Standards for quantitative assessment of lung structure

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The February 15th, 2010, issue of the American Journal of Respiratory and Critical Care Medicine contains an official research policy statement on quantitative assessment of lung structure (1). This document is the product of a Joint American Thoracic Society (ATS) and European Respiratory Society (ERS) task force created in response to a widespread recognition that many investigators were publishing morphometric studies that were improperly done, leading to the potential for misinterpreting scientific data. The leadership of the ATS and ERS realized that this was a serious problem, and both organizations agreed to fund a task force of 20 experts from around the globe to generate a document that would provide guidelines for the proper ways to quantify lung structure. This published document sets standards and procedures for the quantification of lung structure, not only from histologic sections, but also from in vivo tissue sampling by biopsy and from noninvasive lung imaging by computed tomography, magnetic resonance, or positron emission tomography. The two Societies adopted the report of this task force and designated it as their Official Policy Statement.

The basic challenge of quantifying structural changes in the lung after experimental interventions or disease progression is to make sure that the quantitative methods used are 1) accurate with adequate statistical power to allow meaningful interpretation of results, 2) efficient to yield adequate precision with reasonable effort, and 3) adherent to uniform standards to facilitate comparisons among experimental groups and different labs. These demands manifest themselves at different levels, including fixation methods, measurement of the reference lung volume, sampling the tissue, and choosing the appropriate stereological method that allows 3D information to be obtained from measurements on 2D sections.

The great advantage of stereology is that it allows investigators to obtain accurate quantitative information on a large organ, such as the lung, by looking at a very small number of tiny random tissue samples. This process, however, mandates the use of correct sampling procedures that will not compromise the accuracy and precision of the stereological estimates. A proper approach needs to account for such features as the orientation of surfaces in space and the heterogeneity of lung tissue in not only normal lungs, but also pathologic conditions. The task force document provides the general guidelines for carrying out these proper procedures. However, the document obviously could not deal with the detailed specifics of every experimental situation, but it does discuss a number of model cases. The details of experimental planning still remain the responsibility of individual investigators. It is worth noting that this situation with regard to proper quantitative morphology has similarity with the use of statistics in biomedical research. Modern journals now demand that proper and rigorous statistical analyses be done on published data, but they allow the investigators to choose the most appropriate metric. In both circumstances there are occasional situations where some compromises will need to be made, but these must fall within standardized guidelines. With regard to lung stereology, if the general guidelines are followed and intentional modifications justified and discussed, it should become possible to compare results from different labs even where some specific protocols may differ. With many studies in the existing literature, this comparison is often not possible.

We thus hope that the procedures and guidelines for unbiased quantitative assessment of lung structure by means of stereology described in this recent document (1) will be followed as rigorously as possible by investigators whenever quantitative morphology is required. We hope also that the editors and reviewers of the Journal of Applied Physiology and of other related journals, as well as reviewers of research grant proposals, will account for the rules set out in these guidelines to ensure that proper morphometric analysis is promulgated in the literature and by extramural funded research.

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