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Symposium

Summary of third Nordic symposium on digital pathology

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Abstract

Cross-disciplinary and cross-sectorial collaboration is a key success factor for turning the promise of digital pathology into actual clinical benefits. The Nordic symposium on digital pathology (NDP) was created to promote knowledge exchange in this area, among stakeholders in health care, industry, and academia. This article is a summary of the third NDP symposium in Linköping, Sweden. The Nordic experiences, including several hospitals using whole-slide imaging for substantial parts of their primary reviews, formed a fertile base for discussions among the 190 NDP attendees originating from 15 different countries. This summary also contains results from a survey on adoption and validation aspects of clinical digital pathology use.

Key words: Implementation, pathology informatics, validation

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INTRODUCTION

The potential benefits for clinical pathology of adopting well-designed digital technologies have been solidly established.[1-3] Essentially, there are strong arguments pointing to improved patient care and more efficient care pathways in the digital era. The reality, however, often is that the path toward realizing this potential is not straightforward. The clinical adoption is multi-faceted and for each domain, customized solutions may be required.

There are many efforts around the world aiming to pave the way for digital pathology into routine clinical use, and a particular concentration of development work is happening in the Nordic countries (Sweden, Denmark, Norway, Finland, and Iceland). For example, full histology scanning and extensive digital primary review are a reality since several years in the hospitals of Linköping and Kalmar.[3] Recently, Gävle hospital started a digital review for parts of the clinical routine, and concrete implementation plans are being carried out in many more institutions.

Thus, the Nordic countries are a fertile environment for further digital pathology progress. The Nordic symposium on digital pathology (NDP) was created in 2013 to promote global exchange of state-of-the-art knowledge, taking advantage of this Nordic digital greenhouse. The specific focus of NDP is advancing toward the clinical adoption of whole-slide imaging (WSI) and other digital technologies in pathology. In particular, a founding principle is the insight that effective progress requires strong collaboration among health care, industry, and academia, and NDP is designed to be a forum where professionals from all these domains can meet. This third installment of NDP marks a continued evolution from the two previous events

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in 2013 and 2014,[4] in terms of participant numbers (190 compared to 125 and 144, respectively) and depth of issues discussed. Below we provide a summary of NDP 2015, in the form of a meeting overview, results from the symposium's validation workshop, speaker contributions, and finally brief conclusions.

MEETING OVERVIEW

The NDP symposium 2015 took place November 3–4 in Linköping, Sweden. A total of 190 attendees gathered, of which 43% listed health care as the primary affiliation, 40% industry, and 16% academia. The health care representatives were dominated by pathologists, but also managers, laboratory technologists, and IT staff were in significant numbers. The participants represented 15 different countries with the Nordic attendees making up the majority (82%), but less so than in the 2014 symposium (87%).

Invited talks constituted the backbone of the program, together with a collaborative workshop on validation aspects of digital pathology. The contents of these sessions will be outlined in the sections below. In the science and innovation session, 13 posters were presented, and top contributions were invited to submit full papers. This resulted in three JPI papers published alongside this editorial: "Consultation of urological specimens using real-time digital microscopy: Optimizing the workflow for referred cancer patients" (Henrik Holten-Rossing *et al.*), "Improving the creation and reporting of structured findings during digital pathology review" (Ida Cervin *et al.*), and "Feature-based analysis of mouse prostatic intraepithelial neoplasia in histological tissue sections" (Pekka Ruusuvuori *et al.*).

In addition, the NDP included an industrial exhibition consisting of 13 vendors, showing a wide range of products and services related to digital pathology operations. Figure 1 shows a snapshot from the symposium, and the program details are available at the NDP website www.ndp2015.se.

Workshop on Validation of Digital Pathology

A key part of the NDP program was the workshop discussing validation of digital pathology. The workshop was organized as an open floor discussion with broad participation from the attendees. As an introduction, a systematic review of previous digital pathology validation research was presented by Bethany Williams, Leeds University.[5] Moreover, a survey among the health care attendees themselves, distributed in advance of the symposium, served as fuel for debate. An excerpt of the results from this survey will be presented next.

Figure 1: The Nordic symposium on digital pathology 2015 audience gathered for the keynote presentation of Prof Paul J. Van Diest

It is important to acknowledge that the survey respondents represent a biased selection among the pathology community. Since only NDP participants were asked, this means that respondents are likely to be among the most positive to digital pathology and also among the most experienced. There is also a strong geographical dominance from the Nordics and, in particular, Sweden. Of 83 asked to participate in the survey, 49 responses were gathered. The distribution of roles is given in Figure 2. It is likely that the pathologist dominance was even higher for some questions that require deep knowledge of clinical practice.

The survey first asked: "Today, to what degree do you use digital images of histology slides in your practice? (In percentage of all histology cases)." The results are shown in Figure 3, showing moderate levels of adoption but no use in about 50% of respondents. (Another bias to note for these questions is that several people from the same institution may have responded).

The same question was asked for the predicted situation at the end of 2016. As the 2016 prediction was also asked in the NDP2014 survey, the two predictions can be compared. The comparison is presented in Figure 4. As in the previous year, a vast majority expects to soon do digital to some degree, but the difference in predicted adoption rate indicates that the plans for digitization are progressing slightly slower than anticipated. This development pace moderation is in line with reports from the symposium attendees that both funding allotment and procurement processes are causing delays in their digitization efforts.

Validation of digital pathology means controlling potential risks of the digitization step, i.e., scanning and

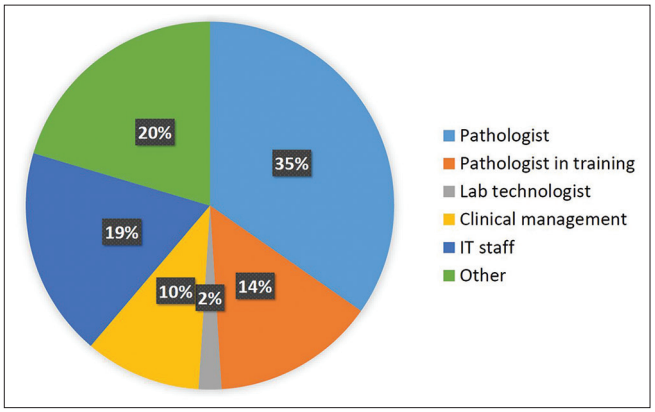

Figure 2: Role distribution of survey respondents

reproduction on a computer screen. In the College of American Pathologists (CAP) guidelines,[6] WSI validation is defined as "a process that aims to demonstrate that the new method performs as expected for its intended use and environment prior to its application for patient care." An important aspect is to decide on an acceptable level of risk. While it is attractive to adopt zero tolerance for errors due to digitization, this may lead to an unbalanced distribution of efforts. If the risks in other parts of the diagnostic chain are much larger than the ones in the digitization step, the mitigation and control efforts in those areas should come first. Therefore, to understand the perceived relative risk of digitization, the survey asked: "Compared with other parts of the sample preparation and diagnostic process, how big do you think the added safety risk of the digitization step is?" The results, presented in Figure 5, show that health care NDP attendees clearly consider the added risk from digitization to be smaller than risks in the diagnostic review, staining, sectioning, and grossing steps.

There is an ongoing debate in the community regarding what type or scale of validation that is needed before adoption of digital pathology in diagnosis. To elicit the overall opinion, the survey asked: "What's your personal view on the need for validation efforts to increase the confidence for digital pathology in clinical practice?" For this group having substantial experience of clinical use of WSI, the dominant view (68%) is that current knowledge is sufficient for going ahead with digital pathology adoption and that further validation is characterized as a continuous improvement effort. This may again reflect the high proportion of early adopters in the audience. As seen in Figure 6, about 20% are more hesitant and require further validation as a condition for adoption.

Validation can be performed, documented, and disseminated in many ways and by several types of stakeholders. As the decision to adopt digital pathology often boils down to the conviction of individuals, it is interesting to know which sources of safety assurance that have the highest credibility. The survey asked: "Assurance that digital pathology is safe for clinical use can come from many sources. For your own decision, if digital pathology is safe, how much confidence would you get from the following sources?" The results in Figure 7 show that personal experience along with high-quality scientific trials is associated with the highest confidence, whereas CE marking and Food and Drug Administration approval of systems are less assuring, relatively.

After the survey results were presented, a guided discussion among all participants took place. Overall, the points of view shared demonstrated the many facets of validation to consider. A fundamental prerequisite is

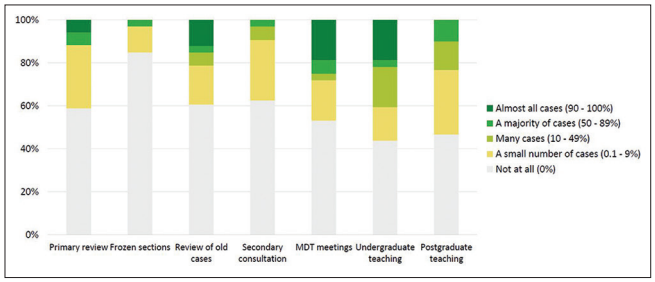

Figure 3: Current use of digital pathology among survey respondents

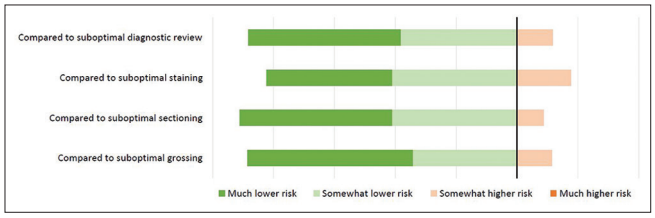

Figure 5: Perceived added safety risk from digitization (scanning and image reproduction on screen) relative to risks stemming from other parts of the diagnostic pipeline. Overall, the results point to lower perceived risk, i.e., that digitization is perceived as less error-prone

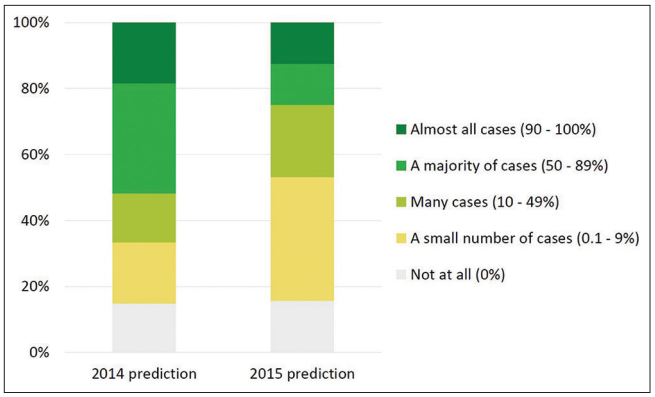

Figure 4: Predicted use of digital pathology for primary review at the end of 2016. Left: prediction from Nordic symposium on digital pathology 2014 survey. Right: prediction from Nordic symposium on digital pathology 2015 survey

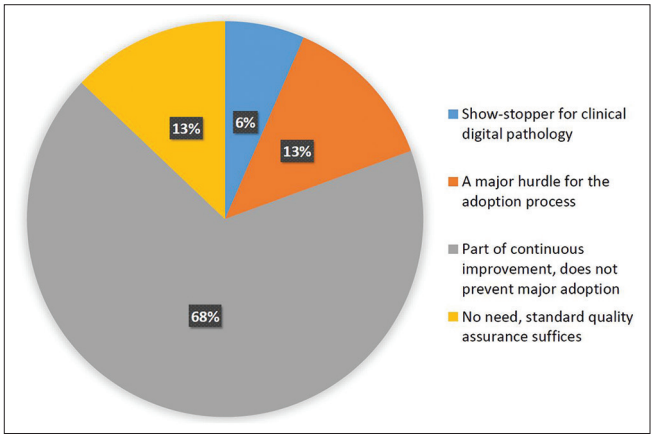

Figure 6: Characterization of perceived validation need for digital pathology. The majority sees further validation as a part of continued progress, but not as prohibitive for adoption in general

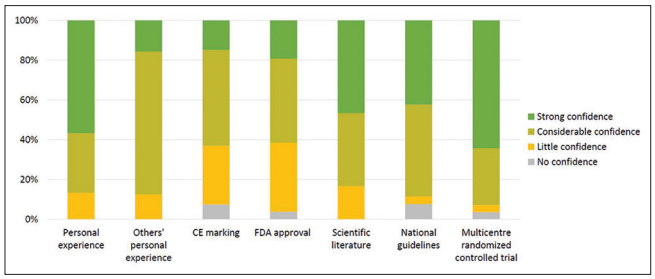

Figure 7: Perceived confidence in different sources of safety assurances regarding digital pathology. Personal experience and high-quality trials are considered the most trustworthy sources

that digital pathology does introduce new process steps that need to be scrutinized: The image digitization and the visualization (display and interaction) in a digital workstation. There are now many concordance studies showing reassuring overall results.[5] At the same time, potential concerns are that there are few well-designed large studies to date and that despite high overall concordance with light microscopy, this may conceal the possibility that for some case types, digitization might introduce problems not existing in microscope glass slide review. In line with the first statement of the CAP guidelines,[6] NDP attendees expressed the need for validation activities at each individual laboratory implementing WSI. In this preliminary stage, no clear consensus on scope and depth of such activities emerged from the discussion, but ongoing initiatives in Sweden and the United Kingdom are directed toward developing concrete support for validation work.

Another aspect voiced was that even if agreeing that digital pathology adds a slight risk, this should be compared to the risk of nonadoption. For example, an increased risk may be acceptable if the benefits of increased reproducibility or easier consultations across the healthcare enterprise clearly outweigh any additional risk. A positive effect of the validation effort of digital pathology can also be that components of current practice, actually having evolved with a low level of scrutiny, are revisited with a critical eye.

The conclusion from the discussion is that there is a broad consensus in this group that continued efforts to scrutinize digital pathology are needed, whereas the views differ as to what degree this affects the pace of adoption.

Speaker Contributions

Dr. Paul J. Van Diest, professor and head of pathology at the University Medical Center Utrecht, the Netherlands, presented their digital pathology program, including both past efforts and future plans. The experience includes many years of scanning all slides, working integration with their report system, and validation efforts with positive results. Currently, Utrecht is implementing new systems and workflows to take the step to digital primary review, and Prof. Van Diest emphasized the need for establishing a solid and continuous change management process in the department, in contrast to a one-off implementation activity.

Dr. Nasir Rajpoot, associate professor at Qatar University, Qatar, and University of Warwick, UK, gave a comprehensive overview of opportunities and challenges in image analysis for pathology. He presented a wide range of methods developed in his research groups constituting a toolbox for detection and classification on several levels: Nucleus, cell, gland, and entire tissue. Dr. Rajpoot also stressed the benefits of an open exchange of methods and data for the scientific community to effectively make advances in the field.

Petra Lindstedt, former head of the diagnostic division at Region Gävleborg, Sweden, spoke to the benefits that had been the main motivation for their decision to go fully digital, a process now underway with several pathologists doing their main primary review on digital slides. A benefit particular to smaller, rural hospitals is that a digital environment opens new possibilities for specialist careers based on a consultation volume from other providers.

Johnny Eriksson, CTO at Telemedicine Clinic, Spain, and CTO Radiology IT at the University Hospital Örebro County, Sweden, described the opportunities stemming from enterprise-wide digital image management. The experience from radiology, including services such as running off-hour diagnostic routine for European hospitals from Australia, demonstrates the potential but also the need to assiduously address the technical challenges involved.

Dr. Anna Bodén, pathologist and digitization project manager at Linköping University Hospital, Sweden, presented the experiences from implementing a second generation of large-scale digital pathology in their clinic. Issues given increased consideration this time around included achieving highly stable and fast viewing, running scanners from multiple vendors in parallel, careful selection of monitors, and support for large slides.

Dr. Manuel Salto-Tellez, professor and molecular pathologist at Queen's University Belfast, UK, provided a compelling vision of improved health care, thanks to advances within reach for joint efforts in pathology and genomics. Several examples of such efforts from his research group were presented, including testing for BRAF, KRAS, and EGFR mutations in cancer. Dr. Salto-Tellez strongly emphasized the need for effectively combining the two disciplines of molecular and digital pathology, since the genomic findings require a context of phenotype and morphometry.

André Homeyer, scientist at the Fraunhofer Mevis research institute in Bremen, Germany, presented their group's software framework for image analysis in

pathology. Key objectives are to exploit image features across several scales and to meet high interactivity requirements by carefully designed feature extraction in the preprocessing stage. Many examples of successful pathology applications built on this framework were described.

NDP also included a number of special sessions. Three lectures were organized by industrial contributors. Simon Häger of Sectra, Linköping, Sweden, talked about how to construct a business case for digital pathology. Courtesy of GE Healthcare, Dr. Yee-Wah Tsang from Coventry University, UK, presented the large validation study recently performed in Coventry.[7] Visiopharm arranged a talk from Henrik Holten-Rossing from Rigshospitalet Copenhagen, Denmark, presenting studies and experiences of advanced quantitative image analysis. Finally, a special session on education and collegial exchange was held, led by Dr. Mats Wolving, head of quality development at the Swedish Society of Pathology and pathologist at Sahlgrenska University Hospital, Gothenburg, Sweden, and Martin Svenson of Sectra. They presented ongoing innovation efforts to develop new tools and workflows in this domain, and the audience contributed in an enlightening discussion regarding possibilities and obstacles with regards to this area of clinical practice.

CONCLUSIONS

The need for, and interest in, knowledge exchange with regards to the clinical routine use of WSI and related IT tools continues to be strong, as demonstrated by the increasing attendance at this third installment of the NDP. As digital pathology evolves and initial hurdles are managed, new questions arise. The symposium touched on many topics of digital pathology, some of which are growing in importance with increased digital maturity. The feedback from the attendees is that this type of experience sharing across organizations, disciplines, and sectors is important for the progress in the field. As organizers, we are happy to conclude that NDP 2015 has made a substantial contribution to this end. Finally, we gladly note the increasing ratio of non-Nordic attendees and encourage colleagues from all over the world to come and benefit from future NDP symposia.

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Conflicts of Interest

Claes Lundström is an employee of the company Sectra AB. Anders Persson is a board member for Sectra AB. Darren Treanor is a member of the Aperio/Leica Advisory Board and Sectra Advisory Board. Marie Waltersson has no competing interests to declare.

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