



Leica

BIO SYSTEMS

Advancing Cancer Diagnostics
Improving Lives

IMAGE QUALITY IN AI ALGORITHMS

David de Mena

*For In Vitro Diagnostic Use
The clinical use claims described for the products in the information supplied
have not been cleared or approved by the U.S. FDA or are not available.*

Confidential - Company Proprietary

150+ YEARS OF IMPACT AND INNOVATION

1.6M+ Patient Diagnoses Enabled Per Week

More than 150 years tackling pathology challenges head on, from better slide production to world-leading Digital Pathology empowering AI development.

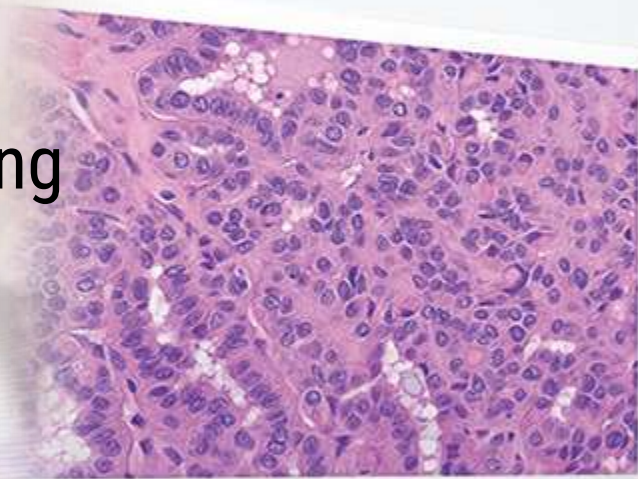
1872



Present

DIGITAL PATHOLOGY APPROACH

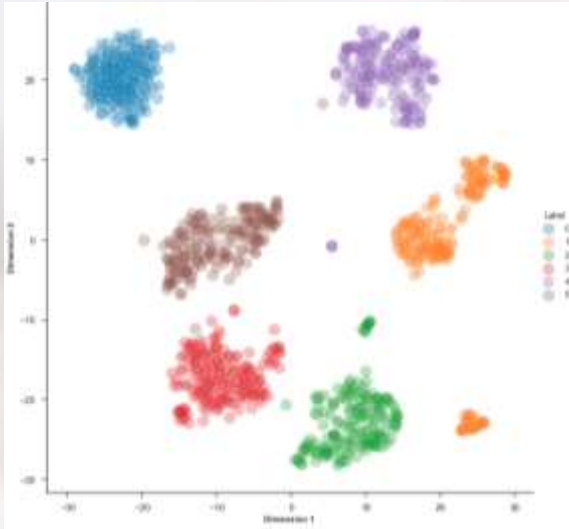
- Exhaustive computing
- Ability to quantify
- Efficient
- Learn the underlying relationships based on the data



CHALLENGES IN DIGITAL PATHOLOGY

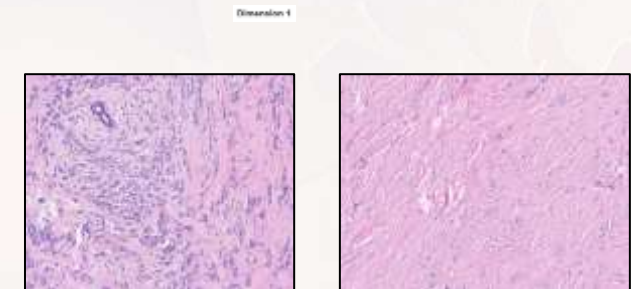
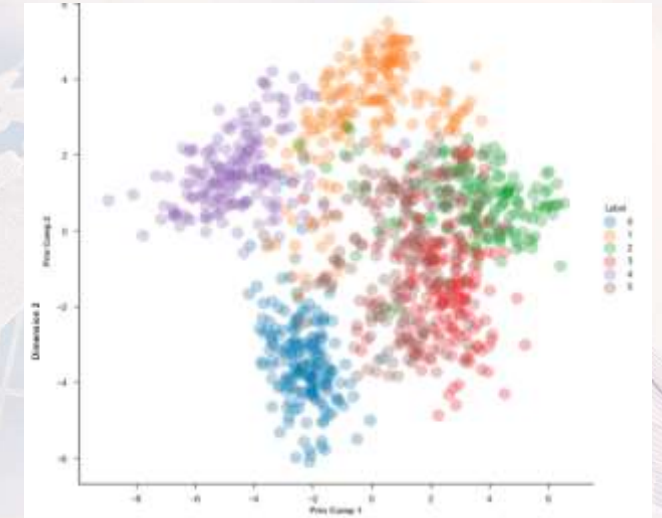
PREDICTION COMPLEXITY SCALE

Highly Separable



- High Intra-Class Variance, Low Inter-Class Variance
- Morphological heterogeneity

Large Overlap

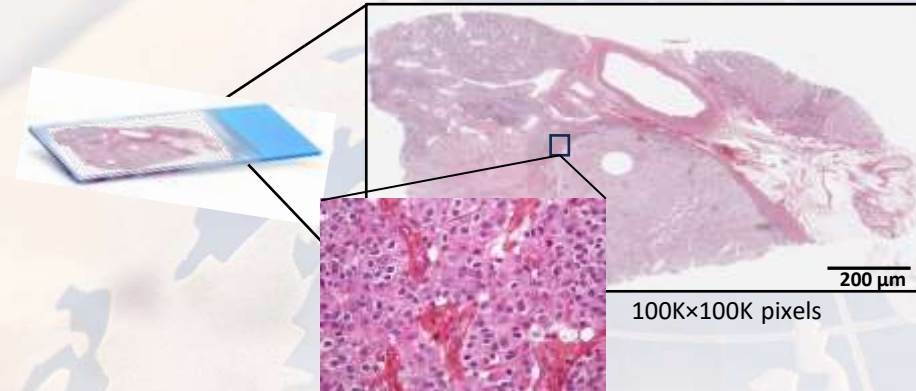
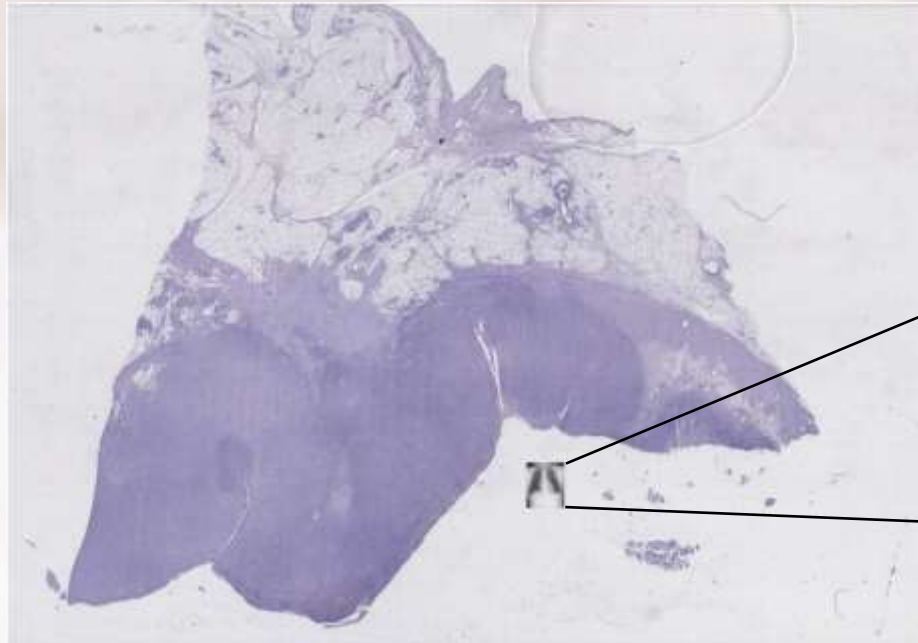


Problem complexity

CHALLENGES IN DIGITAL PATHOLOGY



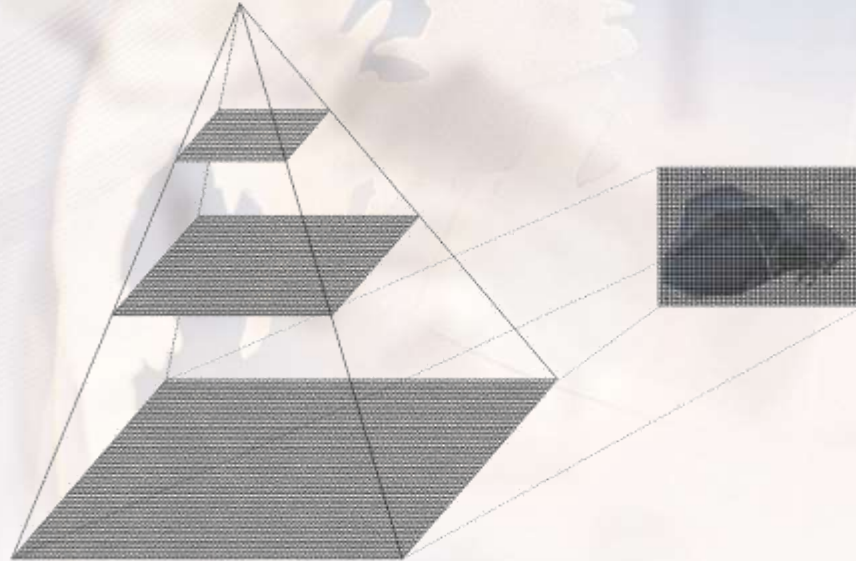
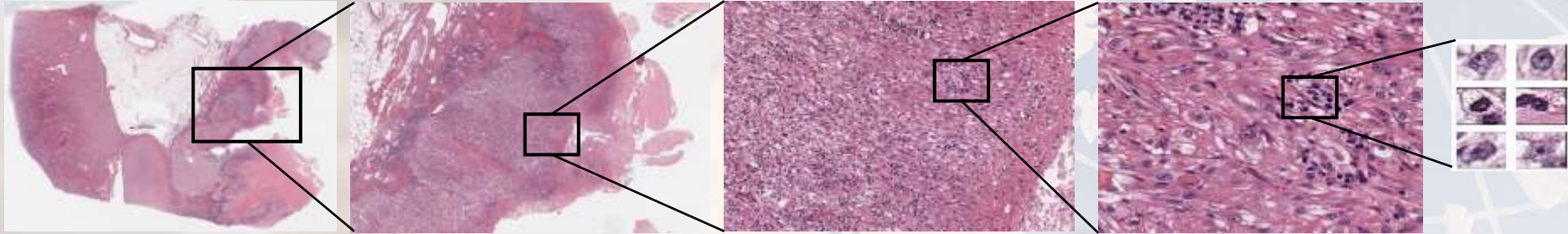
4096×4096 pixels



- **Humongous size images**
- **Giga-pixel images**

CHALLENGES IN DIGITAL PATHOLOGY

- Digesting the whole slide for pathologists is not feasible

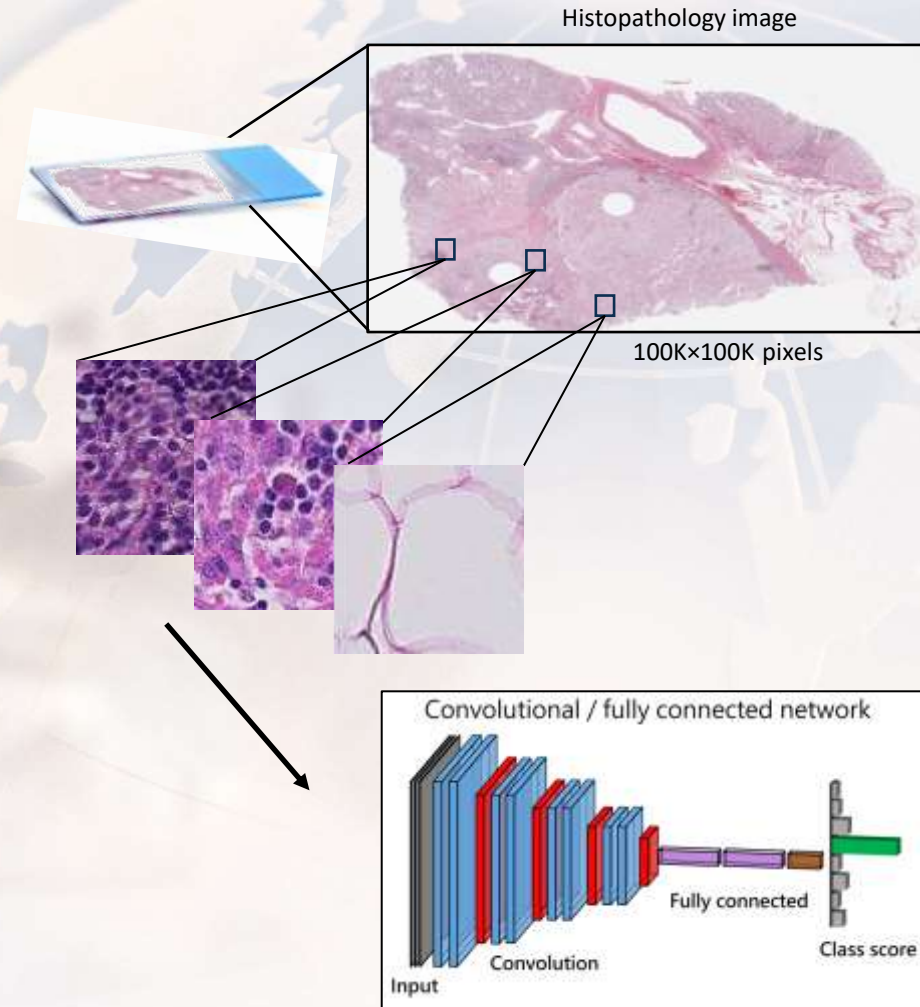


For In Vitro Diagnostic Use

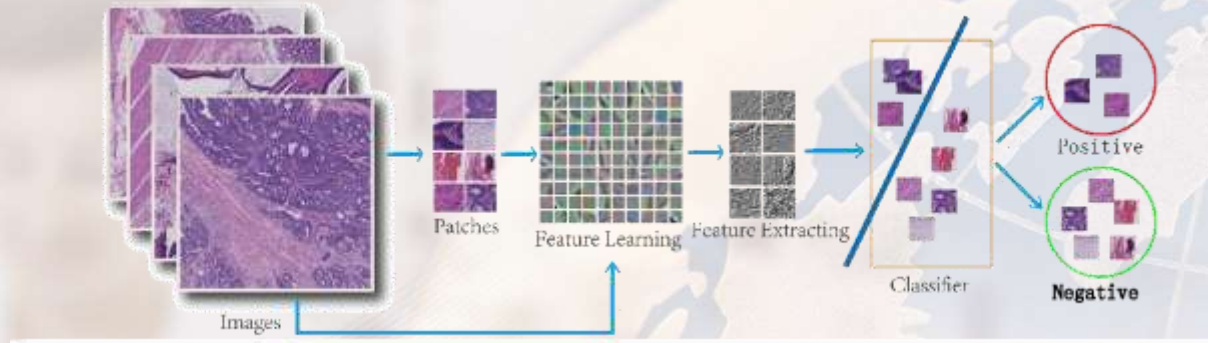
The clinical use claims described for the products in the information supplied have not been cleared or approved by the U.S. FDA or are not available.

DEEP LEARNING IN HISTOPATHOLOGY

- Convolutional Neural Nets are state-of-the-art in computer vision
- Produce optimal network architecture
- Common approach is to extract patches from WSI and use as input




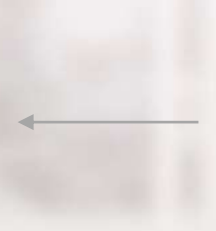
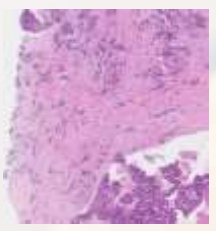
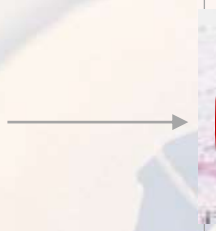



BINARY CLASSIFICATION EXAMPLE



The inputs include both cancer images and noncancer images. All images are used to generate patches. In feature learning processing, images/patches are used to downsample receptive fields.

Source: [Deep learning of feature representation with multiple instance learning for medical image analysis](#)
Yan Xu, Tao Mo, Qiwei Feng, Peilin Zhong, Maode Lai, Eric I-Chao Chang

WHOLE SLIDE IMAGES - ANNOTATION TYPES

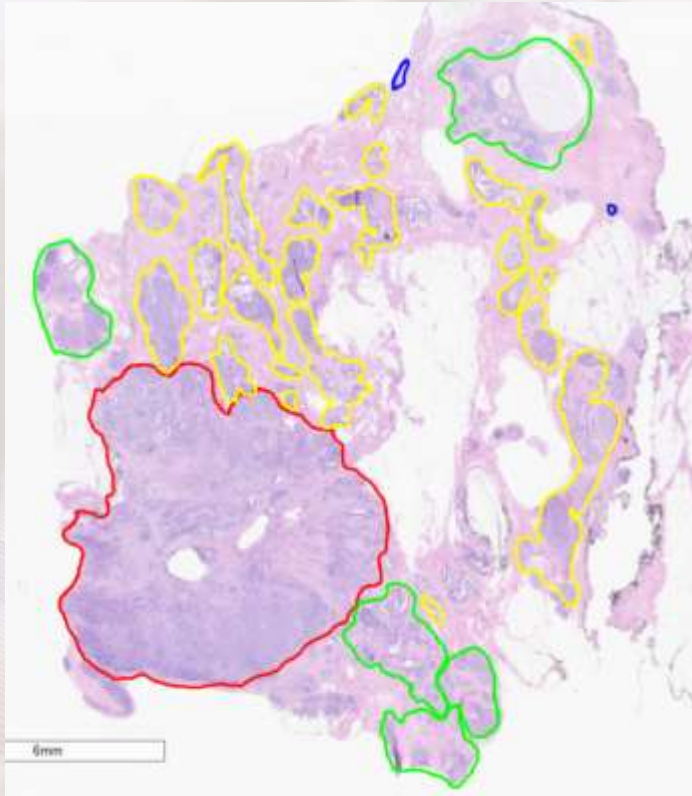
	Diagnosis	Archived Image	Slide Level Annotation	Areas of High Discordance	Lesion Area Annotation	Pixel Annotation	Detailed Pixel Annotation
Image example							
Objective	Inform treatment and prognosis	Provide clinical slide image for use in research	Full description of features important to project	Drive pathologist alignment on high discordance parameters	Highlight location/presence of specific lesion	Classify every area of the slide at lesion level	Classify every area of the slide at lesional and cell type level
Annotation Complexity	Line; only select slides annotated	Slide diagnosis (nothing circled)	Slide diagnosis (nothing circled)	Variable, but usually slide diagnosis	Free hand, broad	Free hand, within 200 microns of lesion	Free hand or assisted at cellular level
Time to Annotate (Per Pathologist)	< 1 minute	<<1 minute	~ 1 minute	~1 - 5 minutes	~1 - 5 minutes	15 - 30 min	Usually over 1 hour; may be multiple hours
Number of Pathologists	1 (most cases)	1	1 - 5	5 - 15	1 - 5	3 - 5	Variable, usually 3 - 5

← Less Detail → More Detail

In the field of computational pathology, datasets consisting of whole slides images are essential to the development of AI-based image analysis systems

DEVELOPMENT AI

The difference in image quality between scanners can pose multiple challenges



Inter-scanner variability can affect downstream image quality and deep learning solutions

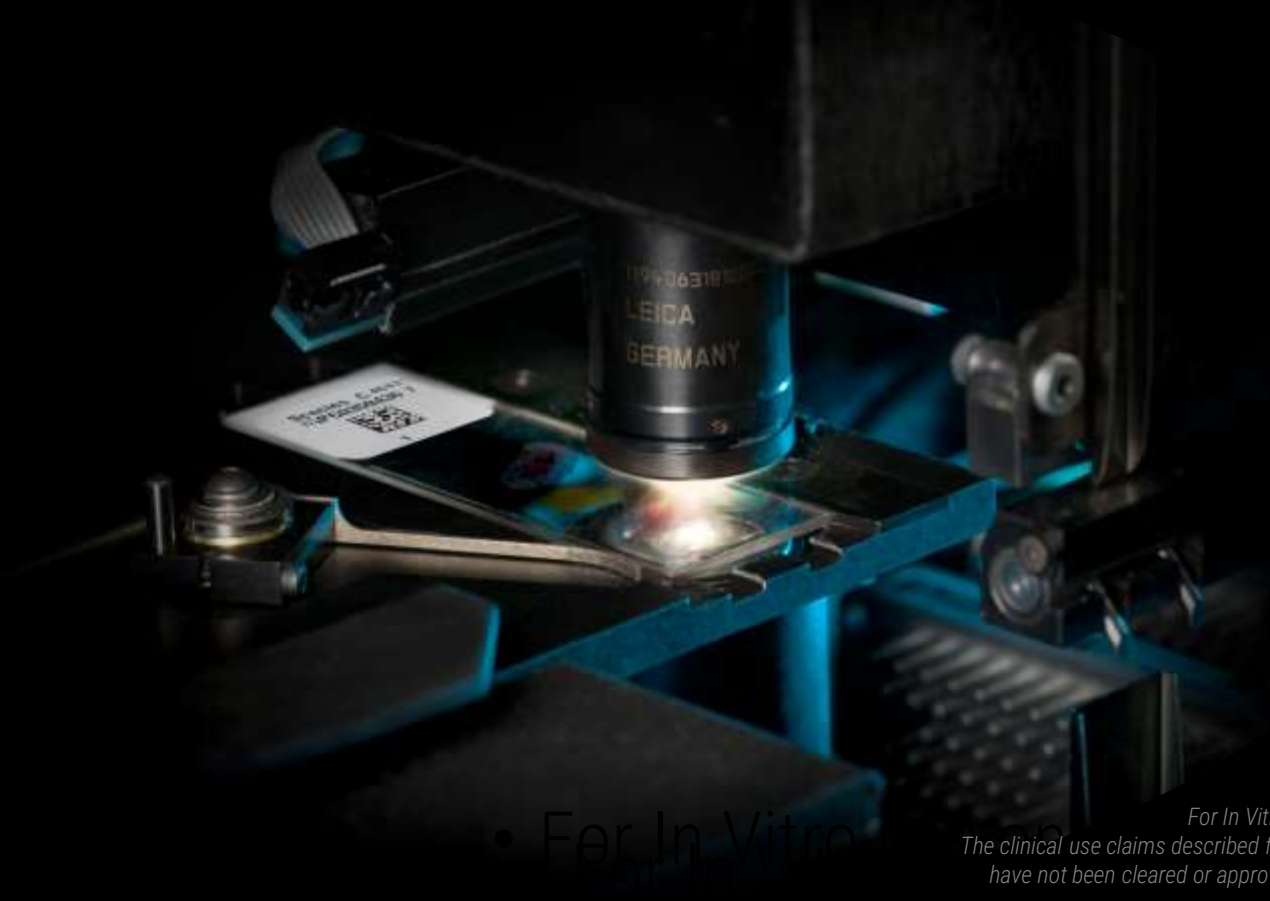
- Image compression
- Color profile
- Contrast
- Brightness
- Sharpness

Source: Assessment_of_image_quality_of_whole_slide_images_digitized_by_the_Aperio_GT450_DX_scanner.

YOUR FOCUS IS OUR OBJECTIVE

Leica Biosystems (LBS) and Leica Microsystems (LMS) optics engineers worked together to solve the problem:

- “What objective design can maximize field of view, handle very fast accelerations and decelerations, and deliver excellent image quality during extremely fast scanning speeds using real-time focusing?”



• For In Vitro
Use Only

For In Vitro Diagnostic Use

*The clinical use claims described for the products in the information supplied
have not been cleared or approved by the U.S. FDA or are not available.*

CAREFUL DESIGNED SOLUTION

- ✓ Extra-wide flat field correction that enabled a large FOV (more than 1mm) that could accommodate extremely large digital image for fast scans
- ✓ A lightweight and robust design that could handle very fast accelerations and decelerations
- ✓ An objective that resulted in 0.26 $\mu\text{m}/\text{pixel}$ resolution at 40x magnification
- ✓ A novel design that the digital pathology market has not yet seen before

REAL TIME FOCUS (RTF)

RTF not only eliminates focus time spent in traditional Point Focus Method (PFM) to speed up total scan time significantly, but also provides better focus quality in a few aspects:

- Continuous focusing over discrete point focusing offers orders of magnitude and more focus data
- Continuous smooth motion over radical point-to-point move during focusing requires no slide or stage settling time
- Short exposure over long exposure of tissue under light prevents tissue from potential thermal deformation or bleaching



AUTO-QUALITY CONTROL

- International Color Consortium (ICC) correction

The industry standard protocol for color reproduction, is used in Aperio GT 450 for color consistency and color accuracy of the images. The ICC profile was created based on the spectrum of the illumination, the spectral response of the camera, and the spectral properties of stained tissue. It represents the true color of a slide if it's viewed under a daylight illuminated microscope.

- Auto-Quality Control (QC)

If a stripe-focus error remains, an auto-QC procedure uses a series of parameters extracted from the image data against thresholds, which was pre-configured using a SAM (Scanner Administration Manager), to show an image quality warning note on the console screen for further investigation.

OPTICS IN Aperio GT450DX

Excellent Image Quality

- Excellent image quality using Leica optics
- 40x scans with 0.26 $\mu\text{m}/\text{pixel}$ resolution
- Image quality proven - tested with Pathologists
- Consistent high-quality images enable on-time, on-screen diagnosis

German Craftsmanship

- Objective custom made by Leica Microsystems in Germany
 - FOV 1.0mm vs AT2 0.5mm
 - DOF 1.7 microns
- Utilizes Real-Time Focusing technology

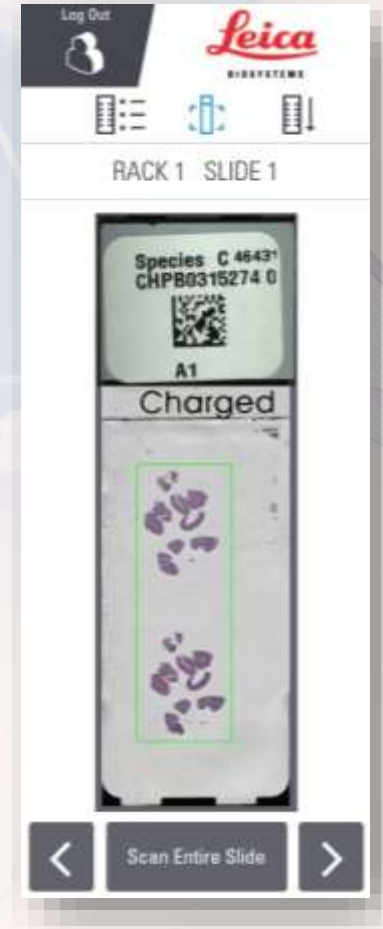
Confidence

- Every slide is calibrated during scanning
- 99.5% accurate tissue finder
- Automated Image Quality Check



READY FOR DIAGNOSES

- The results indicated that diagnoses made using the Aperio GT 450 DX were accurate and comparable to diagnoses made using light microscope and had an acceptable level of precision.
- This creates an efficient, and ergonomic diagnosis workflow resulting in improved turn-around time which benefits healthcare professionals, and ultimately the patient





Thank you!

We envision a world where comprehensive insights enrich cancer diagnosis and offer reassurance to all patients.

Advancing Cancer Diagnostics, Improving Lives

Advancing Cancer Diagnostics
Improving Lives

*For In Vitro Diagnostic Use
The clinical use claims described for the products in the information supplied
have not been cleared or approved by the U.S. FDA or are not available.*

Confidential - Company Proprietary

Leica
BIO SYSTEMS