
BREAKING THE GLASS SLIDE HABIT: How digital pathology is revolutionizing tissue biomarker research and diagnostic pathology

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2nd European Workshop on Tissue Imaging and Analysis
Heidelberg June 25-26, 2010



Image Analysis in Pathology is not new !

Harley TJ Jr, Kanal LN, Randall NC: System considerations for automatic image screening. *Pictorial Pattern Recognition*. Edited by GC Cheng, RS Ledley, DK Pollock, A Rosenfeld. Thompson, Washington D.C., 1968

THE JOURNAL OF HISTOCHEMISTRY AND CYTOCHEMISTRY
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PERFORMANCE TESTING FOR AUTOMATED PRESCREENING DEVICES IN CERVICAL CYTOLOGY¹

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Vol. 27 No. 1, pp. 613-620, 1979
Printed in U.S.A.

An Image Analysis System for Cervical Cytology Automation Using Nuclear DNA Content

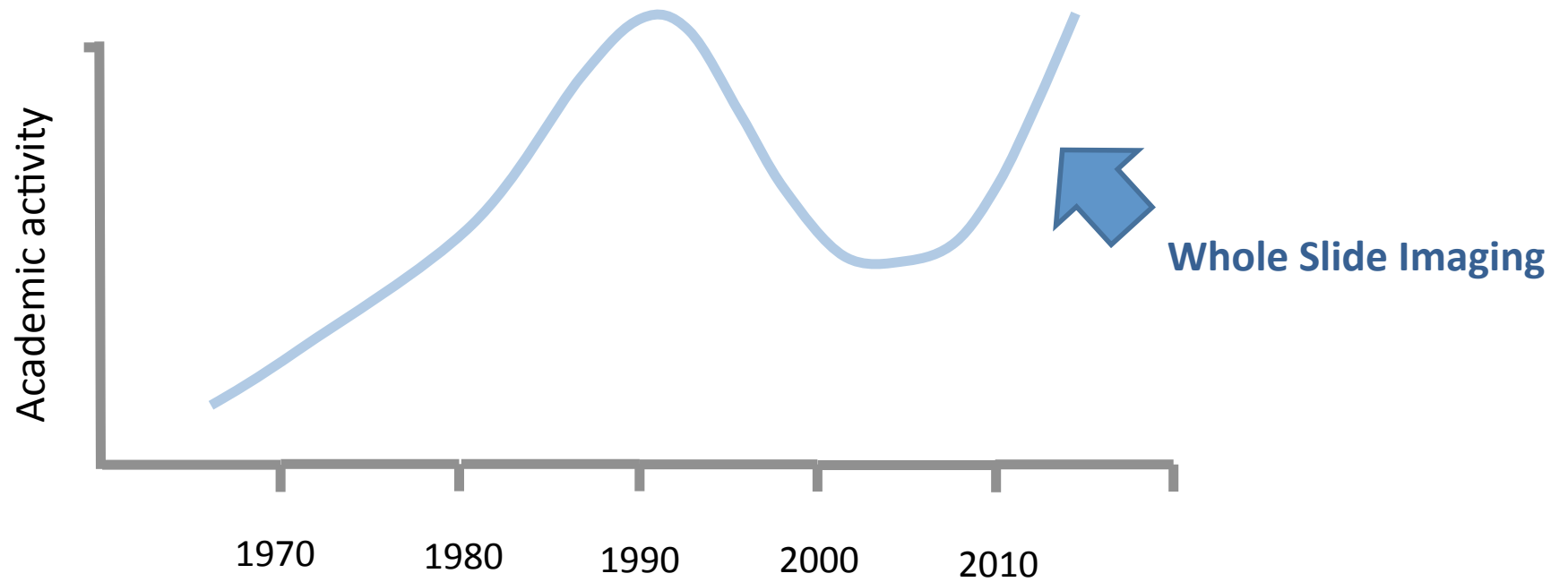
JAMES H. TUCKER

MRC Clinical and Population Cytogenetics Unit, Western General Hospital, Crewe Road, Edinburgh, EH4 2XU, Scotland

Received for publication July 7, 1978

Digital Pathology

Morphometry, Cytometry, Stereology, Image Analysis, Machine Vision, etc. Etc.



Scanning Hardware Technology

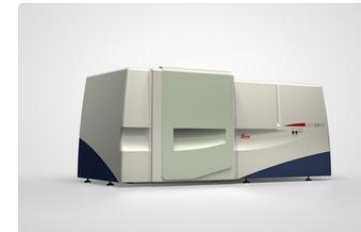
HAMAMATSU



ai APPLIED IMAGING



Olympus .slide

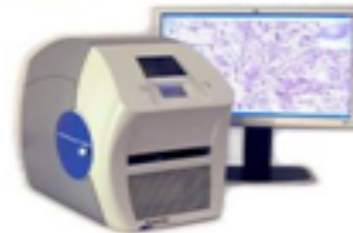


Leica
MICROSYSTEMS



Bioimagine

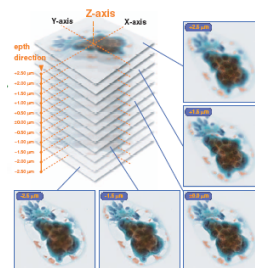
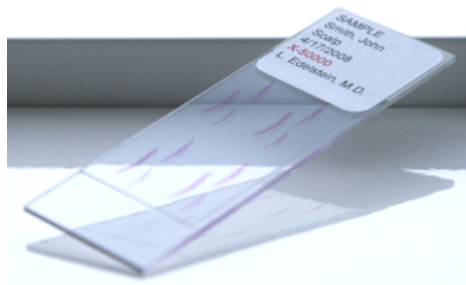
Aperio
TECHNOLOGIES



ZEISS



A change is coming: Virtual Microscopy



Digital Pathology

Education



Research

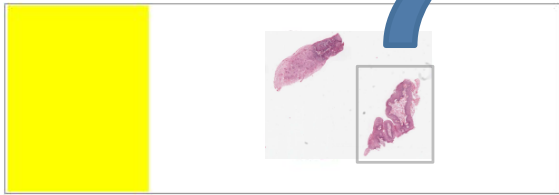


Clinical Diagnosis

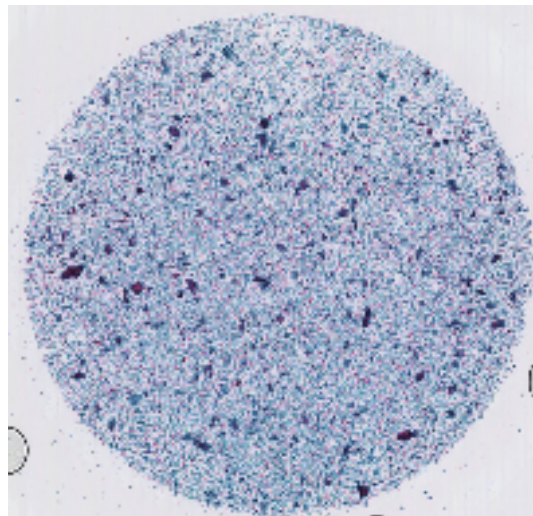
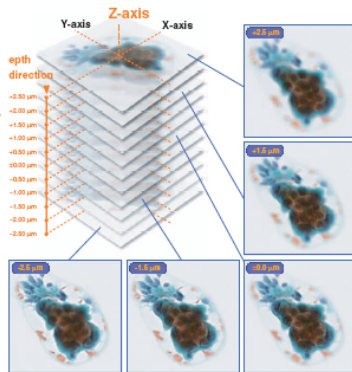
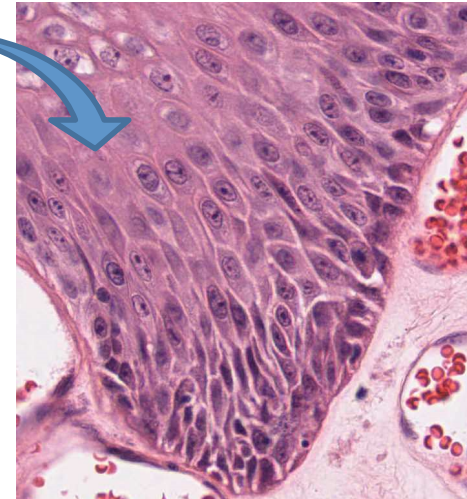
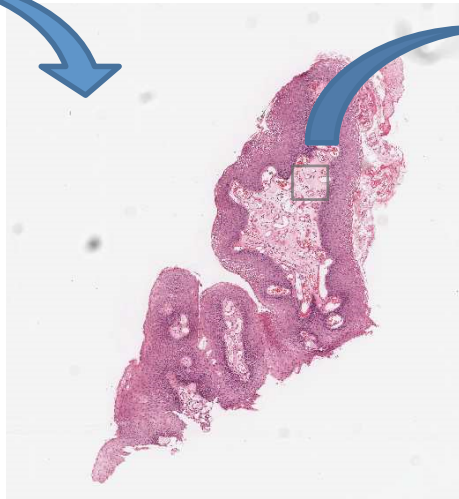




Virtual Slides are very large images !



0.23 microns per pixel
104,000 x 85,000 linear pixels
Billions of pixels
Gigapixel images
300 cases per day = 100 terabytes per year

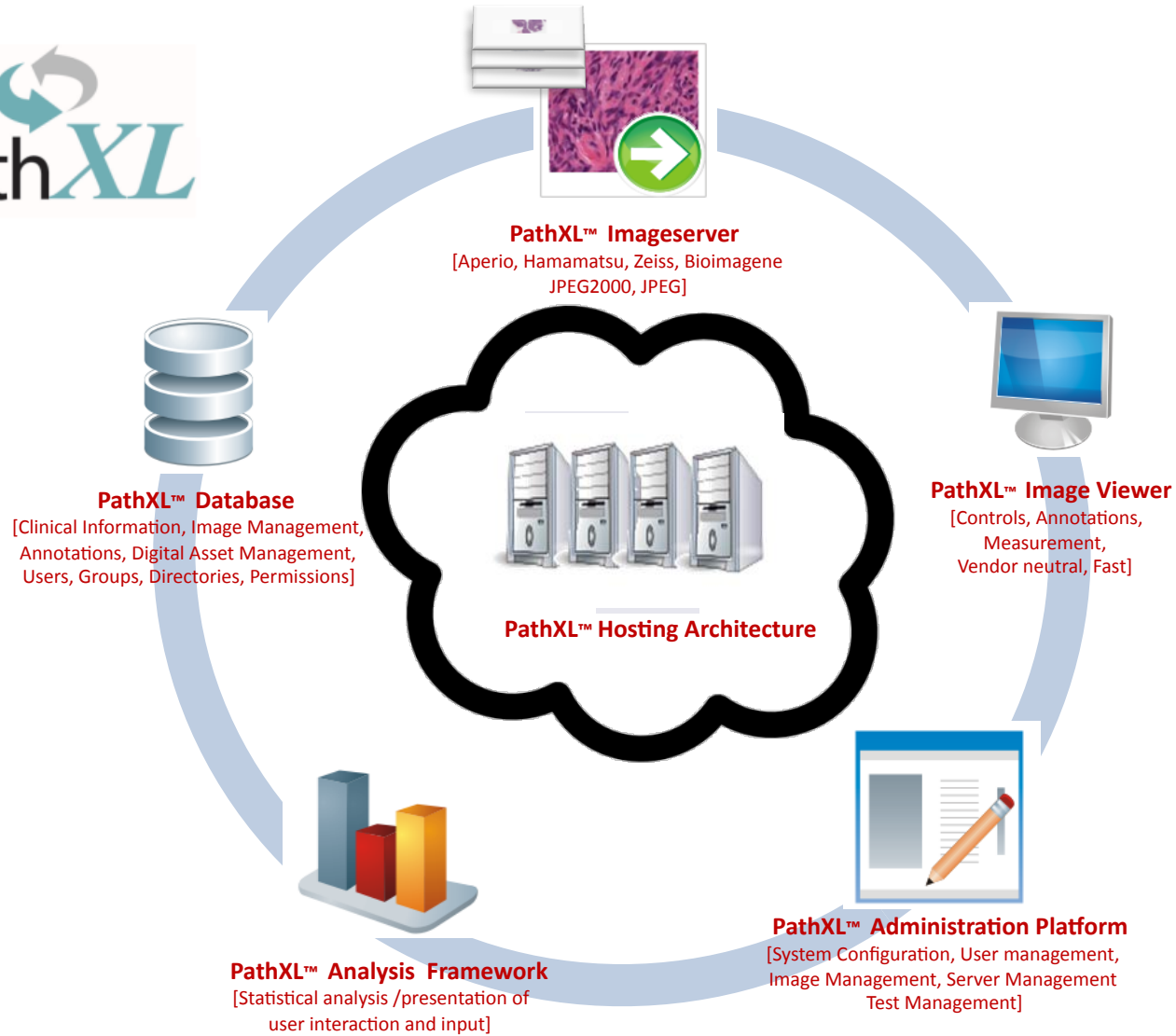


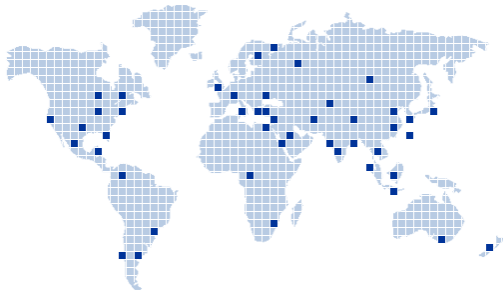
16 Gigabyte : TIFF JPEG compressed

Teaching Series
Cervical LBC
100 samples
54 layers
4 Terabytes
Slide catalogue

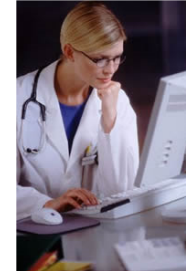
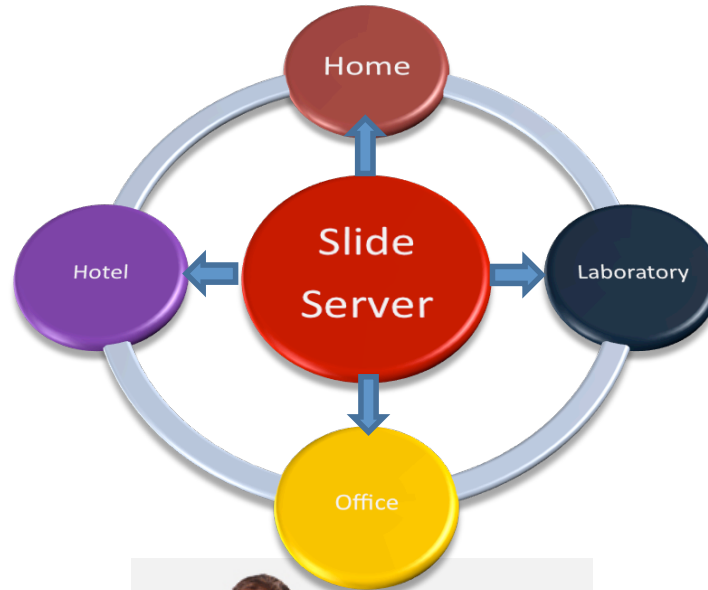
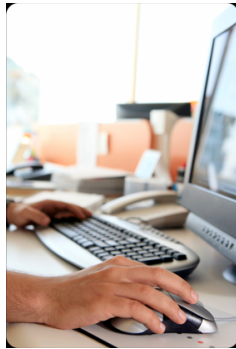


Managing Virtual Slides?





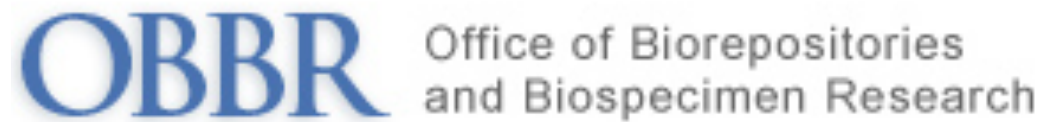
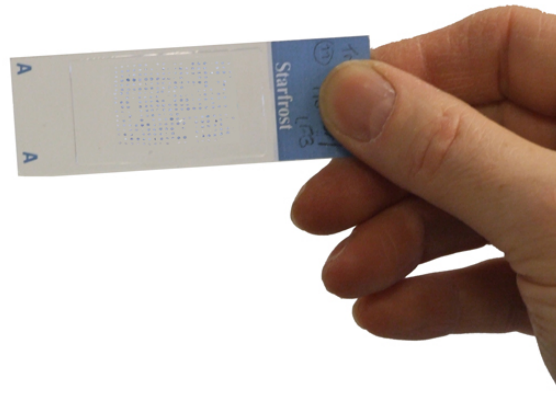
Access to virtual slides, anytime, anywhere



**How does this support tissue research
and diagnostic practice?**

**Virtual Tissue Banking
Biomarker Research
Routine Diagnostic Laboratory**

Biobanking and Tissue



Northern Ireland Virtual Tissue Archive



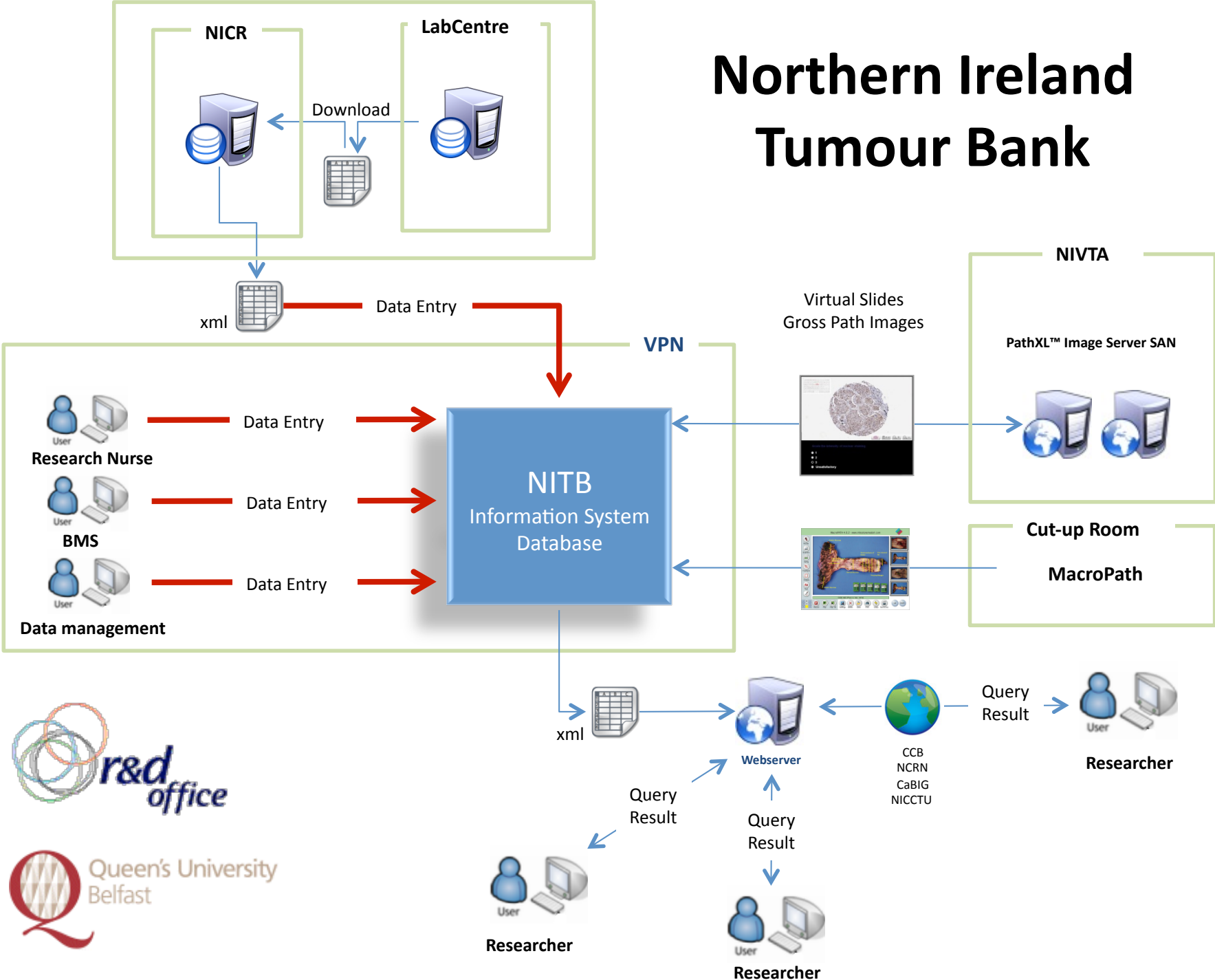
(NIVTA)



invent



Northern Ireland Tumour Bank

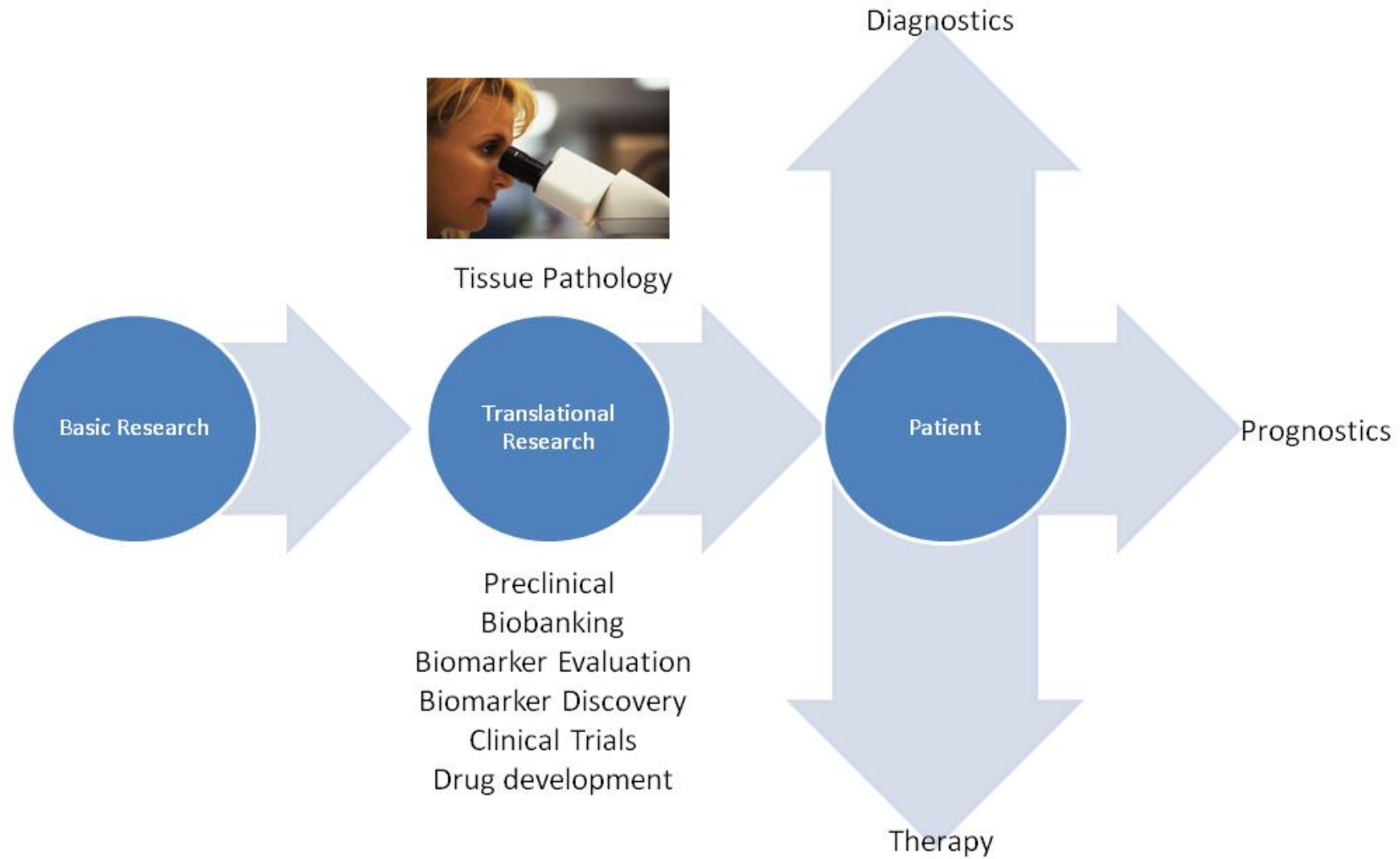




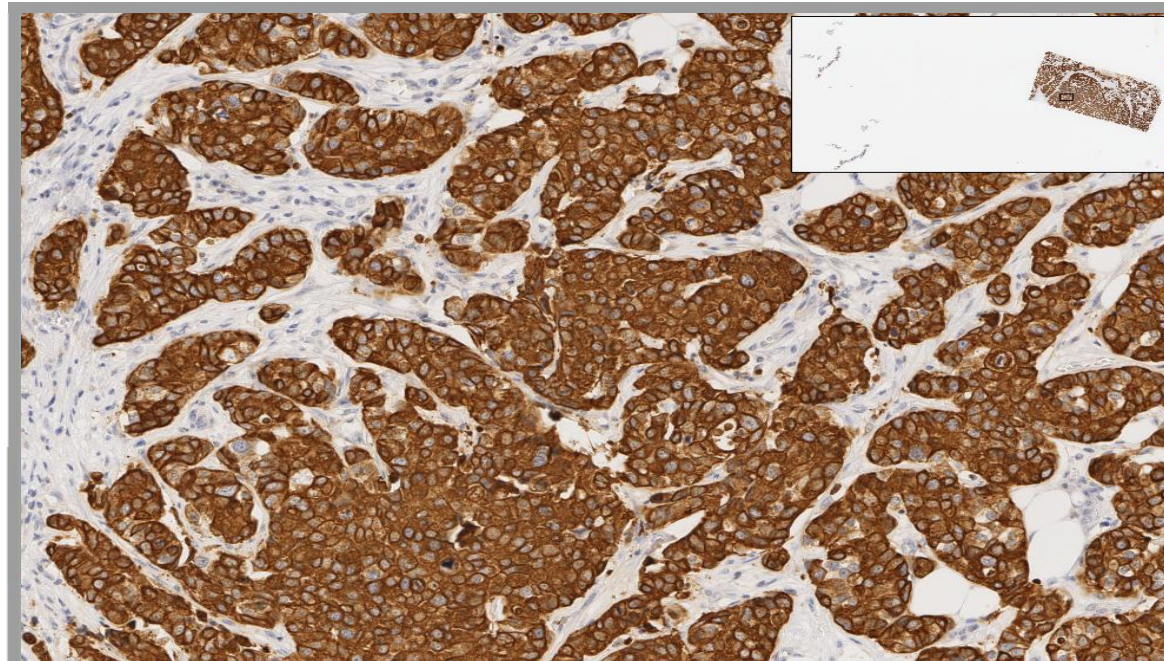
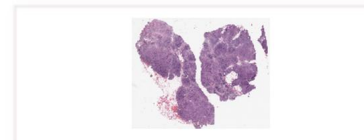
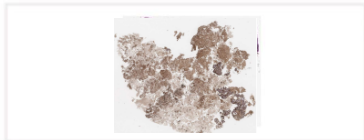
Biomarker Research



Tissue Research and the Pathologist



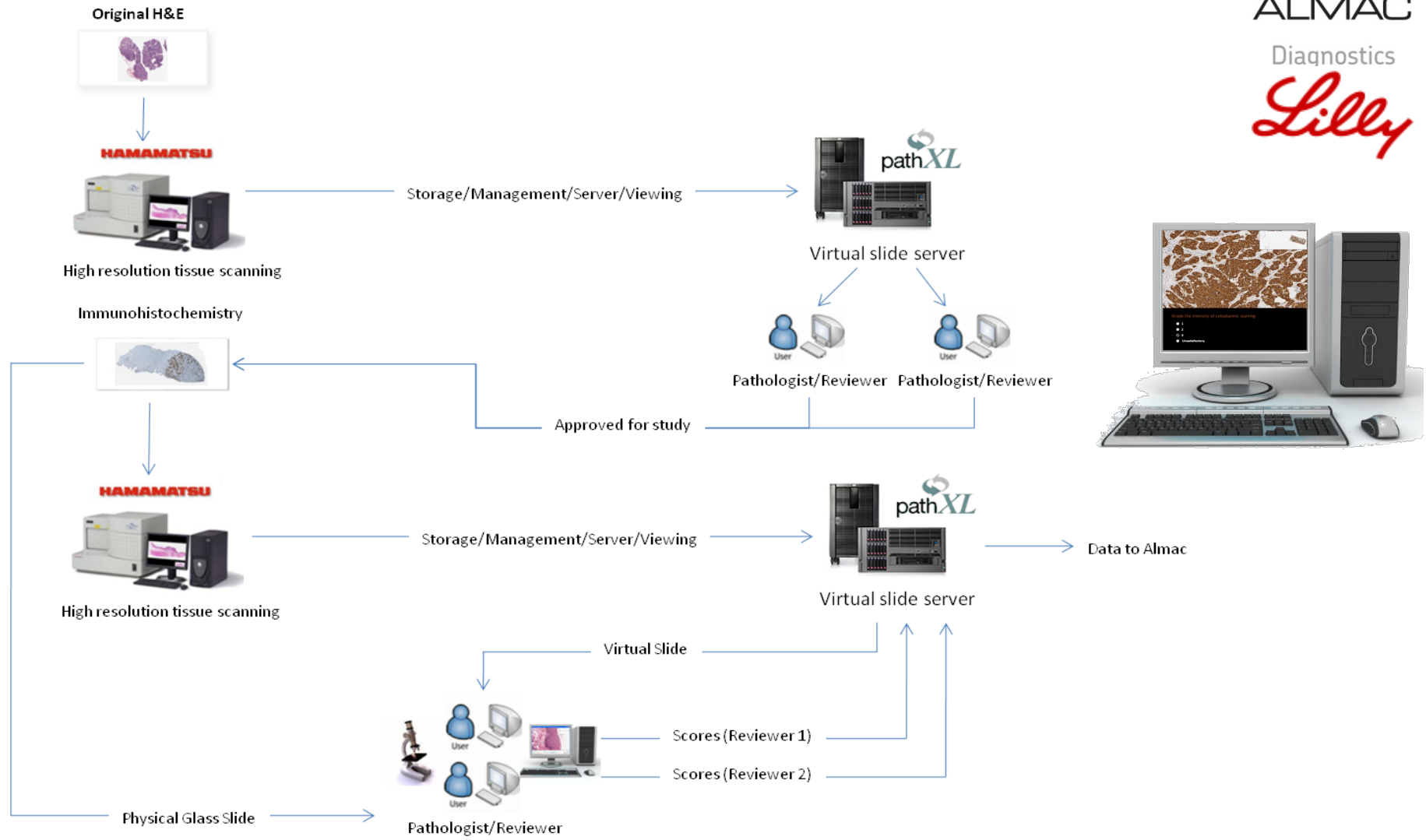
Biomarker Scoring Interface



Grade the intensity of cytoplasmic staining

- 1
- 2
- 3
- Unsatisfactory

Remote Evaluation of Biomarkers of Response in Lung NCCLC



Remote TMA Scoring

TMA Toolbox

Core Information

Slide ID: TMA52P
Core ID: F16LMP
Column: B
Row: 2

Patient Data:
Sex: Male
Age: 67

Anatomic Site:
Gastrointestinal

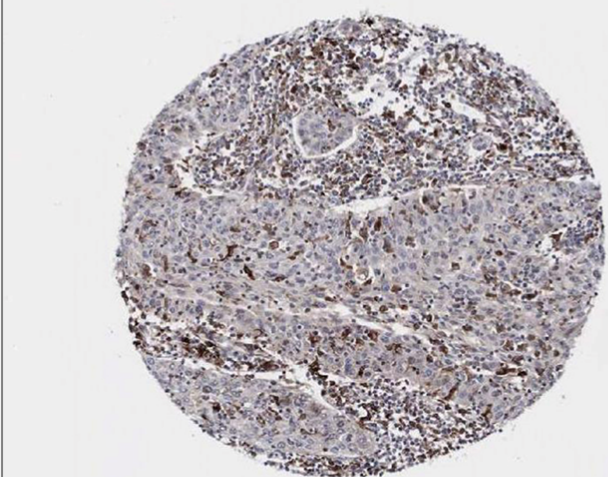
Tissue type:
Stomach

Diagnosis:
Adenocarcinoma

TNM Classification:
T2b

Immunohistochemistry:
ERK2


Image View Tools



TMA Core Image

⊕ ⊖ x8 ▲

TMA Map



A B C D E F G H I J K L
1 2 3 4 5 6 7 8

Navigation

⏪ ⏩ Column: Row:

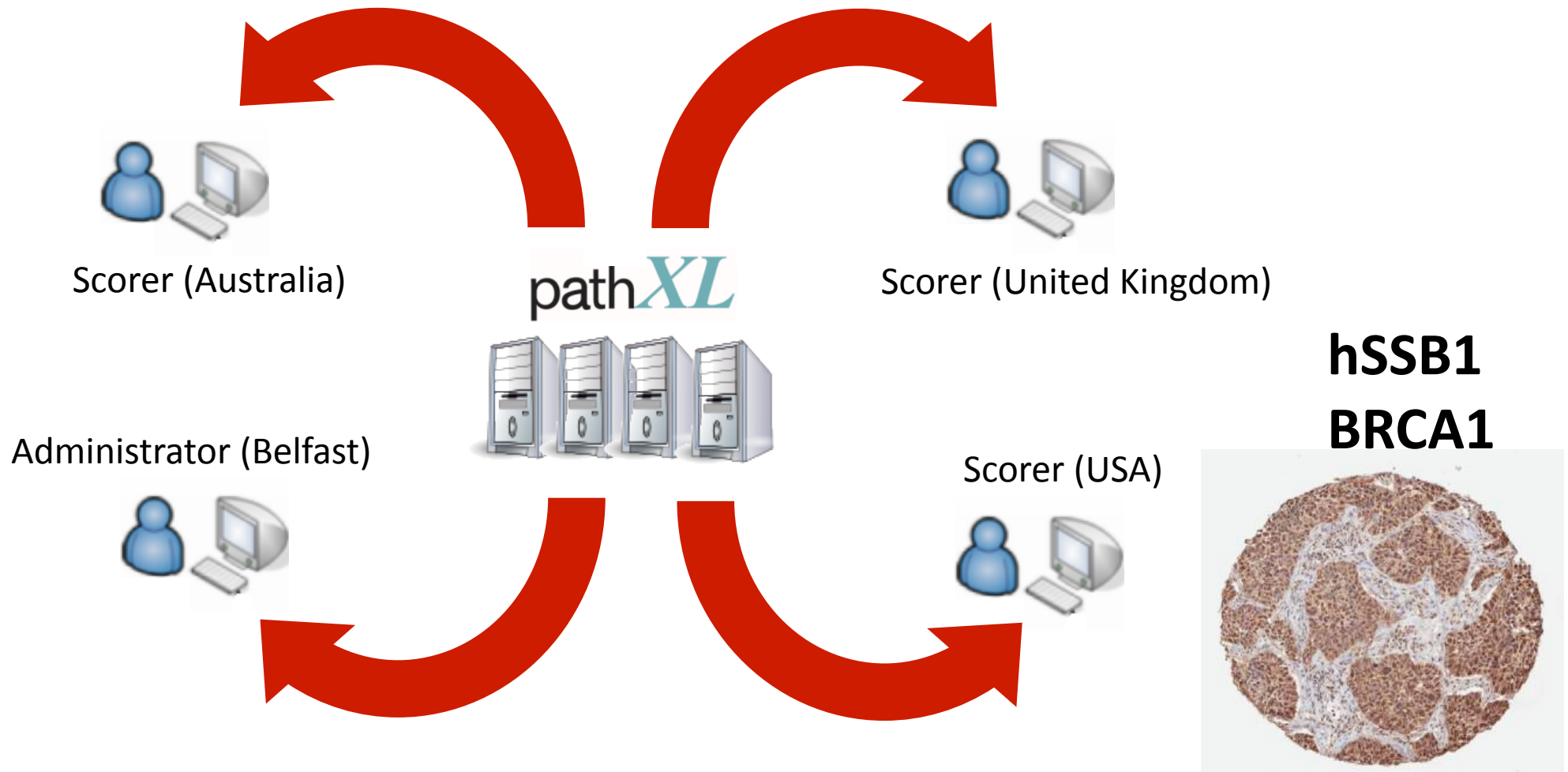
Scoring

Question 1 Score the intensity of nuclear staining

- 1
- 2
- 3
- Unsatisfactory

Next question ☰

Remote Biomarker Scoring

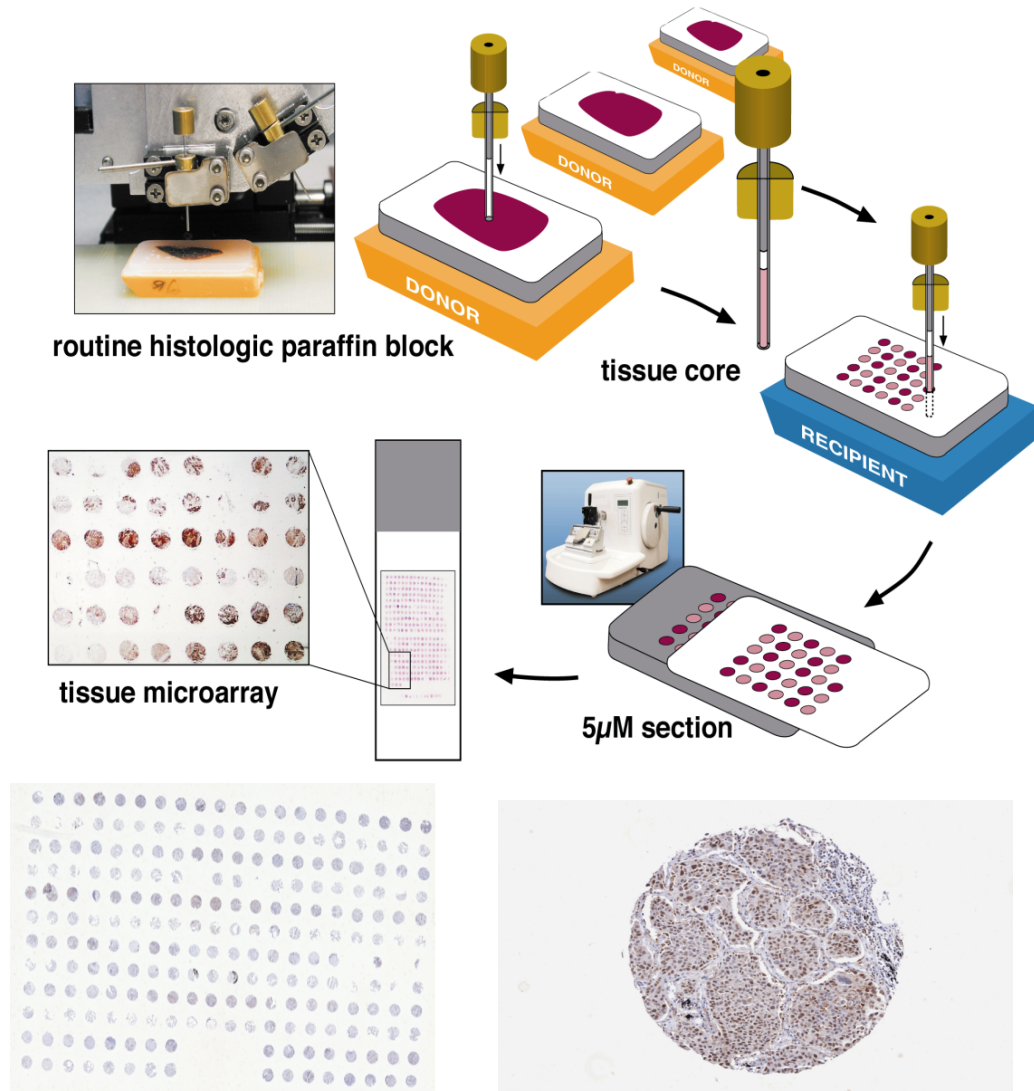




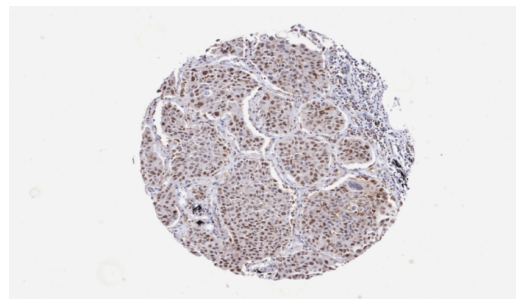
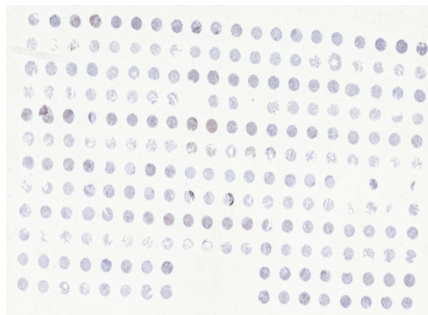
High Throughput Biomarker Imaging



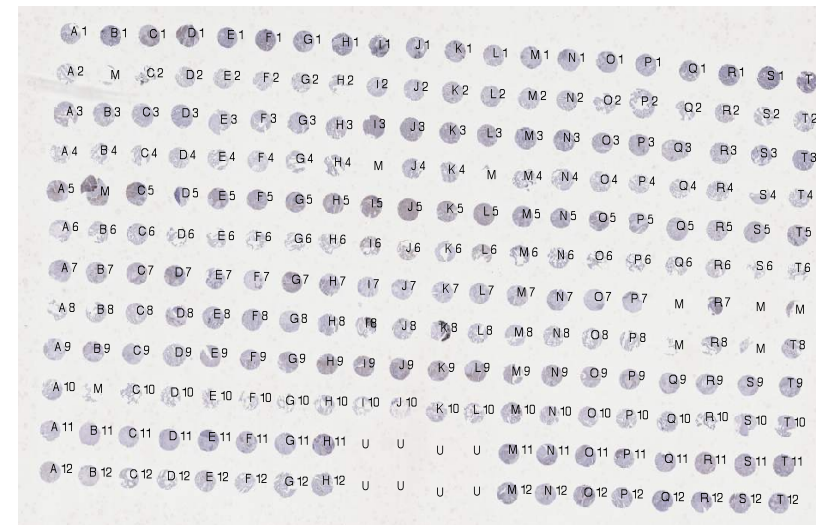
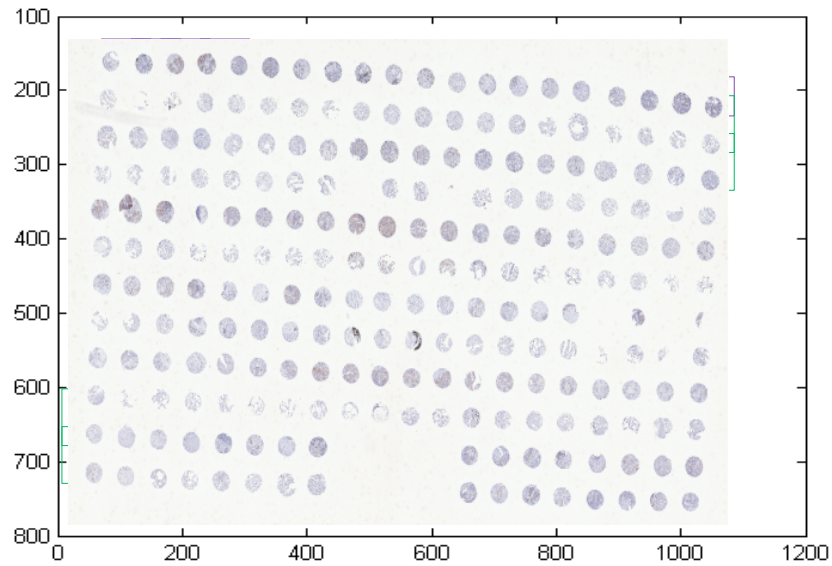
Tissue Microarrays (TMAs)



Single experimental assay
Complex analytics
Visual Interpretation
Time consuming
Subjective
Reliable?

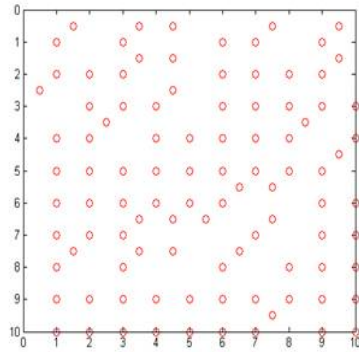


De-arraying algorithm

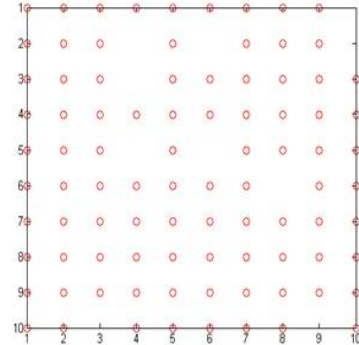


Models for Testing De-arraying

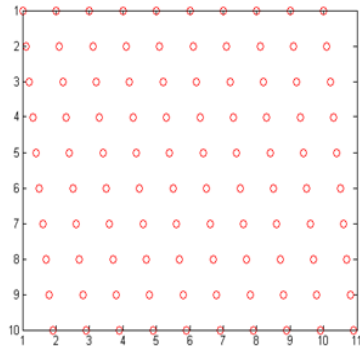
Misalignment



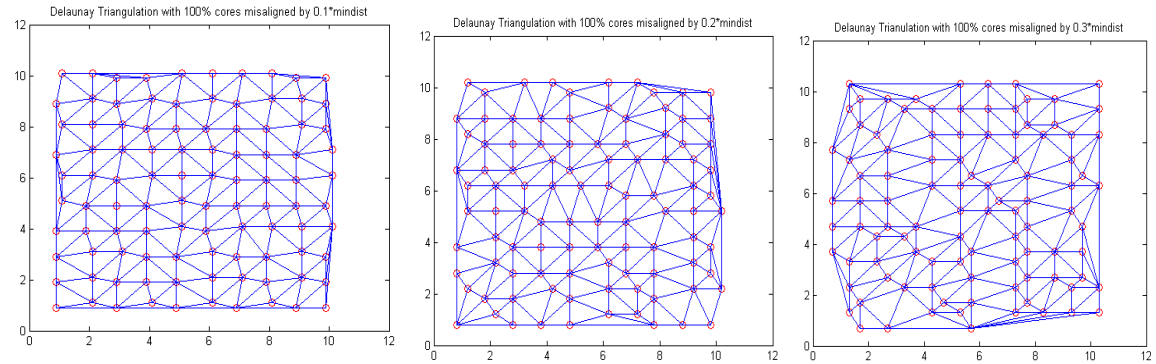
Missing



Skewing



Irregularity Index



30,000 model TMAs of increasing irregularity

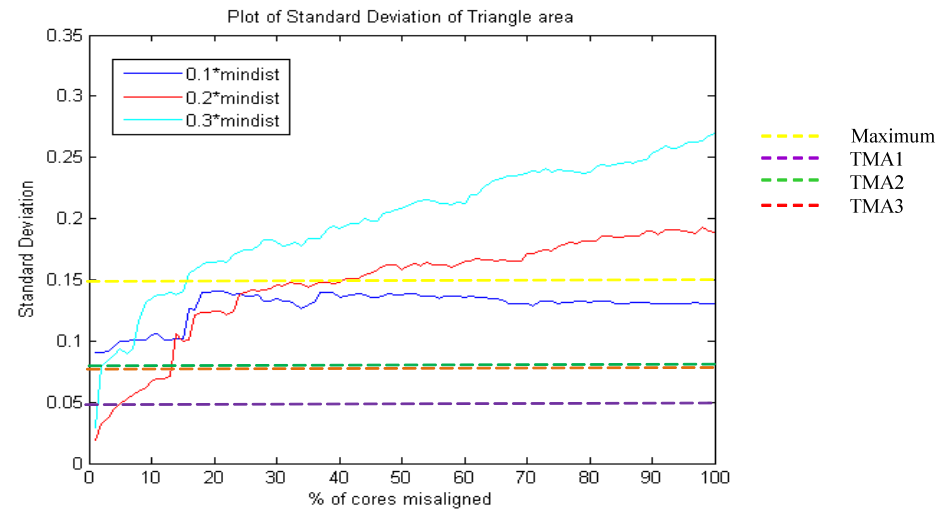
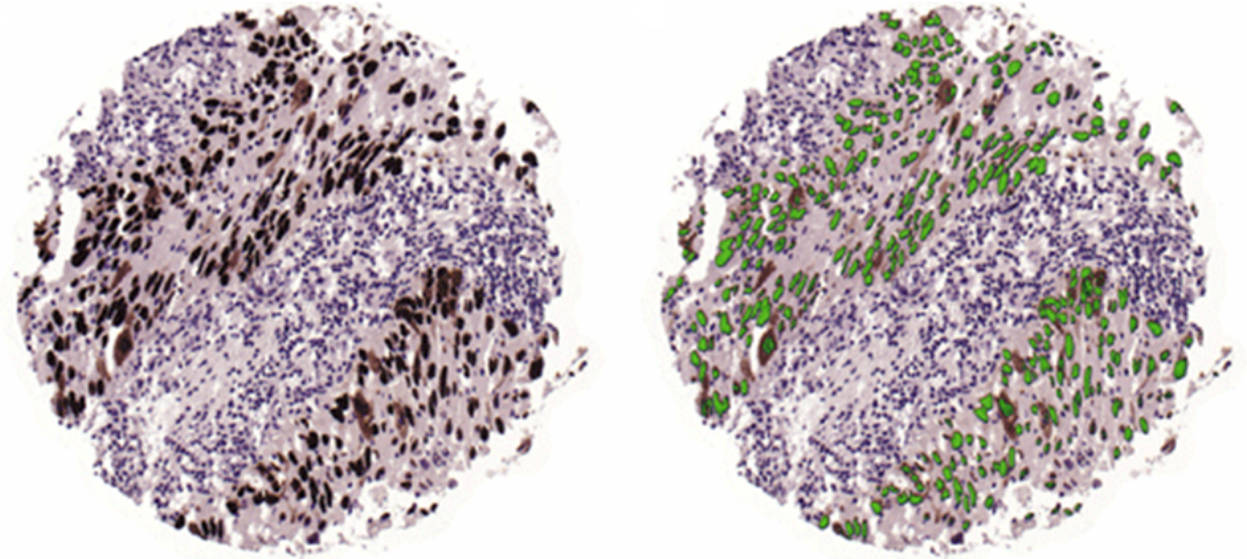
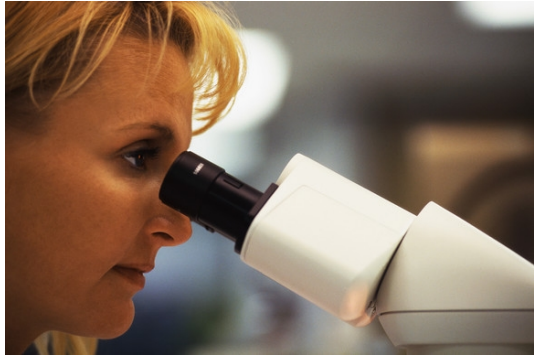


Image Analysis on Virtual TMAs and virtual slides

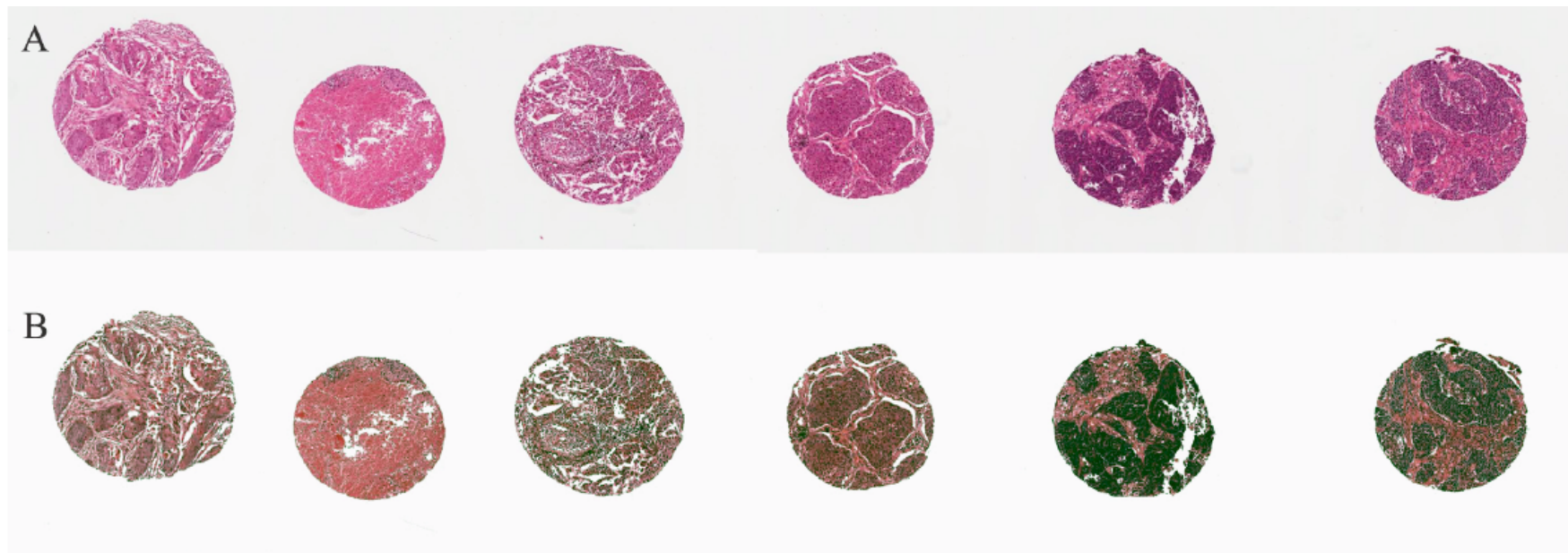


Objectivity
Speed



Biomarker Studies in Non-Small Cell Lung Cancer [NSCLC]

Pemetrexed (Alimta) Treatment for Non-Squamous tumours only

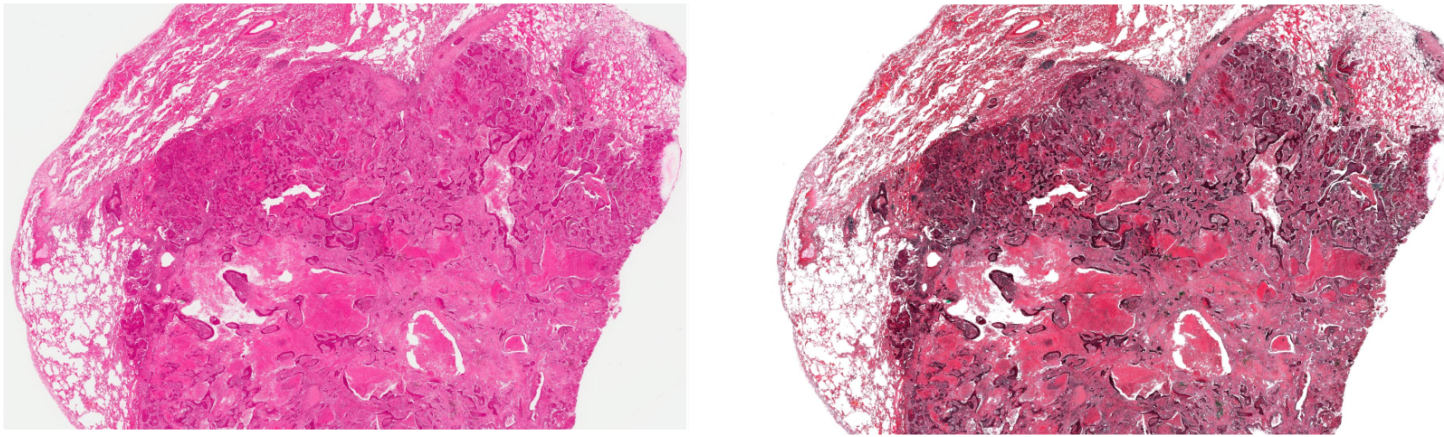


	Squamous	Non-squamous
Squamous	261	11
Non-squamous	22	75

CWW algorithm
Adaptive Boosting
92% correct classification

Biomarker Studies in NSCLC

Whole section analysis

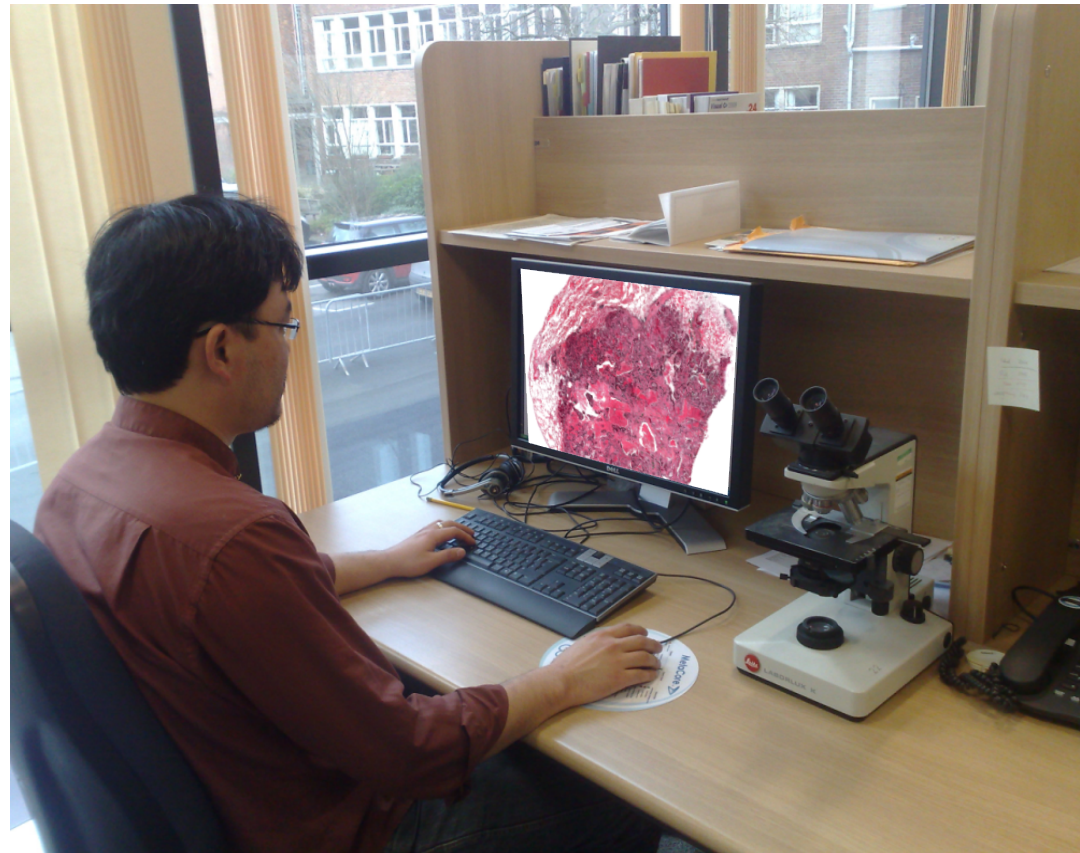


	Squamous	Non-squamous
Squamous	84	9
Non-squamous	4	187

95% correct classification

Augmented Visualisation

Visual support for NSCLC squamous/non-squamous classification



Biomarker Studies in NSCLC

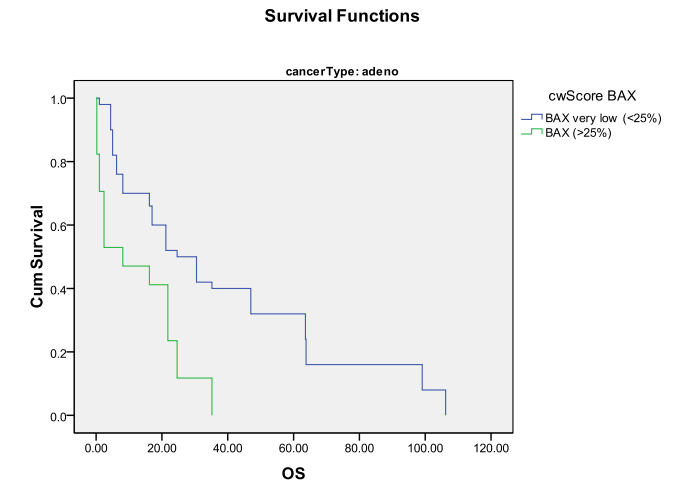
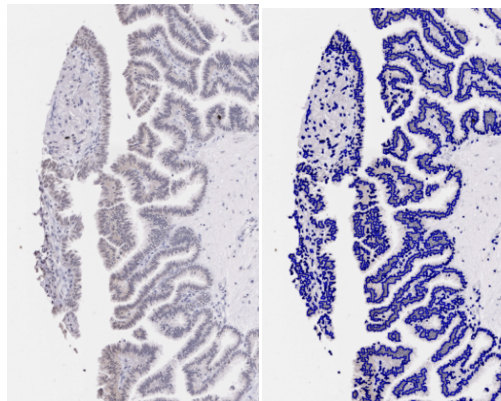
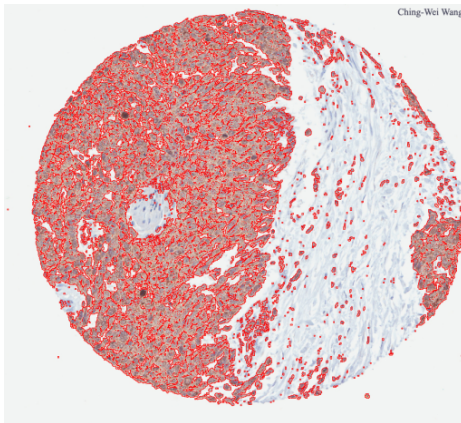
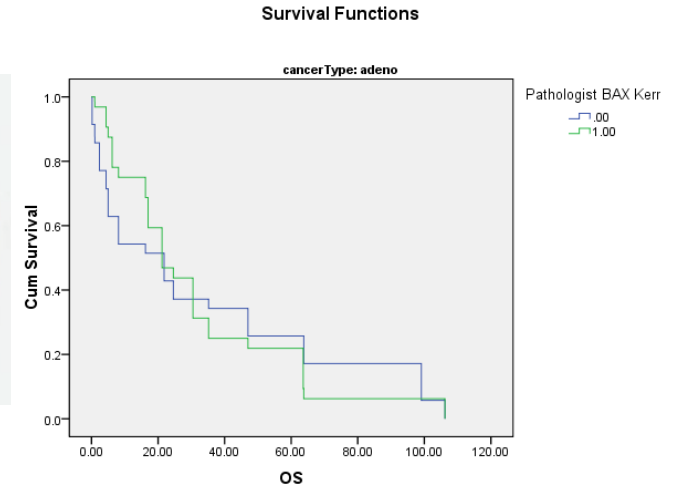
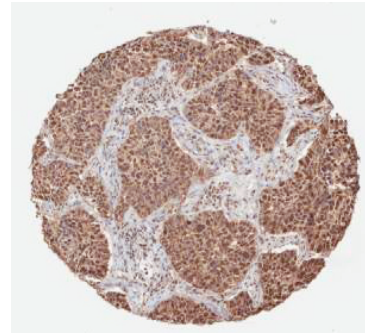
Automated imaging of BAX, BAK, BRCA1, hSSB1 as predictors of patient outcome

458 samples across 4 TMAs

BAX IHC

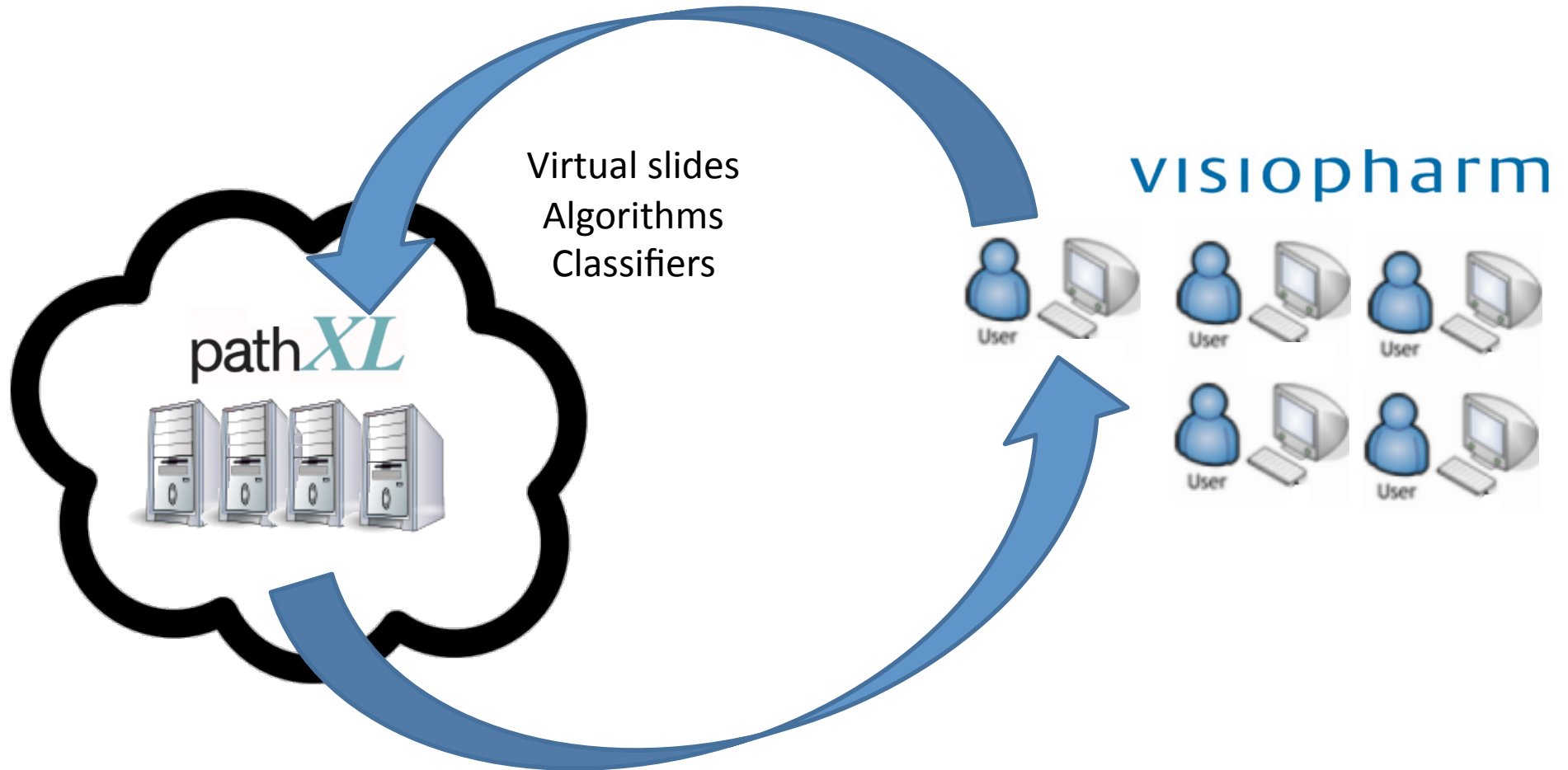
(1) Scored by x2 experienced pathologists

(2) Automated scoring using image analysis

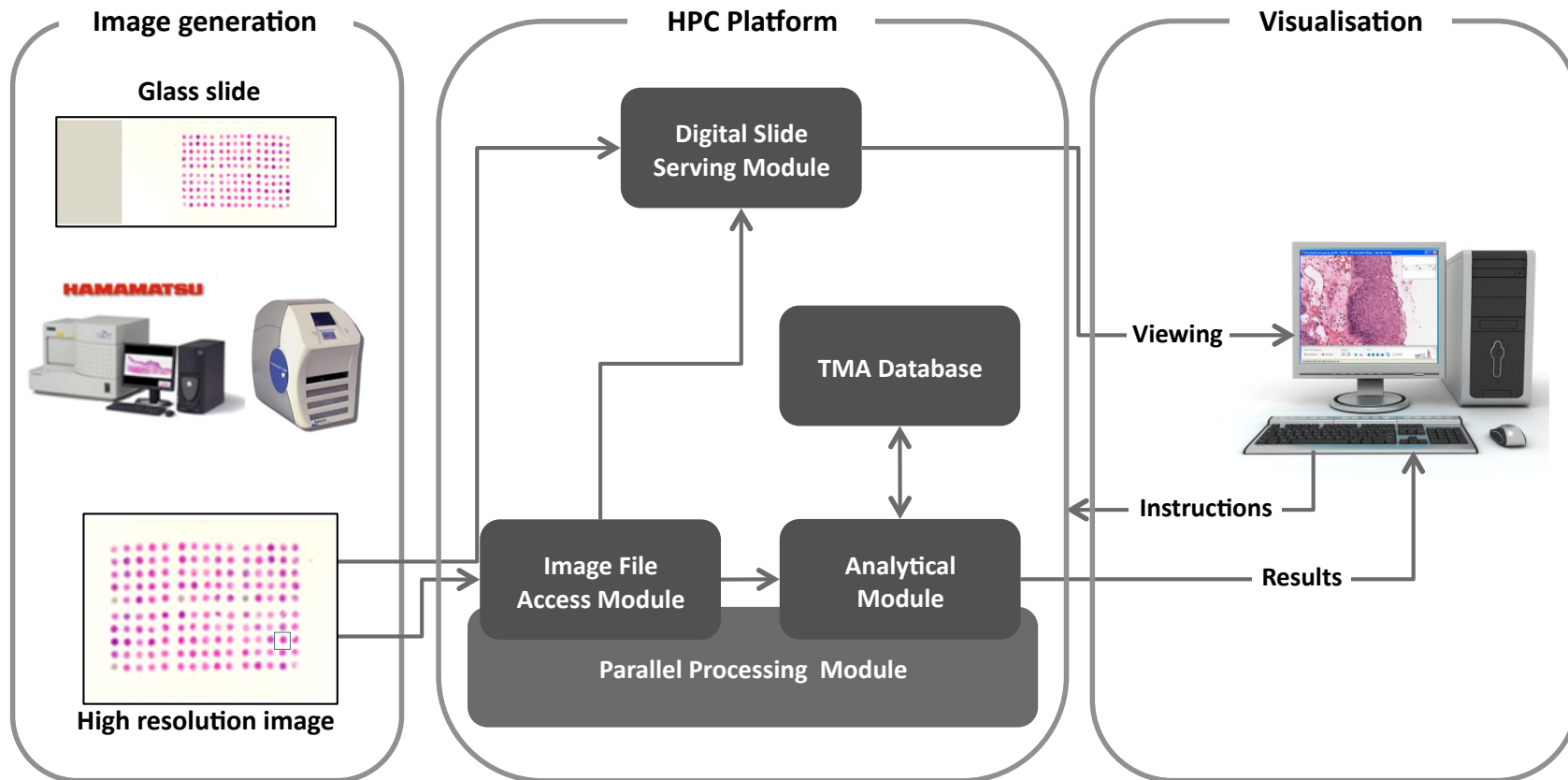




Cloud Computing and Image Analysis



High Performance Computing Architecture



HP Blade System Cluster 9000 processor cores

C++ programming

MS Message Passage Interface (MPI)

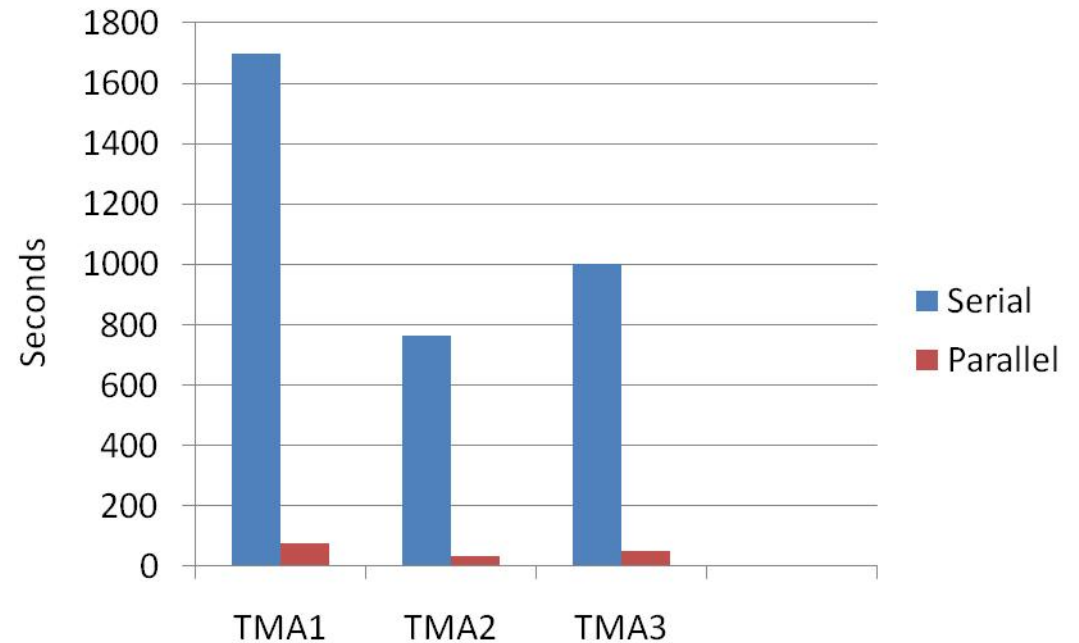
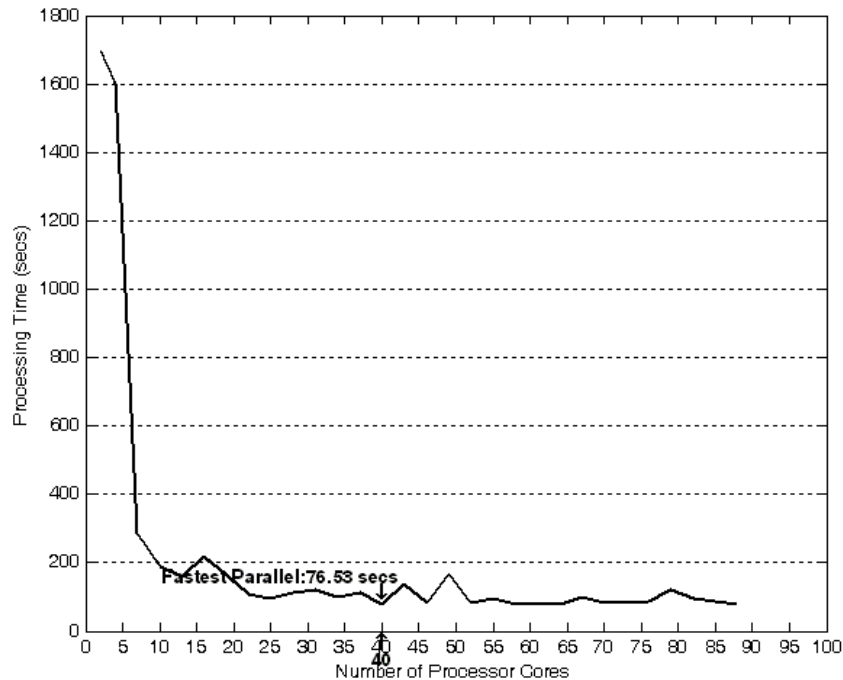
Centralised Dynamic Load Balancing



i n v e n t

Dr Yin Hai Wang

HPC provides significant analytical speedup for TMA analysis



Processing time: 30minutes → 77seconds
Speedup=22.19

Clinical Diagnostics



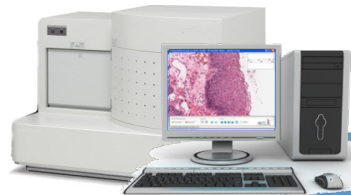
Request form and Specimen Processing



Glass slides



Slide Scanner



Pathology PACS Image Server Cluster

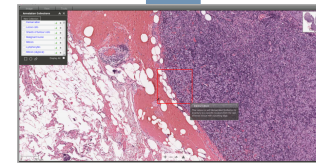


pathXL

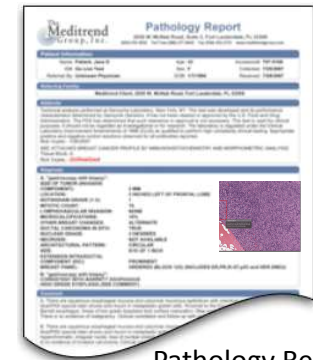
Digital Archive



Laboratory LIMS



Whole Slide Scan



Pathology Report

Consultation network



Pathologist

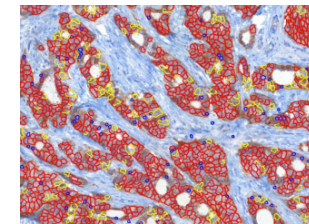
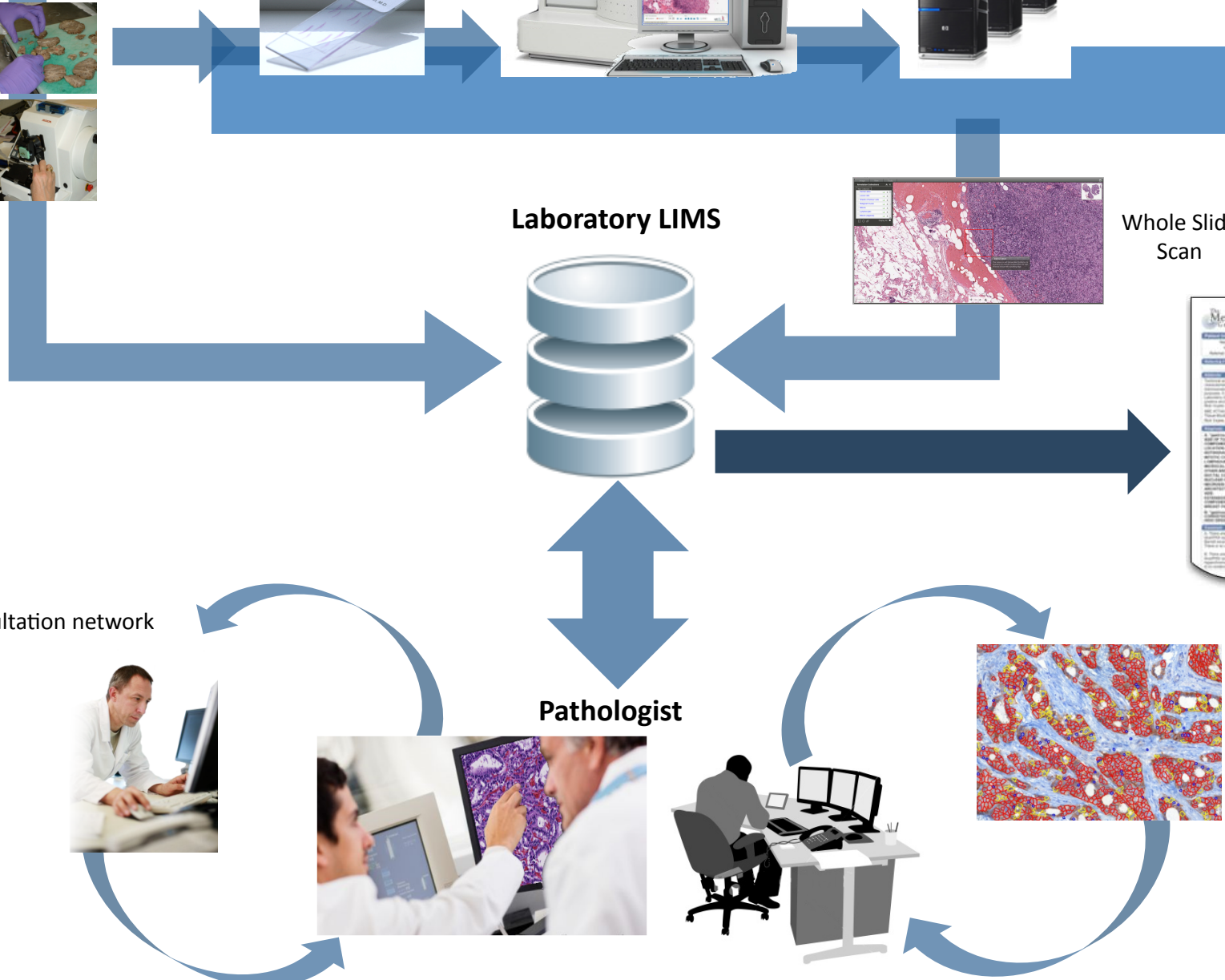
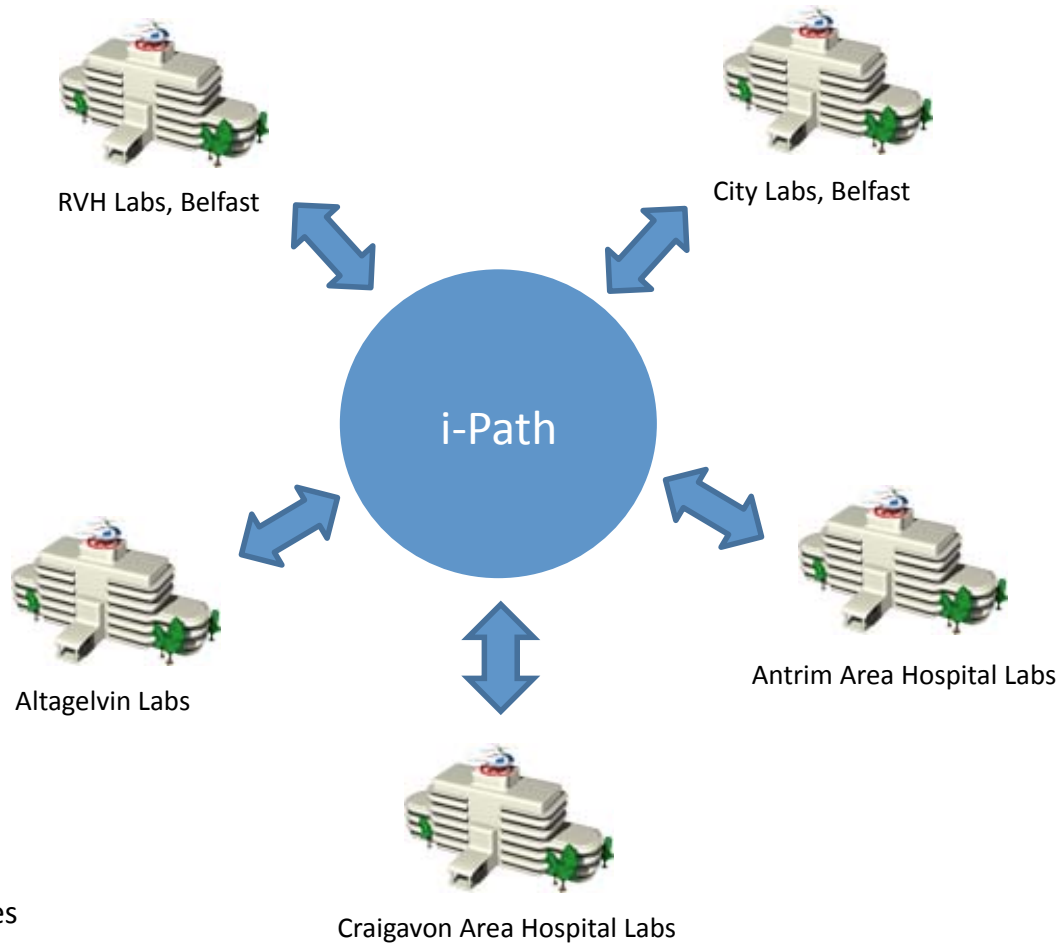


Image Analysis Decision Support





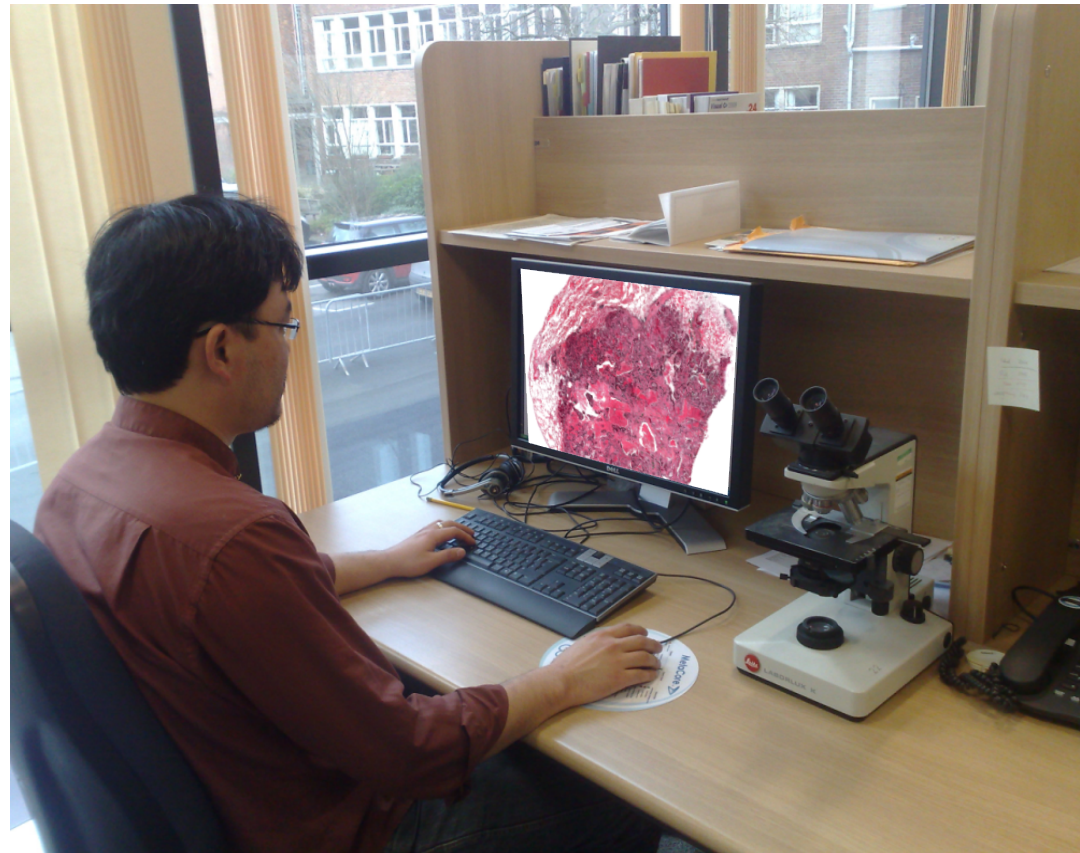
Northern Ireland Trial of Digital Pathology



- Bowel Cancer Screening Programme
- Lung Pathology
- Routine scanning of all specimens
- Image Quality
- Scanning requirements
- Storage requirements
- Networking requirements
- Diagnostic Precision by comparison with slides
- Integration with LIMS

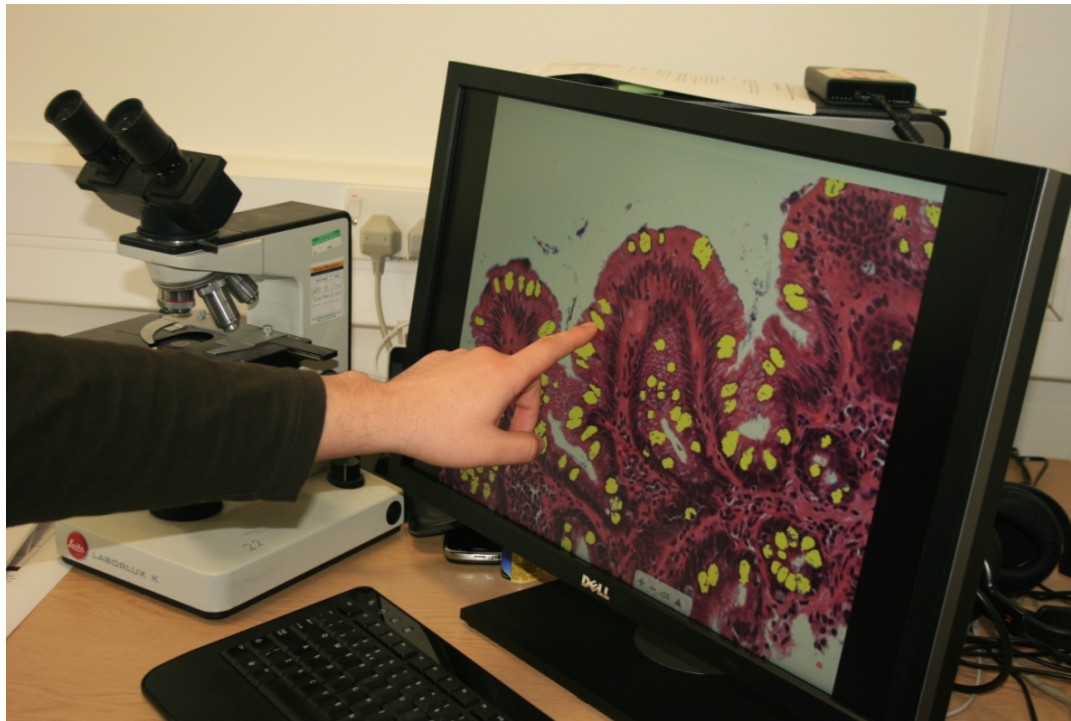
Augmented Visualisation

Visual support for NSCLC squamous/non-squamous classification

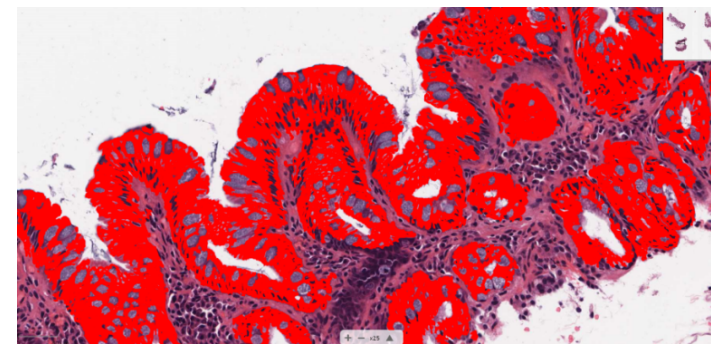
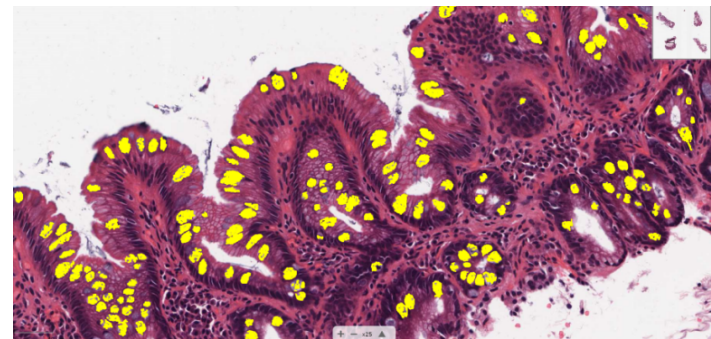
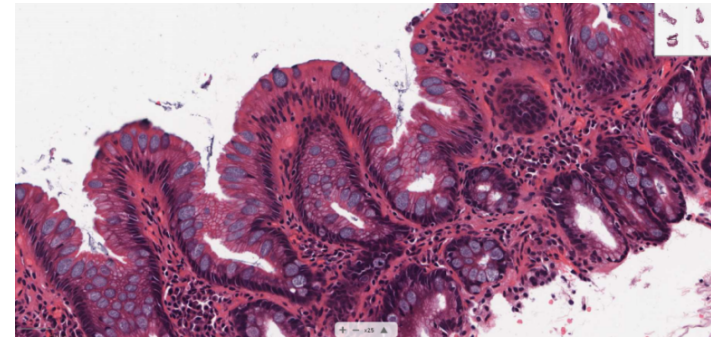


Augmented Visualisation

Diagnostic support and biomarker evaluation
in Barret's oesophagus assessment

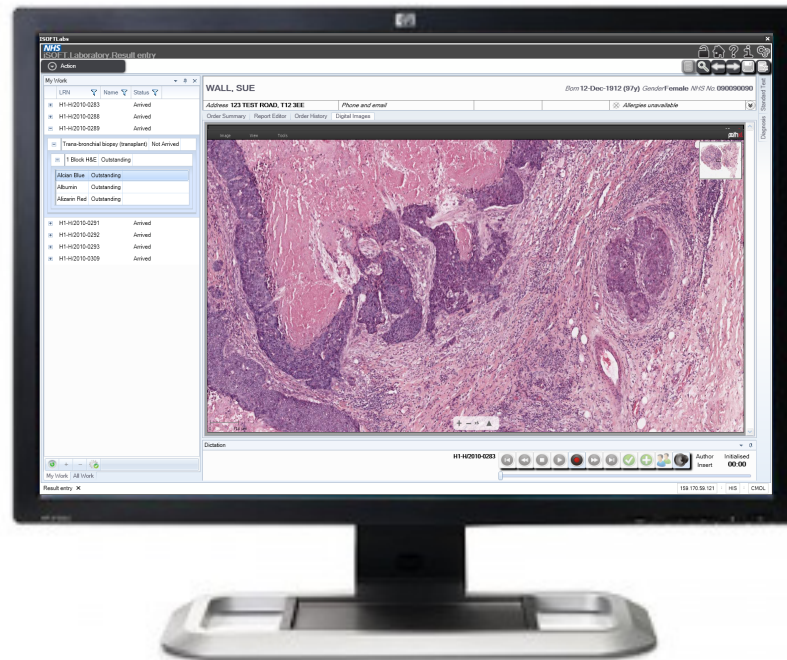


Providing the diagnostic pathologist with a
library of new tools to strengthen diagnosis
as an integral part of their diagnostic process



Augmented Visualisation and Multitouch Surface Technology





The Digital Pathology Tipping Point