

# ESO-ESP Digital Pathology Seminar

ONLINE COURSE

## PORTO DIGITAL WORKFLOW

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No conflict of interests to declare

Survey: *Implementação da digitalização de lâminas nos Laboratórios de Anatomia Patológica*

Population: portuguese pathology labs

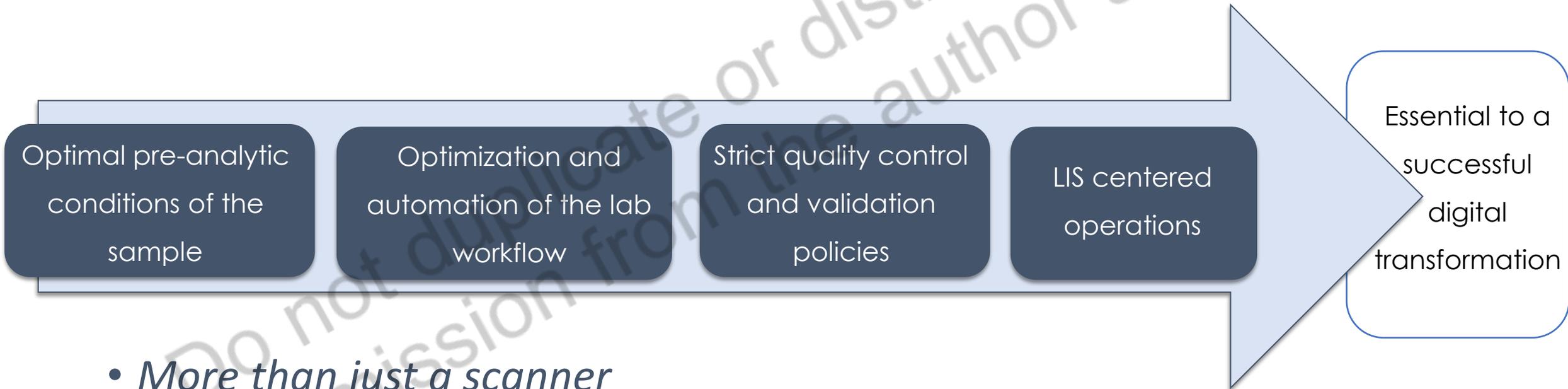
- 14 valid replies
  - Is there a digital workflow in your lab? : 9 (64.3%) no/5 (35.7%)yes
  - Those who reply NO:
    - Anticipate that telepathology for primary diagnosis and second opinion are the major advantages (66.6%)
    - Anticipate that costs may represent the major obstacles to digital pathology implementation (88.9%)
    - One participant does not consider relevant to undergo digitization (11.1%)
  - Those who reply YES:
    - Admitted that the major alterations operated in the lab contemplated instruments (1-2 scanners), space organization and technical staff scheduling
    - All had educational opportunities regarding digital pathology
    - Only 2 use the scanner for primary diagnosis, one of them does not have a LIS-scanner integration



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# The digital transformation (for primary diagnosis)

- The holistic concept of *digital pathology* comprehends innovative interventions in all areas of the pathology laboratory



# A new methodology

*in-silico* reporting represents an advantage in the diagnostic process

- Digital versus analogic/optical pathology: non inferior accuracy and reliability even in the context of biomarker studies and clinical trials

**Blueprint 2 PD-L1 IHC Comparability Study 1305**

**Table 1. Reliability (Intraclass Correlation Coefficient) of Scoring PD-L1 Expression on Tumor Cells among All Pathologists (Excluding the Trainer) for All Cases and NSCLC Biopsy Samples/Resected Cases**

Assay	Glass Slide Scoring		Digital Scoring	
	All Cases	NSCLC Tissue Only	All Cases	NSCLC Tissue Only
22C3	0.89	0.88	0.91	0.91
28-8	0.92	0.94	0.86	0.88
SP-142	0.88	0.86	0.80	0.84
SP-263	0.89	0.92	0.90	0.93
73-10	0.93	0.95	0.91	0.93
All assays	0.86	0.89	0.91	0.93

PD-L1, programmed death ligand 1.

Original Paper | Published: 31 October 2020

## Digital Versus Optical Diagnosis of Follicular Patterned Thyroid Lesions

[Ayat Aloqaily](#) , [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](#)

# A safe and efficient methodology

The laboratory standards for routine diagnostics in a digital setting are part of the standard accreditation procedures internationally

## Validating Whole Slide Imaging Systems for Diagnostic Purposes in Pathology

Guideline Update From the College of American Pathologists in Collaboration With the American Society for Clinical Pathology and the Association for Pathology Informatics

Andrew J. Evans, MD, PhD; Richard W. Brown, MD; Marilyn M. Bui, MD, PhD; Elizabeth A. Chlipala, BS, HTL(ASCP)QIHC; Christina Lacchetti, MHS; Danny A. Milner Jr, MD, MSc(Epi), MBA; Liron Pantanowitz, MD; Anil V. Parwani, MD, PhD; Kearin Reid, MUS, MT(ASCP); Michael W. Riben, MD; Victor E. Reuter, MD; Lisa Stephens, MBA, HTLA(ASCP)<sup>CM</sup>; Rachel L. Stewart, DO, PhD; Nicole E. Thomas, MPH, CT(ASCP)<sup>CM</sup>

The usage of WSI stimulates an increment in the quality control measures

Digital pathology is a cost-effective model with direct and parallel significant achievements



# The main advantages of using WSIs

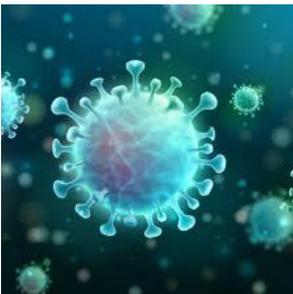
Digital pathology and COVID-19: with the COVID-19 crisis, many national and international agencies have revisited their criteria to encourage the adoption of digitalization into routine pathology

## EDITORIAL

J Pathol Inform 2020, 11:15

### The future of pathology: What can we learn from the COVID-19 pandemic?

Bethany J Williams<sup>1</sup>, Filippo Frassetto<sup>2</sup>, Matthew G Hanna<sup>3</sup>, Richard Huang<sup>4</sup>, Jochen Lennerz<sup>2</sup>, Roberto Salgado<sup>5</sup>, S Joseph Sirintrapun<sup>6</sup>, Liron Pantanowitz<sup>2</sup>, Anil Parwani<sup>7</sup>, Mark Zarella<sup>8</sup>, Darren E Treanor<sup>9</sup>



#### Sharing

Using the digital image to reduce the distance between people and maintain quality of diagnoses

- Internal and external consultation of cases
- Annotation of specific diagnostic doubts
- Validation of staining at distance and using archived images
- Pathologists and technicians work at distance

Digital pathology and the opportunity for integrating artificial intelligence (AI) into routine pathology practice

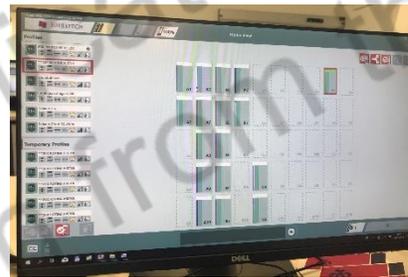
# Digital transformation (2016-2020) at IPATIMUP



Integration with LIS



Protocol optimization



QA program

Validation for primary diagnosis

Full digital



8th July

21st October

6th November

11th November

January – July 2020

July

2019

2020

Time line

Time line

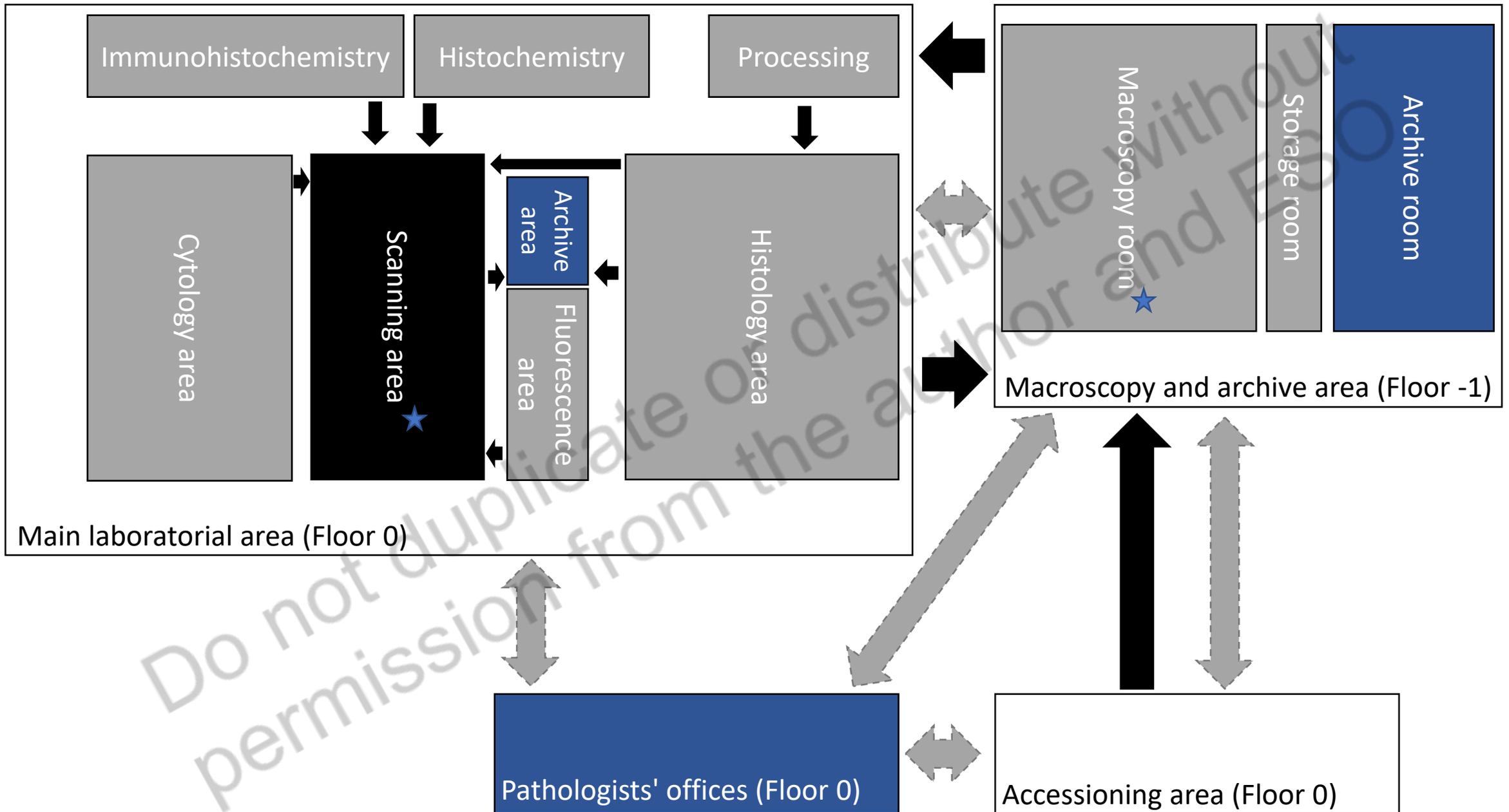


Involving the team in the process of digital transformation

Training the staff: technicians and pathologists

- Improvement /automation of the pathologist's and technician's workstations

- Equipment
- Environment
- Space management
- Workload management

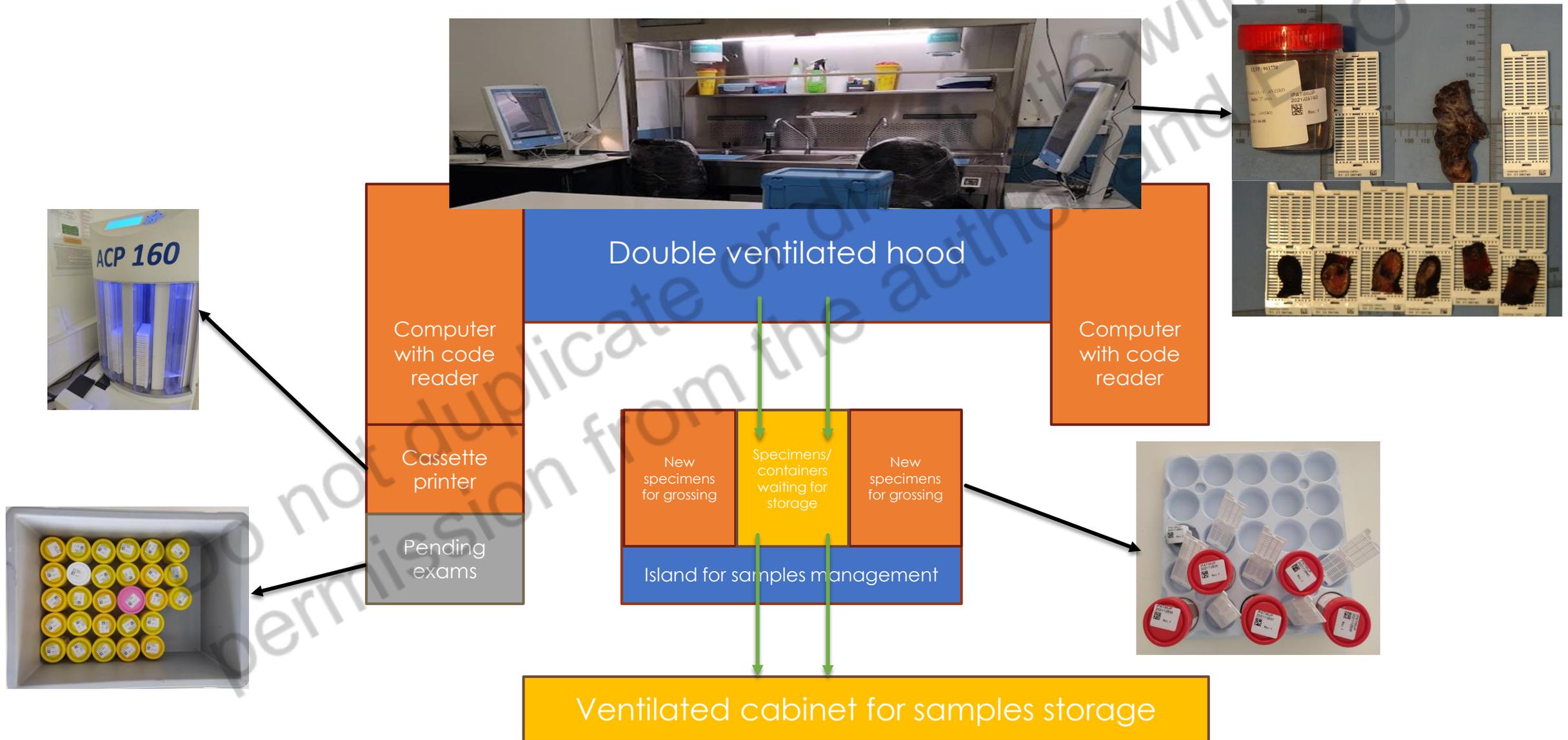


# Sparing valuable resources Space, time, people and instruments (Lean)

The tracking system



# Spare valuable resources – macroscopy room

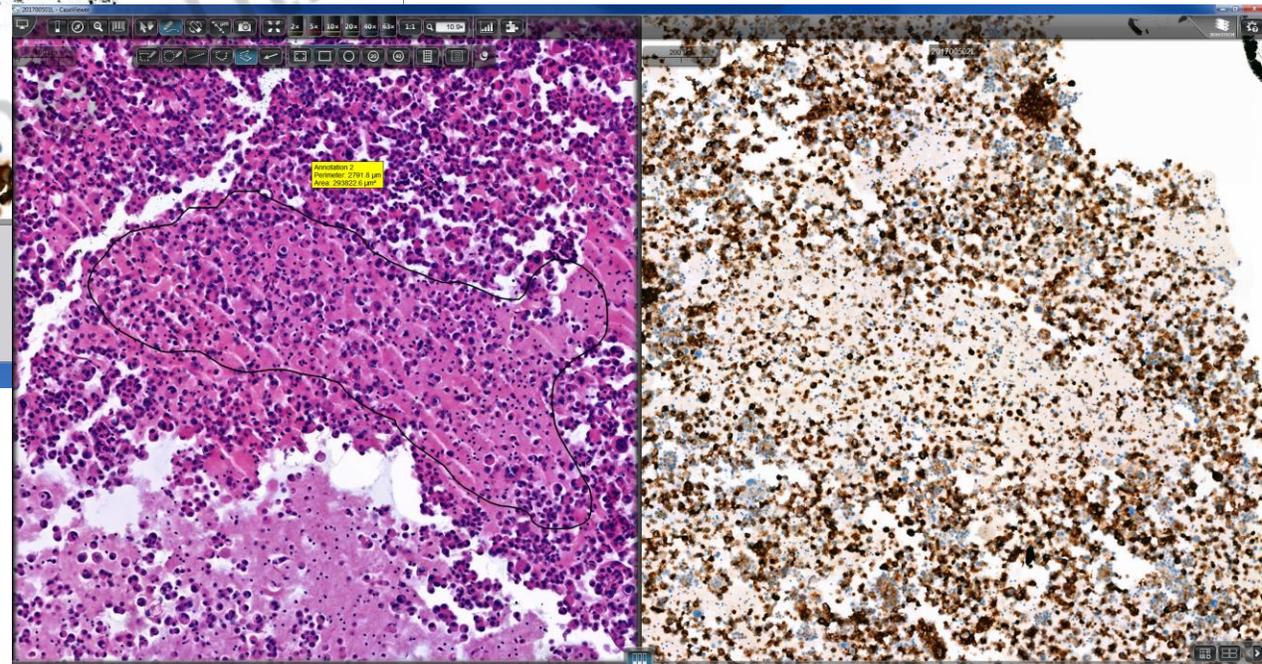
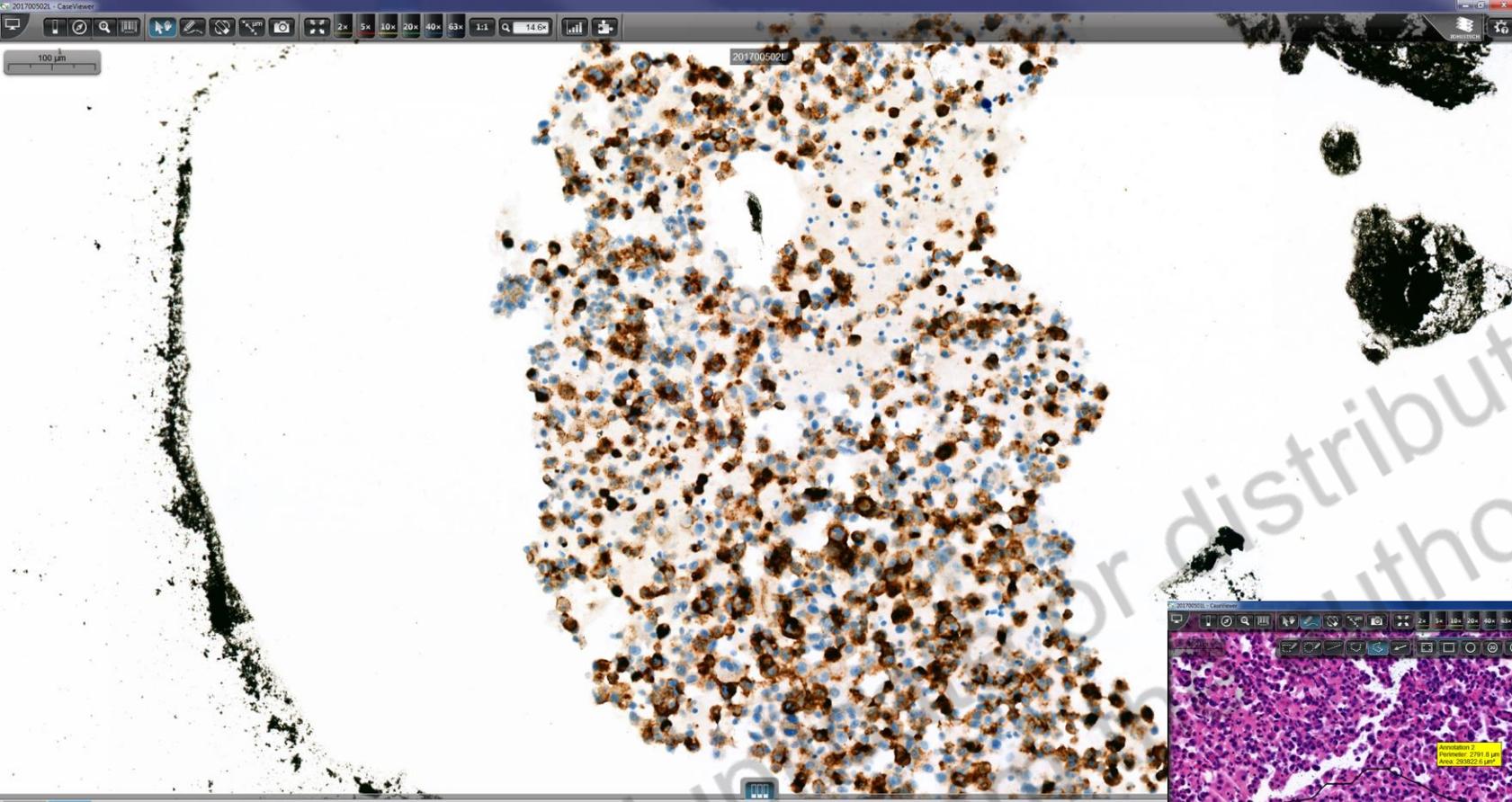


# Change attitude early in the flow - embedding



- ✓ Fragments as close as possible to each other and centered on the embedding mold;
- ✓ Always include in such a way as to create less knife resistance to avoid artifacts;
- ✓ Respect the side margins of the embedding mold;
- ✓ One by one.

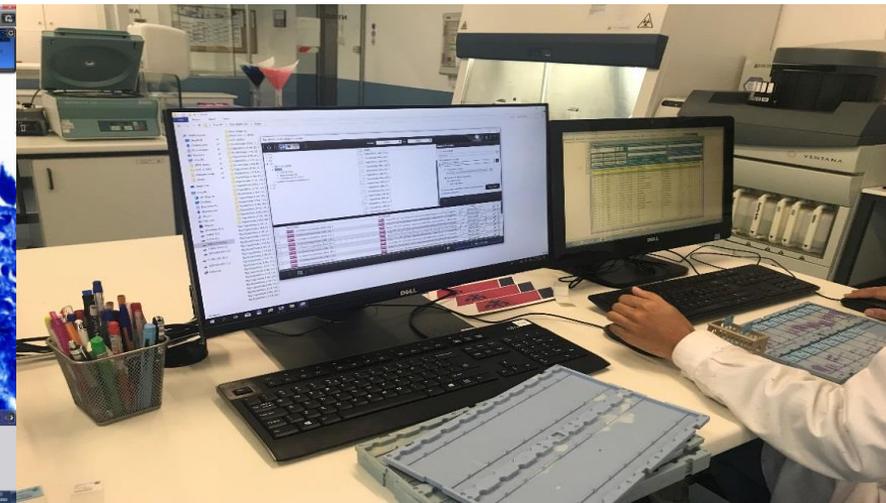
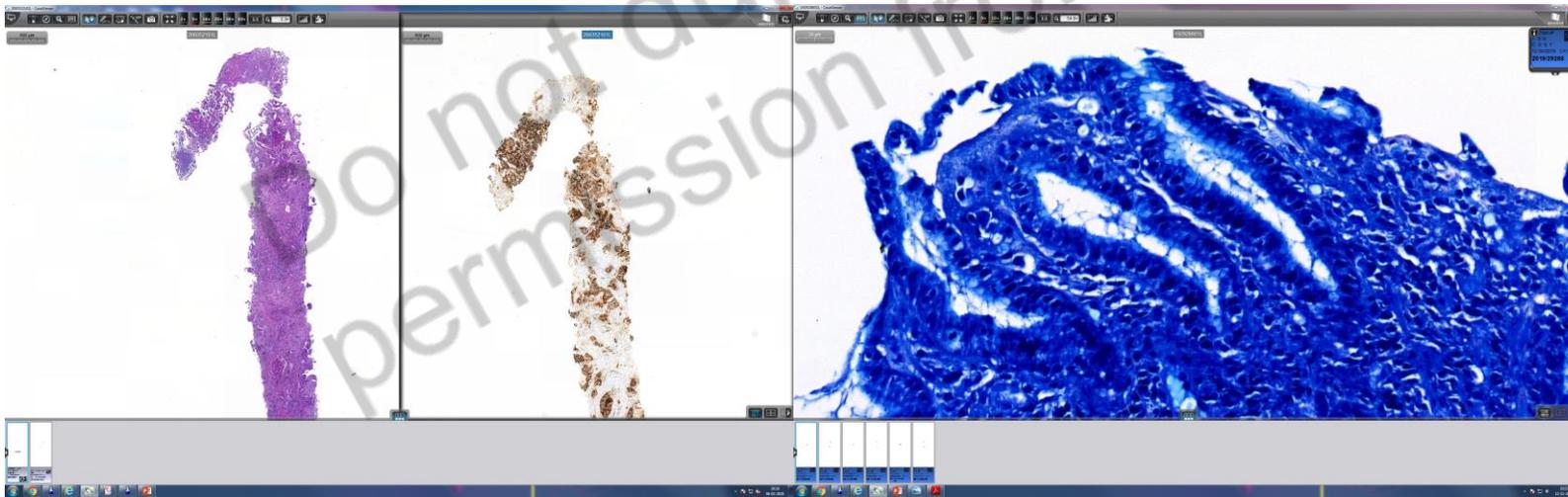




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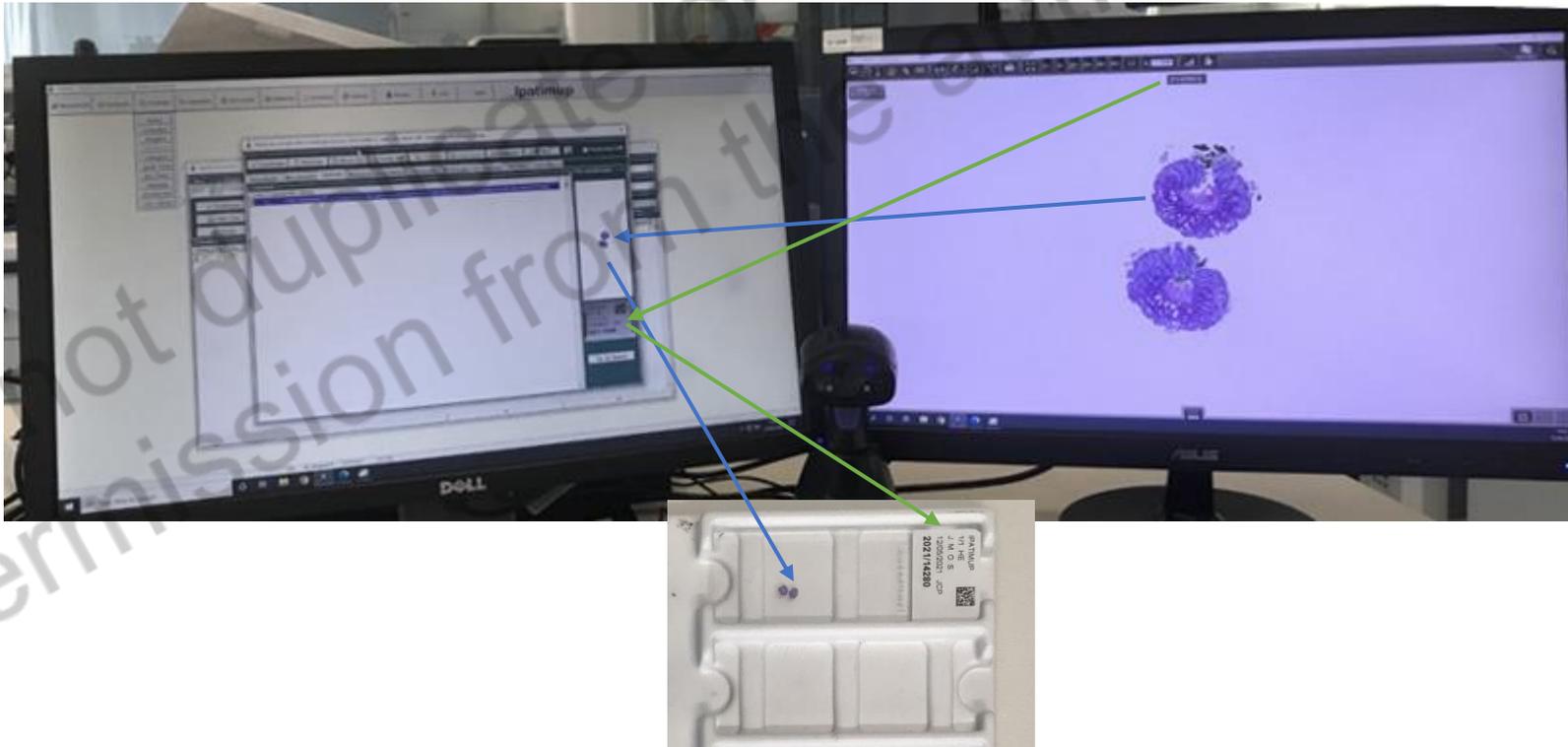
# Modifications in the lab work

- Adapting to “full charge” schedule keeping with TaT (daily scanning)
- Validated 20x rapid magnification scanning protocol followed by quality control in the screen of the LIS for all scanned slides



# Scanner performance control

- Technical verification of 100% of digital images



# 1GB network LIS centered



Intel(R) Xeon(TM) Gold 5120 @ 2.20GHz processor, 96GB of memory, a 240GB SSD disk for 64 bit OS, 960GB SSD for SWAP and a 2TB mechanical disk to local storage that gathers the images, convert them and then stores these slides in the CaseCenter server (Intel(R) Xeon(TM) E3-1270 v6 @ 3.80GHz, 24GB of RAM, 2x 240GB SSD for 64 bit OS in RAID 1, and 20TB mechanical disk, from 3DHISTECH).

Rotina do circuito: Micro histologia (Exame: 2020/31740-1) Sexo: F Idade: 29A Instituição: Hospital Cuf Porto

Confirmar Retornar Novo Circ. Cons. Ext. Exames Caso Index Consulta Sair Protocolos CAP

Requisição Macroscopia Lâminas Máscaras Diagnóstico Topografia Morfologia Inf. Internas Circuitos Fotos Macro Cabeçalho

Rev.	Lâmina	URL Lâmina
0	1	http://casecenter.i3s.up.pt/CaseCenter/index.php?ContainerType=CaseView&ContainerID=08SlideID=aa4338a61549104de1f5f66db0e0d236
0	2	http://casecenter.i3s.up.pt/CaseCenter/index.php?ContainerType=CaseView&ContainerID=08SlideID=19b739606b4141f4648e004125fe8121
0	3	http://casecenter.i3s.up.pt/CaseCenter/index.php?ContainerType=CaseView&ContainerID=08SlideID=f03e06696249f75d12d5b095fa30ca2
0	4	http://casecenter.i3s.up.pt/CaseCenter/index.php?ContainerType=CaseView&ContainerID=08SlideID=4d8bdcdd80067bb71615121e61d3819c
0	5	http://casecenter.i3s.up.pt/CaseCenter/index.php?ContainerType=CaseView&ContainerID=08SlideID=bff885fc8b6f22a08ad17e389d5da179
0	6	http://casecenter.i3s.up.pt/CaseCenter/index.php?ContainerType=CaseView&ContainerID=08SlideID=7ea985106099eac5963a15b8700eb0c4
0	7	http://casecenter.i3s.up.pt/CaseCenter/index.php?ContainerType=CaseView&ContainerID=08SlideID=254932081611f1640e3614e00b0fbc053
0	8	http://casecenter.i3s.up.pt/CaseCenter/index.php?ContainerType=CaseView&ContainerID=08SlideID=680f5d5e340af9d83548e9f1194048b
0	9	http://casecenter.i3s.up.pt/CaseCenter/index.php?ContainerType=CaseView&ContainerID=08SlideID=412aba0c413c81e8d0365611d95ad42f
0	10	http://casecenter.i3s.up.pt/CaseCenter/index.php?ContainerType=CaseView&ContainerID=08SlideID=4c3bf6070813c2500ceebab2146f8c438
0	11	http://casecenter.i3s.up.pt/CaseCenter/index.php?ContainerType=CaseView&ContainerID=08SlideID=48b09e4c57e645e43645c85701755c27

Pré-visualização

IPATIMUP  
1/11 HE  
R. B. C. A.  
18/11/2020 CAT  
2020/31740

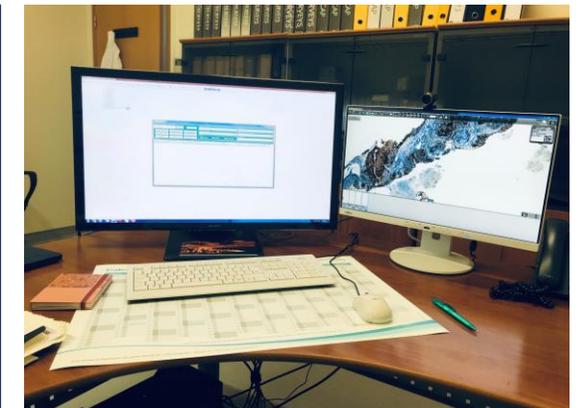
3D-Histech

Storage - 220TB storage that can scale up to 960TB (fast and slow disks, images are not erased after diagnosis)

3DHISTECH (viewer) is integrated with LIS (SISPAT)

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.



# QA program and tissue control bank

The image displays a screenshot of a medical software interface, likely used for quality assurance (QA) and tissue control. The window title is "Rotina do circuito: Micro histologia (Exame: 2019/30277-1) Sexo: M Idade: 75A Instituição: Hospital Cuf - Porto".

The interface features a top navigation bar with buttons: Confirmar, Retornar, Novo Circ., Cons. Ext., Exames, Caso Index, Consulta, Sair, and Protocolos CAP. Below this is a menu bar with tabs: Requisição, Macroscopia, Lâminas, Máscaras, Diagnóstico, Topografia, Morfologia, Inf. Internas, Circuitos, Fotos Macro, and Cabeçalho. The "Qualidade" tab is selected, showing a form with the following sections:

- Qualidade do corte
- Qualidade da coloração
- Qualidade da macroscopia
- Qualidade da digitalização no scanner

A blue arrow points to the "Qualidade da digitalização no scanner" section. To the right, a smaller window shows a digital image of a tissue slide with a red outline, and a blue arrow points to a grey bar at the bottom of this window. Below the main interface, there are several circular images of tissue slides, some showing blue-stained tissue and others showing different staining patterns.

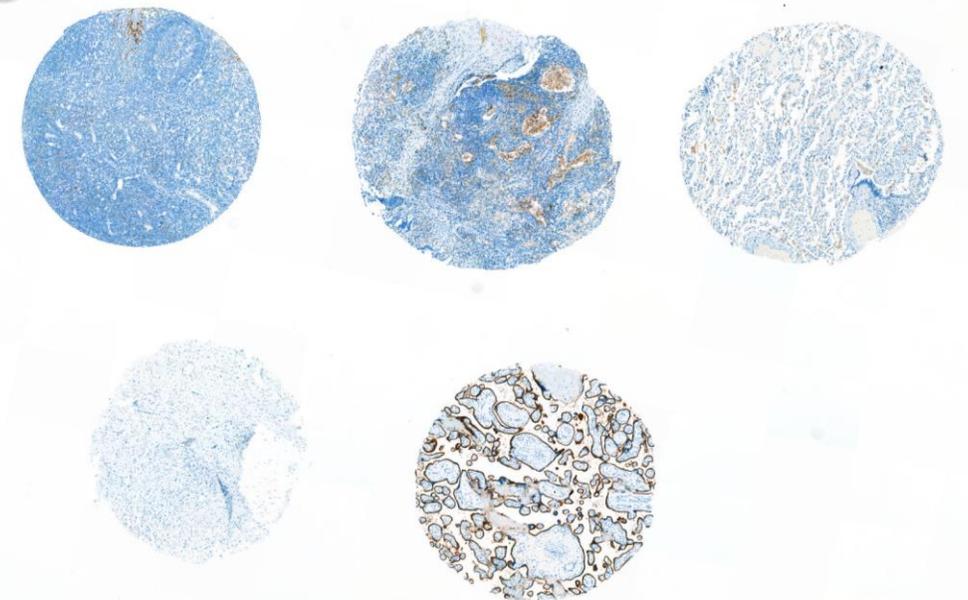
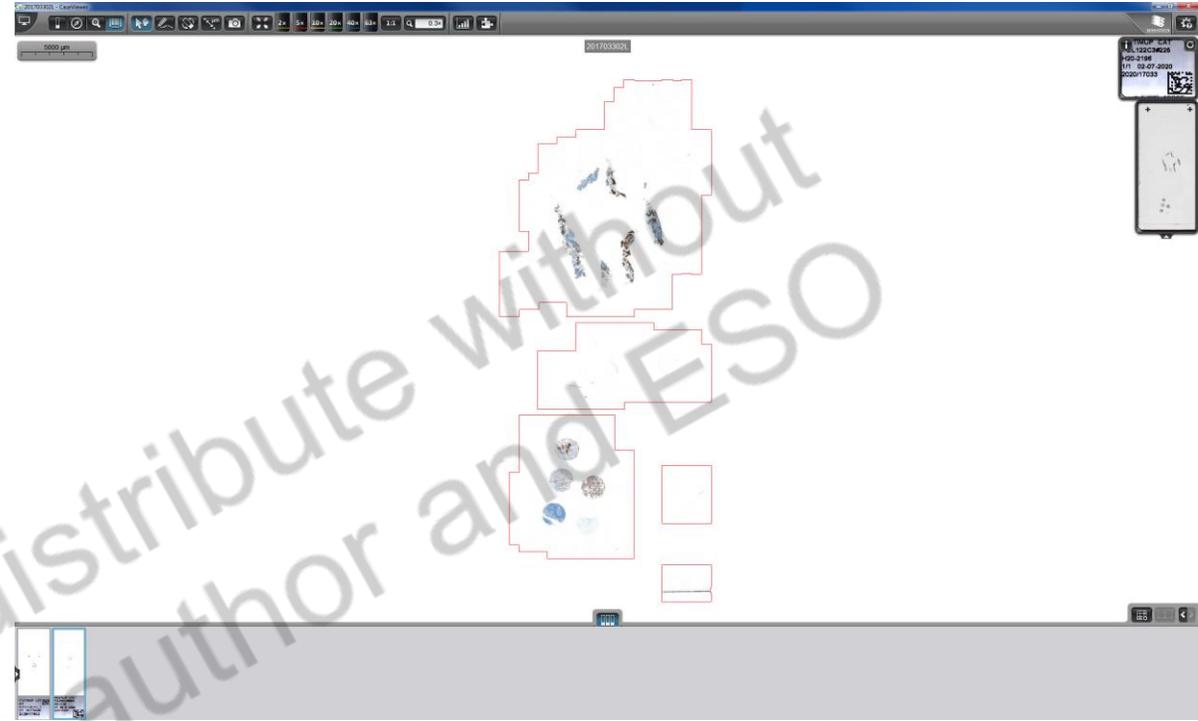
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# Standardization

*Tissue control bank*

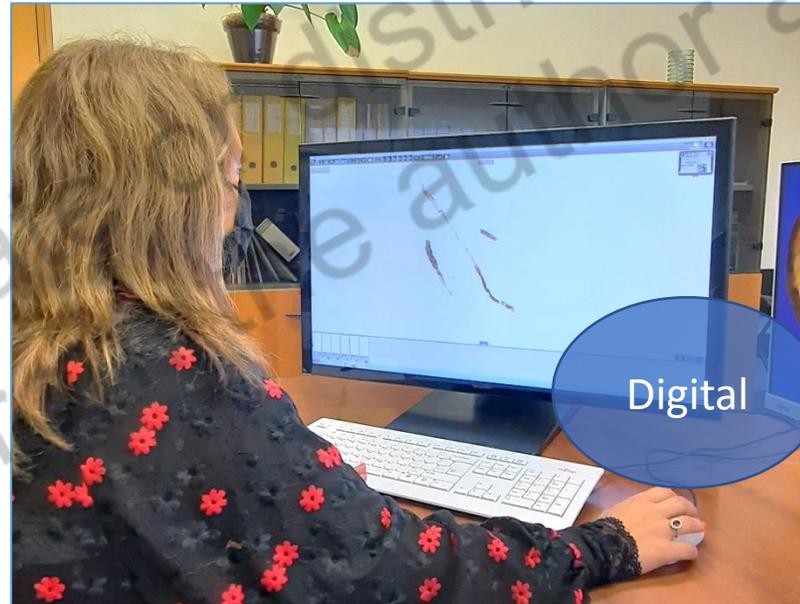
Core: Ref: Tecido:	Core: Ref: Tecido:	Core: Ref: Tecido:	Core: Ref: Tecido:	Core: Ref: Tecido:	Core: Ref: Tecido:	Core: Ref: Tecido:	Core: Ref: Tecido:	Core: Ref: Tecido:
Core: Ref: Tecido:	Core: Ref: Tecido:	Core: Ref: Tecido:	Core: Ref: Tecido:	Core: 3 Ref: 353 Tecido: Amigadala	Core: 4 Ref: 336 Tecido: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

Core: 3 Ref: 353 Tecido: Amigadala	Core: 4 Ref: 336 Tecido: Adeno Pul+	Core: 5 Ref: 347 Tecido: Adeno P-
Core: 1 Ref: 53 Tecido: Leiomioma	Core: 2 Ref: 3 Tecido: Placenta	Core: Ref: Tecido:



PD-L1 (Lung) TMA

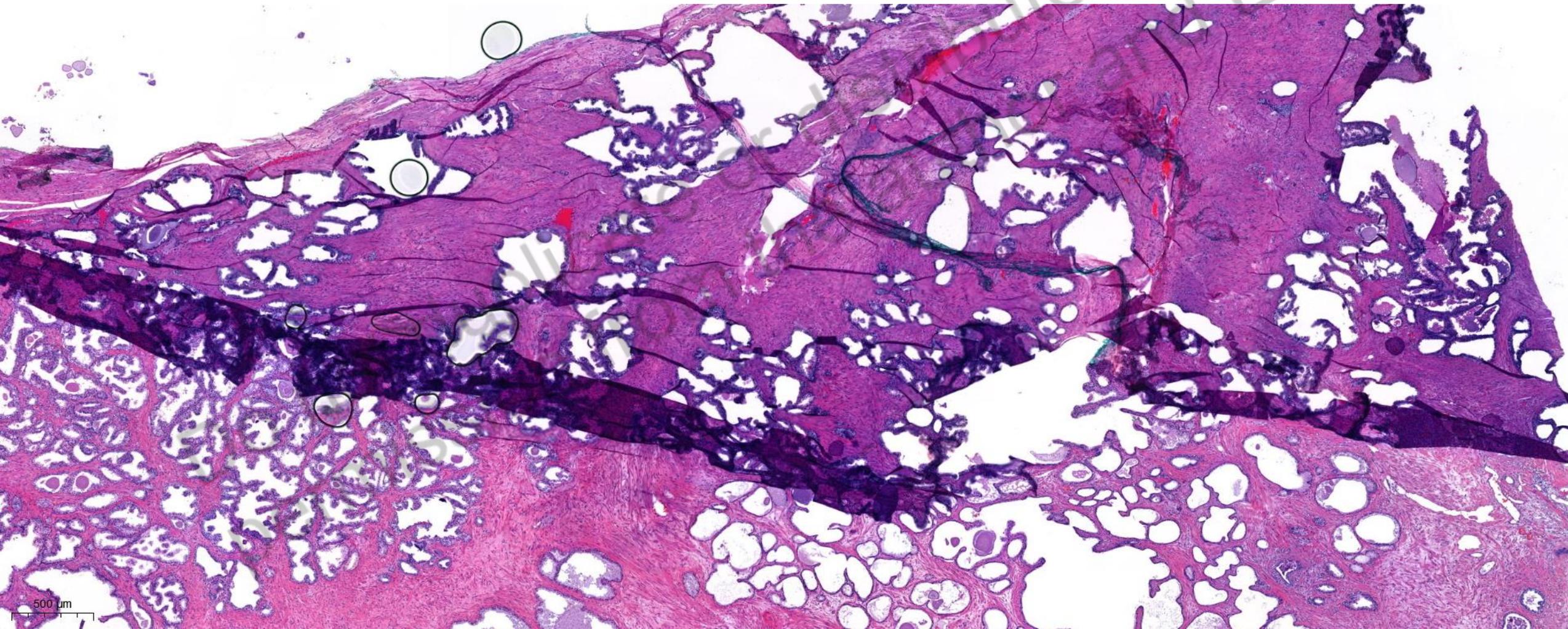
# All issues are *amplified* in the digital image



*Multilayers and transparency are lost*

- Navigation changes
- Ergonomics and environment modifications
- Two tracks' observations (training)
- Quality triage

# Artifacts



# Results

- Staff

14 pathologists

4 internal/10 external

8 using DP/6 not using DP

Cytology

Consultation cases

Telepathology model

Less than 10 cases/month

10 technicians

5 administrative

- Production

- 30 000 samples/year

- Paraffin blocks 40 000

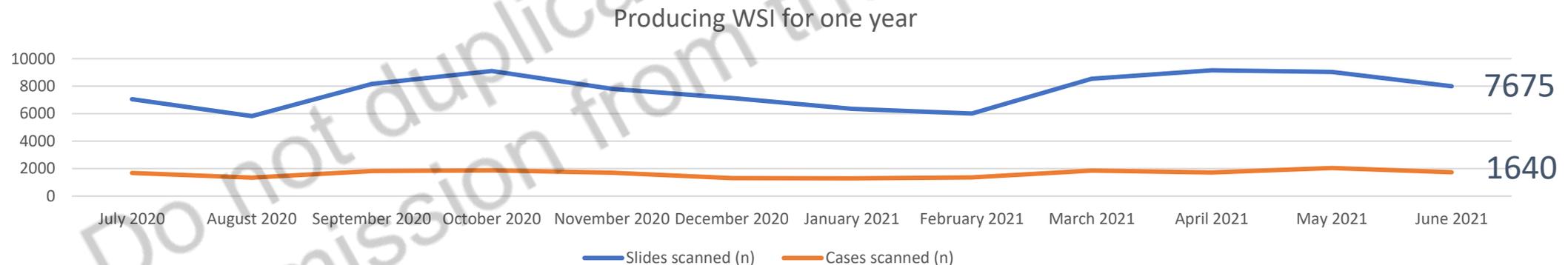
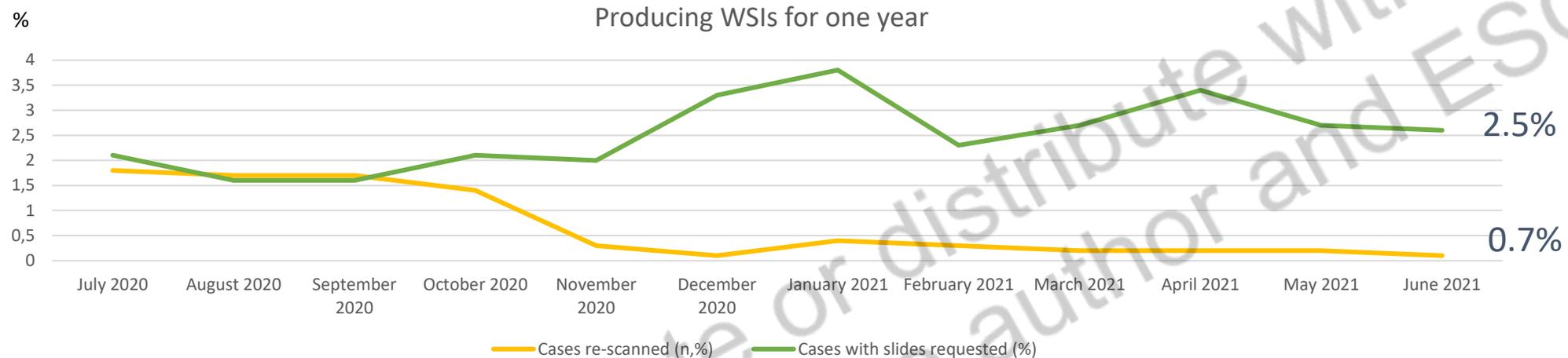
- Slides 60 000 (plus external sources)

- Histology, cytology, histochemistry (both types), immunohistochemistry, in situ hybridization (dark and bright field) & immunofluorescence

- Turn around time: 2 days

## Scanner performance control – monthly statistics

# Results



No impact in the quality of the diagnoses produced (external QA program)  
No impact in the quality of the laboratory product (internal QA program) – 98.8% good WSIs  
Turn-a-round time was kept after the digital transformation with the same amount of personnel

# Adopting the digital workflow

- Choose the scanner
- Validate WSI for clinical usage and optimize the digital navigation for diagnosis
- Establish data retention policies and a digital archive



## Validating Whole Slide Imaging Systems for Diagnostic Purposes in Pathology

Guideline Update From the College of American Pathologists in Collaboration With the American Society for Clinical Pathology and the Association for Pathology Informatics

*Andrew J. Evans, MD, PhD; Richard W. Brown, MD; Marilyn M. Bui, MD, PhD; Elizabeth A. Chlipala, BS, HTL(ASCP)QIHC; Christina Lacchetti, MHSC; Danny A. Milner Jr, MD, MSc(Epi), MBA; Liron Pantanowitz, MD; Anil V. Parvani, MD, PhD; Kearin Reid, MLIS, MT(ASCP); Michael W. Riben, MD; Victor E. Reuter, MD; Lisa Stephens, MBA, HTLA(ASCP)CM; Rachel L. Stewart, DO, PhD; Nicole E. Thomas, MPH, CT(ASCP)CM*

**GPS 3.** The validation study should closely emulate the real-world clinical environment in which the technology will be used.

**GPS 4.** The validation study should encompass the entire WSI system. It is not necessary to separately validate each individual component (eg, computer hardware, monitor, network, scanner) of the system or the individual steps of the digital imaging process.



# Adopting the digital workflow

- Evaluate the result of the transformation
- Prepare the next step – the digital transformation is just the beginning



# The acknowledgement of all data embedded in a simple tissue section stained by haematoxylin-eosin obtained by AI techniques represents a true epistemological transformation

Computed aided diagnostic tools, tools for staging or extracting other morphologically-based prognostic relevant data

Quantification

> [Am J Clin Pathol](#). 2020 Oct 29;aqaa151. doi: 10.1093/ajcp/aqaa151. Online ahead of print.

## Artificial Intelligence Improves the Accuracy in Histologic Classification of Breast Lesions

António Polónia<sup>1 2</sup>, Sofia Campelos<sup>1 2</sup>, Ana Ribeiro<sup>3</sup>, Ierece Aymore<sup>1 2</sup>, Daniel Pinto<sup>4</sup>, Magdalena Biskup-Fruzynska<sup>5</sup>, Ricardo Santana Veiga<sup>6</sup>, Rita Canas-Marques<sup>7</sup>, Guilherme Aresta<sup>8 9</sup>, Teresa Araújo<sup>8 9</sup>, Aurélio Campilho<sup>8 9</sup>, Scotty Kwok<sup>10</sup>, Paulo Aguiar<sup>2 11</sup>, Catarina Eloy<sup>1 2 12</sup>

Research opportunities for understanding the disease - identifying a causal agent of a disease or a pattern of disease

Taxonomy

Algorithms that predict molecular biomarker *status* with relevance to select therapy

Markers



### Classification and mutation prediction from non-small cell lung cancer histopathology images using deep learning

Nicolas Coudray<sup>1,2,9</sup>, Paolo Santiago Ocampo<sup>3,9</sup>, Theodore Sakellaropoulos<sup>4</sup>, Navneet Narula<sup>3</sup>, Matija Snuderl<sup>3</sup>, David Fenyo<sup>5,6</sup>, Andre L. Moreira<sup>3,7</sup>, Narges Razavian<sup>8\*</sup> and Aristotelis Tsirigos<sup>13\*</sup>

**TABLE 2 |** List of the key challenges that face the translation of computational pathology into clinical practice.

### Key challenges in diagnostic AI in pathology

Access to large well-annotated data sets  
Context switching between workflows  
Algorithms are slow to run  
Algorithms require configuration  
Properly defined protocols for training and evaluation  
Algorithms are not properly validated  
Lack of health economics

*These typically slow down access to diagnostic apps or make pathologists hesitant to adopt. It is critical to ensure that apps are embedded in digital workflows to allow seamless access to AI.*

Serag A et al. Front. Med. 2019. 6:185.

Digital pathology  
(holistic concept)

Full digital (100%)

## MODERN PATHOLOGY

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Article | [Open Access](#) | Published: 24 June 2021

### Quality control stress test for deep learning-based diagnostic model in digital pathology

Birgid Schömig-Markiefka, Alexey Pryalukhin, Wolfgang Hulla, Andrey Bychkov, Junya Fukuoka, Anant Madabhushi, Viktor Achter, Lech Nieroda, Reinhard Büttner, Alexander Quaas & Yuri Tolkach [✉](#)

*Modern Pathology* (2021) | [Cite this article](#)

1611 Accesses | 20 Altmetric | [Metrics](#)

# ESO-ESP Digital Pathology Seminar

ONLINE COURSE

## Porto digital workflow

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