STEREOMETRY AND MORPHOMETRY IN PATHOLOGY: AN INTRODUCTION

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ABSTRACT

Experimental pathology has used the methods of stereology and morphometry and these methods have been valuable in that context. Diagnostic histopathology can also derive advantage from these methods. Stereology and morphometry are able to analyse the visual patterns of the microscopic image in any detail. Pattern recognition is an approach which usually deals with automatic instrumentation, and aims at recognition of patterns and features which we know are relevant for us. But also patterns of thinking are important in the diagnostic context. These thinking patterns lead to diagnosis. Stereology and morphometry offer a good background for diagnostic decisionmaking, and at the University of Kuopio stereology, morphometry and decisionmaking are jointly studied during the pathology course for medical students.

THE NATURE OF DIAGNOSTIC PATHOLOGY

I will start by describing an incident which occurred a couple of days ago. I was driving my car in rain. I heard some noise from the front but because I did not see anything special at the moment I went on driving. Then I turned towards left at a crossroads and when looking to the right to see other traffic I noticed that the right windscreen wiper was no longer there. I stopped my car about 100 meters from the crossroads, stepped out and looked down the road I had followed so far.

It was an early morning and the road was lonely. At first it all looked completely normal — a scenery I could expect any rainy morning in that place which was familiar to me. But I
had the idea about the windscreen wiper in my mind, and because I wanted to find it I looked at the scenery a bit more carefully. And there it was. About 300 meters away there was a small horizontal dash in the middle of the road. I did not know what it was but in the pattern of a road it was unusual because the central parts of the lane are usually free from any material. So I run to the thing and when at a distance of about 10 meters I could definitely say it was a windscreen wiper. And because of the context, my windscreen wiper. I took it up, walked back to the car, fixed it and it works today as well as ever.

You may ask why I am speaking about windscreen wipers. And you do it because it does not suit into the pattern you are expecting under a title which includes pathology. But it is your question which leads us to the answer. I talked about windscreen wipers because the story was full of patterns and we handle patterns in diagnostic pathology. Contextual patterns, and patterns of visual images, to be exact. We have been taught how normal tissue looks like in sections. Thereafter we have been taught how different diseases look like in sections. In doing diagnostic work we have to decide whether the tissue is normal or abnormal, and when abnormal what disease entity it presents. In doing that, we detect patterns,
and see clues in these patterns which lead us to a decision about the nature of the disease. This decision about the nature of disease we call diagnosis. The clues may appear minimal and we may not even know what they represent but they may be very helpful. It is exactly what happened to me and my windscreen wiper. I saw something not knowing exactly what it was, and I am a bit richer now than I was when I had lost it.

STEREOMETRY AND MORPHOMETRY

But it has turned out that finding those faint clues and interpreting them right is not easy and not always reproducible (Collan 1982). So physicians have turned to measurements, which have allowed them to estimate their own performance but in addition allowed the detection of changes which by other means might have been left unnoticed. They have dealt with measurements of form, morphometry. In pathology, morphometry has mostly been applied in experimental pathology but also diagnostic pathology has benefited in recent years. Measurements on sections, however, were first made by geologists, anatomists and histologists who tried to get an idea about 3-dimensional structure of tissues. Because they had 3-dimensional structures in mind the methods applied were called stereometry (Underwood 1970, Weibel 1979). The principles of geometry were and still are very important in such studies.

 PATTERNS IN DIAGNOSTIC PATHOLOGY

But before I go on I want to return to patterns. We should realise that studying histological samples and reporting findings need not be dull or far from the frontlines of science even though there may be people who feel like that. Today we should really be interested of what we do, and how we do our work - and also interested of this in the psychological sense. When we dare to look at our performance, we are very near the frontlines of scientific research of today.

You remember the contextual patterns of the story at the beginning of this presentation. With contextual patterns I mean complexes like: noise in front of the car - windscreen wiper missing - a faint dash on the rainy road, or: a patient with enlarged liver - earlier history of melanoma - anaplastic neoplasm in liver biopsy. Such patterns are interpreted by us and may lead to action from our side. We think in terms on these patterns and after thinking we decide what to do next. In fact it has been suggested that such patterns are always necessary in thinking and that intelligence is basically nothing else than recognition of various kinds of patterns. It is easy to agree because intelligent people no doubt handle patterns more efficiently than less intelligent people. That is my
experience anyway; simply because I call people intelligent if they seem to handle patterns and especially contextual patterns efficiently. But if the basis of intelligence is in similar patterns on which we base our diagnostic decisions we should realise how near the frontline of science we are working. And we should realise how basic and uniformly relevant points in science are touched when we start to think what we really do in diagnostic pathology. The time does not allow me to go further but to say that the research in psychology, human factors, safety planning, international politics, decisionmaking, artificial intelligence, mathematics, automatic data processing, and computer research are all dealing with related problems. We see pathologists who tell us, often slightly embarrassed, that they left research and turned to routine pathology, as if that would mean a good bye for brain-teasing. The truth is that they are now dealing with the side of pathology which is very badly known, and needs intellectual contributions to make us understand diagnostic decisionmaking in histopathology. But patterns do not play a part in decisionmaking only. In histopathology visual patterns are important and especially such patterns interest us today. For handling of these patterns there are three potentially fruitful approaches available. One approach deals with pattern recognition. This approach aims at a complete description of visual patterns and usually also at completely automatic computer-aided description, so that with its help we could recognize features which we have already defined. Designing of instruments which could recognize patterns is a very important aspect of pattern recognition. Stereology and morphometry, the other two, do not need complicated instruments, although they can derive benefit from them. Stereology and morphometry are often considered identical and this may be true in some practical problems, although the definitions of these entities are distinctly different. In histopathology we have to make a distinction between these two because the transformation of 2-dimensional information to 3-dimensional information may be extremely laborious. The visual image that we analyse is 2-dimensional. We have been happy with the information it gives us and there is lots of evidence that histopathology has been and still is very important in the care of sick patients. When we measure details in the microscopic image, the results are certainly relevant for diagnosis even without the transformation to the 3-dimensional space. If such transformation is laborious, one would rather leave it out from the procedure than abandon measurements altogether. One thing is certainly true of morphometry, stereology, and patterns recognition: if you are going to use them to make your diagnostic system perform better you should know the principles of those methods. You have to know what you are doing, before you can even think of being more exact than you used to.
ARE WE AFRAID OF MEASUREMENTS?

Principles of stereology and morphometry have been applied in experimental and basic research in histology and histopathology. In diagnostic histopathology these methods have not been applied to the same degree. One reason for this is that pathologists have been afraid of losing their jobs. True, the intuitive reaction to talks about automatic patterns recognition, stereology or morphometry is that of suspicion. Who is going to do all that? We pathologists or those guys from the local Institute of Technology? There is a misunderstanding behind this suspicion. Misunderstanding of the place of the physician in the medical community. In the medical community and in the diagnostic context, no automatic instruments or users of those instruments can replace physicians. Good medical background is absolutely necessary for any conclusions drawn for diagnostic purposes from any measurement, be it automatic or manual. It is also understandable that decisions leading to practical applications can be made by physicians only. This is because a broad understanding of the nature of disease states is necessary for such decision. On the other hand it can be said that because measurements no doubt are valuable, they should necessarily be applied to give the diagnostic decision a more accurate and reproducible basis. If physicians can apply the methods the benefits are more immediately recognised for the good of the patient. We should not be afraid of these methods, we should rather try to find the good they offer for the medical community.

STEREOLOGY AND MORPHOMETRY IN PATHOLOGY: THE WAY AHEAD

In fact we know quite well what these methods can offer. They can help us find image features which might have diagnostic significance and do this in an accurate and reproducible fashion (Baak 1983). Reproducibility studies have taught us that experience does not increase intraobserver reproducibility (Ringsted et al. 1978). It is probable that experience helps specialists to work faster but the quality of the performance (in terms of reproducibility) does not change. This makes it quite clear that the quality of our performance cannot be much increased with experience only—new methods have to be applied for that purpose. Diagnostic pathology has not had many methods for objective quality control. One has been the follow-up of the patient. Now stereology and morphometry are offering other methods for quality control. Interpretation of image features can now be challenged by morphometric measurements, which are able to characterise the image in any detail. Stereology and morphometry also offer a method for testing and evaluating the limits of human performance and the influence of human factors (Collan 1984).
all this: no doubt these methods are able to lead diagnostic histopathology from art to science. "Complete" pattern recognition may also give us a new insight into the diagnostic process and possibly even detect features which are not known to be important today. Without education, however, the impact of these methods will not be what it should.

EDUCATION IN STEREOLOGY AND MORPHOMETRY

Morphometry offers us an exact way to describe the image on which the diagnosis is based. Because we can speak in terms of exact image features, the diagnostic system can be characterised in more detail than has been possible earlier. Also diagnostic philosophy can be based on exactly determined parameters. Understanding of these features results in decreased dispersion on diagnostic suggestions. At least education can be monitored by applying morphometric methods. Education can also be made more efficient because accurate methods are available to test alternatives.

Diagnostic decisionmaking is central in diagnostic histopathology. So, when morphometry or stereology are applied in the diagnostic context, the decisions need be handled also. This is why decisionmaking has an important part in the morphometry training for medical students in the University of Kuopio.

Stereology and morphometry are introduced during the course in pathology. The pathology course is in 3 phases: general pathology (one term during the third year of studies), organ pathology I (one term after general pathology), organ pathology II (a shorter course with lectures and demonstrations on gynecologic, skin, otorhinolaryngologic, pediatric and neuropathology). During each phase 2 hours are given for lectures and 2 hours for exercises on stereology and morphometry. The study plan is as follows:

General pathology
Lectures on geometric probability, volume fraction estimation, length density estimation, surface density estimation, numerical density estimation.

Exercises on subjective estimation of histological parameters, and measurements with point and line grids.

Organ pathology I
Lectures on principles of disease classifications, the concept of diagnosis, variation in diagnostic histopathology, variation in morphometric studies, principles of diagnostic decisionmaking.
Exercises on measurements with point and line grids, and on decision patterns.

Organ pathology II
Lectures on scientific basis of diagnostic decisions, evaluation of prognosis, basic philosophy related to the cause of death.

Exercises on decisions based on subjective evaluation of histological samples, on decisions based on morphometric analysis of histological samples, exercises on prognostic decisions, exercises on cause of death analysis.

What skills should the diagnostic pathologist have in stereology and morphometry? He should know the basic principles outlined above and in addition he should be able to follow the developments on the field. This he has to master to avoid the unhappy situation in which pathologists could be totally dependent on technical experts whose knowledge in medical factors and associations is limited. In the next few pages the special course of this symposium tries to cover the aspects which hopefully will be able to lead the diagnostic histopathologist into the world of stereology and morphometry.

REFERENCES