Final thesis

Reporting in digital pathology: increasing efficiency and accuracy using structured reporting

by

Ida Cervin

LIU-IDA/LITH-EX-A-15/006–SE

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The healthcare today is experiencing a greater burden since diseases such as cancer are more common. The diagnostic parts of the healthcare, such as radiology and pathology, are affected with increased workload. During the past several decades, systems for structured reporting in radiology have become available in a try to facilitate their workflow. The introduction of digital pathology has enabled the possibility to introduce structured reporting in pathology as well. The question is whether it can facilitate their workflow.

Today’s aids for structured reporting in radiology are more or less perceived as distracting, and the challenge in this thesis is to create an aid for structured reporting that is not distracting the pathologist’s diagnostic workflow. To achieve this, a prototype with a template for invasive breast cancer and prostate cancer was implemented in Sectra’s viewer for pathology images. The template for invasive breast cancer was tested by two pathologists in a user study with the main objective to determine the differences in the diagnostic workflow using the prototype and using only paper and pen. The pathologist could see a use of the prototype both for breast assessment and assessments in other areas of pathology. Both pathologists also think that the prototype will save time in their overall workflow, help them organize the information retrieved during the assessment, and create an overall better diagnostic workflow.

Structured reporting, pathology, synoptic reporting
Abstract

The healthcare today is experiencing a greater burden since diseases such as cancer are more common. The diagnostic parts of the healthcare, such as radiology and pathology, are affected with increased workload. During the past several decades, systems for structured reporting in radiology have become available in an attempt to facilitate their workflow. The introduction of digital pathology has enabled the possibility to introduce structured reporting in pathology as well. The question is whether it can facilitate their workflow. Today’s aids for structured reporting in radiology are more or less perceived as distracting, and the challenge in this thesis is to create an aid for structured reporting that is not distracting the pathologist’s diagnostic workflow. To achieve this, a prototype with a template for invasive breast cancer and prostate cancer was implemented in Sectra’s viewer for pathology images. The template for invasive breast cancer was tested by two pathologists in a user study with the main objective to determine the differences in the diagnostic workflow using the prototype and using only paper and pen. The pathologist could see a use of the prototype both for breast assessment and assessments in other areas of pathology. Both pathologists also think that the prototype will save time in their overall workflow, help them organize the information retrieved during the assessment, and create an overall better diagnostic workflow.
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Abbreviations

ER        Estrogen Receptor
HER2      Human Epidermal Growth Factor Receptor 2
INCA      the National Quality Register for Cancer in Sweden
KVAST     the Swedish Quality and Standardization Committee for Pathology
NHG       Nottingham Histological Grading
PgR       Progesterone Receptor
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Chapter 1

Introduction

With a longer living population, some deceases such as cancer have become more common. This gives a greater burden on healthcare, not only for clinicians working with treatment of patients but also the diagnostic parts of healthcare, such as pathology [1] and radiology. Improvement of the radiologist’s workflow has been applied over time to deal with the increased workload. One improvement is the process of generating radiology reports and in the past several decades, structured reporting systems have become available to facilitate the process [2]. With the possibility for pathology to now become fully digital due to whole slide imaging [3], a relevant question is whether structured reporting is suitable for facilitating the pathologist’s workflow. Al-Janabi et al. [4] states that the introduction of digital pathology enables smart ways to improve and facilitate the pathologists’ workflow, such as integration of structured reporting. However, Weiss and Langlotz [2] performed a study on available systems for structured reporting in radiology and found out that current systems are perceived as distracting. They mean that this could partly be due to when the radiologist handles complex cases; a too structured template for reporting will hinder the radiologist to do the descriptive reporting needed for a complex and unique case.

A study performed by Randall et al. (2012)[5] showed that pathologists, in a similar way as radiologists, handle complex cases different from person to person. Some pathologists format the report with respect to the slides and dictate the report while assessing each slide. Other pathologists keep all information in their head during the assessment and take notes to be able to remember what to dictate after finishing the full assessment. Regardless of their way of handling complex cases, there are a lot of things that need to be remembered in order to complete a report with all necessary parameters. The introduction of structured reporting could help the pathologist with this.
1.1 Purpose

The purpose of this thesis is to investigate the possible use of a software for structured reporting that cooperates with Sectra’s viewer for pathology images. The software is a prototype with a template for invasive breast cancer and a simpler template for prostate cancer. The hypothesis is that a fully implemented software will facilitate the pathologists’ diagnostic workflow.

1.2 Question of issue

- Is there a way to create structure in complex and unique cases that allows the pathologists to facilitate their diagnostic workflow?
- Is it possible to implement software that makes the reporting simple without distracting the pathologist’s diagnostic workflow?
- Is the prototype applicable in clinical practice?

1.3 Limitations

The prototype is not a complete product, only sufficient to be used in a user study performed with two pathologists. The templates in the prototype was implemented in Swedish.

1.4 Outline

Chapter two and three present the theory. The first of these two chapters presents today’s status of digital pathology and structured reporting as well as the fundamentals of cancer diagnosis in Sweden. The second one presents the principles of breast and prostate cancer with important key factors for assessment and reporting of these types of cancer. Chapter four presents the method and workflow of this thesis. Chapter five presents the method used to analyze pathology reports to determine if there is any kind of structure present today and get an idea of possible parameters for the templates. It also presents the results of the analysis. Chapter six presents the design and the implementation of the prototype and chapter seven the results and design of the user study with the prototype. The last two chapters in the report is the discussion of the results and conclusions.
Chapter 2

Digital pathology and structured reporting

Today’s status of digital pathology enables numerous possibilities to integrate smart software to facilitate the pathologist’s workflow [4]. One possible tool is structured reporting, that has the potential to facilitate the pathologist’s diagnostic workflow, i.e. their workflow while viewing slides. Systems for structured reporting have been developed for radiology in the past several decades and have both advantages and disadvantages. A big challenge is to create systems that will facilitate reporting and at the same not be distracting to the user [2].

2.1 Digital pathology

Interpretation of tissue and cells at a higher resolution than the human eye is the core of the pathology described in this thesis. Traditionally this has been made by studying specimens with light microscopy, but the introduction of digital slide scanners in the last decade has made digital pathology an alternative to conventional microscopy. The scanners produce whole slide images (WSI) (Figure 2.1) that can be explored with image viewers. There are many advantages of digital pathology and WSI such as; more ergonomic posture while working [3, 6, 7], the ability of remote consultation (telepathology) [3, 4, 7], displaying slides side by side, simultaneous displaying of an overview and a higher-power view of the slide, constant quality over time, no need to set focus during review, ability of automated image analysis and integration with electronic patient records [4]. Despite all advantages, there are also disadvantages. Gilbertson et. al [8] performed a validation study on primary histologic diagnosis using WSI, and found several limitations that can cause diagnostic confusion. Such limitations include areas of suboptimal focus and scanning artifacts that appear to be related to the WSI process.
The scanners are also currently unforgiving to tissue folds, bubbles and poor staining of the material to be scanned [9]. In addition to these advantages and disadvantages, there are numerous possibilities to integrate other useful tools together with digital pathology. One of these tools could be software for structured pathology reports.

![A whole slide image of tissue from a partial mastectomy of breast.](image)

Figure 2.1: A whole slide image of tissue from a partial mastectomy of breast.

### 2.1.1 Structured reporting

The diagnostics parts of healthcare, such as pathology and radiology, have to create reports about the findings when assessing a case. The reports are distributed to the referring clinicians as a basis for what treatment a patient needs. Structured reporting is the idea of a structured format that creates the basic elements and consistent organization in the report. The introduction of structured reporting creates a change in the traditional workflow since it requires keyboard and point-and-click input rather than the traditional dictation. The new workflow can interfere with the image interpreting process and has the potential to affect the diagnostic accuracy. It can also be impractical and distracting when handling complex cases where each finding requires individual attention, and the concept of using the keyboard and mouse for point-and-click reporting becomes limiting [2].

A change in the traditional workflow is difficult but necessary to improve the quality of the care. Even if the introduction of structured reporting might require a workflow change, the goal of any modern reporting system must be to not distract the pathologist and minimize the number of conscious steps necessary for report creation [2].

Systems for structured reporting have become available for radiology in the past several decades and have become more sophisticated and acceptable today. A system like this introduces a structured report format with paragraphs and headings that distinguish the basic elements of the report.
The structured format is preferred by the referring physician presumably since the information is easier to find than in a free text report. Another attribute of structured reporting is the use of standardized language which makes the report more accessible and usable [2].

Casati and Bjugn (2012)[7] investigated the use and long-term effect of a structured electronic template for colorectal carcinoma resections reports in pathology. The study showed that the implementation of a structured electronic template significantly improved the presence of key parameters in the reports. The structured template was used in 1089 cases, and out of these 75.5% of all reports had all key parameters present. This is to be compared with the 97 dictated free text reports where none had all key parameters present. They mean that the implementation of a structured electronic template increased the quality of the reports compared with free text reporting. Feedback from the template users indicated that the time spent completing the structured reports was similar to the time spent dictating the traditional free text. Casati and Bjugn also points out that the use of a template enables immediate sign out of the case, which will decrease the overall workload of the pathologists and clerical staff. If the pathologist dictates a report in the traditional fashion, the clerical staff have to transcribe the report and then the pathologist has to proofread it before the case can be signed out. This process (Figure 2.2 A) usually takes a day to perform leading to a long turnaround time for the report.

Natural language processing is a technology that has the potential to become nondistracting and intuitive in the future. It is the process of extracting information from a text, but it is not yet able to automatically extract all the relevant concepts from a dictated report. If a dictation could make use of natural language processing in combination with structured reporting in the future, this hybrid system could become a nondistracting and accepted reporting system [2]. The changes in workflow between the traditional dictating, structured reporting and natural language processing can be seen in Figure 2.2.
2.2 Diagnosis of cancer in Sweden

The diagnosis of breast and prostate cancer in Sweden follows certain guidelines, set by the Swedish Quality and Standardization Committee for Pathology (KVAST) and the National Quality Register for Cancer in Sweden (INCA).

2.2.1 The Quality and Standardization Committee, KVAST

The Swedish quality and standardization committee (Swedish: kvalitets- och standardiseringskommittén), KVAST, is a nonprofitable committee of
Swedish pathologists. Their purpose is to create documents for standardization in diagnosis of common diseases, as well as guidelines for validation and quality controls of examination and diagnosis methods. The committee consists of different groups with different areas of expertise and each group is responsible for the documents concerning their area, e.g. breast cancer or prostate cancer. The documents for breast and prostate cancer are both consisting of information such as biological and morphological markers and guidelines for possible parameters when writing reports for different procedures and diagnoses [10].

2.2.2 The INCA register

The INCA register is a national quality register for cancer in Sweden. It was applied for breast cancer in all regions 2008 and consists of information about preoperative diagnostics and the tumor, as well as procedure type, information about short- and longterm complication and relapse frequency, treatment, cosmetics, waiting times, and whether the patient is satisfied or not. The patients are only registered once when the first breast cancer tumor is found.

The intention of the register is to objectively standardize a way to follow up the flow from diagnosis to relapse and death, map regional differences, to follow guidelines and requirements of quality, and support progress in breast cancer research. All regions are obliged to report all newly diagnosed cancer to INCA with a few exceptions, such as cancer findings in autopsies or if the patient declines participation in the register [11].

The register for prostate cancer was applied in all regions 1998 and consists of information about diagnostics as well as treatment, the symptoms experienced by the patient over time, and a follow up of men, younger than 70, diagnosed with prostate cancer [12].

2.3 Chapter summary

Digital pathology enables the introduction of structured reporting to facilitate the pathologist’s workflow. Structured reporting has been introduced and developed in radiology in the past decades, and there have been both advantages and disadvantages. Some advantages are:

- a structured format that is easy accessible
- the use of a standardized language creates a more universal understanding of the report
- the use of standardized language facilitates reporting to the INCA register
- consistent reporting of key parameters
• increased quality of the reports
• decreased overall workload for pathologists and clerical staff

Some disadvantages are:

• distraction of the image interpretation process
• limiting in complex cases due to the structured format
• alteration of the traditional workflow without an obvious improvement is hard
Chapter 3

Principles of breast and prostate cancer diagnosis

Cancer, in general, has six hallmarks according to Douglas Hanahan et al. [13], that comprise biological properties that are acquired during the development of human tumors regardless of the site of the tumor. The hallmarks include sustaining proliferative signaling, evading growth suppressors, resisting cell death, enabling replicative immortality, inducing angiogenesis, and activating invasion and metastasis. To be able to diagnose patients with cancer clinicians have to rely on morphological markers and biomarkers that correspond to these hallmarks. This chapter describes the key factors in the diagnosis of breast and prostate cancer.

3.1 The diagnosis of breast cancer

Breast cancer is a widely spread decease with approximately 537000 deaths in 2012 [14] with over 1400 deaths alone in Sweden [15].

3.1.1 Vascular invasion

Vascular invasion is the presence of tumor cells in vessels. It is an early indication of metastasis and is important for the progress of malign tumors. It can be studied as a morphological marker in tissue sections and is a strong prognostic factor of breast cancer [16].

3.1.2 Nottingham Histological Grading

Nottingham combined Histological Grading (NHG) is the most used system for grading of the appearance of the tumor cells [17]. NHG gives a simple and routinely applicable overview of the intrinsic biological characteristics
3.1. THE DIAGNOSIS OF BREAST CANCER

and clinical behavior of the tumor. It is based on the grade of differentiation in the tumor tissue and is evaluated by three morphological properties [18]:

- **The grade of tubule formation** is determined by scanning all parts of each block of tissue, and the proportion of tumor displaying tubule structure is estimated. It is graded with, 1, 2 or 3 where 1 corresponds to tubule formation in the majority of the tumor (>75%), 2 corresponds to moderate degree of tubule formation (10-75%) and 3 corresponds to little or none tubule formation (<10%) [19].

- **Nuclear pleomorphism** is determined by both a quantitative and qualitative judgment of the nuclei. If the nuclei are small, vary little in size, 1 point is appropriate. If the cells appears larger than normal and there is moderately variation in both size and shape, 2 points are appropriate. 3 points are appropriate if there is distinct variability in both shape and size, and very bizarre nuclei are present [19].

- **Mitotic count** is the counting of mitoses in a minimum of ten fields, often in the periphery of the tumor since active growth is most likely there. Only nuclei with distinct morphological evidence of the growth phases metaphase, anaphase and telophase are counted. If the count is less than, or equal to, 9 mitoses per ten fields the grade is 1, 10-19 mitoses are grade 2 and more than 20 mitoses are grade 3 [19].

The grades of tubule formation, nuclear pleomorphism and mitotic count are summarized, giving a total of 3-9 points. 3-5 points corresponds to grade I and well differentiated tumors, 6-7 points are grade II and moderately differentiated tumors and 8-9 points are grade III and poorly differentiated tumors [19].

### 3.1.3 Estrogen and progesterone receptors

Estrogen receptors (ER) and progesterone receptors (PgR) are both receptors of the family steroid receptors. These are of special interest in breast cancer diagnosis since their protein levels are elevated in premalignant and malignant breast lesions, compared with normal tissue [20]. ERs has been used as a biomarker for breast cancer in over three decades [21] and are often used to foresee the response of endocrine therapy [22]. This is because the substantial benefit endocrine therapy has on ER-positive tumors and not on ER-negative tumors [21].

PgRs role in patient management has not yet been established, although guidelines for routine measurement of PgR have been called for. Suggestions are that an ER-positive and PgR-negative patient has worse prognosis than a patient that is positive for both ER and PgR. There is also evidence that a small part of patients with ER-negativity and PgR-positivity will respond to endocrine therapy, and this together with prognosis suggests that it is sufficient clinical value for routine testing of PgR [21].
The results of ER and PgR are both presented as the percentage of cells expressing the receptor. Nuclei stained in brown are considered positive and nuclei without any brown is considered negative (Figure 3.1).

![Figure 3.1: The staining of the cell nuclei (brown) in the tissue corresponds to 100% in the assessment of ER status. Light blue tissue surrounding the tumor cells are stroma and should not be counted. The assessment of PgR status works in the same way.](image)

### 3.1.4 Human Epidermal Growth Factor Receptor 2

Human Epidermal Growth Factor Receptor 2 (HER2) is a member of the family epidermal growth factor receptors that is overexpressed in 15-30% of newly diagnosed breast cancers, due to amplification of the HER2 oncogene [23, 21]. It is a receptor that normally regulates cell growth and cell survival, as well as adhesion, migration, differentiation and other cellular responses. When a HER2 receptor is activated its intracellular pathway inhibits cell death and promotes cell proliferation, which leads to tumor growth when overexpressed. Overexpression is associated with a worse prognosis and decreased overall survival [24]. HER2 status is assessed with 0, 1+, 2+ or 3+ that corresponds to the grade of cell membrane staining. 0 corresponds to incomplete or weak staining in <10%, 1+ to incomplete or weak staining in >10%, 2+ to complete and moderate staining in >10% and 3+ to complete staining. Figure 3.2 is an example of tissue with HER2 status 3+ [10].
3.1. THE DIAGNOSIS OF BREAST CANCER

To assess the HER2 status, two methods are used:

- **Immunohistochemistry (IHC)** is detecting overexpression of the HER2 protein. It is a relatively inexpensive method that is easy to perform and it is used widely in the diagnosis of breast cancer [23]. The tissue in Figure 3.2 is stained by this method.

- **In situ hybridization (ISH)** is sometimes used as a complement to IHC, since the protein quantification with IHC can be affected by several factors, such as fixation time and processing, antigen retrieval, and antibody specificity and sensitivity. ISH detects the amplification of the HER2 oncogene and is often used as a reference standard to confirm ambiguous results from the performed IHC. However, the ISH performed today has high expenses and long turn-around time along with some other limitations and is therefore only performed in some cases [23].

Various studies suggest that agents targeting the HER2-receptor are remarkably efficient both in metastatic and adjuvant settings. An approach to treat HER2-positive patients is to target the HER2-receptor with a humanized monoclonal antibody (Trastuzumab) and inhibit the activation of its intracellular pathway [24]. Treatment with agents as Trastuzumab improves response rates, time to progression as well as survival when it is used alone or in combination with chemotherapy [21]. Unfortunately, this treatment is expensive and only patient with status 2+ or 3+ are considered for treatment.

Figure 3.2: The staining of the cell membranes (brown) in the tissue corresponds to the value 3+ in the assessment of HER2 status.
3.1.5 Ki67

The expression of the protein Ki67 is strongly associated with cell proliferation. It is present during the cells active phases (G1, S, G2 and mitosis) and absent from resting cells (G0) [25].

Tumor cell proliferation is a cornerstone in cancer progression and are thus a good tumor marker. Today, mitotic index is the most established method to determine proliferation, but it has limitations since the number of mitoses per area unit is not linearly related to the rate of proliferation. The use of Ki-67 to determine cell proliferation could be an alternative method, but there is no consensus about the usage, which hinders full clinical implementation [26].

The assessment of Ki67 index in Sweden is performed in areas with a high content of Ki67 positive cells. At least 200 cells should be included in an area and all brown cells are counted as positives and all blue cell as negatives (Figure 3.3). The percentage of positive cells represents the index [10].

![Image of Ki67 index assessment](image)

Figure 3.3: The assessment of Ki67 index is performed in areas with a high content of Ki67 positive cells. The arrow in the image is pointing on a brown Ki67 positive cell while the blue cells are negative. An area of at least 200 cells has to be counted and the percentage of the positive cells represents the index.

3.2 The diagnosis of prostate cancer

Prostate cancer is the most common malign cancer in western countries [27] and is the sixth most common cancer related cause of death amongst men, with 32200 deaths worldwide in 2012 [14]. An average of 2399 men per year died during the years 2009-2011 in Sweden alone [15]. The markers described in this section are the key factors in the assessment of prostate cancer on specimens from biopsies performed with a hollow core needle.
3.2. THE DIAGNOSIS OF PROSTATE CANCER

3.2.1 Gleason score

In the 60’s and 70’s, Donald F. Gleason et al. discovered various architectural patterns in prostate cancer and grouped them in five different patterns or gradings [28]. The grading of the two most common patterns in the specimen are summarized and represents the Gleason score [29]. The score has become a key factor in the diagnosis of prostate cancer, and has been used unrevised until 2005 when the International Society of Urological Pathology (ISUP) clarified and standardized it [28]. A schematic diagram of the updated and modified Gleason grading is shown in Figure 3.4.

![Figure 3.4: The sum of the two most common patterns in a specimen represents the Gleason score. There are five different patterns and a higher value is associated with a worse prognosis. The image is an adaption of the original image of the updated and modified Gleason score from Epstein et al. [29]](image)

3.2.2 Markers of metastasis

Perineural invasion (PNI) is a well known route for metastasis. In prostate cancer, PNI is the process of neoplastic invasion of nerves by cancer cells that spreads beyond the prostate by the innervation rich posterior part of the prostate. However, there are conflicting studies about PNI’s significance in prostate cancer, but there seems to be a statistically significant higher presence of extraprostatic extensions (EPE) in patients with PNI. EPE is the presence of tumor outside the prostate and is associated with a worse prognosis, especially in combination of positive surgical margins (PSM)[30].

PSM can be seen by pathologists in the inked surgical resection margin in prostatectomy specimen if the local resection have been incomplete[31].
This means that the tumor has not been fully removed and the cancer is spread outside the prostate[31, 32].

3.2.3 TNM classification

The extent of a cancer is a key factor to determine which treatment to use and evaluate the chance for a successful outcome of the treatment. In 1992, a system for classification of anatomical extent of cancer was introduced by the American Joint Committee on Cancer (AJCC) and International Union for Cancer Control (IUCC). The system has been revised several times since its introduction and was last updated in 2010 to the 7th edition [33, 34]. The classification is called TNM and is defined as follows:

- **Primary tumor (T)**, also called pathologic classification of primary tumor (pT) when assessed by pathologists. pT, in prostate cancer, is classified from pT2-pT4 where class two means that the cancer is confined in the organ, class three that there are extraprostatic extensions and class four that the cancer has invaded rectum, levator muscles and/or the pelvic wall. The classes pT0 and pT1 are never set in prostate cancer [27, 35].

- **Regional lymph nodes (N)**, also called pathologic classification of regional lymph nodes (pN) when assessed by pathologists. pN is classified as pNX, pN0 or pN1 where pNX means that regional lymph nodes were not assessed, pN0 corresponds to absence of metastasis in regional lymph nodes and pN1 corresponds to metastasis in regional lymph nodes [35].

- **Distant metastasis (M)** is classified as M0 or M1. M0 corresponds to no distant metastasis and M1 corresponds to metastasis in distant regions. M1 is divided in subcategories a-c where a corresponds to nonregional lymph nodes, b to bone(s), and c to other site(s) with or without bone disease [35].

Together with Gleason score, these two classifications evaluate the anatomic state/prognostic group that is an assessment for disease outcome [35].

3.3 Chapter summary

Cancer is a widely spread disease today. Clinicians have to rely on certain morphological markers and biomarkers to be able to diagnose patients with cancer. The individual markers work as prognostic factors and/or an indication of what treatment to use on the patient and are all assessed and reported during a diagnosis session.
Chapter 4

Method

A crucial part of the thesis was to obtain an explicit understanding for the pathologists and their diagnostic workflow. It was obtained through several steps and started with a literature study concerning digital pathology, today’s status of structured reporting, the pathologist’s workflow and breast and prostate cancer. The next step was to study and analyze how reports are written and formatted today as well as evaluate possible parameters to use in the templates. This was done with anonymized pathology reports provided by Sectra. The third step was a meeting with a pathologist to study the pathologist’s diagnostic workflow in real life. With this knowledge, the design, implementation and evaluation of the prototype were started. The development of the prototype was divided in two iterations and the design and implementation of the first iteration was finished halfway through the thesis. The evaluation of the first iteration was performed with the help of two pathologists which gave feedback on a demonstration video of the prototype. One of the pathologists corresponded through email while the other participated in a meeting to give feedback. The feedback from the two participant pathologists was the foundation of the second iteration. The design was updated due to the pathologists’ feedback and was then implemented. When the second iteration was done, a user study was run with two pathologists. Figure 4.1 shows a schematic picture of the workflow during the thesis.
Figure 4.1: A schematic picture of the workflow during the thesis. The first step was a literature study to gain knowledge of digital pathology, structured reporting, the pathologist’s diagnostic workflow, breast and prostate cancer. The second step was an analysis of old pathology reports to get an understanding for reporting in pathology and possible template parameters. The third step was a meeting with a pathologist to study the diagnostic workflow. Then two cycles of design, implementation and evaluation of the prototype were done. The whole thesis was then finished by a user study.
Chapter 5

Pathology reports

Old pathology reports were studied in order to get an understanding for the reporting in pathology, determine if there was any kind of structure present and to get an idea of possible parameters for the templates. Sectra provided anonymized pathology reports from three different regions in Sweden. The reports were from different types of pathology diagnoses and were therefore sorted using regular expressions in C++. An initial sorting was performed to separate the breast and prostate reports from the rest using certain keywords associated with breast and prostate cancer diagnosis as regular expression. Statistics and potential parameters for the templates were derived from the sorted reports in the same way as the initial sorting. The keywords for the regular expressions were determined using the Swedish quality and standardization committee’s recommended parameters associated with prostate respectively breast cancer diagnosis. 100 of the 1491 prostate reports were randomly chosen and categorized as descriptive reports, semistructured reports and structured reports by visual inspection. The C++ library cstdlib was used to generate a vector of random numbers and the reports corresponding to these number were categorized.

Additionally, reports addressing the same types of cancer and same type of procedure were sorted out using keywords for procedure type and final diagnosis. This to be able to compare the diverseness between different reports addressing the same issue as well as regional differences and the appearance of long and complex reports.

5.1 Results

The country councils from where the reports have their origin are hereon called site A, site B and site C. All the line breaks were removed in the anonymization process and therefore the structure in all reports are assumed.
5.1. RESULTS

5.1.1 Long and complex reports

Figure 5.1 is a report on a lumpectomy for breast cancer. In general, this type of report is voluminous, containing many parameters to be assessed and included in the clinical review.

The micro part of the report consists of a list of assessed parameters and their results. The descriptive text about findings and the final diagnosis based on the other two parts of the report are the second and third parts, respectively.

The report is divided into three parts: one part with the total of 25 assessed parameters, another part with descriptive text regarding the histological diagnosis, and the last part where the assessed parameters are summarized to a diagnosis.

Figure 5.1: A voluminous report from a breast cancer lumpectomy that is divided into three parts. One part is the micro part that consists of a list of assessed parameters and its results, the second part is descriptive text about the histological diagnosis, and the third part is the final diagnosis based on the other two parts of the report.
5.1.2 The structure of prostate reports

The reports for prostate cancer were sorted in three categories; descriptive reports, semistructured reports and structured reports. The distribution of the reports (Figure 5.2) shows that two thirds create reports with some kind of structure and approximately half of these create their report with a fully structured format, whereas the other half uses a semistructured format. One third is using only descriptive reporting with no structure. Examples of the three categories of reports can be seen in Figure 5.3, Figure 5.4 and Figure 5.5.

![Distribution of prostate reports](image)

Figure 5.2: The distribution of pathology reports. Descriptive reports corresponds to 30%, semistructured reports to 34% and structured reports to 36%.

The report, presented in Figure 5.3, originates from site A and is from a prostate biopsy performed with a hollow-core needle. The report is descriptive and consists of only free text with no obvious structure.
A summary of the findings in the biopsies containing cancer

Figure 5.3: A descriptive report from a prostate biopsy performed with a hollow core needle. The number of fractions is summarized in the beginning, the length of the biopsies are inserted in the middle of a sentence and the cancerous findings and its extent and Gleason score are described in three sentences. The findings are summarized in a separate diagnosis in the end.

The report, presented in Figure 5.4, originates from another site, site B, but is from the same type of procedure as the first report. It is a semistructured report that still contains descriptive text when presenting the findings of each biopsy.
### 1-7 Mellannålsbiopsier prostata.

| 1 | Sparsamt fragmenterat material. Fett- och bindväv samt muskulatur. Ingen glandulär vävnad. Inga tumörstrukturer. |
| 2 | Fragmenterat material med innehåll som i fraktion 1. |
| 3 | 11 mm lång biopsi med centralt 2 mm stort cancerfocus. Perineural växt. |
| 4 | 15 mm lång biopsi. Centralt cancer i 5 mm. |
| 5 | 5 mm lång biopsi med kapselvävnad. Inga glandulära strukturer. Inga tumörvegetationer. |
| 6 | 15 mm lång biopsi. Cancer inom 11 mm. Ett par mm till tuschad ände. |
| 7 | 15 mm lång biopsi. Cancer i drygt 12 mm. 1 mm till tuschad ände. Material är delvis lite klämt men bedömer Gleason score till 4+3=7. |

PAD 1-7 Sju mellannålsbiopsier från prostata: Adenocarcinom 4+3=7 med utbredning enligt ovan.

**A merged Gleason score for every finding of cancer in the biopsies.**

**The summary of the findings in a final diagnosis.**

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**Figure 5.4**: A semistructured report from a prostate biopsy performed with a hollow core needle. The report is divided in a title describing what type of specimen it is and thereafter each biopsy is described on separate rows with descriptive text. The Gleason score for each cancer findings are merged to a common result and presented in a separate sentence. The final diagnosis is presented last in the report.

The report, presented in Figure 5.5, is also from site B and is also from a prostate biopsy performed with a hollow-core needle. It is a structured report and contains no descriptive text other than the final diagnosis.
5.1. RESULTS

All fractions listed in numerical order
The length of all biopsies/fraction
The number of biopsies/fraction
The extent of cancer in the biopsies
The summary of the findings in a final diagnosis
Slutdiagnos prostatacancer Gleason score 7 (3+4). Anmäl till tumörregistret

Preparat nr 1: 2 biopsier. Längd 18+16 mm. Cancer 0 mm.
Preparat nr 2: 2 biopsier. Längd 13+18 mm. Cancer 0 mm.
Preparat nr 3: 2 biopsier. Längd 13+17 mm. Cancer 0 mm.
Preparat nr 4: 2 biopsier. Längd 19+18 mm. Cancer 0 mm.
Preparat nr 5: 2 biopsier. Längd 16+16 mm. Cancer 2+1,5 mm. Gleason 3+4
Preparat nr 6: 2 biopsier. Längd 20+18 mm. Cancer 6+8 mm. Gleason 3+4

Figure 5.5: A structured report from a prostate biopsy performed with a hollow-core needle. The report is written with one line for each fraction. Each line is starting with the fraction number followed by the number of biopsies in the fraction. After this, the length of the biopsies and the extent of cancer are written. If there is cancer in the biopsy, the Gleason score is reported last in each line.

All three reports are formatted in different ways and it indicates that different sites formats reports differently, but at the same time it does not exclude the possibility that different pathologists at the same site chose to write reports differently. This can be seen in report two and three, that are from the same site but written/dictated by different pathologists. Irrespective of the reasons, the reports tend to have different format even though the examination type is the same and the diagnosis is very similar. One thing they have in common though, is the use of multiple measurements.

Out of ten reports with the same type of procedure and similar diagnosis, three were semistructured, six were descriptive and only one was structured.
Chapter 6

Design and implementation

The prototype was implemented in Sectra’s viewer for pathology images, seen in Figure 6.1, and involved only client side programming using JavaScript and the JavaScript libraries Knockout and Durandal. JavaScript and the Javascript libraries were chosen since the viewer is implemented with these languages. The prototype makes use of already built in functions for distance measurements and bookmarks.

Figure 6.1: Sectra’s viewer for pathology images. The viewer has a bar in the bottom for displaying all the slides and a small window in the upper left corner to facilitate the users navigation. A measurement annotation is also added in this image, seen as a green line in the middle of the image. The measurement is manually added by a user and is displayed together with its length.
6.1 The breast cancer template

The implementation of the template for invasive breast cancer was divided in five major categories that consist of all parameters necessary for reporting and are described in the subsections. All parameters were chosen from and influenced by private templates from a pathologist at Linköping University Hospital, as well as proposals of standardized templates from the quality and standardization committee in the Swedish Association of Pathology. A complete list of all parameters can be seen in Appendix A and the template is shown in Figure 6.2 with the placement in the viewer in Figure 6.3.

![Figure 6.2: The template with the parameters for the assessment of invasive breast cancer.](image-url)
6.1.1 Single feature parameters

The parameters histological tumor type and the number of cancers were both implemented with a title and subsequent text field. The feature is the clickable title that automatically puts the marker in the subsequent text field.

Vascular invasion was implemented as two radiobuttons with the feature that the options "yes" or "no" can be chosen by the user.

6.1.2 Measurements

A major part of the measurements was the categorization of the measurement values. The user manually creates measurements and afterwards it can be added to a parameter in the report. The measurement is added by clicking a button, as in Figure 6.4. It is the user that decides where the measurement is added by clicking a specific button, and this is the initial step in the categorization of the value. The value is then displayed in the report in different categories (Figure 6.5), dependent on the user’s decision. The four parameters; largest invasive focus, extent of all malign structures, minimum margin of the invasive cancer component and the minimum margin for the in situ cancer component are all dependent on measurements and are all following this principle (Figure 6.6).
Figure 6.4: The different colored buttons appear when the user has created a measurement for any of the parameters for minimum margin. The user manually categorizes the measurements by clicking the different buttons. The measurement will be listed in a table that corresponds to the clicked color and chosen parameter.

Figure 6.5: The report where the measurements are listed. The measurements are sorted in tables under the parameter the user has chosen to import it to. The user’s navigation in the report is facilitated by the gray area that shows the user its current position in the report.
Figure 6.6: The principle of adding a measurement to the report. The user creates a measurement in step 1, and chooses where to add it in step 2. Based on the user’s choice, the measurement is automatically categorized in the report in step 3.

All values of the measurements are shown in a table as clickable links that redirect the user to the corresponding measurement annotation in the viewer. The user is able to select the measurement wanted for the final report by marking it in the table. The selected value is highlighted and the rest of the values in the table are grayed out (Figure 6.7).

Figure 6.7: If a user selects a value for the final report, the value is highlighted and the rest of the values in the table are grayed out.

The values populating the tables are dependent on the communication with the server. Every time the user adds a measurement it is possible to add exactly that measurement to the report by clicking a button, as in Figure 6.6. If the user updates or removes a measurement annotation that is present in a table, the value will be updated/removed.

6.1.3 Nottingham Histological Grading

The three parameters tubule; formation, nuclear pleomorphism and mitotic count are automatically summarized and displayed beside the title for NHG in the prototype, provided that the values are set between 1-3 by the user (Figure 6.8). If a value is not set between 1-3, the text field will become red to give the user an indication that the input is incorrect. The inputted
values correspond to a NHG grade which is displayed beside the summation of the individual parameters. The summation and grade are updated simultaneously with value changes.

Besides the summation, the parameters for tubule formation, nuclear pleomorphism and mitotic count was implemented in the same way as a single feature parameter. Mitotic count though, has an additional feature for keeping track of the number of mitoses counted. The user can use the plus and minus sign on the keyboard to add or subtract mitoses to the total count. The total count is continuously transformed to its corresponding NHG grade and the grade is displayed in the text field for mitotic count.

![Diagram showing the assessment of NHG parameters](image)

Figure 6.8: The three parameters of NHG and the summation of them displayed as an integer and its corresponding NHG grade. The aid for keeping track of the mitotic count is displayed as the number of mitoses per 10 high power fields (HPF).

### 6.1.4 Receptors and Ki67

The titles of the estrogen receptor, progesterone receptor, HER2 and Ki67 are all links (Figure 6.9). The user gets redirected to the slide with the correct staining for the assessment if the link is clicked.
The implementation of Ki67 has an additional feature for automatic indexing of the status using cell detection. The algorithm is under development and is not a part of this thesis, but was used as an aid for automatic population of the Ki67 value in the report. The user chooses the tool for cell counting, surrounds the area of interest and then the algorithm calculates the percentage of positive cells. The value is automatically inserted in the report and if the user performs several measurements, the highest percentage is displayed.

6.1.5 Additional features

Other functionality, to facilitate the usage of the template, was implemented as well. A two dimensional measurement type was derived from two ordinary distance measurements. If two distance measurements are crossing each other when the user lets the mouse up, the two distance measurements are converted to a two dimensional measurement that will act as a group (Figure 6.10).
A feature to add descriptive text to a parameter was implemented. If the user double clicks on the title to a parameter, a text area appears under the title (Figure 6.11). The user can enter the desired information and thereafter leave the text area. The area is then collapsed and is accessible again by clicking a link under the corresponding parameter title (Figure 6.12).
6.2 The prostate cancer template

The template for assessment of prostate cancer (Figure 6.13), when performing a biopsy with a hollow-core needle, was implemented in a table structure with the following parameters:

- the length of the biopsies in mm
- the extent of cancer in mm
- Gleason score

In addition, a column for comments about extraprostatic extension, perineural or vascular invasion and histological tumor type was added. The parameters were chosen based on the results in the analysis of old pathology reports and proposals of standardized templates from the quality and standardization committee in the Swedish Association of Pathology.
Chapter 7

User study

A user study was run with the main objective to determine the differences between using the prototype and using only paper and pen while reviewing a case. Each participant performed two diagnostic sessions on two different breast cancer cases with the prototype as an aid in one case and only paper and pen as an aid in the other. The order of the aid used and cases was counterbalanced.

7.1 Experimental task

The experimental task was performed on a laptop with an attached external screen, keyboard, mouse and the prototype with the template for invasive breast cancer. The participants were given two different cases of breast cancer, one complex and one simpler, that they were supposed to diagnose answering the following parameters; histological tumor type, largest invasive focus, the size of all malign structures in the specimen, the minimum margin of the invasive cancer components, the minimum margin of the in situ cancer components, the number of cancers in the specimen, the grade of tubule formation for NHG, the grade of nuclear pleomorphism for NHG, the grade of mitoses for NHG, estrogen receptor status, progesterone receptor status, HER2 status and Ki67 index. After the participants completed the review a semistructured interview was held, lasting around 20 minutes.

The parameter for vascular invasion was intentionally omitted since the assessment of it is time consuming and is just a simple radiobutton in the report with no further features. HER2 ISH was omitted as well since the specific case did not include a specimen for this assessment.
7.2 Participants

Two pathologists from different regions in Sweden, participated in the experiment. One resident pathologist with experience of assessing breast cancer, and the other, a breast cancer specialist with five years of experience. The participants work in two different regions in Sweden.

7.3 Procedure

Before the experiment, the participant was given a one-to-one training on how to use the prototype with the template for invasive breast cancer. The participant was guided through the prototype’s functionalities, and was then allowed to try it out themselves and ask questions. The training lasted in an average of 15 minutes until the user felt comfortable using the prototype.

While the participants were undertaking the experimental tasks, a webcam and a software for screencapture were recording the session. A mobile device for sound recording was used as well.

7.4 Analysis

The evaluation of the user study was divided in two main areas; workflow and clinical practice. Workflow includes changes in the diagnostic workflow, memory management and disturbances, while clinical practice includes patient safety and applicability.

The material recorded from the user study was analyzed based on activities. The user’s actions were divided in activities associated to the parameters in the template. Each time the user performed something associated with a parameter, the time duration was noted and later on transformed to the percentage of the total time of the diagnosis session.

The material was also evaluated using Norman’s [36] definitions on slips and mistakes. Every time the user did a slip or a mistake, it was registered. A slip was counted every time a user was meaning to perform one action but accidentally performed another unintended action, and a mistake was counted every time the user performed the planned action but the action itself was incorrect regarding to the wanted outcome.

7.5 Results

The participant pathologists are hereon called P1 and P2.

7.5.1 Changes in the diagnostic workflow

An analysis based on activities shows a difference in the diagnostic workflow when P1 uses the prototype. The analysis indicates that P1 is alternating
between different parameters throughout the session when using the prototype while working with one parameter at a time without the prototype. Figure 7.1 shows P1’s distribution of activities during both diagnosis sessions during the user study.
Figure 7.1: The activity analysis of pathologist P1 during the diagnosis session with the prototype (upper) and the diagnosis session without the prototype (lower). With the prototype the user choses to work with one parameter at multiple times and alternating with other parameters during the session. Without the prototype, the user choses to work with one parameter at a time and the work progresses without altering which parameter to assess. The white spaces correspond to activities not belonging specifically to any parameter and can for instance be the user trying to get an overview of the specimen.
P1 realizes that the prototype enables the ability of parallel assessment of parameters, in comparison with P1’s normal workflow where the assessment is much more reliant on what can be kept in the mind. The risk of being interrupted or disturbed, while keeping data stored in the mind, makes the diagnosis process more static and systematic. P1 means that the prototype creates a more structured format that reduces the things needed to be remembered to fulfill the assessment of a parameter.

P2 on the other hand does not change the diagnostic workflow. P2 still uses a systematic approach when assessing parameters with the prototype as aid. P2’s activities can be seen in figure 7.3. A big difference between P1 and P2 though, is that P1 did three measurements when assessing the largest invasive focus, while P2 did only one measurement. The same goes for the assessment of minimum margin for the invasive component, where P1 did three measurements while P2 did only one. P2 meant that the invasive cancer component was only extended on one slide and therefore did not have to do multiple measurements, while P1 meant that the component was extended over several slides. P1 also did a measurement on the invasive cancer component on the estrogen receptor slide as a control, resulting in a larger total amount of measurements.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>P1</th>
<th>P2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimum margin invasive</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Extent of all malign structures</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Largest invasive focus</td>
<td>3</td>
<td>1</td>
</tr>
</tbody>
</table>

Figure 7.2: A comparison of P1 and P2’s measurements while using the prototype. P1 conducted in total seven measurements while P2 conducted three.
Figure 7.3: The activity analysis of pathologist P2 during the diagnosis session with the prototype (upper) and the diagnosis session without the prototype (lower). The two diagnosis sessions have no distinct differences and the user choses to work with one parameter at a time in both with and without the prototype. The white spaces correspond to activities not belonging specifically to any parameter and can for instance be the user trying to get an overview of the specimen.
CHAPTER 7. USER STUDY

P2 does not think that the prototype will change the diagnostic workflow, but thinks that the prototype will save time in P2’s overall workflow. Especially in bigger cases where there are a lot of measurements and other parameters to assess.

7.5.2 Memory management

P1 experiences that the prototype eases the burden of the short term memory, in other words, the things needed to be kept in the mind. P1 also states that it is easy to overview the values in the prototype and revisit measurements done during the diagnosis session. The functionality to revisit measurements excludes the need of choosing the desired value on one slide and then compare it with new values on the next slide, and possible reprioritize which value to chose in the report. P1 also means that the functionality also makes it possible to get a simultaneous overview of all measurement values which excludes the need of putting the slides with measurements side by side for comparison.

P1 used a separate paper to take notes once during the diagnosis session with the prototype. The notes were a helper to remember on which slides there were interesting findings and which slides to not include in further assessment of the parameters due to no cancer findings. P1 has a wish that this could be done using the prototype and exclude the need of taking separate notes to remember what slides to use in the assessment.

P2 can see the use of this prototype when assessing cases where a lot of measurements and different parameters are required. The prototype will create a structure that will decrease the time spent on organizing parameters and values, that otherwise is necessary to be able to overview and chose what value to use in the report.

7.5.3 Disturbances

Both P1 and P2 made some slips during the diagnosis session with the prototype. P1 also did a mistake when opening the prototype, wanting to add an measurement, while assessing with only paper and pen as aid. P1’s slips were:

- added the minimum margin of the invasive component to the largest invasive focus
- added the same measurement two times
- added another measurement to the wrong parameter
- started using the hotkey for mitotic count while having the marker in an input field
- used the hotkey for stepping through a slide while having the marker in an input field
P2’s slips were:

- started using the hotkey for mitotic count while having the marker in an input field
- did not control the value of Ki67 in the prototype after manually altering the cell count in the algorithm for assessing Ki67 (manual update is required here)

Both P1 and P2 did the slip trying to use hotkeys while having the marker in an input field. P1 finds this disturbing and thinks it is a bit tricky to work around this.

P1 and P2 are both missing functionality for separating measurements and other parameters if the case has multiple tumors. P1 would like to have the possibility to separate and report measurements, NHG grading and receptor status on each tumor. P2 is simply stating that it would be desirable to be able to report different tumors in the same case separately.

### 7.5.4 Patient safety

Both P1 and P2 cannot see any risk for the patient when using the prototype. P2 thinks this may improve the patient safety since the values are stored and displayed in the prototype, decreasing the risk for mixing numbers up. P2 is also a bit thoughtful about the algorithm for assessing the Ki67 value since the algorithm gave a different value than the assessment P2 did. P2 thinks there should be some further evaluation before the algorithm is taken into clinical practice. P1, on the other hand, thinks that the ki67 algorithm does not introduce any patient risk, since the assessment of the value is not that exact in practice, due to P1.

### 7.5.5 Applicability

P1 and P2 are both positive of having an aid like the prototype while assessing a case. They also think that the prototype is applicable in more areas than just breast cancer.
Chapter 8

Discussion

8.1 Pathology reports

The voluminous report in Figure 5.1 has 25 parameters that have been assessed. It is a large amount of parameters, and some parameters such as measurements can be done multiple times over multiple slides. Therefore, there is a lot of information to be categorized and processed by the pathologist. Some sort of tool is necessary to be able to do this. Today that tool can be ordinary paper and a pen which not necessarily creates a structure that helps the pathologist to categorize and process. The introduction of a tool, such as the prototype, categorizes and displays data automatically and could be helpful. As P1 said, the prototype creates a structure with more ordered values that are easier to access and process than in P1’s normal workflow. P2 had a similar opinion and could see the advantages of using an aid like the prototype when assessing long cases, such as the one assessed in the report in Figure 5.1.

The shorter reports on prostate biopsies performed with a hollow-core needle in Figure 5.3, 5.4 and 5.5 are good examples how reports concerning the same procedure and similar diagnosis can have different appearance. The differences in the pathology reports indicate that some kind of standardization can be of use for different reasons. One reason is that it could facilitate the mandatory reporting to the INCA register, since data is easily extracted when using the prototype, leading to the possibility of a semi-automatic process for reporting to INCA. Another reason could be the facilitation of keeping statistics when each parameter is being more structured and standardized. This means that the data is more easy to access and put together in the wanted fashion, for example the distribution of a parameter at a specific site. P1 thought that there is profit in the possibility of a more uniform way of reporting in the pathologist’s workflow, since it is easy for the pathologists to diverge in different ways of reporting otherwise. The prototype would exclude the diversion and create a more universal understanding
when reading pathology reports.

8.2 Workflow

8.2.1 Changes in the diagnostic workflow

In P1’s case it was pretty obvious that the prototype changed the diagnostic workflow and allowed assessment of multiple parameters at the same time. P1 also seemed to find a confidence in the prototype to ease the burden on the short term memory allowing P1 to work less strict and not having to worry about being interrupted during the diagnosis session. P1 felt that the prototype is organizing and storing the data and makes it easy to access and process during the session. There is a possible drawback though, with the opportunity of simultaneous assessment of multiple parameters. The attention might be too divided between different parameters and affecting the diagnostic workflow in a manner that slows down the whole diagnostic process, that usually is pretty static and systematic without the prototype. This is hard to say something about today when a more extensive investigation will have to be done to determine if the prototype is slowing down the workflow. However, both P1 and P2, had the opinion that the prototype will save time in their overall workflow. P1 with the opinion that the static and systematic workflow without the prototype is slower and P2 with the opinion that there is time to gain, especially in long cases. If there is no obvious increase in time while using the prototype, or at least no increase that disturbs the pathologist, this is not going to be a problem.

In P2’s case, it was no indication of a change in the workflow, but in this case it is necessary to note that P2 did not do multiple measurements over multiple slides. If P2 had felt the need of doing multiple measurements over multiple slides, the result may have been different. P2 felt that the prototype did not change the diagnostic workflow and did not think that it would do it in other cases either. Worth mentioning, is that P1 did not think that the diagnostic workflow had changed at first either, until P1 was asked to actively compare the workflow when using and not using the prototype. Regardless if the diagnostic workflow is changed or not, both P1 and P2 think that the prototype is useful and would like to use it as an aid to facilitate their everyday work.

8.2.2 Memory management

The burden of the short term memory seems to be decreased, since the prototype’s functionality of categorize and display the data requires less effort than if the pathologist was going to do this manually. The pathologist no longer has to make decisions how to store and display data to get an overview that is suitable to make a relevant decision on what values to use in the report. The process of remembering values by creating a structured
format is now handled by the prototype. When this is handled by the prototype it also allows the pathologist to let values go temporarily and then easily access the value again by refreshing the memory of the performed activity, for example using the links to revisit a measurement. Consider this in contrast to values that are written down on a paper which becomes just characters without linkage to an activity previous performed. The memories are more easily accessed with the prototype, and thus the pathologist does not have to be able to store as much information in their short term memory that otherwise is necessary without the prototype.

The easiness of refreshing the memory of a value creates an opportunity to do simultaneous assessment of several parameters. This could be positive for the assessment, letting the pathologist evaluate and save important information at the same time it is discovered, and still keep a structured format of the information. The confidence gained by knowing that the prototype is remembering the information might do that the pathologist is more open to findings other than the one parameter meant to be assessed at the time, leading to findings that otherwise may be forgotten or even unnoticed.

8.2.3 Disturbances

The disturbances while using the prototype are mainly directed to two areas; the measurements and the fact that the prototype is based on text field preventing hotkeys to work while inside a field. The functionality that makes the measurement values populate the report is dependent on the communication with the server. This is not a sustainable way of doing it, since the only time it is possible to add a measurement is right after it is created and the only way you can remove the measurement value from the report is if you delete the corresponding annotation. There are scenarios where it is desirable for the pathologist to mark an earlier created annotation and add it to the report. This action is not possible today. In the same way, the pathologist should be able to mark a value in the report and remove it. This comes in handy when a value is reported under the wrong parameter, but the annotation is still to be used for a different parameter. The adding of measurements should be dependent on which annotation is active, i.e. marked by the pathologist, and the removal of values from the report should be dependent on the interaction with the value in the table.

The fact that the prototype is based on text field creates a bit of trouble since all functionality of hotkeys is lost while inside a text field. How this problem should be solved is a bit tricky, since the functionality of inputting text in a text field cannot be excluded from the prototype. However, the use of ordinary text field should be limited to parameters where a more descriptive answer is needed, such as histological tumor type. Some parameters that today are based on input fields, for example nuclear pleomorphism, would preferably be based on user orientation and hotkeys. In other words, if the user has chosen the parameter nuclear pleomorphism (orientation), certain
hotkeys are coupled to populate the parameter instead of the ordinary use of an input field. The user’s experience will be that the inputting works just as any ordinary input field, but all other hotkeys will still be working. The limitation of this is that it will only be applicable on parameters with simple and standardized answers, such as 0, 1, 2 or 3 in the assessment of HER2 status or the parameters of Nottingham Histological Grading. How to solve this problem fully, has to be considered.

8.3 Clinical practice

8.3.1 Patient safety

In general, both P1 and P2 did not think that the prototype would introduce some kind of patient risk. Their opinion is rather that there is an increase in patient safety since there is less risk of mixing numbers up. Both P1 and P2 thought that it is easy to get an overview of the values, and therefore it is easy for the pathologist to control that the values are reasonable. Even though reports are proof read today before distribution, it can be a good thing to be able to easily control the values while still having the case fresh in mind, instead of refreshing the memory of the case when the report returns from a medical secretary.

The variations in format of reports seen in Figure 5.3, 5.4 and 5.5 can make it harder for the referring physician to sort out useful data important for future treatment of the patient. By introducing a more structured format with the prototype, the universal understanding for the report is increased. This leaves less for the referring physician to interpret due to a diversity in the pathologist’s way of reporting.

8.3.2 Applicability

P1 and P2 were both positive to use an aid like the prototype to facilitate their everyday work. Since both P1 and P2 were positive to an introduction of an aid like this, a discussion of how this could be done is held in the next chapter.
Chapter 9

Conclusions

The results indicates that a template based structure for structured reporting is an aid that facilitates the pathologists diagnostic workflow. If a template based structure were to use in clinical practice it would require that every type of cancer assessment got its own template. Each template would then be well adjusted to every type of assessment and would be an aid for the pathologist.

With the positive results, it would be an appealing feature to integrate in Sectra’s viewer for pathology images. The way the prototype works today, with template based structure, might not be a sustainable method to use since there would be tremendous work to implement all templates for all kinds of different cancers that pathologists assess. The functionality that would be appealing though in all types of assessment, is to be able to categorize, order, and display the important data. For example, the way measurements are categorized and displayed is a functionality that could be generalized and used in many more areas than just breast cancer.

My suggestion, if this were to be implemented in Sectra’s viewer for pathology images, is that the template based approach is rejected and a more general approach with three major groups is applied. The three groups are; measurements, categorization and counting aids. With these three groups it would be possible for the pathologists to configure a suitable template that would facilitate their workflow.

9.1 Measurements

Measurements are conducted in several areas in the cancer assessment done by pathologists and if an aid for measurements were introduced it would be useful for most pathologists. The measurements should:

- be stored in a ordered fashion under a chosen parameter (if they are added to the report)
9.2. CATEGORIZATION

Measurements are the only parameters that make use of categorization today. The user has to categorize measurements when adding them to the report and other parameters could make use of this functionality as well. There are two kinds of categorization; value categorization and parameter categorization. Measurements are dependent on value categorization, where the values of each measurement is categorized and displayed under a certain parameter (Figure 9.1). Parameter categorization is basically when an assessment of a parameter has to be done multiple times but be distinguished from each other. Multiple tumors in a diagnosis session is an example of this. The user has to categorize the parameters with respect to the tumors since the tumors are assessed individually. Figure 9.2 shows an example where the NHG value is to be assessed in two tumors. The displaying follows the same principle as value categorization seen in Figure 9.1.

![Figure 9.1: Categorization based on values. The values of a parameter are categorized and displayed under that certain parameter.](image)

- be clickable links in the report in order to allow the user to revisit the corresponding measurement
- be removable from the report without removing the corresponding annotation
- be updated when the corresponding annotation is updated
- be selectable in the report to highlight which value the user has chosen to the final report

This is very similar to the functionalities of the measurements implemented in the prototype.
CHAPTER 9. CONCLUSIONS

9.3 Counting aids

Some activities during assessment are dependent on the pathologist counting some factor, for example mitoses. The process of counting can be divided over multiple slides or multiple fields of vision and an aid would be helpful to keep count. The count would preferably be coupled to hotkeys, as the plus and minus key coupled to the mitotic count today. The current count also has to be displayed in the report, i.e. as in Figure 9.3.

Figure 9.3: The current mitotic count is displayed to the right and is updated when the plus or minus key is used.
Bibliography


Appendices
Appendix A

Template parameters for invasive breast cancer

A full list of parameters used in the template for invasive breast cancer.

- histological tumor type
- vascular invasion
- largest invasive focus
- extent of all malign structures
- minimum margin of the invasive cancer component
- minimum margin for the in situ cancer component
- tubule formation
- nuclear pleomorphism
- mitotic count
- estrogen receptor status
- progesterone receptor status
- HER2 status
- Ki67 status
På svenska

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