Digitalizing Healthcare: The Potential to Transform Pathology Labs

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by:
Martin Fortou
Noah Goodman
Sycamore Herlihy
Brandon Vuong

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Sponsor:
Phoebe Liang, Overseas Business Development
aetherAI

Submitted to:
Dr. Grant Burrier
Dr. Alex Sphar

Abstract

The study of disease through the examination of tissues and bodily fluids is known as pathology. Since digital pathology is relatively new, only a few hospitals and labs in the United States have implemented the technology. To identify the barriers to greater implementation of digital systems into pathologists' workflow, our team conducted interviews with members from the Digital Pathology Association (DPA) and non-DPA members. Our research discovered several challenges to digitalization, including financial limitations, regulations, interoperability issues, resistance to change, and inefficiency. We proposed several solutions to these challenges, including investing in digital pathology education, collaborating with other specialists, utilizing a top-down or bottom-up marketing approach while also exploring more effective methods for introducing the technology.

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Authorship

Section	Author	Editor
Abstract	Noah/Martin	Brandon/Martin
Executive Summary	All	Brandon
Digital Pathology	Sycamore	Brandon/Sycamore
Improvements to Accuracy	Sycamore	Brandon/Martin
Workflow Integration	Brandon/Martin	Sycamore
Monetary Barriers	Noah/Sycamore	Brandon/Martin/Sycamore
Ethical Concerns	Martin	Brandon/Sycamore
Healthcare and Biotechnology in Taiwan and the United States	Brandon	All
Current Digitalization Solutions	Sycamore/Noah	Brandon/Martin/Sycamore
Archival Research	Sycamore/Noah	Brandon/Sycamore
Interviews of Pathology Experts	Brandon/Sycamore	Brandon
Market Research	Martin	Brandon
Surveys	Brandon	Brandon
Case Studies	Sycamore	Brandon/Sycamore
Data Analysis & Visualization	Sycamore	Brandon/Sycamore
Current Market	Sycamore	Brandon/Sycamore
Benefits of Digitalization	Sycamore/Martin	Martin
Finances	Brandon	Sycamore
Regulations	Sycamore	Brandon

Practicality	Noah/Sycamore	Sycamore
Interoperability	Noah/Martin	Martin/Sycamore
Technophobia	Martin/Noah	Martin
Continued Collaboration with Research Institutions	Brandon	Sycamore
Education	Noah/Sycamore	Brandon
Top-down Approach and Bottom-up Approach	Martin/Noah	Martin
Research into Human-Computer Interaction	Noah/Martin	Martin
Limitations	Noah/Martin	Brandon/Sycamore
Future Research Opportunities	Brandon/Martin	Sycamore

Table of Contents

Abstract i
Acknowledgements ii
Authorship iii
0 Executive Summary 1
0.1 Motivation 1
0.2 Approach 1
0.3 Results 2
0.4 Conclusions 3
1 Introduction 6
2 Background 7
2.1 Digital Pathology 7
2.2 Digitalization: Potential and Challenges 10
2.2.1 Improvements to Accuracy & Efficiency 10
2.2.2 Workflow Integration 12
2.2.3 Monetary Barriers 14
2.2.4 Ethical Concerns 15
2.3 Healthcare and Biotechnology in Taiwan and the United States 16
2.4 Current Digitalization Solutions 19
3 Methodology 20
3.1 Archival Research 21
3.2 Interviews of Pathology Experts 22
3.3 Market Research 24
3.4 Surveys 25
3.5 Case Studies 26
3.6 Data Analysis & Visualization 26
3.7 Ethical Considerations 27
4 Findings 28
4.1 Current Market 28
4.2 Benefits of Digitalization 29
4.3 Barriers to Digitalization 31
4.3.1 Finances 33
4.3.2 Regulations 36
4.3.3 Practicality 37
4.3.4 Interoperability 38
4.3.5 Technophobia 40
5 Conclusion 41
5.1 Recommendations 41
5.1.1 Continued Collaboration with Research Institutions 42
5.1.2 Education 43
5.1.3 Top-down Approach and Bottom-up Approach 44

5.1.4 Research into Human Computer Interaction 44
5.2 Limitations 45
5.3 Future Research Opportunities 46
6 Bibliography 47
7 Appendix 54
7.1 List of Interviews 54
7.2 Interview Questions 55
7.3 Competitor Analysis 57

0 Executive Summary

0.1 Motivation

In recent years, there has been a surge in the application of new technologies within the practice of pathology. Traditionally, pathology has relied on the use of glass slides and microscopes to analyze tissue samples; the digitalization of systems has been a recent consideration for hospitals and laboratories. The implementation of digital systems in pathology labs is essential in order to utilize artificial intelligence applications in the near future. The initial AI applications in pathology have been proven to effectively distinguish and detect cancer as well as count cells accurately and are one of the most enticing features to digitalizing.

aetherAI is a Taiwanese-based medical imaging company that focuses on digital pathology and providing AI solutions. With plans to expand into the US market, our team was assigned by aetherAI to identify barriers that may be hindering their entry into the US market. By identifying these barriers, aetherAI can make informed decisions on how to effectively and successfully enter the US market.

0.2 Approach

We conducted our research using multiple methods, including archival research and interviews with pathologists in the United States and in Taiwan. Among other methods considered were case studies and surveys, which were decided against.

The interviews included nine professionals in the industry, eight of them being from the United States, and were hosted using online meeting platforms such as Zoom. These interviews were hosted during the months of March and April, lasting about thirty minutes each. The interviews began with questions about the individual pathologist including how long they had been practicing and what their specialty was. We then asked about their practices' use of digital pathology, what made them implement it, and what challenges they faced in doing so. We also asked them if they used AI at all in their practice as well as what they used it for. As we planned a semi-standardized interview format, each interview included unique follow-up questions as well.

For the archival research we mainly used peer-reviewed journal articles and the websites of digital pathology companies to find our information on costs, barriers, products, and more. This included articles from many publications including PubMed, Jstor, and ScienceDirect. For our market research we used the company websites and articles about them to find information such as their product portfolios, FDA clearance status, collaborations with other companies, and who they receive funding from.

In order to protect the data of our interviewees, we stored all interview transcripts in a Google Drive folder only accessible by team members. Before each interview we read an informed consent statement to ensure that our interviewee knew the risks and benefits associated with our study and obtained consent to record the interview for later transcription.

0.3 Results

Regarding the global market for digital pathology, we found that the compound annual growth rate (CAGR) is 13.2% and the total value is projected to reach 1.3 billion USD by 2026. This has given rise to many digital pathology companies globally in both image management (IM) systems and artificial intelligence (AI) applications. Among these companies, only four have FDA-cleared products on the United States medical device market. We found that AI applications are usually focused on prostate, breast, and lung cancer, which all fall in the top five most common cancers globally. There are several digital health funding programs within the United States, including the NSF's seed fund and the FDA's Digital Health Center of Excellence.

Through interviews with nine pathologists, we were able to determine benefits and barriers to digitalization. The most common benefit stated by far was that the main reason for digitalization is for the potential to integrate AI applications, as IM systems are a prerequisite for AI. Pathologists also shared that the ability for digitalization to enable faster transportation and collaboration of slides is a benefit that can improve the overall efficiency and turnaround time of a patient case, despite digitalization often slowing down pathologists on an individual level.

Our interviewees named several barriers, including finances, regulations, practicality, interoperability, and technophobia. The cost to entry for digital pathology is steep; scanners alone cost $200-300k. Since a pathology lab often needs multiple scanners, this combined with the software, maintenance costs, and increased IT support, the cost of digitalization can easily surpass a one-million dollar investment. As of 2023, 13 new billing codes for digital pathology are being implemented to track its usage. This will be an important step toward hospitals being able to get reimbursement for services performed using digital pathology, hopefully lessening the impact of the financial barrier.

A few of our interviewees also named the difficult FDA clearance process as a reason more labs might not be digitalized. As previously mentioned, there are only four companies with FDA-cleared digital pathology products on the United States market. However, there is an important clarification to make here; non FDA-cleared medical devices can still be used clinically with secondary verification of results. So even though digital pathology products can be used clinically regardless of FDA clearance, the real barrier presented is

that it is seen as a seal of approval, making hospitals more reluctant to implement non FDA-cleared products.

The practicality of using digital pathology clinically is also a factor in labs' adoption of the technology. Some pathologists have expressed the concern that digitalization actually slows them down due to the time it takes to scan a slide and due to their unfamiliarity with the technology. However, as explained previously, even though digitalization has the potential to slow down individual pathologists it does improve workflow efficiency as a whole.

Digitalization is also not possible for all subspecialties within pathology, such as cytology. Cytology slides are "3D" in that they are examined layer by layer via changing the magnification on the microscope, something that cannot currently be replicated with digital technologies. However, there is progress being made towards this, such as aetherAI's own aetherScope product.

Digital pathology products currently lack robust interoperability. Since there is no widely-used standard image format for whole slide images (WSIs), many scanners produce images in proprietary image formats which can then only be viewed with a viewer from the same company. This prevents compatibility between different companies' products as well as hindering integration with a patient's electronic health record (EHR). To combat this, the American College of Radiology (ACR) is working towards developing a standard image format called DICOM that can be created from any proprietary image format.

The main barrier–that is also the most difficult to overcome–is technophobia. Pathologists have become accustomed to their way of working through decades of training and experience, and thus are reluctant to change something that already works for them by introducing a new technology to their workflow. This resistance can be alleviated over time by pushing digital pathology education in training, so that pathologists are already accustomed by the time they enter the workforce, in addition to continuing to show existing pathologists how the use of digital pathology can change their workflow for the better.

0.4 Conclusions

Our team's research and interviews with pathologists revealed strategies that aetherAI can employ to overcome these barriers and expand their presence in the United States market. From our interview with Dr. Pantanowitz, we found that junior pathologists were more hesitant to use digital pathology compared to more senior pathologists. The reasoning behind this is their unfamiliarity with what they were taught during their schooling. Senior pathologists were more confident in their abilities and were more willing to do virtual signouts. However, some senior pathologists that transitioned into digital systems noted that the interaction between them and computers was not as friendly.

For these reasons listed, we suggest continuing collaboration with research institutions, tapping into the education market to develop tools to train the new generation of pathologists, adopting a top-down or bottom-up approach depending on the targeted institution, and looking into more tailored human-computer interaction tools.

With continued collaboration, aetherAI can sustain its innovation, validate its existing AI systems, enhance its brand, and tap into the expertise of top professionals within the field. Working with top industry experts allows them to continue to develop new AI algorithms which will not only develop the field of pathology as a whole, but will help with building brand recognition. aetherAI faces challenges building brand recognition within the United States as opposed to Taiwan, so partnering with more prestigious institutions can help with this issue. Working closely with digital pathology pioneers will help advance both the field of digital pathology and the company's brand.

Furthermore, working with research institutions will connect aetherAI with industry-leading professionals and possible pathology professors looking to incorporate a digital system into their curriculum. With aetherAI's aetherWeb, we believe that its usage within educational settings will promote the digital pathology workflow for the next generation of pathologists. As the most important feature of digital pathology, the ability to digitize glass slides and send them through the internet will improve the overall quality of pathology education. Dr. Pantanowitz visited the first institution in the world that uses digital pathology for primary diagnosis, where he met a pathology resident who he called *the very first digital pathology native* that he ever met (Liron Pantanowitz, personal communication, 4/10/23). The resident, as he recounts, found that after being trained on digital pathology for their entire career was unable to go back to a traditional workflow. Being trained solely on digital will allow for assistance when utilizing the bottom-up approach.

The bottom-up approach involves pathologists seeking funding for a digital pathology system from hospital executives. This approach is suitable for hospitals with pathologists who are already familiar with digital pathology and are interested in transitioning their workflow to a digital system within their workplace. Pathologists will be able to provide insights on how the technology can improve their workflow and patient outcomes, which can be more persuasive to hospital executives than a top-down approach. On the other hand, a top-down approach will be more effective at ensuring that the hospital as a whole is committed towards the transition to digital pathology. Hospital executives also may have more influence when negotiating with insurance companies to create reimbursement codes for digital pathology services, which can address the financial barrier as well.

As noted by multiple interviewees, the current state of interaction between

pathologists and digital workflows is sub-par at most. As Dr. Huang states *[W]hen I try to view the slides through the screen I have to use the mouse to scroll and pan around the slide. I think that it takes me more time to do this compared to what I traditionally do. During daily practices I find myself still using traditional slides* (Shih-Chiang Huang, personal communication, 3/23). Further investment into research and development into human-computer interaction is a possibility. Development of a new physical controller is not the only necessary component. Researching ways to improve the user experience of the software will also be beneficial.

Our research was not without limitations, notably the small sample size and similar backgrounds of most pathologists. Most interviewees were pathologists that were either members of the Digital Pathology Association or had a digital system already implemented. The conclusions may be influenced by this sampling bias, as all of our interviewees did agree that digital pathology is the way forward. Our interviewees also were from bigger medical centers that have the means to implement these systems. Scheduling interviews was also a challenge due to the significant time zone difference, which may have resulted in missed opportunities with other medical professionals.

1 Introduction

According to the Center for Disease Control and Prevention (CDC), an estimated 40,000-80,000 deaths occur per year due to preventable diagnostic errors. Combined with the knowledge that 70% of medical decisions are based on laboratory test results, the need for improvement in clinical laboratory standards to ensure good patient incomes is evident (*Strengthening Clinical Laboratories | CDC*, 2018).

aetherAI seeks to provide artificial intelligence (AI) solutions to improve healthcare standards and human quality of life. The company is based in Taiwan and currently has several AI technologies in the Taiwanese healthcare market. We examined the market for AI technology in the United States healthcare system–specifically within pathology–to determine barriers to its adoption. With this analysis of the United States market, we were able to develop and understand what recommendations could be made for aetherAI's continued expansion outside of Taiwan.

We developed a comprehensive market evaluation to aid aetherAI as they contemplate expansion to the United States. To conduct this evaluation, we performed archival research and interviews with pathologists in varying positions and other professionals, such as university professors. We then triangulated the data we received from the interviews and archival research to form an overview of what barriers there are to the adoption of AI pathology in the United States and how aetherAI can overcome these barriers.

2 Background

To develop a detailed market analysis, we needed to gather the necessary background needed for digital pathology, its integration with current workflows, government policies between the United States and Taiwan, and current efforts to digitalize. We first researched digital pathology and how it is currently used to establish our understanding of pathology and digitalization. We then moved into determining and analyzing the potential and challenges of digitalizing by researching current trends of digitalization and history of pathology. The analysis of current trends on digitalizing and the effects of path dependence allowed us to understand potential barriers to the adoption of this new technology. As we gained a deeper understanding of the challenges and past experiences in implementing new technologies in pathology, we compared the healthcare and biotechnology policies of the United States and Taiwan due to our sponsor's location in Taiwan. Government economic stances such as the developmental state of Taiwan and the strongly regulated market of the United States further refined the barriers we determined in the previous section. We then researched current solutions that exist globally, which allowed us to develop a deeper understanding of market trends and contextualize where aetherAI stands amongst its competitors.

2.1 Digital Pathology

A pathology lab is a clinical laboratory in which tissue, blood, or other patient samples are examined and interpreted to diagnose a disease (*About Pathology and Laboratory*

Medicine, n.d.).[1] According to the Center for Medicare & Medicaid Services (CMS), there are over 300,000 CLIA-certified pathology labs in the United States that collectively run nearly two billion tests per year. The CMS also provides data on the volume of tests run by various types of pathology labs such as hospital-based, independent (e.g. Quest Diagnostics), and physician-office labs (*S&C QCOR*, 2023). As shown in Figure 1.1, hospital and independent labs make up only about 6% of CLIA-certified labs in the United States while performing over 60% of total annual tests. This points to these types of pathology labs being of high interest in market research, as they have the potential to benefit greatly from increased efficiency.

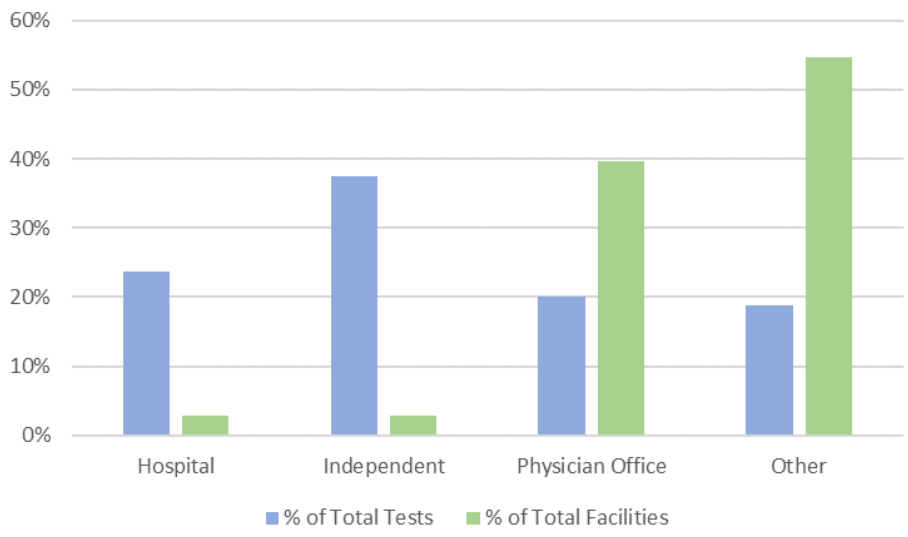

Figure 1.1: Percent of total annual tests versus percent of facilities in each category.

[1] Every lab in the United States (with the exception of New York and Washington) that analyzes human specimens must be certified under the Clinical Laboratory Improvement Amendments (CLIA).

Digital pathology refers to the transformation of the traditional pathology workflow into an entirely digital process, from sample preparation to diagnosis. After slides of patient samples are prepared, they are scanned and uploaded into an image management (IM) system for storage, viewing, management, and collaboration (Bury & Griffin, 2019). Recently, digital pathology as a term has grown to include the use of artificial intelligence as a diagnostic assistant. This creates the need to differentiate between the two main devices in digital pathology: 1) image management (IM) systems, and 2) AI solutions.

The requirements for an IM system differ greatly from what is needed for traditional slide management. The typical components of an IM system are features for organizing, sharing, and viewing whole slide images (WSIs). After a slide with a patient sample is prepared, it must be loaded into a WSI scanner for digitization. A high-throughput scanner can process 300-400 slides per batch at a speed of approximately one minute per slide. Depending on the size of the pathology department, up to 10 scanners might be needed to process slides efficiently, where each scanner costs approximately $300,000 (aetherAI, 2022). Since each WSI is approximately 1-2GB at a 20k megapixel resolution, adequate storage is needed to store the images, in addition to a sufficient graphics processing unit (GPU) to display the images. It is important to note that an IM system is required in order to use AI; in other words, a pathology lab must have all of the above requirements before implementing an AI tool (Sean Yu, personal communication, 2023).

2.2 Digitalization: Potential and Challenges

Digitalization has been described as the future of healthcare. Although there have been notable advancements, the integration and utilization of digitalization and AI pathology in healthcare systems worldwide has been slow. We examined experts' perspectives on the current state of digitalization in pathology and what is hindering its further progress in the United States.

2.2.1 Improvements to Accuracy & Efficiency

The benefits of IM systems include increased efficiency and ease of collaboration. Pathologists commonly request second reviews, especially for challenging cases, which has been shown to increase diagnostic accuracy (Geller et al., 2017). Sharing glass slides for this purpose can be difficult, as only one person can have the slide at a time. Additionally, pathologists working on a slide only view a specific area of it, making it highly difficult for pathologists in different locations to collaborate with glass slides because locating the same area on a microscope after moving the slide is highly unlikely (Sean Yu, personal communication, 2023). In contrast, WSIs can be annotated and shared instantly to be viewed by multiple pathologists at a time. In this way digitalization opens new avenues for collaboration, allowing for multiple experts to view and validate the same slide at the same time. In addition to collaboration support, IM systems provide efficient storage; slides can be easily accessed for future reference.

The implementation of AI pathology products provides further benefits to the field of pathology. Recent studies have shown that AI models have the potential to detect disease

markers earlier than they could be reliably seen by the human eye. For example, models have been developed that enable pathologists to give a diagnosis with higher sensitivity, or the ability to correctly give a positive diagnosis, than unassisted pathologists (Steiner et al., 2018; Oren et al., 2020). It is important to note that when training AI, a high sensitivity usually comes with a low specificity; in other words, fewer false negatives tend to lead to an increase in false positives. Raciti et al. (2022) assuage the concern of AI sensitivity being too high in a 2020 study on the effectiveness of Paige Prostate, an FDA-cleared AI model for detecting prostate cancer based on scans of slides. Their study shows that when pathologists use Paige Prostate to aid in their diagnoses, there is higher sensitivity with a very minimal impact on the specificity, or the ability to correctly rule out a diagnosis. Pathologists were able to identify tumors with Paige Prostate that are otherwise frequently missed more often than they were able to detect the tumors unassisted.

In addition to improving accuracy, the use of AI can also allow pathologists to make significantly faster diagnoses compared to unassisted work (Chen et al., 2021; Raciti et al., 2020; Steiner et al., 2018). Faster diagnoses decrease turnaround time for results, a benefit for both physicians and their patients. Another factor in the efficiency of diagnoses is how many resources are required to perform necessary tests, such as patient tissues, glass slides, and stains. AI can be used to identify disease markers in a shorter amount of time based on fewer factors, meaning fewer samples are needed from the patient and less time and money is needed from the pathology lab (Go, 2022).

2.2.2 Workflow Integration

Many digital pathology experts have questioned the relative slowness of the digitalization of the field. Scholars believe this slow adaptation occurs due to a “translation gap”, defined as “the failure to prospectively validate and successfully integrate AI models into real-world clinical workflows” (Berbís et al., 2023). Others elaborate that the power and accuracy of the algorithms are not the only things necessary for digitalization to develop. Instead, to achieve the goal of increased diagnostic accuracy and efficiency, Steiner et al. (2021) discuss various factors that need addressing to close the “translation gap.” In addition to thoughtful implementation into current workflows, they discuss the importance of human-centered design and interoperability between existing computer infrastructure. Gu et al. looked to do just that with their development and study of xPath.

Gu et al. (2022) developed a “human-AI collaborative diagnosis tool–xPath–that shares a similar examination process to that of pathologists.” Seeking to improve AI’s integration into routine examinations, the development of this tool gave insight into challenges that needed to be solved to bridge the “translation gap.” Gu et al. define three challenges: comprehensiveness, explainability, and integration, which prevent AI from being adopted in a clinical setting. They propose xPath as a step toward a solution to these problems. They also bring the conversation to Human-Computer Interaction researchers to collaborate with pathologists to assist with what Steiner et al. (2021) identified as “thoughtful implementation.”

Another challenge in workflow integration is resistance to change. Path dependence is defined as the tendency for technologies and institutions to resist change; also based on the idea that “history matters'' (Path Dependence | Definition & Facts | Britannica, n.d.). Scholar

Paul Pierson (2000) explains that path dependence is used to support key claims: patterns of timing and sequence, repetition of similar conditions, small events lead to large consequences, and political development is marked by critical moments. One of the key ideas that Pierson (2000) expresses about path dependence is that similar factors that contribute to the resistance to change have the tendency to repeat. Since pathology has existed for centuries while digital technology is just beginning to emerge, there might be hesitancy to change a system that already works, even if a new system might be better. This can be seen in other applications of technology in healthcare; for example, the transition from paper to digital medical records. According to Barrett et al. (2016), many physicians agree with the concept of digitizing their records but are reluctant to put it into practice due to tedious startup work such as the entry of all existing files. This suggests that for pathology labs to be open to integrating AI technology, it must either be easy to set up or it must be clear that the benefit is worth the setup time and costs.

Between the invention of the microscope and its first use in pathology there was a gap of about 250 years. A few factors contributed to this delayed adoption: scarcity, high cost, neglect by universities, and technical difficulties (Majno & Joris, 1973). In 1744, scholar Henry Baker published a manual called *The Microscope Made Easy* where he details how the microscope was only available to a select few people and had a huge price tag. Baker also explains that people feared the use of the microscope because they believed that it required a deep understanding of optics (Majno & Joris, 1973). According to Hajdu (2011), physicians in the 17th and 18th centuries were performing autopsy findings solely based on the naked eye. It was not until the 19th century where pathologist Gabriel Andral first used the microscope to

focus on alterations in blood cells (Hajdu, 2011). One of the largest barriers that contributed to the late adoption was distrust due to the pessimistic attitude of the scientific community towards using optical devices (Majno & Joris, 1973). Currently, the integration of AI into the pathology workflow has been inhibited due to the incompatibility between the two (Gu et al., 2022). In the context of path dependence, the adoption of such a keystone instrument was a slow process, spanning 250 years of resistance. As such, in the implementation of digital systems in current workflows, it is imperative to resist the status quo to prevent a repetition of historical patterns.

2.2.3 Monetary Barriers

Pathology labs need to have a slide scanner, viewer, and storage server to implement digital technologies, which can present a large cost barrier to the adoption of digital systems. Even then, the cost is only part of the whole picture as labs also have to deal with the time, manpower, and collaboration with other departments it would take to implement (Go, 2022). Fortunately, lower-cost AI systems have been presented, but digitalization of slides is still needed as a precursor to utilize AI algorithms.

A group of pathologists has developed a promising algorithm for digital pathology called clustering-constrained-attention multiple-instance learning, or CLAM (Lu et al., 2021). This algorithm is more data efficient than many other deep-learning methods and only requires slide-level labels. And CLAM does not stand alone – several other models have recently been developed that also are only trained with slide-level labels (Chuang et al., 2021; Schrammen et al, 2020). It reduces the load and computational power needed to use these AIs, which in turn

cuts costs by reducing demand for hardware processing power. Still, CLAM has additionally been tested on microscopic images taken with just a smartphone and a microscope. This test showed that using the lower quality images only made a drop of about 0.037 percent AUC (area under the curve) meaning that for only a negligible accuracy drop, pathology labs using the pre-trained algorithm could have an astronomically lower barrier to entry for AI pathology.

Additionally, a three-year study on a hospital by Hanna et al. (2019) showed that while implementing digital pathology systems resulted in an initial cost increase, it resulted in net lower costs as pathologists became acclimated and the need for glass slides went down. She found that the cost of dealing with glass slides and the storage of said slides for later reference would incur an extra $267,000 a year in costs as compared to digital, showing that the entry cost into digital slide imaging could pay for itself over time. Instead, digitizing slides allow compact storage that can be accessed at any time and anywhere, and last indefinitely.

2.2.4 Ethical Concerns

The implementation of artificial intelligence and digitalization in pathology must be considerate of consent, privacy, and bias. Most medical AI systems require large amounts of data derived from patient records. With medical AI systems comes the issue of the collection and sharing of personal data (McKay et al., 2022). For United States data to be anonymized, it must be stripped of any identifiers such as age and dates, following the United States Health Insurance Portability and Accountability Act (HIPAA) guidelines. Under these guidelines, AI companies are strictly required to obtain informed consent from patients before using any of their data for model training (Jackson et al., 2021; Sorell et al., 2022).

The trustworthiness of medical AI has been doubted due to the potential for bias in training. Chauhan and Gullapalli (2021) state that a reason for bias is mainly due to sample availability and socioeconomic factors such as access to healthcare. Although there may be instances where AI displays biased results due to skewed data sets, bias can be avoided with comprehensive data samples (Sorell et al., 2022). Without comprehensive data samples, the AI model would be incompletely trained, also called underspecification (Chauhan and Gullapalli, 2021). When it comes to cancer diagnoses the risk of bias is minimal because almost every type of cancer exhibits common markers (McKay et al., 2022).

2.3 Healthcare and Biotechnology in Taiwan and the United States

Our sponsor is based within Taiwan and seeks to expand into the United States market, making it necessary to examine similarities and differences between the United States and Taiwan. Specifically, we want to examine differences between the healthcare systems and economic policies between the two countries. The healthcare systems of the United States and Taiwan have two very different approaches when providing healthcare to their citizens. As a general overview, the United States relies on a combination of public and private insurance programs whereas Taiwan has a single-payer, government-run National Health Insurance (NHI) system that provides mandatory coverage to all citizens. Understanding the similarities and differences of both healthcare systems allow us to understand barriers that may inherently lie within the systems themselves. The highly centralized healthcare system of Taiwan is overseen by the National Health Insurance Administration (NHIA), which is under the Ministry of Health and Welfare (MoHW). In addition to the NHIA, parliament also controls the premium of the NHI

requiring an amendment to be passed if the premium rate rises more than 6%. Hospitals also rely on subsidies from the government for funding research, new technology, employee wages, and covering expenses. According to The Commonwealth Fund (n.d.), all citizens of Taiwan receive an affordable copay of 50-420 NTD or 1.67-14 USD for their visits. To ensure quality of care, performance based incentives are given to physicians such as the pay-for-performance plan.

Relying on the combination of public and private insurance programs, the United States healthcare system looks to provide healthcare on a high standard. Some individuals are covered by a government program such as Medicare, Medicaid, or provided care by the Veterans Health Administration. Even with the high quality of care, the affordability of care is a problem within this system. 91.5% of citizens have some form of insurance, leaving a staggering 8.5% of the population, or 27.5 million people, uninsured. On the contrary, 99% of Taiwanese citizens are covered through the NHI (The Commonwealth Fund, n.d.). The Veterans Health Administration, is however, the largest centralized healthcare system in the United States. Also funded by the government, the VA has a unified process in determining budgeting and implementation of systems which must be approved by Congress. The VA provides care to 171 VA Medical Centers and 1,113 outpatient sites of care, covering nine million veterans (Veterans Health Administration, n.d.).

Compared to Taiwan, the United States does not have incentives for physicians to ensure quality of care. Instead, the Affordable Care Act (ACA) required the U.S. Department of Health and Human Services to establish a National Quality Strategy (The Commonwealth Fund, n.d.). This strategy outlines the national goals and priorities to guide local, state, and national

governments towards quality improvements. The 2018 National Healthcare Quality and Disparities Report found that improvement in quality has been inconsistently increasing, but the affordability was consistently decreasing.

The Taiwanese developmental state played a crucial role in the growth and development of the biotechnology sector in Taiwan. A developmental state refers to a model of economic development where the government takes a more active approach in shaping the economy. This is usually done through policies, regulation, and investments. In 1982, the government deemed biotechnology to be an essential sector that would allow for further Taiwanese economic development. The establishment of the Development Center for Biotechnology (DCB) in 1984 sought to nurture biotech start-ups through the offering of fiscal and tax-based benefits (Wong, 2005). In addition to these policies, the government has assisted with promoting collaboration between academia and industry through the establishment of several biotech parks. Through the passing of the "Asia Silicon Valley 2.0" developmental plan, the Taiwanese government further solidified its stance on improving the startup development environment (Executive Yuan, 2021). By further providing resources, funding, and incentives for biotech research and development, the government continues to not only stimulate the growth of the biotech industry, but its economy as well.

On the other hand, the United States has a system relying on strong regulations, which can have both positive and negative effects on the development of start-ups. With limited resources, start-ups may struggle with meeting the regulatory standards that the government sets. Specific to our sponsor, the fact that no guidelines exist for AI technology, combined with already strict approval standards, are inherently a barrier of entry into the United States.

However, these standards can also ensure equal opportunity or competitive advantages for all start-ups. Similar to Taiwan, the United States government also passes legislation on industry funding looking to house more domestic production. In December of 2022, the National Biotechnology and Biomanufacturing Initiative (NBBI) was launched (The White House, 2022). Through the NBBI, a stance to develop the domestic biotechnology sector was adopted, similar to that of the Asia Silicon Valley 2.0 developmental plan of Taiwan.

2.4 Current Digitalization Solutions

Taiwan's strong promotion of the development of the biotechnology industry set the stage for aetherAI, a digital pathology company based in Taipei. Their mission is "to use state-of-the-art information technology to improve standards of healthcare and quality of human life", shown by their work towards providing solutions in digital pathology, AI diagnosis services, and biopharmaceuticals. The company was founded in 2015 in Taiwan by Steve Yeh, Joe Yeh, and KJB. As of now, they have approximately 70 employees.

aetherAI offers products in both the IM systems and AI application sides of digital pathology. Their image management system, aetherSlide, allows for viewing, storage, and organization of digitized slides in addition to easy integration with AI tools and the capability to automatically triage cases. AI products offered by aetherAI cover a wide range of pathology specialties, including but not limited to analysis of bone marrow samples, analysis of lymph nodes for gastric cancer metastasis, and analyzing breast cancer prognosis.

Companies outside of Taiwan have also developed digital pathology products. Philips, a Dutch company, produces scanners and provides Intellisite, an IM system for viewing slides and

collaborating on cases (*Philips IntelliSite Pathology Solution*, n.d.). Sectra and Indica Labs both provide similar image management systems that can be easily integrated with AI. (*Sectra Digital Pathology Solution*, n.d.; "HALO AP," n.d.). There are also several companies that, like aetherAI, provide both IM system and AI pathology solutions. Aiforia, a digital pathology company from Finland, claims that their cloud-based model reduces bias while increasing the speed and accuracy of results (Aiforia, n.d.). Paige AI, a US-based company, provides an IM system in addition to breast cancer detection AI and an FDA-approved prostate cancer detection AI. (Paige AI, n.d.). Path AI is another US-based biotechnology company whose IM system product, AISight Dx, is FDA 510(k) cleared and produces high-quality in-vitro diagnostic images (AISight, n.d.).

Our research into the pros and cons of digital pathology, the barriers of its acceptance in the US, and the differences between the Taiwan and United States healthcare systems has painted a much clearer picture of the background of our topic. Our data shows how digitalization seems to be the path of innovation in the field of pathology, however, it is disputed by underlying barriers found within the adoption of new technologies. Whether that be the steep entry cost, the difficulty in changing the workflow of companies, or the lack of easy ways to get the technology approved for clinical use, digital pathology has a long way to go before it can be adopted en masse.

3 Methodology

The goal of our project was to identify barriers to the digitalization of pathology labs in the United States and propose how they could be overcome. To do this, we needed a solid

background in the benefits, limitations, and ethics of digitalization in addition to real-world accounts from experts in the field. We used a multi-method research design to accomplish this task. By combining archival research with interviews, we expected to attain a well-rounded view of the state of digitalization and AI technologies to guide aetherAI's expansion into the United States digital pathology market.

3.1 Archival Research

We used archival research to gain an understanding of what pathology is, limitations of digital pathology, the similarities and differences between the Taiwanese and US healthcare and biotechnology sectors, and the current progress in the digitalization of pathology. Most of our literature was found via searches on Google Scholar, PubMed, and the WPI Gordon Library database. According to Lune and Berg (2016), a common problem in the execution of a literature review is being too restrictive when searching for references. To avoid this, we used varied terms in our searches; for example, "ethics in AI", "AI in healthcare", "ethics of AI pathology", and "ethical concerns of AI in healthcare".

Additionally, as we continued to research, selection bias was present as a limitation. Selection bias is described as the inability to achieve randomness from a selection of cases, resulting in an unrepresentative sample of a population (Lustick, 1996). To avoid selection bias, we used triangulation, which involved the use of scholarly sources that corroborated our points and discussed dissenting opinions by experts. It was necessary to look at differing viewpoints so that a cohesive argument with minimal bias could be constructed. The information discovered

then allowed us to generate a refined list of barriers and limitations found within the digital pathology market.

3.2 Interviews of Pathology Experts

Between March 23rd and April 19th, we conducted nine interviews of researchers and pathologists in both Taiwan and the United States, including those who do and do not use digital systems. Pathologists within the United States generally do not have experience with using digital systems clinically (Phoebe Liang, personal communication, 2023). Moreover, less than 20 percent of pathology labs use digital pathology within their workflow as a second opinion, while less than 1 percent use digital pathology for clinical exams (*Legal and Regulatory Hurdles in Digital Pathology and Telepathology*, n.d.). Interviewing these professionals allowed us to understand traditional clinical pathology workflows within labs and concerns regarding digitalization. Pathologists within Taiwan, and some research hospitals in the United States, use digital systems and served to help us understand the workflow change, benefits and limitations of a new system, and possible improvements. Of these interviews of pathologists who have implemented digital systems, two utilized aetherAIs IM system and AI products in their workflow.

To locate interviewees, we used our team's connections with pathologists, recommendations from aetherAI, and cold emailing pathologists found via searches online. The recommendations from aetherAI included both two interviews that they set up for us as well as the contact information of attendees from the 2019 Digital Pathology Association (DPA) conference. After each interview, we also asked our interviewee if they recommended anyone

else to reach out to. Receiving recommendations from our interviewees allowed us to both expand our sample and increase the chance of getting a response, as we were reaching out with a connection rather than with a cold call or email. This variety of sources for interviewees allowed us to build a representative sample of pathologists that minimized bias towards certain populations. The pathologists and researchers that we interviewed can be found in the appendix along with the questions that guided our interviews.

All of our interviews took place over Zoom or Google Meet. Using video call interviews rather than telephone interviews made sure that we kept the advantage of a wider reach than what telephone interviews provided (as not everyone can make long-distance calls) while retaining the ability to have face-to-face communication, which is a key factor in maintaining rapport and a personal connection. Each interview lasted 20-45 minutes, varying based on the lengthiness of responses to our questions and what follow-up questions we asked. To maximize the information we got from our interviewees, we used a semi-standardized interview format. This format allowed us to stay on track with a schedule while also allowing scripted and unscripted follow-up questions when necessary. Our team conducted each interview as a group, with one team member leading the interview, one sub-leader supporting, and the two remaining members focused on taking detailed notes. This interview structure allowed the team member interviewing to be completely engaged with our interviewee.

To ensure the informed, consensual participation of the interviewees, we read an informed consent statement before any questions were asked. The statement can be found in the appendix and included the risks and benefits associated with the study and how their information would be used as well as asking permission to record video and/or audio of the

interview. All participants gave us their consent to record, so we were able to transcribe the full text of every interview. This explanation served as implied consent instead of a formally signed consent form; this style of informed consent provided the additional benefit of removing any written records of who exactly participated in our study (Lune & Berg, 2016).

As stated by Lune and Berg (2016), interviews are a fundamental way to learn about people's lives; generally, people are honest during interviews because they have no reason to mislead. Interviews must be crafted in a way to make the interviewee comfortable, which can be achieved by providing an inviting environment and establishing rapport. We structured our interviews to have fewer in-depth questions at the beginning to let the interviewee acclimate. The script included a brief small talk before the interview began, then slowly moved towards more in-depth questions. We also considered that self-reported data is not always reliable; Lune and Berg state "memories fade, or change, so you can't be sure about what they reported…" This is a limitation that is inherent to interviews and is something that we kept in mind.

3.3 Market Research

To find other barriers, market research was conducted into the current industry of digital pathology, looking to discover past, current, and future trends. The primary focus of the market research was an analysis of aetherAI's competitors in both IM systems and AI solutions. Several factors were included, such as an overview of each companies' project portfolio, hospital collaborations and implementations, FDA approval/CE mark status, and funding sources. This information was obtained from news articles and reports or brochures from each

companies' website. In addition to an analysis of competitors, we used information from our interviews to determine differences in the market for digital pathology between different types of hospitals.

3.4 Surveys

Originally, we wanted to include a survey to gather a general census of the US population. The objective of the survey was to understand US citizens' thoughts on the use of AI within the medical field. We believed that it would be important to understand the patient's point of view in a market study; however, we did not consider the fact that patients have no control over technology usage within hospitals and likely are unaware of diagnostic processes. Therefore, the responses collected from the survey would not have helped us determine any barriers or develop a detailed market report, which was our main research goal. The inability to gather a representative population further pushed us to drop our survey section. Since the United States population covers a wide variety of demographics, our survey results would have likely suffered from selection bias due to convenience sampling; such a sample would be skewed towards certain demographics, most likely college students in the northeast. After reviewing last year's study, we also considered developing a survey geared towards pathologists and hospital executives. However, we also dropped the idea as they were unable to obtain a substantial amount of responses to further their study.

3.5 Case Studies

Our team's initial goal of talking with Dr. Huang at the Chang Gung Medical Foundation (CGMH) was to start developing a case study on how the pathology department digitalized and adopted AI technology. We were hoping to use this case study as a basis for understanding what barriers other hospitals might face in trying to digitalize their pathology departments through learning about what CGMH needed before integrating aetherAI's technology. A case study is most beneficial due to the intense study it entails (Lune & Berg, 2016), so we reasoned that one interview would not be enough to gather the depth of information we wanted. However, during a meeting with our sponsor we learned that CGMH approached digitalization in a top-down manner–that is, higher-level administration decided to digitalize the entire hospital system, including the pathology department (Phoebe Liang, personal communication, 2023). Due to this, the pathology department did not face any barriers in digitalizing as it was a decision made for them, not an idea they had to propose. Therefore, we chose to not do a case study on CGMH as their situation is not representative of the digitalization process most other pathology labs must undertake. Though we are not doing a full case study, our interview with Dr. Huang provided useful information about the process of integration and adaptation after implementing the new technology.

3.6 Data Analysis & Visualization

Content analysis is a tool used to "identify patterns, themes, assumptions, and meanings" of the given content, which is typically content generated from human

communications such as interviews (Lune & Berg, 2016). Performed after all of our interviews, it allowed us to identify trends in pathologists' stances on digitalization. A concern with content analysis is that what you are analyzing is limited to what has been transcribed completely; but since we performed content analysis on interviews we have transcribed ourselves, this issue is virtually nonexistent (Lune & Berg, 2016).

For our analysis, we were planning to use Voyant, a free software for performing text analysis. To get the interview content in the proper format, we recorded and transcribed the interviews. We were going to use Voyant's word correlation and word cloud tools in order to determine associations between certain words and frequency of words respectively However, upon beginning we found that the analysis was not particularly useful for what we wanted to see. Since the sample size was small, it proved easier and more beneficial to read through the interview transcripts ourselves to determine themes between them and to pick out relevant quotes to support our findings and our conclusions.

3.7 Ethical Considerations

We must also consider our ethical protocols as we conduct our research. According to Lune and Berg (2016), it is necessary to disclose the usage of the collected data with our interviewees, which can take the form of a verbal or written agreement. The informed consent to use interviewees' responses in our research is vital to ensure that they are comfortable answering the questions we pose.

Our goal is to provide an overview of the market for digital pathology in the United States. For this, we must be aware of the importance of data privacy. To uphold the privacy of

our interviewees, we have kept their names and contact information private. We also considered the group of people that would have access to our data, restricting it only to ourselves and advisors. In addition, our informed consent statement ensured that interviewees understand that we are not providing their information for marketing purposes, but for the sole purpose of bolstering our knowledge on digital pathology. All potentially identifying information, including interview transcripts, is kept in an encrypted Google Drive folder that cannot be accessed by anyone outside of our team.

4 Findings

4.1 Current Market

The current global digital pathology market expects a compound annual growth rate of 13.2% and an expected market value of 1.3 billion USD by 2026 (Digital Pathology Market Trends, Drivers & Opportunities, n.d.). The global market value as of 2021 was $736 million. According to a report done by Markets and Markets (n.d.) the market is driven by factors such as enhanced lab efficiency, linking to electronic medical records, and the rising prevalence of cancer.

As the market for digital pathology products has grown, companies globally have established themselves in the industry. Most digital pathology companies produce products only within hardware/IM systems or within AI solutions, with few exceptions. Among the most notable of aetherAI's competitors are Philips, Sectra, and Paige. Philips and Sectra both offer FDA cleared scanners and IM systems, while Paige produces several AI applications–including

an FDA cleared prostate cancer diagnostic assistant–as well as an IM platform to work with their applications. Overall, breast cancer, prostate cancer, and lung cancer are the most covered by AI solutions, all falling within the top 5 most common cancers worldwide ("Worldwide Cancer Data," n.d.). Several other companies produce IM and AI solutions, but most are designated for research use only within the United States. More detailed information about these and additional companies can be found in section 7.3.

In recent years, the United States government has begun initiatives toward advancing digital health. The Agency for Healthcare Research and Quality (AHRQ), an agency within the Department of Health and Human Services (DHHS), provides funding for research into the development of digital systems within healthcare and how digitalization can improve standards of healthcare for patients (AHRQ, n.d.). The FDA's Digital Health Center of Excellence (DHCoE) helps actualize this development by providing support, including funding and guidance through the FDA approval process, for new and established companies to develop digital medical devices (FDA, 2022). Finally, the National Science Foundation's (NSF) seed funding program provides R&D for digital health companies, among other industries (NSF SBIR, n.d.). These funding programs suggest that the United States is making progress into digitalizing healthcare overall, which will hopefully include the field of pathology.

4.2 Benefits of Digitalization

A common sentiment held by the interviewees is that there is "*very little incentive to digitizing slides in the first place"* (Woon Chow, personal communication, 4/4/2023). Despite this sentiment, most pathologists that we interviewed still agreed that pathology is moving

towards digitalization. After conducting multiple interviews, it became apparent that digitalized systems do offer some advantages. The most emphasized point across all our interviews was that incorporating digital systems into a lab workflow has the advantage of enabling future integration of AI systems, as an image management system is a prerequisite for AI applications.

> *To use some of the new tools like AI, you have to digitalize slides first. That was part of the motivation because that's the future.* (Woon Chow, personal communication, 4/4/23).
>
> *[T]he ability to use any AI tool to improve our practice was really critical knowing that the field is moving towards that way.* (Marie-Christine Aubry, personal communication, 4/10/23).
>
> *[T]he [...] most powerful [advantage], which is not fully realized, is the AI aspect of it.* (Anil Parwani, personal communication, 4/14/23).

Pathologists also noted that while the time taken to analyze an individual slide may be longer, the overall turnaround time for analysis was reduced. This is mainly due to the capability to diagnose and collaborate from any location in the world, a significant advantage of implementing digital systems.

> *[T]he most phenomenal powerful advantage is sharing images with somebody around the globe rapidly [...] this approach saves both time and money as the transportation of physical slides can be a lengthy and costly procedure.* (Anil Parwani, personal communication, 4/14/23).

Effective collaboration becomes imperative in emergency situations, particularly when a diagnosis needs to be made by a specialized pathologist located thousands of miles away. As shared by Dr. Chow, *"[a] lot of bad things happened with the COVID pandemic, but digital pathology really moved the field forward with the pandemic"* (personal communication, 4/4/23). The ability to share slides virtually is also extremely useful in educational and other academic settings. In most cases, classrooms are furnished with microscopes that have multiple viewing heads, limiting the number of students who can simultaneously observe slides to

around five. However, by utilizing digital slides, entire classrooms can now view high-definition slides together (Phoebe Liang, personal communication, 2023).

> *Let's say I'm presenting at a conference, instead of cutting slides and distributing the slides–which is a lot of work–sending a link to everyone in the conference who can then preview the slides beforehand is much more manageable*. (Woon Chow, personal communication, 4/4/23).

The ability to collaborate improves all areas of pathology, including in clinical, research, and academic settings.

4.3 Barriers to Digitalization

Over a 5-week period our team conducted 9 interviews via Zoom and Google Meet. Through these interviews, we were able to get pathologists' valuable insights into the current market of digital pathology and barriers that are slowing adoption of this technology. Out of our eight interviews in the United States, we interviewed three pathologists from the east coast, one pathologist from the west coast, and four pathologists from the midwest, as represented in Figure 4.1.

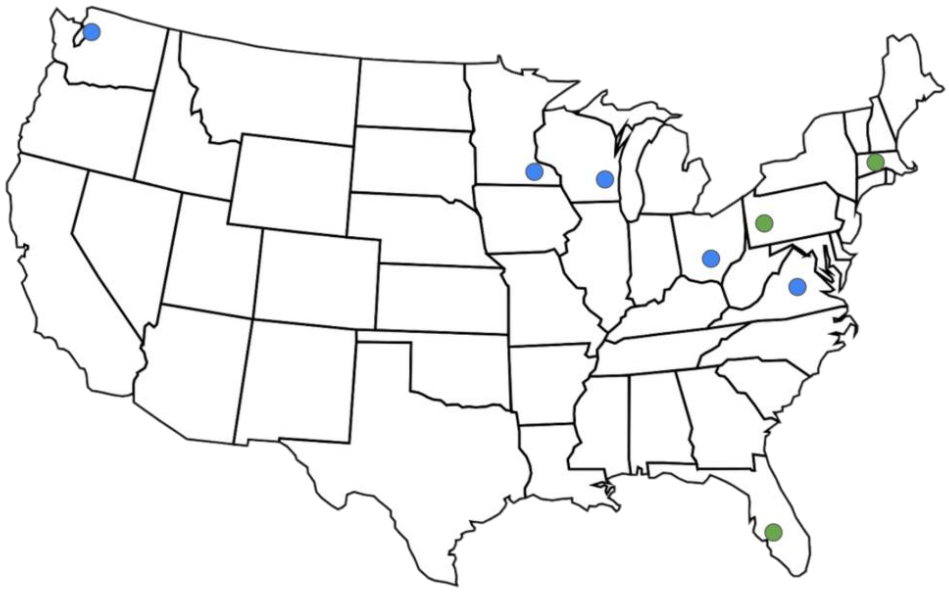

Figure 4.1: Map showing the United States pathology labs we interviewed, where blue dots represent DPA members and green dots represent non-DPA members..

We determined five barriers based on our interviews–financial barriers, US regulations, utility of digital pathology, interoperability between existing systems, and technophobia of pathologists, which we deem the most prevalent barrier. Although each pathologist interviewed had different views on the barriers to adopting digital pathology, most of them pointed out the five main barriers that we will discuss. The range of years as a practicing pathologist (seen in figure 4.3 below) spans from 6 to 27, providing us with a diverse range of perspectives.

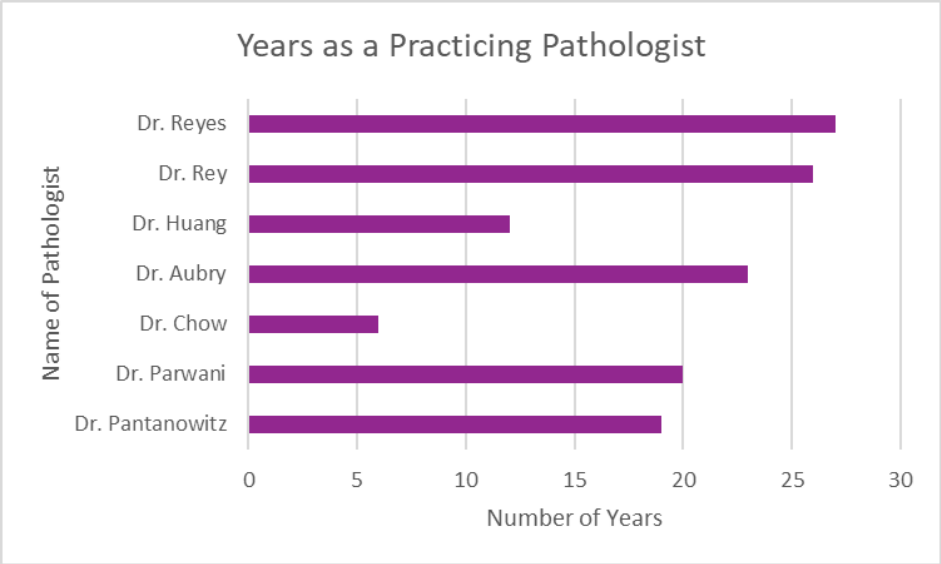

Figure 4.2: Bar chart displaying the years of experience across all of our interviewees.

4.3.1 Finances

Between our nine interviews, eight of them discussed cost as one of the barriers preventing the implementation of digital pathology. After cross referencing all of our interviews with each other, we were able to discern multiple financial issues that arise once a lab or hospital decides to digitalize–the steep entry and upkeep cost of digital devices, the lack of reimbursement, and difference of budgeting between different organizations. These financial issues that arise with the implementation of emerging technologies are a common occurrence, but they are likely to diminish over time as pathology becomes more widespread. However, despite the potential of digital pathology, the poor return on investment is still leading hospitals to stray away from the technology.

The high cost of scanners, need of sufficient digital storage, computers with sufficient hardware to display the images, monitors, and the digital pathology software systems are main

expenditures needed to facilitate the implementation of a digital system. Digital pathology systems rely on a scanner to facilitate the digitization of slides, however

> *[s]canners themselves are just a few hundred thousand dollars. If you get one you kind of need two for the redundancy of the system. So that's like a million dollars right there for the scanners alone* (Woon Chow, personal communication, 4/4/23).

Faculty, maintenance, and upkeep costs appear even after overcoming the million dollar entry fee–hundreds of thousands of dollars are needed in subsequent years, making the overall investment *"in the order of millions in order to digitalize"* (Dr. Aubry, personal communication, 4/10/23). Besides scanners, digital storage must be taken into account. An advantage of digitizing slides is the ability to store and organize the slides for an indefinite time. The continued scanning of glass slides into WSIs brings with it the need for hospitals to have sufficient storage space to keep these digitized slides for future use.

> *[I]n pathology the images are about 1-2 gigabytes. That's just one image, [...] you'll need like 50 slides all for one case. That's 100 gigabytes for one case [...] so from a cost benefit perspective it's really not great.* (Woon Chow, personal communication, 4/4/23)

This is where healthcare professionals benefit from the use of Current Procedural Terminology (CPT) codes, which are maintained by the American Medical Association (AMA). These codes provide a standardized language for tracking medical procedures and technology changes over time, and are also used by healthcare providers to bill insurance companies for the service they provide. By using CPT codes, healthcare providers can ensure they are receiving appropriate reimbursement for the digital pathology services they provide, including the storage of WSIs. However, in previous years, digital pathology did not have a set of CPT codes.

> *There isn't an actual billing code yet, but what we have now seen is, actually, the US Government CMS set up for Medicaid services, has issued 13 CPT codes for billing.*

> *They are only for tracking out to see who's using it, and how much, but eventually the billing will come. (Liron Pantanowitz, personal communication, 4/10/23)*

While billing codes do not currently exist for digital pathology services, the establishment of these tracking codes by the CMS suggests that progress is being made towards establishing said codes. This is a positive sign for future adoption of digital pathology services and will be important for reducing financial barriers and ensuring appropriate reimbursement for healthcare providers.

The management of budgets in service based hospitals and private labs also have implications for the adoption of digital pathology. Service based hospitals may be more limited in terms of budgeting due to government budget cuts or restrictions, which can impact their ability to invest into new technology. Conversely, private labs have more flexibility in terms of budgeting decisions and have the ability to allocate more resources towards new technology (Phoebe Liang, personal communication, 2023). Healthcare providers must also consider potential benefits and drawbacks of adopting digital pathology, namely AI. With the lack of regulations, healthcare providers must make their own judgements on whether or not to utilize AI within current workflows.

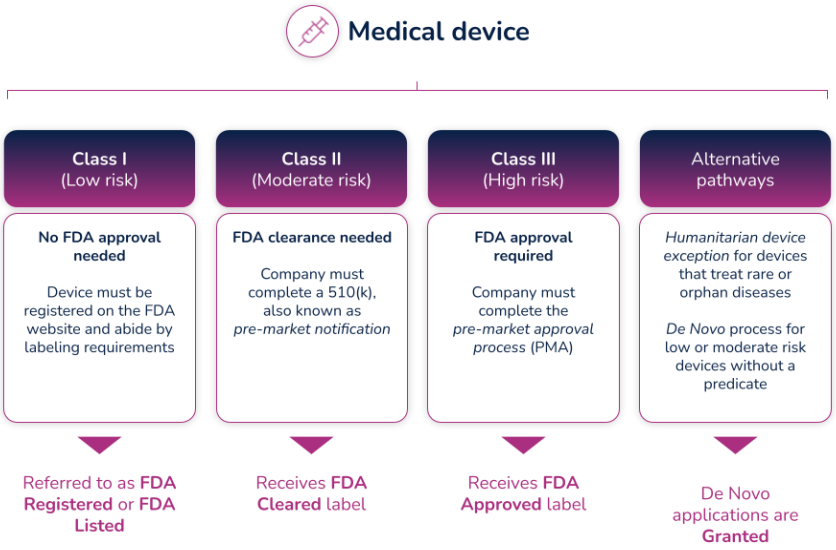

Figure 4.3: Infographic showing different medical device registration processes by risk class (Source: (FDA Listed, Cleared, Approved, Granted - What Do These Mean, and What's the Difference? n.d.)

4.3.2 Regulations

Currently, IM systems and AI must undergo the same approval or clearance process as other medical devices in the United States. This process can last weeks to months, depending on the determined risk of the product and if there is already a similar product on the market (see Figure 4.3 above) ("510(k) Submission Process," 2022). The FDA classifies digital pathology devices into four broad categories: Digital Pathology Image Management and Viewing Software, Whole Slide Imaging System, Digital Pathology Display, and Software Algorithm Device to Assist Users in Digital Pathology. As of April 2023, there are only 10 devices across all four categories (*Product Classification*, n.d.).

The strict regulations for medical devices have been pointed to as a factor in the slow adoption of new technology. FDA-approved medical devices are able to be used for primary diagnosis, meaning that no external validation is needed before using the device clinically. The

importance of this clarification is that non-FDA-approved medical devices can still be used in a clinical setting, given that there is external verification; for example, using a microscope in tandem with WSIs, or manual review of suspicious regions highlighted by an algorithm. This could increase the time it takes to review a slide, but data from interviews has shown that many pathologists tend to check their digital work manually regardless of FDA approval. With this, FDA regulations present only a perceived barrier rather than a true barrier. Even though pathologists can use any digital system clinically as long as it is validated, there is reluctance as FDA approval is a gold standard (Woon Chow, personal communication, 4/4/2023).

4.3.3 Practicality

Some of our interviewees expressed the concern that digital workflows are less efficient than traditional pathology. This is typically caused by physical discomfort or lack of familiarity with the new technology. As Dr. Huang mentioned, "*[i]t's more labor intensive and time consuming when we try to use digitized slides on the screen, compared to using a microscope*" (personal communication, 3/23/23). As a result of this, he typically uses glass slides in his daily work despite having every slide available digitally. Lack of familiarity with technology also negatively impacts the efficiency of digitalization due to the tendency to double check work done with digitized slides.

> *Sometimes it's still pretty new, so we're still building our diagnostic acumen or confidence, so if I'm looking at the digital and I am not sure 100% what I'm looking at I might go back to the glass slide because this is still our comfort zone.* (Marie-Christine Aubry, personal communication, 4/10/23).

> *But in all honesty, I need to see the slides first to make sure that I have my own answer.* (Shih-Chiang Huang, personal communication, 3/23/23)

But even though the time taken to analyze an individual slide may be longer, the overall turnaround time for a case is reduced. This is mainly due to the capability to diagnose and collaborate from any location in the world, a significant advantage of implementing digital systems.

> *[T]he most phenomenal powerful advantage is sharing images with somebody around the globe rapidly [...] this approach saves both time and money as the transportation of physical slides can be a lengthy and costly procedure.* (Anil Parwani, personal communication, 4/14/23).

While digitalization has the potential to streamline most types of pathology, certain specialties such as cytology still require the use of physical slides. This leads to concerns about practicality, as the requirement of glass slides means that it is impossible to digitalize all aspects of a pathology lab.

> *That comes from adjusting the depth that we can look with our microscope and that's not there with the digitized imaging, […] we lose that third dimension. [...] So there's some parts of our practice that just can't go completely digital yet.*
> (Marie-Christine Aubry, personal communication, 4/10/23).

As shared by Dr. Aubry, sample analyses in cytology rely on the depth in a slide. In order to see different layers of the slide, cytologists adjust the magnification on the microscope, something that currently cannot be replicated using WSIs. However, there is progress being made toward a digital solution for cytology; aetherAI's own product aetherScope is a virtual microscope that can be used for cytology and integrated with their AI applications.

4.3.4 Interoperability

Several companies produce scanners that generate images in proprietary file formats. This leads to scanners only being compatible with IM systems from the same company, or to

companies needing to support many file formats–for instance, Indica Labs employs an image platform that supports 19 different file formats. These 19 formats are still only a small proportion compared to the vast majority of formats available on the market. Attempts have been made to establish a standardized format, notably, the Digital Imaging and Communications in Medicine (DICOM) format, established by the American College of Radiology and the National Electrical Manufacturers Association. The goal of this initiative is to enhance industry interoperability by creating an easily accessible format to reduce the burden of dealing with various file formats. This format has the added benefit of allowing patient, case, specimen, and staining information to be added to the image files, making them more practical than images alone. Conversion tools, such as Infinitt, can transform whole slide images into DICOM format, which presently supports most vendor file types (Mori, 2022).

Efficiency is a primary goal in the medical sector, and it is essential to have a shared file type to promote seamless collaboration between hospitals and labs. Unfortunately, there are numerous challenges to achieving this goal, including the desire of companies to sell their own scanners and software packages to increase revenue and retain customers. There are also high costs associated with implementing DICOM imaging, which pose a significant obstacle to laboratories.

> *Scanning companies will make more sales if they sell non-DICOM viewers [...] it's going to cost another $100,000 [for a lab] to use these DICOM features so it's not an incentive for the scanning company to sell DICOM scanners.* (Anil Parwani, personal communication, 4/14/23).

So although the DICOM format is being developed as a potential solution to the lack of interoperability, financial challenges still pose a barrier to its widespread adoption in pathology labs.

4.3.5 Technophobia

The hardest barrier to overcome in the expansion of digital pathology is inherent resistance to change. It has always been a difficult challenge to persuade individuals to alter the way they carry out their work, especially medical professionals. Medical professionals undergo years of rigorous education and training where they become accustomed to specific methods of performing their job. According to Dr. Pantanowitz, senior pathologists are usually not the people against the switch to digital pathology as they will usually jump at any opportunity to make their job easier. Pantanowitz continued that the junior pathologists are the most wary to change as they learned how to perform the tasks recently and are reluctant to leave their comfort zone (personal communication, 4/11/2023). The concept of technophobia contributes to the notion of path dependence, wherein individuals tend to adhere to established practices and resist change; "*even if the opportunity is there [to digitalize], not everybody is embracing it at the same speed*" (Marie-Christine Aubry, personal communication, 4/10/23).

Dr. Pantanowitz made it clear that the root of resistance to change comes from a closed mindset, giving an instance of a Swedish hospital that relies exclusively on digital slides for initial diagnosis (personal communication, 4/11/2023). According to him, they have achieved favorable outcomes owing to their exclusive utilization of digital techniques for learning. The aforementioned example demonstrates how adopting and embracing digitalization can lead to positive outcomes. To alleviate technophobia, an alternative approach could involve incorporating a physical adjustment knob into the computer system that emulates the natural feeling of a microscope (Phoebe Liang, personal communication, 2023). This feature would be

beneficial for certain pathologists, particularly those who are older and may struggle with using a mouse and keyboard.

5 Conclusion

Through our interviews with experts and research from multiple accredited sources, we discovered that many medical institutions implemented digital pathology for research, telepathology, and for the potential to apply AI technology in the future. However, the implementation of this technology has been stunted by barriers that we have determined: high costs, lack of regulations, practical use, and resistance to change. Just as there are barriers, there are solutions to these problems. In addition, the return on investment of a digital pathology system has not been shown to improve profits. While the initial investment may be significant, digital pathology is a new technology that is likely to decrease in cost over time. Obtaining official FDA approval for the devices is not a significant barrier, as it is not mandatory for clinical use as long as the microscope confirms the results. Although some pathologists may find digital pathology to be more time-consuming than manual slides, it can increase efficiency by reducing the overall turnaround time and allowing for easy collaboration.

5.1 Recommendations

To promote digital pathology's widespread adoption, it is necessary to overcome existing barriers which can be accomplished through a combination of further research and development into human computer interaction and employing either a bottom up or top-down

decision-making model that suits the institute's needs. aetherWeb and other digital pathology education platforms can be valuable tools in training new pathologists about the technology.[2] By using the digital slide repository provided by aetherWeb, future practitioners can gain valuable experience with digital pathology and lay the foundation for future pathologists to build upon. To encourage companies to adopt digital pathology, a top-down approach may be the most effective, as decision-makers at the highest level have the power to allocate resources towards this technology. In addition, attending conferences and presentations can be an effective way to promote and demonstrate the benefits of digital pathology to those who may be skeptical. One possible way to address technophobia is to include an analog adjustment knob in the computer system that mimics a microscope; the inclusion of this feature could prove beneficial for pathologists who have become accustomed to using microscopes over several years of practice.

5.1.1 Continued Collaboration with Research Institutions

To foster innovation and validate existing AI systems, aether AI should continue to cultivate and expand partnerships with research institutions. Research institutions are generally more eager to adopt new technology as they are highly motivated to advance their research goals, unlike clinical practices that may prioritize cost-effectiveness. Due to AI being the most enticing reason to digitalize, further development and refinement of AI will help the growth of digital pathology as a whole. Collaboration with more prestigious institutions can also assist

[2] AetherWeb is a repository of slides from pathologists to be used in an educational context.

with creating a reputable name within the world of digital pathology, which will be important when implementing both a bottom-up and top-down approach in hospital systems. While the geographical location of hospitals may play a role within the spread of digital pathology, we believe that the technology needs to prove to hospitals that the system is more profitable. Collaboration will give access to industry leaders, progressing the overall quality of software that aetherAI can produce. Furthermore, research institutions may have connections with pathology professors who are seeking to implement digital pathology systems into their curriculums, creating a new generation that has familiarity with digital systems.

5.1.2 Education

The importance of digital pathology in education cannot be understated. Promoting digital pathology as it applies to educational settings would help give rise to a new generation of pathologists trained with the technology from the start, which would greatly improve the chances of them carrying that technology into the workforce. aetherAI can help increase education in digital pathology by more heavily promoting the use of aetherWeb in the United States. It would also allow for easier teaching as the use of these premade WSIs takes out the need for each student or group of students to need a physical slide and microscope to view it with. Groups of students could also collaborate on viewing the same slide without having to use lab space saving areas in the school for other students. This new generation, with their familiarity of digital pathology, can help implement a bottom-up approach.

5.1.3 Top-down Approach and Bottom-up Approach

Introducing digital pathology systems into a medical practice can be approached in two ways–the top-down or bottom-up approaches. The top-down approach involves persuading executives to implement digital systems, forcing pathologists to adhere. This method is particularly advantageous because the executives at the top can dictate budget decisions and coerce pathologists to use the technology. On the other hand, the bottom-up approach involves the pathologists persuading executives for the implementation of the technology. This is an approach that is likely to be more useful in the future as the incoming generation of pathologists begins to be educated using digital pathology. One advantage of this approach is that it allows pathologists to embrace the technology because they advocate for it. While it may be difficult to connect with executives, the top-down approach appears to be the more effective method since executives ultimately make the final decision.

5.1.4 Research into Human Computer Interaction

One recurring sentiment among the interviews and articles on digital pathology is the importance of conducting research on pathologists' interactions with the computer. The problem is that some pathologists are not used to using a mouse, keyboard, and a large screen so it can be hard for them to become acclimated to using these different tools.

> *On the other hand, when I try to view the slides through the screen I have to use the mouse to scroll and pan around the slide. I think that it takes me more time to do this compared to what I traditionally do. During daily practices I find myself still using traditional slides.* (Shih-Chiang Huang, personal communication, 3/23/23)

While the inefficiency could be a result of pathologists being unaccustomed, there is a need for users to get comfortable with digital systems. One solution could be attempting to emulate microscope controls with a new interface or even using a tablet interface with touch controls. These possible solutions are to make users feel as little disruption as possible when making the change from microscope to digital. Further research into improving the user experience and user interface of aetherAI's software may improve pathologists' interactions with digital systems. This would entail making navigation and collaboration easier and faster, optimizing the software so it can work on as many systems as possible, And making sure that every part of the software runs smoothly and efficiently. The combination of physical control scheme and ease of use of the software is very important for any software on the market.

5.2 Limitations

As with any research, there are certain limitations associated with this study. The pathologists who were interviewed all worked at facilities where digital pathology was already implemented, and most of them were members of the DPA. As a result, our conclusions may have been influenced by this bias, since all of the pathologists were in favor of digitalization and have already had first-hand experience. Many of the pathologists we interviewed worked in large practices at academic medical centers, making it possible that there was bias related to their greater financial resources. Additionally, the sample was also skewed toward the eastern United States as seen in Figure 4.1, but this does not pose a great issue as regional differences between pathologists are negligible compared to other factors such as practice size and

research activity. Finally, scheduling the interviews proved challenging due to significant time zone differences, which may have resulted in missed opportunities.

5.3 Future Research Opportunities

Future research projects into the implementation of digital pathology can look into connecting with hospital or lab executives to gain a comprehensive understanding into how digital systems are implemented at an executive level and if there are any associated barriers. We suggest interviewing private labs, both pathologists and executives, because their budget management approach is different from service-based hospitals. Additional research could be conducted to explore the impact of telepathology in the non-contiguous United States. Additionally, due to many of our sources pointing towards the poor return on investment of digital pathology, future studies can look towards solutions that mitigate this poor outlook. Research and surveys of additional features that pathologists feel would justify the investment costs into digitalization could be considered. Understanding the entire workflow of digital pathology would also be helpful. Getting first hand experience on the average day of a pathologist will give great insights on which areas could be subject to improvement. Research into Linköping, the first place in the world that used digital pathology for primary diagnosis, could also give insight on how it is being used and what factors led to their full digital transformation.

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7 Appendix

7.1 List of Interviews

1. Dr. Sakthikumar Ambady, Worcester Polytechnic Institute
2. Dr. Shih-Chiang Huang, Chang Gung Medical Foundation

3. Dr. Woon Chow, Virginia Commonwealth University
4. Dr. Marie-Christine Aubry, Mayo Clinic
5. Dr. Liron Pantanowitz, University of Michigan
6. Dr. Miguel Reyes, University of Pittsburgh Medical Center
7. Dr. Monica de Baca, Pacific Pathology Partners
8. Dr. Anil Parwani, Ohio State University
9. Dr. Luis Rey, Palmetto General Hospital

7.2 Interview Questions

Thank you for taking the time to meet with us today! [various small talk]

Before we begin, I will need your informed consent to participate in this study. Your participation will consist of one interview that will last approximately thirty minutes. You will receive no personal benefit for your participation, but your answers will be used to help an emerging technology find its footing in the United States. There is no risk taken by participating in this interview. You may decide to stop participating in the research at any time without penalty or loss of other benefits. This includes your right to refuse to answer any question, stop the interview at any point in time, or contact us after your interview to request that your responses not be used for our research. Any audio, video, or transcription of this interview will be stored in a secure location and will not be accessed by anybody apart from myself, our research group, and our two faculty advisors.

Do we have your consent to proceed with the interview?

Do we have your consent to record the audio and video of this interview?

1. How many years have you been in practice as a pathologist?
2. Can you tell us more about your specialty?
3. Does your lab currently use any digital pathology technology?
    a. What equipment or systems do you use?
    b. What factors led to the decision to digitalize your lab?
    c. Can you describe the process of integrating the technology into your lab?
    d. What benefits or disadvantages have you found in implementing digital pathology?
4. Does your lab currently use any AI technology?
    a. What applications do you use AI for?
    b. How long did it take to become acclimated to using AI?
    c. Can you describe your experiences with the technology, both positive and negative?
    d. What was your experience with the integration of the technology into your workflow?
    e. No: Has your department ever considered utilizing AI? If so, why was it not implemented?
5. Do you have any other thoughts you would like to share on digital pathology that we haven't asked about?
6. Is there anyone else you would recommend we reach out to for an interview?

7.3 Competitor Analysis

AI Solutions								
	Location	Products	Authorization	Partnerships	Clinical trials	Collaborations/Implementation	Funding	Compatibility
Paige	NYC, USA	Platform/FullFocus	FDA Cleared*/CE mark	Philips & Mindpeak				iSyntax (Philips), SCN, LIF (Leica)
		Prostate Detect	FDA Cleared*/CE mark		Memorial Sloan Kettering	University of Louisville	Startup funding, Series C (Casdin Capital, J&J, Goldman Sachs)	
		Prostate Grade & Quantify	FDA Cleared*/CE mark					
		Prostate Perineural Invasion	RUO					
		Breast	RUO					
		Lymph Node	RUO					
PathAI	Boston, MA, USA	AIM-PD-L1 NSCLC	RUO				Series C (D1 Capital Partners and Kaiser Permanente)	iSyntax (Philips)
		AISight DX	FDA Cleared*/CE					

			mark					
Ibex	Tel Aviv, Israel	Galen Prostate	RUO/CE mark	Philips	Maccabi Healthcare Services	UPMC	Kreos Capital	
		Galen Breast	RUO/CE mark					
		Galen Gastric	RUO/CE mark					
Aiforia	Helsinki, Finland	Prostate	RUO/CE mark	Microsoft		Mayo Clinic	Series B (Epredia)	most file types
		Breast***	RUO/CE mark					
		Lung	RUO/CE mark					
Visiopharm	Horsholm, Denmark	Breast	RUO/CE mark	Hamamatsu				
		General	RUO/CE mark					
Mindpeak	Hamburg, Germany	Breast	RUO/CE mark	Paige			European Innovation Council	
		Breast Metastasis (LN)	RUO					
		Lung	RUO					
		Onychomycosis	RUO					

Image Management							
	Location	Products	Authorization	Partnerships	Collaborations/Implementation	Funding	Compatibility
Philips	Amsterdam, Netherlands	IntelliSite	FDA Cleared/CE mark	Ibex, Paige, Proscia			
Sectra	Linkoping, Sweden	Digital Pathology Module	FDA Cleared*				Most image formats and devices
Indica Labs	Albuquerque, New Mexico, USA	Halo AP	CE Mark	Hamamatsu			Most image formats and devices
		Halo Link	RUO				Most image formats and devices
Proscia	Philadelphia, PA, USA	Concentriq	CE Mark	Ibex, Visiopharm, Philips, Leica, 3DHISTECH, Hamamatsu	Hospital Of Jaén, Bristol Meyers Squibb, abbvie, AMGEN, Bayer, Johns Hopkins University, Takeda, Teva, NSA		
Tribun	Paris, France	CaloPix	CE Mark	Hanamatsu, Leica, Roche, Zeiss, Philips, Akoya, Deep Bio, Owkin, Mindpeak, Primaa, Gustave Roussy, Assistance Publique	Saclay Hospital	Startup Campus Incubator, Medical Valley, Investir L'	Most image formats and devices
		AI apps	RUO				Most image formats and devices
		Teleslide Patho	CE Mark				Most image formats

				Hopitaux de Paris, cypath, Chum, Hopital Erasme, LBO France, and ULB		Avenir, agence nationale de la recherche(anr), bpifrance, Region iledeFranc e, Paris Region, eit Health, and the European Union	and devices