total number of alveoli in the human lung has been a matter of interest and of some dispute for many years. This measurement, as well as the size of the individual alveoli are of fundamental biological importance in terms of the growth and development of the lung, as well as in its aging. Further, the number of alveoli is of interest and significance to pulmonary physiologists.

One method of calculation presently in use is based upon a random sample of lung tissue from which can be determined the average number of alveoli per unit area of tissue. The latter is obtained by visually examining the sample under magnification and counting the number of alveoli which can be related through a known formula to the internal surface area. However, the technique is an extremely tedious one for a human and has been shown not to yield repeatable results. In order to overcome these problems, a method of computerized image processing which would automatically perform the computation was invoked.

The computer analysis of the lung tissue first involves the digitization of the image on the histological slide by the McGill Scanner (McScan) System. Next a binary matrix representation of the image is calculated using a normalization procedure which takes into account image variability. The alveolar walls are thinned and topological considerations are then used to determine the number of alveoli per unit area.

The application of the method to lung samples previously processed visually has yielded comparable results.

INTRODUCTION

A lung, in part, is an intricate series of air passageways that connects the external atmosphere to the tissue that performs the exchange of carbon dioxide for oxygen in the blood. As such, it is a multiply-branched structure whose smallest branches, called bronchioles, terminate in a cluster of small pockets or sacs known as alveoli. Alveolar walls form the air-blood interface needed for gas exchange. Clearly the total area of all the alveolar walls is a major factor in determining the capacity of a lung to oxygenate blood. We define the internal surface area (ISA) of a lung as the sum of the surface areas of all the alveoli in that lung.

The pathologist is interested in quantitatively determining the ISA of lungs for several reasons. First, he desires a fundamental knowledge of physical lung properties and would like to correlate ISA with various body parameters such as normalized size and age. Secondly, he wishes to measure the extent of various disease processes such as emphysema. Finally, quantitative physical measurements of lungs could lead to useful mathematical models with which to analyze and predict lung behaviour.

Statistical methods for calculating lung ISA have been developed by Weibel [2]. One technique involves estimating the average number of alveoli per unit area of lung tissue. By assuming a certain general shape for the alveoli and a certain distribution of the alveolar volumes, lung ISA can be calculated by determining the average number of alveoli per unit area, N_a. This method has been implemented visually at the Department of Pathology, McGill University. Problems have arisen, however, largely due to the fact that the procedure is a long and tedious one and because the results are difficult to reproduce with any great accuracy. Because of the success in computerizing an alternate method based on the calculation of the mean linear intercept for the alveolar structure [1], it was decided to also automate the counting technique.

The main goals of the computerization of this approach were economy, accuracy, and speed (in that order). The McGill Scanner (McScan) System which is built around a Digital Equipment of Canada 4K PDP-8 computer, and an ITT image dissector scanner coupled to a Zeiss microscope, was used for the experiments.

BINARY PICTURE ACQUISITION

The small core size of the PDP-8, coupled with the elimination of any peripheral mass-storage devices (in the interest of economy) require that the image be read into core memory in a binary format. The binary image is obtained by choosing a threshold light intensity, such that all brighter points are labelled "white" (Ø), and all darker points, "black" (1). This is complicated by the fact that the microscope lighting is not always uniform, the scanner output sometimes drifts, and the lighting intensity is set manually and so is not necessarily repeatable.

To overcome these problems, a preliminary scan is made which records the number of points in the image at each grey level. A short thresholding algorithm is then applied to this histogram in order to calculate an appro-

priate threshold. The threshold depends on a knowledge, based on experimentation, of the general shape of the grey level distribution.

Having calculated a threshold, the program rescans the same area, this time using the threshold to acquire the binary image and pack it into core.

BINARY PICTURE ANALYSIS

A histological section of lung tissue, as shown in Figure 1, resembles highly irregular chicken wire with its network-like properties. Assume that each closed loop (dotted line in the figure) of tissue represents the cross section of an alveolus or a bronchiole and that each "dangling" piece of tissue (solid circle) is evidence of an incomplete alveolus, perhaps one of several alveoli arranged around the inner periphery of a bronchiole. The dangling pieces of tissue are characterized by their endpoints. The program is written to search a filtered and thinned version of the binary image for disjoint white areas (binary Ø) that represent complete alveoli or bronchioles and for endpoints. A distinction is made between white areas that do not contain endpoints (assumed to be alveoli) and white areas that do contain endpoints (assumed to be bronchioles). The program estimates the number of alveoli (NAL) by counting all white areas without endpoints (NWOE) and adding to this the number of endpoints (NEPT), the latter quantity representing the effect of "completing the alveoli". Finally a correction factor (CORN) which is equal to the sum of the numbers of white spaces on two adjacent borders of the image is subtracted from the count so that white spaces are not counted twice. The final formula is thus:

$$NAL = NWOE + NEPT - CORN .$$

This result is then typed out and the program resumes scanning on an adjacent area of tissue.

RESULTS

We can compare the results obtained by the computer and the pathologist on the basis of the calculated number of alveoli per unit area (NAL). These are presented in TABLE 1, where the numbers are given as number of alveoli per square millimeter. It can be seen that in general the computer matches the pathologist's average to within 5 or 10%. Note that in fact no "correct" answer is presently available.

Both types of ISA measurements are now being reprogrammed to run more efficiently, later to be used as a tool for basic research on the morphology of the lung.

Lung No.	1	2	3	4	5	6	7
Pathologist	23.4	27.9	32.0	31.9	38.2	19.6	18.0
Pathologist	22.3	25.0	29.4	28.9	31.8	22.9	23.4
Computer	23.6	25.3	27.1	33.3	34.1	23.6	20.9
Lung No.	8	9	10	11	12	13	14
Pathologist	19.0	16.8	22.7	23.8	29.0	30.5	28.4
Pathologist	19.7	21.2	26.9	25.2	31.9	29.0	25.9
Computer	20.0	19.6	24.0	23.2	31.8	24.4	21.2

TABLE 1

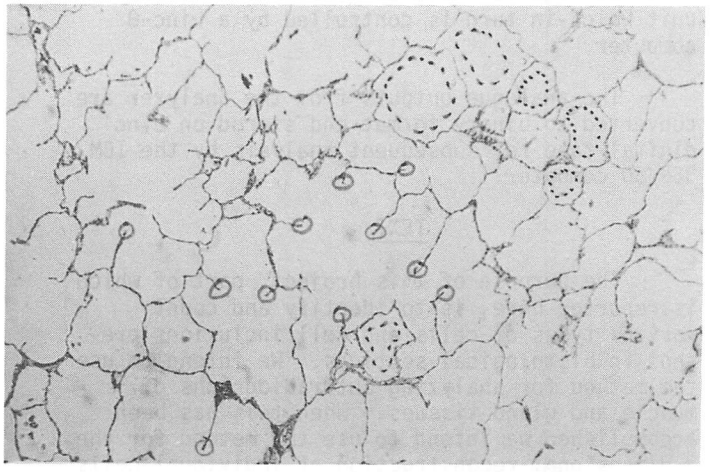

FIGURE 1

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