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A practical roadmap to implementation of in-house developed computational pathology algorithms

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Abstract

Despite rapid advances in artificial intelligence (AI) for digital pathology, translation from algorithm development to routine clinical use remains rare. Most studies focus on technical performance, overlooking the different implementation steps needed for safe, sustainable deployment. This study addresses that gap by detailing the real-world integration of a laboratory-developed AI tool into the daily workflow of an academic pathology department. Our approach encompasses regulatory compliance, IT integration, validation studies, workflow redesign, and user training, essential for lasting adoption under current regulation. Through this process, we developed a flexible, locally adapted system which is now used in routine care. This work offers a practical, replicable framework for other laboratories, highlighting that successful implementation takes far more than technical accuracy alone.

Introduction

The landscape of anatomical pathology is rapidly changing. The introduction of digital pathology, creating digital representations of entire microscopic slides, has opened the possibility for integrating artificial intelligence (AI) into clinical workflows, offering transformative potential for improving diagnostic efficiency and accuracy. This has resulted in an explosion of AI-related studies in the field of pathology over the last ten years. An expert Delphi study by Berbis et al.[1] showed that experts foresee specific AI applications to be routinely used by 2030, with some tasks even to be fully delegated to AI. Numerous studies have demonstrated AI's capability to analyze whole slide images (WSI) with high precision, often rivalling or exceeding human performance in controlled settings [2, 3]. Examples of AI applications in pathology include automated assessment of prognostic biomarkers, tumor grading, diagnosis of metastatic cancer in lymph nodes, and streamlining clinical laboratory workflows through automated quality control [4, 5]. Many tech companies are therefore moving into the pathology domain and many AI-based products are introduced to the market. AI is deemed to have the potential to support pathologists, both by entrepreneurs and investors and by pathologists [6]. Despite promising advances, the translation of AI algorithms into real-world pathology practice remains very limited [7, 8]. While new research largely focuses on model development and validation, only few studies address implementation within clinical workflows. Factors that block this transition are the slow worldwide adoption of digital pathology [9, 10], uncertainty around reimbursement, cost and complexity of AI integration into existing workflows, clinician acceptance, and regulatory barriers[7, 11]. In particular, workflow integration is often overlooked as a parameter for successful innovation in healthcare. In the past years some insightful documents have been published with guidelines and roadmaps about implementation[12–15]. Regardless of their innovative character, only a few demonstrate a successful workflow integration and deployment within routine clinical practice [16, 17]. Hence, there is a need for studies that go beyond proof-of-concept. The present study aims to present a path towards successful implementation of an in-house developed AI algorithm into the routine workflow of a surgical pathology department. Steps to reach this goal include a tight integration of the AI algorithm into the existing digital workflow, as well as analytical and clinical validation while complying with applicable regulations (in Europe, mostly regulated by the In Vitro Diagnostic Regulation (IVDR), General Data Protection

Regulation (GDPR) and the AI-act [18–20]). For every step, we illustrate both the feasibility and the challenges of integrating AI into standard diagnostic practice. We refer to the Supplemental pages for extensive study details. This work not only demonstrates the potential of AI to enhance pathology workflows but can also pave the way for broader adoption of AI in clinical settings. As a result, in our department, a large Dutch academic hospital, AI is no longer a concept, but supporting pathologists in daily diagnostics.

Results

The implementation of the AI-assisted sentinel lymph node assessment was evaluated through sequential analytical validation, clinical validation, workflow safety analysis, and clinical deployment. The results of these steps are presented below.

Analytical validation demonstrates high specificity and robust performance across laboratory variability

The goal of analytical validation is to assess the technical robustness, reproducibility, and consistency of the algorithm under controlled conditions. Our results show that all negative sections (n = 48) were correctly classified as negative by the algorithm, resulting in a specificity of 100%. Across the different scanning time points, an average sensitivity of 82,7% was obtained (n = 100 cases). Missed cases all contained micrometastases. Regarding variability in scanning and staining, a slightly higher stain intensity was visually noticed after the weekly maintenance of the stainer. However, this minimal difference did not influence the performance of the algorithm. These results support the robustness of the algorithm in standardized lab conditions and provide the foundation for clinical validation.

Clinical validation confirms improved diagnostic sensitivity and high specificity with AI assistance

Clinical validation focused on assessing the algorithm’s performance in a real-world diagnostic setting, using a selection of representative archived cases. As shown in Table 1, the use of AI support led to improved performance in several areas. For two out of four readers, the algorithm improved specificity, resulting in an overall score of 100%. The average sensitivity across all readers increased from 87% without AI to 91% with AI. For two readers, this represented individual improvements of 17% and 9%, indicating enhanced detection of metastases with AI assistance. Importantly, a correct positive diagnostic decision means that no additional immunostaining is required. Based on this principle, the use of AI in this study could have led to a reduction in the number of immunostains needed.

Table 1
Sensitivity and specificity for readers with and without AI, compared to standalone AI performance. For Reader A and D the sensitivity score went down with the use of AI.

Reader	Sensitivity (%)			Specificity (%)		
	Without AI	*With AI*	*AI only*	*Without AI*	*With AI*	*AI only*
A	89	84	100	98	100	100
B	78	95	100	100	100	100
C	86	95	100	100	100	100
D	95	89	100	98	100	100

To evaluate efficiency, we measured the time readers needed to reach a diagnostic decision. For negative cases (no metastasis) without AI, an average of 67 seconds was required to confidently review the haematoxylin and eosin (H&E) slide (Fig. 1). With AI supported workflow, these negative cases would directly proceed to an CK8.18 immunostain, eliminating the need for manual H&E review. For positive cases (with metastasis), the average time to reach a decision decreased from 9 seconds without AI, to 4 seconds with AI (Fig. 2). These findings demonstrate the algorithm's reliable performance under clinical conditions, supporting its readiness for integration into the daily workflow. Quality management and risk analysis The HFMEA was performed by a multidisciplinary team including pathologists, laboratory technicians, clinical informatics staff, and quality management representatives.

Risk analysis confirms safe integration with no high-risk failure modes identified

To ensure safe clinical deployment following validation, a prospective HFMEA-based risk analysis was performed. None of the analysed process steps were classified as medium or high risk in terms of severity or occurrence. These outcomes informed mitigation strategies and quality control checkpoints, supporting safe integration into clinical workflow.

Implementation and user experience

Following a step-by-step implementation plan, the AI tool was successfully integrated into the clinical workflow. All relevant personnel were trained to the changes in task distribution. The tool is currently used in daily diagnostics, and the underlying IT infrastructure has been designed to support scalable integration of future AI tools.

Discussion

While the development and validation of AI tools in digital pathology have progressed rapidly, real-world clinical integration remains rare. This study addresses that gap by going beyond algorithm validation to detail every step required for safe and effective implementation with full workflow integration. We present a structured approach to integrating an in-house developed AI tool into the routine pathology

workflow, involving not only analytical and clinical validation, but also technical integration, quality management, and user-centered design. By providing a practical roadmap, this work supports the adoption of future AI tools in our lab and can serve as a guide for other pathology laboratories seeking to integrate AI into their workflows.

In the past year, numerous studies mainly describe the possibilities and possible future strategies/barriers for implementation, only a few studies have highlighted the process of implementation. Dooijeweert et al.[16] demonstrated the feasibility of a company-built AI tool in a clinical setting, by investigating the safety and potential for cost and time savings of AI assistance for sentinel node metastasis detection. They conclude that the employment of this AI-assisted workflow not only leads to a significant reduction in IHC use and subsequent costs, but also supporting pathologists by saving time and making their work more enjoyable. Recent work from Jia et al. [15] proposed a comprehensive deployment safety case for AI-assisted prostate cancer diagnosis, with a strong emphasis on risk assessment, validation, and alignment with regulatory expectations. Their work sets an important precedent for safe AI deployment in pathology. Even if a device receives CE/FDA clearance from regulators, real-world implementation may still reveal unforeseen risks and challenges that were not apparent during the approval process. While similar in scope, implementation studies regarding commercially developed AI tools differ from ours in a key aspect: the allocation of responsibility for validation, quality control, and regulatory compliance. In the case of company-built tools, the vendor is responsible for these processes, under IVDR. In contrast, our study reflects the reality of implementing a laboratory developed test (LDT), where the clinical laboratory is fully accountable for ensuring safety, performance, and compliance with applicable standards, such as having ISO 15189 accreditation. This distinction required us to conduct extensive local validation and integrate the tool into existing quality management systems, which, while resource-intensive, allowed for greater flexibility, contextual adaptation, and alignment with the specific needs of our diagnostic workflow well beyond a commercially available application. To our knowledge, this study is the first to fully describe and successfully employ the implementation process of an in-house developed AI application to clinical workflow.

As with any implementation study, several limitations should be acknowledged to contextualize the findings. Firstly, the work was conducted in a single academic pathology laboratory, which may limit generalizability to institutions with different infrastructures, workflows, or resources. Secondly, although our results suggest potential efficiency gains and reduced use of immunohistochemistry, a formal cost effectiveness analysis was beyond the scope of this study. Thirdly, although the current setup still requires a manual step by the lab technician to initiate the AI and request IHC stains, we aim to move toward full automation. This would further streamline the workflow, reduce reliance on assessment and rule-based decision making, manual input, and enhance the scalability of AI integration in pathology practice. More importantly, the scope of our study was limited to short-term evaluation; long-term outcomes such as sustained diagnostic accuracy, evolving user interaction, or clinical impact were not assessed. To ensure sustained safety and effectiveness in clinical practice, continuous monitoring is essential. Post-market surveillance (PMS) is therefore a key requirement in the life cycle of any medical

device or AI tool, and mandatory for manufacturers under international and national regulations [18, 29]. Our PMS plan encompasses performance tracking, user feedback, error logging, regular re-evaluation of clinical relevance, and reporting of findings. At the moment of writing, PMS has started, but no long-term results can be shared yet. This study sets the stage for future prospective studies, which will yield the real-world data showing AI impact on pathology diagnostics. More broadly, health technology assessment may be used to study the impact of AI on the whole clinical trajectory, also taking into account potential effects of AI on patient management and outcomes.

We presented a path to implementation and pathology diagnostic workflow integration of a lab-developed AI algorithm to improve the breast cancer sentinel lymph node diagnostic accuracy, diagnostic focus and turnaround time in pathology. This study has resulted in a real-world implementation, compliant with all applicable regulations in the European Union. As such, it may serve as a blueprint for future LDT AI tool implementations.

Methods

Diagnostic application

In 2016 and 2017, the CAMELYON challenges showed that AI is capable of detecting lymph node metastases of breast cancer in digitized H&E slides, with an accuracy comparable to pathologists [4]. The present study aims to implement an AI algorithm for assessment of lymph node status, confined to nodes of breast cancer patients that were acquired through the sentinel node procedure. The workflow (before introduction of AI) for sentinel lymph nodes (SLN) in our practice is shown in Fig. 3a. WSI of H&E-stained SLN are first assessed by the pathologist. If no metastatic tumor is detected, the pathologist will request for cytokeratin immunohistochemistry (IHC) to confirm, according to national clinical protocol [21], and in a subsequent session the IHC stained sections are examined by the pathologist.

AI algorithm

In the present study, we implemented a previously developed AI algorithm for SLN assessment into our departments' routine digital workflow [22]. The algorithm is provided as a containerized application, taking as input a WSI of a H&E-stained SLN and producing as output a large bounding box around the tissue (when negative) or smaller bounding boxes around metastases (when positive). The bounding boxes are visually labelled with 'SNB: negative' (negative node) or 'SNB: positive' (positive regions, see Fig. 4) To enhance the value of the AI algorithm as a workflow optimizing tool, it processes WSI before it reaches the pathologist for the first time. In case the AI does not detect any metastasis in a negative lymph node, a lab technician will request IHC without involving the pathologist. The case will reach the pathologist when either at least one of the sections of a lymph node is flagged positive, or all sections are flagged negative and come with the request of an accompanying keratin-stained slide. Ideally, this will allow a single-pass sign out by the pathologist, resulting in a decrease in reading time, less case tracking for the pathologist, and an overall decrease in turnaround time. See Fig. 3b.

Technical integration

To implement the algorithm in clinical practice, a dedicated software framework (called Nexum) was custom developed to connect AI models with the digital pathology environment in a robust and scalable way. The primary goal of this system was to ensure that large-scale WSI analysis could be carried out reliably and securely, without disrupting the existing clinical workflow. Nexum was specifically designed to integrate seamlessly with the Sectra IDS-7 (Sectra AB, Sweden) digital pathology system, which is being routinely used in our diagnostic setting for 5 years. Nexum acts as a bridge between the image management system, WSI viewer, and the AI algorithm, ensuring smooth exchange of images and results, including overlay and annotation. From a technical perspective, Nexum acts as a broker between Sectra and AI services. It receives requests from Sectra, downloads the corresponding digital slide, and places the task on a queue. The AI service then picks up the request, runs the appropriate algorithm, and pushes the results back to Nexum. Nexum translates these results into Sectra's coordinate system and returns them directly to Sectra IDS, where the technician can review them as annotations on the original image. Whenever all sections of a single SLN are flagged negative, the technician immediately requests IHC. Because Nexum tracks every request from start to finish, it always knows which result belongs to which case. This design keeps the workflow straightforward for the user, while ensuring scalability: one Nexum broker is enough, and AI services can be scaled horizontally as workers to speed up processing. In this way, AI support becomes seamlessly available at the point of care without complicating daily pathology routines.

Security

To safeguard patient data and ensure compliance with healthcare information security standards, all data processing by our AI tool is performed locally within the hospital's secure IT environment, hence no data is transferred to or stored in the cloud. Additionally, the hospital's Information Management (IM) department is closely involved throughout the implementation to ensure that all data handling processes meet institutional and regulatory standards (in accordance with ISO 27001 and NEN 7510), for privacy, security, and system integrity.

Case selection

To perform analytical and clinical validation, we obtained archived formalin-fixed paraffin-embedded tissue blocks from breast cancer patients from the Radboudumc pathology reporting system (UDPS, Palga, Houten, The Netherlands) from both in house patients as well as from a tertiary hospital for which our department offers her pathology services. All blocks contained sentinel lymph node tissue sections from breast cancer cases. To establish a reference standard, digital images of both H&E and if present CK8.18 stained cases, together with the pathology report, were reviewed by a board-certified pathologist with special expertise in breast pathology. Cases were categorized as either negative or containing macrometastasis (tumor > 2 mm), micrometastasis (tumor > 0.2 mm and ≤ 2 mm) or isolated tumor cell clusters (ITCs; ≤ 200 scattered tumor cells or tumor cluster ≤ 0.2 mm) according to clinical guidelines

[23]. Currently no clinical implications exist for breast cancer patients with sentinel lymph nodes containing ITC, therefore these cases were considered negative.

Analytical validation

Before introducing any computational pathology algorithm into clinical practice, it is crucial to establish its technical reliability under controlled laboratory conditions. This step is particularly important in pathology, where small technical inconsistencies can significantly impact visual interpretation—both by the human eye and by AI algorithms. To assess the reproducibility and robustness of our algorithm, we designed a validation study that simulated typical pre-analytical variations. Archived tumor blocks with a representative range of lymph node involvement were selected to cover the spectrum of clinical scenarios. By including both micro metastases and macro metastases, we aimed to challenge the algorithm's sensitivity across different morphological presentations. Sections were prepared over several days, with intentional variation in the timing of staining and cutting (morning vs. afternoon), to mimic subtle differences in the pathology lab output. Each slide was scanned multiple times on a Pannoramic 1000 (3DHistech) which is used in routine clinical practice, on the day of preparation to examine the consistency of algorithm output across repeated digital acquisitions. For the AI analysis of the slide, we used a high-confidence detection threshold, prioritizing specificity in this early phase to avoid overcalling and to better assess the algorithm's precision in true negative cases. Altogether, this analytical validation phase confirmed the algorithm's ability to operate reliably under standardized, but realistic, laboratory conditions. For all study details, see Supplementary Information Table 1.

Clinical validation

Following the analytical validation, the next step was to evaluate the algorithm's performance in a daily pathology diagnostics context, taking into account the complexities and variability inherent in pathology practice. The goal of the clinical validation was twofold: first, to measure the efficiency of pathologists with and without the aid of the algorithm, and second, to explore whether the algorithm could streamline the diagnostic process by reducing the need for immunohistochemistry (IHC) slides, which are costly and time-consuming. Both objectives are crucial for understanding how the algorithm could be integrated into routine diagnostic workflows in a way that enhances, rather than disrupts, the pathology process. We designed a multireader multicase study that included (resident) pathologists with different levels of experience. By assessing their performance in a randomized crossover setting (with and without the AI tool), we aimed to capture the algorithm's impact on diagnostic decision-making and time efficiency. To avoid any effect of memory from the first round, we introduced a four week washout period between sessions. Comparable to the analytical validation study, a variety of cases was selected representing a range of clinical scenarios. To mimic daily practice, each case contained one H&E image of the original breast tumor, as comparison with the original tumor morphology is often critical for accurate diagnosis. Participants reviewed the cases in the Sectra IDS environment, using tools they normally use in their daily work. We measured the time it took to make a diagnosis and noted any

additional comments by the readers. During the AI-supported session, the algorithm showed simple positive or negative annotations. For all details on this study, see Supplementary Information Table 2.

Quality management and risk analysis

Implementing AI in a diagnostic setting requires alignment with the quality and safety standards expected of medical laboratories. Under IVDR, in house developed tests require validation, implementation in compliance with ISO 15189 norms and accreditation. ISO 15189 accreditation is a field standard for Dutch pathology departments and requires all processes within the laboratory to be documented, monitored, and integrated into a Quality Management System (QMS). This includes not only the analytical performance of an AI algorithm, but also its interaction with other parts of the workflow, such as data handling, result reporting, and clinical interpretation. Ensuring traceability, auditability, and ongoing performance monitoring of the AI system is essential for safe and sustainable use in patient care. In compliance with the ISO 15189 norm, we conducted a prospective risk inventory using the Healthcare Failure Mode and Effects Analysis (HFMEA-light) methodology. This structured approach enabled us to assess the entire pathology workflow, from tissue grossing and staining quality to image analysis, and the overall management and safety of the AI algorithm. By mapping out each step, we were able to identify which failures would influence the algorithm and prioritize actions to reduce risks. Embedding this risk inventory into the broader QMS framework ensures that the AI solution not only performs as intended, but also supports the lab's overall commitment to quality and patient safety and continuous improvement [24, 25].

Implementation and user experience

Successful implementation of any new medical technology critically depends on the acceptance, understanding, and engagement of the personnel who interact with the tool [26]. Specifically in healthcare, ensuring good integration of the system, training, and early involvement of users were facilitating factors for acceptance of AI systems [27]. Therefore, early on, a multidisciplinary team (pathologists, lab technicians, lab managers, researchers, data scientists) was gathered to make sure that the AI algorithm would naturally integrate in the existing workflow. During several collaborative sessions, special attention was paid to the Sectra IDS interface usability to ensure that status updates, annotations, and alerts were visually clear, intuitive, and not overwhelming to the user. Also, tailored training sessions were organized for personnel in which the tool was thoroughly explained and possible troubleshooting (e.g. whom to contact for errors) was discussed. Additionally, to gain insights into the user experience and acceptability, we conducted think aloud sessions (task-based interviews during interaction with the AI tool) with the relevant users and distributed surveys with questions adopted from the System Usability Scale and the Technology Acceptance Model [26, 28]. The surveys contained statements that were answered on an 1 to 5 Likert scale.

Declarations

Data availability

The datasets generated and/or analyzed during the current study are not publicly available due to patient privacy considerations and institutional data-sharing restrictions.

Author contributions

F.M. wrote the original manuscript draft. M.B. curated the datasets used for evaluation. G.L. supervised the development of the AI algorithm and contributed to its methodological readiness and deployment for this study. D.G., L.v.E., R.L., R.v.d.L., and P.v.O. developed the Nexum platform and realised the technical integration of the algorithm into the digital pathology infrastructure. M.B., K.F.-W. and S.v.d.K-H conducted the risk analysis and prepared the quality management documentation. J.G. coordinated the project. F.M., M.B., G.L., K.G., and J.v.d.L. contributed to study design, supervision, and interpretation of results. All authors reviewed and edited the manuscript and approved its contents.

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Competing interests

J.v.d.L. reports consulting fees from Philips, ContextVision and AbbVie, and grants from Philips, ContextVision and Sectra, outside the submitted work. He is chief scientific officer and shareholder of Aiosyn BV, the Netherlands. G.L. reports grants from the Dutch Cancer Society and the NWO, and grants from Philips Digital Pathology Solutions and personal fees from Novartis, outside the submitted work. All other authors declare that they have no competing interests.

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Figures

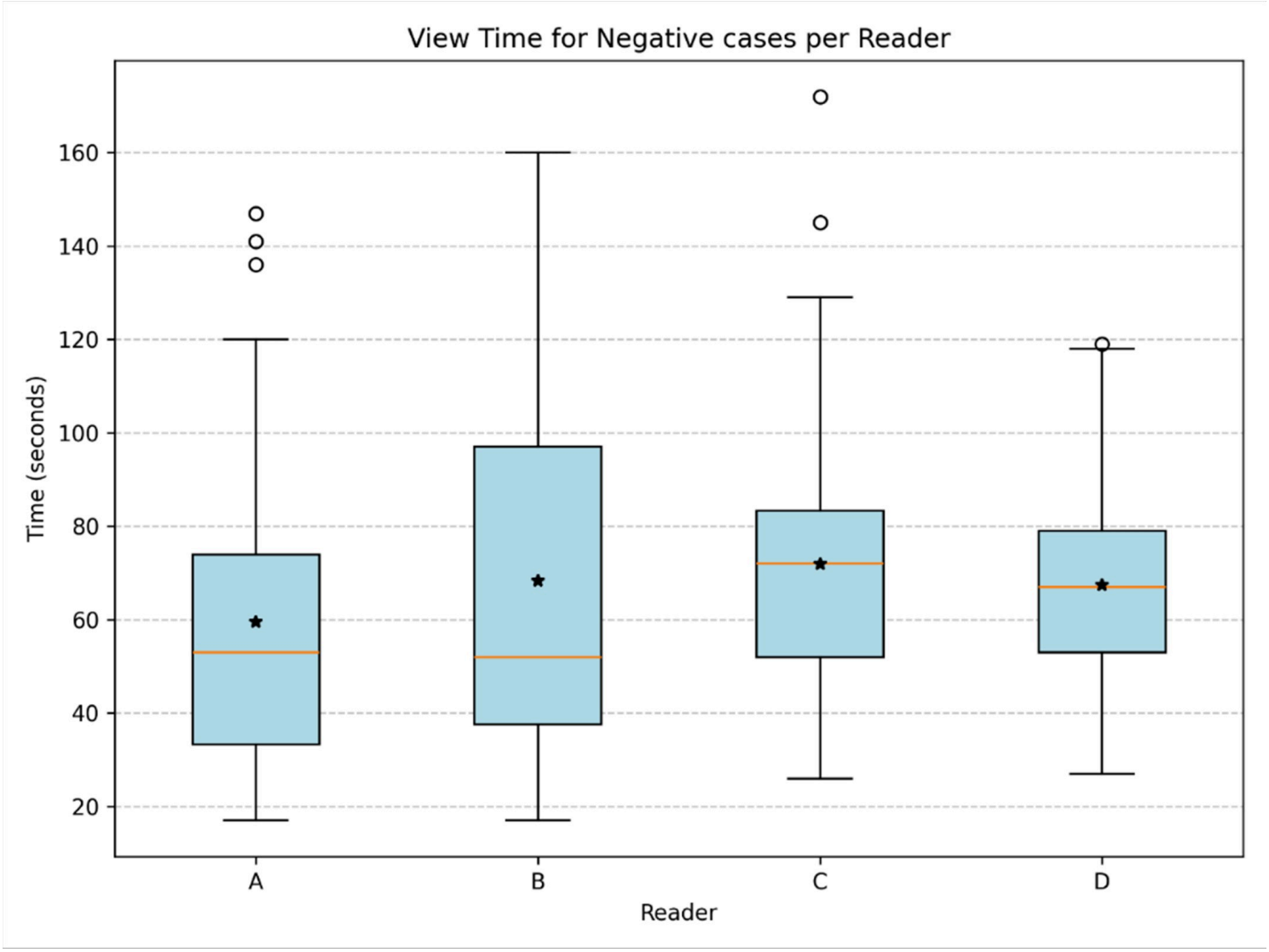


Figure 1

Distribution of view times (in seconds) for negative diagnosed cases without AI assistance, grouped by reader. The boxplots show median and interquartile range, with the asterisk (*) marking the mean time (A=59 sec, B=68 sec, C=72 sec, D=67 sec).

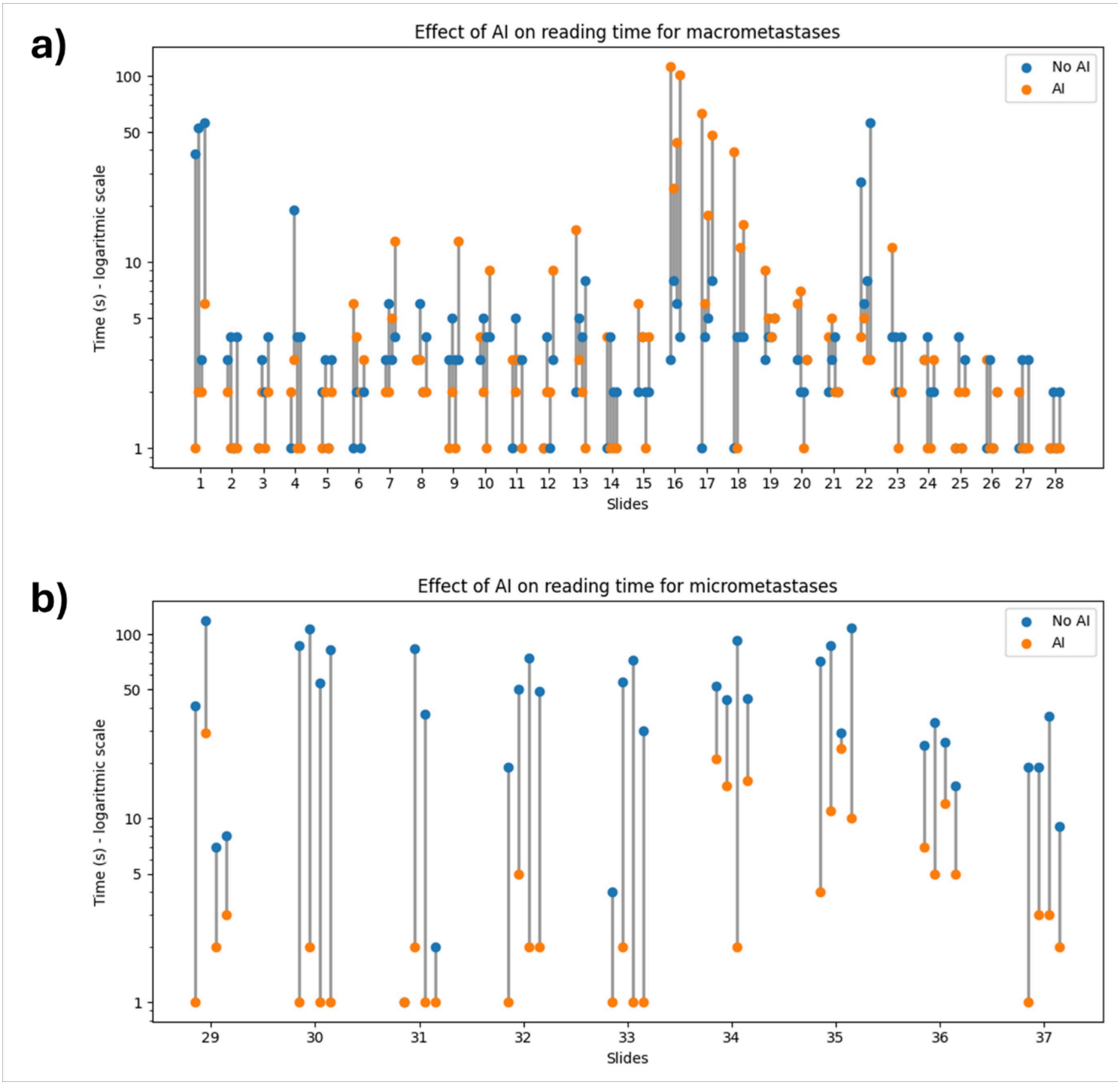


Figure 2

Reading time per case with and without AI support. For each case, dumbbell plots show paired reading times for four readers without AI (blue) and with AI (orange). Vertical lines connect paired measurements for the same reader and case. Cases are ordered by macrometastases (A) and micrometastases (B). The y-axis is shown on a logarithmic scale.

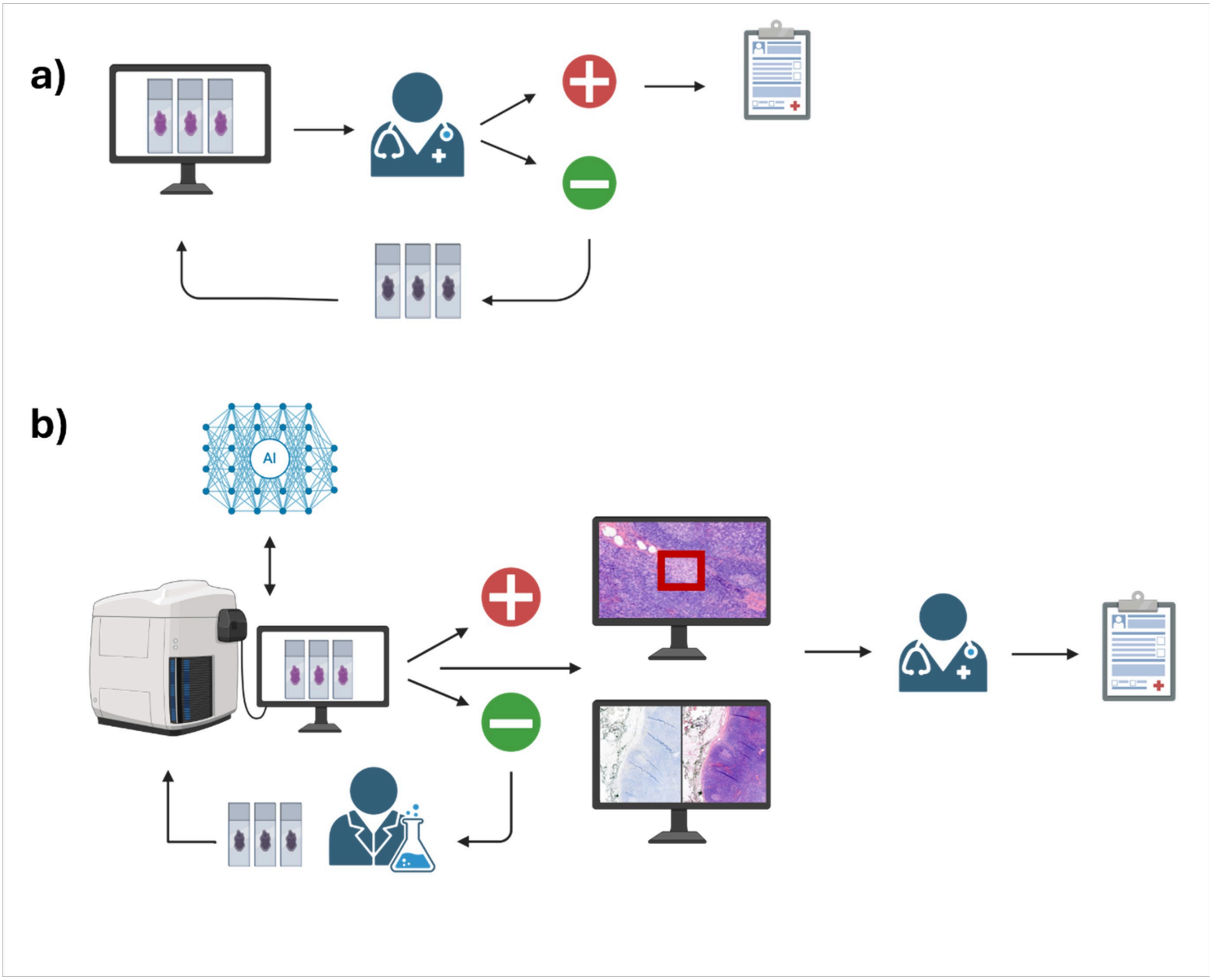


Figure 3

Outline of the current routine diagnostic pathology workflow (a). The digital images of axillary lymph nodes H&Es are examined by a pathologist. When one or multiple metastases are found (the red plus sign), the pathology report is finalized. Whenever the tissue is morphologically negative or the presence of metastasis is uncertain (the green minus sign), additional immunohistochemistry is requested. Outline of the AI-supported workflow (b). The algorithm analyses the images and whenever a negative node is detected, the lab technician can already request for IHC. In this way, the pathologist receives positive nodes (flagged) and negative nodes (with additional IHC). Created with BioRender.com.

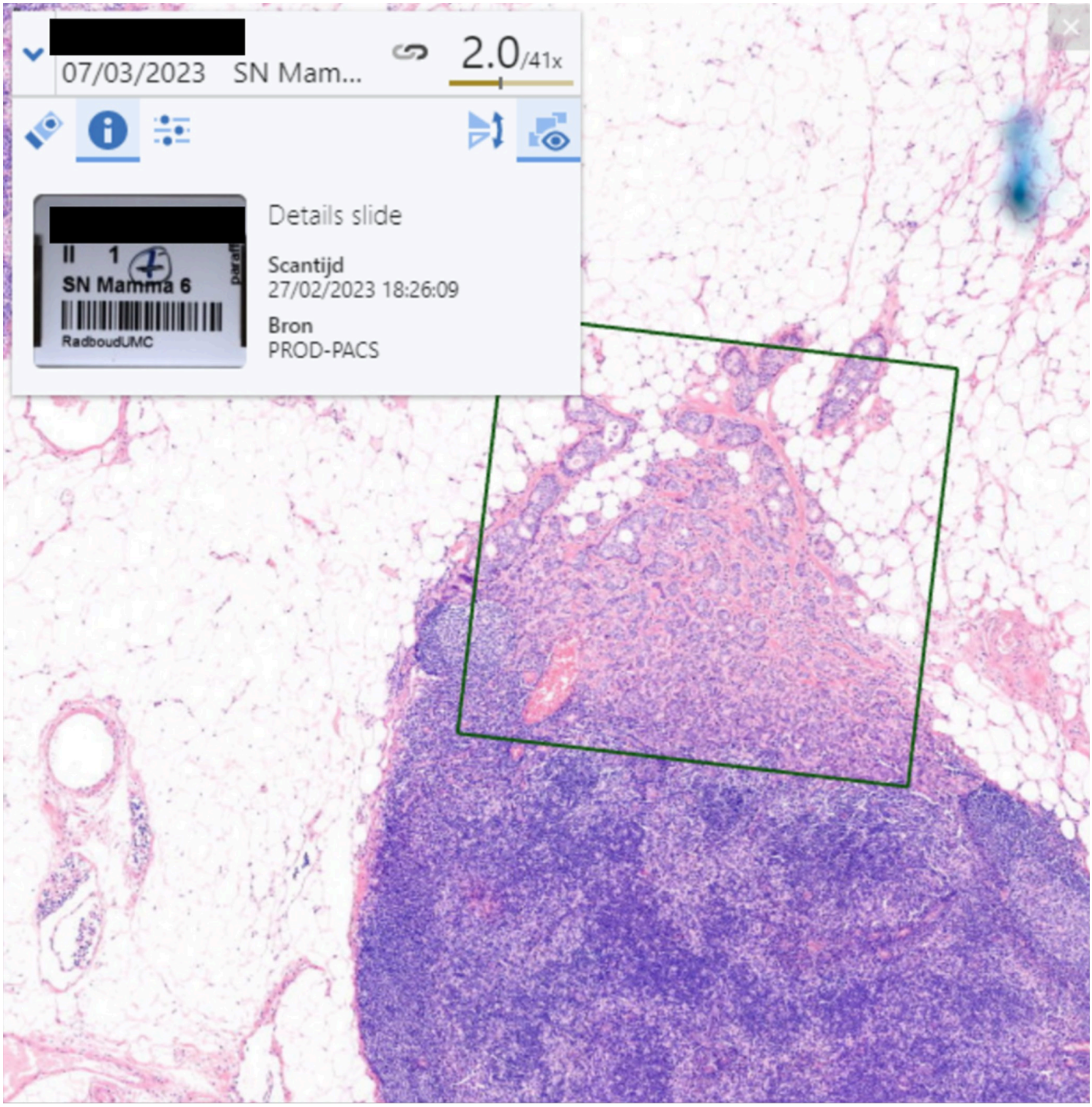


Figure 4

Scanned H&E slide of a sentinel lymph node with breast cancer metastasis, annotated by a green bounding box.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- supplementaryinfo.pdf