University Hospitals Coventry and Warwickshire NHS Trust

# Digital pathology – disease processes by pixel analysis

Professor David Snead

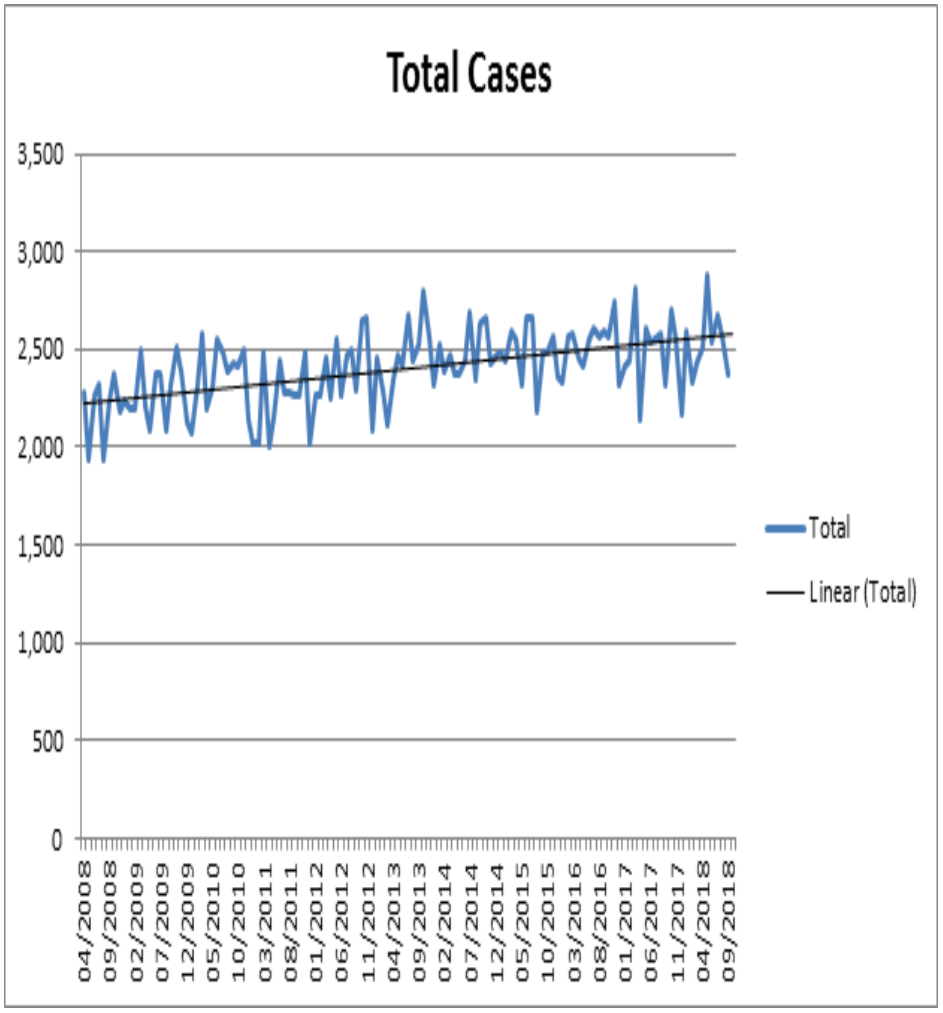
University Hospitals of Coventry and Warwickshire NHS Trust

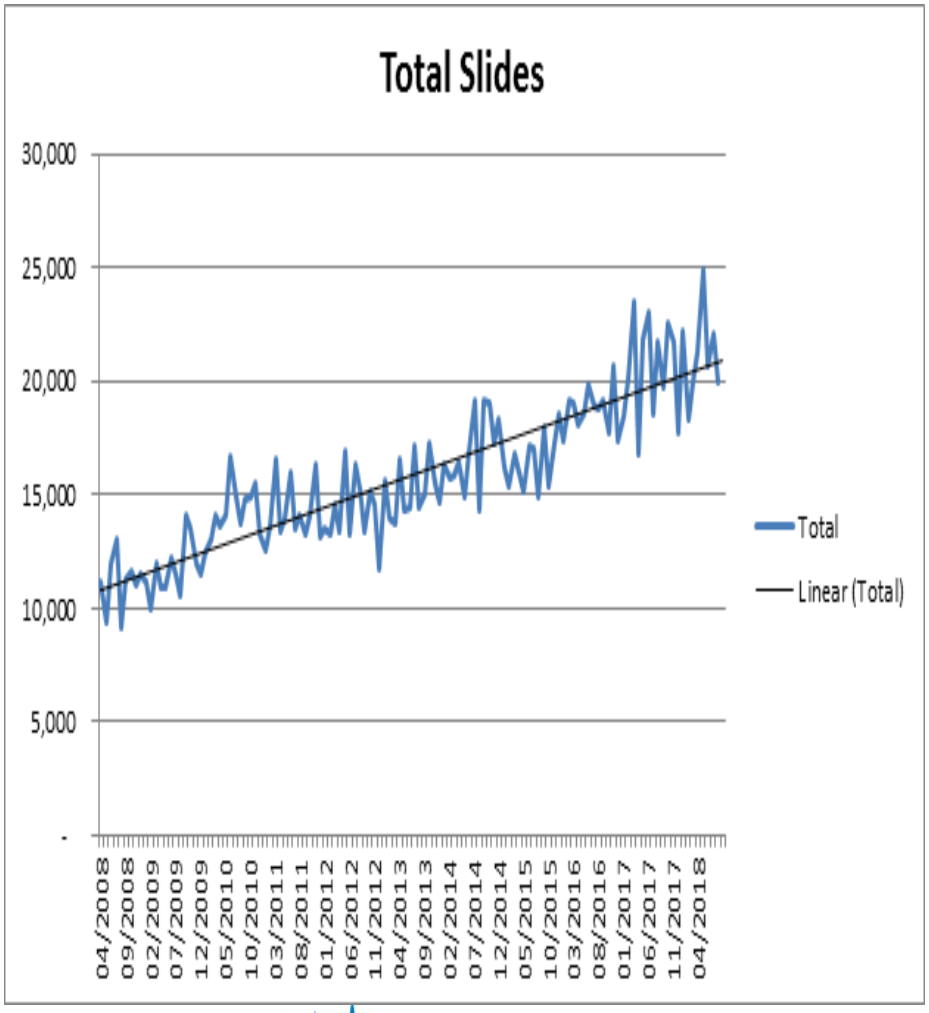
University of Warwick

# Disclaimer

- Philips Computational Pathology Board

# Pathology workload 2008-2018



Laboratory Number: H18-27654

CLINICAL DETAILS:
URGENT 31/62
A) Exc BCC left post auricular area marker 12 o'clock.
B) Wide exc melanoma in-situ left arm, marker 12 o'clock

SPECIMEN TYPE:
A) SKIN EXCISION left post auricular

B) SKIN EXCISION left arm

MACROSCOPY:
A) . SKIN EXCISION left post auricular
- Disc or skin measuring 25 x 22 x 4mm. Surface bears a pale lesion measuring 17 x 17mm. S = 12, 3 = B, 9 = G, sectioned 12-6. All of lesion processed.

B) . SKIN EXCISION left arm
- Ellipse of skin measuring 50 x 15 x 13mm. Surface bears a linear scar measuring 32mm in length. S = 12, 3 = B, 9 = G, sectioned 12-6. Representative sections taken scar submitted. Cut surface shows a focus of haemorrhagic measuring 5mm across. No other lesion seen.

MICROSCOPY:
a) Basal cell carcinoma
Low risk component: nodular

High risk component: none
Maximum diameter 9mm.
Thickness 1.2mm
Extradermal invasion: no.
Perineural invasion: no.
Lymphovascular invasion: no.

Radial margin 4mm.
Deep margin 1.2mm.

Stage T1N0 pT1
High risk case for MDT -no.

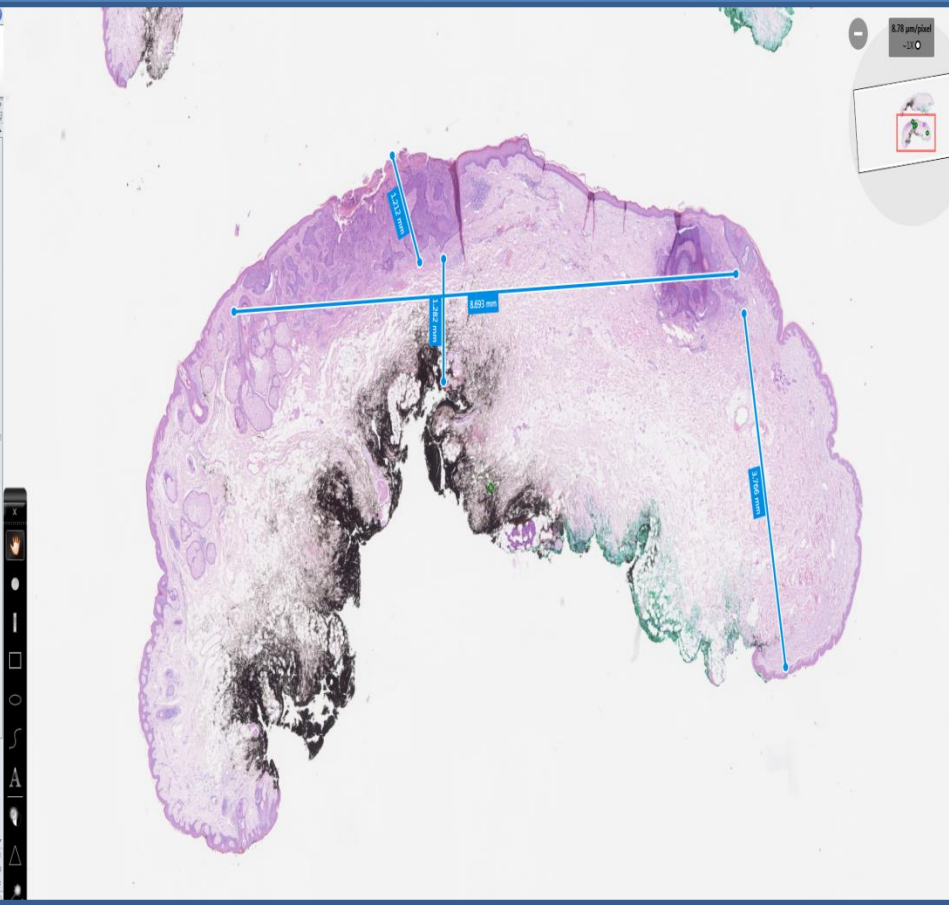
b) Skin containing a healing scar tissue. There is no residual melanoma. Excision appears complete.

DIAGNOSIS:
Basal cell carcinoma

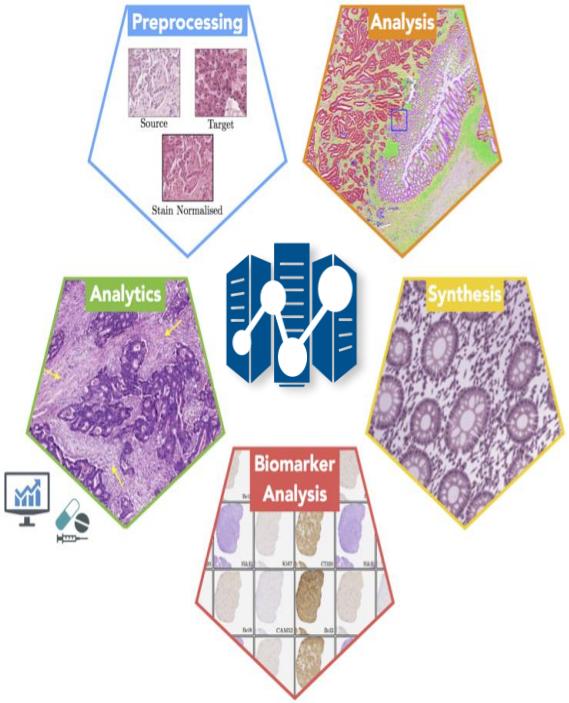
Reporting Pathologist:

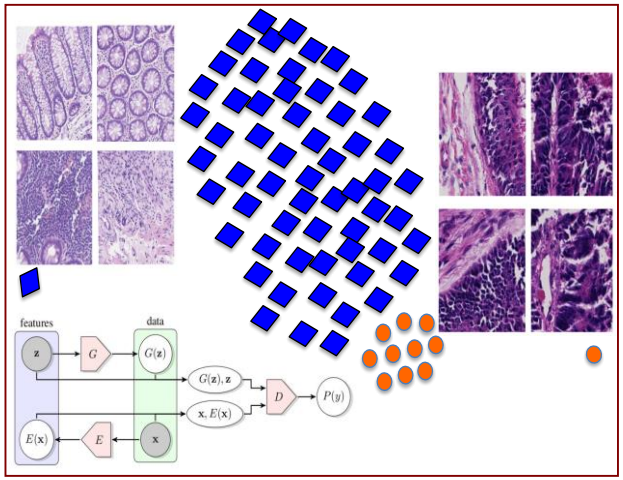
Authorising Pathologist:

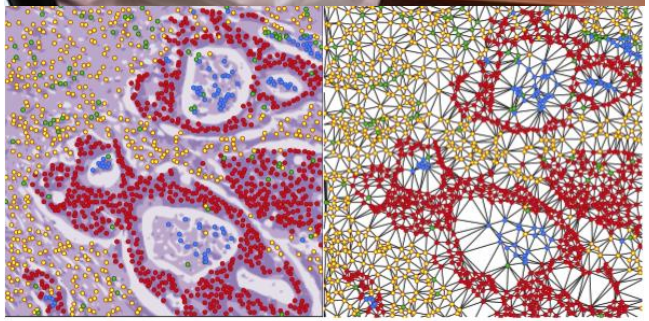
Date of Report:

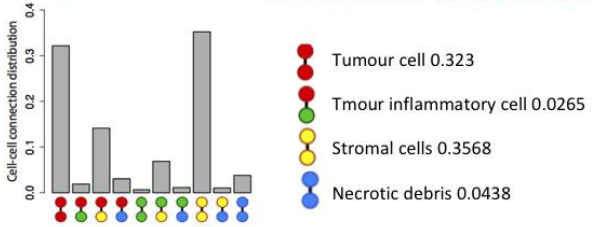


# Pathology Image Analytics



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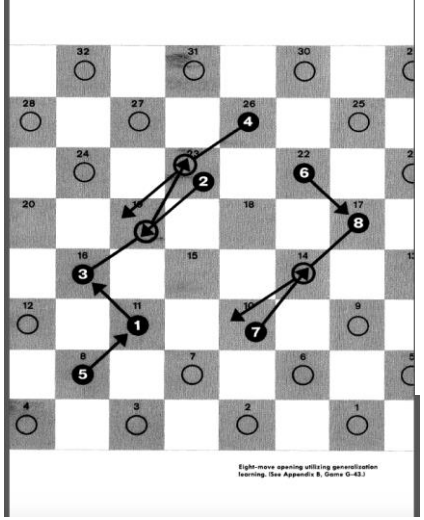
# Scope for AI in cellular pathology

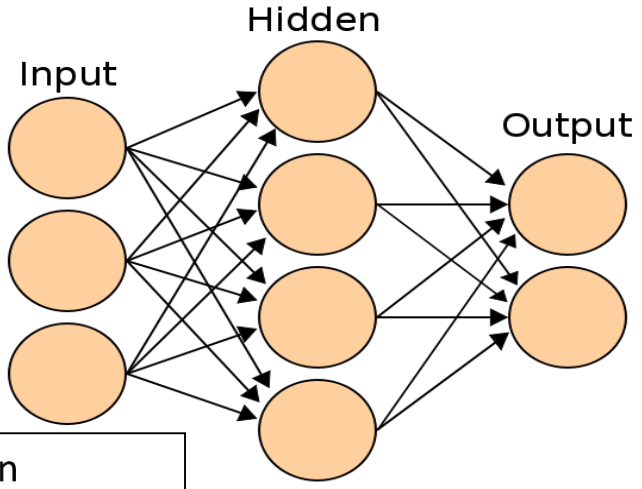
- Automation
- Biomarker assessment
- Cancer detection
- Cancer grading
- Prognostic and predictive tools
- Research



A. L. Samuel

# Some Studies in Machine Learning Using the Game of Checkers

IBM JOURNAL • JULY 1959




Perceptron neural network 1958
F Rossenblatt

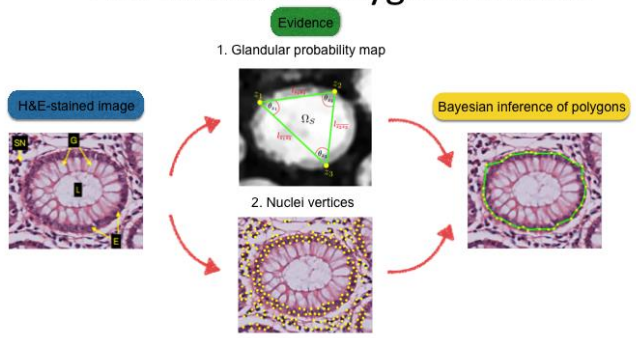
*Cytopathology* 1997, **8**, 265–273

## Image analysis of low magnification images of fine needle aspirates of the breast produces useful discrimination between benign and malignant cases

S. S. CROSS, J. P. BURY, T. J. STEPHENSON AND R. F. HARRISON*
*Department of Pathology, University of Sheffield Medical School, and *Department of Automated Control and Systems Engineering, University of Sheffield, Sheffield, UK*

*Accepted for publication 4 February 1997*

## Tubule formation
## The Random Polygons Model




Sirinukunwattana *et al.*, IEEE *Trans Med Imaging* (Nov 2015)

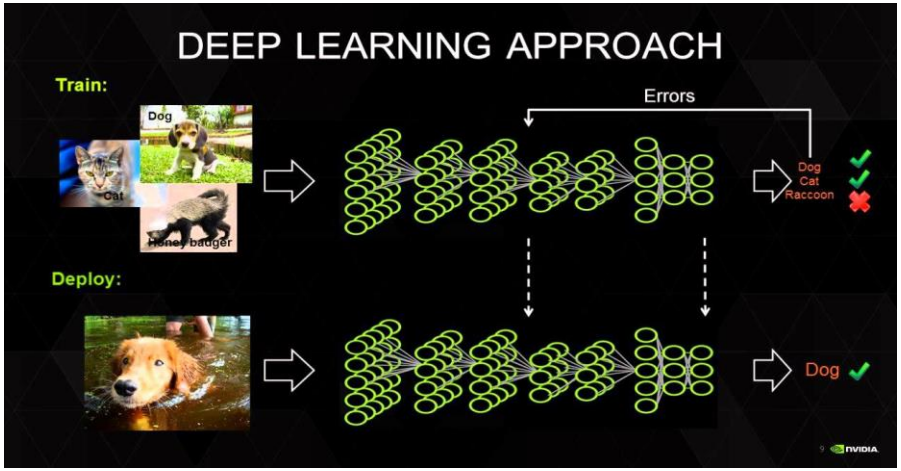
US patent application number 61452293

*CURRENT ISSUES*

## PAPNET Computer-Aided Rescreening for Detection of Benign and Malignant *Glandular* Elements in Cervicovaginal Smears: A Review of 61 Cases

Charles D. Sturgis, M.D.,* Carol Isoe, S.C.T. (A.S.C.P.), C.M.I.A.C., Nodee E. McNeal, S.C.T. (A.S.C.P.), C.M.I.A.C., Gordon H. Yu, M.D., and Denise V.S. DeFrias, M.D., F.I.A.C.

*Diagn. Cytopathol. 1998;18:307–311.*



ELSEVIER

Canadian Association of Radiologists Journal 69 (2018) 120–135

CANADIAN ASSOCIATION OF RADIOLOGISTS JOURNAL

www.carjonline.org

Health Policy and Practice / Santé: politique et pratique médicale

# Canadian Association of Radiologists White Paper on Artificial Intelligence in Radiology

An Tang, MD, MSc[a,b,*], Roger Tam, PhD[c,d], Alexandre Cadrin-Chênevert, MD, BIng[e], Will Guest, MD, PhD[c], Jaron Chong, MD[f], Joseph Barfett, BESc, MSc, MD[g], Leonid Chepelev, MD PhD[h], Robyn Cairns, MSc, MD[i], J. Ross Mitchell, PhD[j], Mark D. Cicero, MD, BESc, FRCPC[g], Manuel Gaudreau Poudrette, MD[k], Jacob L. Jaremko, MD, PhD[l], Caroline Reinhold, MD, MSc[f], Benoit Gallix, MD[f], Bruce Gray, MD, FRCPC[g], Raym Geis, MD, FACR[m]; for the Canadian Association of Radiologists (CAR) Artificial Intelligence Working Group

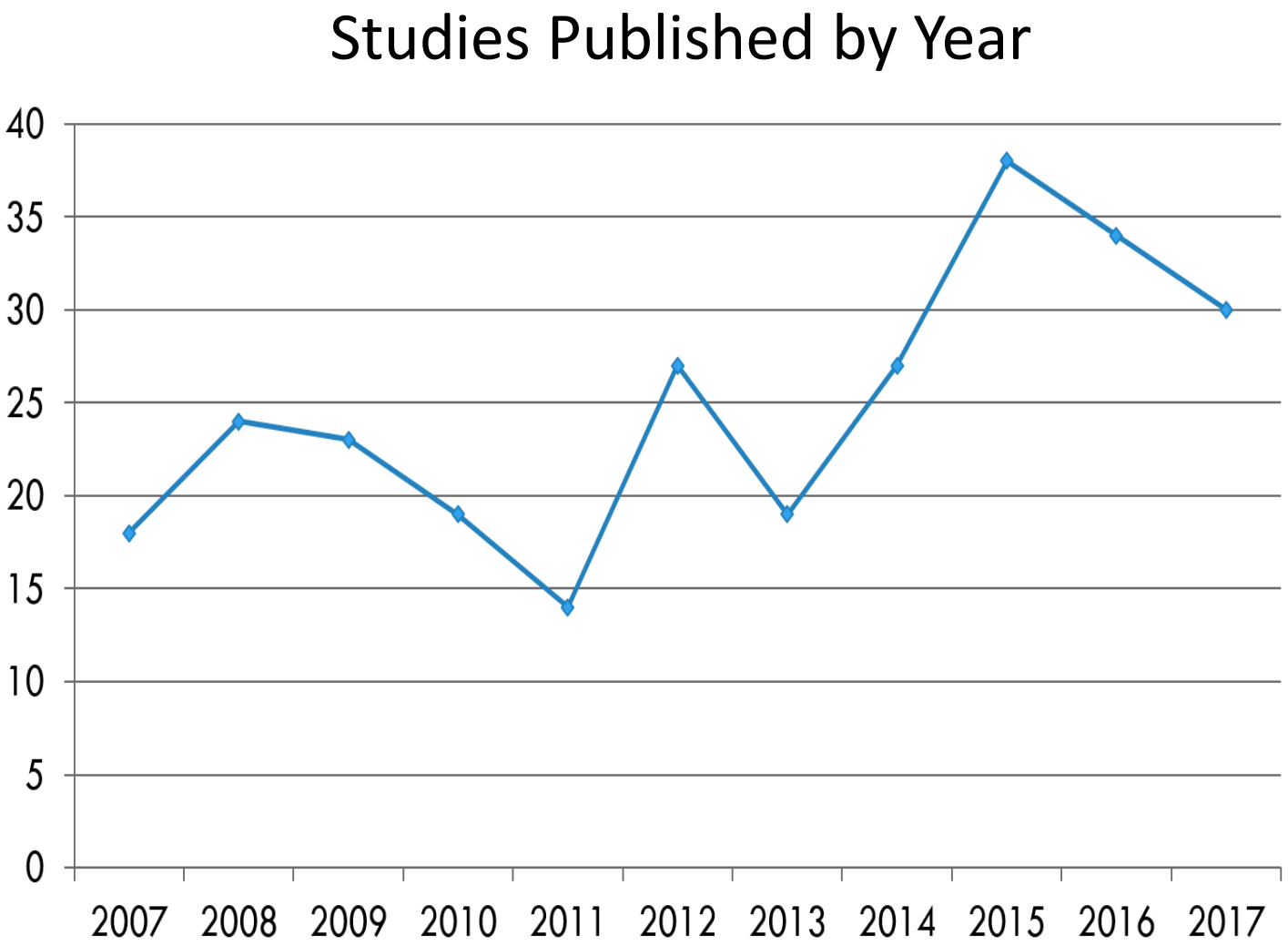
[a]*Department of Radiology, Université de Montréal, Montréal, Québec, Canada*
[b]*Centre de recherche du Centre hospitalier de l'Université de Montréal, Montréal, Québec, Canada*
[c]*Department of Radiology, University of British Columbia, Vancouver, British Columbia, Canada*
[d]*School of Biomedical Engineering, University of British Columbia, Vancouver, British Columbia, Canada*
[e]*Department of Medical Imaging, CISSS Lanaudière, Université Laval, Joliette, Québec, Canada*
[f]*Department of Radiology, McGill University Health Center, Montréal, Québec, Canada*
[g]*Department of Medical Imaging, St. Michael's Hospital, University of Toronto, Toronto, Ontario, Canada*
[h]*Department of Radiology, University of Ottawa, Ottawa, Ontario, Canada*
[i]*Department of Radiology, British Columbia's Children's Hospital, University of British Columbia, Vancouver, British Columbia, Canada*
[j]*Department of Research, Mayo Clinic, Phoenix, Arizona, USA*
[k]*Department of Radiology, Université de Sherbrooke, Sherbrooke, Québec, Canada*
[l]*Department of Radiology and Diagnostic Imaging, University of Alberta, Edmonton, Alberta, Canada*
[m]*Department of Radiology, National Jewish Health, Denver, Colorado, USA*

**Abstract**

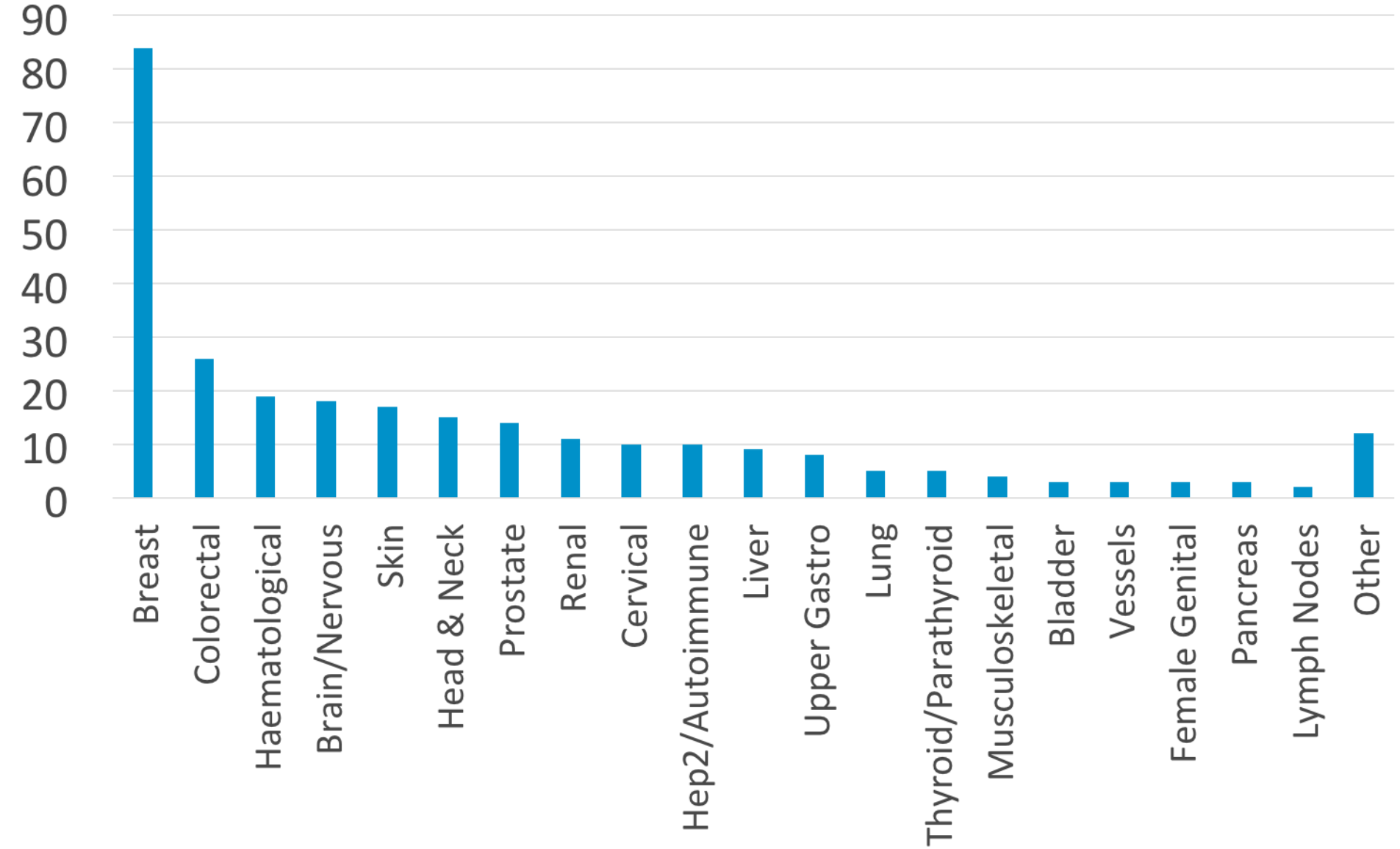
Artificial intelligence (AI) is rapidly moving from an experimental phase to an implementation phase in many fields, including medicine. The combination of improved availability of large datasets, increasing computing power, and advances in learning algorithms has created major performance breakthroughs in the development of AI applications. In the last 5 years, AI techniques known as deep learning have delivered rapidly improving performance in image recognition, caption generation, and speech recognition. Radiology, in particular, is a prime candidate for early adoption of these techniques. It is anticipated that the implementation of AI in radiology over the next decade will significantly improve the quality, value, and depth of radiology's contribution to patient care and population health, and will revolutionize radiologists' workflows. The Canadian Association of Radiologists (CAR) is the national voice of radiology committed to promoting the highest standards in patient-centered imaging, lifelong learning, and research. The CAR has created an AI working group with the mandate to discuss and deliberate on practice, policy, and patient care issues related to the introduction and implementation of AI in imaging. This white paper provides recommendations for the CAR derived from deliberations between members of the AI working group. This white paper on AI in radiology will inform CAR members and policymakers on key terminology, educational needs of members, research and development, partnerships, potential clinical applications, implementation, structure and governance, role of radiologists, and potential impact of AI on radiology in Canada.

delivered rapidly improving performance in image recognition, caption generation, and speech recognition. Radiology, in particular, is a prime candidate for early adoption of these techniques. It is anticipated that the implementation of AI in radiology over the next decade will significantly improve the quality, value, and depth of radiology's contribution to patient care and population health, and will revolutionize

# Digital pathology peer reviewed publications



# Tissue type

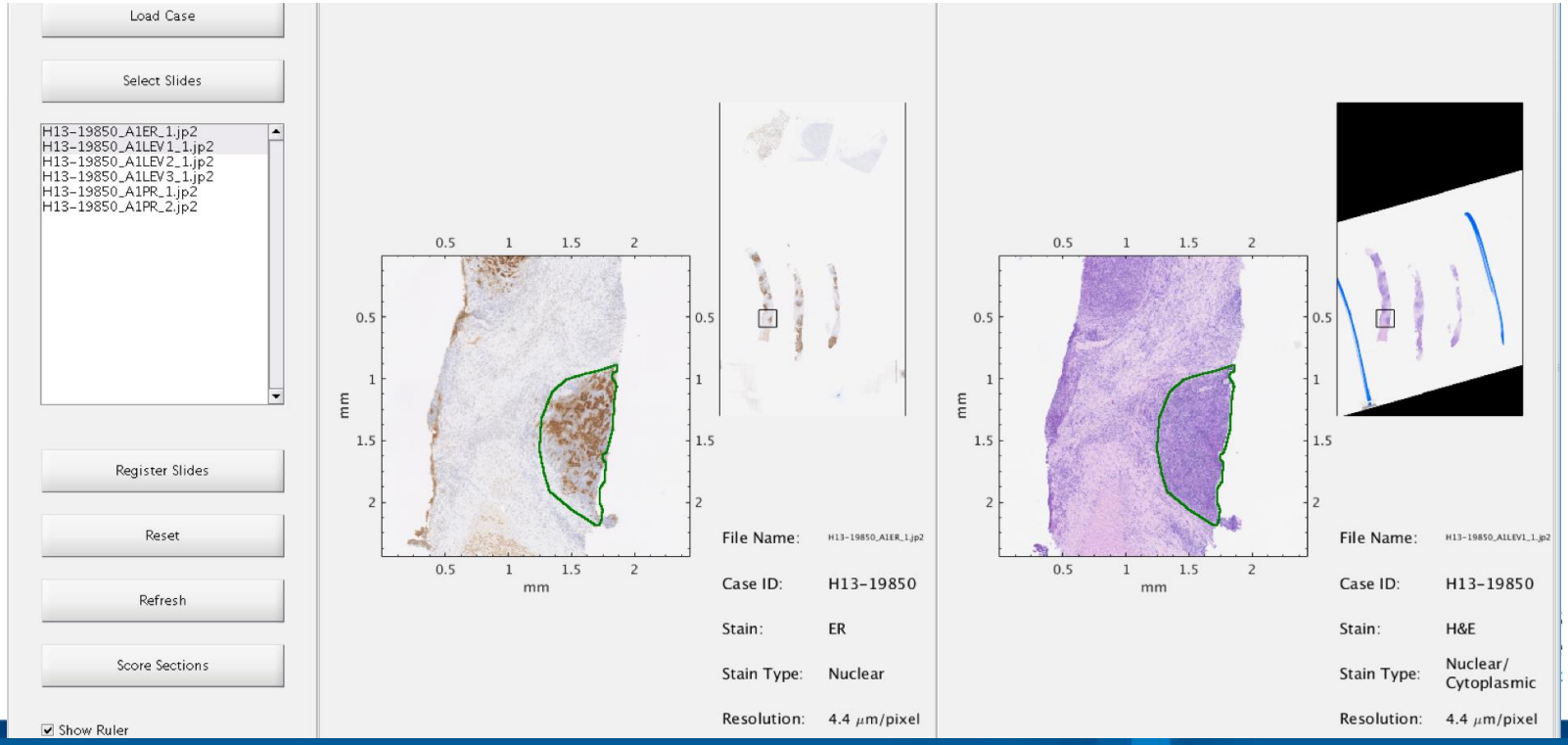

90
80
70
60
50
40
30
20
10
0
Breast
Colorectal
Haematological
Brain/Nervous
Skin
Head & Neck
Prostate
Renal
Cervical
Hep2/Autoimmune
Liver
Upper Gastro
Lung
Thyroid/Parathyroid
Musculoskeletal
Bladder
Vessels
Female Genital
Pancreas
Lymph Nodes
Other

# Automated ER & PR scoring

**Simultaneous Automatic Scoring of Hormone Receptors in Tumour Areas in Whole Slide Images of Breast Cancer Tissue Slides**

Nicholas Trahearn[a], Yee Wah Tsang[b,c], Ian Cree[c], David Snead[b,c], Nasir Rajpoot[a]

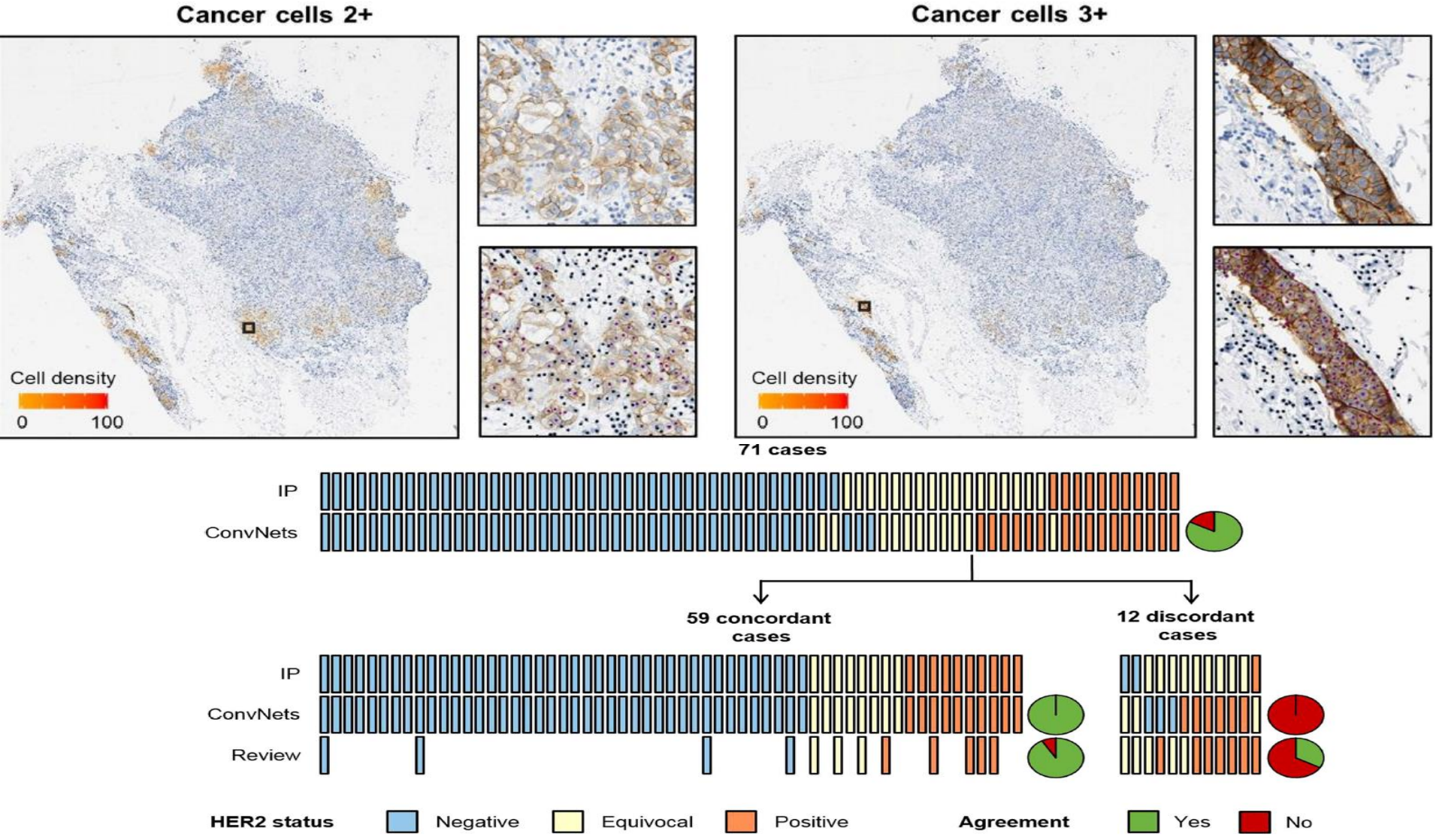
[a] Department of Computer Science, University of Warwick, United Kingdom
[b] Department of Pathology & [c] Centre of Excellence for Digital Pathology, University Hospitals Coventry and Warwickshire, United Kingdom
Cytometry Part A 91A: 585-594, 2017.



# Relevance of deep learning to facilitate the diagnosis of HER2 status in breast cancer

Scientific Reports | 7:45938 | DOI: 10.1038/srep45938 2017

Michel E. Vandenberghe[1], Marietta L. J. Scott[1], Paul W. Scorer[1], Magnus Söderberg[2], Denis Balcerzak[1] & Craig Barker[1]



# Automated Her2 Scoring

Pathological Society
Understanding Disease

The University of Nottingham
UNITED KINGDOM · CHINA · MALAYSIA

UCLM
UNIVERSIDAD DE CASTILLA-LA MANCHA

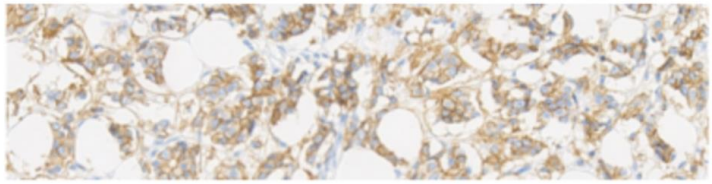
University Hospitals Coventry and Warwickshire NHS
NHS Trust

AID PATH
http://aidpath.eu

## Her2 Scoring Contest

Home | Background | Contest Registration | Contest Rules| Contact

HER2 Contest



Welcome to the contest page of **HER2 scoring in histology images**. This challenge will be held in conjunction with Nottingham Pathology 2016 (The Pathological Society of Great Britain & Ireland).

http://www.warwick.ac.uk/TIAlab/Her2Contest

Qaiser et al., Histopathology 72;227-238 2018

# Her2 Scoring – Man *vs* Machine

| Rank | Team Name | Score | Bonus | Score+Bonus |
|---|---|---|---|---|
| **1** | **Team Indus** | **220** | **12.5** | **232.5** |
| **2** | **Pathologist 2** | **210** | **20.5** | **230.5** |
| 3 | Visilab | 212.5 | 15 | 227.5 |
| 4 | MUCS (Ireland) | 205 | 20.5 | 225.5 |
| 5 | Pathologist 1 | 185 | 10 | 195 |
| 6 | Pathologist 3 | 180 | 13 | 193 |

http://www.warwick.ac.uk/TIAlab/Her2contest/

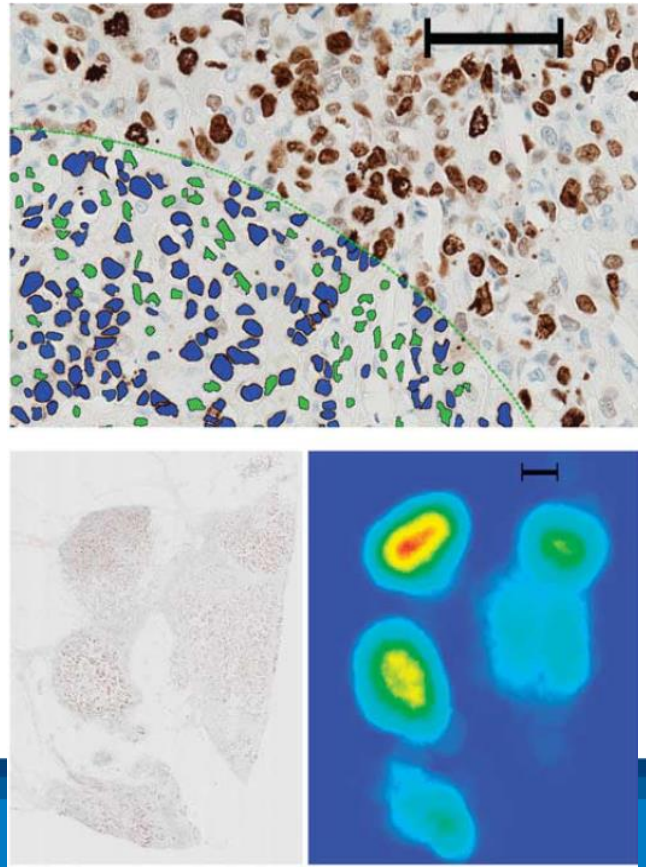
Qaiser et al., Histopathology 72;227-238 2018

# Digital image analysis outperforms manual biomarker assessment in breast cancer

MODERN PATHOLOGY (2016) 29, 318–329


Gustav Stålhammar[1,2], Nelson Fuentes Martinez[1,3], Michael Lippert[4], Nicholas P Tobin[5], Ida Mølholm[4,6], Lorand Kis[7], Gustaf Rosin[1], Mattias Rantalainen[8], Lars Pedersen[4], Jonas Bergh[1,5,9], Michael Grunkin[4] and Johan Hartman[1,5,7]

*[1]Department of Oncology and Pathology, Karolinska Institutet, Stockholm, Sweden; [2]St Erik Eye Hospital, Stockholm, Sweden; [3]Södersjukhuset, Stockholm, Sweden; [4]Visiopharm A/S, Hoersholm, Denmark; [5]Cancer Center Karolinska, Stockholm, Sweden; [6]Department of Applied Mathematics and Computer Science, Technical University of Denmark, Kongens Lyngby, Denmark; [7]Department of Clinical Pathology, Karolinska University Hospital, Stockholm, Sweden; [8]Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden and [9]Department of Oncology, Karolinska University Hospital, Stockholm, Sweden*



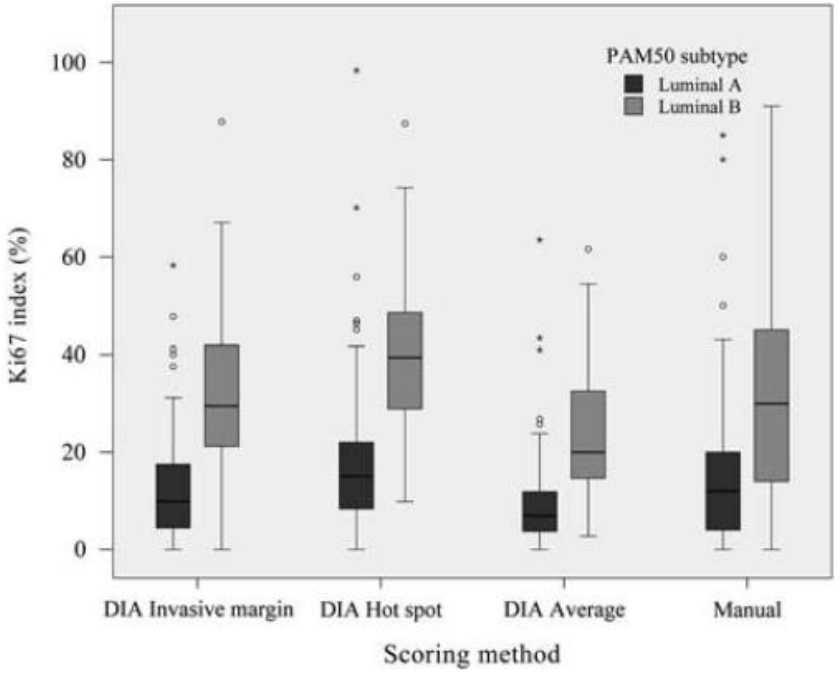



**Figure 2** Clustered box plot for Ki67 index (%) by each scoring method in PAM50 Luminal A and B subtypes. Error bars represent 95% confidence interval. Circles represent outliers and asterisks represent extremes. DIA, digital image analysis ($n=214$).

# Digital image analysis outperforms manual biomarker assessment in breast cancer

MODERN PATHOLOGY (2016) 29, 318–329


Gustav Stålhammar[1,2], Nelson Fuentes Martinez[1,3], Michael Lippert[4], Nicholas P Tobin[5], Ida Mølholm[4,6], Lorand Kis[7], Gustaf Rosin[1], Mattias Rantalainen[8], Lars Pedersen[4], Jonas Bergh[1,5,9], Michael Grunkin[4] and Johan Hartman[1,5,7]

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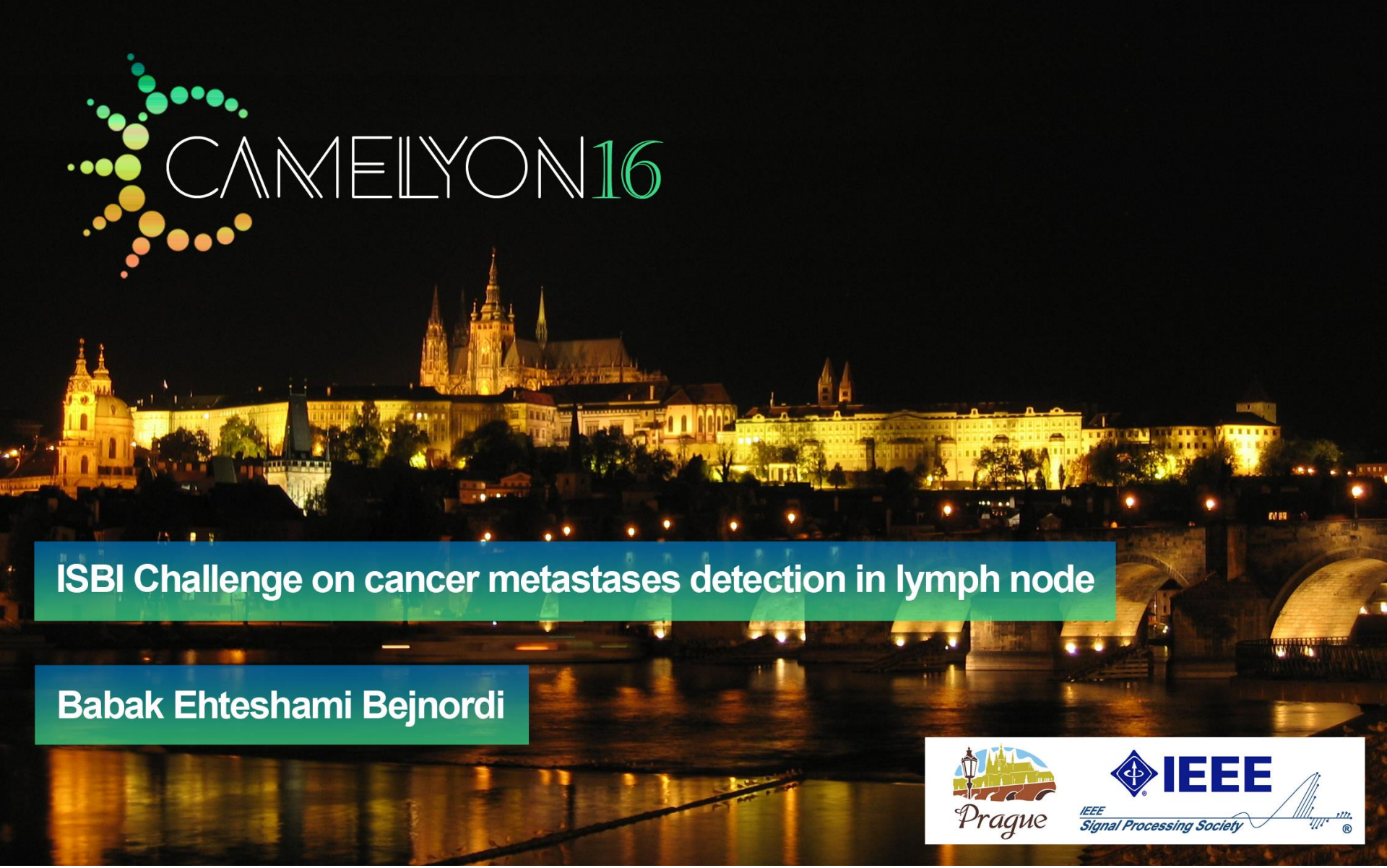
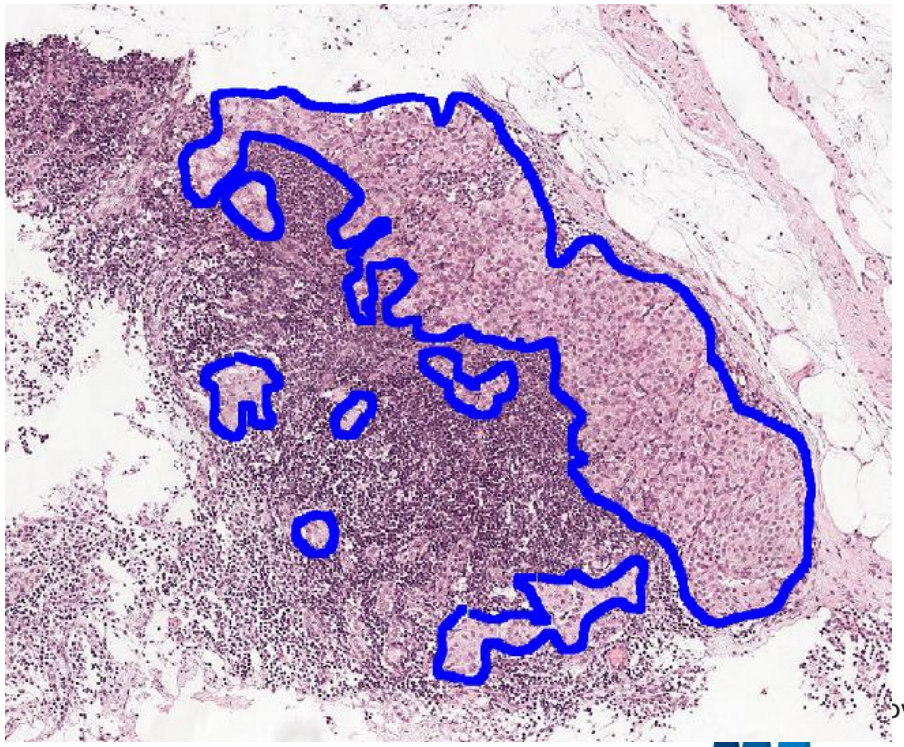
| *Ki67 scoring method* | *Sensitivity for PAM50 Luminal B vs A* | *Specificity for PAM50 Luminal B vs A* | *Proportion misclassified* |
|---|---|---|---|
| *DIA invasive margin* | | | |
| Cutoff ≥ 20% | 84% | 78% | 20% |
| Cutoff ≥ 20.2%* | 82% | 79% | 20% |
| *DIA hot spot* | | | |
| Cutoff ≥ 20% | 90% | 65% | 24% |
| Cutoff ≥ 25.2%* | 86% | 77% | 19% |
| *DIA average* | | | |
| Cutoff ≥ 20% | 60% | 90% | 31% |
| Cutoff ≥ 15.5%* | 80% | 83% | 19% |
| *Manual* | | | |
| Cutoff ≥ 20% | 75% | 70% | 30% |
| Cutoff ≥ 22.5%* | 74% | 75% | 29% |

Manual scores retrieved from patient records.
* = Adjusted cutoffs.


CAMELYON16
ISBI Challenge on cancer metastases detection in lymph node
Babak Ehteshami Bejnordi
Prague
IEEE
IEEE Signal Processing Society
Radboudumc
university medical center
UMC Utrecht
TU/e
Technische Universiteit
Eindhoven
University of Technology
Where innovation starts
PHILIPS
innovation you
trait
a ctmm project
ST
stichting
IT
PRO
IT projecten

# Camelyon16 dataset

- Most of the tumor slides were exhaustively annotated
- The average time for annotating each slide was 1 hour

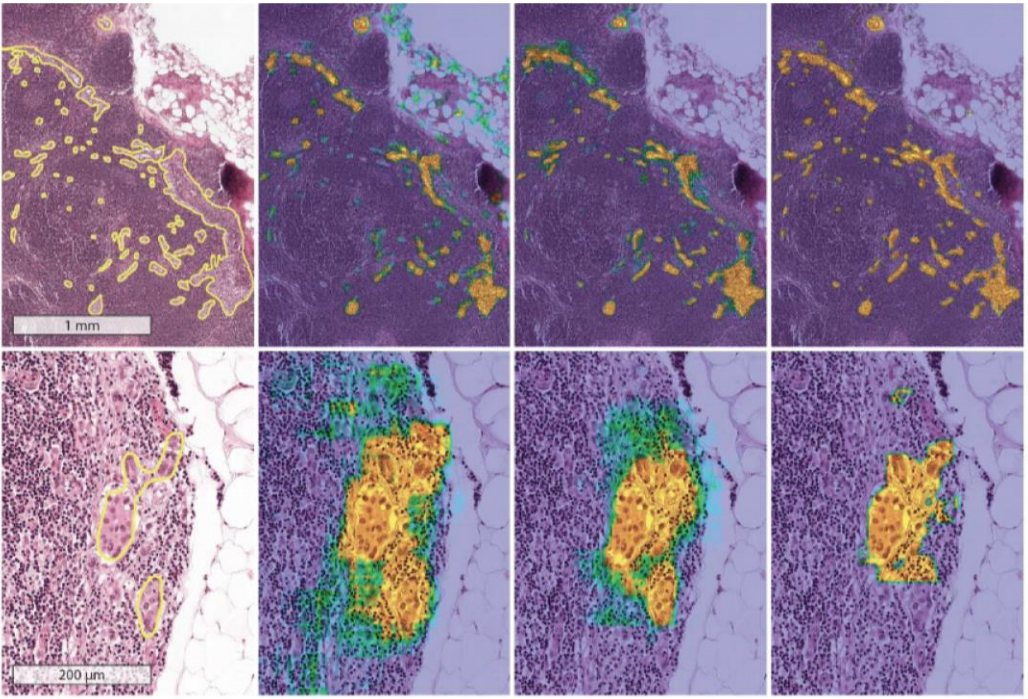


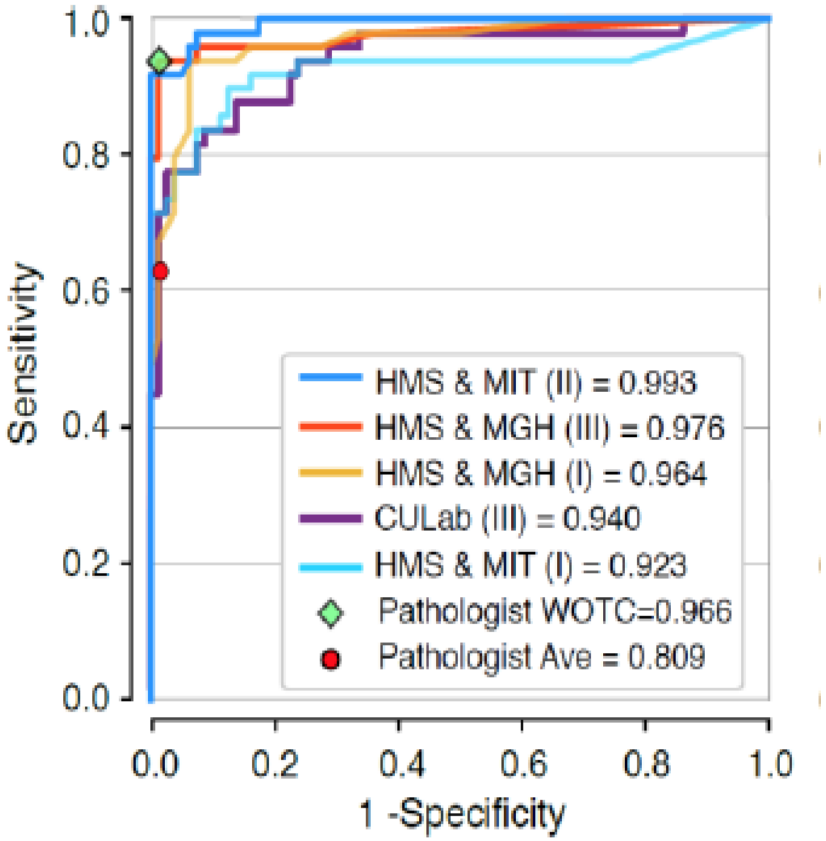
JAMA | Original Investigation

# Diagnostic Assessment of Deep Learning Algorithms for Detection of Lymph Node Metastases in Women With Breast Cancer

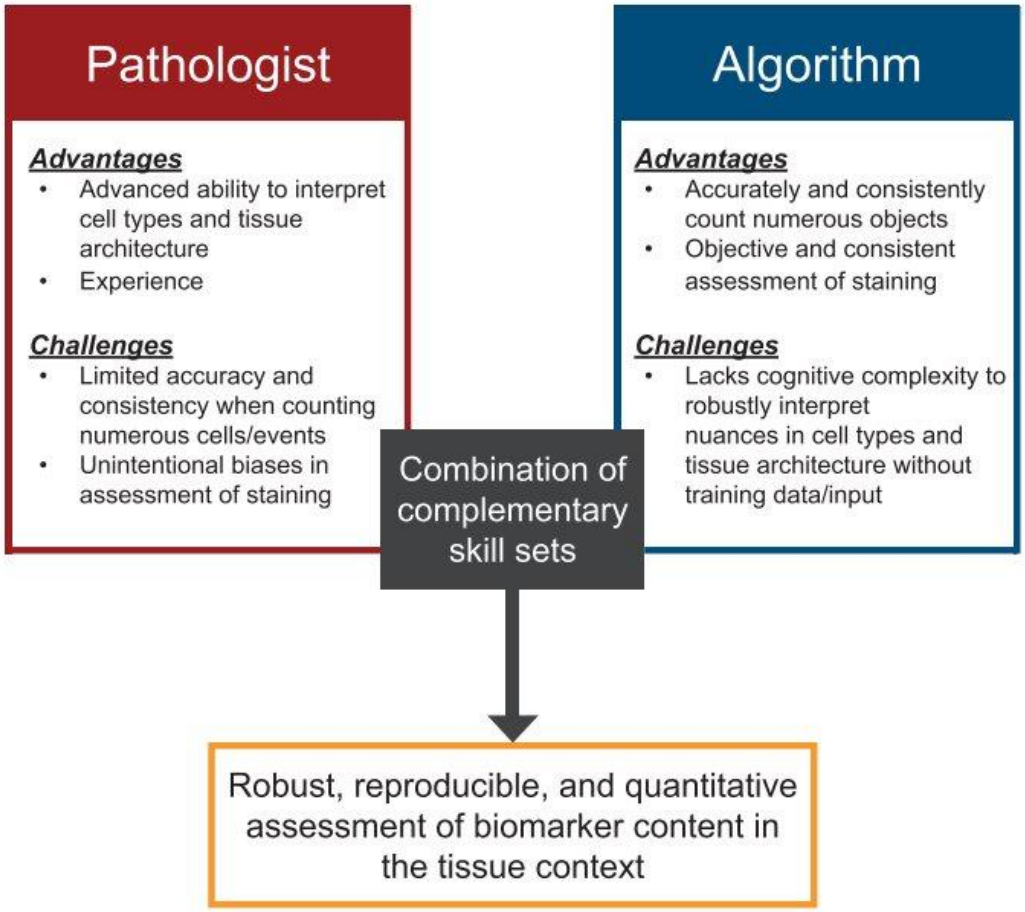
Babak Ehteshami Bejnordi, MS; Mitko Veta, PhD; Paul Johannes van Diest, MD, PhD; Bram van Ginneken, PhD; Nico Karssemeijer, PhD; Geert Litjens, PhD; Jeroen A. W. M. van der Laak, PhD; and the CAMELYON16 Consortium

JAMA. 2017;318(22):2199-2210.



# Pathologist + Algorithm

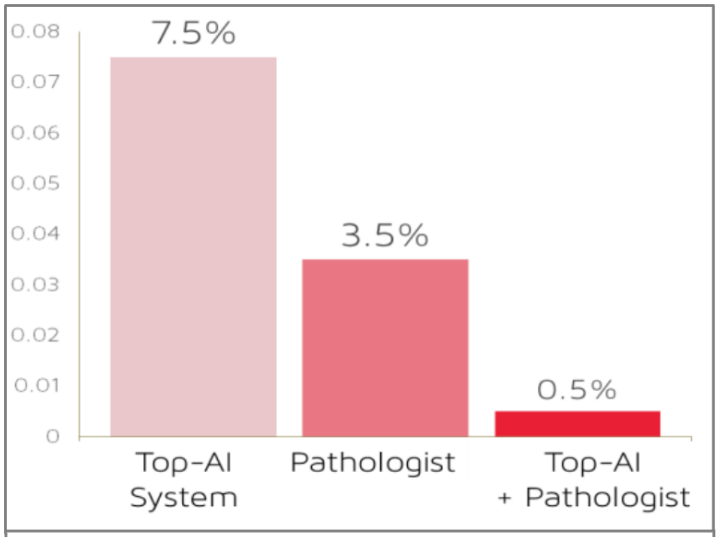



Aeffner *et al*., Arch Path Lab Med (Sep 2017)

# The White House Takes Note

ARTIFICIAL INTELLIGENCE FOR COMPUTATIONAL PATHOLOGY

*Image interpretation plays a central role in the pathologic diagnosis of cancer. Since the late 19th century, the primary tool used by pathologists to make definitive cancer diagnoses is the microscope. Pathologists diagnose cancer by manually examining stained sections of cancer tissues to determine the cancer subtype. Pathologic diagnosis using conventional methods is labor-*



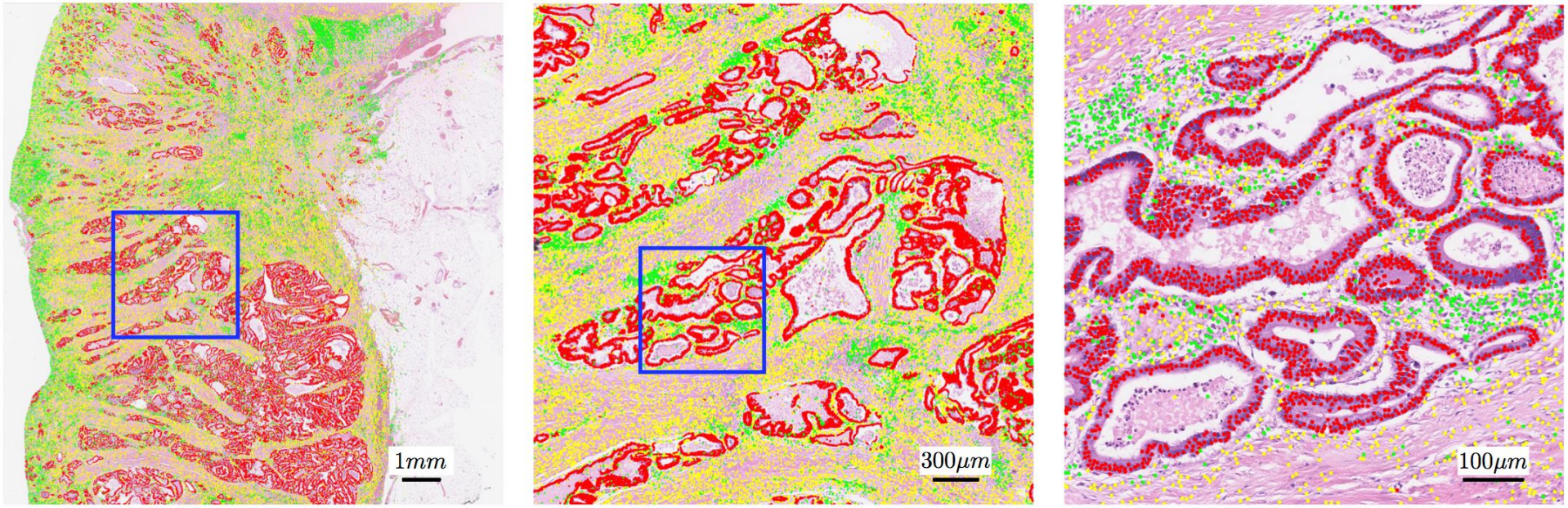

AI significantly reduces pathologist error rate in the identification of metastatic breast cancer from sentinel lymph node biopsies.

THE NATIONAL ARTIFICIAL INTELLIGENCE RESEARCH AND DEVELOPMENT STRATEGIC PLAN

October 2016

# Deep Learning - Profiling Tumour Microenvironment

- Cell recognition in large sets of whole-slide images
- Analytics for profiling the tumor micro-environment




Sirinukunwattana *et al.*, ***IEEE Trans Medical Imaging*** special issue on ***Deep Learning in Medical Imaging*** (May 2016)

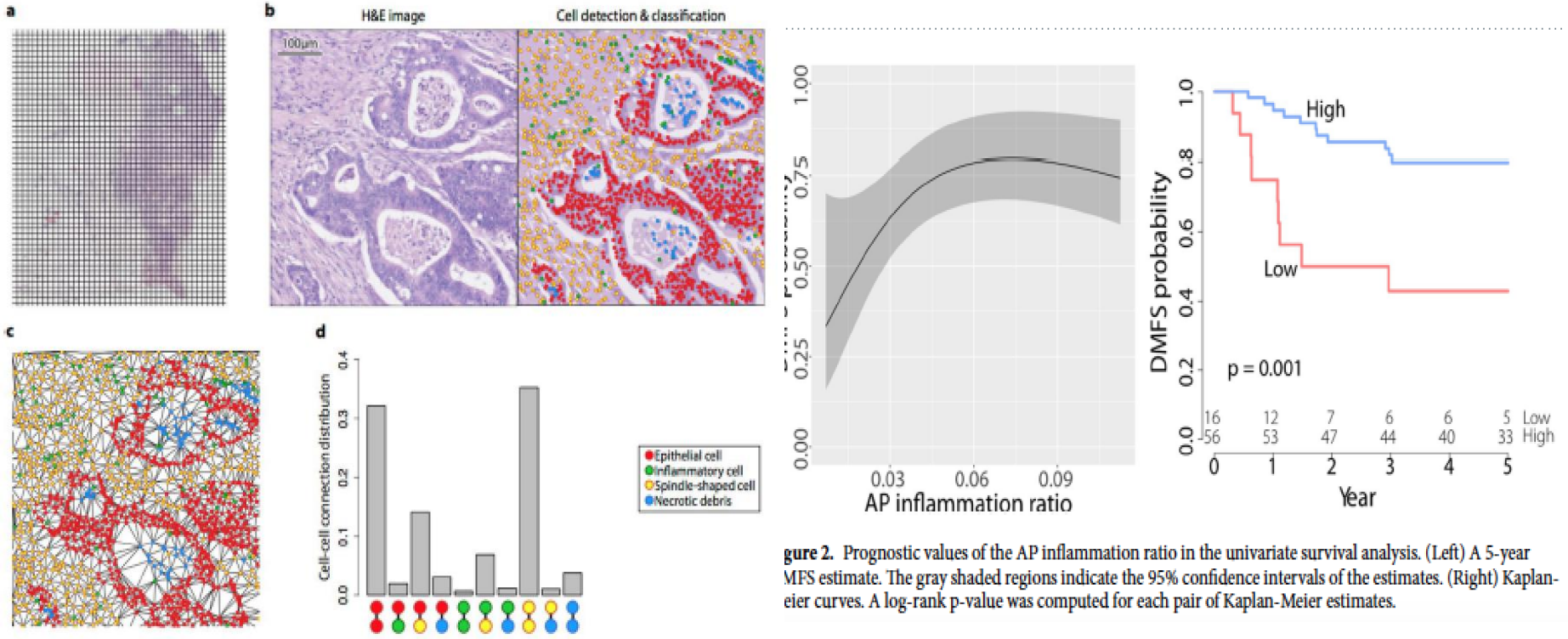
SCIENTIFIC REPORTS

OPEN

# Novel digital signatures of tissue phenotypes for predicting distant metastasis in colorectal cancer

Received: 23 January 2018
Accepted: 7 August 2018

Korsuk Sirinukunwattana[1], David Snead[2], David Epstein[3], Zia Aftab[4], Imaad Mujeeb[4], Yee Wah Tsang[2], Ian Cree[5] & Nasir Rajpoot[6,2,7]




**gure 2.** Prognostic values of the AP inflammation ratio in the univariate survival analysis. (Left) A 5-year MFS estimate. The gray shaded regions indicate the 95% confidence intervals of the estimates. (Right) Kaplan-eier curves. A log-rank p-value was computed for each pair of Kaplan-Meier estimates.

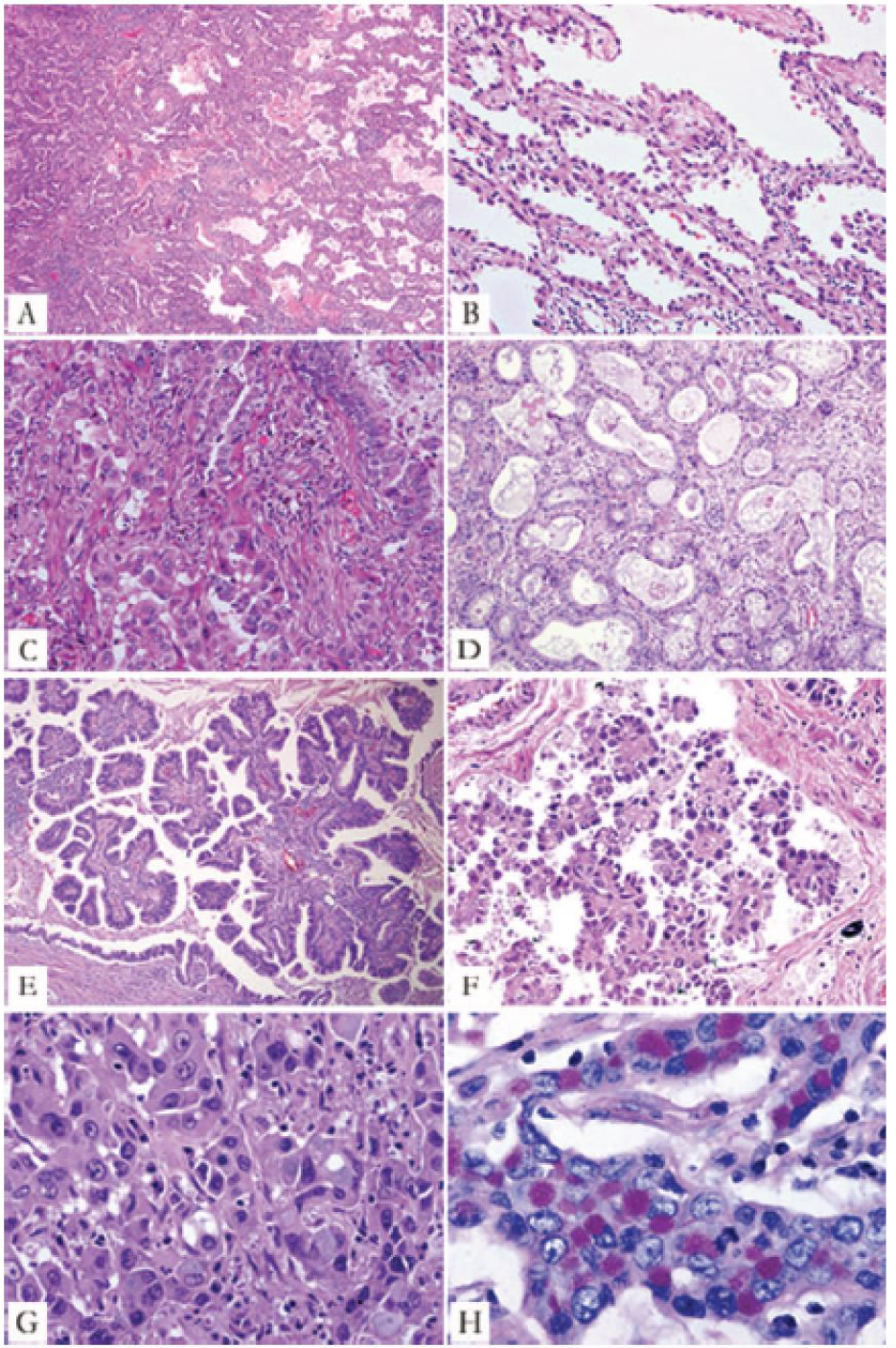
STATE OF THE ART: CONCISE REVIEW

*Journal of Thoracic Oncology* • Volume 6, Number 2, February 2011

# International Association for the Study of Lung Cancer/American Thoracic Society/European Respiratory Society International Multidisciplinary Classification of Lung Adenocarcinoma

*William D. Travis, MD, Elisabeth Brambilla, MD, Masayuki Noguchi, MD, Andrew G. Nicholson, MD, Kim R. Geisinger, MD, Yasushi Yatabe, MD, David G. Beer, PhD, Charles A. Powell, MD, Gregory J. Riely, MD, Paul E. Van Schil, MD, Kavita Garg, MD, John H. M. Austin, MD, Hisao Asamura, MD, Valerie W. Rusch, MD, Fred R. Hirsch, MD, Giorgio Scagliotti, MD, Tetsuya Mitsudomi, MD, Rudolf M. Huber, MD, Yuichi Ishikawa, MD, James Jett, MD, Montserrat Sanchez-Cespedes, PhD, Jean-Paul Sculier, MD, Takashi Takahashi, MD, Masahiro Tsuboi, MD, Johan Vansteenkiste, MD, Ignacio Wistuba, MD, Pan-Chyr Yang, MD, Denise Aberle, MD, Christian Brambilla, MD, Douglas Flieder, MD, Wilbur Franklin, MD, Adi Gazdar, MD, Michael Gould, MD, MS, Philip Hasleton, MD, Douglas Henderson, MD, Bruce Johnson, MD, David Johnson, MD, Keith Kerr, MD, Keiko Kuriyama, MD, Jin Soo Lee, MD, Vincent A. Miller, MD, Iver Petersen, MD, PhD, Victor Roggli, MD, Rafael Rosell, MD, Nagahiro Saijo, MD, Erik Thunnissen, MD, Ming Tsao, MD, and David Yankelewitz, MD*

- Adenocarcinoma in-situ
- Minimally invasive adenocarcinoma
- Lepidic adenocarcinoma
- Papillary adenocarcinoma
- Acinar adenocarcinoma
- Micropapillary adenocarcinoma
- Solid adenocarcinoma



ORIGINAL ARTICLE

# Comprehensive Computational Pathological Image Analysis Predicts Lung Cancer Prognosis

Xin Luo, MD,[a] Xiao Zang, BS,[b] Lin Yang, MD,[b,c] Junzhou Huang, PhD,[d] Faming Liang, PhD,[e] Jaime Rodriguez-Canales, MD,[f] Ignacio I. Wistuba, MD,[f] Adi Gazdar, MD,[g,h] Yang Xie, MD, PhD,[a,b] Guanghua Xiao, PhD[a,b,*]

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[b]*Quantitative Biomedical Research Center, Department of Clinical Sciences, University of Texas Southwestern Medical Center at Dallas, Texas*
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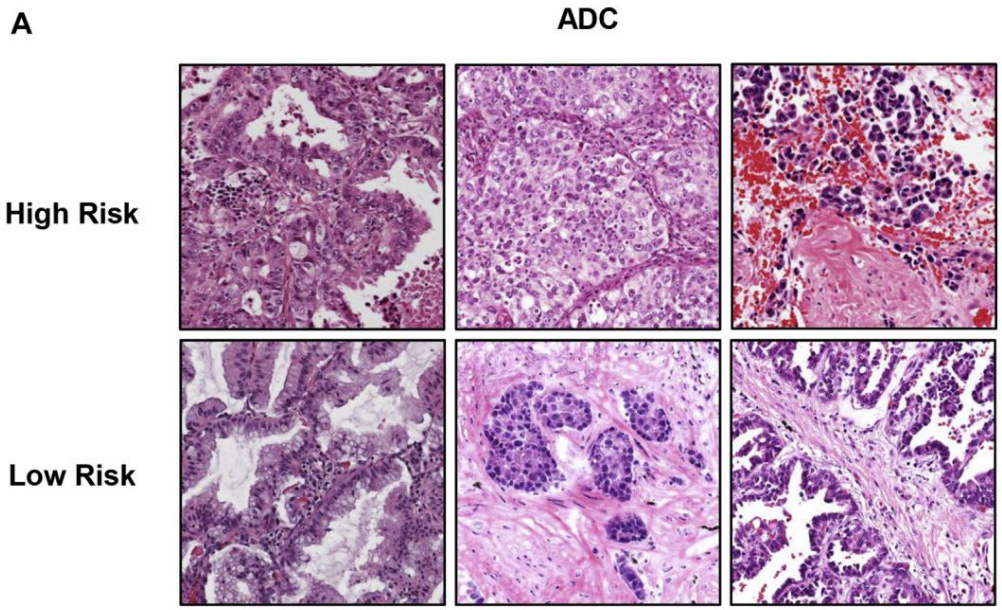
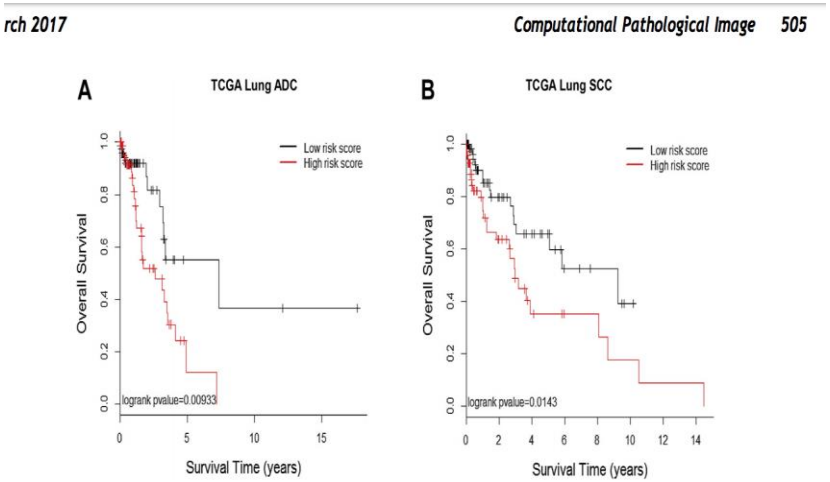
[h]*Hamon Center for Therapeutic Oncology, University of Texas Southwestern Medical Center at Dallas, Dallas, Texas*

Received 9 June 2016; revised 28 September 2016; accepted 24 October 2016
Available online - 4 November 2016




ure 2. Associations between survival outcomes and morphological feature-defined risk groups in The Cancer Genome Atlas GA) cohorts of patients with adenocarcinoma (ADC) and squamous cell carcinoma (SCC). Kaplan-Meier survival curves for ients in the high-risk group (*red*) and low-risk group classified by morphological feature-based prediction models for both C ($p = 0.009$) (*A*) and SCC ($p = 0.0143$) (*B*). The features and prediction model were derived from the training data, and survival analysis was performed in the testing data set.

# Tumour Cell Morphometrics Predict Survival in Lung Adenocarcinoma

Najah Alsubaie[1,2], David Snead[3], Nasir Rajpoot[1,3,4]
[1]Department of Computer Science, University of Warwick, UK
[2]Department of Computer Science, Princess Nourah University, KSA
[3]Department of Pathology, University Hospitals Coventry and Warwickshire, UK
[4]The Alan Turing Institute, UK

TISSUE IMAGE ANALYTICS LAB

## Background

Tumour cell morphometrics are one of the most significant indicators of cancer aggressiveness. Pathologists assessment is limited to some morphological features due to their biological meaning and usefulness in most types of cancer. Besides the subjectivity of the assessment, it also requires time and effort. In this study, we characterise the heterogeneity of lung adenocarcinoma (LUAD) using morphometric features of tumour cells automatically extracted from the whole slide images (WSIs).

## Dataset and Methods

We build the TCM (Tumour Cell Morphometric) system using a dataset of **78** LUAD patient collected from **2011** to **2014**. The system aims to quantify standard nuclear morphometric features along with the topological, textural and global heat map statistics. We extracted **malignant nuclei** by combining nuclei detection and segmentation algorithms. Features are calculated for tumour cells on **40x** magnification. We used **75%** of the data to perform features selection and find the Cox model. The other **25%** of the data is used to test the model.

## Results

We find that nuclear graph and nuclear texture features are highly correlated with patient survival. Using the selected features, the Cox model is able to stratify patients into better and worse prognosis in both training and testing sets, see **Figure 1**. **Figure 2** shows clustered heatmap for the average number of connected nuclei per nuclear cluster in low and high survival cases. The Maximum cluster is higher in the low survival case compared to the high survival case.

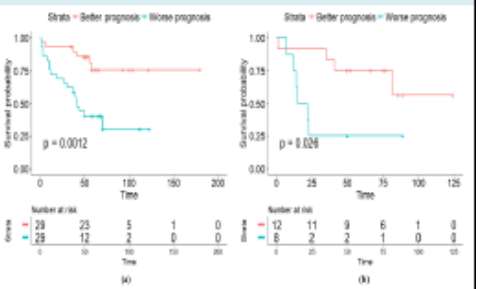



**Figure 1: A Kaplan-Meier survival plots for the model prediction. Plots a and b show LUAD survival estimation on the training and testing sets; respectively.**

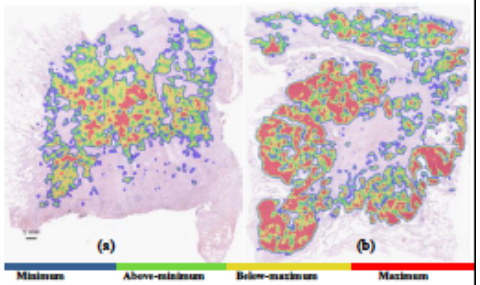



**Figure 2: Heat map of average number of connected nuclei per nuclear cluster for higher survival case (left) compared to the lower survival case (right).**

## Conclusion

In this work we quantity heterogeneity of nuclear features in WSI of LUAD. We find that statistics extracted from the heatmap is highly correlated with patient overall survival.



# Automatic Quantification of Lung Adenocarcinoma Growth Patterns Predicts Five-Year Survival

Najah Alsubaie[1,2], David Snead[3], Syed Ali Khurram[4], Nasir Rajpoot[1,3,5]
[1]Department of Computer Science, University of Warwick, UK
[2]Department of Computer Science, Princess Nourah University, KSA
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[5]The Alan Turing Institute, UK

TISSUE IMAGE ANALYTICS LAB

## Background

Identifying lung adenocarcinoma (LUAD) growth patterns (GP) is critical for diagnosis and treatment of lung cancer patients. There are five main growth patterns: **Acinar**, **lepidic**, **papillary**, **micropapillary** and **solid**. The new LUAD classification system is based on the predominant growth pattern when measured semi-quantitatively in 5% increments. Clinical studies have shown show that some of these patterns might be correlated with prognosis and could predict patient response to therapy. LUAD GPs can have variable appearance, size and location with overlapping features, where it might be difficult to avoid inter-observer variability.

## Dataset and Methods

We automatically locate and classify GPs of LUAD in whole slide images (WSI). The percentages of each pattern in relation to the tissue sample size is combined to build a features vector per case. **Five-year survival** is treated as a binary variable, i.e. patients with greater than five-year survival have an outcome of one and zero otherwise. We split our dataset of **78** LUAD patients into **60%** for training and **40%** for testing. We fit logistic regression model using training set and test the model on the testing set.

## Results

The model has an accuracy of **0.826** on the training set and an area under curve of **0.65** on the testing set.

The logistic model shows that percentages of lepidic and micropapillary are significant predictors ($p<0.05$). The model is able to stratify patients in our dataset into long and short term survival based on percentages of GPs ($p = 0.009$).

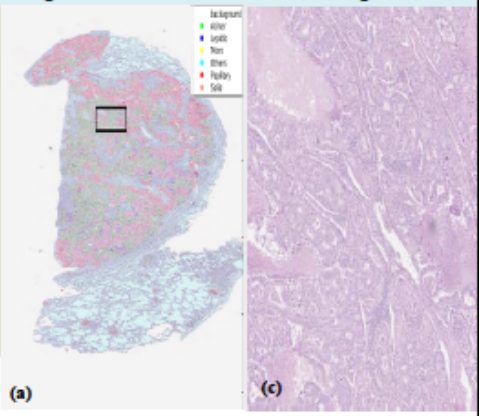



**Figure 1: Whole slide image classification of GP for automatically identifying of pattern percentages.**

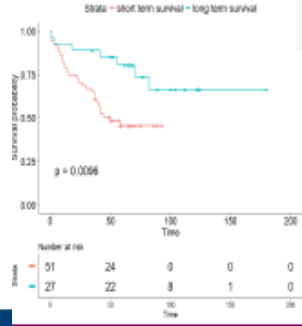



**Figure 2: A Kaplan-Meier survival plot using the model prediction is able to stratify patients into short and long term survival using automatic quantification of GPs percentages.**

## Conclusion

In this work, we automatically quantity LUAD GPs on WSIs. Percentages of GPs are combined to build a feature vector per case. We train on GPs percentages and find that model prediction is strongly correlated with patient survival.

nature medicine

ARTICLES

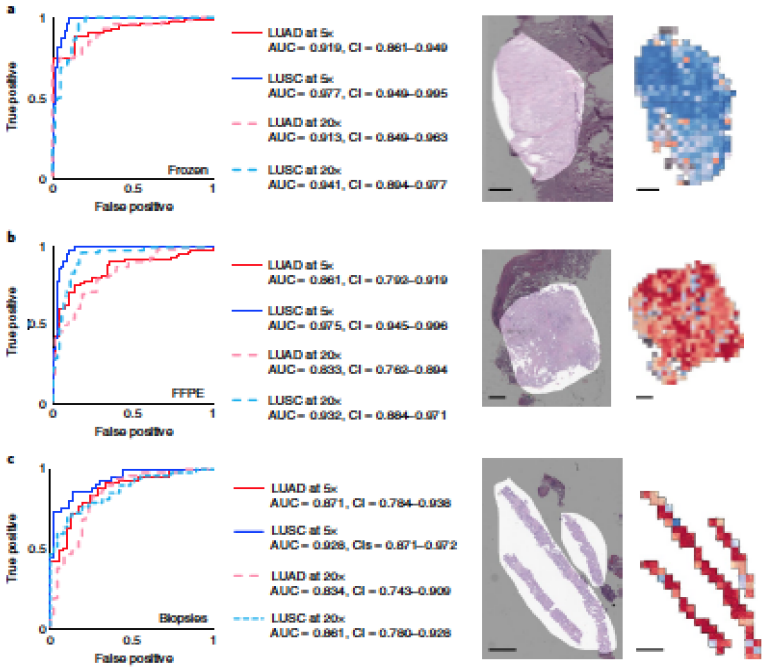
https://doi.org/10.1038/s41591-018-0177-5

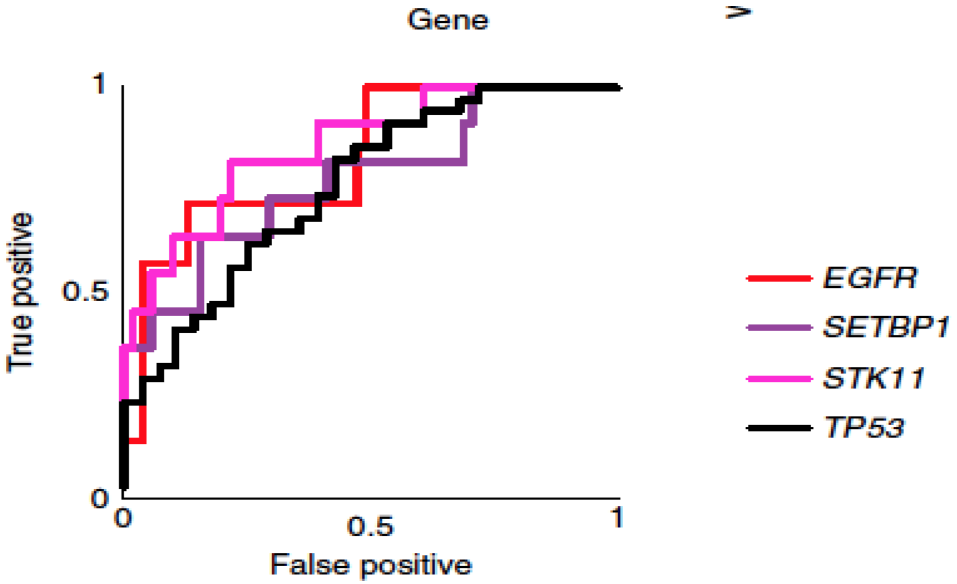
Nat ure Medicine | VOL 24 | OCTOBER 2018 | 1559–1567 |
www.nature.com/naturemedicine

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

Nicolas Coudray[1,2,9], Paolo Santiago Ocampo[3,9], Theodore Sakellaropoulos[4], Navneet Narula[3], Matija Snuderl[3], David Fenyö[5,6], Andre L. Moreira[3,7], Narges Razavian[8*] and Aristotelis Tsirigos[1,3*]

**Visual inspection of histopathology slides is one of the main methods used by pathologists to assess the stage, type and subtype of lung tumors. Adenocarcinoma (LUAD) and squamous cell carcinoma (LUSC) are the most prevalent subtypes of lung cancer, and their distinction requires visual inspection by an experienced pathologist. In this study, we trained a deep convolutional neural network (inception v3) on whole-slide images obtained from The Cancer Genome Atlas to accurately and automatically classify them into LUAD, LUSC or normal lung tissue. The performance of our method is comparable to that of pathologists, with an average area under the curve (AUC) of 0.97. Our model was validated on independent datasets of frozen tissues, formalin-fixed paraffin-embedded tissues and biopsies. Furthermore, we trained the network to predict the ten most commonly mutated genes in LUAD. We found that six of them—STK11, EGFR, FAT1, SETBP1, KRAS and TP53—can be predicted from pathology images, with AUCs from 0.733 to 0.856 as measured on a held-out population. These findings suggest that deep-learning models can assist pathologists in the detection of cancer subtype or gene mutations. Our approach can be applied to any cancer type, and the code is available at https://github.com/ncoudray/DeepPATH.**



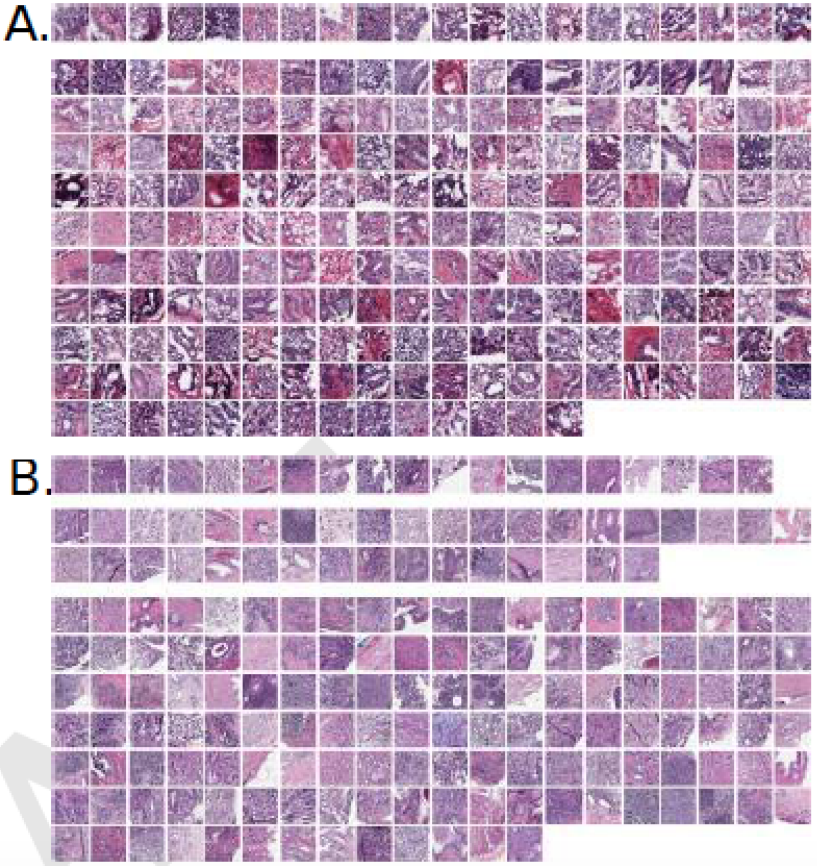
# H&E-stained Whole Slide Image Deep Learning Predicts SPOP Mutation State in Prostate Cancer

**Andrew J. Schaumberg**[a,b,*], **Mark A. Rubin**[c,d,e,*], **and Thomas J. Fuchs**[f,g,*]

[a]Memorial Sloan Kettering Cancer Center and the Tri-Institutional Training Program in Computational Biology and Medicine; [b]Weill Cornell Graduate School of Medical Sciences; [c]Caryl and Israel Englander Institute for Precision Medicine, New York Presbyterian Hospital–Weill Cornell Medicine; [d]Sandra and Edward Meyer Cancer Center at Weill Cornell Medicine; [e]Department of Pathology and Laboratory Medicine, Weill Cornell Medicine; [f]Department of Medical Physics, Memorial Sloan Kettering Cancer Center; [g]Department of Pathology, Memorial Sloan Kettering Cancer Center

This manuscript was compiled on October 1, 2018

**A quantitative model to genetically interpret the histology in whole microscopy slide images is desirable to guide downstream immunohistochemistry, genomics, and precision medicine. We constructed a statistical model that predicts whether or not SPOP is mutated in prostate cancer, given only the digital whole slide after standard hematoxylin and eosin [H&E] staining. Using a TCGA cohort of 177 prostate cancer patients where 20 had mutant SPOP, we trained multiple ensembles of residual networks, accurately distinguishing SPOP mutant from SPOP non-mutant patients (test AUROC=0.74, p=0.0007 Fisher's Exact Test). We further validated our full metaensemble classifier on an independent test cohort from MSK-IMPACT of 152 patients where 19 had mutant SPOP. Mutants and non-mutants were accurately distinguished despite TCGA slides being frozen sections and MSK-IMPACT slides being formalin-fixed paraffin-embedded sections (AUROC=0.86, p=0.0038). Moreover, we scanned an additional 36 MSK-IMPACT patients having mutant SPOP, trained on this expanded MSK-IMPACT cohort (test AUROC=0.75, p=0.0002), tested on the TCGA cohort (AUROC=0.64, p=0.0306), and again accurately distinguished mutants from non-mutants using the same pipeline. Importantly, our method demonstrates tractable deep learning in this "small data" setting of 20-55 positive examples and quantifies each prediction's uncertainty with confidence intervals. To our knowledge, this is the first statistical model to predict a genetic muta-**



npj | Breast Cancer

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ARTICLE OPEN

# Correlating nuclear morphometric patterns with estrogen receptor status in breast cancer pathologic specimens

Rishi R. Rawat[1], Daniel Ruderman[1], Paul Macklin[2], David L. Rimm[3] and David B. Agus[1]

In this pilot study, we introduce a machine learning framework to identify relationships between cancer tissue morphology and hormone receptor pathway activation in breast cancer pathology hematoxylin and eosin (H&E)-stained samples. As a proof-of-concept, we focus on predicting clinical estrogen receptor (ER) status—defined as greater than one percent of cells positive for estrogen receptor by immunohistochemistry staining—from spatial arrangement of nuclear features. Our learning pipeline segments nuclei from H&E images, extracts their position, shape and orientation descriptors, and then passes them to a deep neural network to predict ER status. After training on 57 tissue cores of invasive ductal carcinoma (IDC), our pipeline predicted ER status in an independent test set of patient samples (AUC ROC = 0.72, 95%CI = 0.55–0.89, $n = 56$). This proof of concept shows that machine-derived descriptors of morphologic histology patterns can be correlated to signaling pathway status. Unlike other deep learning approaches to pathology, our system uses deep neural networks to learn spatial relationships between pre-defined biological features, which improves the interpretability of the system and sheds light on the features the neural network uses to predict ER status. Future studies will correlate morphometry to quantitative measures of estrogen receptor status and, ultimately response to hormonal therapy.

*npj Breast Cancer* (2018)4:32 ; doi:10.1038/s41523-018-0084-4

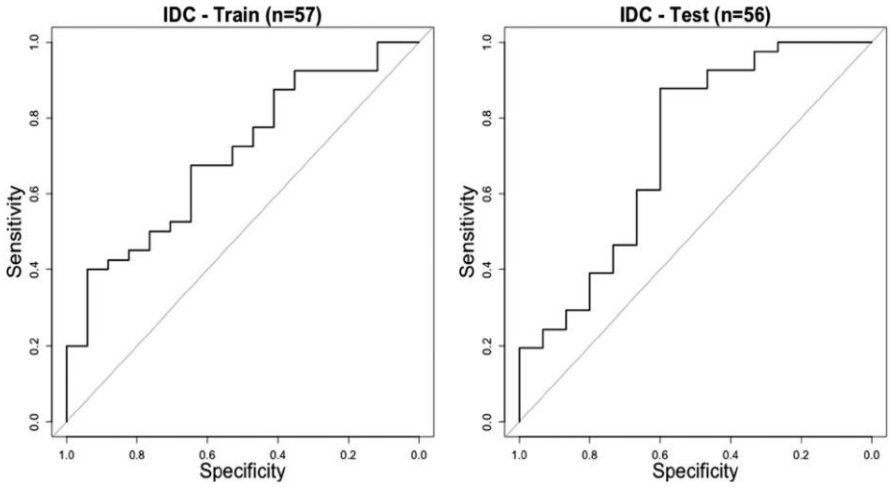
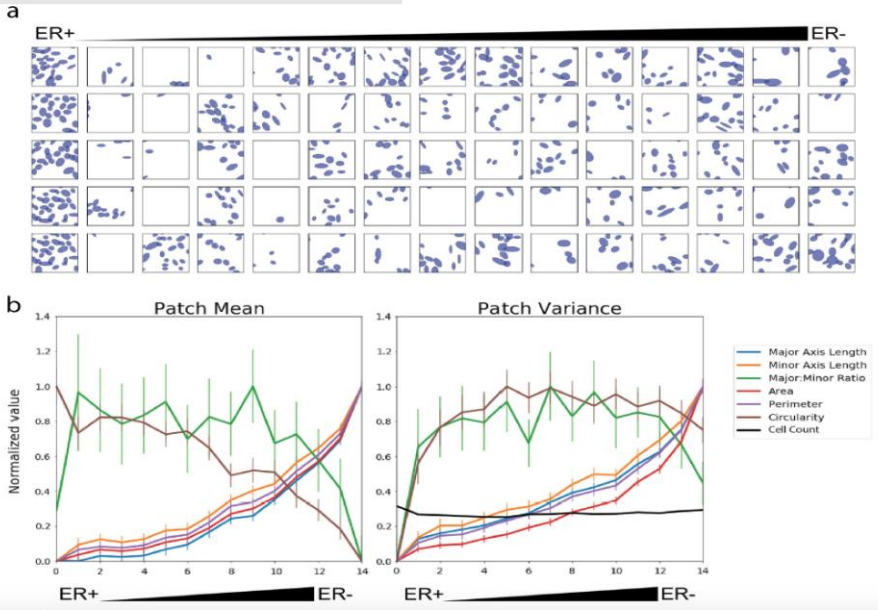



Fig. 1 Receiver operating characteristic (ROC) curves for the training dataset (AUC = 0.70, 95%CI = 0.56–0.85) (left), and test dataset (AUC = 0.72, 95%CI = 0.55–0.89) (right)






Press release

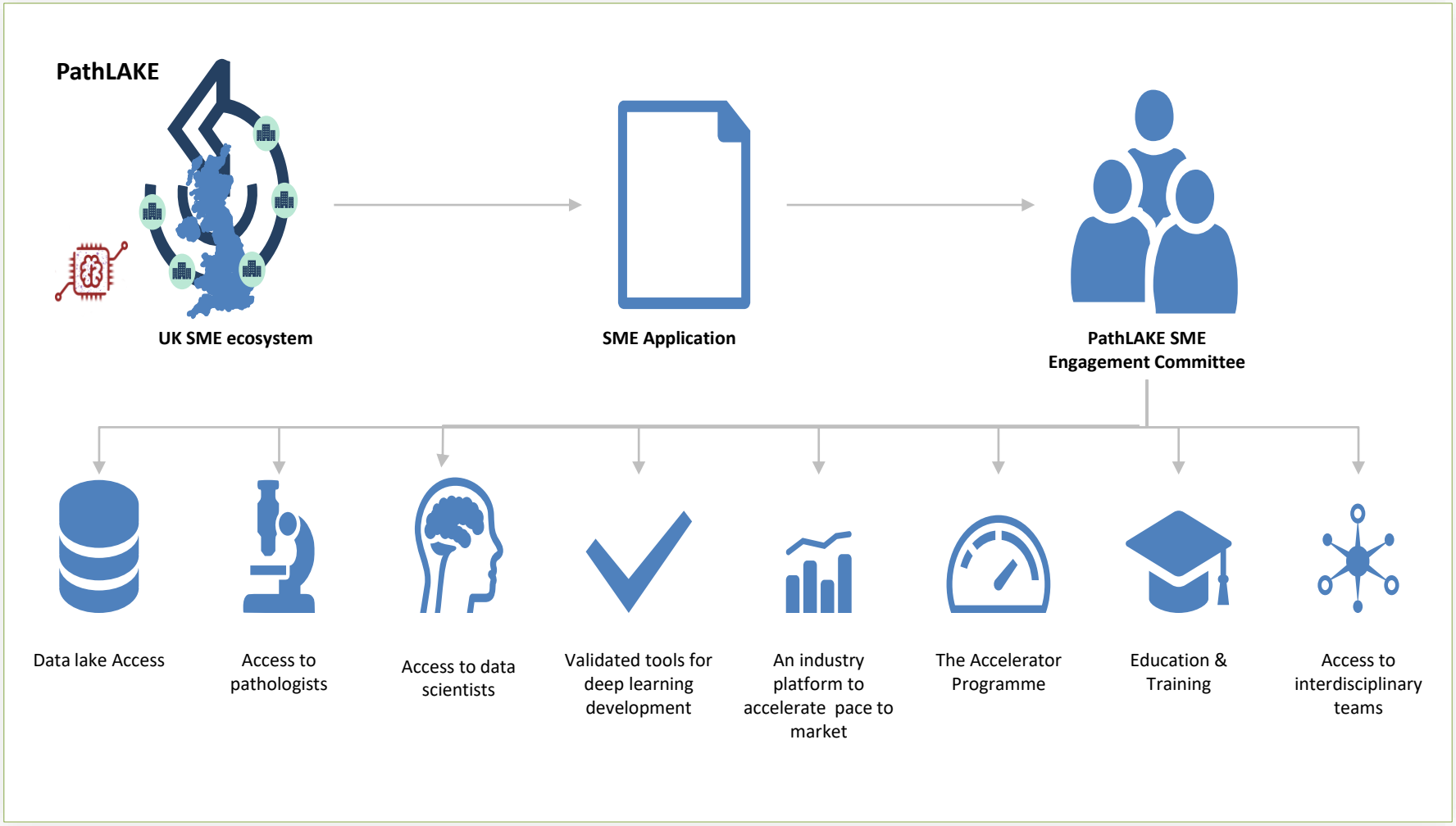
# Artificial Intelligence to help save lives at five new technology centres

The UK's Artificial Intelligence revolution gets new backing, as the Business Secretary announces five new centres of excellence for digital pathology and imaging, including radiology, using AI medical advances.

Published 6 November 2018
From: Department for Business, Energy & Industrial Strategy, UK Research and Innovation, Innovate UK, The Rt Hon Greg Clark MP, and The Rt Hon Matt Hancock MP


- Patients are set to benefit from radical advances in medical technology using artificial intelligence to diagnose diseases at an earlier stage
- The centres will use AI, an area the government is backing in its modern Industrial Strategy, to find new ways to speed up diagnosis of diseases to improve outcomes for patients
- Based in Leeds, Oxford, Coventry, Glasgow and London – but each with partners across many parts of the UK – the centres will develop more intelligent analysis of medical imaging, leading to better clinical decisions for patients, and freeing more staff time for direct patient care in the NHS

# SME Engagement: Ensuring Access



## CM-Path and BIVDA Artificial Intelligence/Image Analysis in Histopathology Workshop

This workshop will focus on the use and potential use of image analysis and artificial intelligence tools in clinical histopathology laboratories. The aim is to identify the steps in a roadmap from development to diagnostic use in a UKAS accredited laboratory with an emphasis on identifying challenges and potential solutions.

**Britannia Room, The Tower Hotel, St Katharine's Way, London, E1W 1LD**
**Thursday 7th June 2018, 10.00am – 16.30pm**

**Agenda**

| | | |
|---|---|---|
| 09.30 | Arrival and registration | |
| 10.00 | **Welcome and Introductions** | Professor David Snead<br>Professor Clare Verrill |
| 10.10 | **"The bigger picture". The Industrial Life Sciences Strategy, AI and Pathology.** | Professor David Snead |
| 10.20 | **Overview of AI development from inception to clinical trial** | Professor Nasir Rajpoot |
| 10.40 | **Post-trial implementation of AI solutions, including regulatory approval** | Professor Dirk Vossen |
| 11.00 | **Regulatory processes for AI in clinical practice** | Dr Stephen Lee |
| 11.20 | Coffee break | |
| 11.35 | **Concept to regulatory approval**<br>• Purpose: Groups work together to highlight the stages in the development of algorithms<br>• Groups: Attendees will be mixed into set groups including a variety of disciplines<br>• Outputs: An outline of the journey and associated challenges with possible solutions | Breakout Sessions |
| 12.20 | **Feedback from breakout groups and discussion** | All |
| 12.40 | Lunch | |
| 13.25 | **Using digital pathology in an NHS histopathology laboratory – what do UKAS expect?** | Dr Jonathan Bury |
| 13.45 | **The role of UKAS in monitoring Digital Pathology and use** | Mrs Alyson Bryant |

# Artificial Intelligence product development

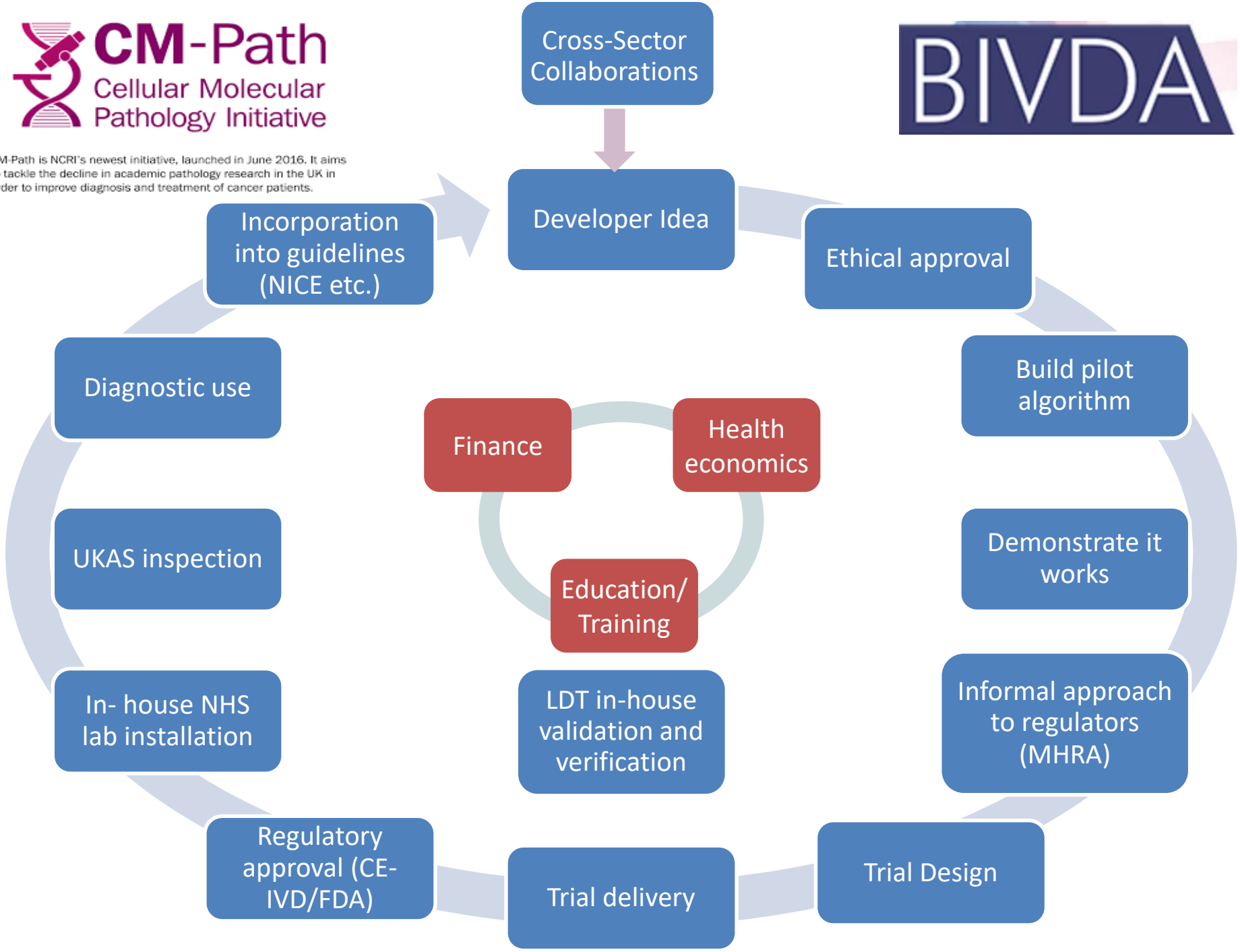
- Product purpose
- Engage with regulators early
- Entire pathway scrutinised
- Control of software used
- Pathologist certification
- Quality assurance of annotations
- Trial design

University Hospitals Coventry and Warwickshire NHS Trust

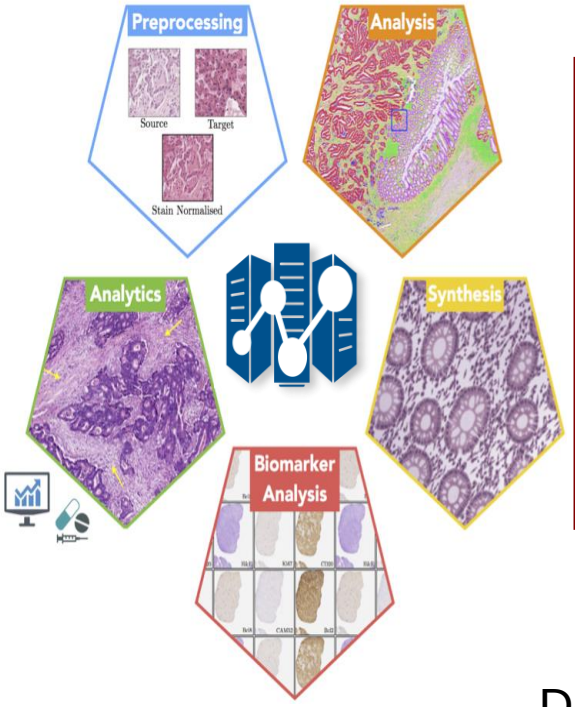
CM-Path
Cellular Molecular Pathology Initiative

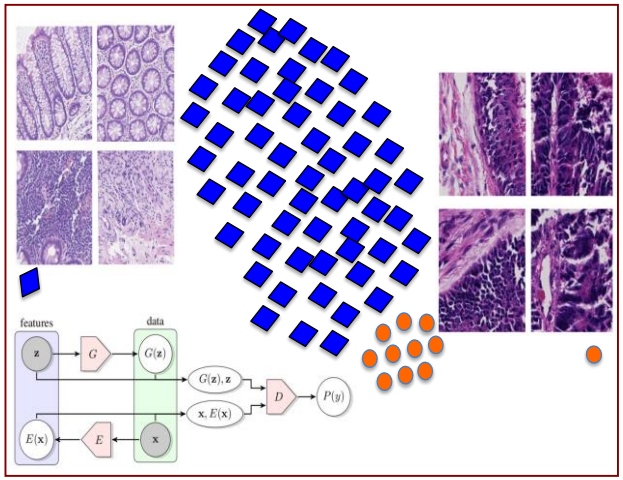
CM-Path is NCRI's newest initiative, launched in June 2016. It aims to tackle the decline in academic pathology research in the UK in order to improve diagnosis and treatment of cancer patients.

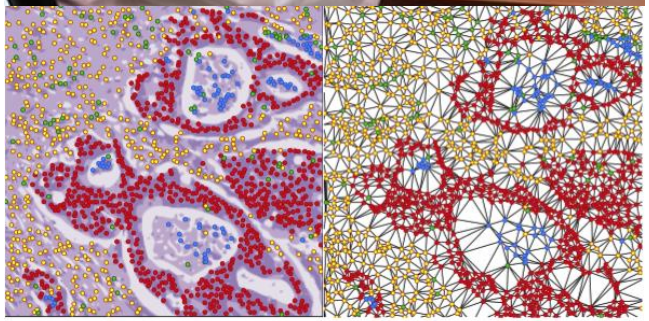
BIVDA

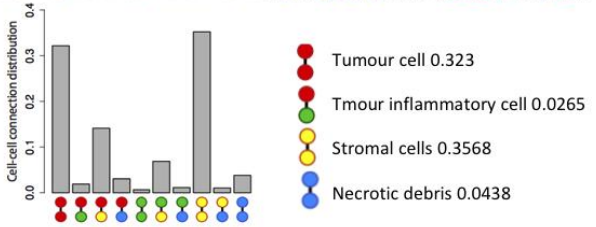


# Pathology Image Analytics






Deployment in practice
Interoperability across platforms
Variability of sections
Variability of staining
Quality assurance of performance
Implementation controls
Accreditation

# Acknowledgements

Innovate UK

NHS National Institute for Health Research

PHILIPS innovation + you

EPSRC Engineering and Physical Sciences Research Council

BBSRC bioscience for the future

THE ROYAL SOCIETY

الصندوق القطري لرعاية البحث العلمي Qatar National Research Fund Member of Qatar Foundation

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Dr Adnan Khan (ICR)

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# 15th EUROPEAN CONGRESS ON DIGITAL PATHOLOGY (ECDP) 2019

11-13 April 2019 | ecdp2019.org @ESDIPatho

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