Digital transformation: towards efficiency and precision in Pathology

Catarina Eloy, MD, PhD

ipatimup

epredia
Enhancing precision cancer diagnostics

PHC GROUP

Learning objectives

- **To understand the technical challenges in building a high-quality whole slide image**
- **To learn about quality and production control in a digital setting**
- **To envision how can the digital product impact on the computational pathology outputs**

Disclosure information

Diapath | Consultation
Sakura | Consultation
Biocartis | Consultation
Paige AI | Consultation
Epredia | Consultation

Virchows Archiv
https://doi.org/10.1007/s00428-025-04090-w

ORIGINAL ARTICLE

Check for updates

Digital transformation of pathology - the European Society of Pathology expert opinion paper

Catarina Eloy[1,2] · Filippo Fraggetta[3] · Paul J. van Diest[4] · António Polónia[1,5] · Mónica Curado[1,6] · Jordi Temprana-Salvador[7] · Inti Zlobec[8] · Elvira Purqueras[9] · Cleo-Aron Weis[10] · Xavier Matias-Guiu[11] · Peter Schirmacher[10] · Aleš Ryška[12]

Received: 22 January 2025 / Revised: 18 March 2025 / Accepted: 20 March 2025

Digital transformation of pathology
(Digital pathology)

is a process that entails the implementation of procedures at the pathology departments ultimately aiming to produce high-quality whole slide images (WSIs) for diagnosis.

Laboratory Investigation
Available online 13 October 2023, 100261
In Press, Journal Pre-proof What's this?

Research Article

Real-World Implementation of Digital Pathology: Results from an Intercontinental Survey

Daniel Gomes Pinto [a b c], Andrey Bychkov [d], Naoko Tsuyama [e], Junya Fukuoka [d f], Catarina Eloy [c g]

127 laboratories

- 52 Asian and 75 European
- 72 with digital pathology (38 Asian and 34 European)

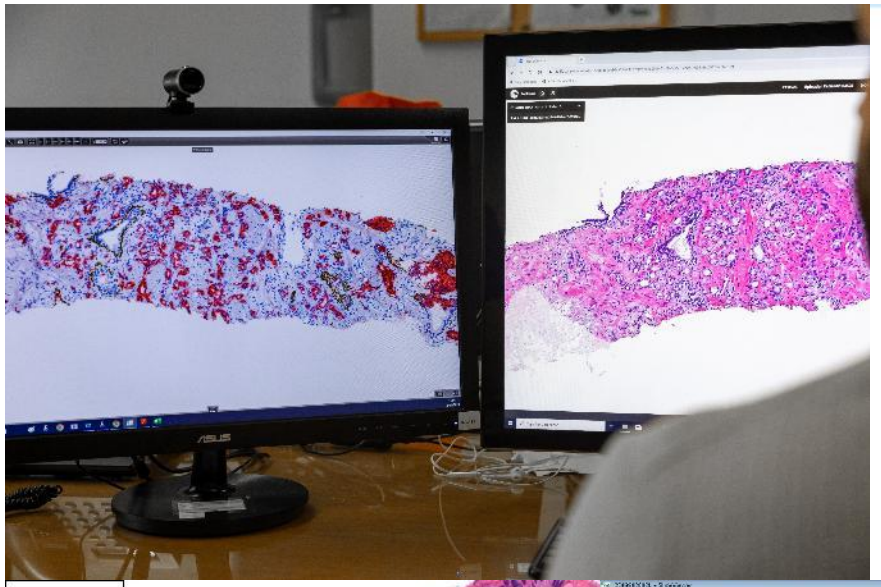
44% maintain the microscope due to lack of quality of WSIs

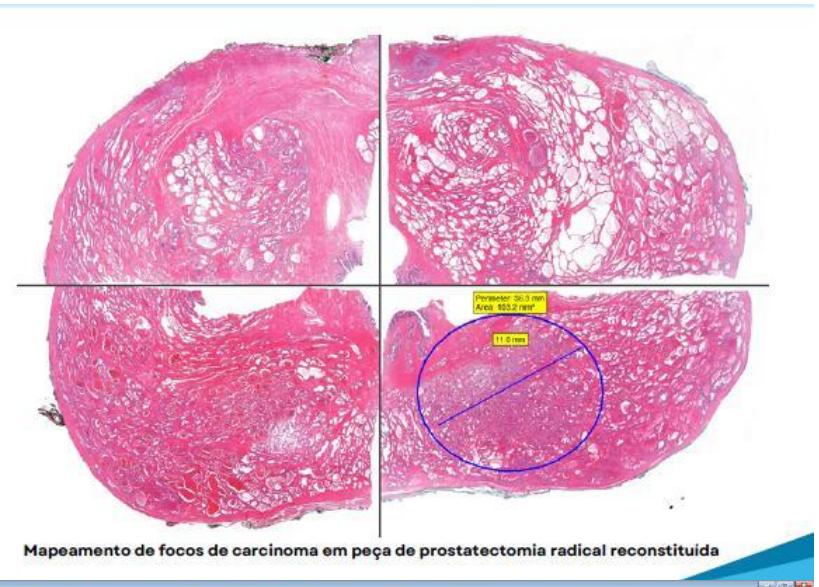
47% have pathologists doing quality triage of WSIs

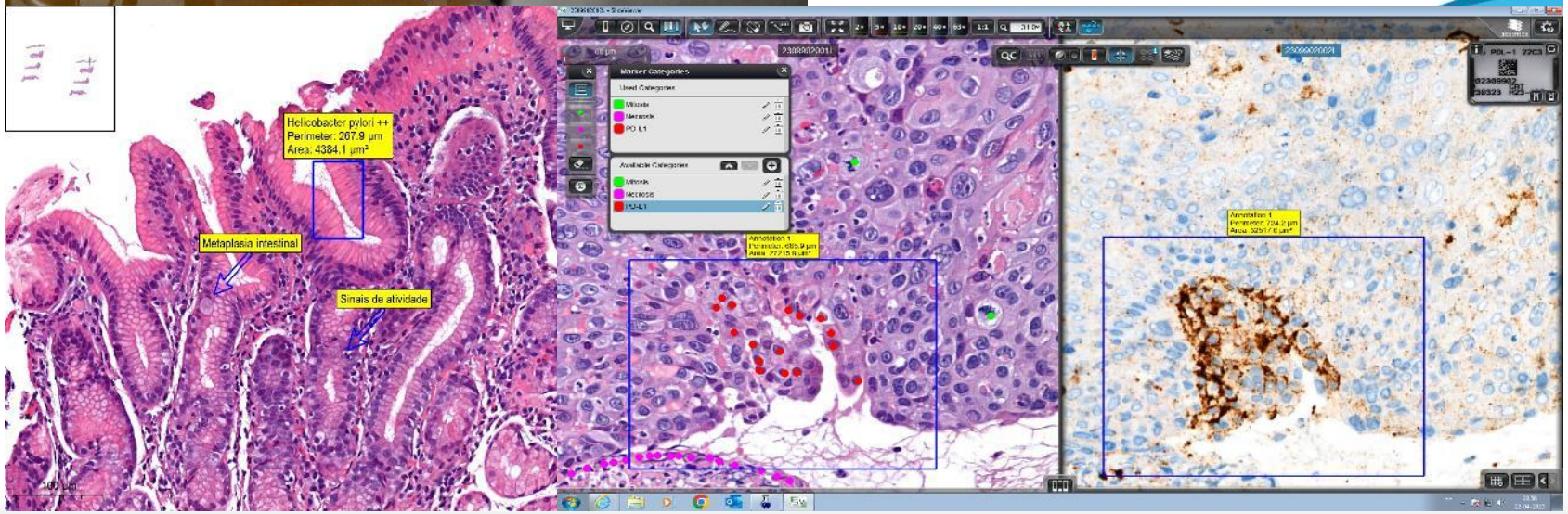
29% record the scanning error rate

57% do not validate their scanning protocols

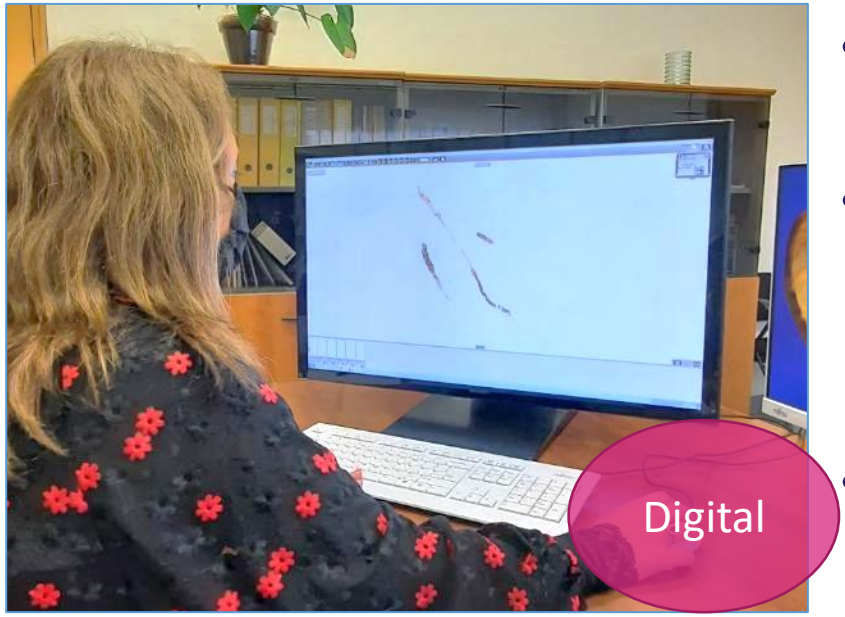
Digital navigation





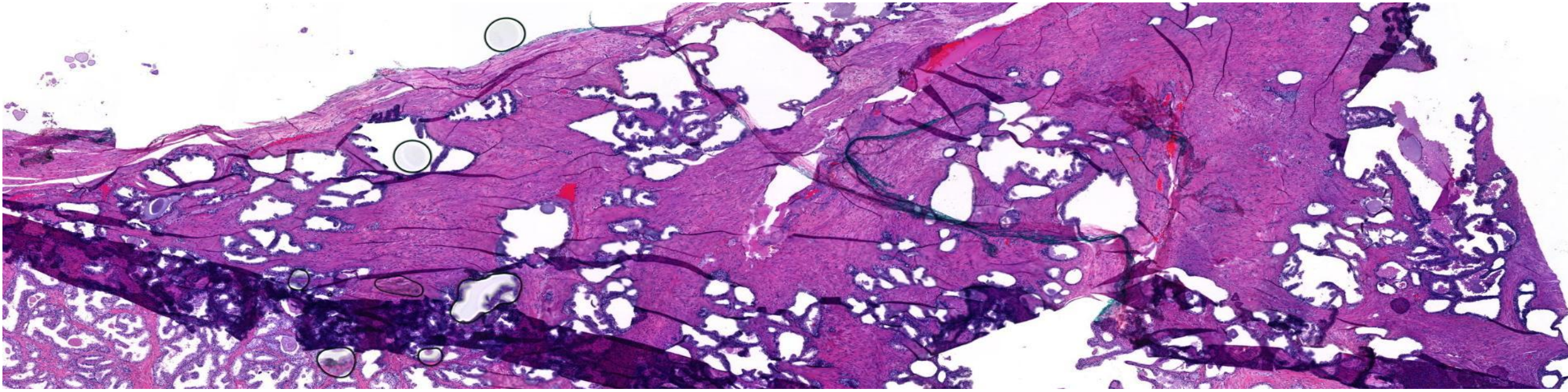


Navigation conditions change



- Navigation changes
- Ergonomics and environment modifications
- Colors and intensities change
- Multilayers and transparency are lost

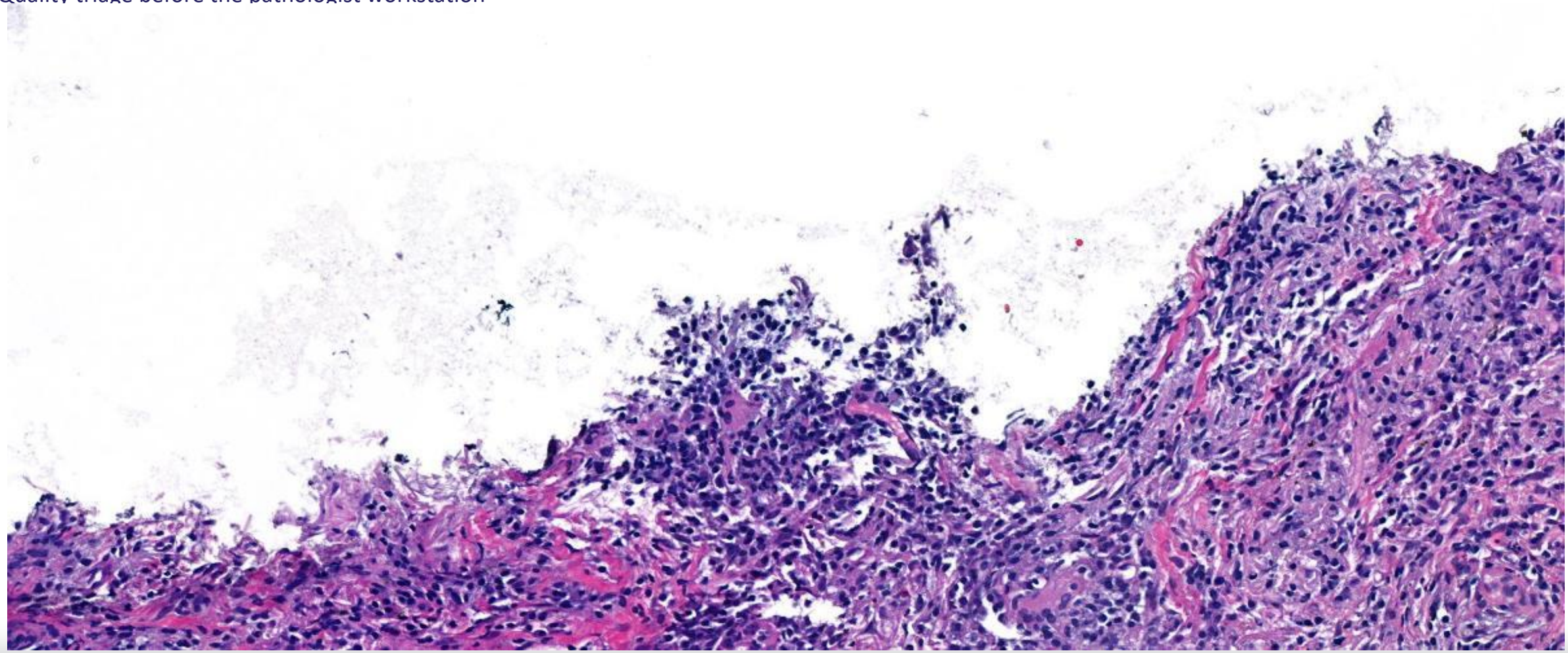
All issues are *amplified* in the digital image



???Only visible in WSI???

Active surveillance of the quality of the lab work and tracking of possible interferences

Quality triage before the pathologist workstation



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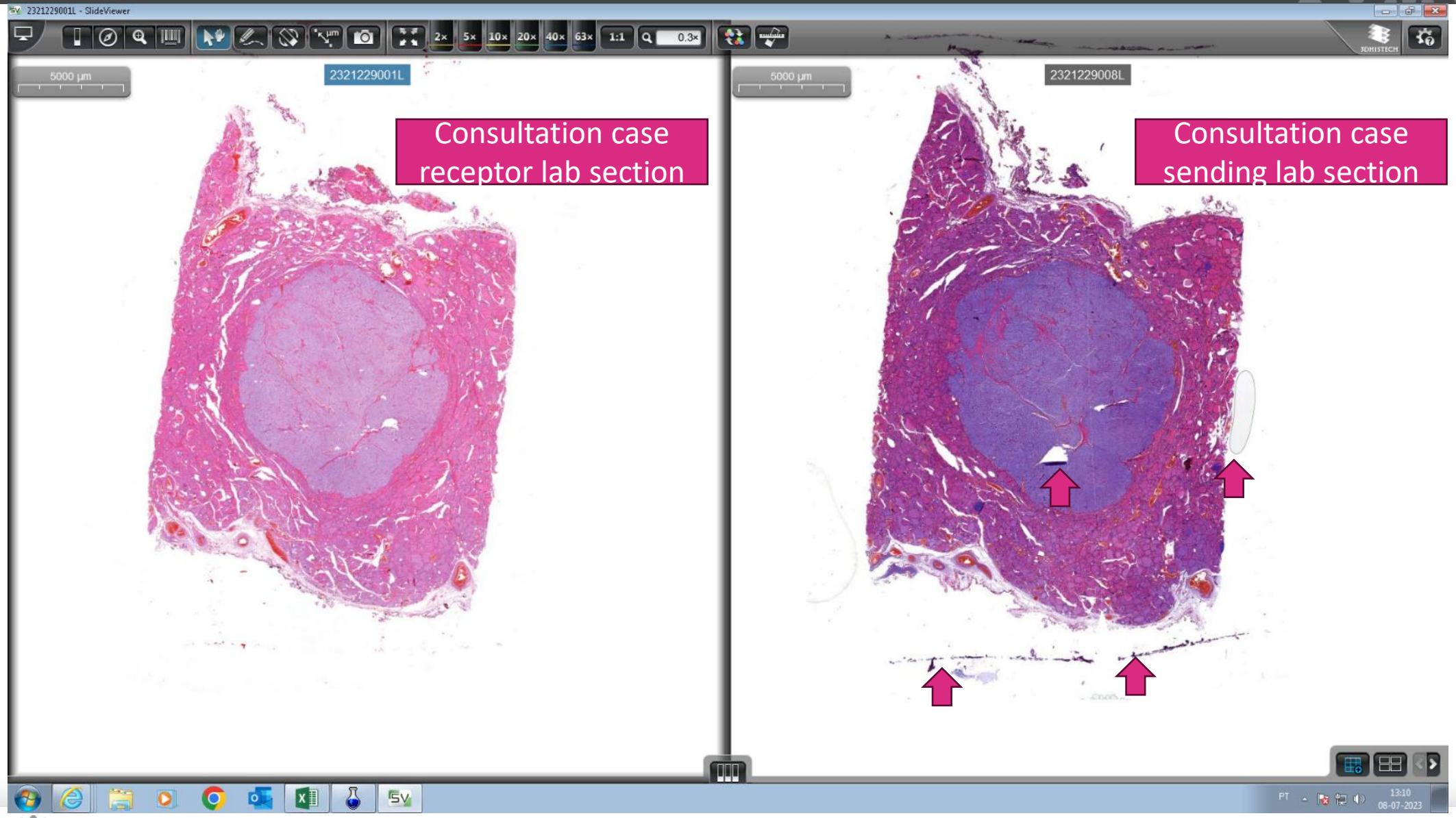
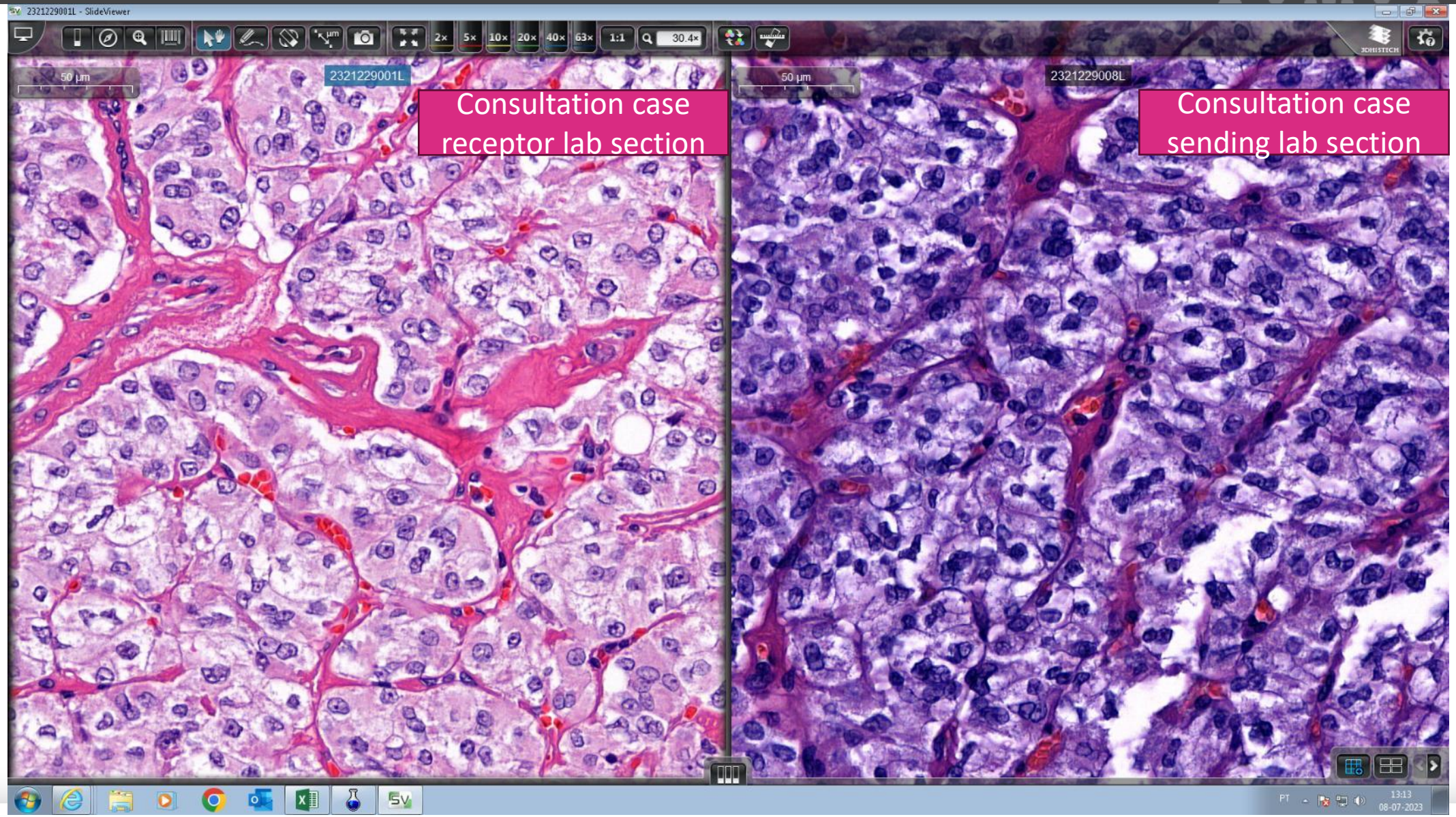
Understand the limits of good practice



Understand the limits of good practice



100% Digital

(tissue)

The holistic concept of digital pathology comprehends innovative interventions in all workstations of the pathology laboratory, as well as before and after the analytic process.

diagnostics

MDPI

Article

Digital Pathology Workflow Implementation at IPATIMUP

Catarina Eloy [1,2,*], João Vale [1], Mónica Curado [1], António Polónia [1,2], Sofia Campelos [1], Ana Caramelo [1], Rui Sousa [1,2] and Manuel Sobrinho-Simões [1,2]

Digital Pathology Workflow Implementation at IPATIMUP

Catarina Eloy [1,2,*], João Vale [1], Mónica Curado [1], António Polónia [1,2], Sofia Campelos [1], Ana Caramelo [1], Rui Sousa [1,2] and Manuel Sobrinho-Simões [1,2]

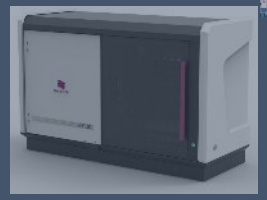
Pre-analytic optimization

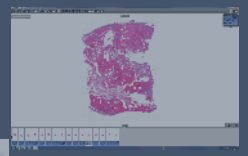
Analytics automation and control

Post-analytic surveillance

Beyond scanning, transcending the perfect whole slide image

Digital transformation at IPATIMUP





Transformation started

July

Integration with LIS

October

Protocol optimization & QA program

November

Validation for primary diagnosis

January

Fully digital

July

2016 2017 2018 2019 2020 2021 2022 2023

Time line

Adopting the digital workflow

- **Get to know the possibilities of your LIS/LIMS and informatic resources**
- **Instal a reliable tracking system**
- **Design a quality control program mapping the necessary quality control checkpoints**
- **Invest in a good production control design**

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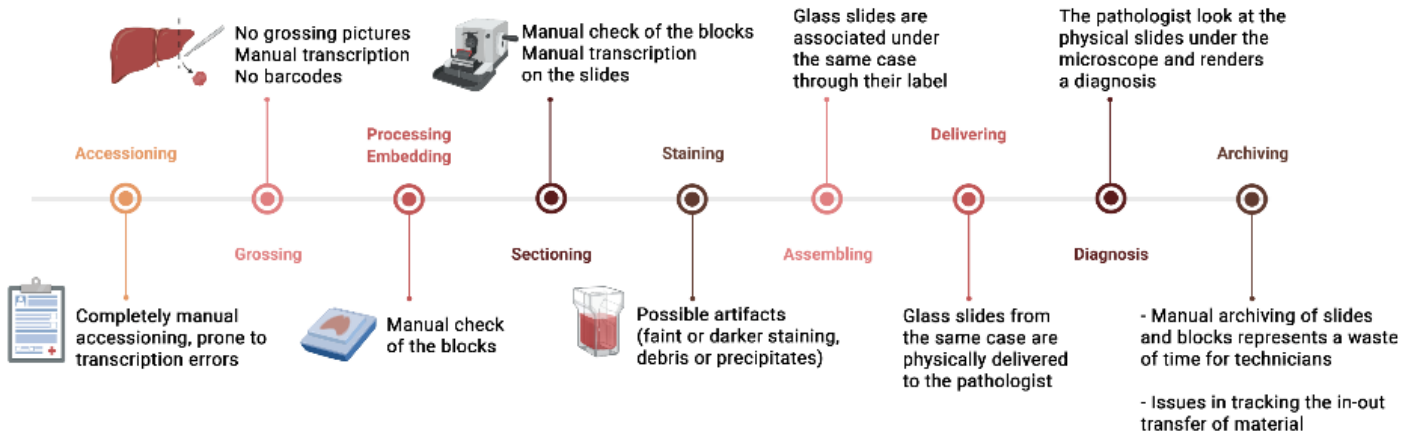
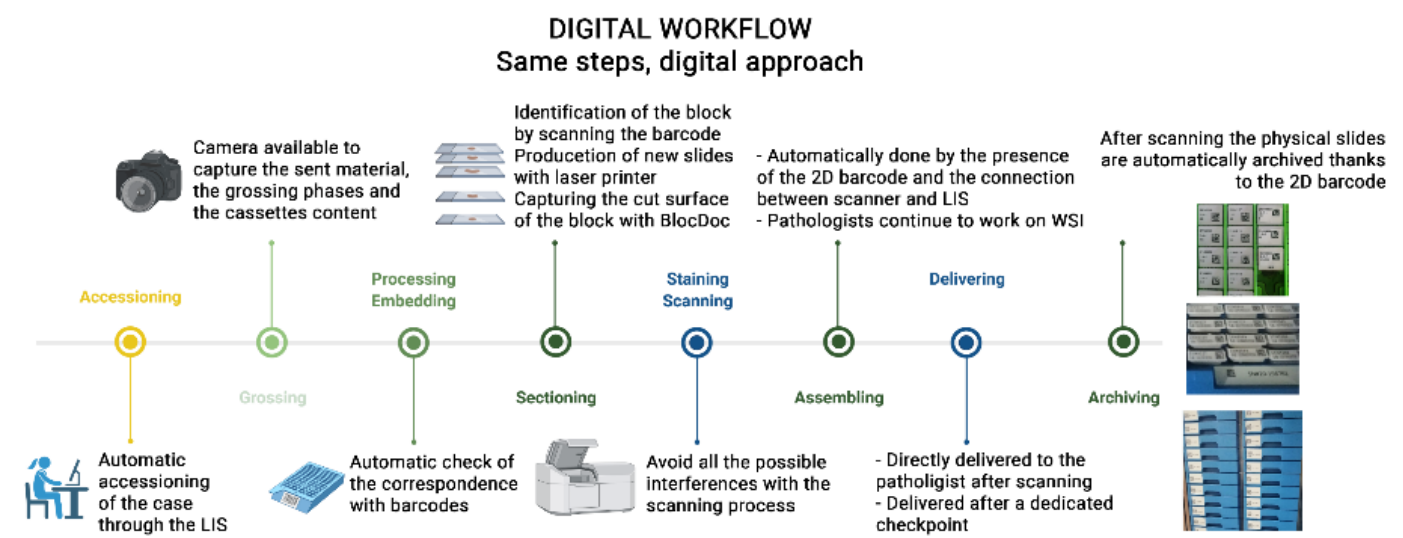
Guidelines

Best Practice Recommendations for the Implementation of a Digital Pathology Workflow in the Anatomic Pathology Laboratory by the European Society of Digital and Integrative Pathology (ESDIP)

Filippo Fraggetta [1,2], Vincenzo L'Imperio [1,3], David Ameisen [1,4], Rita Carvalho [1,5], Sabine Leh [1,6,7], Tim-Rasmus Kiehl [1,5], Mircea Serbanescu [1,8], Daniel Racoceanu [1,9], Vincenzo Della Mea [1,10], Antonio Polonia [1,11,12], Norman Zerbe [1,5] and Catarina Eloy [1,11,12,*]





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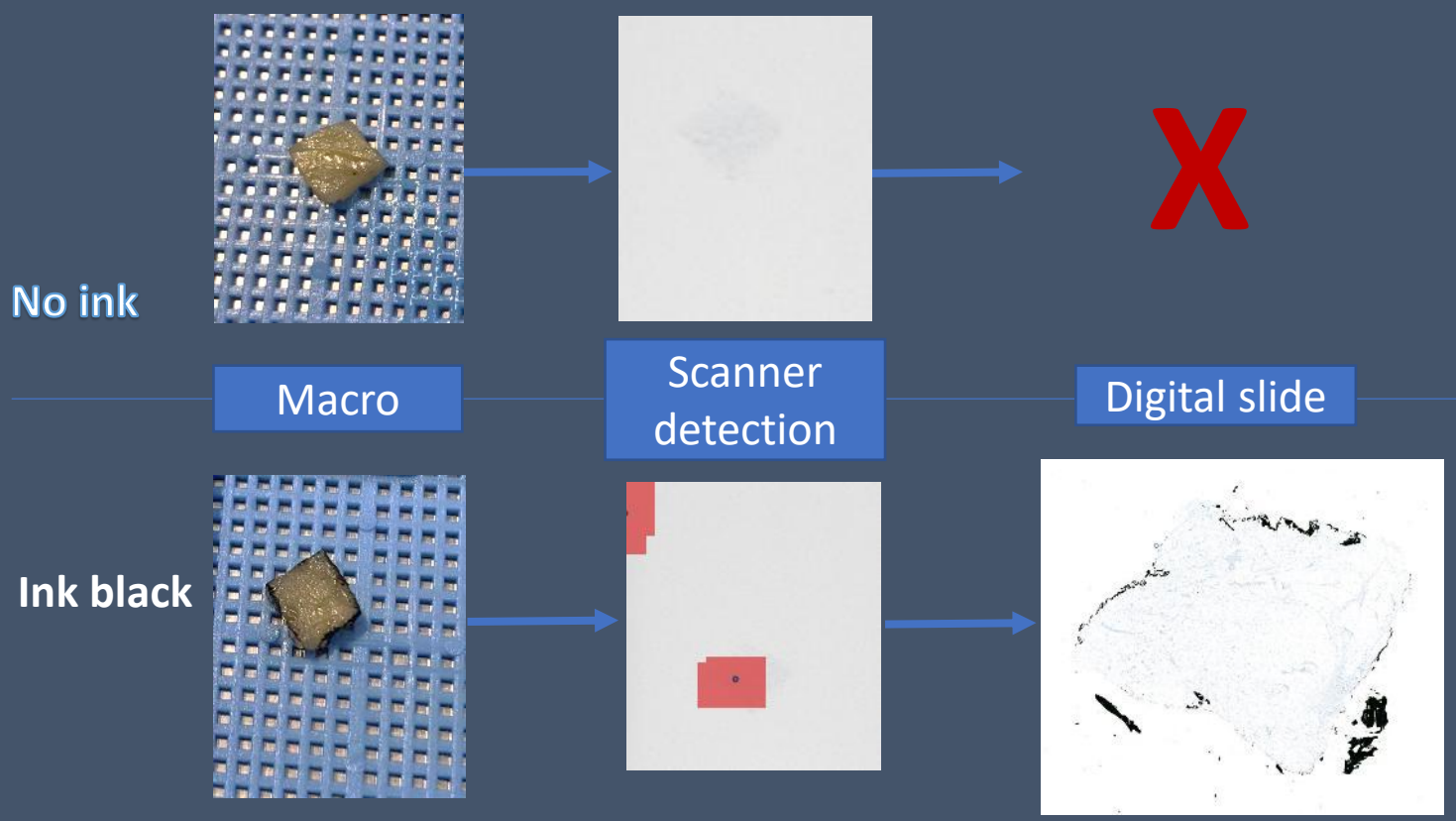
Macroscopy

2 fragments of adipose tissue of the same type and size, 3µm cut
IHC – TTF1
P1000, 20x routine scanning protocol



(Internal data, by Catarina Eloy)

Inking breast cancer biopsies
(Internal data, by Catarina Eloy)

Received: 15 May 2023 | Revised: 6 September 2023 | Accepted: 7 September 2023
DOI: 10.1002/dc.25224

ORIGINAL ARTICLE

WILEY

Inking cell blocks improves scanner detection for diagnosis in pathology

Catarina Eloy MD, PhD [1,2,3] | Beatriz Neves BSc [1] | João Vale MSc [1,4] | Sofia Campelos MD [1] | Mónica Curado BSc [1,4] | António Polónia MD, PhD [1,2]

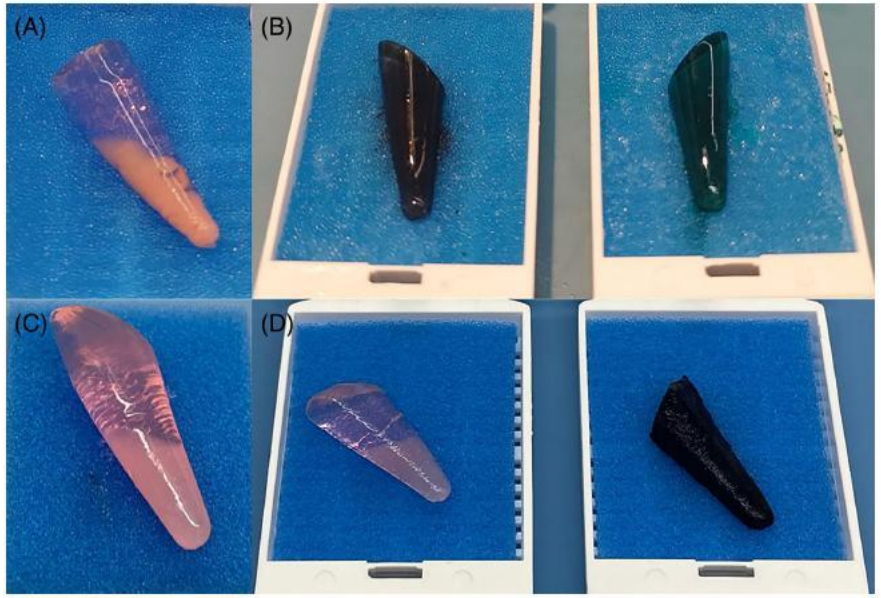


FIGURE 1 (A) Non-inked cell block used in Test 1. (B) Cell block after sectioning in two half cones, one inked black (left) and one inked green (right). (C) Non-inked cell block used in Test 2. (D) Cell block after sectioning in two half cones, one non-inked (left) and one inked black (right).

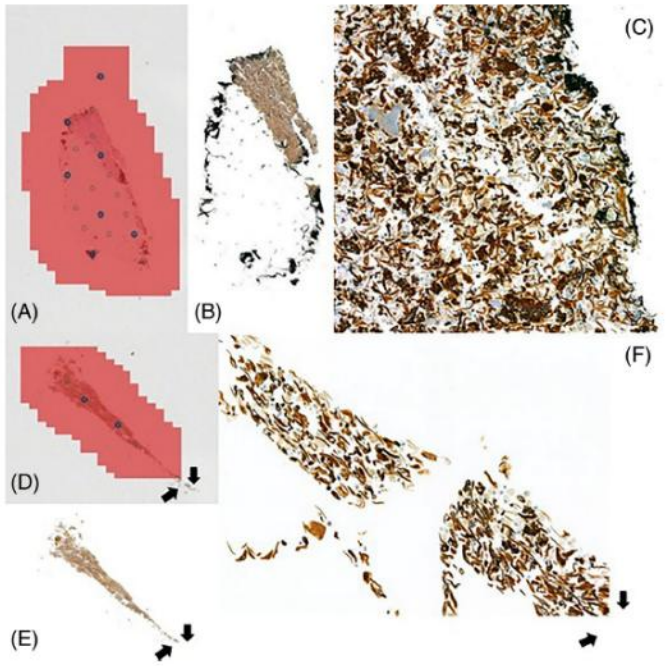


FIGURE 3 CKAE1AE3 stained WSI of inked black half cone of a cell block: (A) area of total scanner detection expressed in Case Center software, (B) CKAE1AE3 WSI, 0.5×, and (C) CKAE1AE3 WSI, 10.0× demonstrating low infiltration of the ink within the cell content. CKAE1AE3 stained WSI of non-inked/null half cone of the same cell block: (D) partial scanner detection expressed in Case Center software with missing areas (black arrows), (E) CKAE1AE3 WSI, 0.5× with missing areas (black arrows), and (F) CKAE1AE3 WSI, 10.0× demonstrating missing areas (black arrows).

Virchows Archiv
https://doi.org/10.1007/s00428-024-03762-3

ORIGINAL ARTICLE

Optimizing the management of thyroid specimens to efficiently generate whole slide images for diagnosis

Catarina Eloy[1,2] · João Vale[2,3] · Mariana Barros[2] · Diana Oliveira[2] · Morgana Mesquita[2,3] · Mónica Curado[2,3] · João Pinto[2] · António Polónia[2,4,5]

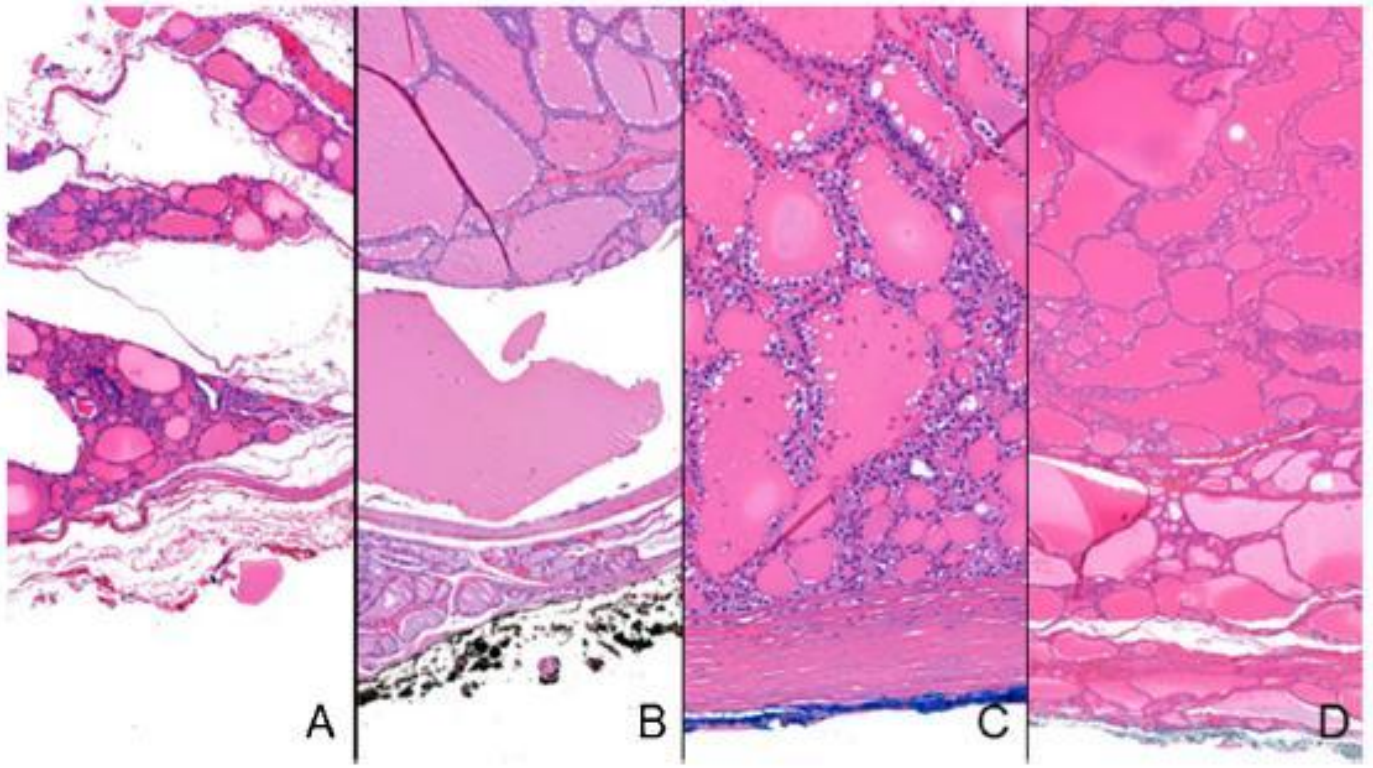


Fig.1 Hematoxylin and eosin (H&E) whole slide images of four cases with their surgical margins inked with different colours: **A** red, **B** black, **C** blue, **D** green

Embedding

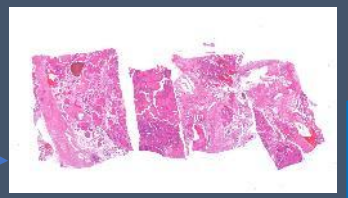
1cm^2 tissue divided in 4 fragments of similar size, 3µm cut, H&E P1000, 20x routine scanning protocol

A

Scanning area: 94kx102k px
Time to scann:49 sec
File size: 727Mb

Macro | Embedding | Scanner detection | Digital slide

B



Scanning area: 84kx46k px
Time to scann:39 sec
File size: 466 Mb

- Spare 56% digital archive
- Optimize navigation
- Decrease 127% scanning area
- Increase scanning speed 25%

(Internal data, by Catarina Eloy)

Cutting

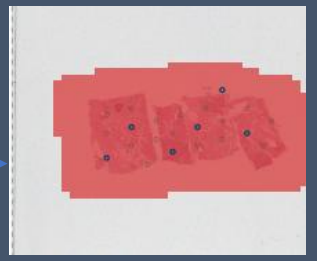
1cm^2 tissue divided in 4 fragments of similar size, H&E
P1000, 20x routine scanning protocol

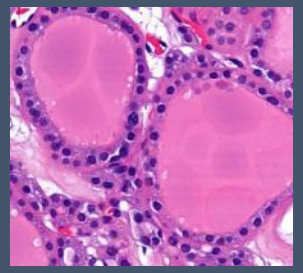
B

Macro

Embedding

3µm cut



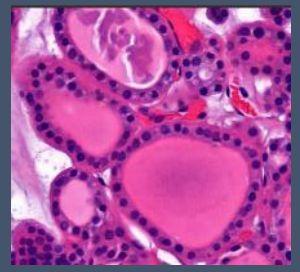


Scanner detection

Digital slide

Scanning area: 84kx46k px
Time to scann:39 sec
File size: 466 Mb

5µm cut



Scanning area: 91kx48k px
Time to scann:45 sec
File size: 504 Mb

Decrease 8% digital archive

Increase scanning speed 15%

Efficient workflow

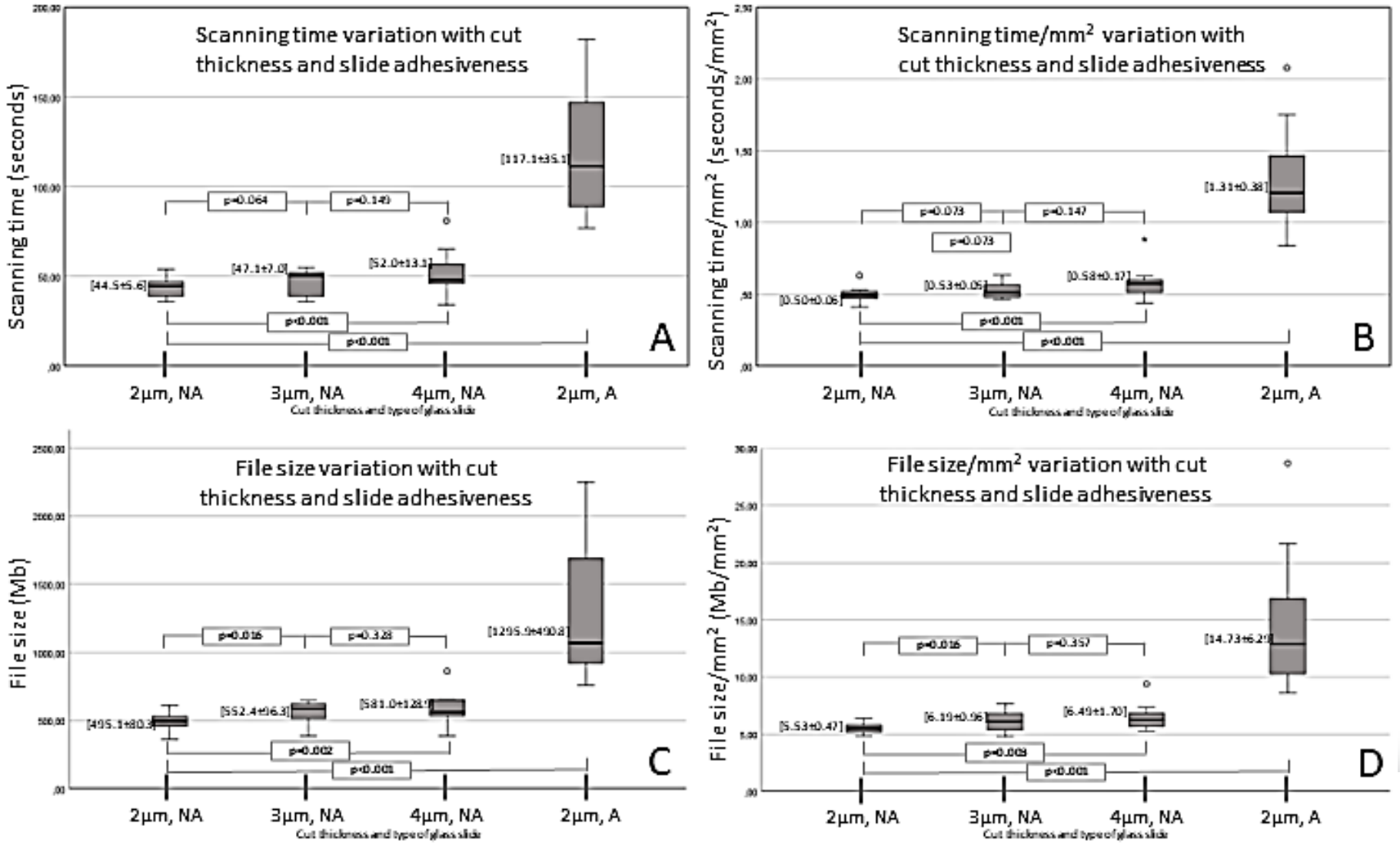
(Internal data, by Catarina Eloy)

Virchows Archiv
https://doi.org/10.1007/s00428-024-03762-3

ORIGINAL ARTICLE

Optimizing the management of thyroid specimens to efficiently generate whole slide images for diagnosis

Catarina Eloy[1,2] · João Vale[2,3] · Mariana Barros[2] · Diana Oliveira[2] · Morgana Mesquita[2,3] · Mónica Curado[2,3] · João Pinto[2] · António Polónia[2,4,5]



Coverslipping

Journal of Pathology Informatics 13 (2022) 100098

Contents lists available at ScienceDirect

Journal of Pathology Informatics

journal homepage: www.elsevier.com/locate/jpi

Technical Note

The impact of different coverslipping methods in the quality of the whole slide images used for diagnosis in pathology

Diana Ferreira [a], João Vale [a], Mónica Curado [a], António Polónia [a,b], Catarina Eloy [a,b,c,*]

digital pathology. The coverslipping method interferes with the quality of the WSIs, as well as with the scanning time and the file size of the WSIs. All coverslipping methods were found suitable for diagnosis. The glass and liquid methods were manual and had similar results concerning the presence of air bubbles/polymer accumulation, air drying artifacts, tissue exposed and staining alterations. The glass method was the one with more air bubbles. The liquid method was associated with more alterations on the WSIs, but with the lowest file sizes. Automation of coverslipping and calibration of the scanner for the coverslipping method chosen by the pathology laboratory are relevant for the final quality of the WSIs.

Table 2
Average evaluation of the pre-scanning and scanning features.

	Glass method	Film method	Liquid method	Friedman test
Air bubbles/polymer accumulation	1.31	1.00	1.06	$P = 0.018$
Air drying artifact	1.03	1.11	1.32	$P = 0.121$
Tissue exposed	1.00	1.00	1.00	$P = 1.000$
Staining alterations	1.37	1.26	1.45	$P = 0.129$
Blurring/out of focus areas	1.39	1.55	2.00	$P = 0.004$

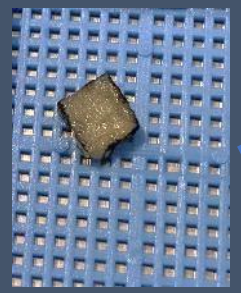
Table 1
Coverslipping methods features after their usage under the conditions created for this study.

Method	Glass method	Film method	Liquid method
Equipment	Dry station	Tissue-Tek Film® Automated Coverslipper Oven	Dry station Oven
Management	Manual	Automatic	Manual
Reagents/consumables	Xylene BioMount®	Xylene Tissue-Tek Film®	Xylene Cristallo®
Average time between staining and scanning (minutes)	21	6	64
Average size of the WSI file (gigabytes)	2.26	1.85	1.68

WSI – whole slide image

Staining

1 fragment of inked black adipose tissue, IHC S100 P1000, 20x routine scanning protocol



Macro

Optimized IHC

Wild IHC

Scanner detection

Digital slide

Scanning area: 50kx40k px
Time to scann:20 sec
File size: 140 Mb

Scanning area: 97kx174k px
Time to scann:138 sec
File size: 776 Mb

Decrease 454% digital archive

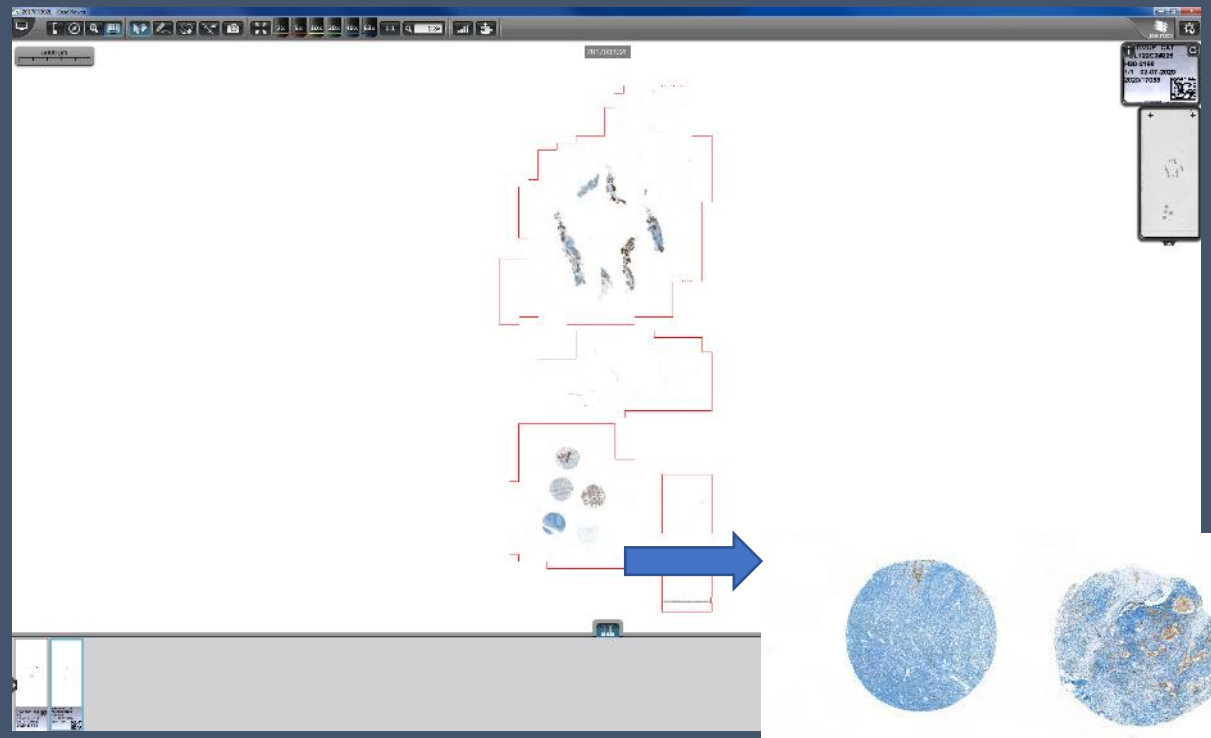
Increase scanning speed 590%

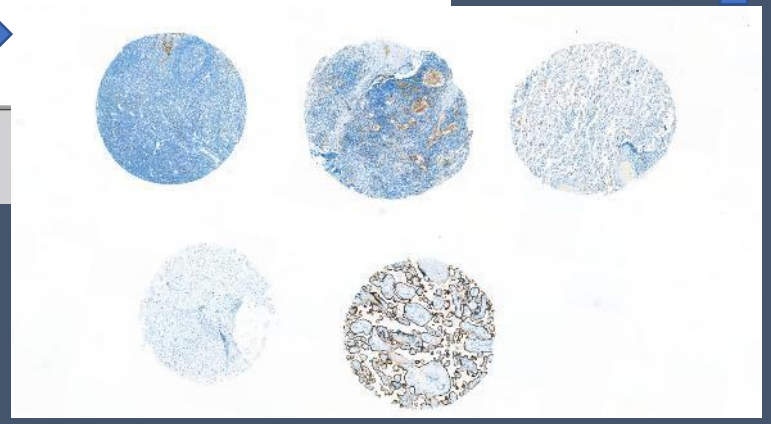
Decrease 401% area

(Internal data, by Catarina Eloy)

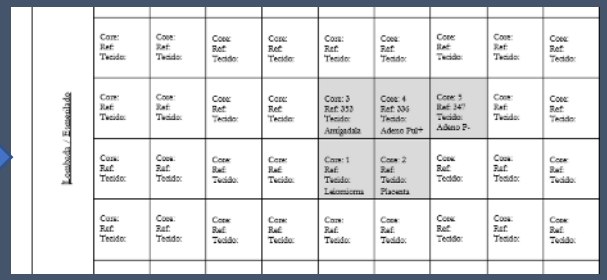
Permanent control of all slides

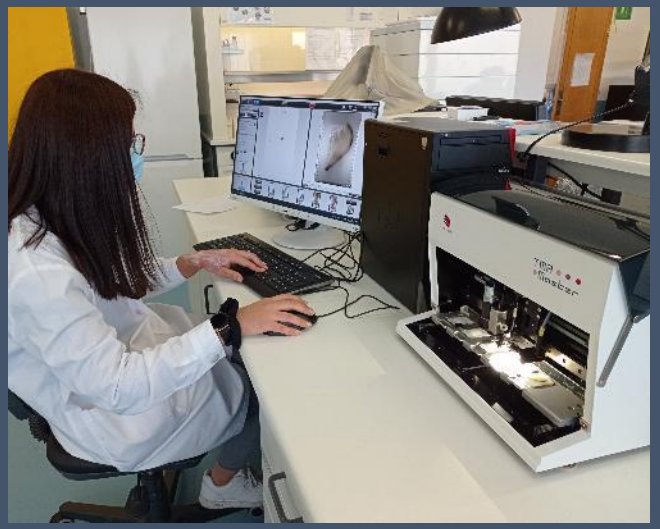
TMA production from clinical purposes





Core: 3 Ref: 353 Tecido: Amígadala	Core: 4 Ref: 336 Tecido: Adeno Pul+	Core: 5 Ref: 347 Tecido: Adeno P-
Core: 1 Ref: Tecido: Leiomioma	Core: 2 Ref: Tecido: Placenta	Core: Ref: Tecido:

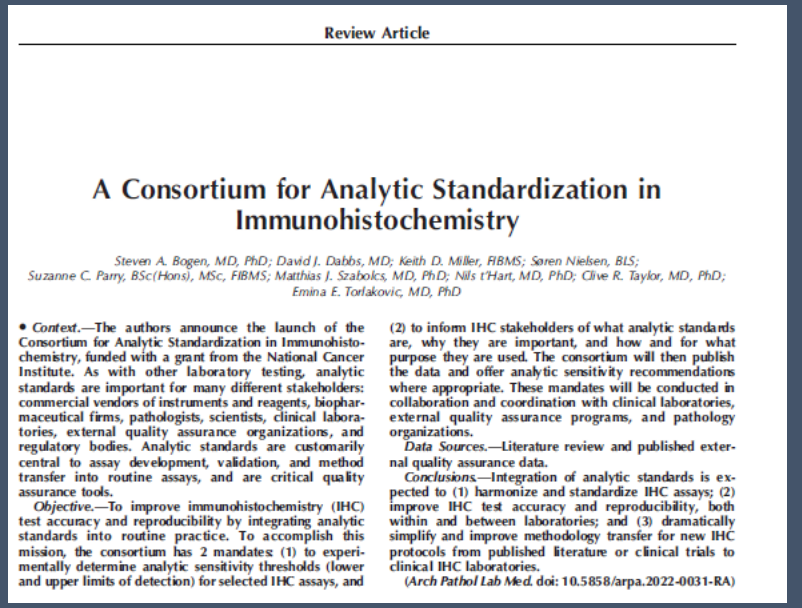




IPATIMUP, PD-L1 (Lung) TMA

(Internal data, by Catarina Eloy)

Tissue control bank



Review Article

A Consortium for Analytic Standardization in Immunohistochemistry

Steven A. Bogen, MD, PhD; David J. Dabbs, MD; Keith D. Miller, FIBMS; Søren Nielsen, BLS; Suzanne C. Parry, BSc(Hons), MSc, FIBMS; Matthias J. Szabolcs, MD, PhD; Nils t'Hart, MD, PhD; Clive R. Taylor, MD, PhD; Emina E. Torlakovic, MD, PhD

• *Context.*—The authors announce the launch of the Consortium for Analytic Standardization in Immunohistochemistry, funded with a grant from the National Cancer Institute. As with other laboratory testing, analytic standards are important for many different stakeholders: commercial vendors of instruments and reagents, biopharmaceutical firms, pathologists, scientists, clinical laboratories, external quality assurance organizations, and regulatory bodies. Analytic standards are customarily central to assay development, validation, and method transfer into routine assays, and are critical quality assurance tools.

Objective.—To improve immunohistochemistry (IHC) test accuracy and reproducibility by integrating analytic standards into routine practice. To accomplish this mission, the consortium has 2 mandates: (1) to experimentally determine analytic sensitivity thresholds (lower and upper limits of detection) for selected IHC assays, and (2) to inform IHC stakeholders of what analytic standards are, why they are important, and how and for what purpose they are used. The consortium will then publish the data and offer analytic sensitivity recommendations where appropriate. These mandates will be conducted in collaboration and coordination with clinical laboratories, external quality assurance programs, and pathology organizations.

Data Sources.—Literature review and published external quality assurance data.

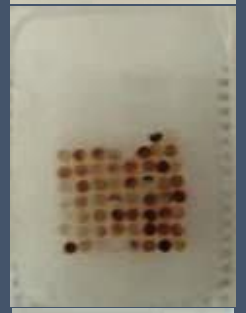
Conclusions.—Integration of analytic standards is expected to (1) harmonize and standardize IHC assays; (2) improve IHC test accuracy and reproducibility, both within and between laboratories; and (3) dramatically simplify and improve methodology transfer for new IHC protocols from published literature or clinical trials to clinical IHC laboratories.

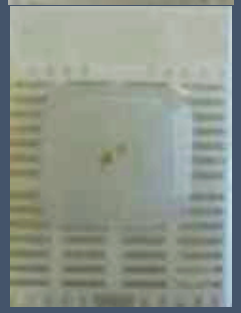
(*Arch Pathol Lab Med.* doi: 10.5858/arpa.2022-0031-RA)

- Establishment of patterns of reaction
- Search for stability of the staining aiming to standardization
- Prevent modification after new lots of reagents/instruments/conditions

- Bank of donor blocks that feed well designed TMAs
- Each TMA is conceived to control one or more stains
- All slides carry a routine TMA copy (+/-)
- All stains are verified with a validation TMA when hard changes occur

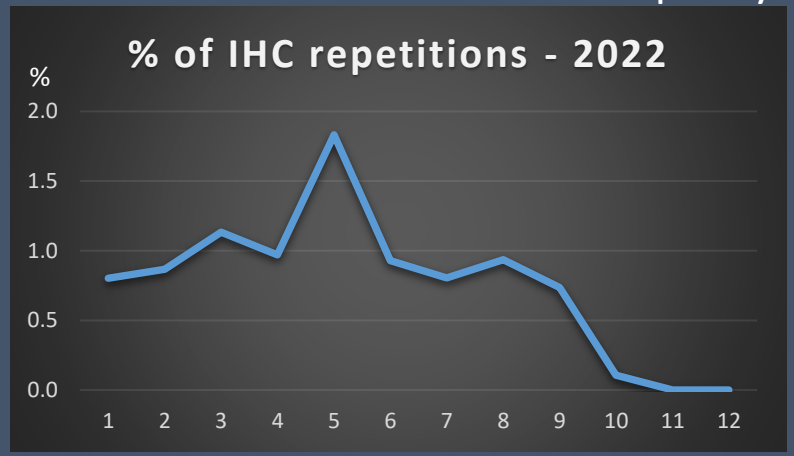
Tissue bank at IPATIMUP



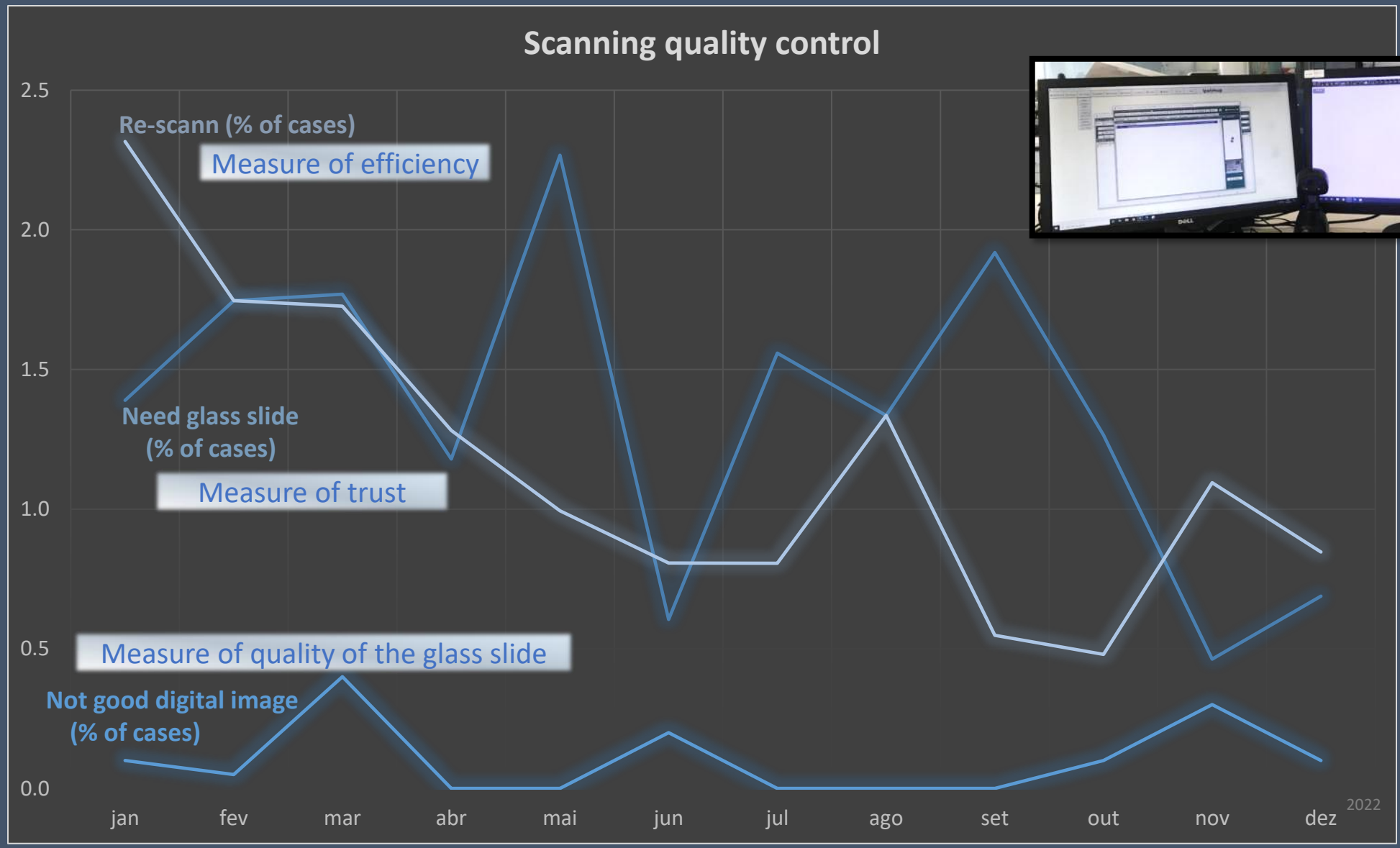


- 2207 donor blocks
- 15 validation TMAs (20-94 cores)
- 72 routine TMAs (2-5 cores)
  - Histochemistry – 18
  - Immunohistochemistry – 51
  - Fluorescence - 3

Surveillance of IHC quality



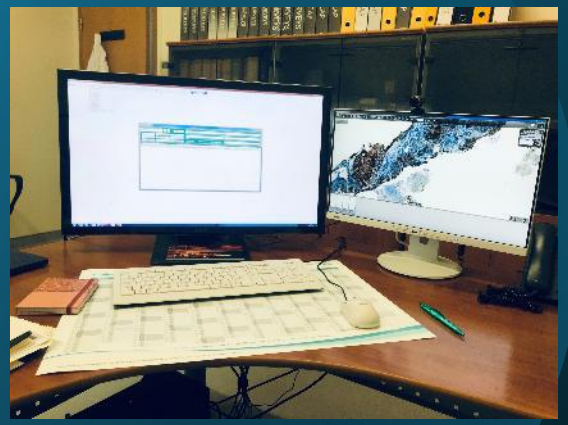
(Internal data, by Catarina Eloy)



DIGITAL & QUALITY are two faces of the same coin

(Internal data, by Catarina Eloy)

Confortable & safe navigation
1GB network LIS centered



Dell Precision Tower 3620 equipped with an Intel(R) Core(TM) i7-6700 CPU @ 3.40GHz, 8GB of RAM, ST500DM002-1SB10A ATA Disk with 466GB and a NVIDIA Quadro M2000 with 4GB.

The workstation has two monitors, one Sharp PN-K322BH 4K, 32”, touch screen

Storage - 220TB storage that can scale up to 960TB

Low power view
&
High power view

Original Paper | Published: 31 October 2020

Digital Versus Optical Diagnosis of Follicular Patterned Thyroid Lesions

Ayat Alqaily, Antonio Polonia, Sofia Campelos, Nusaiba Alrefae, Joao Vale, Ana Caramelo & Catarina Eloy

Head and Neck Pathology **15**, 537–543 (2021) | Cite this article

189 Accesses | **2** Altmetric | Metrics

Endocrine
https://doi.org/10.1007/s12020-022-03104-w

ORIGINAL ARTICLE

Nuclear score evaluation in follicular-patterned thyroid lesions using optical and digital environments

Helton Estrela Ramos[1,2] · João Vale[3] · Sara Lopes[4] · Ana Marques[3,5] · Jorge Pinheiro[3,5] · Fabyan Esberard de Lima Beltrão[1] · Gabriel Rodrigues[1] · Pedro Resende Ferreira Rende[1] · Fabio Hecht[6] · Catarina Eloy[3,7]

Received: 29 March 2022 / Accepted: 29 May 2022

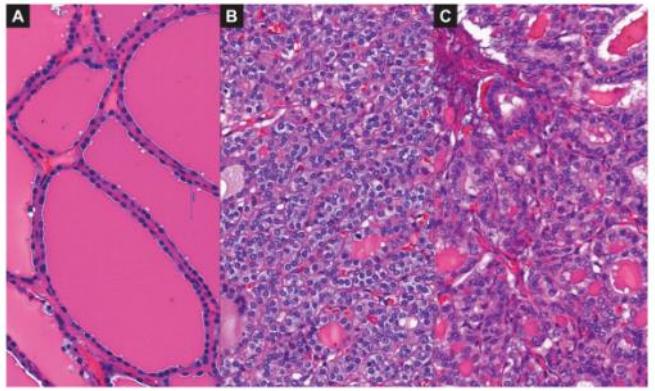


Fig. 1 Pictures of cases illustrating the evaluation of the nuclear scoring of thyroid pattern lesions unanimously classified under the microscope by the 3 pathologists (captured at 40x after scanning with P1000 20x scanning protocol). **A** case 20 classified as nuclear score of 0/1; **B** case 8 classified as nuclear score of 2; **C** case 6 classified as nuclear score of 3


diagnostics

MDPI

Article

Digital Pathology Workflow Implementation at IPATIMUP

Catarina Eloy [1,2,*], João Vale [1], Mónica Curado [1], António Polónia [1,2], Sofia Campelos [1], Ana Caramelo [1], Rui Sousa [1,2] and Manuel Sobrinho-Simões [1,2]

Evaluation of the result of the digital transformation

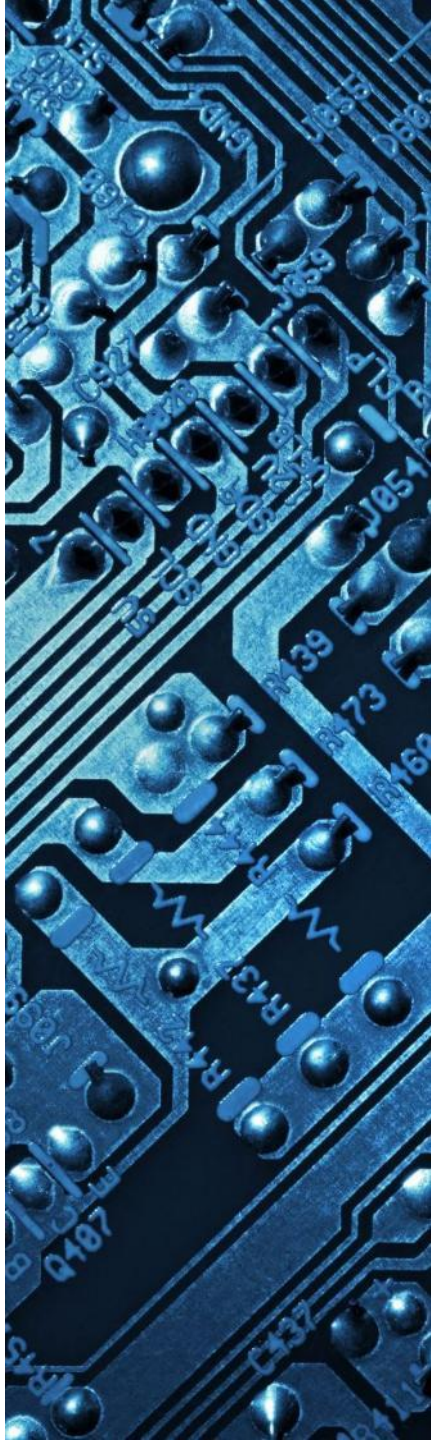
Return of the investment 2022

- Maintenance of the space, people and instrument numbers
- Maintenance of the excellent results in the external quality control programs

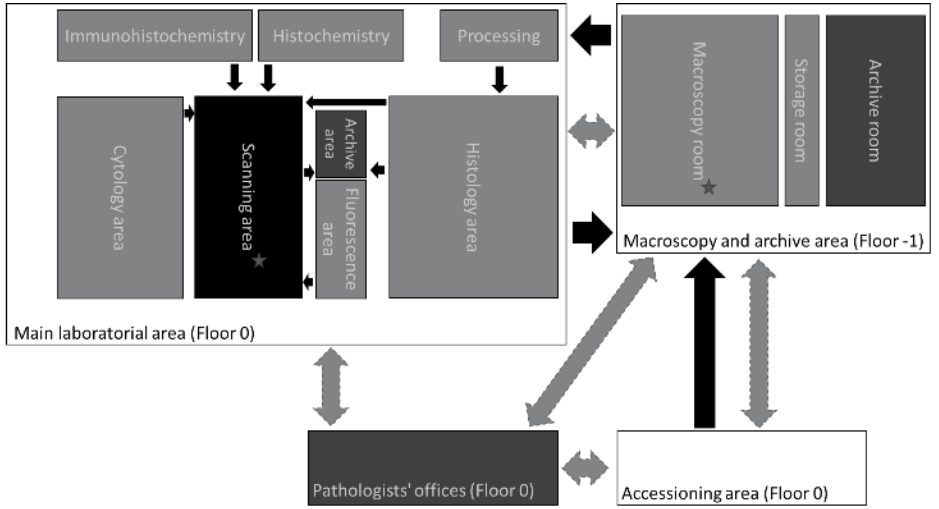
CAP ACCREDITED
COLLEGE of AMERICAN PATHOLOGISTS

INSTITUTO PORTUGUÊS DE ACREDITAÇÃO IPAC acreditação

- Improvements in the internal quality control program
- **10-20%** improvement in the turnaround time
- Flexible scheduling with the possibility to work at distance
- Paper *free* lab



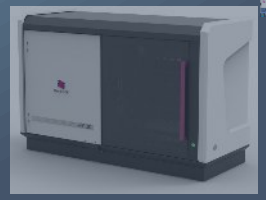
Time matters



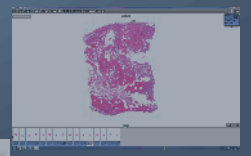
- Turnaround time is a measure of quality
- If turnaround time is increased maybe, you are not carrying a full benefit to the patients
- Keeping with the turnaround time contributes to increase trust in the process
- Turnaround time may be kept after the digital transformation with the same amount of personnel provided that the workflow is carefully optimized (Lean approach: identify *bottle necks*, continuous loading, scanning during the day)

Digital transformation at IPATIMUP

Transformation started



July



Integration with LIS

October

Protocol optimization & QA program

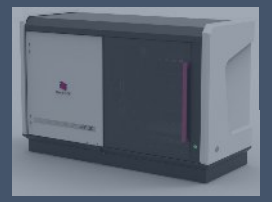
November

Validation for primary diagnosis

January

Fully digital

July



October

Production control

January

AI

May

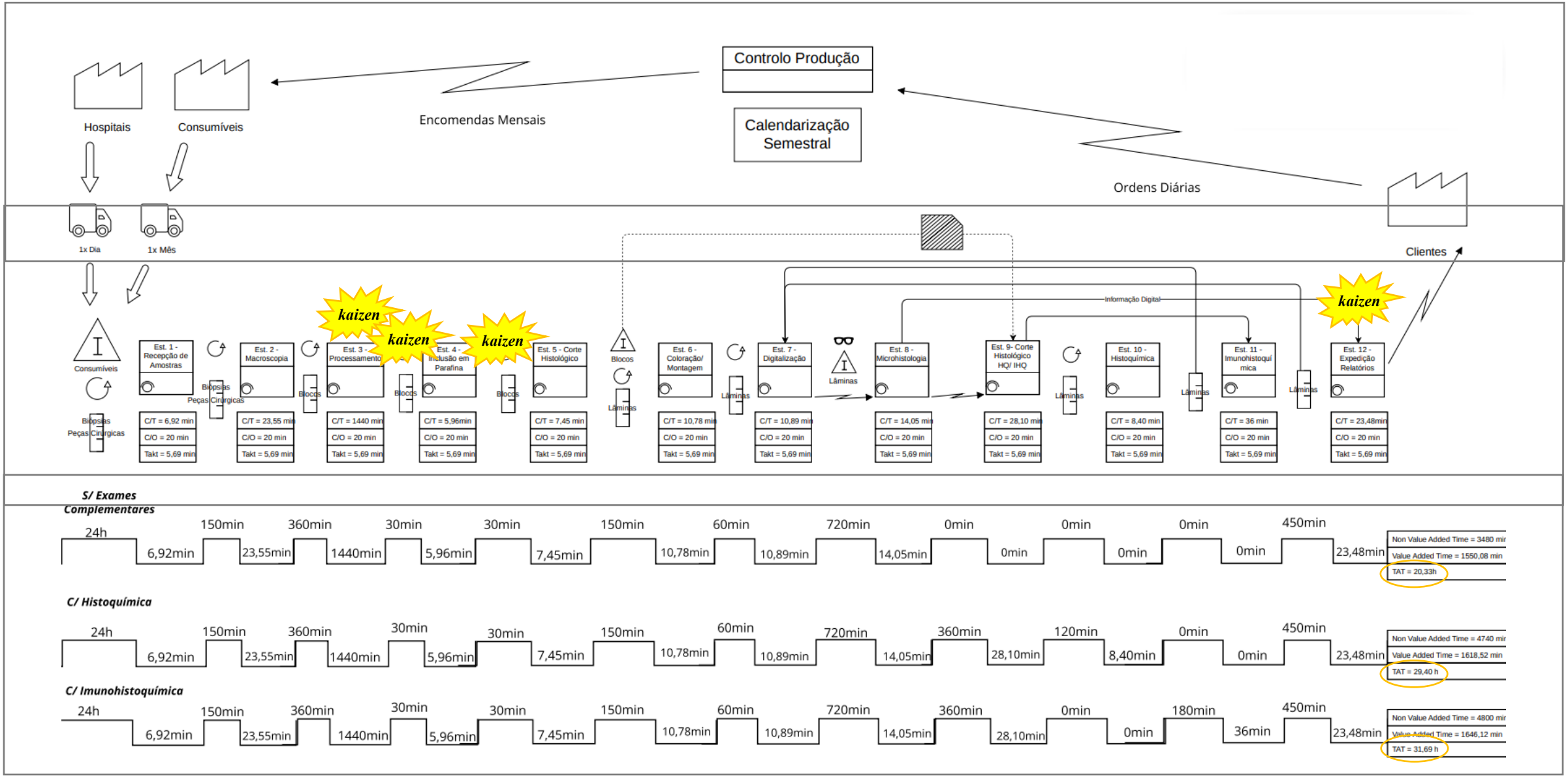
Time line

2016 2017 2018 2019 2020 2021 2022 2023 2024

Lean methodology

- Maximize efficiency
- Improving turnaround time

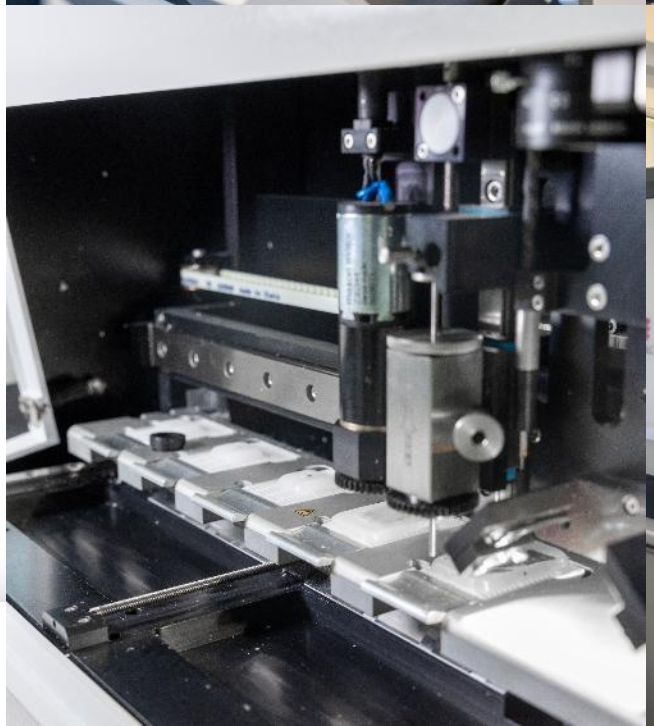
Before Lean



Value Stream Mapping

Standardization of the lab product and automation

- Fast processing
- Automatic embedding
- Continuous staining
- TMA control bank
- Accelerated and high-quality scanning



epredia

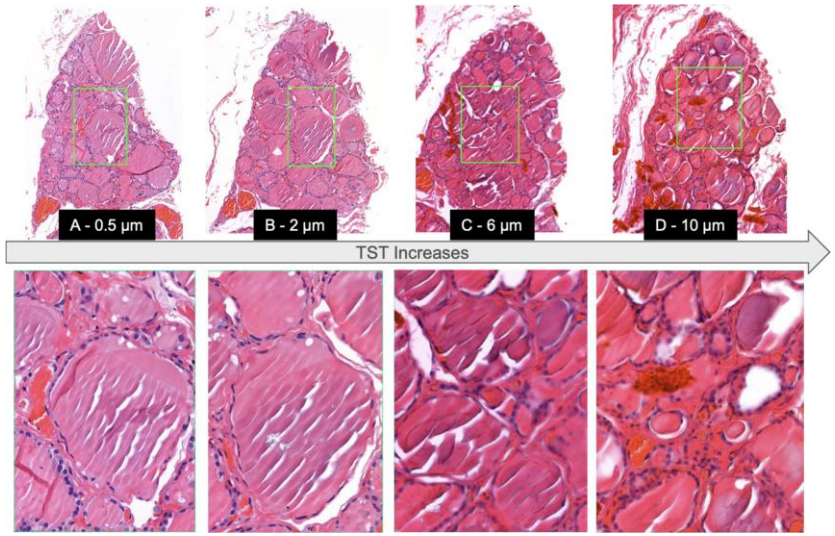
Interference of the lab product in the performance of AI

Endocrine Pathology (2025) 36:10
https://doi.org/10.1007/s12022-025-09855-2

RESEARCH

Impact of Tissue Thickness on Computational Quantification of Features in Whole Slide Images for Diagnostic Pathology

Manav Shah[1] · António Polónia[2,3] · Mónica Curado[2] · João Vale[2] · Andrew Janowczyk[1,4,5] · Catarina Eloy[2,6]



Increment in tissue thickness leads to:

- 13.7% decrease in nuclei
- Fewer complex textures
- Intensity decreased by 30.4% at the nuclear level
- WSI contrast exhibited an increase of 92.6% when transitioning from 0.5 to 10 µm

These findings demonstrate that variations in tissue thickness can obscure or alter the appearance of biological signals, complicating both visual diagnostics and computationally extracted features.

Reporting AI at IPATIMUP

- **2 years use in synergy**
  - Select the team (pathologists & technicians)
  - Workflow changes
  - Parallel control - **(HE+IHC+AI)**
  - Specific quality control
    - Platform downtime
    - Diagnosis agreement
  - Reporting design

(Internal data, by Catarina Eloy)

Reporting AI results

ESMO GOOD SCIENCE BETTER MEDICINE BEST PRACTICE

ESMO REAL WORLD DATA AND DIGITAL ONCOLOGY

PERSPECTIVES

The 1 million words pathology report or the challenge of a reproducible and meaningful message

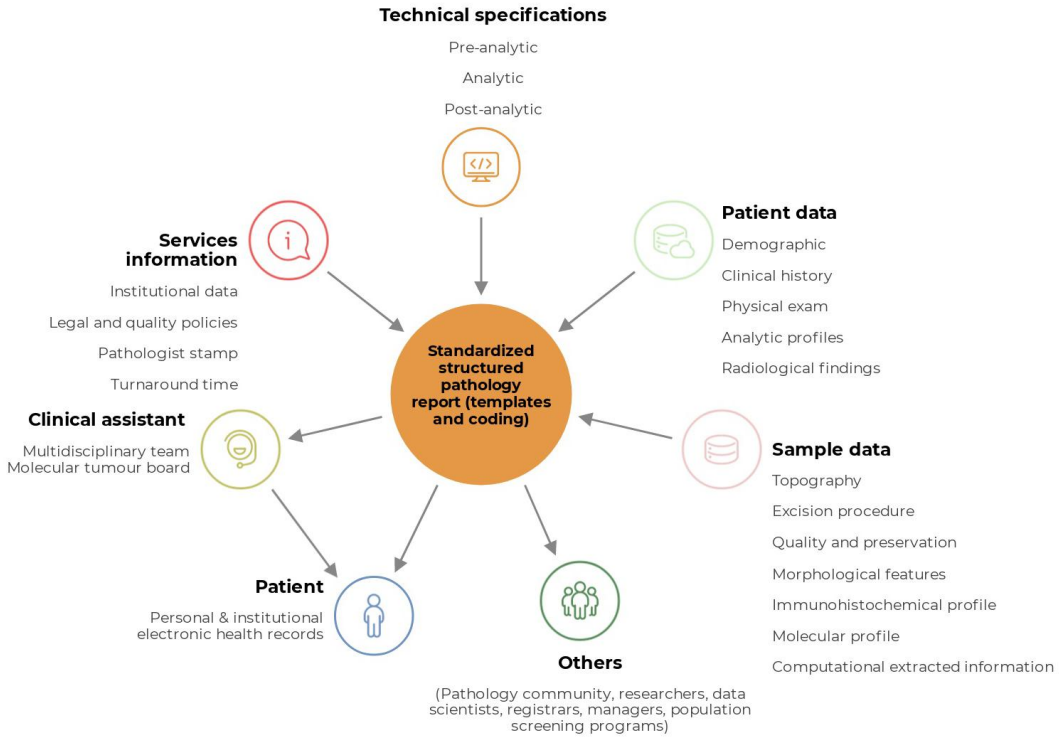
C. Eloy[1,2*], P. Seegers[3], E. Bazyleva[4] & F. Fraggetta[5]

[1]Pathology Laboratory, Institute of Molecular Pathology and Immunology of University of Porto (IPATIMUP), Porto; [2]Pathology Department, Medical Faculty of University of Porto, Porto, Portugal; [3]Palga, National Pathology Databank, Houten, the Netherlands; [4]Belgian Society of Pathology, Brussels, Belgium; [5]Pathology Department, Gravina Hospital, Caltagirone, ASP Catania, Italy

Available online xxx

Many years have passed since the pathology report was all about a single-sentence diagnosis based on morphology. The pathology report is an invaluable source of data that needs to evolve from a narrative reporting to a synoptic reporting system by standardizing data elements to ensure consistency and structured formats that improve completeness, interoperability, and scalability across different health care systems. The convergence of technology, structured data, and artificial intelligence propels the field of pathology toward a future where the synthesis of information benefits not only health care professionals and patients but also serves as a wellspring of knowledge for machines, paving the way for unprecedented strides in data mining and health care innovation.

Key words: digital pathology, digital transformation, pathology report, computational pathology, synoptic reporting



epredia

Evaluation of the result of the digital transformation

Return of the investment
2025

100 000 WSI/year
5 years

- **Increment** in space, people and instruments
- **Automation and standardization**
- Maintenance of the excellent results in the external quality control programs

- Improvements in the internal quality control program
- **>50%** improvement in the turnaround time
- Flexible scheduling with the possibility to work at distance
- **Introduction of AI towards precision medicine**
- **Teaching tool**
- Paper *free* lab

Investing on the digital transformation

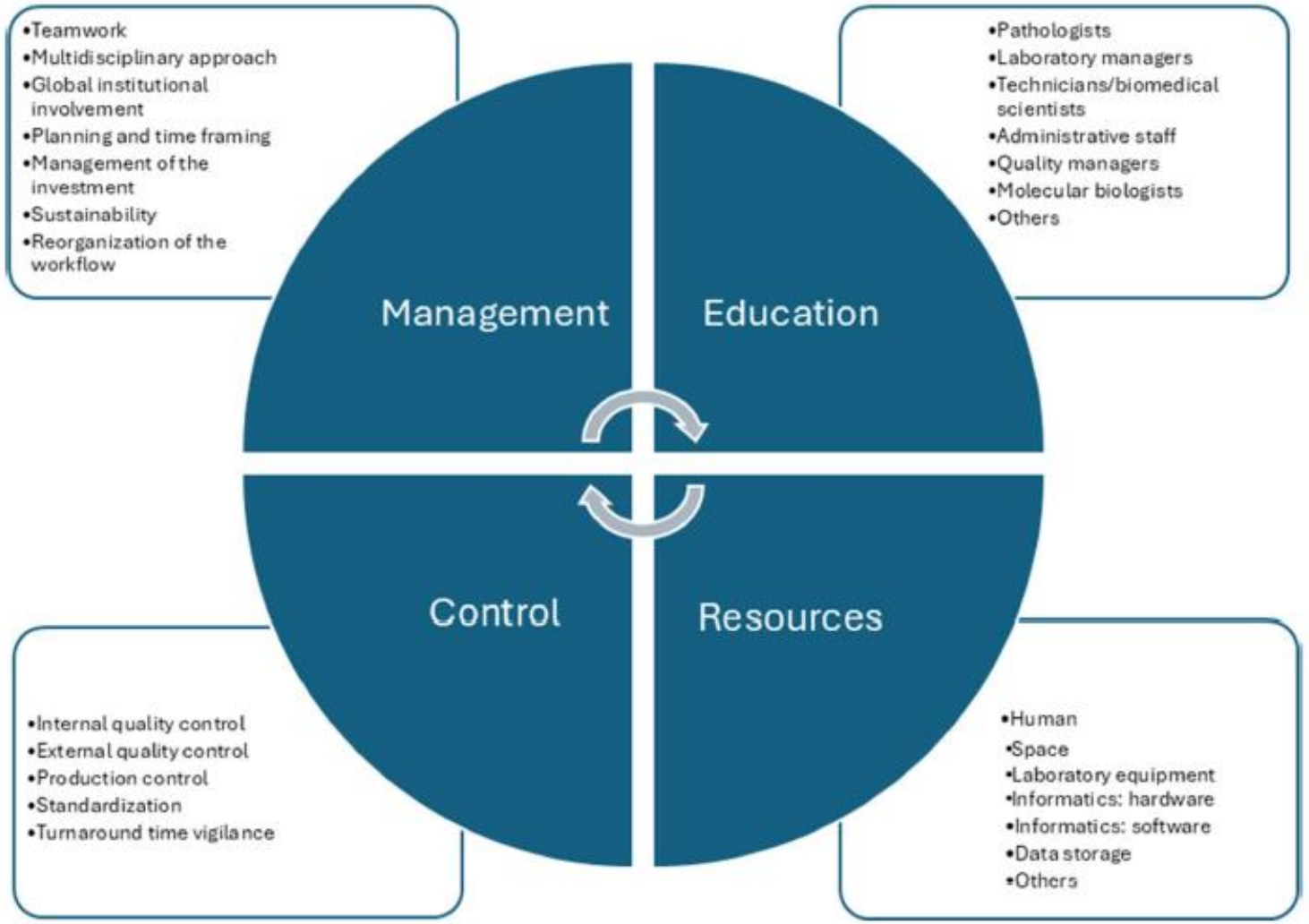


Fig. 1 Management, education, resources, and control policies involved in the digital transformation of pathology

epredia

Eloy *et al*, 2025, Digital transformation of pathology – the European Society of Pathology expert opinion paper

Thank you

Virchows Archiv
https://doi.org/10.1007/s00428-023-03714-3

COMMENTARY

Postponing evolution: why are we choosing to ignore the need for a digital transformation in pathology?

Catarina Eloy[1,2]

Received: 6 October 2023 / Revised: 20 November 2023 / Accepted: 27 November 2023