An architectural concept for implementing the socio-technical workflow of Digital Pathology in Chile

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STATUTORY DECLARATION

I, Stefan Sigle, ensure hereby, that i developed and written my thesis on the topic

> *An architectural concept for implementing the socio-technical workflow of Digital Pathology in Chile*

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Heilbronn, November 27, 2014

STEFAN SIGLE

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Abstract

Virtual Microscopy opens up the possibility to remotely access high quality images at large scales for scientific research, education, and clinical application. For clinical diagnostics, Digital Pathology (DP) presents a novel opportunity to reduce variability [Bauer et al., 2013] due to the reproducible access to Whole Slide Imaging, quantitative parameters (e.g. HER2 stained membrane) [Al-Janabi et al., 2012], second opinion and Quality Assurance [Ho et al., 2013]. Despite of the mentioned advantages, the challenge remains to incorporate DP into the pathologists workflow within a heterogeneous environment of systems and infrastructures [Stathonikos et al., 2013]. Different issues must be solved in order to optimize the impact of DP in the daily clinical practice [Daniel et al., 2012] [Ho et al., 2006]. The integration needs precise planning and comprehensive evaluation for adopting this technology [Stathonikos et al., 2013]. This thesis will focus on an organizational development approach based on a Socio-Technical System (STS). The socio-technical approach covers: (i) the technical issue: tissue-scanner, NDP.view, NDP.serve, analysis software, and (ii) the social issue: pathologists, technicians. In order to improve the integration, a joint optimization (of i and ii) is necessary. The developed STS approach will optimize the integration of DP towards improved workflows in clinical environments. The improved workflows will reduce the pathologists turnaround time, improve the certainty of the diagnostics, and provide a more effective patient care within the covered institutions. An overt multi-site Participatory Observation, Questionnaires, and Business Process Modelling Notation will be used to analyse the existing pathological workflows. Based on this, the system will be modelled with the 3lgm2-Toolkit [Winter et al., 2007] under consideration of various technical subsystems that are present in the clinical environment. Afterwards, the interfaces between subsystems and its possible interoperabilities will be evaluated, taking into account the different existing standards and guidelines for image processing and management, as well as business processes in DP. In order to analyse the existing preconditions a questionnaire will be evaluated to establish a robust and valid view. In addition, the overt participatory observation will support this elevation, giving a deeper insight on the social part. This observation also covers the technical side including the whole pathological process. The socio technical model will then reveal measurable potential for optimization with incorporated DP (e.g. higher throughput for slides).

The organizational development approach consists of a Socio-Technical System based on overt multi-site participatory observations, questionnaires, business process modelling and 3LGM2, will optimize the use of Digital Pathology in the daily

clinical practice and raise the acceptance to incorporate integrate the new technology within the dayly workflow through the user centred process of incorporation.

- *Perform and evaluate a questionnaire and a participant observation of pathologists work days in private & public institutions*
- *Create and evaluate a 3lgm2 model*
- *Model the current pathological process (viewpoint of pathologist & technical assistant) & perform and evaluate a contextual inquiry to elevate the pathologists requirements & expectations towards the system*
- *Test the future WF according the model parameters*

This project will detect unsuspected interrelations and interdependencies within the socio- technical workflow with a pathology laboratory. The observation will reveal the action conformity as well as the environment in which the process has to be embedded. Furthermore it will establish an optimized workflow for a specific clinical environment to prepare the implementation of DP. Additionally it will be possible to quantify digitized images in order to improve decision making and lastly to improve patient care. In the future it will be possible to extend automated image analysis in order to support clinical decision support. Depending on acceptance, this can lead towards an automated clinical decision support for cases with low complexity.

Contents

Glossary

3LGM^2 .... 3-Layer Graph Meta Model
AP .... Anatomic Pathology
APIS .... Anatomic Pathology Information Systems
BPM .... Business Process Modelling
BPMN .... Business Process Modelling and Notation
CI .... Contextual Inquiry
CLC .... Clinica Las Condes
CSF .... Critical Success Factor
DICOM .... Digital Imaging and Communications in Medicine
DIHIT .... Diagnostic Intelligence and Health Information Technology
DP .... Digital Pathology
HCI .... Human Computer Interaction
HL7 .... Health Level 7
IHE .... Integrating Healthcare Enterprise
ISO .... International Organization for Standardization
KPI .... Key Performance Indicator
LIS .... Laboratory Information System
LMS .... Laboratory Management System
MITA .... Medical Imaging and Technology Alliance
MPPS .... Modalities Performance Procedure Setup
MWL .... Modalities wordlist
PACS .... Picture Archiving and Communication System
PMS .... Patient Management System
PO .... Participatory Observation
QMS .... Quality Management System
SNOMED CT .... Systematized NOmenclature of MEDicine Clinical Terms
STS .... Socio Technical System
UML .... Unified Modelling Language
WSI .... Whole Slide Imaging

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1. Introduction

1.1. Motivation

Since the early 2000s the term telemedicine is continually growing and offering more and more options to provide medical advice and treatment to remote areas without causing long travels of qualified personnel. Innovations like virtual microscopy are offering solutions in the area of Pathology. But the transition from classic- to virtual microscopy is afflicted with many challenges.
Though there are many successful transition-stories in a similar field of telemedicine: teleradiology, where radiologic (image) material is sent via telecommunication to a remote place, there are no such overarching solutions to pathology. A new dimension adds up to the challenge as soon as the scope is set to emerging economies. This thesis focusses, as the title suggests, on the introduction of Digital Pathology (DP) in South America, more precise Chile. The challenge lies within the geographic structure of the country: from north to south the country is measuring more than 4000km offering everything from the lonely desert to the urban jungle in the capital. The total population of Chile consists of 16,3 million inhabitants, from which 6,5 million are living in the capital city Santiago[1]. Through the high degree of centralization on the capital the medical care supply is impaired in remote areas. The most severe impairments are experienced due to a lack of infrastructure, equipment and expertise. These problems affect the availability and accuracy of pathological diagnosis. In order to minimize and eventually overcome these problems the SCIAN-Laboratory[2] has acquired a next generation slide scanner[3]. This device will provide reproducible access to high quality images of organic tissue samples without the exposition to natural decomposition due to the preparation process of the laboratory technicians.

The introduction of this technology is controversial all over the world and though some nations e.g. Canada or Denmark are, or are close to use DP in the medical routine, other countries are hesitating to use this technology for various reasons, one of them being acceptance. But reasons are more manifold than this, and even

[1] see http://www.auswaertiges-amt.de/DE/Aussenpolitik/Laender/Laenderinfos/01-Nodes_Uebersichtsseiten/Chile_node.html, accessed on 18.10.2014
[2] see http://scian.cl/portal/globals.php?COD_SECCION=2988, accessed on 18.10.2014
[3] Hamamatsu NanoZoomer XR

though there are some convincing benefits lying in inter institutional second opinion and education, success of the implementation also depends heavily on the given preconditions of the health system in a specific country. In Chile the health-care landscape is offering not the best preconditions. 74% of the population are covered by public health institutions, around 17% are privately ensured and 9% are taken care of by other semi private institutions like the army[4].

The CPDAI FONDEF project aims for a stepwise introduction of a slide scanner, a new piece of technology and all of its benefits like the reduction of inter- and intraobserver variation to all Chilean health care providers. In order to provide a full DP solution several points have to be considered.

1.2. Objectives

As mentioned in chapter 1.1 it requires precise planning and a steady evaluation of the conducted steps. Therefore a multi sided approach has been chosen to achieve the primary goals of this project. The aim of this thesis is to present a detailed architectural concept of the implementation under consideration of the critical success factors and the key performance indicators involved in this project. Since this project is residing interdisciplinary an appropriate approach, the so called "socio technical system" approach has been followed. The components of this approach will be explained in more detail later on. *The thesis will answer the hypothesis if this organizational development approach based on multi sided participant observations, questionnaires and modelling will optimize the use of Digital Pathology and raise acceptance to incorporate the new technology through the user centered process of incorporation.* With the elaborations of this thesis it is possible to get an overview about the existing technical and social preconditions, weighing up risks and chances implementing DP in a specific health institution, being public or private. Additionally the complete process from preparing the tissues up to transporting and re-sending it to the original owner is covered by a business process model (BPM). Based on this model, another consecutive model has been elaborated (3LGM^2) showcasing the preconditions necessary between institutions on a technical level, which is not covered in detail by the business process. The expected acceptance can be identified with the aid of evaluation questionnaires, which is an important factor to the success of a project like this. Additionally critical success factors will be elaborated and addressed to spot project critical details. Lastly the performance and maturity of the processes will be evaluated with the established key performance indicators (KPIs).

[4]see http://web.minsal.cl/, accessed on 18.10.2014

1.3. Structure of the thesis

This thesis is structured in four major points. The fundamentals chapter will give an insight into the external preconditions to understand the methodology justifying the approach. The methodology block covers everything that has been done in the context of this thesis allocated by phase. In order to be able to offer a solution concept a requirement analysis has been done. The result chapter is concentrating on the outcomes of the applied implementation of the methodologies. The final chapter "conclusion" is engaging critically the conducted project together with all used methodologies. In the discussion the work is judged for applicability and interoperability within the scope of the context. The final chapter describes the future opportunities for this project, where it can lead and where are the definite limitations.

2. Background

2.1. Pathology

Pathology describes the doctrine of sufferings in which all the morphological changes that can be observed are examined. It is based on the assumption, first made 1700 by Morgagni, that dysfunctions caused by diseases are correlated with characteristics and morphological changes in organs and tissue [Büttner et al., 2003]. In order to observe these structural changes it was necessary to help the human eye by magnifying the regions of interest. Since the early 20th century the microscope has been the tool of choice as a part of medical research [Kriss & Kriss 1998]. Ever since then the methodology of observing did not change much while new possibilities for the classification of diseases arose.
Pathology can be divided in several specialist fields, such as:

- Autopsy Pathology
- General Pathology
- Cytological Pathology
- Specialized Fields:
  - Neuro-pathology
  - Haemato-pathology
  - Dermato-pathology
- Molecular Pathology

All disciplines, despite the fact that the education is slightly different, share the unified need for microscopically analysis and can thereby be enhanced by the latest IT-developments [Weinstein et al., 2009].

2.2. Telemedicine

Telemedicine first came up around 1990 and is described accurately as a method by which patients can be examined, investigated, monitored, and treated, with the patient and the doctor being located at different places [Kumar & Dunn 2009]. Shortage of resources, is a growing topic in today's society and has to be considered. Additionally mandatory judicial regulations from the correspondent country ensure the best possible practice of telemedicine. This arises a new challenge for standardization institutions. A special relevance is applied when introducing technology to a development country. Naturally, resources are limited and necessary infrastructure is not necessarily provided. Thus the potential benefit is extremely high since the population may not have the possibility to travel to an institution due to long journeys and lack of funding.

2.3. Virtual Microscopy

Virtual microscopy describes the access to histological material via the internet, any time and from anywhere. Hereby the quality is comparable to conventional histology. Earlier microphotography was utilized since there were no broadband internet connections available. These methodology offers, in comparison to Virtual Microscopy, several shortcomings.

Microphotography	**Virtual Microscopy**
• Recording of a picture (extract) • *static* image with a fixed magnification • Image section without reference to the whole image	• Digitalization of the whole object holder • *dynamic* image including zooming functionalities • Simultaneous view of an overview in combination with a detailed view

Table 2.1.: Comparison Microphotography and Virtual Microscopy

As seen in table 2.1 the advantages of Virtual Microscopy are obvious and therefore the current standard in telepathology. Virtual Microscopy is not a synonym for telepathology or digital pathology since it describes only the modality of which images are acquired or presented.

2.4. Whole Slide Imaging

Whole Slide Imaging (WSI) covers two main areas, the creation (caption) and viewing of high quality digital slides [Weinstein et al., 2009] containing tissue samples. These slides are typically captured by a high resolution scanning process [Webster & Dunstan 2014] on a slide scanner. To view the acquired images a specialized viewer software is necessary. The term WSI is not equal to telepathology or digital pathology, since it is neither covering the context of patients nor their diseases. WSI also does not incorporate the topic of automation but in order to provide an efficient resource management this topic cannot be untreated. Vendors came up with the solution of automated WSI, which allows to process several slides in one batch. The processed slides then have to be managed by an image management software in order to be accessible.

2.4.1. Technical aspects

There is a multitude of techniques for acquiring images with a slide scanner. The amount of data produced by this technique varies by the means of the given parameters like magnification or utilized compression. The file size of images can be characterized as large, it can range from gigabytes up to terabytes of data depending the size of the tissue, compression rate and used algorithms. A typical example would be the capturing of a tissue with the size of 20mm x 15mm with a resolution of 40X. As a result the image is 80,000 x 60,000 pixels or 4,8Gp. Adding a standard 24-bit color depth results in a file size of 15GB [DICOM Standards Committee, Working Group 26 2010]. This case considers only one plane of focus (Z-plane) but in practice it becomes more and more relevant to have multiple z-stacks which rapidly increases scan time and storage space up to several terabytes. Scan times per Z-plane are vendor dependent but generally around 30 seconds per plane. To achieve this minimal amount of time and to handle the large amounts of data different procedural approaches are used, e.g.:

- Tiling
- Line Scanning

For *tiling* the slide itself is split into several small tiles of the requested magnification (e.g. 20X / 40X). Concurrent or afterwards the tiles are stitched together to be able to deliver the whole image in the appropriate resolution. A problem is the focus region that is needed to deliver sharp images, here one of two focus strategies is utilized either focusing the camera every tile or every n^{th} tile, which is speeding up the process by impairing quality.

In contrast *Line Scanning* divides the picture into small strips and the camera is going aligned to these strip taking pictures. The favored focusing strategy is a focus map where fixed points on the slide are distributed. The microscope is then focusing only on these areas. This technique is faster but also more error-prone due to variability on the slide induced by tissue treatment.

As described before to access these images a special viewing software is needed which is able to dynamically navigate on the virtual slide. In addition to the context of the DICOM Supplement 145 the committee presented a way how access this kind of image data can be realised which is widely practised by many vendors already.

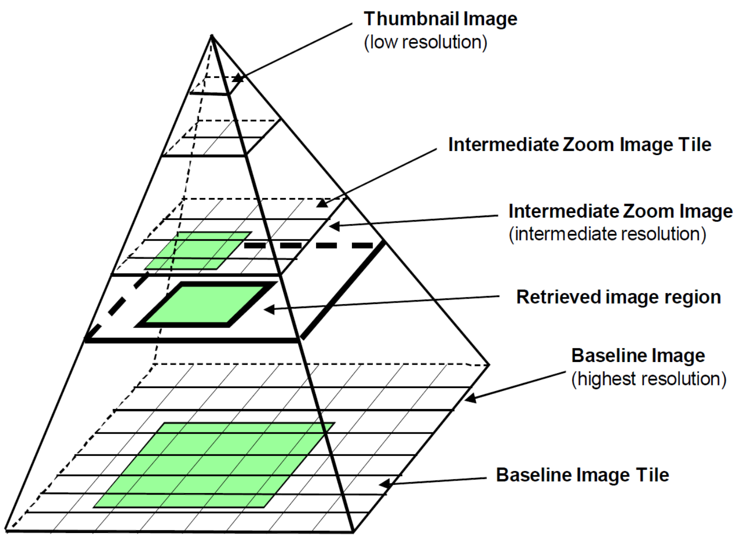

Figure 2.1.: Whole-slide Image as a "Pyramid" of Image Data following [DICOM Standards Committee, Working Group 26 2010]

As shown in figure 2.1, the viewer only receives the specific region of interest in full resolution. Depending on the zoom level, thumbnails are created to save bandwidth. The base image (at highest resolution) is split into smaller tiles. Known impairments of this approach are illustrated as blotted stitching of the tiles, which result in a picture with cognizable borders of the stitching process.

2.4.2. Manufacturers

The selection of manufacturers is broad and rapidly growing nowadays. All scanner manufacturers offer different specifications for their scanners, ranging from relatively cheap scanners with less capacity to scanners that can process up to 400 slides in one batch. Therefore an extensive evaluation of the needs for a specific institution is necessary. According to [Rojo et al., 2006] these are the main competitors on the market:

- Aperio
- Hamamatsu
- Leica
- Nikon
- Olympus
- Zeiss

Vendors are using proprietary file formats, that an exchange between the systems is often not possible.
Open source projects like *Open Slide*[5] are trying to overcome these limitations by providing vendor neutral libraries to access WSI files. Additionally Integrating the Healthcare Enterprise Committee (IHE)[6] is working on a unified (DICOM based) exchange standard which is described in 2.4.4. The advances in this field are comprehensibly necessary to spread acceptance and usability of WSI in daily clinical practice since the heterogeneity between hospitals systems is high.

2.4.3. Software

After acquiring the digital images from the slides further processing is necessary to enable access and tracking of the images. Since vendors are not using the same formats, every vendor has its own image management and viewing software. The requirements to this software reach from a secure access through user management and encryption on the management side on to a fast navigation and easy to use functions in the viewer software such as zooming, scrolling, annotating, rotating and image data export. There may be other specific features which are differing by vendor. The software is often bundled and shipped together with the hardware.

2.4.4. Standardization

Since the choice of WSI suppliers is very versatile a standardization becomes necessary in order to enable inter institutional collaborations. Also the integration in hospitals existing Picture Archiving System (PACS) is important as it already exists in the clinical environment. To address this topic there are several institutions

[5] see http://openslide.org/, accessed on 19.10.2014
[6] see http://www.ihe.net/, accessed on 19.10.2014

that aggregate involved interests. For example the Digital Imaging and Communications in Medicine (DICOM) committee is giving recommendations for the image transfer within hospitals in their supplement 145 [DICOM Standards Committee, Working Group 26 2010]. Since 2005 there is the integrating the healthcare enterprise (IHE) with the initiative for anatomic pathology (AP) as sub-group of the IHE. The initiative is trying to establish an integration profile for unifying AP and WSI. Differing from the DICOM standards the IHE is giving specific instructions for an implementation and utilizes groundwork done by the supplement 145 [Daniel et al., 2011]. If the integration profile is implemented correctly, a communication with the hospital internal communication protocol of the Health Level 7 (HL7) standard is guaranteed. However, agreements in various points for example image compression to JPEG2000 already had impact and will continue to raise acceptance of DP [Zwönitzer et al., 2007] due to vendor neutrality. All these efforts strive towards one standardized solution for all digital pathology workflows and to reduce uncontrolled growth of vendor dependant, non interoperable formats. Despite the DICOM extension and the IHE integration profile not a huge progress can be reported in terms of vendor neutrality yet. To this day vendor neutrality are utopia and the concepts of implementing the technology is rather poorly conceived.

2.5. Telepathology

This term is best described in this short citation: "Telepathology is the practice of pathology over a long distance" [Weinstein et al., 1987] but it is not defined what a long distance is. Nowadays this would typically mean around the world since the internet as a medium is ubiquitous. Typically pathological images are transmitted electronically for the purpose of finding an interpretation or diagnose but also for educational purpose. Potential use-cases for telepathology can be:

- Routine consultation
- Intraoperative section analysis
- Second Opinion for difficult cases

In all of the mentioned use-cases the patient's full clinical picture is needed in order to provide a diagnosis. Telepathology itself can then be classified in four different kinds

1. Static Telepathology
   Single images are transmitted via Internet or E-Mail
2. Dynamic Telepathology
   Remote Control of the Microscope
3. Semi-static Telepathology
   Static Telepathology combined with a consultation (e.g. via phone)
4. Virtual Microscopy
   see chapter 2.3

Nowadays the most promising approach for telepathology is Virtual Micrscopy since it offers an on demand, dynamic and almost lossless transmission of the image material. The downside of this technique is the high consumption of digital storage capacity and necessary bandwidth, which is explained in more detail in chapter 2.4.1.

2.5.1. Digital Pathology

The term digital pathology (DP) evolved over the years and is now used equivalent to the term of telepathology. It involves the patient's context and the specimen to produce a diagnosis. Based on this diagnosis the patient will receive a treatment. In the following the term DP will be used.

2.5.2. Differentiation Virtual Microscopy and Digital Pathology

At first glance the terms seem to cover approximately the same contents. But the difference becomes more obvious if you put focus on the Pathology in Digital Pathology. As described in 2.1, pathology deals with the illness and consequently also the morphological changes in an organism. To find a diagnose to any kind of the mentioned changes it is necessary to consult the patient's clinical background, which makes DP an expansive approach.

2.5.3. Potential benefits of Digital Pathology

To justify the investment into a DP system the possible benefits have to be analysed. In prior validation studies non inferiority of WSI compared to conventional light microscopy has been proven without significant discrepancies [Bauer et al., 2013]. But what are more benefits of DP? According to [Evans et al., 2014] the evaluation of the same can be split up into two main suitors:

1. The pathologist
    - Reduced travelling times
    - Access to diagnostic tools
    - Improved turnaround times
    - Increased collaboration between pathologists
2. The health care institution and the patient
    - Reduced amount of lost / broken slides
    - Reduced cost for pathologist travels
    - Improved access to diagnostic materials
    - Service quality is improved

The mentioned potential benefits seem to be obvious and overwhelming when fulfilled, but having a closer look reveals its shortcomings, e.g. improved turnaround times for a pathologist cannot be realized without special training and / or high performance pathologist workstations.
Another downside not mentioned by this listing is the additional time that is necessary to prepare a digitalized version of a slide. In order to maximize the benefit of DP the workflow has to be adapted in the LIS, which is tied together with a lot of effort and cost. Additionally the storage question has to be considered when implementing DP [Stathonikos et al., 2013].

In order to maximize the benefit of DP a close assessment of the pathologists workflow is necessary to secure an efficient implementation of DP [Ho et al., 2013]. Therefore methods of the user requirements engineering are suited in this scenario, such as contextual inquiry, workflow modelling methods and the application of HCI guidelines for an efficient implementation.

2.5.4. Comparison Digital Pathology to Radiology

The similarity in requirements and used environment in WSI suggests a certain analogy to the field of radiology. In radiology all these technical challenges have been overcome, yet they differentiate greatly when taking a closer look.

Regarding 2.2 teleradiologie's standards are already established since several years in the clinical environment, so naturally there are less problems integrating. Also the file sizes are incomparably different. So far standards were missing and DP could not be integrated in existing environments easily. Developers had to 'reinvent

Teleradiology	Telepathology
• Picture already digitalized • Transmission of original data • No quality loss • Digital standards established • Cost savings in comparison to analog imaging • File-size: MB scope	• Digitalizing through scanning • Transmission of reduced data (sections) • Quality loss inevitable through big file size • Standards not yet fully established • Additional cost compared to analog imaging • File-size: GB / TB scope

Table 2.2.: Comparison Teleradiology and Digital Pathology

the wheel' every time they wanted to integrate a new component as described by [Singh et al., 2011]. The latest efforts by the IHE as described in chapter 2.4.4 will ease up these processes leading towards a new and fully integrated era aiding DP to the break through.

2.5.5. Quality Assurance in pathology

When it comes to clinical application quality assurance is always a very important topic to deal with since it was mandated by the College of American Pathologists (CAP). Studies without the use of WSI have shown that Inter institutional error rates were at 6,7% [Raab et al., 2005], so a harm for patients cannot be excluded when not using WSI for diagnosis. The evaluated cases were revised randomly a second time after a wash out phase to fortify the result. [Ho et al., 2006] compares the performance of WSI against conventional microscopy and came to the conclusion that it is a promising modality for practising surgical pathology.

According to the Nordic immunohistochemical Quality Control[7] (Nordic QC) an independent scientific organization, promoting the quality of immunohistochemistry and assessing tissue stains, the main issue is related to the immunohistochemical staining. This procedure of quality assurance could also be an archetype for implementation in Chile.

[7] see http://www.nordiqc.org/, accessed on 06.10.2014

[Pantanowitz et al., 2013] are trying to establish a guideline for slide validation approved from the College of American Pathologists[8] (CAP) when using WSI. Stated within the guidelines there are several recommendation and expert consents:

- Institution independent validation studies
- Specimen preparation used in the studies should be relevantly involved
- The tested environment should be close to the practical application
- The process should involve all components of the WSI system
- Revalidation needed after significant changes to the system
- ...

CAP together with the American Society of Clinical Oncology[9] (ASCO) is editing guidelines in pathology. These recommendations were developed from initially over 700 studies carried out in the field of digital pathology. Collaborating with the U.S. Food and Drug Administration (FDA) the mentioned institutions are representing an authority in North America and are seen as role-model for worldwide adaptations.

2.6. Human Computer Interaction

2.6.1. Socio Technical System approach

The term Socio Technical System (STS) first came up around the late 1950's when technical system were only used by experts [Boulding 1956]. Over the years the users of computerized system changed from well trained experts to laypersons. So the concept for developing applications involving computers changed dramatically. Suddenly a social component was added to the ancient focus on technical aspects.

As 2.2 suggests the development of new applications for computers has to be separated into a technical- and a social component. The complete system, because of interdependencies, can only be optimized when both sub-systems are optimized concurrently, a so called joint-optimization is necessary to fulfil the systems purpose sufficiently.

[8] see http://www.cap.org/, accessed on 06.10.2014
[9] see http://www.asco.org/, accessed on 06.10.2014

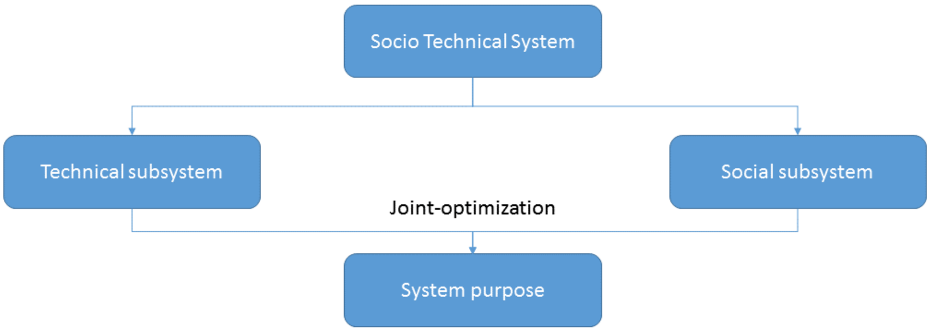

Figure 2.2.: Schema of the STS's components

2.6.2. Contextual Inquiry

Contextual inquiry (CI) is part of the User-centered design process. Since the earliest HCI development approaches the challenge is to integrate systems designs into the everyday work [Beyer & Holtzblatt 1998]. In practical use CI is organized as one on one interaction between system developer and customer (= future user). Furthermore the process is divided into two sub parts:

1. Participant Observation (PO)

2. Discussion of the observed

The involvement of the user has been critically seen because of logistic and financial issues [Hughes et al., 1992]. Nevertheless in a project that depends so strongly on acceptance from interdisciplinary stakeholders and has been proven to lack acceptance in the past, collaboration is necessary to avoid failure and frustration. Furthermore it is necessary to involve not only the primary users (pathologists) but also the secondary or intermediate users (technicians). According to [Sharp et al., 2007] not all groups mentioned before have to be within the CI but have to be considered when designing the system.
The PO is a discipline of the applied research to gather mostly qualitative data in an iterative research process. The biggest benefit arises when conducted in the beginning of a project together with other methods like interviews or focus groups. Regarding the research of [Mack & Woodsong 2005] Conducting a PO involves the following steps:

1. Determine the purpose of the PO
2. Determine the population to be observed
3. Consider accessibility and place of the PO
4. Find possible sites for the PO
5. Find suitable times and anticipate duration
6. Decide which way to be dressed
7. Plan how you will take notes

After conducting the PO the taken notes should be brought in a normalized format to improve comparability [Mack & Woodsong 2005]. POs can be separated in two classes[10].

Covert Observation	**Overt Observation**
Description: • Research is carried out secretly or covertly	• Researcher is open about the reason for presence
Problems: • Researcher has to lie about his presence in the group	• Observer effect affects the participating persons
Advantages: • Avoidance of the observer effect • Access to groups that otherwise would not agree to cooperate	• Participants can be observer in their natural environment • Data can be recorded openly

Table 2.3.: Comparison covert and overt observations

Often a PO is delivering more qualitative data than quantitative, which makes the interpretation more defective to biases, such as the observer effect (referring as Hawthorne-effect[11]). Another source of bias to POs are the non standardized form of reports denounced by [Becker 1958].

Since the scale of this project does not aim to be secretly conducted, an overt observation approach can be used. The participant in this fact gathering process should be well aware of the purpose of the observation to elaborate the most relevant information closest to the everyday life. The observer effect cannot be excluded but minimized as there is no direct pressure put on the participants.

[10] see http://wps.pearsoned.co.uk/ema_uk_he_plummer_sociology_3/40/10342/2647687.cw/content/, accessed 23.09.2014
[11] see http://psychology.about.com/od/hindex/g/def_hawthorn.htm, accessed 07.10.2014

2.7. Modelling

Modelling is the link between theory and practical experience. Process orientation is also essential in Quality Management Systems (QMS) which are widely spread in the health care sector [Rojo et al., 2008].However, modelling is always a matter of perspective, hence many approaches for modelling are co-existing. According to [Macintosh 1993] processes can be classified into the following levels of process maturity:

1. initial - setting up for processes
2. repeatable - repeatable processes
3. defined - documented processes standardized throughout an organisation
4. managed - measured and controller processes
5. optimising - continuous process management

According to Macintosh, depending on the classification (level 1-3 need to improve the knowledge about the processes, while level 4+5 need monitoring and controlling) different modelling techniques are required. Subsequently [Aguilar-Savén 2004] suggests classifying the processes even more fine granular into core- and supportive processes. The core (or primary) process is initiated from outside the organisation triggering a chain of activities. Supportive (or secondary) processes, concentrate on more strategical character, which are providing the preconditions for core processes to be executed. Since the processes are not yet established initially the focus should lie on the core processes, which have to be planned.

Especially when it comes to multidisciplinary project like this, a unified language that every involved profession can understand is needed. For these cases the Business Process Modelling and Notation (BPMN) has been developed which is combining the ability to illustrate complex processes with an easy to read semantic. As mentioned before this approach may fit when viewed out of the perspective of process orientation. Since this is to a high percentage an IT project, the technical details can not be neglected. Here the BPMN cannot provide sufficient informations, so another modelling tool must be used. In this case we decided to utilize an approach developed in Germany, the 3LGM[2]. The combination of the two modalities will lead to an all-embracing model.

2.7.1. Business Process Modelling and Notation

The Business Process Modelling and Notation (BPMN) has been introduced in version 1.1 in 2008[12]. Since then it has been consequently improved until it has been formally published by the ISO 2013 as standard for business process modelling. The purpose of BPMN is the unified communication model throughout all business users and stakeholders of a project [Rojo et al., 2008]. Furthermore the BPMN wants to provide a solution between the gap of process design and process implementation through its connectivity to the XML Business Process Execution Language (BPEL) [International Standardisation Organization 2013]. The BPMN features a set of elements (objects) to describe visually and textually the steps inside of a process divided by the involved institutions shown as so called pools. Within the pools lanes can be established which are used to categorize activities. To illustrate the process itself, activities and events are utilized which are connected via different connector types. For further reference on objects and their usage see the BPMN poster[13].

2.7.2. Three Layer Graph Meta Modell ($3LGM^2$)

The Three Layer Graph Meta Modell ($3LGM^2$)[14], based upon the Unified Modeling Language (UML), aims to display processes at the domain layer and communication paths between application components and their interdependencies [Winter et al., 2007]. Basically the $3LGM^2$ is divided into 3 sub-domains, each with different tasks:

1. Domain Layer - describes enterprise functions
2. Logical Tool Layer - describes application components
3. Physical Tool Layer - describes hardware components necessary to support enterprise functions

The domain layer is accommodating the enterprises functions in order to provide effective services. Additionally object types are defined which are created during tasks or help to solve these. Typical object types would be a report or a glass slide. The logical tool layer on the other hand is modelling application components. There are computer based- and paper based application components. Computer based application components are components of an information system which are installed on a specific machine, examples would be a patient management

[12] see http://www.omg.org/spec/BPMN/index.htm, accessed on 17.09.2014
[13] see http://www.bpmb.de/images/BPMN2_0_Poster_EN.pdf, accessed on 17.09.2014
[14] see http://www.3lgm2.de/index.jsp, accessed on 17.09.2014

system or a digital picture archive. As the name suggests paper based application components involve the utilization of physical resources. An example for a paper based application component would be the biopsy form. Finally the logical tool layer is accommodating physical data processing components, which are defined as server- or computer systems which are connected within an enterprise wide network. For communication modelling it is possible to create interlayer relations for all layers to reveal dependencies. Hereby message types are respected and if necessary a communication server model has to be considered. However, the $3LGM^2$ is not able to replace business process modelling due to limited vocabulary [Thomas Wendt 2006] and should more be seen as a valuable addition to process modelling.

2.7.3. Introduction to Critical Success Factors

This term, as the name suggests are critical factors within a project that, if not addressed and fulfilled due to limited resources, will lead to the failure of a project. [Pinto & Slevin 1987] extracted, after comparison of several approaches of other researchers, success factors 9 essential factors that can be classified in tactical and strategic factors:

- Strategic
  - Top management support
  - Sufficient resource allocation
  - Clearly defined goals
  - Adequate communication channels
- Tactical
  - Competent project manager
  - Competent project team members
  - Control mechanisms
  - Feedback capabilities
  - Responsiveness to clients

In a further publication Pinto and Slevin are pointing out that these factors vary in weight according to the projects life-cycle phase and that the examination did not take into account a weight to the single factors, but are assuming that these factors are positively correlating. Over time the concept of project success changed away from only the customer's satisfaction over to the satisfaction of all the project's stakeholders. At this time project completion without changing to date was the highest priority. Another approach named Analytic Hierarchy Process was established by [Saaty 1990]. First suggested as a decision making approach with its factors arranged in a hierarchical structure, [Chua, D. K. H. et al., 1999] Suggests a different approach, classifying in objectives of budget, schedule and quality. Chua relies on- and acknowledges previous approaches but analyses critically under consideration of expert opinions.

2.7.4. Key Performance Indicators

Key Performance Indicators (KPI) are defined as special operating figures which are addressing success, degree of utilisation of a company, its organizational entities or machines[15]. To be able to use these operating figures for management purposes, the following requirements should be kept[16]

- Comparability
- Target orientation
- Continuity
- Actuality
- Comprehensibility
- Sustainability

KPIs have to be comparable in order to illustrate change over time. The target orientation should be set on improvements that can be achieved e.g. the employee through changes in the process. Continuity secures a permanent record of the KPIs, which are taken in a regular basis (hour, day, month, ...) to avoid outdated figures and allow control over the command variable. Furthermore the KPIs should be reduced on the key indicators to keep clarity and ease up comprehensibility. Finally the improved circumstances should be kept further in focus to avoid drawbacks.
Based on KPIs graphs can be developed which illustrate the current situation and outline the gap between the performances. This can motivate employees and gives a tool for justification in front of stakeholders.

[15] see http://wirtschaftslexikon.gabler.de/Definition/key-performance-indicator-kpi.html, accessed on 16.10.2014

[16] see http://www.awf-arbeitsgemeinschaft.de/download/Kennzahlen-in-der-Produktion-awf.pdf, accessed on 16.10.2014

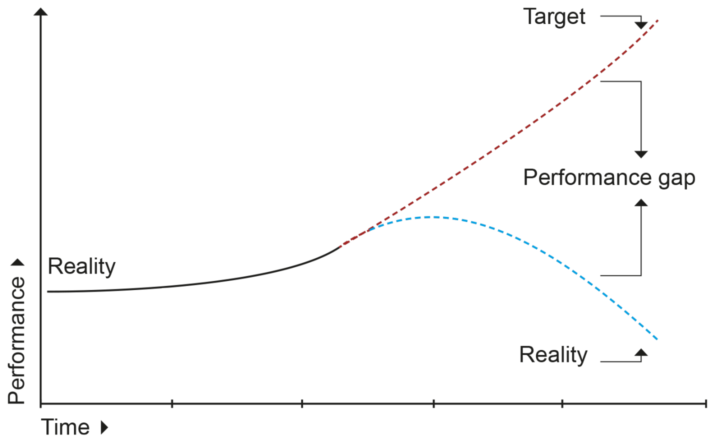

Figure 2.3.: The performance gap following [Turner 2009]

Shown in figure 2.3 is the actual performance of a project on the basis of the previously measured indicators. The divergence between the target and reality curve are representing the performance gap that needs to be adjusted. [Turner 2009] Suggests comparison to other institutions with similar performance indicators with benchmarks in order to compare performance between comparable projects and keep the ability to compete successfully against competitors. A term closely related to performance indication is the organizational efficiency which can be improved by changing workflows, the usage of automation and supply chain management. In order to raise the organizational efficiency the performance indicators have to have a positive trend.

But before KPIs can be measured they have to be identified. Figure A.2 shows this process.

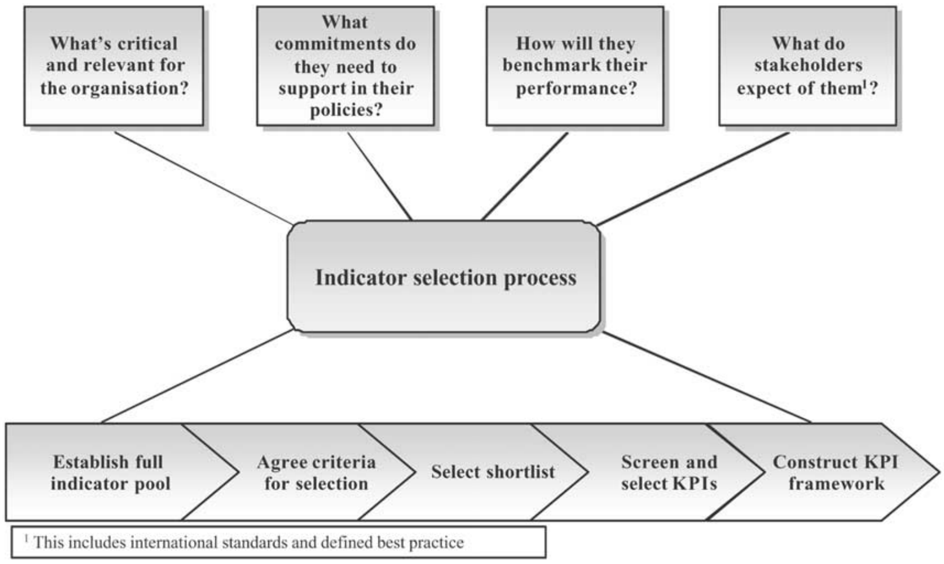

Figure 2.4.: Indicator selection process following [Keeble 2003]

Based on the questions at the top of figure A.2 a pool of possible KPIs is created. [Marr 2011] suggests the 75 most common KPIs divided into sub classes from which afterwards the pool of indicators has to be discussed to select the most applicable indicators, or new ones can be estimated. Furthermore combined or related KPIs can be used to visualize trends or ratios more clearly. Then a classification is done based on whether or not the activity is related to the core business functions. Lastly the KPI framework is established, defining the conditions like the effort or frequency of reporting [Keeble 2003]. Additionally a visualization system can be developed with methodologies like balanced scorecards, trend analysis, SWOT-analysis, traffic-light system or ratio systems.

3. Methodology and implementation

3.1. Fact gathering

In order to be able to conduct a project of this scale and complexity it was necessary to tie down a scope first. Initially this project was set out to provide a digitalization service for organic tissue sent via ways of conventional transport. The area provided with digitalization should be all Chile. So far no other project like this exists in South America. Later on the service should be expanded to be able to handle DP, which makes interfaces to the institution's laboratory management system (LMS) necessary to deliver the needed patient related context. The projects participants were organized in a team specific organisation including a flat hierarchy. The team itself was organized interdisciplinary, with participants from different areas of study e.g. biotechnological engineering, medical computer science, medical engineering and anatomic pathology. Time for conducting the project was limited by the Chilean government to three years, from which one was needed to acquire the tissue scanner. Exchange between all team members was possible during meetings in a two week interval due to different involvement of the project participants. For the context of this thesis, the following roadmap has been developed[17].
Since DP has been growing for the last 20 years the Job training involved extensive literature research. To establish a general overview and order the terms creative techniques like mind maps were used[18]. DP requires a certain level of present infrastructure in the facility that wants to incorporate it, to examine this, it was necessary to visit external institutions (hospitals) to investigate working methods on-site. Additionally a team meeting was scheduled to keep track of the other team members work, exchange findings and discuss future steps.

[17] see A.1
[18] see A.2

3.2. Requirement Analysis

3.2.1. Covered Institutions

Since the Chilean healthcare system is divided into a private and public sector the existing preconditions in terms of infrastructure are very diverse. Typically the empathy for new investments is higher in a private environment since new technology is raising the institution's reputation. As described in chapter 3.1 the project itself is aiming to supply the service of digitalization and later the ability to practise DP for all institutions within Chile. Naturally the area of expertise and area of activity on which the institutions are present differ, therefore the institutions have been selected to cover a broad variety.
Clinica Las Condes (CLC) is one of the biggest private hospitals in Santiago. The pathology department employs 8 pathologists, 20 technicians and carries out up to 15.000 biopsies a year. The second institution is *Clinica Alemana*, also one of the largest private health care providers of Chile. With up to 13.000 biopsies per year and up to 7 pathologists working at peak times.
The third institution is the semi-private *Hospital Clinico Universidad de Chile*, located next to the medicine faculty of the university. Finally the *Instituto Nacional del Cancer* is a public health care provider specialized on cancer which is located near the university of Chile. The institute is employing 3 pathologists which are located on the same site to ease up exchange between them. Additionally 4 technicians and 2 secretaries are present (+ additional temporary workers). The diversified selection of institutions is helping to improve robustness of planning when implementing the project.

3.2.2. Meta-process

Approaching the project a meta process has been established, which then was repeated, with exception of the requirement analysis questionnaire, in all of the covered institutions mentioned in chapter 3.2.1. This should secure the reproducibility and prevent dependencies which are only occurring in one specific institution. This chapter will give a brief overview about the methodologies utilized during the project, which will then be exemplary described together with practical experiences in an example institution later on.

Figure 3.1 shows the first three steps of the process. In all of these steps future users have been consulted in different quantities. The requirement analysis questionnaire due to its characteristics to only build up the foundation of requirements, was only conducted within the Clinica Alemana documented in chapter 3.2.3. The

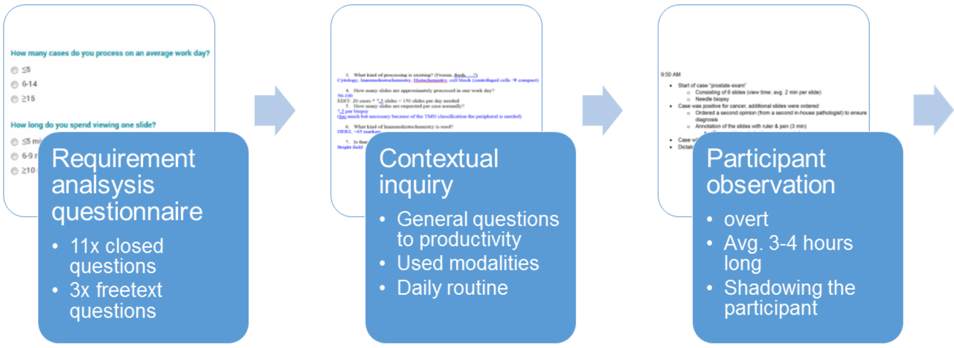

Figure 3.1.: Meta process of requirement analysis, part I

contextual inquiry (QI) was performed before the participant observation to roughly identify the institutions scale as well as used techniques, an example can be found in chapter 3.2.4. Afterwards the core of the requirement analysis was performed: the PO. Acting as a shadow and following the participant throughout his work day, this process was the main source of information. For an example case study please see chapter 3.2.5.

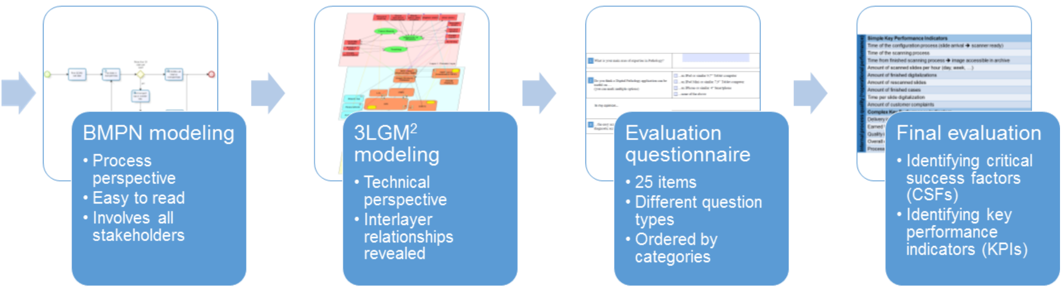

Figure 3.2.: Meta process of requirement analysis, part II

The second part as seen in figure 3.2 is consisting of four further parts. In contrast to the first part, this part involves the user less strong and has an emphasis on modeling processes of technical systems (see chapters 3.3.1 and 3.3.2). After the modeling process which was based on the results of the previously collected data a second questionnaire was distributed to validate the model and reveal its shortcomings in terms of functionality. After revising adjustments revealed by the evaluation were applied to the model. Finally, to ease up project management, the critical success factors (CSFs) as well as key performance indicators (KPIs) were identified to derive implementation possibilities (chapter 4.2) and, given the right maturity of processes, their efficiency (chapters 4.5 and 4.4).

3.2.3. Requirement analysis questionnaire

The requirement analysis questionnaire[19] was intended to elaborate basic performance informations about pathology laboratories in Chile and the general attitude towards DP. The questions should be simple and easy, combined questions where doubled negotiation should be avoided. Furthermore ambiguity, suggestive questions and strong generalizations were avoided, too. Sources of error can be the Error of central tendency, social credibility and social expectancy. Aware of the problems mentioned a combination of the different question types has been created. The questionnaire can be split up in three parts:

1. Particular questions (about institutional performance)
2. General questions (about DP)
3. Free text questions

1. Is designed to elaborate general information about the workload of the pathologist. Questions contain informations about quantity like the amount of cases reviewed on one day and how long the pathologist spends time on one slide. In literature the time saving possibilities often played an important role, so it was questioned in the beginning.
2. Is scaled with the Likert-type scale with three expressions to quantitatively measure the attitude towards DP and additions that are coming with it. Questions are defined as items and are evaluated on outcome. When the answers are agreeing on a higher rate than 80% a ceiling[20]- or floor effect[21] occurred.
3. Free text questions are representing the creative part of the questionnaire. The goal is to elicit aspects that have not been thought of before. In total there were 14 questions to answer on this questionnaire.
Exemplified on *Clinica Alemana*, this questionnaire has been filled out by 4 pathologists to elaborate the preconditions as they are perceived by the pathologist.

The overall impression is, that the pathologists in Chile, despite the fact that they did not grow up as digital natives[22], are relatively open towards new technology which is making use of the internet. Consequently participants are willing to participate in a study when the groundwork is done. Surprisingly the amount of time travelled according to the opinion of the pathologists can be reduced, which will later be

[19] see A.5
[20] see http://link.springer.com/chapter/10.1007%2F978-3-211-89836-9_170, accessed on 06.10.2014
[21] see http://www.springerreference.com/docs/html/chapterdbid/334262.html, accessed on 06.10.2014
[22] Persons who grew up with digital technology from an early age, see http://jpalfrey.andover.edu/2007/10/28/born-digital/, accessed on 25.09.2014

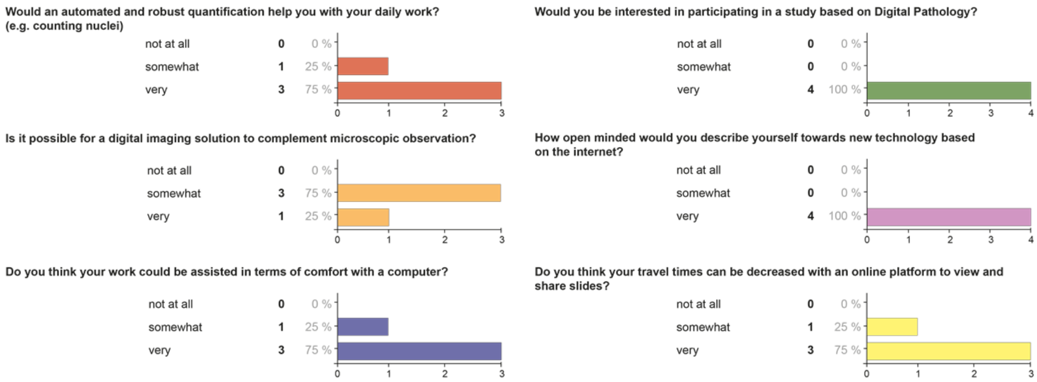

Table 3.1.: Results of requirement analysis questionnaire

proven not to be first priority since most of the participants are working on only one pathological site. A second benefit of this questionnaire was the first orientation on how many slides a pathologist is viewing per day and for how long. This is a first indicator for what can be provided with this project and what benefit can be achieved given the extra processing time. Interestingly the Clinica Alemana already implemented some kind of LIS to their workflow as they use barcodes to track specimens throughout the procedure. This makes it easier and more efficient for the pathologist to gain further information on the patients context, since they just scan the barcode and the hospital information system (HIS) which is connected to the LIS will return patient context information like personal information, prior diseases and diagnosis. One measurement index of the efficiency for pathology labs is the amount of slides requested per case which in this case is 2.4 slides per case. Even though the amount of slides needed to solve a case is highly dependent on the kind of biopsy this indicator can be utilized to measure a laboratory's performance. Most of the time only one screen was available and the desktop computers were older single core CPU'S. Field tests with the digital image library of the Tissue Imaging and Analysis Center (TIGA[23]) have shown that the bandwidth is sufficient to access the high quality images with reasonable performance. In practice the latency is supposed to be smaller since the image server will be located in Chile.

3.2.4. Contextual inquiry

Within the contextual inquiry modality an interview is conducted which is about 1 hour in length. Location for this is the user's work place where the researcher observes the actions and discusses them with the user to clarify project importance and relevance. Important is the partnership between user and researcher so that

[23]see http://tigacenter.bioquant.uni-heidelberg.de/, accessed on 26.09.2014

the CI alternates between observing the users work and the discussion why he did what action. The goal is to exchange impressions to enable comprehension for the context of actions for the researcher. This also involves complementation of records written down earlier by the researcher during the process. Another advantage of this approach is that the researcher can exactly set the focus of observation and discussion, this reduces overhead on non-usable information which has to be discarded afterwards. Due to the fact that CI mostly acquires qualitative data, statistical inference is limited.

The example institution covered here is located closest to the slide scanner and the image storage solutions, the *Hospital Clinico Universidad de Chile*. This institution provides health care on a semi-private level. In general it can be said that the amount of paper based work is increased compared to other institutions mentioned before. In practice there are also minor discrepancies for example the labels for slides and the paraffin blocks are written by hand and are not registered in any kind of tracking system. This increases the time per case since additional information has to be searched manually. Throughput itself is decreased since everything has to be written by hand. An additional impairment is that to get further information about a patient the responsible clinician has to be called. The followed pathologist[24] was expert in nephrology had an average estimated workload of viewing 60 slides per day. The approximate amount of slides per case is 5, doubled to the Clinica Alemana. This was the first pathologist to cover more than one pathological site, in fact 4 sites are covered including the one on which the CI took place. Surprisingly all the sites were within a radius of 5 km so that long travel times were, if not inducted due to the traffic, no issue. Archiving, a point that has potential being improved with DP is a huge issue in all institutions.

Figure 3.3.: Pathological archive of Hospital Clinico Universidad de Chile

[24] Dr. Paula C. Segura Hidalgo (psegura@hcuch.cl)

Figure 3.3 shows the organization within the institution. According to the Chilean law it is necessary to store the paraffin block holding the tissue as well as the glass slide for at least 10 years. In practice the samples are kept forever which is consuming a lot of space within the institution. In the concluding discussion after the PO Mrs. Hidalgo mentions the lack of possibilities for efficient second opinions, many slides are broken on transport and the amount of time needed to get a second opinion is very high. Also the amount of paperwork is considerably higher than in other institutions of same or larger scale.

3.2.5. Participant Observation

As described in chapter 2.6.2 the PO is a tool for the explorative discovery of users' needs and expectations towards a newly introduced system. The future users of this project have been assigned to a group:

1. primary users - the pathologist
2. secondary users - the technician

Correspondent to this classification the PO's have been conducted, focusing on the primary group, but also with one case to consider the secondary users. The observations have been conducted within an equal scope between all institutions. Participants were asked to undergo a typical work day. This includes everything even if it is not directly involved within the projects scope, for example researching in books to find a diagnosis. Two case studies will be described in more detail one covering the pathologist as primary user and one study dealing with the secondary users, the technicians.
The PO itself was conducted overt, so that the participants knew that they were under observation.
A brief introduction was made on how the PO works, to avoid interruptions during the observation itself. Critics of this method often mentions the observer effect which is the effect of altering behaviors when under observation.
1. Case study - the pathologist at CLC
Observed was a typical day of a pathologist which had his specialist field in lymph nodes[25].

As seen in figure 3.4 the workspace itself was equipped with a single core computer as well as an Olympus bright field stereoscopic microscope with an 8 mega pixel digital camera mounted on top. The microscope's camera is connected to a memory card system to save pictures. Displays are two 19 inch flat screens (Samsung

[25]Dr. Pablo Matamala Bastian (pmatamala@clc.cl)

Figure 3.4.: Pathologists workspace at Clinica Las Condes

& HP). The internet is accessed via a wired 100 MB Ethernet connection. These informations have later been used to establish the 3LGM[2]. During the observation a time scaled observation log was filled out to keep track of the actions and their duration [26].

9:50 AM

- Start of case “prostate exam”
  - Consisting of 6 slides (view time: avg. 2 min per slide)
  - Needle biopsy
- Case was positive for cancer, additional slides were ordered
  - Ordered a second opinion (from a second in-house pathologist) to ensure diagnosis
  - Annotation of the slides with ruler & pen (3 min)
    - Does not have to be “super accurate”
- Case will eventually be presented in the tumor board for its difficulty
- Dictate protocols (some of them have template in the HIS)

Figure 3.5.: Extract from the observation log

The extract shows a prostate biopsy case where it had to be decided whether the patient has cancer or not. Noticeable during the procedure was the very quick and very distinctive handling with the microscope. In less than 3 minutes a first opinion was found which then had to be assured with further material which was ordered electronically via the HIS. Additionally a second opinion has to be gathered by a colleague, which was sitting next to the pathologist, so the exchange and response rate of the case was quick. Furthermore annotations were necessary on the slides,

[26] see A.6

which were done by hand using a ruler and pen.

2. Case study - the technician at Instituto Nacional del Cancer

The technician also plays an important role in the workflow of establishing a diagnose for a patient. After the gross examination, he has the task to prepare glass slides for the pathologist to examine. This is process which requires a high level of fine tuning regarding staining and processing. Steps during the preparation process are: the dehydration and clearing of the tissue which is then embedded in a paraffin mold. Afterwards the tissue is cut, mounted upon a glass slide and processed within an automated but not error free staining process. After this procedure the slide can be presented to the pathologist. Given the high amount of preparation time which is necessary to arrange a probe, DP would add another step onto it: the digitalization which has to be done for some or all slides within a case.

To get insights into the preparation process the same principle as utilized with the pathologist was applied. The PO with the technician[27] took place on site.

Figure 3.6.: Slide preparation of Instituto Nacional del Cancer

Explanation with numbers according to figure 3.6: [1] When the tissue is first brought to the laboratory a new entry within the registration book is put, containing identification number of the biopsy, name, billing number, date, responsible pathologist and a signature. All of this is done by hand, since there is no LMS. [2] The samples are stored together with the according paper request for the gross examination. [3] The sample is then mounted on the cutting device to remove fine sections of the tissue for putting on a glass slide. [4] For frozen sections the process of preparation has to be speed up from 24 hours to 20 minutes, therefore the

[27] Pedro Escandon (pedro.escandon@gmail.com)

dehydration and preservation process is skipped. Cutting the sample is done at -24 degrees Celsius to avoid denaturation. [5] This is the autostainer which gives the characteristic colour to the slide. Slight variations can cause a variation in diagnosis, therefore a good quality assurance is necessary.

3.3. Modelling

3.3.1. BPMN

All the previous work (the CI, consisting of the questionnaire, PO and discussion) was done to elaborate a general idea of the pathological workflow in Chile. Based on this a future workflow model, integrating the digital acquisition and distribution of the slides, could be established. Since this was an interdisciplinary approach, a modelling notation was required that can be understood by all participants yet holds enough information to be of use. The Business Process Modelling and Notation was used in version 2.0.1 which was declared as standard 19510:2013 in 2013 by the International Standardisation Organization (ISO). Additionally it offers the possibility to close the gap between the modelling language and the machine readable generation of code using an XML based exchange format, this is done via the Business Process Execution Language (BPEL), helpful for computer based simulations. Since the whole process[28] is rather complex the process will be split up into smaller parts for the sake of clarity.
The involved actors, represented as pools, are:

- The health care provider
- The Scientific Image Analysis Laboratory (SCIAN)
- The external transport company

All mentioned parties are collaborating during the process and were therefore modelled as Pools. In this case the modelled process does not consider these pools as black box and describes activities within them. Lanes are used to distinguish between certain organisational units within a big institution. However for the sake of clarity some processes have been left out or modelled as sub-processes.

3.7 shows the hospitals process of handling pathological requests during routine sections. Before a digitization can be performed several steps have to be completed. The process starts with the clinician that orders a pathological examination

[28] see A.3

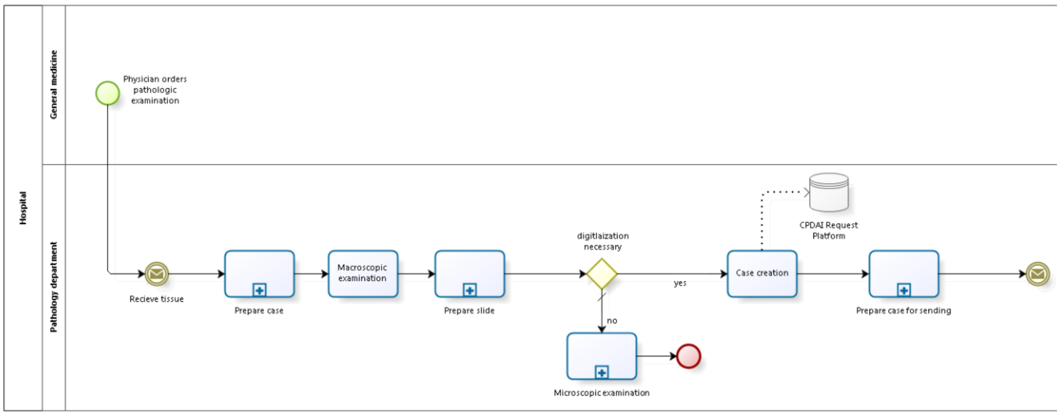

Figure 3.7.: BPM extract from the hospital's processing

from tissue that has been taken from a patient in a biopsy. The pathological laboratory receives the specimen, registering the case details in their system which are specified as a sub-process 'prepare case'. Afterwards the pathologist conducts the macroscopic (= gross) examination on the specimen. Before a digitization can be considered the glass slide has to be prepared explained in the sub-process of 'prepare glass slide'.

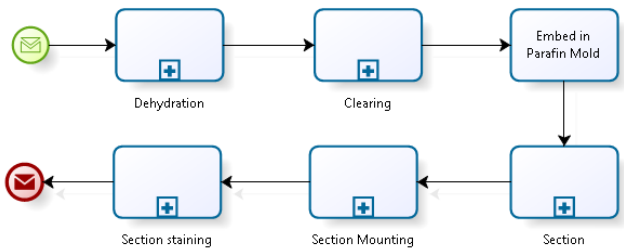

Figure 3.8.: BPM sub-process - prepare glass slide

This process is modelled as described in pictures on figure 3.6 and consists of the following processes: dehydration, clearing, embedding, sectioning, mounting and staining which can again be modelled as a sub-process.
Following back on the main process illustrated in figure 3.7 the next step in the process is a gateway which is requiring a decision whether a digitalization is necessary or not. Given the extra cost it would be possible the institution is agreeing on a policy which cases are needed digitally, for example only hard cases or cases that can be used for educational purposes. In case the digitalization is not necessary the case continues to the classic microscopic examination conducted by the pathologist. The process has its unspecified end event here, because this model is not focussing on the classic approach on pathology but. Following the other pathway at

the gateway a new case has to be created via the CPDAI on-line platform[29]. This platform is taking in the scanning parameters as well as eventual requested image processing. Furthermore the billing is made via the users account. After that, the slide has to be prepared for sending.

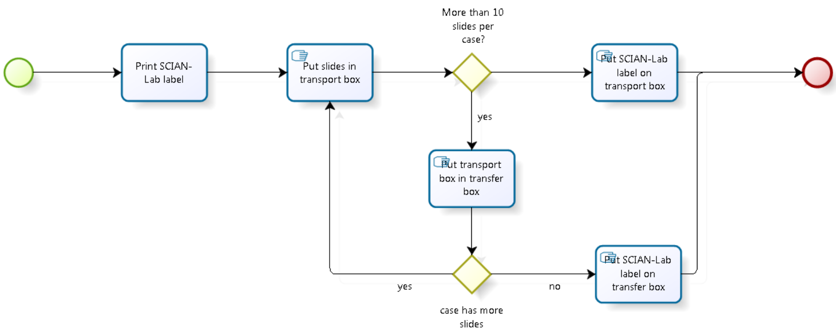

Figure 3.9.: BPM sub-process - prepare slide for sending

Figure 3.9 shows the sub-process embedded to the preparing process. First the slide label (QR-code[30]) which is provided by the SCIAN Lab has to be printed out to be able to establish the connection between the internal hospital tracking system and the SCIAN-Lab internal slide tracking management. For sending slides two modalities are existing, supporting varying case sizes: [1] *Transport box* - can hold up to 10 slides from one case, in case the case has more than 10 slides a [2] *Transfer box* is used which can hold multiple transport boxes. Once a case is completely transacted the label is put on and the box(es) are stored until the daily transport to the SCIAN Lab is carried out.

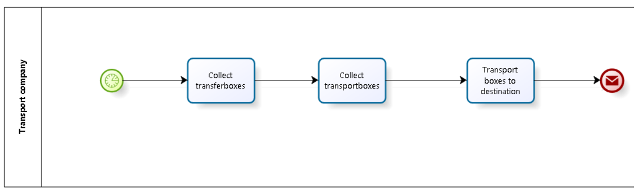

Figure 3.10.: BPM transport company

Based on a timed event which is triggered once a day at a specified hour, the carrier company is collecting the transfer- and transport boxes and delivering them from the remote institution to the SCIAN Laboratory. For scalability reasons this process could be extended for trawling several institutions for a higher efficiency.

When the slide is received at the department for digitization a revision is done in order to ensure the boxes have arrived without broken slides. Missing or mistakable

[29] see http://cpdai2.medicoresponde.biz/invitado/, developed by Mattoli Ingeneria, Parque Riesco 3407, Santiago - Chile
[30] Quick response code, see http://qrcode.wilkohartz.de/, accessed on 28.10.2014

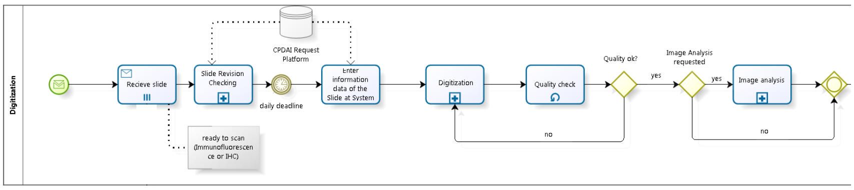

Figure 3.11.: BPM digitization within SCIAN Laboratory (1)

labelled slides will be identified in the next step with the aid of the CPDAI request platform to increase fail safety. The case informations are entered in the slide management software manually before the actual digitization is happening as showed in figure 3.12.

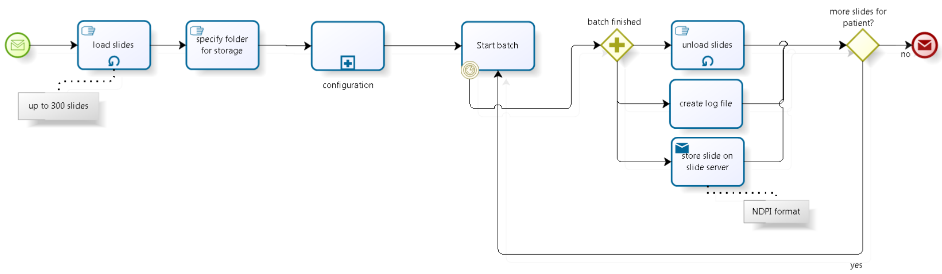

Figure 3.12.: BPM sub-process - configuration and digitization

After the manual configuration of the slide scanner and server the batch, which for this machine can hold a maximum of 300 slides, is processed. Once it is finished and no more slides for case are existing a log file for traceability is created and the digital slide is stored on the slide server in the NDPI[31]-Image format. Referring to 3.11 once the sub process is completed a quality check is performed to check for out-of focus regions or other shortcomings. In case the quality is not consistent, the sub-process 3.12 this case is triggered again. If a quantification of a slide is requested another sub-process is triggered. Where the image is manually loaded and the parameters are adjusted according to the request. Afterwards the quantification is executed on the server and a report together with the original image is being made available to the customer.

When either the image processing is finished or no quantifications have been ordered the next gateway is passed asking if a backup of the files is requested or not. If yes an intermediate event is fired to the datacenter of the SCIAN Lab. Here the process is archived for a preselected amount of time. If no such thing as a backup is requested by the customer, the case with all its components is brought back into the boxes from before and checked out of the internal slide management which ideally is connected to the CPDAI request platform. Afterwards two simultaneous

[31] Proprietary file format of Hamamatsu Nanozoomer micorscopes

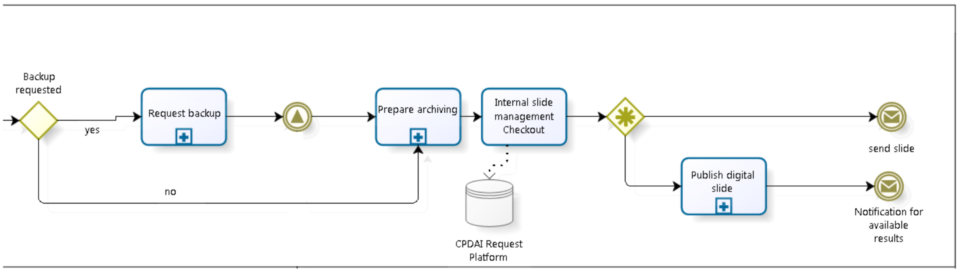

Figure 3.13.: BPM digitization within SCIAN Laboratory (2)

paths are being processed. One sending the slide back to the originating institution, the other one is publishing the digital slide to be able to access it from remote places via the internet and finally giving a notification to the person that requested the digitization.

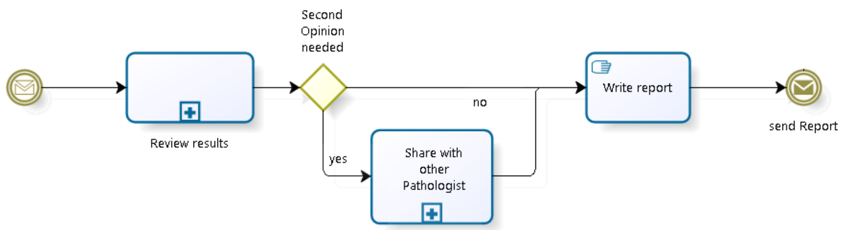

Figure 3.14.: BPM digital slide review process within the institution

After reviewing the results of the digitization by a pathologist and if necessary, one of the large benefits of DP comes into play: the second opinion, providing a solution for difficult cases in terms of flexibility. The digitalized images can be shared inter institutional with other pathologists, offering the possibility for improving the patient care and decreasing inter observer discrepancies just by sending a link to a specific slide. After the decision whether or not a second opinion is necessary in the according case a report is written or dictated, depending the institution. After signing out the case it is sent to the clinician which then decides the further treatment of the patient.

The illustrated process displays the standard case of digitizing glass slides into digital slides which are then accessible from remote locations, given the right permissions have been set. Storage is expensive and as described before (see chapter 2.4.1) digital slides are producing gigabyte often terabyte of data for one case only. Therefore another business process is dealing with the storage of the digital slides. No matter for which storage-type (long- or short term) the slide has been ordered, a specific storage duration has to be selected. After reaching the specified storage time limit for a case the owner of the slides is asked if he wants to renew the subscription for the access to his digital slides or they will be deleted within certain period of time. This procedure guarantees that no files are being deleted without

notification.
The SCIAN Lab does not only want to offer these services to external institutions but also use it for research purposes. In this case the digitization process is altered since no patient information will be needed to keep track off. Additionally the originating institution is the same than the one offering the service so that the transportation layer is omitted.

3.3.2. 3LGM^2

While the business process now has been elaborated to a reasonable extent, the technical aspect on how to implement this within the SCIAN Lab and the according institution has not been covered. To overcome this challenge a 3LGM^2 has been created to propose a solution. Given the background knowledge from chapter 2.7.2 the 3LGM^2 should be seen as an addition to the traditional process modelling conducted in the previous chapter.

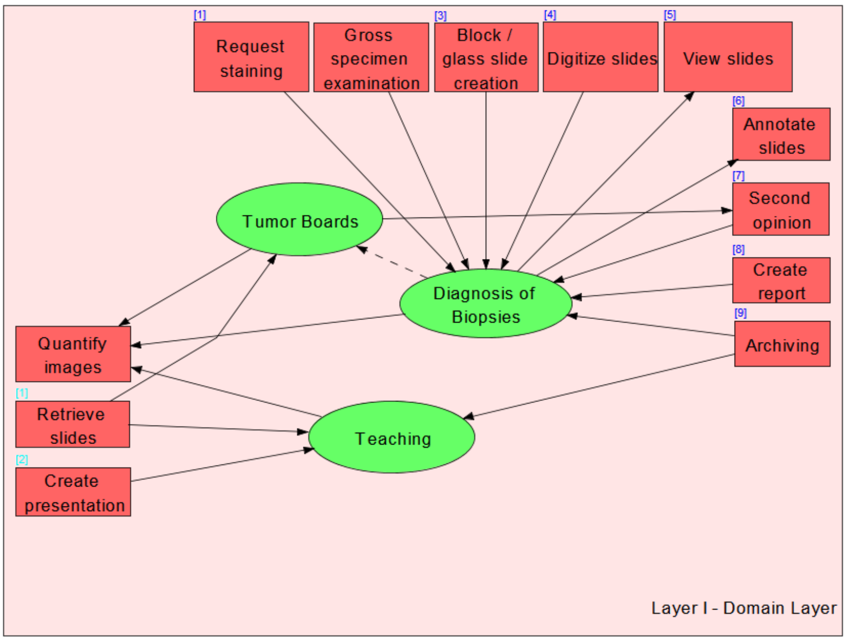

Figure 3.15.: 3LGM-Model, domain layer

Figure 3.15 shows the domain layer which holds the enterprise functions which can be described as the tasks of the pathologist in his daily work. In addition to the functions so called object types are defined. To be congruent to the business process orders of the different objects can be placed. Here are the shortcomings of the modelling capabilities of the 3LGM^2 in terms of business processes are revealed for not having gateways or decisions in general. The three main tasks what the pathologist has to do are:

- Diagnosing biopsies
- Teaching
- Attending Tumor Boards

The diagnosing of biopsies consists of steps shown in figures 3.7, 3.9, 3.11, 3.13 and **??**. For teaching slides have to be retrieved from an (presently from an analog, as seen in figure 3.3) case archive. The introduction of DP in the institution will change this process significantly since there is no need to go to the archive and retrieve a case by hand, everything can be accessed and retrieved by the pathologist directly from the workstation. Afterwards and with the right tools an educational application, involving dynamic image material can be created. Optionally the images which are used can be quantified by an algorithm to be able to create exercises that can be evaluated more easily. Tumor Boards display the last application where DP can increase quality and efficiency: before presentations containing screen-shots had to be created to provide other fellow clinicians with material that can be viewed by many people simultaneously, alternatively the use of a multi-headed microscope was considered, limiting the number of participants. Additionally quantification of images can provide comprehensible explanations for certain hard to decide cases. To conduct all this steps as in every profession, tools are used to increase efficiency.

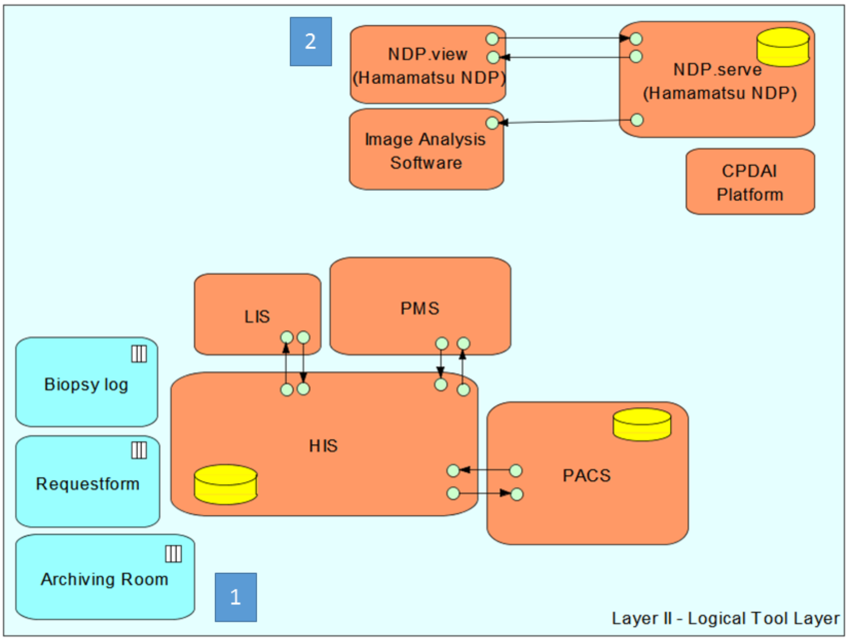

Figure 3.16.: 3LGM-Model, logical tool layer

The figure 3.16 above shows the logical tool layer. This layer accommodates computer- and paper-based application components (orange and light blue). The

software applications can be supported by a persistent storage solution like a database. Simultaneously computer based applications can host interfaces for communication to other components (represented through green dots). Naturally and because of regulatory requirements in medicine many processes are paper based which is represented through light blue colour.
This layer is separated into two sub parts: [1] in the bottom left corner, which is representing the institutions internal software landscape. The HIS is the connecting hub for the LIS and the Patient Management System (PMS). Additionally the HIS is providing the interface to the Picture Archiving System (PACS). Furthermore the paper-based biopsy log is needed to keep the overview about the conducted biopsies and the request form provides the possibility for the pathologist to order additional staining or special treatments [2] located on the top, which contains the necessary software to save and process the generated images. Given the preconditions of the Hamamatsu Nanozoomer XR NDP software is required to produce and handle digital slides supplemented by the CPDAI platform which enables pathologists or technicians to order digitizations.

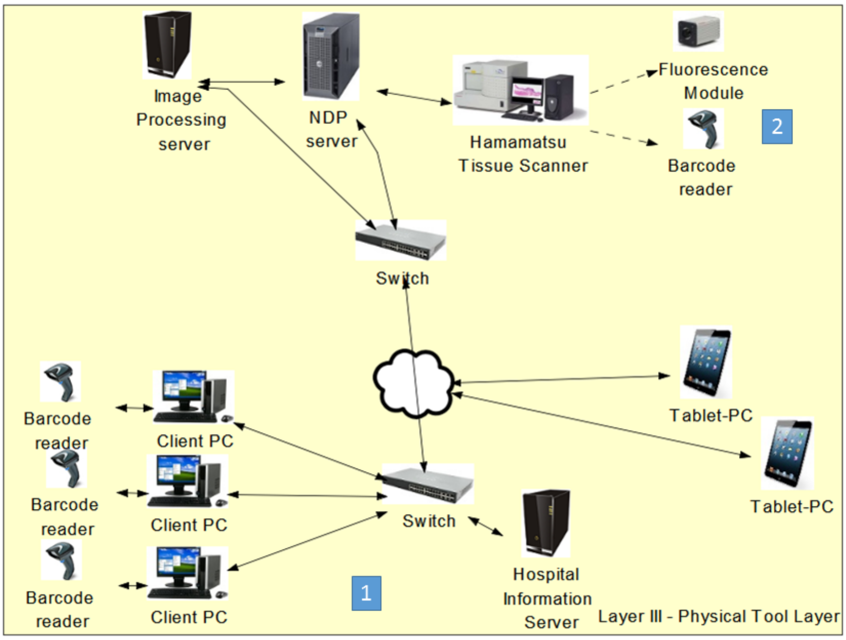

Figure 3.17.: 3LGM-Model, physical tool layer

Figure 3.17 represents the physical tool layer. Here the same differentiation into sub systems has been considered. As before [1] stands for the health provider institution environment, displayed simplified as Hospital Information Server and client PCs, which have access on a barcode reader and printer. Additionally tablet computers connected via the internet are introduced. The SCIAN Labs system [2] consists of the Hamamatsu scanner as well as an NDP server to store the images on.

The scanner itself is equipped with a fluorescence module to be able to process immunofluorescent slides. For image processing an additional high performance server is provided. The two systems are connected via the internet and proper authentication systems are guaranteeing data security. Ideally the NDP server is backed up in regular intervals to secure data integrity and minimize the risk of data loss.
The benefit the 3LGM^2 is offering lies within the connection between the different layers. As seen in A.4 each object is connected to an underlying object. An object type refers to a tool which is used to acquire it. The tool which was utilized is on his part connected to a hardware component on which it is running in order to provide sufficient functionality to solve the tasks on the domain layer.

3.4. Evaluation

The evaluation is structured into two parts: a questionnaire and respectively the evaluation of it. The evaluation questionnaire[32] has been conducted after evaluating the first questionnaire, the CI and the process of modelling has been finished. The extent of items is significantly higher than in the requirement analysis questionnaire (now 25 questions) and consists of different types of questions.

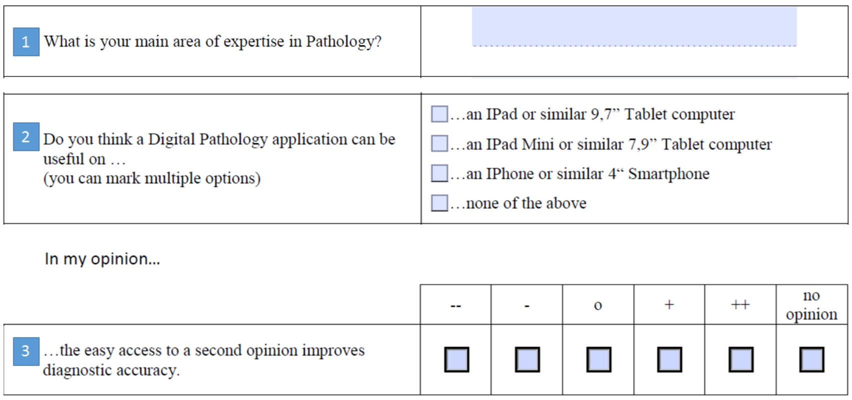

Figure 3.18.: Question types overview

[1] shows a free-text question. There are two types of free-text questions, the here displayed one line question and the essay question, typically used when a longer response is expected. [2] displays a multiple choice answer typically utilized when the expected answer has more than one occurrence. Special form is the multiple choice with the 'other...' possibility where the participant can insert his or her ideas that are not mentioned. Another special variation used is the single choice answer

[32] see A.7

with the respective options yes, no and do not know. This question type is often used when it is not clear whether or not the pathologist has experience in a certain field. [3] lastly is the question which are answered with a Likert-type scale[33]. This type has been proven of being especially adequate for elaborating attitudes and trends.

To cover a broader audience this questionnaire was distributed to more people than the first questionnaire. The questionnaire is consisting of the following categories:

1. Personal information
2. Expectations towards digital pathology
3. Access to second opinions
4. Access to quantitative parameters in images
5. Teaching and education

1. asks for personal information as free text fields, covering questions like the area of expertise and the experience within. Furthermore the informations like the amount of slides analysed per day is evaluated to be able to compare to the first questionnaire. Additionally it was asked how many tumor-boards are attended and whether or not the term DP is familiar to the participants. Finally the extent to which the term DP is known is asked within a multiple choice question.
2. covers the expectations. It is a controversial topic if pathologists should be allowed under certain circumstances to review cases from home. Therefore this sub-section asks from where the pathologist would like to work and from which device. Since technical progress enabled access to the internet even from mobile devices a distinction has to be made which devices and display is ideal for using with DP. The final question in this section is aiming to reveal the general attitude towards DP when it comes to ease up the workflow.
3. elaborates how frequent a second opinion is necessary to establish a secure diagnosis. Before closing this section is asking whether or not it can improve the diagnostic security and the time needed for it can be decreased. Finally the access to a worldwide network of pathologists should be judged.
4. Is dealing with the benefit of having access to quantitative parameters enabled by DP. For a better understanding how the pathologist is working in this field so far, some methods are being questioned for utilization (DAKO Hercep-Test[34], 4B5-Roche[35]). Finally the question is raised if pathologists would use algorithms that

[33] see http://core.ecu.edu/psyc/wuenschk/StatHelp/Likert.htm, accessed on 06.10.2014
[34] see http://www.dako.com, accessed on 06.10.2014
[35] see http://www.roche.com/de/products/product-details.htm?type=product&id=169, accessed on 06.10.2014

are approved by the American Society of Clinical Oncology (ASCO)/ College of American Pathologists (CAP). Additionally asked is the opinion about the potential of benefiting diagnostics and quality when having quantitative parameters.
5. Education is a topic containing high potential for DP and many pathologists are educating students additional to their working pensum. By obtaining concrete numbers of how long the pathologist spends to prepare educational material a possible benefit could be outlined.

4. Results

4.1. Evaluation

The evaluation questionnaire was distributed to 11 pathologists so far and a further distribution within the society of pathologists in Chile is triggered, ideally generating around 100 participants. The questionnaires results should, together with the other modalities utilized (such as modelling, CI, PO) lead towards a robust solution concept for implementing DP.
As mentioned before in chapter 3.4 the questionnaire was divided into sub-parts. The first one asking for personal work-related information and rough productivity indicators. The pathologists' area of expertise was manifold, covering everything from Neuropathology over Renal pathology to Cytopathology. As diversified as the area of expertise was the experience which the pathologists had, ranging from 4 to 30 years, with an average of the test population having 10,2 years of experience. Interestingly, and much lower than expected, was the number of different locations where the pathologists practise medicine, ranging from 1-3 locations with a clear accumulation on only one location. This bias might be inflicted due to the fact that two institutions covered were private organisations so employees are less likely to have several work places due to good salary.
The amount of diagnosed cases per day were estimated to be approximately 20-30, depending the position of the pathologist within the organisation. The number of slides viewed per day is also underlying the oscillation depending the pathologist's position. The minimum was 30, reaching up to 200 slides that are viewed per day through a conventional bright-field microscope. 55,4 slides was the average taking into account the minimal readings possible. The following question was not dependant on the hierarchical position within the organizational structures but on the area of expertise. Therefore the amount of viewed Fluorescent in situ Hybridisation (FISH) slides were varying revealing an average of 1,63 FISH slides per week and pathologist. Lastly the question about tumour boards was answered relatively consistent ranging from 1 to a peak of 6 tumour boards. According to the participants the average pathologist attends 1,9 tumour boards per week.
Summing up the first section of the questionnaire it is to say that the demands vary strongly dependant on the position (focussed more on management or operational

functions) a pathologist is representing. This leads up to the second part of the evaluation covering the expectations of the pathologist about DP. The initial question of the term digital pathology sounds familiar was answered with yes by 82% of the participants.

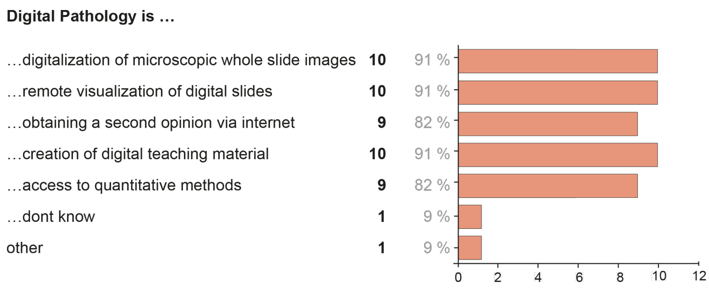

Figure 4.1.: Evaluation questionnaire: understanding of the term DP

To the question on what DP is for them many participants answered similarly. Continuously over 80% agreed, that all previously mentioned areas that can be covered are part of DP. Since there is no such system established in Chile all participants with one exception (the participant was working in Europe before) have not worked with a DP system. Interestingly the question from where the pathologists wanted to view their slide was answered with a high diversity as shown in figure 4.2.

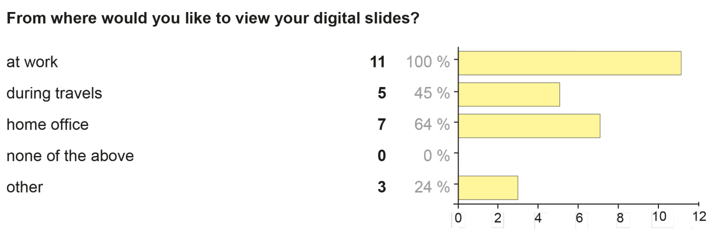

Figure 4.2.: Evaluation questionnaire: possible slide access locations

All participants agreed about viewing slides on the work place. However when it comes to travels only around half the participants are willing to view slides related to work. An increase is noticed when it comes to home office: 7 participants have seen a potential benefit for viewing slides from home.

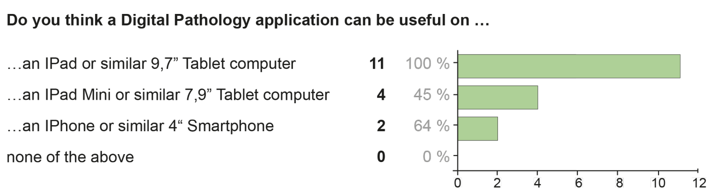

Figure 4.3.: Evaluation questionnaire: on which devices DP can be useful

Another important question is the one of devices where DP should be practised on. Lacking guidelines of image quality everything, including mobile devices as tablets are possible target devices. Mobile devices, despite the fact that there are constantly new developments, come in several semi-standardized sizes. Given the age profile of the participants, most of them were not raised with this kind of technology, but the survey results show a certain familiarity with this devices. The general trend, starting from 100% accordance with utilizing standard 9,7 inch tablets, states a decline towards the smaller sized devices, culminating in the utilization of Smartphone devices which are only 4 inch in average display size.

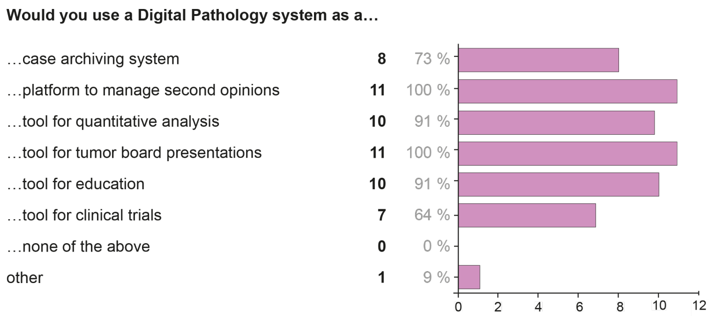

Figure 4.4.: Evaluation questionnaire: application fields of DP

Figure 4.4 shows that the expectancy for applications on a DP system relies heavily on the benefits outlined earlier, such as second opinion, quantitative analysis, education and tumour-boards. Less anticipated are the possibilities to build up a case archive or respectively do studies with the aid of a DP system. This might be due to the institutions focus: private institutions are focusing on productivity over research. The general opinion states that the work comfort can be increased by implementing a possibility to view slides from a screen. Interestingly only 45% of the participants have conducted an inter institutional second opinion during the last month. This fact might be due to the high in-house competency which is held by senior pathologists. This circumstance makes second opinions unnecessary, just in case there is a very rare and difficult case, which occurs according to one of the participants approximately once a month a second opinion is requested. From the 45% that used an inter institutional second opinion the frequency of occurrence is varying between 1 and 3 times. Though not all participants are utilizing second opinion regularly all participants think that an easy access to this modality is increasing diagnostic quality. Furthermore everybody except one single participant is agreeing, that the time to solve a case where a second opinion is necessary can greatly be reduced with the introduction of DP. Lastly the access to an international portal to discuss cases has been estimated highly beneficial from 82% of the respondents.
Summing up the expectations towards DP are generally highly positive in almost all aspects of the pathologists work. There are tendencies towards more efficiency

by widening the possibility to view slides from remote places but in the same time estimation run towards the clue, that a higher diagnostic accuracy can be achieved when having access to an easy to use second opinion system.

The next part is broaching the issue of quantification in images, since there are quantitative estimations necessary to evaluate and infer a treatment which, given a digitalized image, can be useful for concluding a diagnosis. An example for this procedure is the HER-2[36] protein expression, where the cells membrane has to be estimated for connectivity of a certain staining. This level of connectivity is then mapped on a scoring (0, 1+, 2+, 3+) regarding the level of staining. The problem is estimating the 2+ cases, where the classification against 1+ or 3+ becomes difficult due to relative estimations of coverage (score 1+ = 10-30% staining, score 2+ = 30-60% staining, score 3+ = more than 60% staining). Algorithms may help finding a more exact estimation of percentages, but are not yet approved for clinical use. The participants were first asked to report on which kinds of tests they utilized during their experience. After this the question if quantification can help diagnosis and deliver some kind of quality assurance for diagnosis was raised. Both questions were strongly agreed and given the difficulty of a 2+ case estimation assistance is definitely needed to increase diagnostic quality.
Finally teaching and education opportunities improved by DP are questioned. Figure 4.5 is revealing that more than half of the pathologists are involved into education in any form.

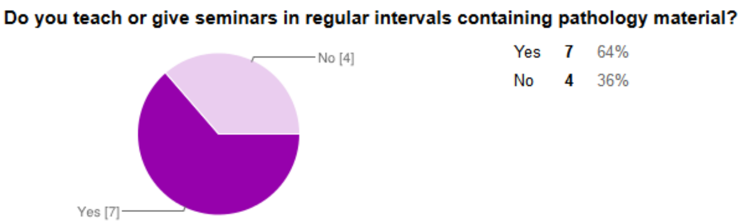

Figure 4.5.: Evaluation questionnaire: education involvement

They accordingly spend between 2 and 5 hours a week to prepare the educational material. Easing up the process of gathering material or presenting already gathered material within an on-line course would be able to reduce the average time spent on this activities. Additionally this material could be forwarded to other teaching institutions maybe providing knowledge to remote teaching institutions and raising overall education quality.

[36]see http://www.nordiqc.org/Epitopes/HER2/HER2.htm, accessed on 23.10.2014

In conclusion this questionnaire revealed the fields that the implemented and finished project should address even further. The classification in several aspects lead towards an incremental implementation strategy based on the modular features of a DP system, prioritizing basic functionality (e.g. digitalization and visualization) at first. Expected acceptance is positive throughout, the participants were informed and creative about the term of DP. A special focus should be lied onto the portability of the applications. As the results suggest many pathologists are willing to continue their work outside of the office, during travels or consider working from their home offices. This subsequently follows to a perspective that should not be neglected involving mobile devices, focussing tablets, into the process of practising DP. Biases as described in chapter 3.2.3 (e.g. social expectancy or central tendency) cannot be excluded due to the relatively small test population. The questionnaire also points out that the scoring of HER2 membrane staining is reasonably hard and image quantification would aid to find a more robust diagnosis. Finally the involvement in education is offering a break through chance of the project providing easy accessible and embeddable solutions for example for presentations or student training.

4.2. Solution concept

The concept is defining and providing the key functionality that is needed by the pathologist in Chile according to his specific environment. Which then can be gradually developed further to tap new fields.
Elaborated by the questionnaires, modelled via the BPMN and $3LGM^2$ this combination of methods should give a robust blueprint for the further development of the project. Given the challenges of implementing a system like this, the full range of functionality that DP can provide is not realistic at first, but with an incremental project management it can be implemented within reasonable time. To identify the effectiveness and efficiency, success factors and performance indicators (see chapter 4.4 and 4.5) will be outlined and measured after the implementation. Though DP offers its benefits, the initial cost for adopting the technique is very high and many institutions may be afraid of the commitment. Therefore the approach centralizing the most expensive resource (the slide scanner) and providing worldwide access to it seems logic. This project will help implement the external system in the heterogeneous environment of the hospital without too deep of an impact on the hospitals IT-infrastructure by providing initially non-invasive browser-based on-line solution.
The suggested implementation can be separated into three stage of expansions showed in figure 4.6.

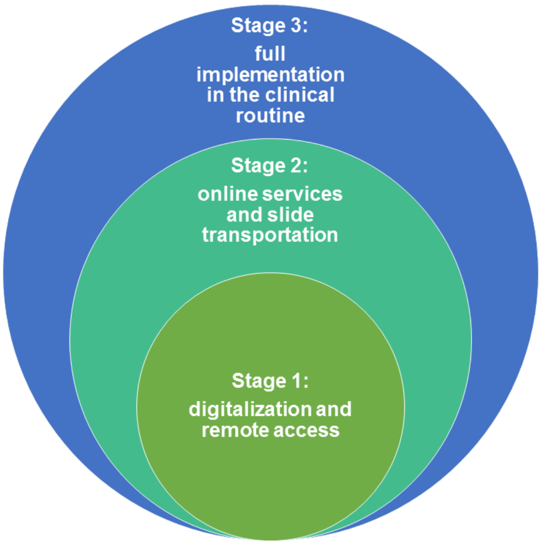

Figure 4.6.: Features of the different expansion stages

All of the mentioned stages have different, yet increasingly higher, technical requirements which but on the same time are increasing the number of features. The final expansion stage requires the highest level of accountability and failure safety due to the direct impact on patient data access and decision of treatment.
To be able to distinguish between the different stages a finer classification of the stages the following the results of the evaluation and modelling have been involved, resulting in the following points:

- Digitalization of slides,
- Remote visualization,
- Online request platform,
- Second opinion,
- Education and presentation,
- Embedding in clinical environment,
- Quantification of images.

To raise the informative value and ease up understanding a graphical representation in form of a radar chart has been chosen. Like this key features which have to be provided following the three stage model cab be identified and its success factors derived.

4.2.1. Stage 1: digitalization and remotely accessible digital slides

The first Milestone is providing digitalization that can be accessed later on from remote sites, such as a hospital. This step suggests the very basic implementation of slide hosting located within the SCIAN Lab. After deployment of the hardware in place the initial configuration of the machine software has to be set up to provide functionality. Since there are no multivendor-capabilities initially there is only one choice: utilizing the software shipped with the tissue scanner. Hamamatsu is shipping their software packages called NDP, consisting of different modules such as *NDP.serve*[37] and *NDP.view*[38].
The specimen itself should be anonymised through the first expansion stage to secure patient privacy. The specimen context is not involved or tracked during the process, therefore no fail safe measurements on mistaken identity have to be considered.

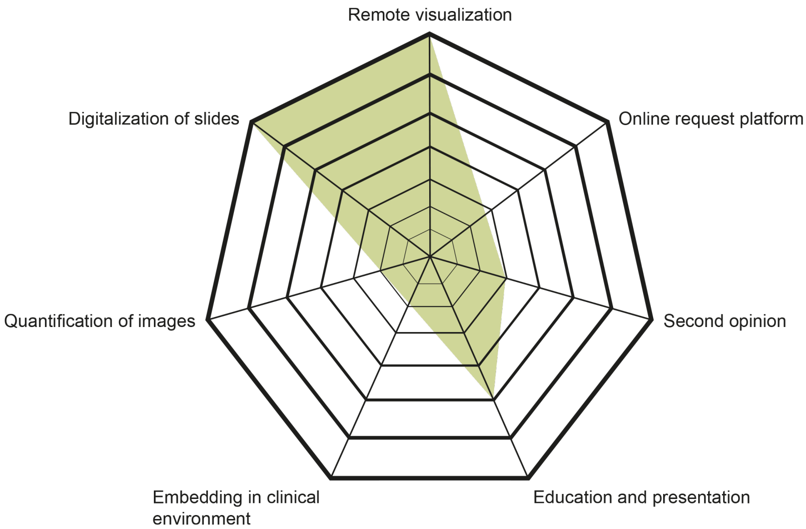

Figure 4.7.: Expansion stage 1 - digitalization and remote access

After a digitalization is complete the specimen should be made accessible via the web browser or the full-screen viewer. Furthermore as seen in figure 4.7 a second opinion can be simulated with forwarding a previously created user with the right permissions. However, the second opinion is not a definitive feature at this point in development. Additionally first educational purposes can be provided with live demonstrations of the viewing application. Thus there is no embedded teaching system underlying which is providing authoring tools.

[37] see http://www.hamamatsu.com/resources/pdf/sys/SBIS0065E02_NDPSERVE.pdf, accessed on 13.10.2014
[38] see http://www.hamamatsu.com/jp/en/U12388-01.html, accessed on 13.10.2014

The *NDP.serve* software application hosts digital slide images and makes them accessible via internal networks or the internet. The software comes with the basic functions of slide hosting and a basic access management systems that provides users, roles and groups. Different user types provide different permissions:

- General user - basic functionality: view slides, search images, change password and annotate slides
- Power user - same permissions as general user, but: adding files to server, attaching document, edit permissions of annotation/folders/files, see server status
- Administrative user - same permissions as power user, but: user management, group management, folder management, define custom user fields

To enable remote access the potential users (the pathologists or researchers) have to have a general user account with user-name and password, initially communicated with the SCIAN Lab. When supplying multiple institutions or multiple users from one institution groups can be included to ease up the file management and is essential for the data privacy of the patient and his specimen. This initial user setup has to be done by an administrative user from the SCIAN Lab. Power users may add new content delivered acquired the scanner so they are also situated within SCIAN Lab.

Type of computer	PC-AT compatibles
OS	Windows Server 2008 R2
CPU	Xeon 2.8 GHz or more
Memory	1 GB or more (More than 2 GB is recommended.)
Available HDD space	100 MB or more
Drive	CD-ROM or DVD-ROM Drive
Screen resolution	1024 × 768 or higher

Table 4.1.: System requirements of the NDP.serve software

The official requirements on NDP.serve such as shown on table 4.1 reveal that no high end machine is needed to provide functionality. Given the purpose of use for clinical use where multiple users are accessing the system simultaneously a maximum of efficiency can only be provided with higher specifications. Since the application relies on time critical streaming of the tiled images additionally a high bandwidth is recommended. This is true for both parts: hosting and viewing. The last mile plays an important role for the fluidity of the service. While this is not a problem in the SCIAN Lab, located on the university campus, this can be a problem on the remote sites. The SCIAN Lab is currently building a 10 Gbps network connecting the image acquisition and the NDP.serve component providing enough bandwidth to the service for many users simultaneously. The server can then be

accessed by internet and is heavily dependent on the last mile in the accessing institution. A bandwidth of constant 5 Mbps is recommended, while a higher rate offers more comfort when viewing slides. Since the server has relatively moderate hardware requirements it can be outsourced on a virtual machine within a server rack to greatly reduce hosting expenses.
NDP.view software is a dedicated viewer for .NDPI files that have been created with the Hamamatsu Nanozoomer slide scanners. The main features of the NDP.view software are:

- Opening digital slides (local file system / published with NDP.serve)
- Navigating on digital slides
- Viewing specimen on different magnifications
- Annotating the digital slide

With this functionality basic research can be conducted and live-presentations can be held. This covers the functionality outlined in chapter 4.2 sufficiently.
The viewer comes in two different solutions on being a full-screen viewer for windows, the other being a browser based solution, working on all latest browsers.

OS	Windows XP, Windows 7, Windows Server 2008 R2
CPU	1.2 GHz or faster
RAM	512 MB or larger
HD	20 GB or larger
Display	Direct X compatible

Table 4.2.: System requirements of the NDP.view software

The requirements for the viewing solutions are outlined in table 4.2 and do not challenge modern personal computers. However the same basic principle 'more is more' in terms of internet connection bandwidth and processing speed applies.

4.2.2. Stage 2: online service for digitalization and access

As seen in figure 4.8 the second stage involves a more advanced approach. Differing from the features outlined in chapter 4.2.1 the service is expanded now and slide ordering is now done via a web platform.

Authorized external users fill out a form specifying the need of processing for a single or a batch of slides on the online platform. Afterwards the process as described in figure 3.9 is triggered, the label as provided by the SCIAN Lab (a template for printing, printed with a special label printer) has to be applied on the slide for later identifying of the specimen. A special case regarding the amount of slides applies

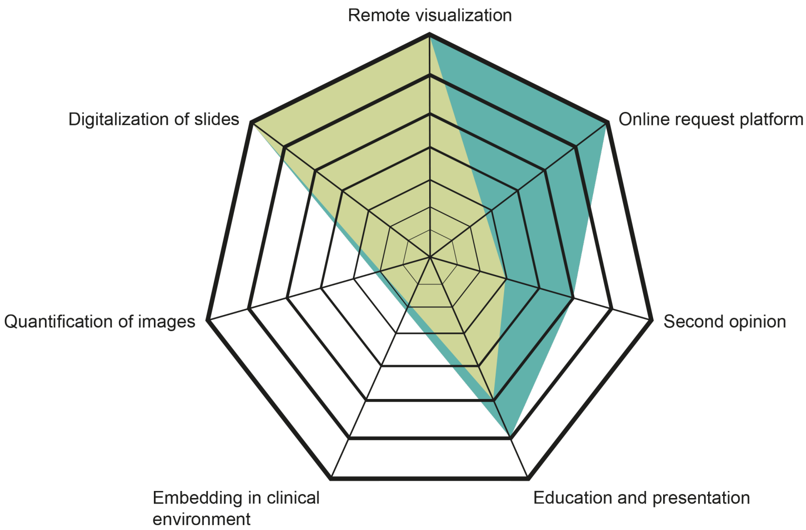

Figure 4.8.: Expansion stage 2 - online service for digitalization

if more than 10 slides per case are needed. In this case a transfer box which can several transport boxes is utilized. These measurements are conducted to minimize the chance of confusion and to uniquely connect one case as registered on the on-line platform (with the aid of an unique id) to one physical case. Patient data can hereby be neglected as just the parameters for the digitalization are needed to process the case. The raised coverage in education and presentation can be explained due to the fact that acquired material can now be selected more easily thanks to the online request platform. The second opinion section is raised, too because of the easier access to it, also owed to the online capability of the service. Transportation is executed by an external transportation company, which is collecting the filled boxes on a timed basis and then transferring them to the SCIAN Lab.
Once the slides arrived in the laboratory, the label (containing a bar-code) on the transport boxes is read by the bar-code reader attached to the scanner and the case is internally registered. Once this is done the status on the on-line portal has to be changed to 'in progress'. If there are errors occurring during the process a flag has to be set with the according slide information found within the case to enable the system to rescan the slide.
After the digitalization process the owner of the case (known by the user-name on the on-line portal) will get a notification about the progress, additionally the status of the case will be updated to 'completed' on the web interface. Together with the notification a link (URL) should be provided to access the case on-line via the web-browser or the full-screen viewer.

4.2.3. Stage 3: full implementation of digital pathology within clinic routine

Stage 3 represents the final goal for this project, the complete implementation of DP within the clinical process of making a diagnosis. Accordingly the highest coverage of features is aimed for, see figure 4.9.

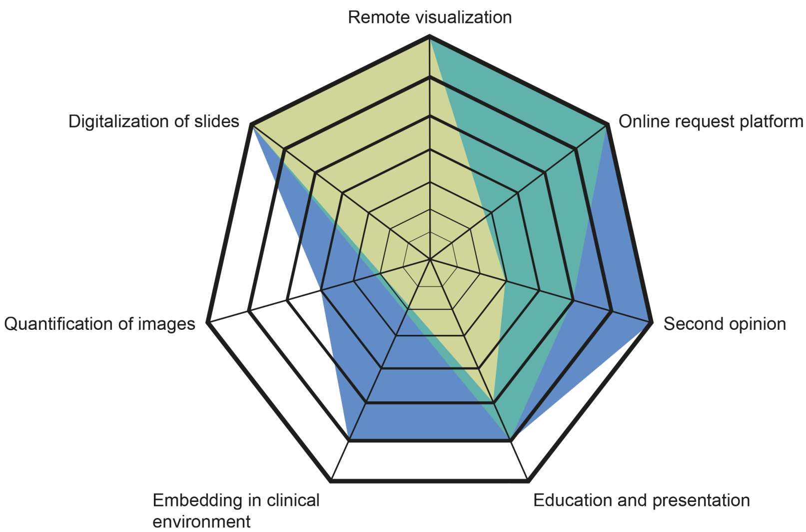

Figure 4.9.: Expansion stage 3 - implementation of DP in clinical environment

Since this stage involves the patient's history for the first time, confidentiality plays a superior role. The challenge upon this stage is the integration and exchange between the image material provided by the SCIAN Lab and the remote institutions patient data within their patient management system (PMS). To diagnose a patient's biopsy it is necessary to examine both the digital images and the patient's context. In the previous stage the focus was lying on tracking slides internally. For combining the two acquired informations of patient information and image it is necessary to bind these together. So far three ways of achieving this task have been thought of:

1. Attach file with patient's history to the image
2. Attach file with (or link to the) patient's images to the patient record in the remote institution
3. Attach file in DICOM format to the patient record

Possibility 1 makes use of the NDP.serve feature to add files on an image-folder. The platform where the parameters are set for the digitalization should offer a possibility to upload documents containing the patients' context, which then are added to the images via the NDP.serve mask by an administrator. The pathologist can then

access this files in case additional information is needed. The pathologist would be able to record his diagnosis as before on a dictating machine and afterwards the transcript could be added up onto the internal hospital patient record.
However there is no proof for the extraction function of the patient's data within the HIS (most likely it will vary from vendor to vendor), and the uploading of the file might be a violation of the law for patient data security which has to be investigated further before starting an implementation. The advantage of this approach lies within its easy implementation, no custom software development would be necessary and in-company training would be minimal. As a conclusion this case is not very promising because of regulatory issues and patient safety concerns.
The second possibility involves the acquired image being put onto the patient's health record. Since the original image would consume too much hard-drive space only a reference to the actual picture could be included in form of an URL. The link could then be followed to the NDP slide archive that holds the digitalized slide. Given the according permissions, the pathologist could view the slides belonging to the case finding a diagnose or share it, if needed, for an inter institutional second opinion to a remote pathologist. The challenge of this approach lies within the extensibility of the involved HIS. Since there is probably no field prepared for this information so far, this would necessitate a custom software change impacting on the HIS. The advantage of this methodology is that the image is still stored within the data-center of the SCIAN Lab, so that the infrastructure is not impaired by the transfer of the huge image files.
The final approach suggestion is taking advantage of the recent developments within the DICOM standard, specifically on the supplement 145. Pre conditional requirements are, that the institution has a PACS archive system which can hold and handle the enormous amount of data. To ensure patient data integrity DICOM comes with a multi-step hierarchy standard: each patient is assigned to a study (equalling a case in DP). Studies are containing time based images of the same modality, grouped into series. The study can be identified using the Study-Instance-UID and specimens via the Specimen-ID. This hierarchy enables the z-stacking of several images by defining studies. However, the DICOM conform protocols are not supported by the scanner and therefore need a reliable image re-encoding in order to work. Depending on the institution that wants to adapt this technology the investments may vary regarding the prior existence of the PACS. On the downside this approach holds probably the highest investment towards DP in both institutions (SCIAN Lab and remote institution). Additional modification of the acquired images is necessary as well as highly expensive transfer of images between institutions over the internet. This might arise discussion for security as well as quality issues regarding the image material.
In conclusion all three approaches might be possible and offer advantages. Ap-

proach 3 is the deepest integration possible within the external institution postulating that it has successfully implemented a PACS and is working with the DICOM standard already, which is yet to be proven. Also it requires the most dedication from both the external institution as well as the SCIAN Lab in terms of preparing the images, modify them and transfer them to the remote institution where they have to be stored. While this approach may offer the most potential when everything is well established, it seems that the second approach offers more start-up potential because of the less complex implementation and less impairments on the existing infrastructure.
Questions that remain are widespread and need to be considered before any of the implementations e.g.:

- Time of archiving
- Trade-off: compression <-> quality
- Failure safety
- Necessity for redundancy and quality of service
- Quality assurance and management

The *time of archiving* plays an important role due to the large file size of the images. One possible approach could be to distinguish between long and short term archiving, this would help to free resources and in the same time give a reference point for a billing model. Short-term archiving could be including storing of digital slides and all related files for up to 6 months. At the end of the 6 months period the owner of the case (which filled out the initial on-line form, or specified a contact person within the process) receives a notification stating that his lease for this set of images is expiring and that he has the option to renew the lease, switch to long term archiving or delete the images. Long term archiving might include less or timed availability owed to higher storage capacity modalities. This topic is only an issue as long as the image is remaining within the SCIAN Lab.
Another important question remaining is the one about the *trade-off between compression and quality*. While many papers and the response received from live demonstrations of the virtual slides for the pathologist resulted that the image quality is more than sufficient it is likely that it will change applying compression formats like JPEG or JPEG2000. This will impact all stated proposals for implementation and requires validation studies to ensure same diagnostic quality is provided when using DP under consideration of the compression.
Failure safety plays an important role throughout any of the proposals made. Since human failure can never be fully be debarred, the priority should be set to make this socio technical system failure tolerant. This can be achieved in various ways,

on process level one being that only one transfer box can be processed at a time. Another being the data model utilized when distributing the bar-code for one process can only be unique usable, ensuring the integrity of the data. Another integrity safety measurement is the bar-code read before the scanning process to verify the current batch of slides against the system that is expecting the case encoding. The slide scanners software has to have sufficient interfaces to verify that images are archived with the proper attributes.
Redundancy and quality of service is another topic worth emphasizing. To be able to offer the service in a sufficient quality to enrol in clinical practice a 100% reliability has to be guaranteed. This can be through redundancy of modules involved in the process. Due to limited resources this might will not be possible for key hardware elements like the slide scanner. Other components like the archive backup can be dealt with easier (but nevertheless immense costs), e.g. with RAID[39] arrays and incremental backup policy.
Finally *quality assurance and management* is an important topic to be discussed. Managing quality in a new process can be difficult and while the quality assurance on slides can be handled easier, quality management can be evaluated using things as KPIs collected while executing the process utilizing information systems which have to be implemented in according states of process. The need for this does not change no matter which approach is used. For further information on this topic please see chapter 4.5.

4.3. Monitoring and visualization

All the CSFs and KPIs gathered are useless without proper management. This includes frequent actualization as well as appropriate visualization to all persons involved to identify drawbacks and being able to respond accordingly. To further extract useful KPIs a review process should be established, evaluating the KPIs with highest information or changing rates. This will help to set the direction towards a consistent growth of productivity while simultaneously utilizing the equipment to the highest grades possible.
In order to gather the KPIs a framework, consisting of different collecting modalities, should be established. To monitor the process later on it is necessary to develop an information system (IS) and subsequently a data warehouse within, where all information is gathered and managed. The actuality factor arises the need for automated process measurement. Once all data is gathered a proper tool is needed to provide a decision-making ability. For this purpose [Kaplan & Norton 2007] sug-

[39]Redundant Array of Independent Discs

gests the Balanced Scorecard in which the comparison between monetary- and non-monetary values is made. Similarly to the data acquisition through the KPIs mentioned before, Kaplan and Norton are suggesting four perspectives:

1. Financial perspective - "how do we look to our shareholders?"

2. Customer perspective - "how do our customers see us?"

3. Internal process perspective - "how well is the business running?"

4. Learning and growth perspective - "how can we create and improve value?"

All these perspectives add up to the projects strategy. Within the goals target values have to be set and periodically evaluated to be able to determine the level of success or failure. Following [Kaplan & Norton 2007] ideally a strategy should consist of not more than 4 strategic goals to achieve, otherwise focus gets lost and progress is impaired. Additionally visualization can increase the employee's motivation when visualized clear and easy to understand.

4.4. Critical Success Factors

Since resources in a project like this are limited, identification of Critical success factors (CSFs) are crucial to the projects development and success. As described in chapter 2.7.3 a classification into strategic success factors (SSF) and operational success factors (OSF) has been conducted. The CSFs have been derived from a variety of sources including general guidelines (following [Pinto & Slevin 1987]) to more specific execution strategies (following [Saaty 1990]). The CSFs then have been preselected and aligned with the projects variables to achieve highest possible relevance.

Strategic Success Factors	
	Internal
	1) Architecture concept
	2) Funding concept
	3) Personnel Development concept
	4) Knowledge management concept
	5) Efficient distribution channels
	External
	1) Service quality
	2) Customer orientation
	3) Support from the scanner vendor (replacement parts, software updates)
	4) Regulatory situation (legislation)

Table 4.3.: Strategic success factors (SSF)

The SSFs as shown in table 4.3 set the stage for the whole project to be realized. Without all of these factors checked the project will fail immediately at the start or after relatively short time after implementation. The present factors can be subdivided further into internal- and external success factors. Internal SSFs build up the core elements to succeed with the project. Essential is a well elaborated architecture concept, which is provided with this thesis is setting up the ground on which the project can be pursued. Having an architecture concept helps keeping the overview on a multi layered project like this and in the same time enables enhancements to be integrated in the already established model without running into uncontrolled growth. However, important is the refreshing period of the modelling process which has to be determined during the projects development. Building up on the architectural concept the funding concept should be established, ensuring a sustainable and sufficient funding. While the cost during business might decrease over time because of a higher efficiency, a high initial commitment is necessary to get the services up and running (for further explanation please see chapter 4.5). Once the service is up and running a fair amount of resources should also go into personnel development. This is important because the operating costs strongly depend on personnel involved in maintaining and operating the device. While the initial installation of the service might require professionals, a skilled worker could be responsible for the operating the system later on. Workshops might be necessary to increase familiarity with the system and will lower overall expenses for maintenance. Due to the fact that changing personal will be involved with the equipment and process a knowledge management concept has to be established to secure the experience and knowledge won during operation. This concept should involve questions dealing with organizational memory (acquisition), -knowledge (knowledge databases) and -learning (Wiki-systems). Lastly efficient distribution channels should increase customer satisfaction to expand and increase revenue stream.
External SSFs are critical to the projects implementation, thus cannot be influenced directly. The regulatory situation plays an important role once the project is rolled out within the medical environment. So far there are no restrictions towards where to practise pathology. However this can change rapidly as the government and societies are learning about the new technology and its possibilities. While this is a potential threat to the project it is also a chance for a regulated implementation once the process is established. Customer orientation implies that the project is strongly dependant on the customer's grace. If there are developments towards a new modality the funding concept can be brought into serious trouble and therefore the customer's satisfaction and tendency have to be monitored closely. The last SSF is concerning the vendor support on which the project is dependant in perpetuity since wear off parts will be needed over time. In this regard a maintenance agreement would be beneficial.

Even though SSFs set the frame for the project, when it comes down to business OSFs are coming more and more into play as there are critical factors for the different stages of the project which were described in chapter 4.2.

Operational Success Factors	
	Stage 1 – digitalization and remote access
	1) Scanner initial setup delivers sufficient quality
	2) Enough hard disk space to handle the initial requests
	3) User-management concept is implemented
	4) Tracking of faulty slides to enable rescanning
	5) Access on digital slide archive is possible
	Stage 2 – on-line services and slide transportation
	1) Online platform is reachable (keyword: quality of service)
	2) Data model supports communication between slide scanner and online platform
	Stage 3 – full implementation in the clinical routine
	1) Connection between case in the external institution and SCIAN Lab is fail safe
	2) Transmissions are sufficiently encrypted
	3) Data is sufficiently secured
	4) Quality assurance

Table 4.4.: Operational success factors (OSF)

As described earlier OSFs are dealing with the operational level of the project. The allocation of different levels arises the composition of different aspects dependant on the expansion stage the project is currently in. It was pointed out before that the stages have increasingly higher requirements towards security and privacy this explains the division into the three stages for the OSFs.

With *stage 1* offering the very basic functions that the slide scanner is providing the OSFs are reasonably to achieve. Of course the scanner has been assembled and tested prior shipping through the manufacturer, nevertheless it is necessary that the image quality that the scanner is delivered with is sufficient for the purpose (1)). Number 2) is dependent on the local structural conditions which is allowing the scanner to deposit the images acquired on some kind of storage media, which is sufficient to handle the scanners batch functionalities (Nanozoomer XR can process up to 320 slides in one batch). Concerning 3) User-management is an important as it is possible to access the digital slide archive via the internet. Roles (as described in chapter 4.2.1) have to be defined in order to restrict access and avoid inconsistencies. The tracking of slides as mentioned in 4) is not as important in later stages as there is no patient information involved in the process yet, but there is another reason concerning quality issues. The tracking mechanism is part of the scanner management system but to ensure quality it cannot be relied on completely. Finally the remote access is picked out as central topic and while accessing a slide archive only from the Intranet is more feasible, the access from the internet holds up more challenging threats in terms of firewalls and encrypted connections. Nevertheless the slide archive has to be accessible from outside in order to deliver the service as there are primarily external institutions involved.

Stage 2 takes into consideration the on-line platform which allows to order digitalized slides with certain attributes such as magnification or quantification. Involving another dimension, as described in 1), to the service is also adding up OSFs to the table. The platform has to have a 100% availability for customers to order, this has to be thought of when choosing a host provider for the platform, cost should play an inferior role compared to availability. Targeting on the long term a high level of automation on-line platform should offer interfaces to interact with the slide scanner to avoid lengthy manual configuration process for e.g. defining folders and user rights via exchange formats. Therefore a data model should be designed to be able to interchangeably communicate between the two components.
Stage 3 states points that could be classified as external factors that cannot be influenced and are the hardest to provide. Simultaneously it is necessary to provide these features reliably to enable implementation into clinical routine. 1) states that physical connection between the institutions has to be fail safe, so in case there is a loss of connection there is redundancy to absorb losses. 2) describes the requirements of the connection between end points which has to be sufficiently encrypted most likely with end-to-end encryption methods. The data itself should be sufficiently secured, this involves the physical access as well as the access over network, restricted through firewalls as well as restrictive user management and isolated physical storage of the image files.

OSFs are highly dependent on the SSFs in this pioneer project as the service can only be delivered when all the aspects are full filled. The combination of the two (OSF, SSF) factor types are complementing the superscript of CSF. The finer differentiation allows a more detailed analysis of the projects chances to be successful.

4.5. Key Performance Indicators

KPIs as previously described in chapter 2.7.4 which are enabling performance monitoring and, according to the shortcomings, improvements. However there are some guidelines to ensure usability of the correspondent KPIs like comparability, comprehensibility and actuality. While the first two points depend on the management decision of defining the KPI, the last one is actually dependant on the modality of reporting. Most likely there is an information system necessary to collect the requested parameters and monitor the KPI accordingly.
For establishing possible KPIs an analytic point of view has to be taken. Thanks to the business process model which has been done earlier this process has been straight forward. The KPIs found have been grouped for clarity issues into four different main areas:

- Internal process quality (operational performance)
- Customer perspective
- Employee perspective
- Financial Performance

These four areas cover the main fields on which the project is based. According to the situation a weight can be given to prioritize the elements according to the need the company has at any given point in time. The KPIs themselves can be further classified into simple and complex KPIs. Simple KPIs being measurements that can be measured directly, for example the time for doing an action. Complex KPIs are often consisting of two or more KPIs put together in a certain way. Like this more complex circumstances or dependencies can be benchmarked. These KPIs enable a company to be comparable to other, similarly working institutions.

Internal process quality (=operational performance)	**Key Performance Indicators**
	1) Time of the configuration process (slide arrival ➔ scanner ready)
	2) Time of the scanning process
	3) Time from finished scanning process ➔ image accessible in archive
	4) Time per slide digitalization
	5) Amount of customer complaints
	6) Amount of finished cases
	7) Amount of finished digitalizations
	8) Amount of rescanned slides
	9) Amount of scanned slides per hour (day, week, …)
	Complex Key Performance Indicators
	1) Delivery in full on time (DIFOT) rate
	2) Earned Value (EV)
	3) Overall equipment effectiveness (OEE)
	4) Process or machine downtime level
	5) Quality index (QI)

Table 4.5.: Indicators of internal process quality

Internal process quality (figure 4.5) is the first area of focus describing the maturity of the process on an internal level. Starting off with the simple KPIs the numbers 1) to 3), are dealing with the time consumption of different sub processes. Since operational costs are increased with higher throughput times they should be ideally minimized. The development will start with a relatively high value but then should be monotonically decreasing as experience with the equipment is increasing until a productivity limit is hit, where only technical improvements can decrease throughput time significantly. The three figures can be added up to indicate a more complex indicator: the complete processing time for a slide. The finer distinction enables us to identify processes which may have more potential for time reduction than others. Number 4) is monitoring the complaints of customers as cases may have been interchanged and can therefore not be processed further or other impairments to the service occurred. This KPI shows how failsafe the process is. Given a proper tracking system, a strictly monotonically decreasing should be targeted. The goal is a reduction of customer complaints on 0. Small changes to the process might increase initially the rate of complaints due to errors, but long term evolution should also be declining. Not only is a mix up of slides a potential cause for complaints: evident from the BPMN other sources of complaints are emerging, such as transport problems with broken slides or misleadingly deletion of files within the digital slide archive. The amount of rescanned slides as shown in number 5) is an indicator for the scanner configuration quality, which is contributing to the process quality. Rescans might occur due to out-of-focus areas and refer to a faulty scanner configuration, other sources for the need of rescanning are varied, one being that the batch processing might be impaired or proper slide tracking cannot be guaranteed. Another throughput indicator is the quantity of slides scanned over a certain period of time, giving information about productivity. Reading this figure enables comparison to other times when the process was conducted disregarding the time needed to process the slides. The tendency should be a steady increase up to a limitation level where the scanner is fully utilised. Supported partially by the simple KPIs the complex KPIs for the internal process quality are derived. Starting off with the *delivered in-full, on-time (DIFOT)* rate is measuring the delivery performance in supply chains from the viewpoint of the customer [Jodlbauer 2008]. In other words this KPI is measuring how often the customer gets what he wants, when he wants it, expressed by the following formula:

$$S = \frac{n_{\text{on time}}}{n} \tag{4.1}$$

where:

S	–	supplier's reliability,
n	–	orders,
$n_{\text{on time}}$	–	orders delivered on time.

Because this project is designed as a contract manufacturer a high DIFOT rate is desirable, which is conflictual with other variables such as a low rate of inventory supplies. The rate itself should increase during time the process is established, ideally to a 100% rate.

Nr. 2) is a KPI originating from the project controlling is the *earned value (EV)* analysis. The method itself utilizes cost, value and schedule. It supports direct measuring in any currency or other metrics available.

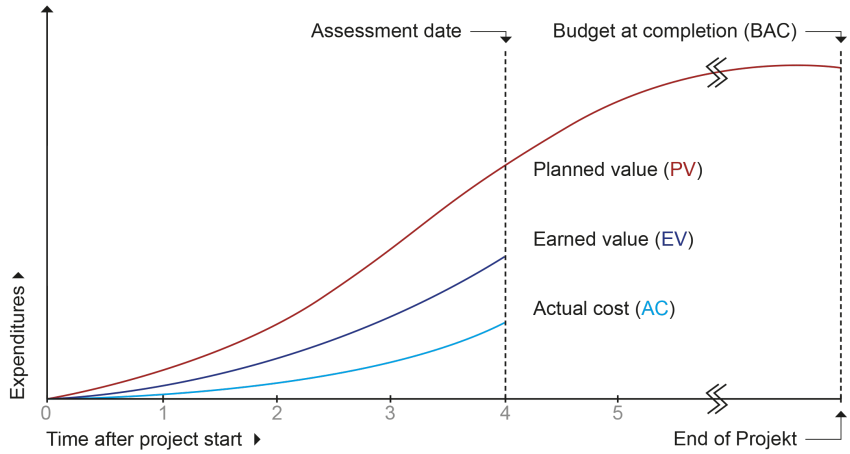

Figure 4.10.: Earned-Value-Graph following [Drews Günter 2007]

The key components of the analysis are the planned value (PV), budget at completion (BAC), actual cost (AC) and the earned value (EV) itself. This method is particularly useful outlined by [Anbari 2003] because it is providing many information about:

- Scheduling situation of the project
- Budget situation
- How efficiently funds are used
- How efficiently time is used
- What the total cost of the project will be
- How big is the cost variance in the end of the project

Problems with this methodology can be over- or under-estimation of investment as well as future problems that are not yet revealed. A common misconception is also the final 10% of a projects value which takes up to 40% development time.
Number 3) *overall equipment effectiveness (OEE)* is the next, more technically oriented KPI focussed on productivity. Based on the fact that machines (in this case the slide scanner) can never run on 100% efficiency basic categorizations on deficiency areas are conducted. The main objective of an OEE calculation is to increase productivity while reducing cost, identifying the equipment's potential and opportunities. According to [Stamatis 2010] the six big losses in equipment are:

1. Breakdowns
2. Setup/adjustments
3. Idle/stops
4. Reduced speed
5. Scrap
6. Start-up yield

Taking these losses into consideration an OEE rate around 85% is considered an ideal trade-off between quality and performance. [Pomorski 1997] suggests the following formula to calculate the OEE:

$$OEE = (A) * (PE) * (RQ) \tag{4.2}$$

where:

OEE	–	overall equipment effectiveness,
A	–	availability,
PE	–	performance efficiency,
RQ	–	rate of quality.

Where availability itself is defined as:

$$\text{Availability} = \frac{\text{Operating Time}}{\text{Net Available Time}} \tag{4.3}$$

Performance efficiency is defined as:

$$\text{Performance efficiency} = \frac{\text{Actual output}}{\text{Operating time}} \tag{4.4}$$

And rate of quality is defined as:

$$\text{Rate of quality} = \frac{\text{Good output}}{\text{Actual output}} \tag{4.5}$$

Measuring the OEE alone does not benefit the institution, the important thing is to link the sources of the previously mentioned six big losses. The acquired targets can then be specifically addressed to be improved and increase the OEE onto a certain limit, e.g. 85%.

Number 4) is suggesting to measure the process or machine downtime level following a simple rule: once a machine is not working or producing anything no money is made. Therefore the downtime level seems to be a reasonable start when thinking about how to optimize productivity calculating a ratio using the formula following [Marr 2011]:

$$\text{Downtime level} = \frac{\text{TA (t)}}{\text{PPT (t)}} * 100 \tag{4.6}$$

where:
TA (t) – actual productive time in a period t,
PPT (t) – planned productive time in a period t.

The downtime level should be minimized in order to provide ideal productivity. Taking into consideration planned and unplanned drop outs after some time the process is established a plateau will be reached where no further decrease of the downtime level will be possible. Additional to the expenses for maintaining the machines the labour cost for the employees cannot be neglected as they are paid, even though the machine might not be running.
The last multi-item measure is the *quality index (QI)* borrowed from the quality assurance, which is combining operational- and service-quality including metrics like first pass yield (FPY) and defect rates [Marr 2011]. FPY establishes a ratio indicating in how many cases corrections or reworks were necessary during the first time digitalizing the slides. The ideal case would be that no reworks are necessary and all slides will pass without problems to be examined by the pathologist.
Summing up the section of internal process quality is measuring performance on every aspect related to this project. Neglected is hereby the diagnostic performance, since this is not within the scope of this project. While the simple KPIs provide better comprehensibility, the complex KPIs are more suited for visual representation for the employee, motivating him for better results within the range of the technical limitations. The complex KPIs generate a more meaningful conclusion which can help to make managing decisions on the (technical) operational tier.

The following section is dealing with the important topic of customer satisfaction (see figure 4.6) which the service is providing, not focussing on acquisition of customers but on keeping them.
Starting off with the simple KPIs, the first KPI is tracking the number of incoming slides in a given time period, valuable to extract trends like seasonal oscillations. Furthermore it is giving a basis for ratios to be calculated for other KPIs. Generally a rising number is desirable.

Customer perspective	Key Performance Indicators
	1) Amount of incoming slides per day / week
	2) Amount of failed scans per day / week
	3) Amount of slides in short-term archive
	4) Amount of slides in long-term archive
	5) Amount of requests for a second opionion user
	6) Amount of broken slides during sending
	7) Customer complaints
	8) Customer reclamation
	Complex Key Performance Indicators
	1) Customer Lifetime Value (CSV)
	2) Customer Satisfaction Index (CSI)

Table 4.6.: Indicators of customer perspective

Number 2) is monitoring the failed scans (out of focus areas or non-assignable) due to a faulty scanner setup or other factors. Besides measuring the general performance of the scanner, this can lead towards a relational calculation together with 7) and 8) which are explained later. The development of this variable should be steadily decreasing towards 0. 3) and 4) are evaluated to track the consumption of necessary storage, it is revealing also the customers intentions for how long they are planning on using the service. This KPI can also give a certain amount of planning reliability once the service is established a few months taking into consideration the growing catchment area over time. Naturally an increasing number is desirable, but comparing the two figures a fixed ratio can be derived on how much space will be necessary in a future time period.
Continuing with number 5) this KPI is a measurement for acceptance of the second opinion. Registered users request another user for second opinion to access the acquired material. The second opinion is usually practised inter-institutional and can be of an international scale.
Number 6) is dealing with the performance of the transport company. A high number indicates a rough treatment to the goods that they are carrying. Since this is verifiable relatively easy (comparing data from online-platform and actual present slides) and in the same time is very important for customer satisfaction a high priority should lie on monitoring this KPI.
KPI 7) is broaching the issue of actual customer complaints. A high amount of complaints indicates a low customer satisfaction and accordingly a shrinking customer loyalty. Especially at the start this should be avoided at any cost to not threat the projects sustainable development. Nevertheless it will not be possible to push the number to 0, but learning from the complaints and make adjustments to provide better service should be targeted.
The last KPI 8) is bringing up the topic of reclamations. Setting apart to complaints

reclamations are less severe, but bringing the provider into need for action to deliver the desired service quality. When combining this indicator with 7) a tolerance limit can be established for the customer, by finding out how many reclamations will be necessary before a complaint is raised.
Moving on to the more complex indicators and starting off with 1) Customer Lifetime Value (CLV). Borrowed from marketing this value is expressing the value of a customer within a number. This is important when thinking about strategic adjustment in customer development. CLV is calculated according to [Berger & Nasr 1998], neglecting the marketing cost part, which is not applying to this project due to the exclusivity of the service in Chile given the following formula:

$$CLV = \{GC * \sum_{i=0}^{n}[r^i/(1+d)^i]\} \tag{4.7}$$

where:

CLV	–	Customer Lifetime Value,
GC	–	gross contribution margin (p. c.),
n	–	length of cash flow projection,
r	–	annual retention rate,
d	–	annual discount rate.

It is possible to determine the worship of one customer, which can then be, once a customer is not utilizing the service any more, expressed in monetary loss. For this reason the risk for losing customers should be minimized splitting the value onto multiple customers. Like this huge financial breakdowns can be prohibited.
The *Customer Satisfaction Index (CSI)* (2)) is the next indicator visualizing the customers alignment towards the provided service. [Fornell 1992] first showed the first satisfaction barometer in 1992.

Seen in figure 4.11 is the closed loop of the customer's satisfaction, whereas the customers' expectations (which have been elaborated during the project) build up the source. They lead, together with the positively correlated perceived performance towards the satisfaction level, which then results in complaints and eventually loyalty towards the service provider. A high satisfaction is the cause for declining complaints and will in the same time rise loyalty, which is then raising the CSV as described earlier.

The following KPIs are centred on the employees involved in the process reclining to the field of human resource management. Number 1) is an indicator related to the complexity of the process itself. Generally the vocational adjustment time for new employees should be on a steadily declining level until a global minimum is

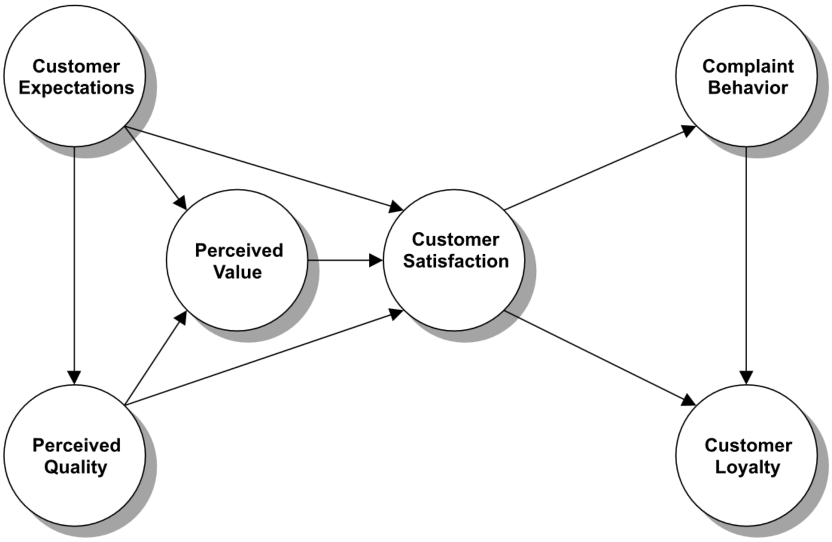

Figure 4.11.: Influences on customer satisfaction, following [Fornell 1992]

Employee perspective	
	Key Performance Indicators
	1) Period of vocational adjustment for new employees
	2) Man-days necessary for maintenance
	3) Administrative effort
	Complex Key Performance Indicators
	1) Workload per employee
	2) Employee satisfaction
	3) Employee engagement level

Table 4.7.: Indicators of employee satisfaction

reached, which is inflicted due to the technical limitations. To reduce operating cost there should be a shift downwards in qualification from an expert technician towards a skilled engineering worker if possible.
Subsequently the next indicator (2)) should be treated, starting with no experience with the technical environment, the maintenance time will be significantly higher than after several circles of maintenance. The man-day value will most likely rise, whenever changes to the system are made or new employees are hired. Good knowledge management should keep the variation between employees on an overall low level.
The last of the simple KPIs is dealing with the administrative effort (3)), also regarding the on-line services in expansion stage 2 as described in chapter 4.2.2. Given that there is a range of customers requesting digitalisations the administrative effort will rise, mostly through tasks like the attribution of images and server maintenance. This problem can be avoided through automation but never completely eradicated. More employees have to be allocated once the service has a certain popularity,

resulting in an instant jump in values. Overall a declining tendency resulting in a minimum level should be aimed for.
This section is dedicated to the complex KPIs related to the employee, first one being the *workload per employee* (1)). This indicator deals with the strain of individuals involved in the process that is going to be implemented. It is common sense that a high workload over a long period of time is contra-productive so an optimal measure should be found. After the service has been deployed and more and more customers are requesting it, it might be appropriate to think about load balancing the work, maybe recruiting more persons. Since every employee is different and every work differs in subjective strain, [Boff et al., 1994] suggests a selection of measurement methods according to certain workload criteria, such as:

- Sensitivity
- Diagnosticity
- Intrusiveness
- Implementation requirements
- Operator acceptance

This KPI is most likely to change during the different phases of the process maturity and should, after an adaptation phase, remain steady. The allocation per employee results up on the subjectivity.
Employee satisfaction is directly related to the workload of an employee, given the right combination a synergy between workload and satisfaction can be achieved resulting in an overall higher productivity. Not only is productivity dependant on the satisfaction but also the service quality stated by [Atkins et al., 1995]. Maintaining a high level of satisfaction is therefore improving the profitability of the service while providing a higher quality and in the end more long term customers. A close and actual monitoring should be kept to optimize this variable. This indicator, together with the CSI is building up a very high priority to monitor and adjust.
The last indicator of employee engagement level holds an ambiguous identifier. In literature many definitions are used simultaneously, yet [Robertson & Cooper 2010] defined this term accordingly: "a positive attitude held by the employee towards the organization and its value. An engaged employee is aware of business context, and works with colleagues to improve performance within the job for the benefit of the organization. [...]". To create a psychological state like this many strategies mentioned by [Kompaso & Sridevi 2010] seem to be suited, which states that providing

- two-way communication,
- satisfactory opportunities,
- everything employees need for doing their job,
- appropriate training,
- feedback system,
- ...

are key elements for a high level of engagement.
To conclude this section it must be mentioned that the part of employee satisfaction often gets neglected and instead the customer's satisfaction is foregrounded. Certainly customer satisfaction is the key factor for sustainable success, the employees are too since they will rise the customers satisfaction when delivering higher quality work which they are trained for. Especially in this projects area technical expertise is needed and should not be reduced to pressing buttons not knowing which processes are underlying.

Financial performance	**Key Performance Indicators**
	1) Cost per slide
	Complex Key Performance Indicators
	1) Return on Investment (ROI)
	2) Marginal utility
	3) Revenue per employee (RPE)

Table 4.8.: Indicators of financial performance

After dealing with the employees' performance finally the financial indicators have to be discussed. The most important KPI is the total cost of a digitalized slide. This depends on many factors. The process has to have reached a certain level of maturity to provide efficient procedures. Also the employee does need the practical skill to usr a minimum amount of time for configuration or other processing of the slide, which is also related to the previous section, e.g. employee engagement. All this determines the invest of the SCIAN Lab to produce a digital slide, respectively it is dictating a minimum price to be asked to demanding remote institution. While the primarily goal lies more on a sustainable continuous execution of the service than on pure profit, this indicator still has to be kept closely in mind.
The complex indicators of this category are introduced with a classical figure *Return on Investment (ROI)*. This allows the calculation of how much benefit is resulting from a certain investment. The ROI is calculated as follows:

$$ROI = \frac{\text{Net profit}}{\text{Investment}} * 100 \tag{4.8}$$

The development of this figure should be rising over time. The RoI is often used when it comes to budgeting a new investment and the danger persists that the initial RoI might not be tempting to do the investment from a sponsor point of view [Phillips 1997]. These doubts can be encountered with a simple, economical and credible RoI process.
2) complex KPI is the marginal utility. Like every technical system the slide scanner has limitations when it comes to productivity which cannot be overcome. Naturally productivity should increase given more resources, but given the specifications of the scanner, which can process up to 320 slides in one batch, each slide has a scan-time of around 30 seconds, this implies the limitations. Even more slides to process or more people preparing the slide attribution will not overcome this bottleneck [Rittenberg & Tregarthen 2009].
The following indicator (3)) is bringing the employee in relation to the revenue stream. The *revenue per employee (RPE)* regards to the sales of a company and is calculated as:

$$RPE = \frac{\text{Revenue}}{\text{numbers of employees}} \tag{4.9}$$

The ratio is particularly useful when comparing to other providers which are offering the same services. Though this might seem not useful at first, it can be valuable to estimate the value of one employee to justify further investment towards the service (especially in the university area). This KPI is also connected to the productivity as a high RPE suggests a higher productivity [Fitz-enz 2000].

5. Discussion

The approach utilized in this project was not new in its components but in the composition. Methods of the HCI were combined with methods of empirical research such as questionnaires and contextual inquiry. This project shows one possible approach to an interdisciplinary project and even though the focus lied within theoretical aspects, it can show a high relevance to the actual on-site implementation. But the used methodologies are not without flaw and these will be discussed within this chapter.

5.1. Participant observation

The participant observation is a controversial topic, it was necessary to observe several pathologists within their work environment which made the process very time consuming and sometimes hard to schedule because the doctor's observation period was limited. Through the form of the 'overt' PO another problem arouse: the observer effect which was indeed hard to reduce. People knew they were under observation and were accordingly changing their behaviour, they often asked questions within the process of the observation which distorted it, even after instructional explanation. This led to a biased result in terms of utilized time for certain actions. Another problem was the amount of incomplete information: while the pathologist was within his work routine, the observer can have difficulties to comprehend why a certain action has been taken. This has to be noted until the final discussion takes place and maybe the observed pathologist forgot the context of the action. In addition not many emergency case situations (so called intra operational frozen sections) could be observed. Given the case of frozen biopsy, only in one of the three covered institutions, where a pathologist was observed, a case like this could be witnessed. Another factor which is impaired is the subjectivity of the participant as well as the observer. This factor was tried to overcome with observing in multiple institutions, yet cannot be completely eradicated since only one person conducted the research. Generally speaking the methodology of the PO is suited very well for the initial research within a new field, without much preparation a lot of information about the workflow can be gathered in short time. The PO should be used only to a limited extent because after visiting two institutions processes repeated and efficiency was lowered, the process then could then already be abstracted to establish the models. Nevertheless the PO pointed out a rough sketch on how to narrow down this project. Though the possibilities for a bias seems to be very wide spread and cannot be neglected, therefore, as done in this case, a combination with other methodologies should be chosen and awareness managed to achieve the best possible result.

5.2. Modelling

While models offer advantages like the simulation of certain scenarios or the rapid process of changing certain components, there are some downsides to be mentioned. Models are always working with a certain point of abstraction, which makes it hard to establish a model for different point of views. According to the preconditions the right modelling technique as well as tools have to be selected. Utilizing the classification mentioned in chapter 2.7 a low level of process maturity is reached since the planning had just begun. A focus more specialized on the core processes is needed and should be sufficiently covered with the utilized modelling techniques. Any kind of modelling can help planning to increase effectiveness and efficiency even before the process is established, once the right tool to do so is selected.

5.2.1. BPMN

The BPMN is offering a structured approach that is capable of a process based modelling interacting between humans as well as machines. Additionally inter-institutional modelling is offered with the pool structure in a set structure of objects and constraints. Another benefit of the BPMN is its readability, all participants of the project could, after a fairly short period of vocational adjustment, read the model and add to it if there was a shortcoming. Overall a very good function of representation is provided with the BPMN. Though the capabilities to model any kind of processes found in a company are very good, there are some downsides: since the BPMN was developed for bridging the gap between customers and developers, some aspects may stay unrevealed when working on the technical side, such as transport protocols, data models and output forms. Luckily these information can be supplemented with auxiliary notes that have no impact to the process itself.
Overall the BPMN offers a very good entry point for modelling processes compared to other modelling approaches like UML, flow charts or Event-driven process chains. The functionality coming with the BPMN, like token simulation is valuable

when the process maturity is more progressed (after the first implementation) and more estimations can be made.

5.2.2. 3LGM^2

The 3LGM^2 proved to be a controversial approach. With its newest scientific publication in 2010 its relevance can of course be questioned. Many authors claim that the functionality is compromised by the limited amounts of objects that can be used and the few locations it is utilized (University of Heidelberg and University of Leipzig) are compromising its relevance. As a matter of fact the 3LGM^2 operates on the underlying an outdated UML schema of 2003[40]. However the capabilities to display business processes are also limited since the domain layer which accommodates the enterprise functions is not capable of decision support such as gateways in the BPMN. The functions themselves can be modelled extensible in terms of structure, functions and the representation form. It is possible to display a sequence of actions or objects but the readability of the notation is suffering. Generally lots of the documentation is hidden not to be seen when looking on the model from a distance. The amount of detail that can go into a model like this is limitless. The separation between the layers is reasonable and also for non-technicians relatively easy understandable. In terms of usability the 3LGM^2 tool-kit needs an overhaul. The ravages of time are clearly visible. A definitive benefit of the 3LGM^2 is the availability to define inter-layer dependencies which visualize in a nice way how a complex IT-infrastructure has to be implemented and configured. No question, the 3LGM^2 is far from being perfect, and the limitations on the domain level prevent this methodology from progressing, but the primarily use case: to display IT-infrastructures with dependencies, offering a wide variety of communication models (including Health Level 7 (HL7)) is fulfilled. Possibilities like the high amount of customization are overwhelming new users easily. But used in combination with the BPMN this can be a good approach for planning an IT- system like this.

5.3. Questionnaires

This presents probably the most classical approach for data acquisition utilized in this project. The goal was to elaborate general facts about the pathologists work as well as estimations for the future in their work, which is most likely becoming more and more digital.

[40]see http://www.clinfowiki.org/wiki/index.php/Three-layer_graph-based_model, accessed 07.10.2014

In this case the paper-based questionnaires were prepared which were translated later on in a digital accessible form for portability. Since the literature shows highly differentiated opinions, this was still the way to go for finding out how pathologists in Chile are embracing DP.
Based on the answer quantitative statistics could be conducted which lead towards a valid and reliable scientific result. The disadvantages of this methodology like a high failure ratio (e.g. participants do not respond) and a high likelihood of external influences are partially eradicated through the execution of the study. Consequently the positive arguments of questionnaires, like clear structured answers, more honest answers and the avoidance of interview mistakes, are outbalancing the weaknesses. Problems arose during the requirement analysis questionnaire when circumstances of the case have not been verbalized clearly enough previously (impacted by the language barrier) or the allocation of the values (e.g. the distinction: high to very high) has not been understood in the sense of the creator. These problems have been tried to overcome through an iterative process to refine the questions with test persons familiar in the field. To ensure data quality the following aspects have been revised and applied to the highest, within this project possible, extent:

- Ensuring quality factors (objectivity, reliability, validity, ...)
- Ensuring the qualification of the participants (only pathologists were asked)
- Ensuring compliance to rules (Data security, avoid threats to personal integrity)

The problems involving the error of central tendency or error of extreme tendency can naturally not be completely barred from the study. Also the acquiescence tendency is not neglected but can neither be eliminated.

5.4. Solution concept

This approach of identifying key success factors and prioritizing them is following on methodologies of different agile project management methods, e.g. PRINCE 2 and Scrum. The structuring into several expansion stages offers a finer subdivision of requirements reducing complexity of the project. Similarly to the Scrum methodology the milestones or expansion stages can be seen as sprints, which differ from the original agile method by increasing in length of a sprint. The adaptation of agile methods in project management can be highly beneficial in terms of change management, due to shorter development cycles and, according to the expansion stage, changing context and involved personnel. Requirements may change rapidly during the development process and a fast adaptation is necessary to ensure to meet them all. A positive side on this fast adaptation is the relatively rare need for changes post development. Though agile methods might be suited, it is recommended establish a process model on how to react upon changes during the development process, securing a documented change-log. The project which is broken up into smaller bits can then be processed by focus groups iteratively providing more and more functionality as they progress. Simultaneously the time to market for the service will be reduced thanks to the intermediate steps in form of expansion stages. Similar to the PRINCE 2[41] method, every stage has its own recommended actions derived from the CFSs to be able to succeed to the next milestone. Hereby the advantages of the PRINCE 2 approach should be focussed on, e.g. the high user centric development avoiding the goal of finishing the project as end in itself but aiming for the business case. Once this project has been conducted successfully, this could establish a standard for following projects in terms of execution even though the standardized documents might need custom adjustment to fit the needs.

5.5. Critical Success Factors

CSFs as perceived during this thesis build the vital core of this new service that will be established. Naturally in a pioneer project many CSFs arise and therefore a classification as in the present case is recommended. However, the source is of theoretical nature and therefore cannot be evaluated before the implementation has taken place. Literature helps out in this case as authors are trying to remove stumbling blocks by providing their own experience like [Stathonikos et al., 2013] or [Pantanowitz et al., 2013]. But the process of implementation is neither viewed from the same condition nor conducted under similar circumstances. The concept of providing a nation-wide open access to digitalization is new and therefore requires practical trial. Because of the projects settlement within a university institution some more challenges like funding and more future-oriented adjustment than in private environments. To visualize the process and in the same time be able to show the progress achieved to the stakeholders will enhance the involvement of investors on the project even further. In fact, they will see how their money is spent on a check-list. Here comes the separation of the CSFs into play: while the strategic success factors allow tracking long term developments within the project and respectively this can be used as justification for stakeholders, the operational success factors offer a way to visualize the milestones for the persons closely involved

[41] see www.axelos.com/prince2, accessed on 21.11.2014

in the project. This might increase the motivation as well as the ability to keep an eye on the bigger picture. During the development of the project new CSFs might arise that lied unrevealed before. Therefore a review of the CSFs should be done in reasonable time periods (e.g. at the beginning of a funding period or when hitting new milestones), regarding the expansion stage as shown in 4.4. The CSFs in all their variations are important for the project's success for involving and updating stakeholders of the project on the status.

5.6. Key Performance Indicators

Since this is the first project of this scale in South America a special role has to be assigned to it. The primary goals are differing from other projects, mostly conducted in the industry. Even though the highest priority goals involved providing a more effective and efficient health care for people in Chile the measurement of how well this goal is achieved is necessary. The project itself was not ready to be implemented when this thesis was written so all KPIs are an estimation and have to be proven in the routine operation and are based on model assumptions for now. Given enough maturity of the involved processes KPIs can improve the productivity of processes with the aid of controlling tools like the Balanced Scorecard. Important when applying this methodology is the clear identification of people responsible for an according KPI, ruling out exogenous factors like a different strategic alignment of a customer which results in lower overall equipment effectiveness due to a lower degree of utilization. Furthermore it is important to apply risk management to the process since the balanced scorecard does not involve this in its basic model. These indicators allow a structured controlling and timing on an operational level that can be used to increase process maturity. It reveals, given a constant and on time monitoring, weaknesses of sub-process and is therefore a tool to identify and improve processes alike. As mentioned before on the CSFs the KPIs have to be evaluated over time to reveal which KPIs have the explanatory power. The KPIs have been derived from the process models that were created earlier in addition to this work. Thanks to the BPMN tools permitting an (XML-) attribution a direct simulation of the established process is possible. While the KPIs itself are only a pure measurement of quantity, appropriately monitored and displayed, it can help motivating employees achieving e.g. a higher throughput or less downtime.

5.7. Conclusion

This project, unique in its current location and type, holds up so many possibilities and yet many sources of failure. Technical progress is overtaking and humans have to adapt to this rapid changes because of global competition. While this seems to be no problem for completely new processes or activities, well established processes face a huge challenge. Grown over the years and burdened with outdated, often paper-based, relics the transition into the digital world, especially in the medical field is difficult. One thing that should not be forgotten within this fast pace spiral of new developments is the human being that is faced with them, in this case the pathologist. He observed specimen all his life (educational and work-related) using bright-field microscopes. Naturally the process of familiarization has taken over. Many scientific works are dealing with the evolution of technology, pointing out the great benefits for the participants of this new technology. But it is forgotten that the people who are using this technology have to be prepared and the development cannot progress without them. There is a reason why younger pathologists are less scared, yet encouraged and curious about the new technologies: they are digital natives. Another argument is, that the clinical environment is not prepared for this kind of extension. The hardware lacks processing power, the infrastructure is not sufficiently strengthened barely capable of providing the basic functionality in terms of e.g. storage and bandwidth. DP forces the institution to new investments in not negligible amounts, offering at least in the beginning, no revenue stream due to longer preparation times and higher cost per slide. Additionally pathologists, under ideal circumstances (experience, technique affinity, ...), will be working with at most the same efficiency. Furthermore as soon as the institution decides for a scanning device it is ending up in a vendor dependency. Missing standardization is prohibiting easy exchange, even though some solutions are trying to overcome those limitations (e.g. OpenSlide).
The idea of the FONDEF project starts exactly here, trying to give solutions to the basic arguments for implementing DP and turning them into benefit. All the negative effects are eradicated for the institution when providing one single scan station in the surroundings of the institution providing the service of digitalization and more. With the aid of the internal tracking system, currently under further development, it will be possible to associate the patients contextual information, which is needed for giving a robust diagnose, with the generated digital slide and enable a world-wide access via the internet. The slide itself will be initially stored on servers of the SCIAN Lab so that the hospital itself does not necessarily need its own storage management, except when additionally implementing the IHE / DICOM profiles. A monthly fee, that is in no way comparable to the investment into

a complete data management solution, will be charged to provide DP to as many institutions as possible. The development is conducted closely together with the pathologists of the institutions that want to adapt this technology. This secures the maximum acceptance onto a technology that will be utilized more and more in the future. As experience is growing the performance and maturity of the processes will increase, which are then monitored through the CSFs and KPIs. The socio technical approach used within the project where the social component (the pathologist, technicians, ...) is not neglected will have a higher accession than other approaches. In consideration of the utilized methodology this project will flatten the way that DP is adopted in South America. Nevertheless extensive modelling cannot overcome practical challenges and not everything can be predicted without actually experiencing it. Standards for diagnostic quality are rising and quality management becomes a more important role in pathology. Digitalized slides are not only offering easy access but also image quantification that can be utilized to display ratios of certain elements in an area of interest, the capacities often overburden internal hospital capacities and are therefore best possible outsourced to SCIAN. Another important role plays DP in education, the current practice is to have multi headed microscopes during educational sessions, or use static pre made screen shots to illustrate. The involvement of DP in education is one forerunner for the future acceptance. Since young pathologists are constantly in touch with the technology prejudice are overcome and efficiency is improved through experience. Lastly the second opinion is so much facilitated when access from anywhere is possible that the option to send a slide via mail seems so outdated like sending a letter with a stage coach. The trend towards DP is unstoppable and will accelerate further in terms of new developments and efficiency.
After intensive literature research and all processes explained, the hypothesis answering the central question if all the modalities utilized within this project are contributing to optimize the use of DP cannot yet be answered and therefore the hypothesis has to be discarded due to the missing implementation within the pathologists clinical practice. Nevertheless this approach seems to be very promising and will be complemented further in the development process.

6. Outlook

Quo vadis digital pathology?

DP will grow stronger, with many research fields covered now or in the near future, the usability will increase. Even today the scan times for a single digital slide lies within 30 seconds or less, depending the parameters. Better algorithms will be able to distinguish finer between good images and out of focus regions and accordingly adapt to the scanning process. Bigger batches will increase, given the proper implementation, the productivity adding more and more slides which are processed autonomously. Scanning of fluorescent slides will be more of an option than it is today, and maybe frozen sections can be processed as well. A huge topic is the standardization within the field. Here expectations lie on the further development of the DICOM supplement 145 and the IHE integration profile to be on the long term able to integrate the modality within the hospitals PACS environment more easily. As suggested by the ASCO / CAP (as described in chapter 2.5.5) subsequent validation studies have to be conducted to ensure maximum patient security on every pathological site. This will raise acceptance and courage pathologists to become more engaged with the technical possibilities of DP. To ensure quality on an international level an institution similar to the Nordic QC should be established to provide reliable standards for practising medicine with the aid of WSI. The Food and Drug Administration (FDA) holds the key to successful commitment towards the use of computed quantitative methods in image analysis in medicine. On the long term decision support systems could be possible which not only quantify but also give advices on possible treatment and eventual reciprocation with other medical treatments. These processes could be supported by the latest developments in machine based learning. Though the idea seems promising these are dreams of the future. One step back to the nearer future leads towards using digital slides on mobile devices efficiently, the area here is just opening up and has huge potential for revolutionizing the market once more. The pathologist, watching his slides via the internet on a vacation island will not long be an illusion, just as radiology put it across before.

Bibliography

Aguilar-Savén 2004
AGUILAR-SAVÉN, Ruth S.: Business process modelling: Review and framework. In: *International Journal of Production Economics* 90 (2004), Nr. 2, S. 129–149. http://dx.doi.org/10.1016/S0925-5273(03)00102-6. – DOI 10.1016/S0925–5273(03)00102–6. – ISSN 09255273 2.7

Al-Janabi et al., 2012
AL-JANABI, Shaimaa ; HUISMAN, André ; VAN DIEST, PAUL J: Digital pathology: current status and future perspectives. In: *Histopathology* 61 (2012), Nr. 1, S. 1–9. http://dx.doi.org/10.1111/j.1365-2559.2011.03814.x. – DOI 10.1111/j.1365–2559.2011.03814.x. – ISSN 03090167 (document)

Anbari 2003
ANBARI, Frank T.: Earned value project management method and extensions. In: *Project management journal* 34 (2003), Nr. 4, S. 12–23 4.5

Atkins et al., 1995
ATKINS, P. M. ; MARSHALL, Brenda S. ; JAVALGI, Rajshekhar G.: Happy employees lead to loyal patients. Survey of nurses and patients shows a strong link between employee satisfaction and patient loyalty. In: *Journal of health care marketing* 16 (1995), Nr. 4, S. 14–23 4.5

Bauer et al., 2013
BAUER, Thomas W. ; SCHOENFIELD, Lynn ; SLAW, Renee J. ; YERIAN, Lisa ; SUN, Zhiyuan ; HENRICKS, Walter H.: Validation of Whole Slide Imaging for Primary Diagnosis in Surgical Pathology. In: *Archives of Pathology & Laboratory Medicine* 137 (2013), Nr. 4, S. 518–524. http://dx.doi.org/10.5858/arpa.2011-0678-OA. – DOI 10.5858/arpa.2011–0678–OA. – ISSN 0003–9985 (document), 2.5.3

Becker 1958
BECKER, Howard S.: PROBLEMS OF INFERENCE AND PROOF IN PARTICIPANT OBSERVATION. In: *American Sociological Review* 23 (1958), Nr. 6, S. 652–660 2.6.2

Berger & Nasr 1998

Berger, Paul D. ; Nasr, Nada I.: Customer lifetime value: Marketing models and applications. In: *Journal of Interactive Marketing* 12 (1998), Nr. 1, 17–30. http://dx.doi.org/10.1002/(SICI)1520-6653(199824)12:1<17::AID-DIR3>3.0.CO;2-K. – DOI 10.1002/(SICI)1520–6653(199824)12:1<17::AID–DIR3>3.0.CO;2–K. – ISSN 1094–9968 4.5

Beyer & Holtzblatt 1998

Beyer, Hugh ; Holtzblatt, Karen: *Contextual design: Defining customer-centered systems*. San Francisco and Calif : Morgan Kaufmann, 1998. – ISBN 1558604111 2.6.2

Boff et al., 1994

Boff, Kenneth R. ; Kaufman, Lloyd ; Thomas, James P.: *Handbook of Perception and Human Performance. Volume 2. Cognitive Processes and Performance*. 1994 4.5

Boulding 1956

Boulding, Kenneth E.: General Systems Theory—The Skeleton of Science. In: *Management Science* 2 (1956), Nr. 3, S. 197–208. http://dx.doi.org/10.1287/mnsc.2.3.197. – DOI 10.1287/mnsc.2.3.197. – ISSN 0025–1909 2.6.1

Büttner et al., 2003

Büttner, Reinhard ; Fend, F. ; Thomas, Carlos: *Pathologie / hrsg. von C. Thomas*. Bd. A: *Allgemeine Pathologie: Mit 15 Tabellen*. 3., erw. Aufl. Stuttgart [u.a.] : Schattauer, 2003. – ISBN 9783794522293 2.1

Chua, D. K. H. et al., 1999

Chua, D. K. H. ; Kog, Y. C. ; Loh, P. K.: Critical Success Factors for Different Project Objectives. In: *Journal of Construction Engineering and Management* 125 (1999), Nr. 3, S. 142–150. http://dx.doi.org/10.1061/(ASCE)0733-9364(1999)125:3(142). – DOI 10.1061/(ASCE)0733–9364(1999)125:3(142). – ISSN 0733–9364 2.7.3

Daniel et al., 2012

Daniel, Christel ; Booker, David ; Beckwith, Bruce ; Della Mea, Vincenzo ; Garc\’\ia-Rojo, Marcial ; Havener, Lori ; Kennedy, Mary ; Klossa, Jacques ; Laurinavicius, Arvydas ; Macary, François et al.,: Standards and specifications in pathology: image management, report management and terminology. In: *Stud Health Technol Inform* 179 (2012), S. 105–122 (document)

Daniel et al., 2011

Daniel, Christel ; Rojo, Marcial G. ; Klossa, Jacques ; Della Mea, Vincenzo ; Booker, David ; Beckwith, Bruce A. ; Schrader, Thomas: Standardizing the use of whole slide images in digital pathology. In: *Computerized Medical Imaging and Graphics* 35 (2011), Nr. 7-8, S. 496–505. – ISSN 08956111 2.4.4

DICOM Standards Committee, Working Group 26 2010
DICOM STANDARDS COMMITTEE, WORKING GROUP 26: Sup145: Whole Slide Imaging: Supplement 145: Whole Slide Microscopic IOD and SOP Classes. (2010). ftp://medical.nema.org/medical/dicom/final/sup145_ft.pdf (document), 2.4.1, 2.1, 2.4.4

Drews Günter 2007
DREWS GÜNTER: Earned Value Analyse. In: DREWS GÜNTER (Hrsg.) ; NORBERT HILLEBRAND (Hrsg.) ; DREWS, Günter (Hrsg.) ; HILLEBRAND, Norbert (Hrsg.): *Lexikon der Projektmanagementmethoden // Lexikon der Projektmanagement-Methoden*. Freiburg : Haufe, Rudolf and Haufe Mediengruppe, 2007. – ISBN 978–3448080520, S. 234 (document), 4.10

Evans et al., 2014
EVANS, Andrew ; GARCIA, BerthaM ; GODIN, Chris ; GODLEWSKI, Marek ; JANSEN, GerardH ; KABANI, Amin ; LOUAHLIA, Said ; MANNING, Lisa ; MAUNG, Raymond ; MOORE, Lisa ; PHILLEY, Joanne ; SLATNIK, Jack ; SRIGLEY, John ; THIBAULT, Alain ; PICARD, DonaldDaniel ; TETU, Bernard ; BERNARD, Chantal ; CHANDRAKANTH, S. A. ; CORNELL, IanScott ; CRACOWER, Hanah ; DALTON, James: Guidelines from the Canadian Association of Pathologists for establishing a telepathology service for anatomic pathology using whole-slide imaging. In: *Journal of Pathology Informatics* 5 (2014), Nr. 1, S. 15. http://dx.doi.org/10.4103/2153-3539.129455. – DOI 10.4103/2153–3539.129455. – ISSN 2153–3539 2.5.3

Fitz-enz 2000
FITZ-ENZ, Jac: *The ROI of human capital: Measuring the economic value of employee performance*. New York : AMACOM, 2000. – ISBN 0814405746 4.5

Fornell 1992
FORNELL, Claes: A national customer satisfaction barometer: the Swedish experience. In: *the Journal of Marketing* (1992), S. 6–21 (document), 4.5, 4.11

Ho et al., 2013
HO, Jonhan ; ARIDOR, Orly ; GLINSKI, DavidW ; SAYLOR, ChristopherD ; PELLETIER, JosephP ; SELBY, DaleM ; DAVIS, StevenW ; LANCIA, Nicholas ; GERLACH, ChristopherB ; NEWBERRY, Jonathan ; ANTHONY, Leslie ; PANTANOWITZ, Liron ; PARWANI, AnilV: Needs and workflow assessment prior to implementation of a digital pathology infrastructure for the US Air Force Medical Service. In: *Journal of Pathology Informatics* 4 (2013), Nr. 1, S. 32. http:

//dx.doi.org/10.4103/2153-3539.122388. – DOI 10.4103/2153–3539.122388. – ISSN 2153–3539 (document), 2.5.3

Ho et al., 2006

HO, Jonhan ; PARWANI, Anil V. ; JUKIC, Drazen M. ; YAGI, Yukako ; ANTHONY, Leslie ; GILBERTSON, John R.: Use of whole slide imaging in surgical pathology quality assurance: design and pilot validation studies. In: *Human Pathology* 37 (2006), Nr. 3, S. 322–331. http://dx.doi.org/10.1016/j.humpath.2005.11.005. – DOI 10.1016/j.humpath.2005.11.005. – ISSN 00468177 (document), 2.5.5

Hughes et al., 1992

HUGHES, John A. ; RANDALL, Dave ; SHAPIRO, Dan: From ethnographic record to system design. In: *Computer Supported Cooperative Work (CSCW)* 1 (1992), Nr. 3, S. 123–141. http://dx.doi.org/10.1007/BF00752435. – DOI 10.1007/BF00752435. – ISSN 0925–9724 2.6.2

International Standardisation Organization 2013

INTERNATIONAL STANDARDISATION ORGANIZATION: Information technology - Object Management Group BPMN. (2013) 2.7.1

Jodlbauer 2008

JODLBAUER, Herbert: *Produktionsoptimierung: Wertschaffende sowie kundenorientierte Planung und Steuerung*. [Online-Ausg. der] 2., erw. [gedr.] Aufl. Wien and New York and NY and [Heidelberg] : Springer, 2008 (Springers Kurzlehrbücher der Wirtschaftswissenschaften). – ISBN 978–3–211–78140–1 4.5

Kaplan & Norton 2007

KAPLAN, Robert S. ; NORTON, David P.: Balanced Scorecard. Version: 2007. http://dx.doi.org/10.1007/978-3-8349-9320-5_12. In: BOERSCH, Cornelius (Hrsg.) ; ELSCHEN, Rainer (Hrsg.): *Das Summa Summarum des Management*. Wiesbaden : Gabler, 2007. – DOI 10.1007/978–3–8349–9320–5_12. – ISBN 978–3–8349–0519–2, S. 137–148 4.3, 4.3

Keeble 2003

KEEBLE, Justin J.: Using Indicators to Measure Sustainability Performance at a Corporate and Project Level. In: *Journal of Business Ethics* 44 (2003), Nr. 2, S. 149–158. http://dx.doi.org/10.1023/A:1023343614973. – DOI 10.1023/A:1023343614973. – ISSN 01674544 (document), 2.4, 2.7.4

Kompaso & Sridevi 2010

KOMPASO, Solomon M. ; SRIDEVI, M S.: Employee engagement: The key to improving performance. In: *International Journal of Business and Management* 5 (2010), Nr. 12, S. p89 4.5

Kriss & Kriss 1998

KRISS, Timothy C. ; KRISS, Vesna M.: History of the operating microscope: from magnifying glass to microneurosurgery. In: *Neurosurgery* 42 (1998), Nr. 4, S. 899–907 2.1

Kumar & Dunn 2009

KUMAR, Sajeesh ; DUNN, Bruce E.: *Telepathology*. Berlin : Springer, 2009. – ISBN 978–3–540–85785–3 2.2

Macintosh 1993

MACINTOSH, A. L.: The need for enriched knowledge representation for enterprise modelling. In: *AI (Artificial Intelligence) in Enterprise Modelling, IEE Colloquium on (Digest No. 078)*, 1993, S. 3 2.7

Mack & Woodsong 2005

MACK, Natasha ; WOODSONG, Cynthia: *Qualitative research methods: A data collector's field guide*. North Carolina : FLI and USAID, 2005. – ISBN 0–939704–98–6 2.6.2, 2.6.2

Marr 2011

MARR, Bernard: *Key performance indicators*. Harlow : Financial Times Prentice Hall, 2011. – ISBN 0273750119 2.7.4, 4.5, 4.5

Pantanowitz et al., 2013

PANTANOWITZ, Liron ; SINARD, John H. ; HENRICKS, Walter H. ; FATHEREE, Lisa A. ; CARTER, Alexis B. ; CONTIS, Lydia ; BECKWITH, Bruce A. ; EVANS, Andrew J. ; LAL, Avtar ; PARWANI, Anil V.: Validating Whole Slide Imaging for Diagnostic Purposes in Pathology: Guideline from the College of American Pathologists Pathology and Laboratory Quality Center. In: *Archives of Pathology & Laboratory Medicine* 137 (2013), Nr. 12, S. 1710–1722. http://dx.doi.org/10.5858/arpa.2013-0093-CP. – DOI 10.5858/arpa.2013–0093–CP. – ISSN 0003–9985 2.5.5, 5.5

Phillips 1997

PHILLIPS, Jack J.: *Measuring return on investment*. Bd. 2. American Society for Training and Development, 1997 4.5

Pinto & Slevin 1987

PINTO, Jeffrey K. ; SLEVIN, Dennis P.: Critical factors in successful project implementation. In: *IEEE Transactions on Engineering Management* EM-34 (1987), Nr. 1, S. 22–27. http://dx.doi.org/10.1109/TEM.1987.6498856. – DOI 10.1109/TEM.1987.6498856. – ISSN 0018–9391 2.7.3, 4.4

Pomorski 1997
POMORSKI, T.: Managing overall equipment effectiveness [OEE] to optimize factory performance. In: IEEE (Hrsg.): *Managing overall equipment effectiveness [OEE] to optimize factory performance*, 1997. – ISBN 0–7803–3752–2, S. A33–A36 4.5

Raab et al., 2005
RAAB, Stephen S. ; NAKHLEH, Raouf E. ; RUBY, Stephen G.: Patient safety in anatomic pathology: measuring discrepancy frequencies and causes. In: *Archives of pathology & laboratory medicine* 129 (2005), Nr. 4, S. 459–466 2.5.5

Rittenberg & Tregarthen 2009
RITTENBERG, Libby ; TREGARTHEN, Timothy: *Principles of microeconomics*. Flat World Knowledge, 2009 4.5

Robertson & Cooper 2010
ROBERTSON, Ivan T. ; COOPER, Cary L.: Full engagement: the integration of employee engagement and psychological well-being. In: *Leadership & Organization Development Journal* 31 (2010), Nr. 4, S. 324–336 4.5

Rojo et al., 2006
ROJO, M. G. ; GARCIA, G. B. ; MATEOS, C. P. ; GARCIA, J. G. ; VICENTE, M. C.: Critical Comparison of 31 Commercially Available Digital Slide Systems in Pathology. In: *International Journal of Surgical Pathology* 14 (2006), Nr. 4, S. 285–305. http://dx.doi.org/10.1177/1066896906292274. – DOI 10.1177/1066896906292274. – ISSN 1066–8969 2.4.2

Rojo et al., 2008
ROJO, Marcial ; ROLÓN, Elvira ; CALAHORRA, Luis ; GARCÍA, Felix ; SÁNCHEZ, Rosario ; RUIZ, Francisco ; BALLESTER, Nieves ; ARMENTEROS, María ; RODRÍGUEZ, Teresa ; ESPARTERO, Rafael: Implementation of the Business Process Modelling Notation (BPMN) in the modelling of anatomic pathology processes. In: *Diagnostic Pathology* 3 (2008), Nr. Suppl 1, S. S22. http://dx.doi.org/10.1186/1746-1596-3-S1-S22. – DOI 10.1186/1746–1596–3–S1–S22. – ISSN 1746–1596 2.7, 2.7.1

Saaty 1990
SAATY, Thomas L.: How to make a decision: The analytic hierarchy process. In: *European Journal of Operational Research* 48 (1990), Nr. 1, S. 9–26. http://dx.doi.org/10.1016/0377-2217(90)90057-I. – DOI 10.1016/0377–2217(90)90057–I. – ISSN 03772217 2.7.3, 4.4

Sharp et al., 2007

SHARP, Helen ; ROGERS, Yvonne ; PREECE, Jenny: *Interaction design: Beyond human-computer interaction*. 2nd ed. Chichester and Hoboken and NJ : Wiley, 2007. – ISBN 978–0–470–01866–8 2.6.2

Singh et al., 2011

SINGH, Rajendra ; CHUBB, Lauren ; PANTANOWITZ, Liron ; PARWANI, Anil: Standardization in digital pathology: Supplement 145 of the DICOM standards. In: *Journal of Pathology Informatics* 2 (2011), Nr. 1, S. 23. http://dx.doi.org/10.4103/2153-3539.80719. – DOI 10.4103/2153–3539.80719. – ISSN 2153–3539 2.5.4

Stamatis 2010

STAMATIS, Diomidis H.: *The OEE primer: understanding overall equipment effectiveness, reliability, and maintainability*. CRC Press, 2010. – 22–24 S. 4.5

Stathonikos et al., 2013

STATHONIKOS, Nikolas ; VETA, Mitko ; HUISMAN, André ; DIEST, PaulJ van: Going fully digital: Perspective of a Dutch academic pathology lab. In: *Journal of Pathology Informatics* 4 (2013), Nr. 1, S. 15. http://dx.doi.org/10.4103/2153-3539.114206. – DOI 10.4103/2153–3539.114206. – ISSN 2153–3539 (document), 2.5.3, 5.5

Thomas Wendt 2006

THOMAS WENDT: *Modellierung und Bewertung von Integration in Krankenhausinformationssystemen*. Leipzig, Universität Leipzig, Diss., 2006 2.7.2

Turner 2009

TURNER, J. R.: *The handbook of project-based management: Leading strategic change in organizations*. 3rd ed. New York : McGraw-Hill, 2009. – ISBN 978–0–07–154974–5 (document), 2.3, 2.7.4

Webster & Dunstan 2014

WEBSTER, J. D. ; DUNSTAN, R. W.: Whole-Slide Imaging and Automated Image Analysis: Considerations and Opportunities in the Practice of Pathology. In: *Veterinary Pathology* 51 (2014), Nr. 1, S. 211–223. http://dx.doi.org/10.1177/0300985813503570. – DOI 10.1177/0300985813503570. – ISSN 0300–9858 2.4

Weinstein et al., 1987

WEINSTEIN, R. S. ; BLOOM, K. J. ; ROZEK, L. S.: Telepathology and the networking of pathology diagnostic services. In: *Archives of pathology & laboratory medicine* 111 (1987), Nr. 7, S. 646–652. – ISSN 0003–9985 2.5

Weinstein et al., 2009

WEINSTEIN, Ronald S. ; GRAHAM, Anna R. ; RICHTER, Lynne C. ; BARKER, Gail P. ; KRUPINSKI, Elizabeth A. ; LOPEZ, Ana M. ; ERPS, Kristine A. ; BHATTACHARYYA, Achyut K. ; YAGI, Yukako ; GILBERTSON, John R.: Overview of telepathology, virtual microscopy, and whole slide imaging: prospects for the future. In: *Human Pathology* 40 (2009), Nr. 8, S. 1057–1069. http://dx.doi.org/10.1016/j.humpath.2009.04.006. – DOI 10.1016/j.humpath.2009.04.006. – ISSN 00468177 2.1, 2.4

Winter et al., 2007

WINTER, Alfred ; BRIGL, Birgit ; FUNKAT, Gert ; HÄBER, Anke ; HELLER, Oliver ; WENDT, Thomas: 3LGM2-Modeling to support management of health information systems. In: *International Journal of Medical Informatics* 76 (2007), Nr. 2-3, S. 145–150. http://dx.doi.org/10.1016/j.ijmedinf.2006.07.007. – DOI 10.1016/j.ijmedinf.2006.07.007. – ISSN 13865056 (document), 2.7.2

Zwönitzer et al., 2007

ZWÖNITZER, Ralf ; KALINSKI, Thomas ; HOFMANN, Harald ; ROESSNER, Albert ; BERNARDING, Johannes: Digital pathology: DICOM-conform draft, testbed, and first results. In: *Computer Methods and Programs in Biomedicine* 87 (2007), Nr. 3, S. 181–188. http://dx.doi.org/10.1016/j.cmpb.2007.05.010. – DOI 10.1016/j.cmpb.2007.05.010. – ISSN 01692607 2.4.4

A. Appendix

A.1. Project Roadmap

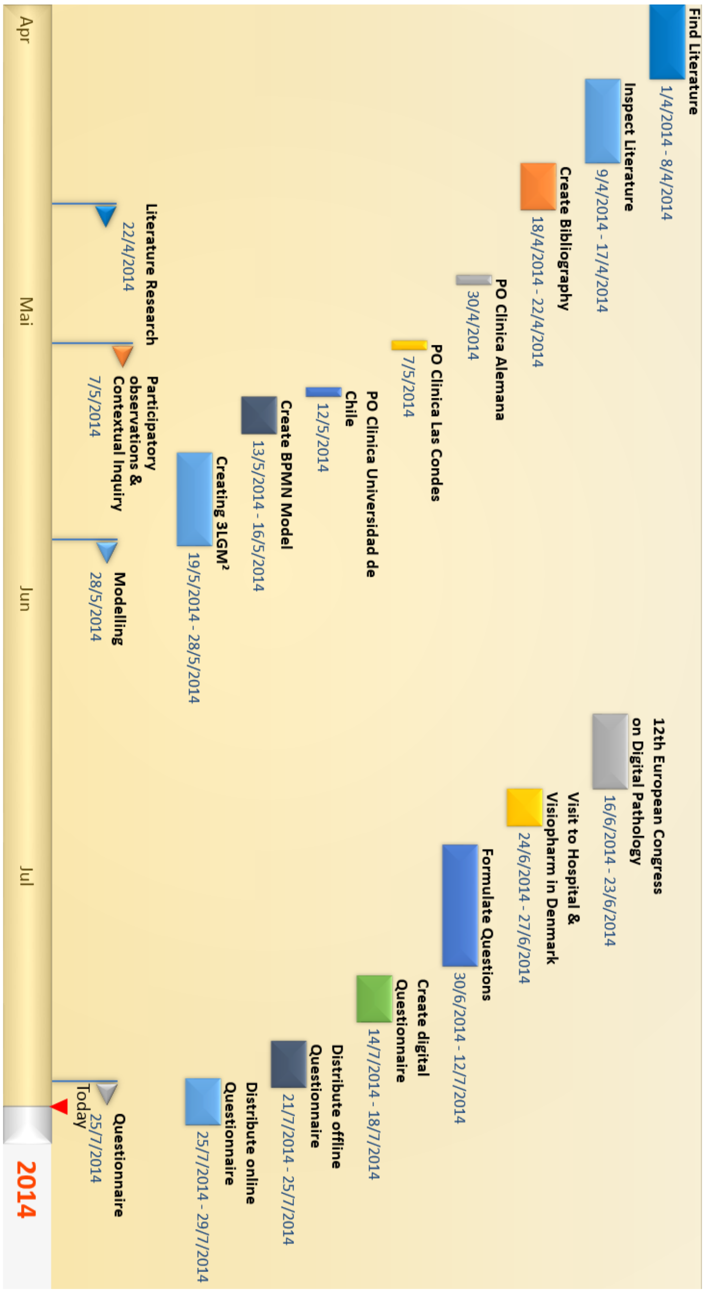

Figure A.1.: Roadmap for the tissue scanner project

A.2. Mindmap virtual microscopy

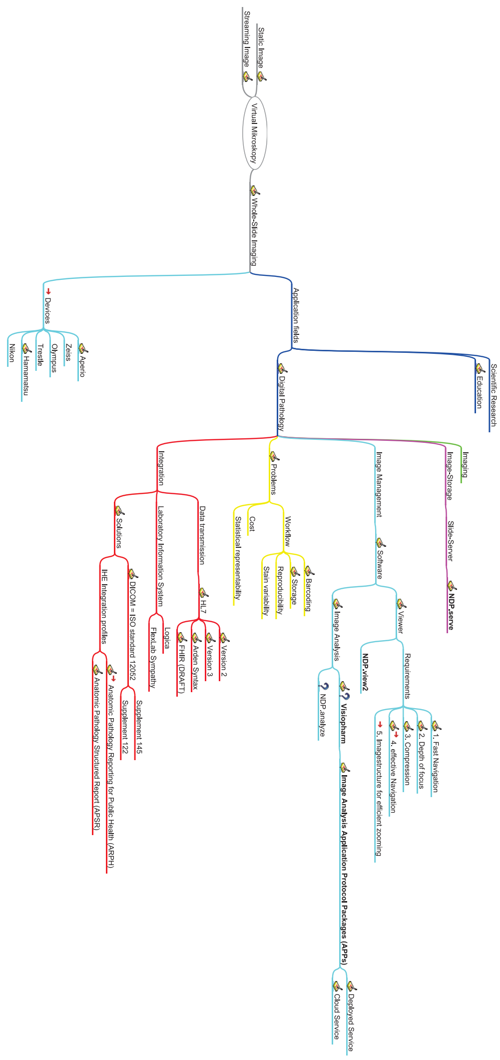

Figure A.2.: Mindmap of the range of topics virtual microscopy

A.3. BPM of the pathology workflow in Chile from the SCIAN Lab perspective

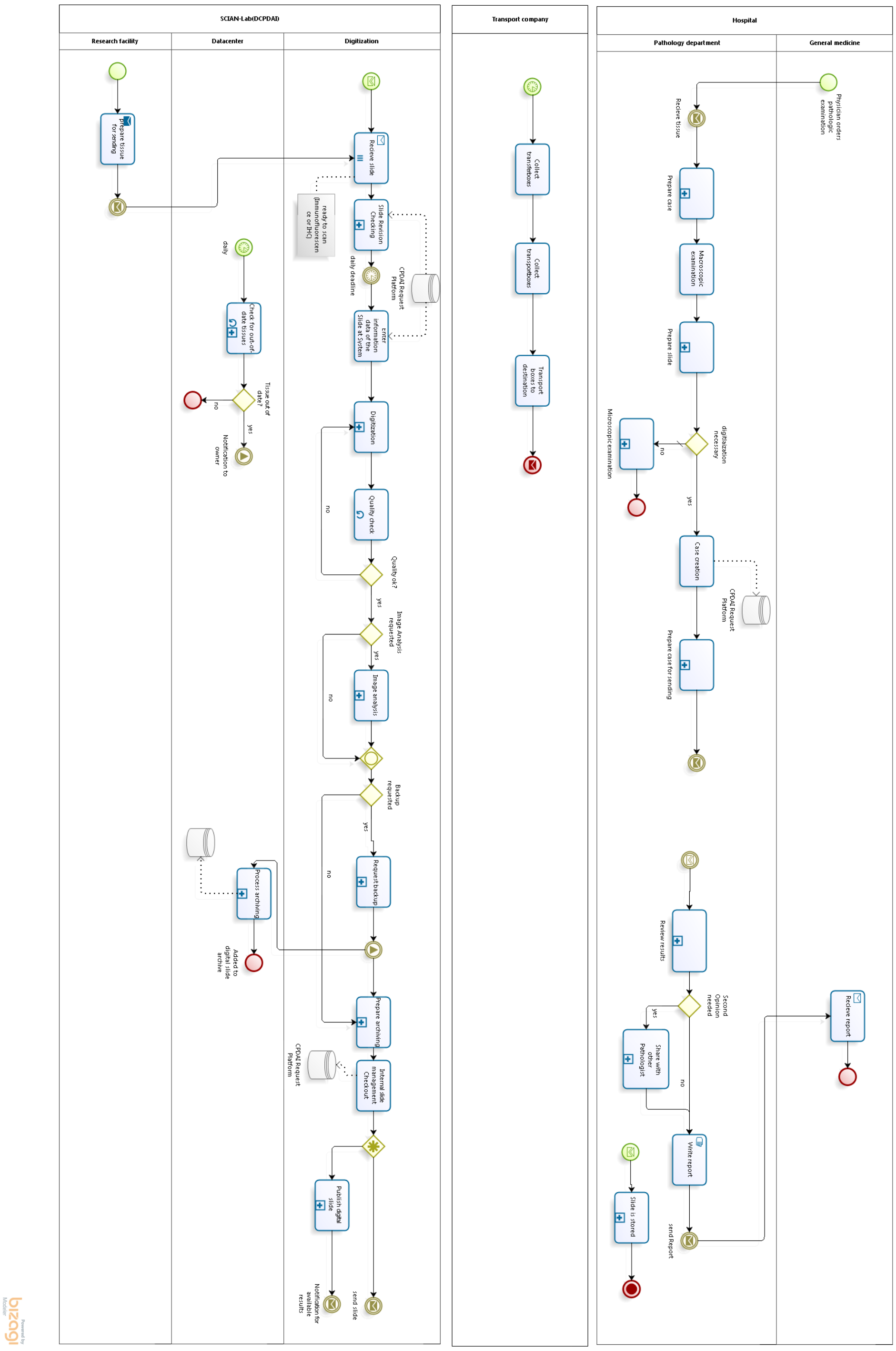

Figure A.3.: Business process model of the Chilean pathology wokflow

A.4. Modelling infrastructure with 3LGM-Model

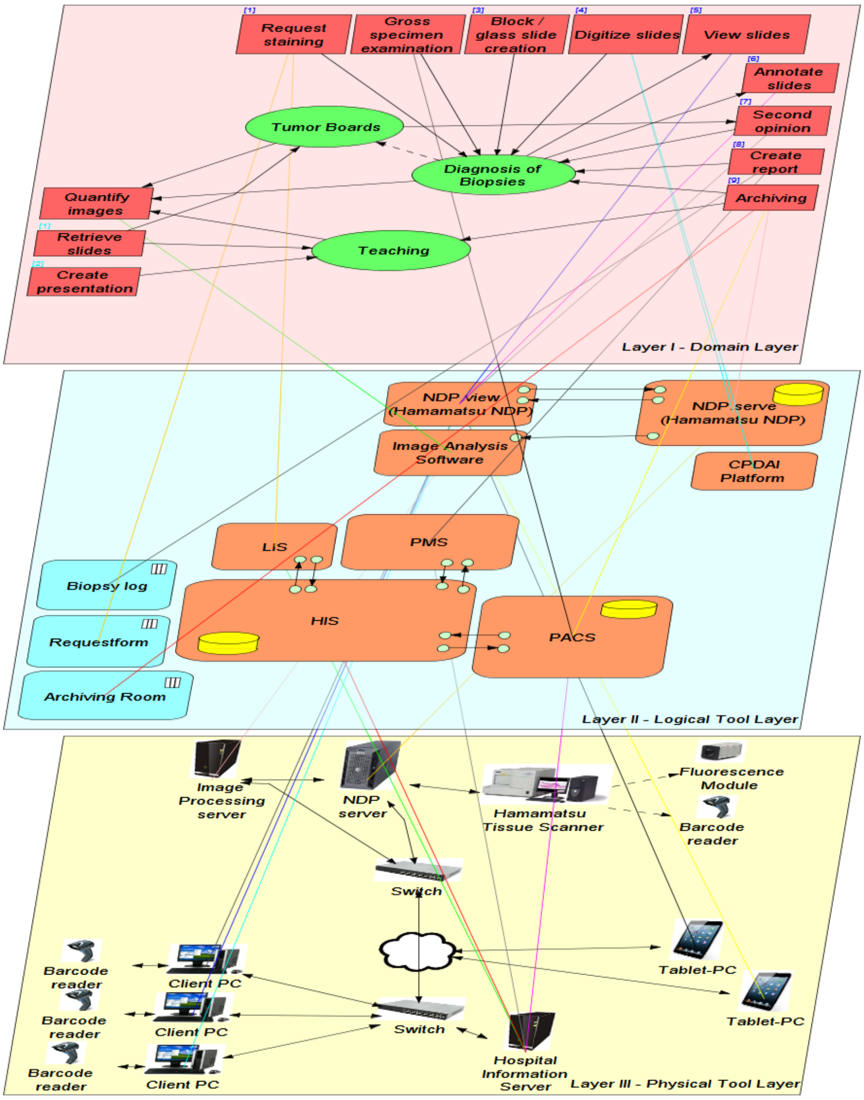

Figure A.4.: The necessary infrastructure modelled with 3LGM-Model

A.5. Requirement analysis questionnaire

Tissue Scanner Project
Questionnaire

Dear study participant:
This questionnaire is designed to assess the impact of **Whole Slide Imaging** and the **remote access to it** on your daily work routine. By completing it, you are enabling us to remedy any shortcomings, with the aim of enhancing your daily work.

Please tick the answers that you find the most fitting according to your opinion. If you do not have an opinion, leave the question blank.

Please note: this questionnaire is completely anonymized to secure data privacy!

Particular questions

	≤30	31-59	≥60
[1.] How many slides do you analyze on an average work day?	☐	☐	☐

	≤5	6-14	≥15
[2.] How many cases do you process on an average work day?	☐	☐	☐

	≤5 min	6-9 min	≥10 min
[3.] How long do you spend viewing one slide?	☐	☐	☐

	≤5 hours	6-9 hours	≥10 hours
[4.] How much travelling time can be saved with a digital slide sharing?	☐	☐	☐

Thank you very much for your cooperation!

30.04.2014

Tissue Scanner Project
Questionnaire

General questions

	not at all	somewhat	very
[5.] How familiar are you with computers?	☐	☐	☐
[6.] How open minded would you describe yourself towards new technology based on the internet?	☐	☐	☐
[7.] Do you think your work could be assisted in terms of comfort with a computer?	☐	☐	☐
[8.] Is it possible for a digital imaging solution to complement microscopic observation?	☐	☐	☐
[9.] Would an automated and robust quantification help you with your daily work? (e.g. counting nuclei)	☐	☐	☐
[10.] Do you think your travel times can be decreased with an online platform to view and share slides?	☐	☐	☐
[11.] Would you be interested in participating in a study based on Digital Pathology?	☐	☐	☐

Free text questions

[12.] Which information, that you do not have, would you find useful at the time of viewing a slide?	
[13.] What improvements or benefits do you expect from digital pathology? (e.g. quantifying images, accessibility)	
[14.] Do you have any general comments or wishes?	

Thank you very much for your cooperation!

30.04.2014

A.6. Observation Log Clinica Las Condes

Observation Log

Participant:

Dr. Pablo Matamala Bastian, anatomic pathologist
Email: pmatamala@clc.cl, Tel: (+56-2) 210 5835
Clinica Las Condes (CLC, www.clc.cl)
Lo Fontecilla 441
Las Condes, Santiago, Chile

Fig. 1: Pathologists workspace

Conducted on 03.06.2014, 9:00 AM

9:00 AM

- Introduction to the team and short explanation of the methodology
  - Explanation of the devices used on the workspace (see Fig. 1)

9:24 AM

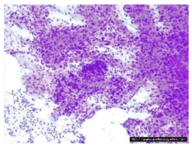

Fig. 2: Cat scratch disease
Source: http://www.surgicalpathologyatlas.com/

- Start of case "cat scratch disease" (see Fig. 2)
- Examination of request (2 min)
- Dictating different case information, including the Immunohistochemistry Information (3 min)
- View slide through microscope (3 min)
  - Second opinion necessary
  - Give slide to colleague next to him
- Meanwhile:
  - Searching for papers (1 min)
  - Correcting orthographic mistakes of cases to sign out in the hospital information system (HIS) (per case: ca. 3 min)

9:47 AM

- Dictation of multiple cases

9:48 AM

- Interuption: approximately 10 new slides are brought in by an assistant and are placed on the table
  - Note: confusing order on the table

9:50 AM

- Start of case "prostate exam"
  - Consisting of 6 slides (view time: avg. 2 min per slide)
  - Needle biopsy
- Case was positive for cancer, additional slides were ordered
  - Ordered a second opinion (from a second in-house pathologist) to ensure diagnosis
  - Annotation of the slides with ruler & pen (3 min)
    - Does not have to be "super accurate"
- Case will eventually be presented in the tumor board for its difficulty
- Dictate protocols (some of them have template in the HIS)

10:14 AM

- Signing out cases with secure diagnosis

10:16 AM

- Coffee break

10:30 AM

- Creating PowerPoint for today´s tumor board (30 min)
    - Copy & paste of diagnosis within the HIS
    - Take pictures with the aid of the camera mounted on the microscope
    - Transfer pictures to computer using a memory card

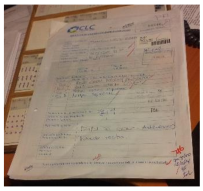

Fig. 3: sheet for second opinion

11:00 AM

- Routine, many slides in short time

11:08 AM

- Result of a second opinion is coming in (see Fig. 3)
    - Sending result to clinician

11:12 AM

- Viewing slides
- Research about specific disease patterns in books
    - Tumor classification of a case with the aid of literature (see Fig. 4)
- Secondly confirm some cancer cases for colleagues (2 min)

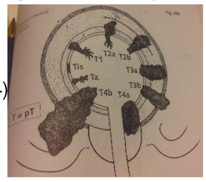

Fig. 4: book extract for tumor classification

11:42 AM

- Short meeting with colleagues
    1. Coordinating the tumor board attendance of the week

11:45 AM

- Case requires further investigation
    1. Fill out request form in the HIS for the technician
    2. 3 layers below are needed to be observed to secure the diagnosis

11:47 AM

- Viewing more slides

12:15 AM

- Lunch break

01:15 PM

- Quality control 10 slides, criteria:
    1. Folding of the tissue on the slide
    2. Coloration of the slide
    3. Broken (ripped apart) tissue

01:25 PM

- Research for the tumor board of the day

01:30 PM

- Tumor board (Fig. 5)
- Several cases are discussed with other doctors (approximately 10 min. per case)
- Sequence:
    1. Case description
    2. Case history
    3. Case specifications (incl. TMN-classification)
    4. Discussion (with the support of static images)

Fig. 5: Tumor board in Clinica Las Condes

02:30 PM

- Routine work, viewing slides
- Correcting cases to sign out

02:45 PM

- Two cases of gross examinations (see Fig. 6)
- Cut specimens
- Place in transport boxes for further treatment
- Fill out report

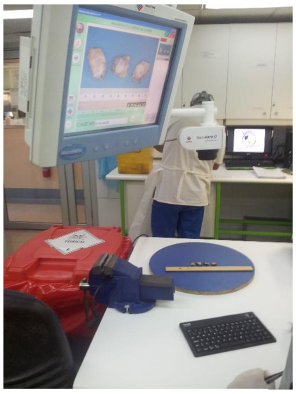

Fig. 6: Gross examination

02:55 PM

- Fluorescence In Situ Hybridization (FISH) cases
- 3 cases per week (1-4 cases in average)
- Calibrating the filter with a control negative / positive slide
- Sequence
    - Take “Screenshots” (software: CelSense Standard)
    - Open image with software: Qcapture Pro
    - Count nuclei (together with 3 assistants)

03:25 PM

- Signing out cases
- Two requests to technicians for more slides from a specimen
    - Electronically

04:00 PM

- End of the observation

Common informations and facts:

- Interesting and difficult cases are signed within a book
- Informations on the patient is gathered via the HIS
- 10 000 Biopsies p.a. in CLC
- 6 Pathologists
- 20 technicians

A.7. Evaluation questionnaire

Tissue Scanner Project
Questionnaire
Appointement:

Dear study participant:

This questionnaire is designed to assess the impact of **Whole Slide Imaging** and the **remote access to it** on your daily work routine. By completing it, you are enabling us to remedy any shortcomings, with the aim of enhancing your daily work.

Please tick the answers that you find the most fitting according to your opinion, reaching from very less agreeing (--) to very high agreeing (++). To express equality between the options please tick (o). If you don't have an opinion please tick (no opinion).

Please note: this questionnaire is completely anonymized to secure data privacy!

Personal information

[1.] What is your main area of expertise in Pathology?	…………………………………………………
[2.] How many years of experience do you have?	…………………………………………………
[3.] How many different locations (pathology) do you cover?	…………………………………………………
[4.] How many cases do you review per day?	…………………………………………………
[5.] How many slides do you view per day?	…………………………………………………
[6.] How many fluorescent slides do you view per week?	…………………………………………………
[7.] In how many tumor board review(s) do you participate per week?	…………………………………………………

Tissue Scanner Project
Questionnaire
Appointement:

Personal Information (II)

[8.] Are you familiar with the term Digital Pathology?	☐ yes ☐ no
[9.] Digital Pathology is … (you can mark multiple options)	☐…digitalization of microscopic whole slide images ☐…remote visualization of digital slides ☐…obtaining a second opinion via internet ☐…creation of digital teaching material ☐…access to quantitative methods ☐…don't know ☐…other: …………………………..
[10.] Did you work with a Digital Pathology system before?	☐ yes, the name was …………………. ☐ no

Tissue Scanner Project
Questionnaire
Appointement:

Expectations towards Digital Pathology

Digitalization and remote access

Whole Slide Imaging allows to digitize slides and view them on a computer without the need of a conventional microscope.

[1.] From where would you like to view your digital slides? (you can mark multiple options)	☐ at work ☐ during travels ☐ home office ☐ none of the above ☐ other: …………………………………………
[2.] Do you think a Digital Pathology application can be useful on … (you can mark multiple options)	☐…an IPad or similar 9,7" Tablet computer ☐…an IPad Mini or similar 7,9" Tablet computer ☐…an IPhone or similar 4" Smartphone ☐…none of the above
[3.] Would you use a Digital Pathology system as a… (you can mark multiple options)	☐…case archiving system ☐…platform to manage second opinions ☐…tool for quantitative analysis ☐…tool for tumor board presentations ☐…tool for education ☐…tool for clinical trials, if yes which: ………………………………………………… ☐…none of the above ☐…other: …………………………………………………

	--	-	o	+	++	no opinion
[4.] Do you think Digital Pathology can increase work comfort?	☐	☐	☐	☐	☐	☐

Tissue Scanner Project
Questionnaire
Appointement:

Access to second opinions

Requesting an evaluation of a case by a remote second pathologist.

[1.] Did you make use of an inter-institutional second opinion in the last month?	☐ yes, how many: ………	☐ no

In my opinion…

	--	-	o	+	++	no opinion
[2.] …the easy access to a second opinion improves diagnostic accuracy.	☐	☐	☐	☐	☐	☐
[3.] …the access to a second opinion via the internet reduces time to solve a case.	☐	☐	☐	☐	☐	☐
[4.] …the access to an international Digital Pathology network is beneficial.	☐	☐	☐	☐	☐	☐

Tissue Scanner Project
Questionnaire
Appointement:

Access to quantitative parameters in images

This part of the questionnaire covers the access to quantification of digital slides.
An example would be the quantification of nuclei on a certain area of interest.

Did you ever…

[1.] …use a Hercep-Test for determination of HER2 protein overexpression in breast cancer tissues?	☐ yes	☐ no	☐ don't know
[2.] …use Pathway (4B5) for determination of HER2 protein overexpression in breast cancer tissues?	☐ yes	☐ no	☐ don't know
[3.] …estimate completeness and intensity of membrane staining to obtain 0, 1+, 2+ or 3+ scoring?	☐ yes	☐ no	☐ don't know

[4.] Suppose that there is a FDA approved Software which uses principles that are not direct translations of the ASCO/CAP and reagent manufacturer's guidelines. However, the Software does not quantify completeness and intensity of membrane staining, but it calculates membrane connectivity which is then translated into a classical diagnostic score (0, 1+, 2+ or 3+). Would it be acceptable for you to use this Software for HER2 protein overexpression assessment?	☐ yes	☐ no	☐ don't know

In my opinion…

	--	-	o	+	++	no opinion
[5.] …quantification can help to improve diagnosis.	☐	☐	☐	☐	☐	☐
[6.] …quantitative parameters can be used as a quality control to obtain reproducible diagnoses.	☐	☐	☐	☐	☐	☐

Tissue Scanner Project
Questionnaire
Appointement:

Teaching and education

The access to location-independent viewing tools aims to reduce time and improve quality of learning material.

[1.] Do you teach or give seminars in regular intervals containing pathology material?	☐ yes, … hours per week	☐ no

	--	-	o	+	++	no opinion
[2.] Different faculties of the world are using Digital Pathology for their students on a regular basis. Do you think there will be a benefit for your teaching?	☐	☐	☐	☐	☐	☐

Thank you very much for your participation!