Digital Pathology - moving on after implementation

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No conflict of interests to declare

Pathology challenges today

- Maintaining high quality students interested in Pathology
  - Need to review the knowledge transmission models and visibility of Pathology
  - Need to re-think workload and turnaround time

TABLE 2 ANNUAL GROWTH IN CELLULAR PATHOLOGY WORKLOAD ACROSS 10 LABORATORIES

Workload Category	Average Annual Percentage Increase 2009-10 to 2014-15
Requests	3.3%
Blocks	4.2%
Slides	3.5%

Source: Responses to 2020 Delivery quantitative request sent to laboratories interviewed as part of this project.

for information at MDT meetings and in order to meet the requirements for increasingly comprehensive, evidence-based Royal College of Pathologists datasets. This growth in complexity has been ongoing for many years – a paper from 1992 examined the content of histopathology reports over 50 years, from 1940 to 1990, finding a 337% increase in the number of words in reports and a 273% increase in the number of items of information included in them over this period.[32]

histopathology requests are linked to cancer investigations but not all of them. These data show on average an increase in histopathology requests per laboratory of 4.5% per year.

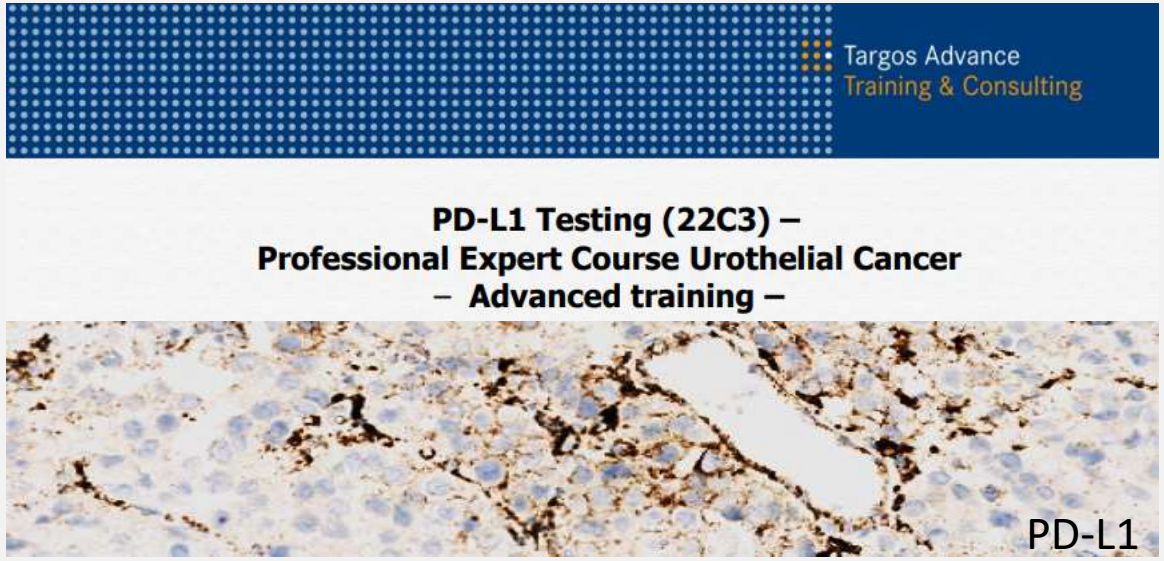
FIGURE 5 HISTOPATHOLOGY AVERAGE TOTAL REQUESTS, UK WIDE

Source: Data from Keele Benchmarking Service, issued May 2016

Cancer Research UK, "Testing times to come? An evaluation of pathology capacity across the UK" (2016).

Pathology challenges today

- Progressive (and aggressive) increment in the number of oncological driven biomarkers, either based upon immunohistochemistry, either determined by molecular pathology techniques
  - Conducing to a decreased interest in benign diseases with consequences on prevention approaches - overdiagnosis
  - Bringing an inherent industry pressure on laboratories



Pathology challenges today

- Announced end of the traditional Pathologist
  - Losing of the integrative clinical approach at the autopsy, together with the mechanistic rational of making a diagnosis and, in a radical position, the decreasing of the creativity/emotion that drives the identification of a new entity


Rembrandt, 1632

Other barriers to digital pathology implementation

- Financial constrains
- Ergonomics and workstation/“reluctance to change”
- Workflow/structure
  - Time
  - Quality assurance
  - Integration of the IT team
  - …

the diagnostic pathology journal DIAGNOSTIC PATHOLOGY

E. Alcaraz-Mateos, et al., diagnostic pathology 2016, 2:232
ISSN 2364-4893
DOI: http://dx.doi.org/10.17629/www.diagnosticpathology.eu-2016-2:232

Research

Research on Devices for Handling Whole Slide Images on Pathology Workstations. An Ergonomic Outlook

E. Alcaraz-Mateos[1], F. Caballero-Alemán[2], M. Albarracín-Ferrer[3], F. Cárceles-Moreno[3], R. Hernández-Gómez[3], S. Hernández-Kakauridze[3], L. Hernández-Sabater[3], I. Jiménez-Zafra[3], A. López-Alacid[3], C. Moreno-Salmerón[3], M. Pérez-Ramos[1], A. Nieto-Olivares[1], N. Sánchez-Campoy[4], I. Martínez González-Moro[5], E. Poblet[6].

Some good news

FDA News Release

FDA allows marketing of first whole slide imaging system for digital pathology

For Immediate Release

April 12, 2017

The Royal College of Pathologists

Pathology: the science behind the cure

Best practice recommendations for implementing digital pathology

January 2018

Authors: Simon Cross, Peter Furness, Laszlo Igali, David Snead, Darren Treanor

Pathobiology. 2016;83(2-3):57-60. doi: 10.1159/000443904. Epub 2016 Apr 21.

Trying to Understand Digital Pathology before We Move to Computational Pathology.

García-Rojo M, Ordi J.

PMID: 27100520 DOI: 10.1159/000443904

[Indexed for MEDLINE] Free full text

J Pathol Inform. 2018; 9: 6.
Published online 2018 Mar 5. doi: 10.4103/jpi.jpi_1_18

PMCID: PMC5869966
PMID: 29619278

Digital Imaging and Communications in Medicine Whole Slide Imaging Connectathon at Digital Pathology Association Pathology Visions 2017

David Clunie,[1] Dan Hosseinzadeh,[2] Mikael Wintell,[3] David De Mena,[4] Nieves Lajara,[5] Marcial Garcia-Rojo,[4] Gloria Bueno,[5] Kiran Saligrama,[6] Aaron Stearrett,[6] David Toomey,[6] Esther Abels,[7] Frank Van Apeldoorn,[7] Stephane Langevin,[2] Sean Nichols,[2] Joachim Schmid,[8] Uwe Horchner,[8] Bruce Beckwith,[9] Anil Parwani,[10] and Liron Pantanowitz[11]

Author information ► Article notes ► Copyright and License information ► Disclaimer

Abstract

Go to:

As digital pathology systems for clinical diagnostic work applications become mainstream, interoperability between these systems from different vendors becomes critical. For the first time, multiple digital pathology vendors have publicly revealed the use of the digital imaging and communications in medicine (DICOM) standard file format and network protocol to communicate between separate whole slide acquisition, storage, and viewing components. Note the use of DICOM for clinical diagnostic applications is still to be validated in the United States. The successful demonstration shows that the DICOM standard is fundamentally sound, though many lessons were learned. These lessons will be incorporated as incremental improvements in the standard, provide more detailed profiles to constrain variation for specific use cases, and offer educational material for implementers. Future Connectathon events will expand the scope to include more devices and vendors, as well as more ambitious use cases including laboratory information system integration and annotation for image analysis, as well as more geographic diversity. Users should request DICOM features in all purchases and contracts. It is anticipated that the growth of DICOM-compliant manufacturers will likely also ease DICOM for pathology becoming a recognized standard and as such the regulatory pathway for digital pathology products.

Keywords: Connectivity, digital imaging and communications in medicine, digital imaging and communications in medicine web, digital imaging and communications in medicine supplement 145, digital pathology, interoperability, picture archiving and communication system, virtual microscopy, whole slide imaging

Increment of Pathology visibility and, hopefully, attraction of young people

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After implementation- resources

- Time sparing process in routine?

Histopathology

Original Article

Evaluating the benefits of digital pathology implementation: time savings in laboratory logistics

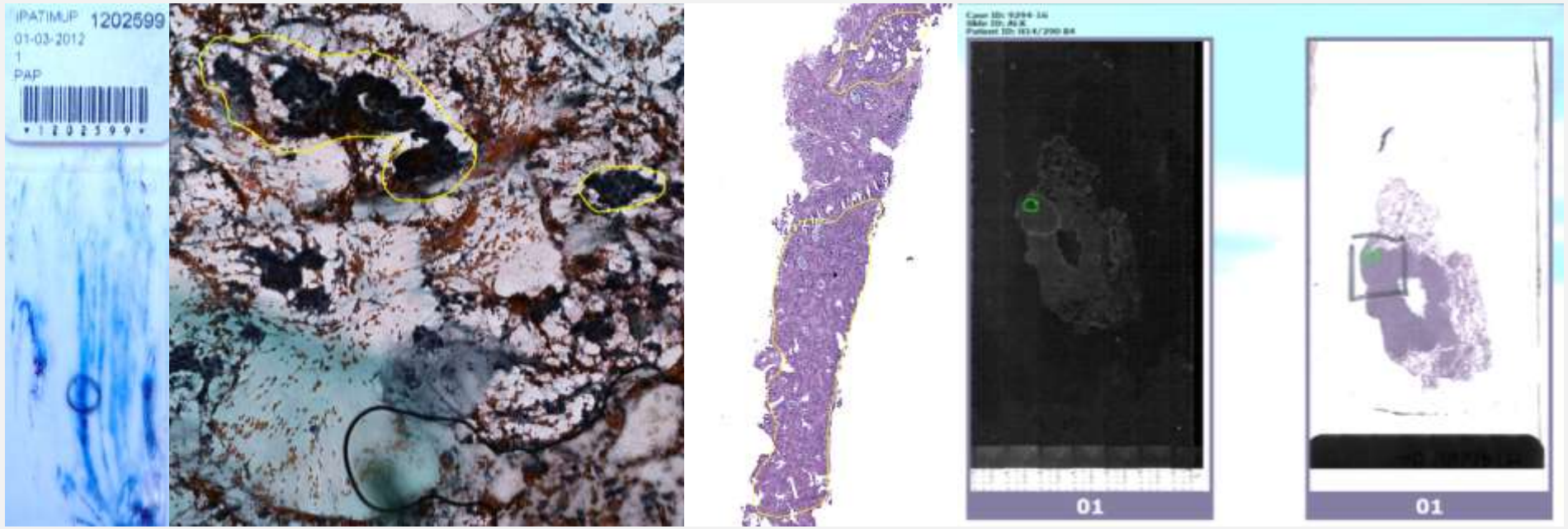
Alexi Baidoshvili, Anca Bucur, Jasper van Leeuwen, Jeroen van der Laak, Philip Kluin, Paul J van Diest

First published: 20 June 2018 | https://doi.org/10.1111/his.13691

PDF TOOLS SHARE

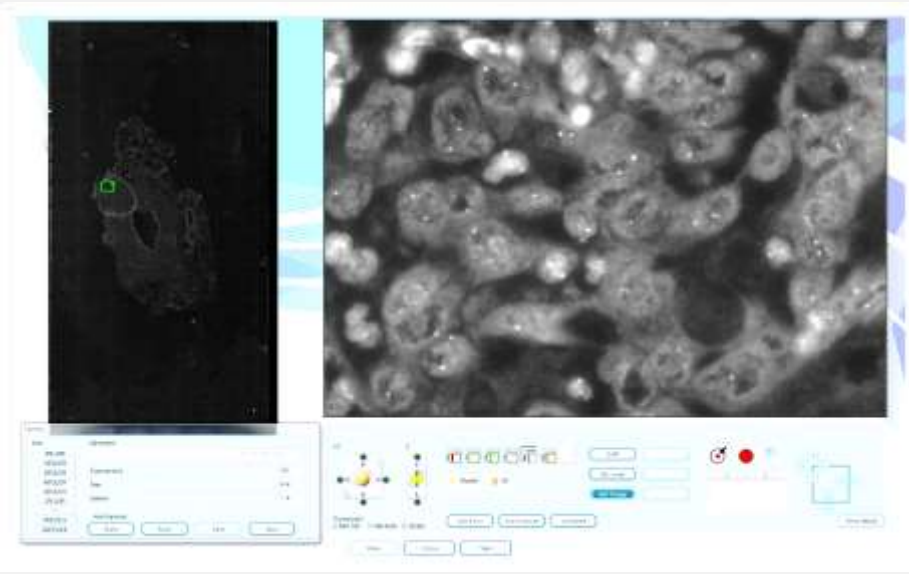
After implementation- resources

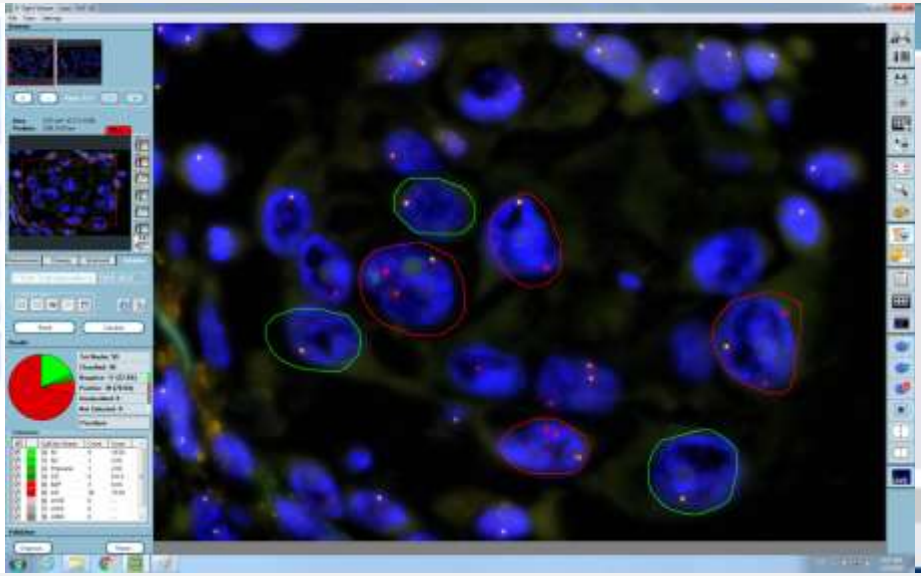
- Time sparing process: our experience with dark field examination of biomarkers
  - FISH semiautomatic image analyses for determination of ALK and ROS1 rearrangement *status* in lung cancer specimens



After implementation- resources

- Gain of more than half of the time in comparison with the use of a regular fluorescent microscope
- Increase in the number of positive cases (less false negatives) – 7% of ALK rearrangements (compatible QA results)
- Easy to maintaining archived documentation of the diagnosis





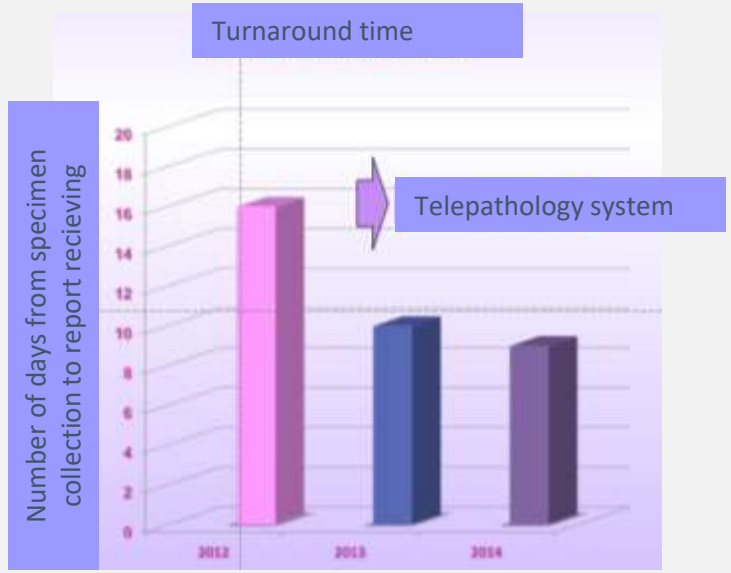
After implementation- resources

- People sparing process: our experience with telepathology system (2013-2018)

Hospital Cova da Beira at Covilhã, at 250 Km from Porto, serves about 100 000 habitants and has no pathologists. Is equipped with an up to date pathology laboratory and has specialized technical staff.

Overall benefits of telepathology in this model

- Samples are always received in very **good conditions**
- Turnaround **time** is reduced
- Strict quality control
- Up to date formation of **staff**
- Continuous improvement of the model
- Support in the setting of unavailable **specialized techniques**
- Lower **costs** at long term experience



After implementation- resources

- Macroscopy and microscopy with adequate validation and quality control

Macroscopy (classic *vs* telepathology model)

Less than 0,1% of the received specimens are evaluated at Ipatimup every year

Microscopy (classic *vs* telepathology model)

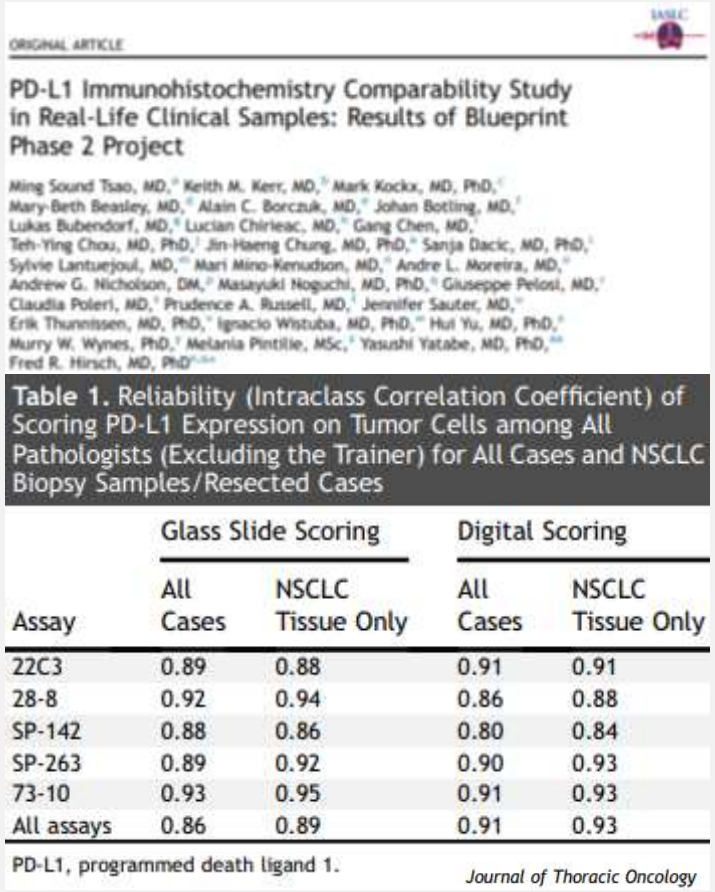
98.5% of the morphological analyses (H&E slides) had a concordant diagnosis

86.4% of the non enzymatic histochemical slides had concordant appreciation

96.6% of the immunohistochemical slides had concordant appreciation

After/during implementation- communication and opportunities

- New and old participants in the process
  - IT team – the pathologist *deep* language
  - Industry
  - Multidisciplinary teams for patient's management
  - Researchers (basics or clinical trials)
  - Residents/students – can we learn **with** the *machine*?



ORIGINAL ARTICLE

PD-L1 Immunohistochemistry Comparability Study in Real-Life Clinical Samples: Results of Blueprint Phase 2 Project

Ming Sound Tsao, MD,[a] Keith M. Kerr, MD,[b] Mark Kockx, MD, PhD,[c] Mary-Beth Beasley, MD,[d] Alain C. Borczuk, MD,[e] Johan Botling, MD,[f] Lukas Bubendorf, MD,[g] Lucian Chirieac, MD,[h] Gang Chen, MD,[i] Teh-Ying Chou, MD, PhD,[j] Jin-Haeng Chung, MD, PhD,[k] Sanja Dacic, MD, PhD,[l] Sylvie Lantuejoul, MD,[m] Mari Mino-Kenudson, MD,[n] Andre L. Moreira, MD,[o] Andrew G. Nicholson, DM,[p] Masayuki Noguchi, MD, PhD,[q] Giuseppe Pelosi, MD,[r] Claudia Poleri, MD,[s] Prudence A. Russell, MD,[t] Jennifer Sauter, MD,[u] Erik Thunnissen, MD, PhD,[v] Ignacio Wistuba, MD, PhD,[w] Hui Yu, MD, PhD,[x] Murry W. Wynes, PhD,[y] Melania Pintilie, MSc,[z] Yasushi Yatabe, MD, PhD,[aa] Fred R. Hirsch, MD, PhD[ab,ac]

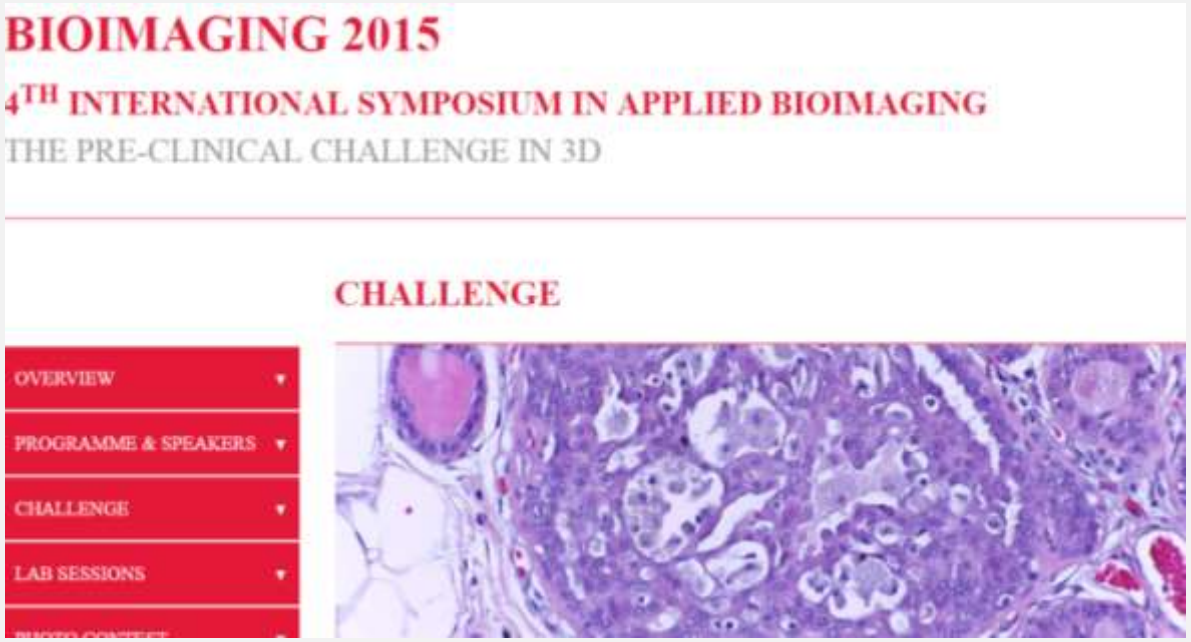
Table 1. Reliability (Intraclass Correlation Coefficient) of Scoring PD-L1 Expression on Tumor Cells among All Pathologists (Excluding the Trainer) for All Cases and NSCLC Biopsy Samples/Resected Cases

	Glass Slide Scoring		Digital Scoring	
Assay	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.

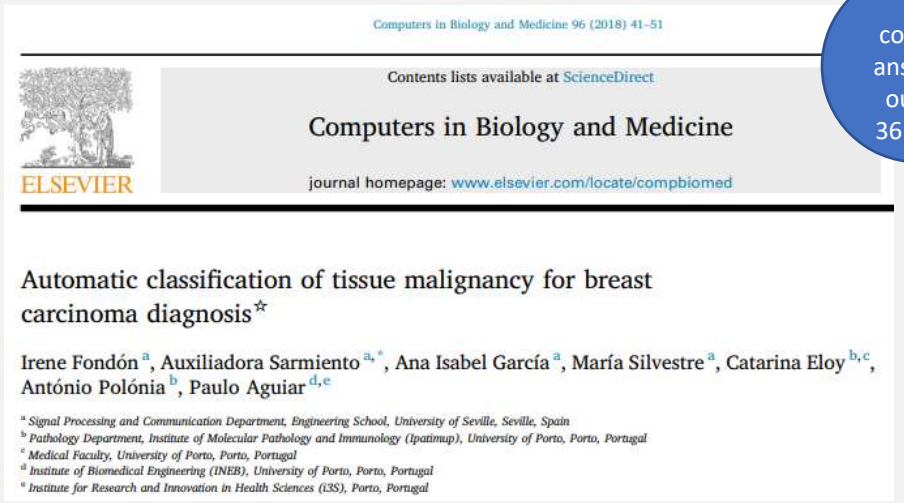
Journal of Thoracic Oncology

After implementation- new tools



- Automatic classification of tumor malignancy on breast histological pictures of hematoxylin & eosin stained slides
  - Aim: CAD in breast specimens
  - 4x30 training + 36 (20+16) test= 156 pictures
  - Distinction between 4 diagnostic categories: normal, benign, *in situ* lesion and invasive carcinoma
  - 13 registered international teams

After implementation- new tools



Computers in Biology and Medicine 96 (2018) 41–51

Contents lists available at ScienceDirect

Computers in Biology and Medicine

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

ELSEVIER

Automatic classification of tissue malignancy for breast carcinoma diagnosis☆

Irene Fondón [a], Auxiliadora Sarmiento [a,*], Ana Isabel García [a], María Silvestre [a], Catarina Eloy [b,c], António Polónia [b], Paulo Aguiar [d,e]

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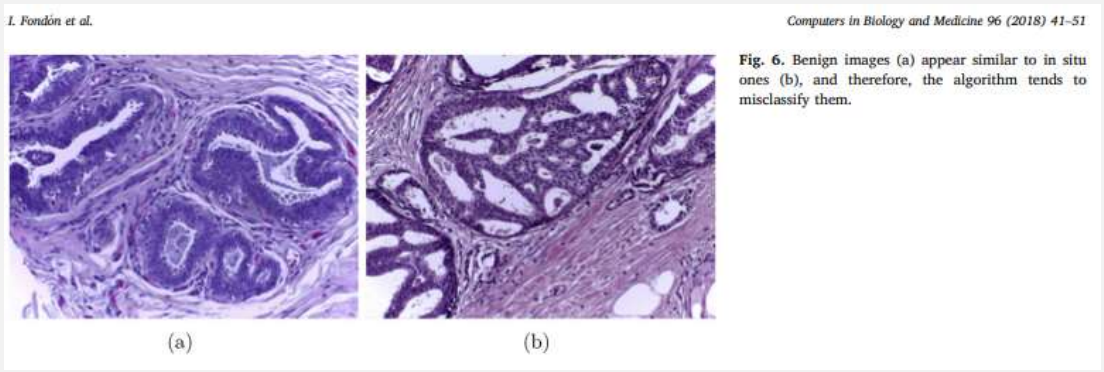
22 correct answers out of 36 tests

- ML based on features descriptors – Support Vector Machine classifier
- Color normalization
- Accuracy for differential diagnosis of 75% - 61%

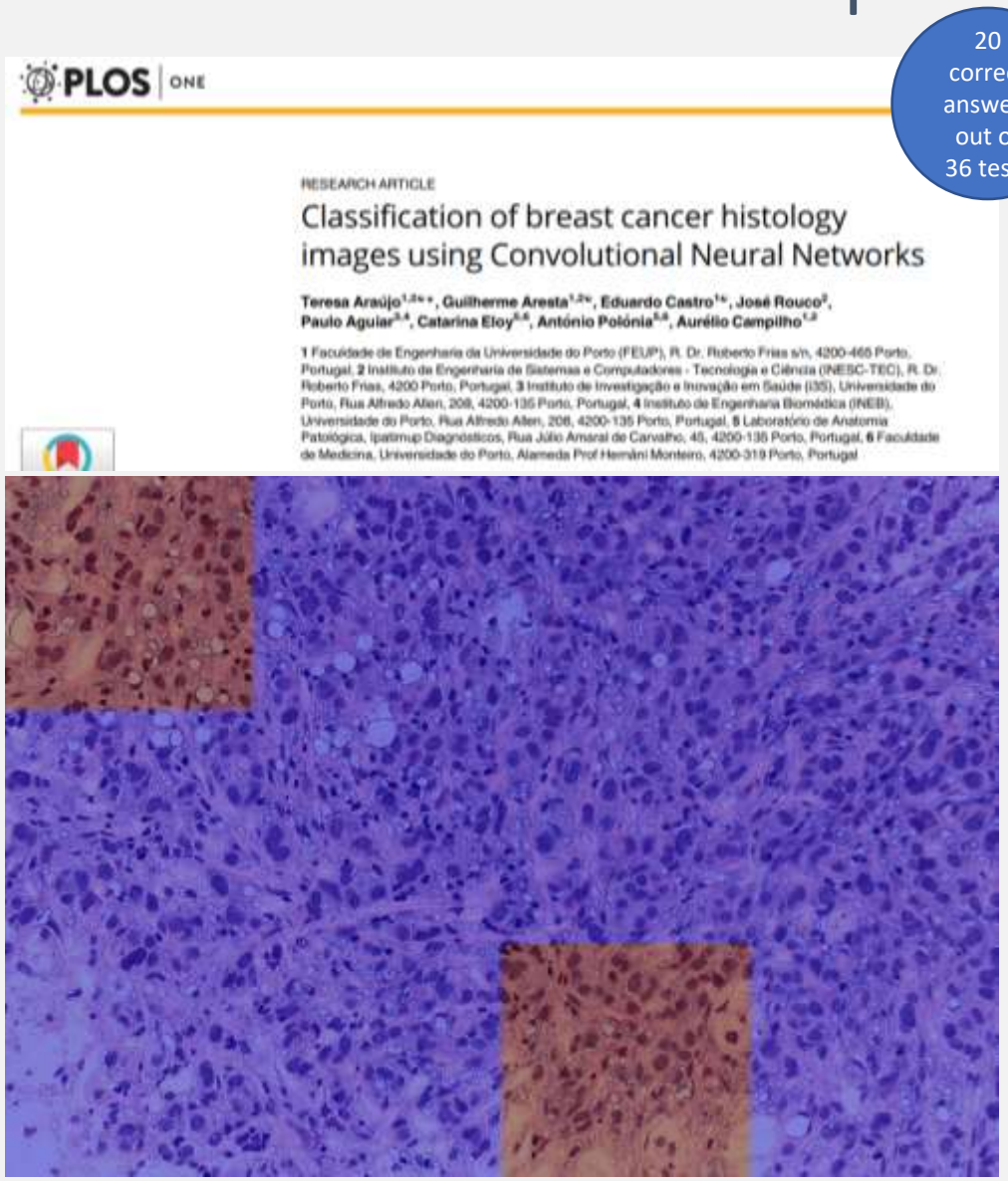


(a) (b)

Fig. 6. Benign images (a) appear similar to in situ ones (b), and therefore, the algorithm tends to misclassify them.

Diagnostic category	Sensitivity (%)	Specificity (%)
Normal	77.8	92.6
Benign	44.4	85.2
In situ lesion	44.4	81.5
Invasive carcinoma	77.8	**92.6**

After implementation- new tools



20 correct answers out of 36 tests

- Convolutional Neuronal Networks model *plus* SVM classifier
- Color normalization
- Accuracy for differential diagnosis of 70% - 56%
- Accuracy for differential diagnosis of 78% - 83% after extended dataset (249 images)

Diagnostic category	Sensitivity (%)	Specificity (%)
Normal	55.6	**96.3**
Benign	55.6	70.4
In situ lesion	55.6	92.6
Invasive carcinoma	55.6	81.5

After implementation- resources

ICIAR — International Conference on Image Analysis and Recognition

AIMI Association for Image and Machine Intelligence

ICIAR 2018
ICIAR 2017
ICIAR 2016
ICIAR 2015
ICIAR 2014
ICIAR 2013
ICIAR 2012
ICIAR 2011

About ICIAR

ICIAR – International Conference on Image Analysis and Recognition aims to bring together researchers in the fields of

- Image Processing
- Image Analysis
- Pattern Recognition

The conference provides a forum for the researchers to present and discuss recent advances in theory, methodologies and applications in the above fields. The scientific program includes invited talks by well expert speakers, panel discussion on current topics and fully refereed contributions. Special sessions are also organized for addressing promising applications in various fields.

BACH: Grand Challenge on Breast Cancer Histology Images

Guilherme Aresta[a,b,*], Teresa Araújo[a,b,*], Scotty Kwok[c], Sai Saketh Chennamsetty[d], Mohammed Safwan[e], Varghese Alex[f], Bahram Marami[g], Marcel Prastawa[g], Monica Chan[g], Michael Donovan[g], Gerardo Fernandez[g], Jack Zeineh[g], Matthias Kohl[h], Christoph Walz[i], Florian Ludwig[h], Stefan Braunewell[h], Maximilian Baust[h], Quoc Dang Vu[j], Minh Nguyen Nhat To[j], Eal Kim[j], Jin Tae Kwak[j], Sameh Galal[k], Veronica Sanchez-Freire[k], Nadia Brancati[l], Maria Frucci[l], Daniel Riccio[l,m], Yaqi Wang[n], Lingling Sun[n,o], Kaiqiang Ma[n], Jiannan Fang[n], Ismael Kone[p], Lahsen Boulmane[p], Aurélio Campilho[a,b], Catarina Eloy[q,r,s], António Polónia[q,r,s], Paulo Aguiar[s,t]

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[f]Chennai, India
[g]The Center for Computational and Systems Pathology, Dpt. of Pathology, Icahn School of Medicine at Mount Sinai and The Mount Sinai Hospital, New York, USA
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[p]2MIA Research Group, LEM2A Lab, Faculté des Sciences, Université Moulay Ismail, Meknes, Morocco
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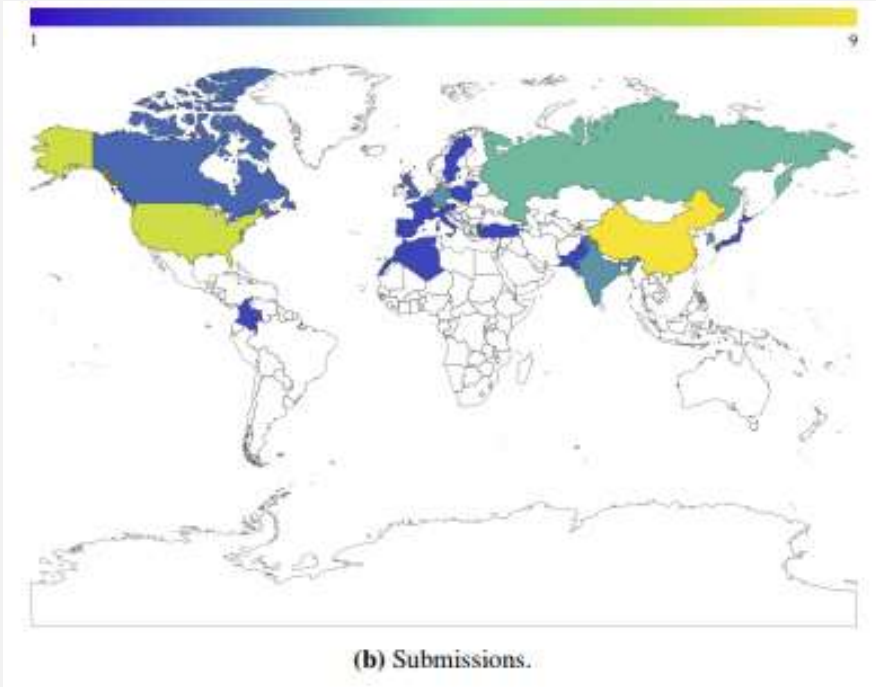
- ICIAR 2018 – BACH (grand challenge on BreAst Cancer Histology images)
  - 64 submissions



(b) Submissions.

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After implementation- resources

- ICIAR 2018 – BACH (grand challenge on BreAst Cancer Histology images)

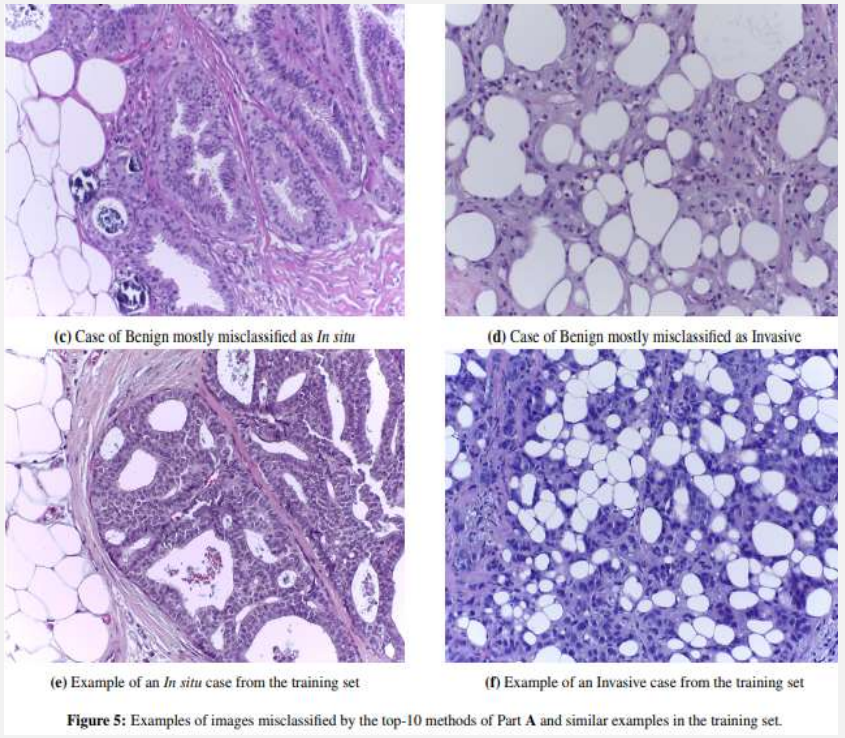
  - Dataset – H&E pictures (400+100) and WSIs (30+10)
  - Training set with 10 annotated WSIs and 20 non-annotated WSIs; test with 10 annotated WSIs
  - Best performance for CNNs models without color normalization
  - Accuracy for differential diagnosis of 87%

Table 4: Class-wise sensitivity and specificity of Part **A** approaches for the classes in study. Benchmarking results via fine-tuning are also shown. Acc - accuracy Se - sensitivity; Sp - specificity.

		Normal		Benign		*In situ*		Invasive	
Team	**Acc**	Se.	Sp.	Se.	Sp.	Se.	Sp.	Se.	Sp.
216 [20]	0.87	0.96	0.88	0.8	0.96	0.84	1.0	0.88	0.99
248 [21]	0.87	0.96	0.93	0.72	0.96	0.88	0.97	0.92	0.96

Table 7: Class-wise sensitivity and specificity of Part **B** approaches for the classes in study. Se - sensitivity; Sp - specificity; Score: Eq. 1.

		Benign		*In situ*		Invasive	
Team	**Score**	Se.	Sp.	Se.	Sp.	Se.	Sp.
248 [21]	0.69	0.36	0.7	0.03	0.59	0.4	0.96
16 [23]	0.55	0.09	0.99	0.05	0.95	0.45	0.92



(c) Case of Benign mostly misclassified as *In situ*

(d) Case of Benign mostly misclassified as Invasive

(e) Example of an *In situ* case from the training set

(f) Example of an Invasive case from the training set

Figure 5: Examples of images misclassified by the top-10 methods of Part **A** and similar examples in the training set.

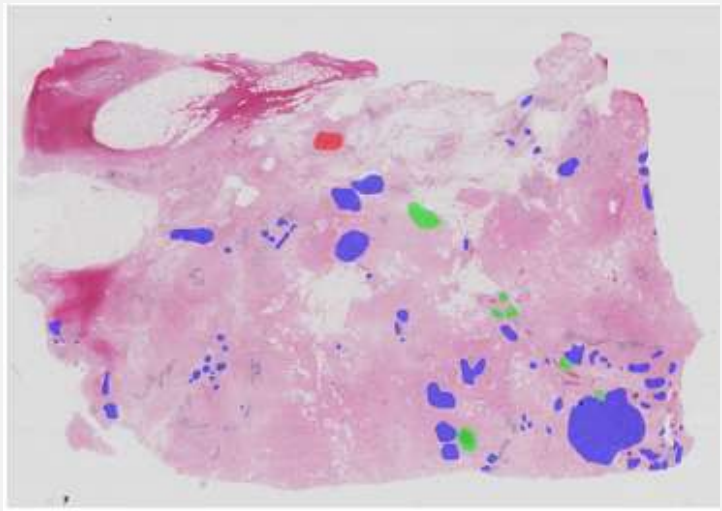


Figure 3: Example of a pixel-wise annotated whole-slide image from the training set . ■ benign; ■ *in situ*; ■ invasive.

It is **not** the time for futurology!
It is time for clinical validation!


V Curso de Patología Digital
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Oporto, Portugal
26 a 28 de octubre de 2016
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http://wwww.conganat.org/

16th European Congress of Digital Pathology

The Augmented Pathologist: empowering for a better patient care

Porto, Portugal
June, 2020

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Catarina Eloy, MD, PhD

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