Exciting experiences in the '*Rocky road to digital diagnostics*'

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The review paper by Professor Paul J van Diest and colleagues entitled '*Rocky road to digital diagnostics: implementation issues and exhilarating experiences*' describes and retraces, in a very attracting way, the path they have followed since 2007 in the fully implementation of digital diagnostics in pathology.[1] We have to admit that we have followed at the beginning with some scepticism and then with enthusiasm, if not with some envy, the development of digitalisation in their institution that eventually has become so successful.

Our scepticism that then became enthusiasm has been linked to the fact that, in one way or another, we witnessed and even participated since the early 1980s in the development and application of what in the past was called 'morphometry' or 'quantitative histopathology' and what can be considered the background of the modern digital diagnostics. The senior author of our contribution still vividly remembers Professor van Diest entering the field of 'morphometry' at the beginning as a medical student and then as a young pathologist, and contributing actively to its development and application in 'diagnostic pathology'.

Several groups were involved in the basic research, developing from scratch theoretical bases, algorithms and applications and even contributing to the development and update of image analysis systems, parallel to the developments in computer science. All this became common knowledge and appreciation among pathologists through publications and meetings. What has currently been achieved by Professor van Diest is the result of such continuous progresses and innovations in the field of 'morphometry' or 'quantitative histopathology' as well as computer science.

We could say here that 'Without the past, there is no future', that is 'understanding where we are going comes from knowing where we've been'.[2]

The field of 'morphometry' was shaped and the road to the current achievements paved by several groups and individuals, in particular by Professors Jan PA Baak (Amsterdam, The Netherlands) and the late Peter H Bartels (Tucson, Arizona, USA) and their groups. Professor Baak, a pathologist by training, succeeded in developing practical computer-based applications that are at the basis of the modern digital diagnostics, with a special focus in breast cancer diagnosis and prognosis. His achievements were condensed in a book entitled 'A manual of morphometry in diagnostic pathology' (figure 1A) published in 1983 and coedited with professor Jan Oort. Professor van Diest was involved in 1991 in its revision that was entitled 'Manual of quantitative pathology in cancer diagnosis and prognosis' (figure 1B).

Professor Bartels, a physic by training who developed a great interest and knowledge in pathology, contributed to the field of 'morphometry' in a slightly different manner. He developed the theoretic background of image analysis and its several applications. This included what was called at his time machine vision and case-based reasoning, that is, the current bases of the modern artificial intelligence (AI) and robotics. His field of interest also included uropathology. One of his works focused on the cribriformity index of prostate cancer with cribriform architecture. At that time this could have appeared of scarce clinical significance. Nowadays, prostate cancer with cribriform architecture is considered the most aggressive form of Gleason pattern 4.[3] Two authors of this contribution (RM and MS) had the opportunity of collaborating with him in the early 90s and to witness the development of a miniaturised microscope array digital slide scanner (Patent No US 7,184,610 B2). Professor Bartels' achievements and contributions were presented in meetings (figure 2A) and books, one of them by the title 'Image analysis. A primer for pathologists', published in 1994 with Professor Alberto M Marchevsky (figure 2B). He also contributed to the revised edition of Professor Baak's book.

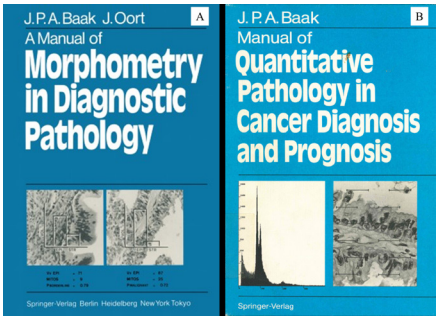

Figure 1 Covers of the two books published by Professors JPA Baak with J Oort in 1983 (A) and in 1991 (B) by JPA Baak as a revision of the former.

In a recent contribution entitled 'Pathology without microscope: From a projection screen to a virtual slide',[4] our group has briefly summarised the successive steps and phases we have witnessed in the 'Rocky road' leading towards greater role of digitalisation in the field of pathology, both in terms of consultation and teaching, as implemented routinely by Professor van Diest. Our main interest, from both the professional and image analysis point of view, is still that fueled by and shared with Professor Bartels, that is, uropathology, in particular the digitalisation the whole mount sections of the prostate (figure 3).

It would be too much reductive not to say that other people and groups were and have been involved with the two scientists mentioned above. One is Professor Peter Hamilton (Belfast, Northern Ireland, UK). He is currently the one who has really inherited Professor Bartels' vision. Others have followed a path different from digital diagnostics in pathology, however, still with success, for instance in robotics and computer science.[5]

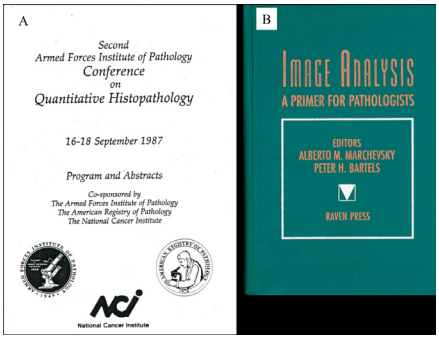

Figure 2 Covers of the Program and Abstract book of the second armed forces Institute of pathology conference on quantitative histopathology published in 1987 (A) and of a book on Image Analysis published by Professor Bartels in 1994 with Professor Marchevsky (B).

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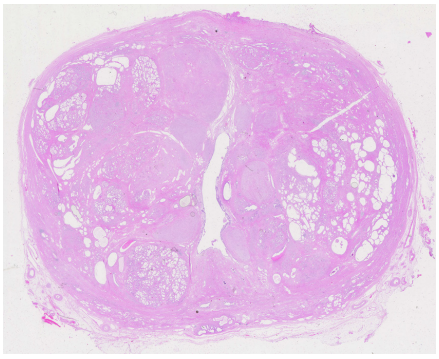

Figure 3 Whole Mount section of a radical prostatectomy as seen in a virtual slide.

Having considered the past contributions by Professors Baak and Bartels and the current situation as reviewed by Professor van Diest, one more consideration should be made, that is, what the situation will be like in 5 years. This involved a bit of vision. For sure routine digital diagnostics in pathology will become routine in many centres, aiming at replacing the microscope with digital slides. However, we have to think that digital diagnostics in pathology depend on the routine work done by technicians and paramedics. There might be a further role for fluorescence confocal microscopy. The acquisition of digital images with this approach with required 2 to 5 min, without the need for conventional processing nor equipped laboratory or dedicated personnel, with interpretation done remotely and even in smart working.[6 7] The adoption of digital pathology will enable the implementation of AI-based algorithms in the routine practice. These algorithms have the potential to go beyond the visual assessment of the main histopathological features to capture subtle patterns which are currently beyond human recognition, such as tumour microenvironment.[8] With multiplex staining on a single slide and high-resolution image analysis, machine vision and deep learning techniques offer diagnostic algorithms, including AI, that can be adopted for precise diagnosis, prognosis and prediction to response to therapy of patients with prostate cancer (PCa).[9] There are future uses of virtual slides, still to be fully explored and implemented.[7] Individual patients, for instance, could carry a microchip with virtual slides, radiological images, clinical records and other data.[7]

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REFERENCES

1 Stathonikos N, Nguyen TQ, van Diest PJ. Rocky road to digital diagnostics: implementation issues and exhilarating experiences. *J Clin Pathol* 2020:jclinpath-2020-206715.
2 Without the past, there is no future. Available: http://www.knutsynstad.com/without_the_past_there_is_no_future/
3 Anderson NH, Hamilton PW, Bartels PH, *et al*. Computerized scene segmentation for the discrimination of architectural features in ductal proliferative lesions of the breast. *J Pathol* 1997;181:374–80.
4 Montironi R, Cimadamore A, Scarpelli M, *et al*. Pathology without microscope: from a projection screen to a virtual slide. *Pathol Res Pract* 2020;216:153196.
5 Montironi MA. From image analysis in pathology to robotics and artificial intelligence. *Anal Quant Cytopathol Histol* 2016;38:268–9.
6 Rocco B, Sighinolfi MC, Sandri M, *et al*. Digital biopsy with fluorescence confocal microscope for effective real-time diagnosis of prostate cancer: a prospective, comparative study. *Eur Urol Oncol* 2020. doi:10.1016/j.euo.2020.08.009
7 Cimadamore A, Lopez-Beltran A, Scarpelli M, *et al*. Digital pathology and COVID-19 and future crises: pathologists can safely diagnose cases from home using a consumer monitor and a mini PC. *J Clin Pathol* 2020;73:695–6.
8 Rakha EA, Toss M, Shiino S, *et al*. Current and future applications of artificial intelligence in pathology: a clinical perspective. *J Clin Pathol* 2020:jclinpath-2020-206908.
9 Huss R, Coupland SE. Software-assisted decision support in digital histopathology. *J Pathol* 2020;250:685–92.