CRITICAL EVALUATION OF NEW TECHNIQUES IN THE MORPHOLOGICAL DIAGNOSIS OF LUNG CANCER

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1. INTRODUCTION

The group of lung cancer constitutes the most important cause of cancer death in men and its incidence rapidly increases in women (1). According to the WHO classification (2) the main types are Squamous Cell Cancer (SCC), Small Cell Lung Cancer (SCLC), Adenocarcinoma (AC) and Large Cell Anaplastic Cancer (LCC), together embracing about 95% of all lung tumors. This classification is based on light-microscopic criteria.

The introduction of fibreoptic bronchoscopy in the diagnosis of lung cancer has considerably added to the difficulties encountered by the pathologist in arriving at a diagnosis as demonstrated by Chuang e.a. (3). This biopsy technique yields tiny pieces of tissue from which conclusions with far-reaching consequences have to be drawn. Are "new techniques" of any help in this dilemma? As demonstrated by a study of Feinstein e.a. (4) there is considerable variability in judgement among different pathologists and even individual pathologists may vary in their diagnosis. Not surprisingly variation especially concerns poorly differentiated tumors. The question therefore arises whether the use of "new techniques" may help in improving the consistency in diagnosis and in better defining difficult and poorly differentiated tumors. Finally as a third area of daily sore we will consider the problem of the diagnosis of proliferative pleural lesions and especially the question whether the use of "new techniques" is of any help in differentiating between malignant mesothelioma and pleural invasion of adenocarcinoma.

What should be included in the heading of "new techniques"? Obviously this paper is primarily concerned with the daily practice of lung cancer diagnosis and we will therefore restrict ourselves to histological techniques other than conventional paraffin embedding and standard histochemical staining as far as they are daily practice in major centres at this moment. Techniques to be discussed are the possibilities of plastic embedding, electron-microscopy and immunohistochemistry. To what extent and in which way can these techniques be applied in smaller pathology departments?

2. THE PROBLEM OF SMALL (BRONCHIAL) BIOPSIES

Although problems encountered in dealing with small fibreoptic biopsies have been illustrated for non-SCLC (3) considerable uncertainty may also exist when a decision has to be made on the possible presence of SCLC.
In fact, given the present state of treatment the single most important decision is that of SCLC versus non-SCLC. But also every effort of course should be made to arrive at a specific diagnosis in cases of non-SCLC.

**Plastic embedding.** For a number of years we have routinely embedded formalin-fixed bronchial biopsies in glycolmethacrylate (5) followed by cutting with glass knives and conventional H&E staining of 2μ sections. Dehydration of the tissue and impregnation with glycolmethacrylate takes place in a Histokinette system overnight. Embedding with polymerization is done during the following morning so that sections will be ready in the afternoon. The procedure generally takes a few more hours than the paraffin procedure. Polymerization is crucial and can be speeded by incubation at a temperature of 400-600°C. As so often, the best approach has to be selected by varying the directions given by the manufacturers. We have made use of chemicals and instructions of both Du Pont company (Sorvall)* and Kulzer & Co (Histoset)** with good results. Plastic sections are undoubtedly of more stable and better quality than paraffin (paraplast) sections in our hands. There is no shrinkage of any importance and morphological and cytological details are well preserved. This difference in quality is nicely demonstrated in figures 1 and 2. Figure 1 is from an H&E stained paraffin section of a bronchial biopsy labeled as a possible SCLC. The tissue was transferred from the paraffin to plastic and figure 2 is from an H&E stained plastic section cut at the same thickness. The eventual diagnosis was poorly differentiated SCC.

![FIG. 1. Paraffin, H&E, x 350](image1)

![FIG. 2. Plastic, H&E, x 350](image2)

An important disadvantage of the plastic embedding is that immunohistochemistry is not easily performed in a routine way. So if one wants to keep the option of performing immunohistochemistry on a routine basis (see later) tissue should be embedded in paraffin or, preferably, two biopsies should be taken. One of these can be used for plastic embedding, the other can be quick frozen to be used for immunohistochemistry. Clearly the "paraffin-only" approach is not ideal.

**Electron-microscopy.** The application of electron microscopy for the study of lung tumors has resulted in fundamental changes of concepts on the histogenesis of lung cancer (6, 7, 8, 9). Ultrastructural studies have revealed details, not visible with the light-microscope, that can be used in classification especially in cases of poorly- or undifferentiated cancers. In this way it was shown that LCC's often represent either poorly differentiated AC's or poorly differentiated SCC's (10). Occasionally a

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