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INSTRUMENTATION IN DIAGNOSTIC MORPHOMETRY

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ABSTRACT

Although any classification is more or less artificial, equipment for quantitative microscopy can be classified into three groups: 1) non-automatic, 2) semi-automatic and 3) mainly automatic instruments. Each group of instruments has advantages and disadvantages, and "more expensive is not necessarily better". In the past years, microcomputers have become widely available at a low price level. Because of this mechanic counters can no longer rival with these instruments in price and certainly not in performance.

Digital image processing computers, DNA-slide scanners and flow-cytometers are still relatively expensive (US $ 50,000 - 120,000). Diagnostic applications mainly require more simple apparatus, such as a projection microscope for stereological analysis or a graphic tablet for nuclear measurements.

INTRODUCTION

The increasing interest in diagnostic morphometry has led to a number of commercially available instruments for this purpose. The explosion of microcomputers is a pleasant accompanying phenomenon, which has caused a drop in the prices. A further reduction seems likely, or, alternatively, the capacities of the image analysis instruments will increase at a constant price level.

Because of this, many pathologists have a somewhat conservative attitude towards instrumentation. In this paper, we will take the same approach.

EQUIPMENT

For a detailed description of the available equipment and commercial companies, see references 1 and 2. For practical reasons, the following distinction is made in quantitative microscopy equipment: 1) non-automatic, 2) semi-automatic, 3) mainly automatic. Of course, such a division is somewhat artificial, and several other classifications are possible. The advantage of the division is that each class represents a certain price level; i.e., non-automatic from approx. US $ 50 to US $ 2,000; semi-automatic from approximately US $ 4,000 to US $ 20,000; automatic from US $ 30,000 to US $ 120,000. At present, only a few companies offer modular instruments (building-blocks which can be added to each other, to expand the system).

1. Non-automatic equipment

Under this heading, ocular grids and counters are grouped. As counters cost approximately US $ 400, their prices are nearly the same as the prices of inexpensive microcomputers. Programs for counting elements are available, and thus, mechanical counters are no longer very interesting. A projection head (US $ 1,000 - 2,000 excluding the microscope) is useful for ergonomic reasons. In addition, self-designed lattices can be attached to the projection head.

2. Semi-automatic equipment

Graphic tables and mechanical scanners are found in this subclass. At present, graphic tablets are most important for diagnostic applications. They cost approximately from US $ 4,000 to US $ 20,000. Self-made programs on low-priced commercially available microscoputers probably will become widely available, but this approach will remain the privilege of the motivated hobby-computerist. A dedicated, user-friendly diagnostic morphometry system is not yet available, but some commercially available graphic tablets are very near to this ideal.

3. Automatic equipment

Electron beam scanners, electron image sensors and flow-cytometers fall in this category. Not only are they much more expensive, but their control and support require a higher level of technical ability. Moreover, the specimens and images needed should be much more perfect, and in this area much work still has to be done. For an overview of flow-cytometers see reference 5.

A warning is necessary to those who believe that this last type of equipment saves time - this is, at present, certainly NOT the case!

APPLICATIONS

For an overview of simple diagnostic applications at the level of point-counting and the graphic tablet, I refer to the "Manual of Morphometry in Diagnostic Pathology (3).

DNA-ploidy measurements form an old, and still diagnostic line, but apart from a few scattered prognostic applications are not yet widely in use (5).

The same is true for digital image processing computers. Cervical smear recognition is mainly used for prescreening, eliminating all PAP-II specimens as "non-positive". Automatic leukocyte recognition computers are used in some large laboratories, but they still are too expensive to be used in smaller institutions.

In our laboratory, we mainly work on those projects which can have diagnostic significance, such as prescreening for the detection of mitoses, nucleoli and stroma. With mitoses, 80% of all non-mitoses in principle can be rejected without loss of the mitoses (4). Special stains are required, and in this direction much work still has to be done. The particles are preselected, and at the end displayed in a composite way. The pathologist then evaluates the particles, and decides for "acceptance" or not.

The advantage of the detection of nucleoli is that in principle, they are simple homogeneous structures. Nuclei are much more complicated images, and mitoses are in between these two. However, not all nucleoli stain equally well with the methylgreen-

pyronin (MGP) stain. We have the impression that reticular nucleoli do stain well, and compact nucleoli do not. In breast cancer, the nucleoli are bright-red with MGP, but in melanomas they do not (unpublished results). Monochromatic stains at present would be ideal, but their number is extremely low. Perhaps monoclonal antibodies will be of help, but we have the impression that they do not stain all areas equally well. In addition, they are rather expensive.

FUTURE TRENDS

Graphic tablets will become less expensive or, alternatively, remain stable in price with more capacities. The rise of 16- and 32-bits computers will help in this direction.

A dedicated, user friendly diagnostic morphometry computer should become available in 2-5 years. DNA-ploidy measurements, either with slide-scanners, or with flow-cytometers will become more accepted as routine measurement in the next 5 years, but only in universities or larger non-university institutes.

Digital image processing computers are now available in several academic pathology laboratories in western Europe. Users should unite to present their demands to the industry. Diagnostic applications will be available within 2-4 years, initially to support a diagnosis, or control a manual measurement. Further expansion of this area is likely in the next decade. For the final acceptance, economic factors will play an important, if not a decisive role.

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