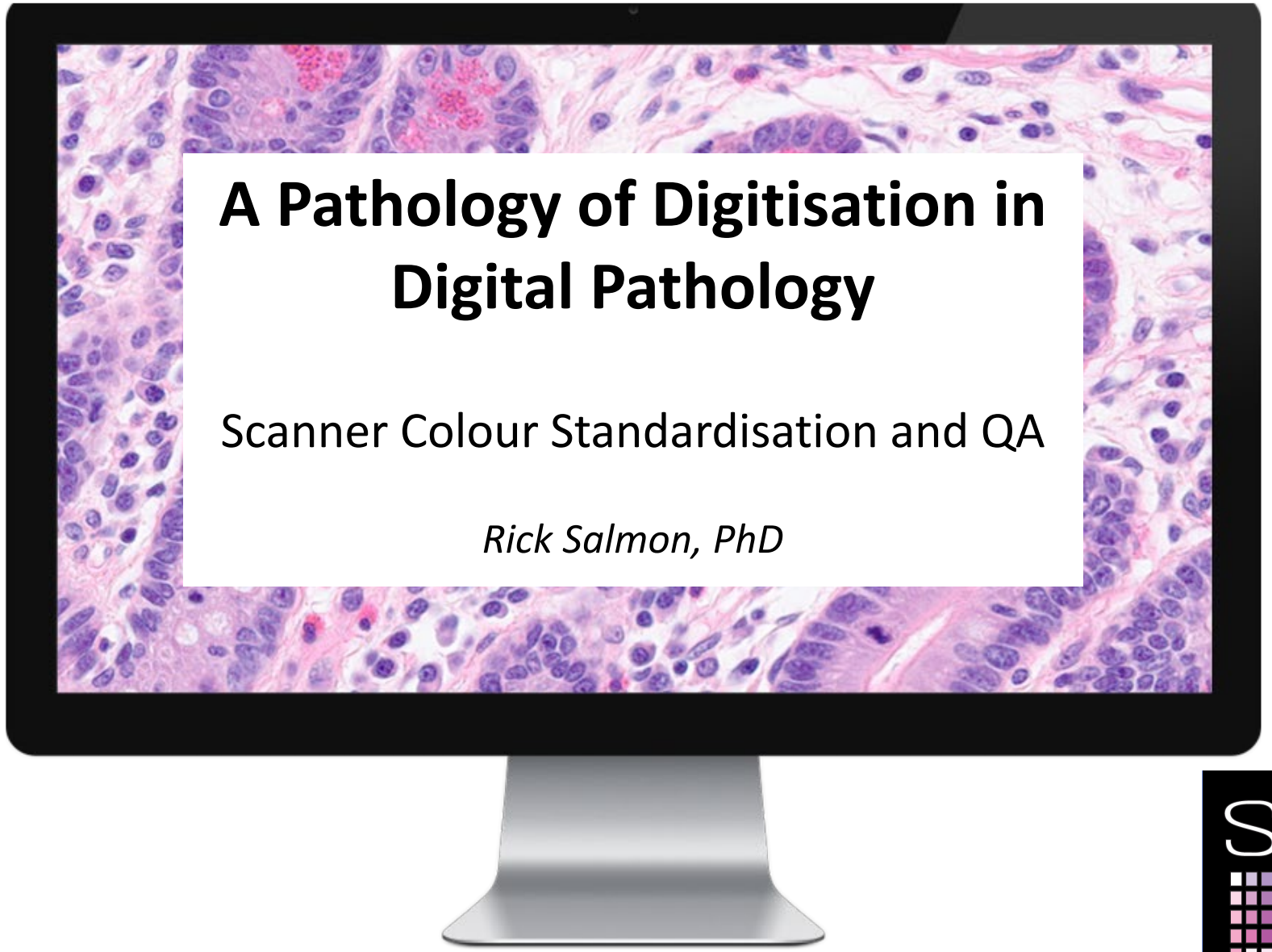
Creative Imaging Technology



A Pathology of Digitisation in Digital Pathology

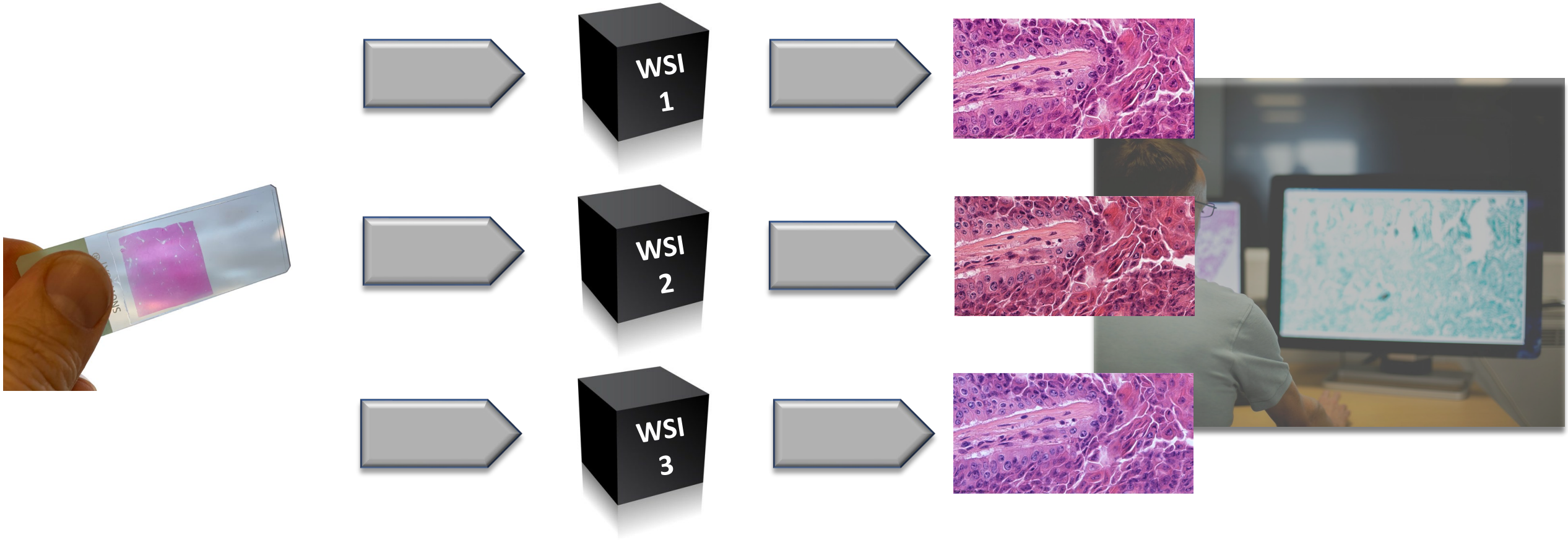
Scanner Colour Standardisation and QA

Rick Salmon, PhD

SIERRA

A ‘Black Box’ Pathology

Symptom: Visible Colour Variation Across Devices



QA/GLP Issue for Pathologists. Scanner-Induced Domain Shift for AI.

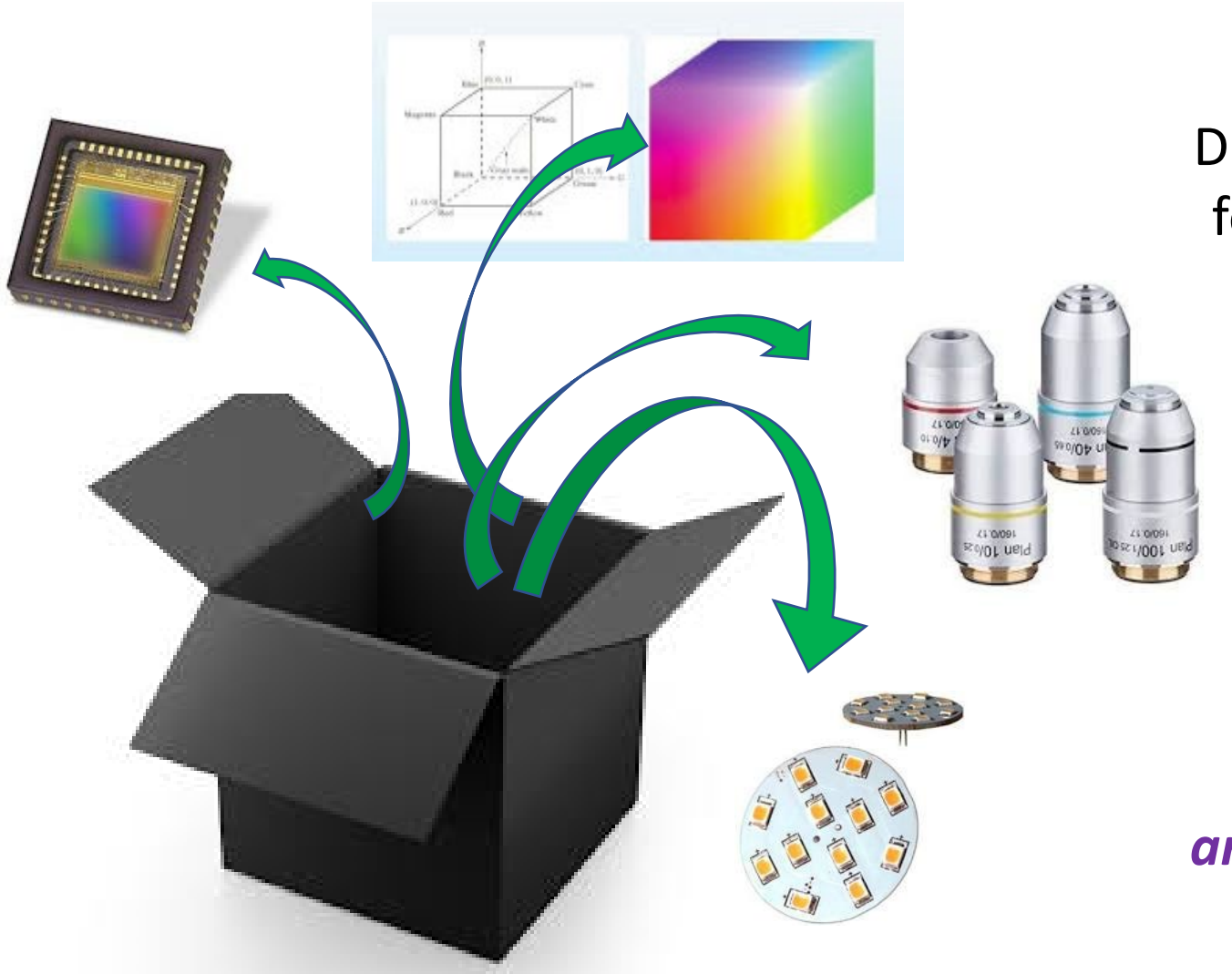
Digital Scanner Colour versus Stain Chemistry Variation

- ***Stain colour variation*** – differences in chemistry and consistency in sample source and technique

- ***Digital scanner colour variation*** – errors in the pixel pathway induced by accuracy of digital imagers

<u>Both are incredibly important</u> in cumulative QA, but have different sources and therefore different solutions

What Causes Scanner Colour Variations?



Digital WSI vendors use different designs for the various modules in the scanner:

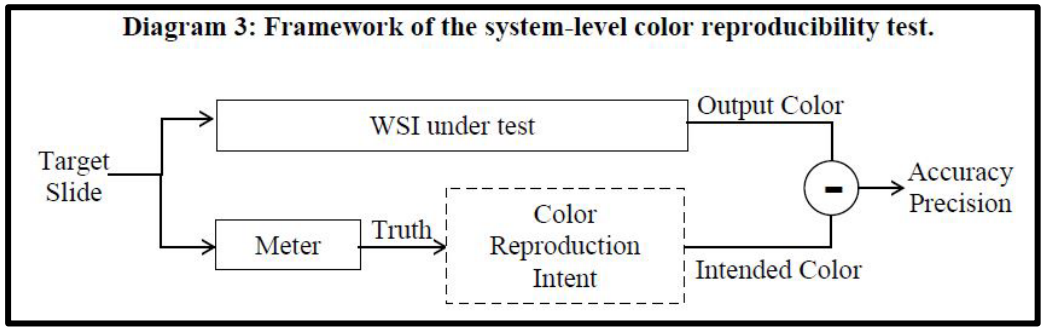
Sensors
Lenses
Illumination
Image processing

WSI devices therefore have different 'Profiles' for how they capture an analogue image and convert it to digital

The ‘Black Box’ of Digital Pathology
…What Can Be Done About Colour Variation?

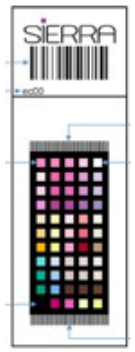
The FDA identified this issue in their guidelines

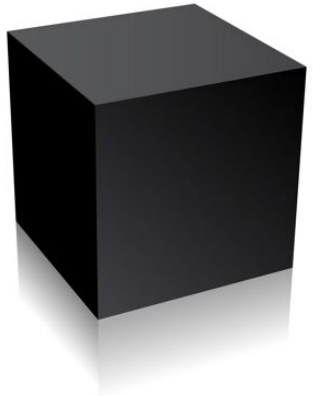
They recommend using a ‘system-level’ colour reproduction intent test to identify the colour ‘Accuracy’ of the WSI device

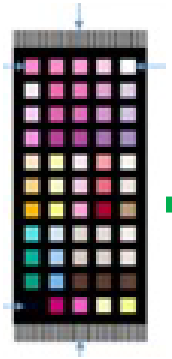


Reference: FDA 2016 Guidance

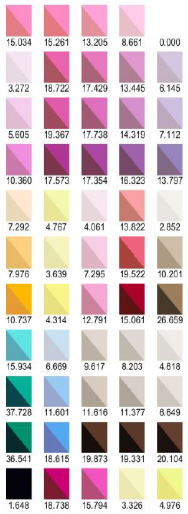
How this works in the real world

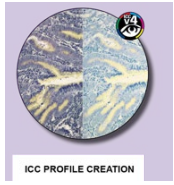






Colour accuracy report / WSI profile

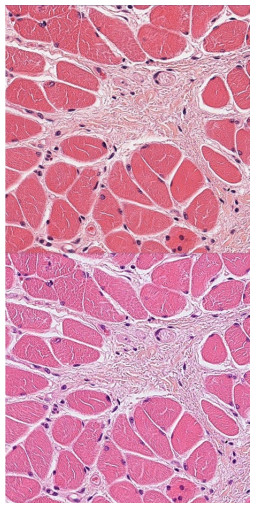




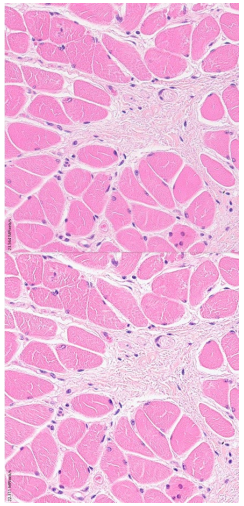
Known reference ‘Target’ slide

Intended ‘Ground Truth’ colour data set

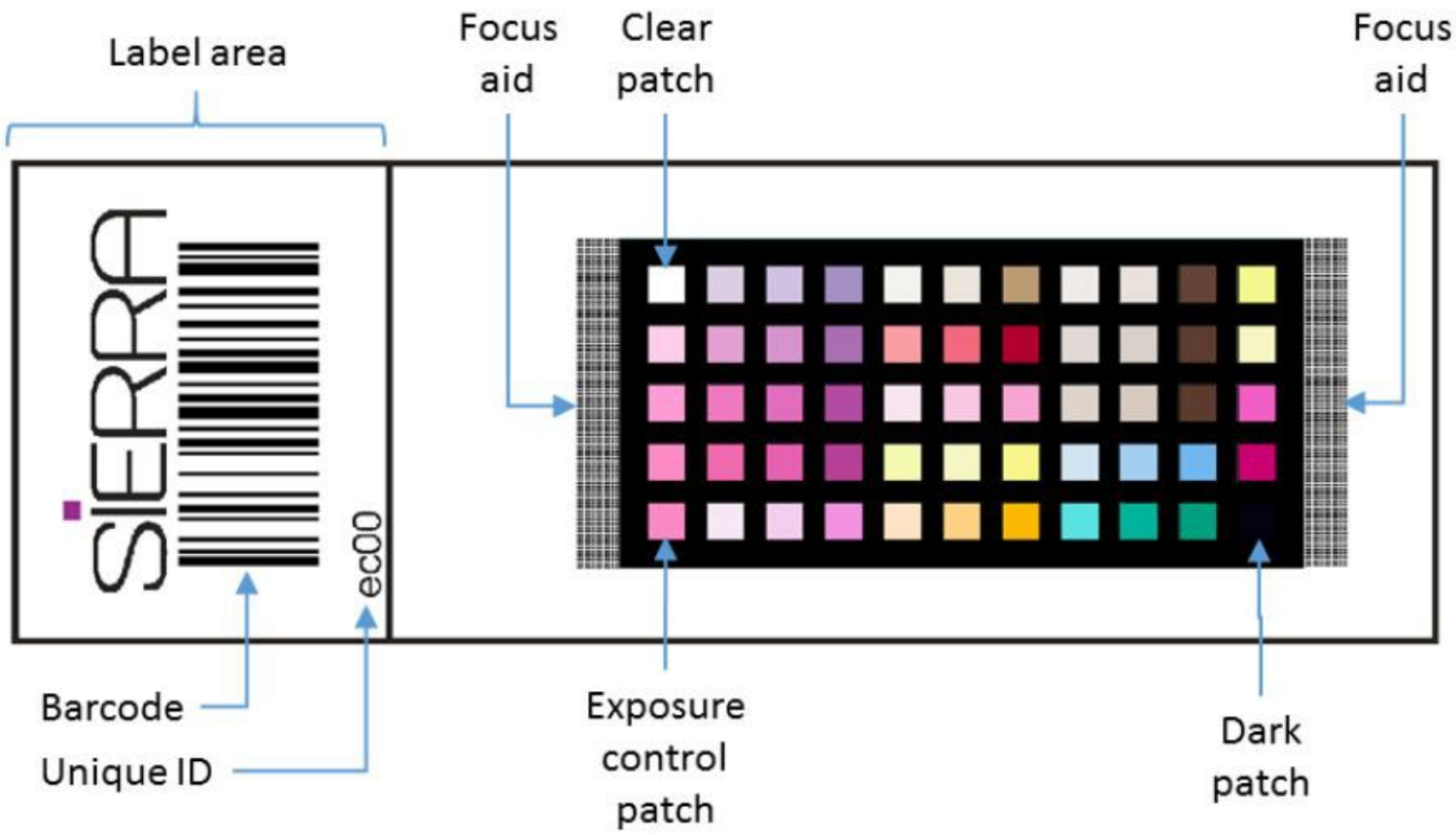
Before ICC



After ICC



The ‘Target’ Reference Slide (Sierra) Must Represent Biological ‘Ground-Truth’ to Ensure Accuracy



Small patches of biopolymer bind pathology stains = tissue mimicry

Creates gamut of pathology colours with **reduced metamerism**

Stained with same protocol as for pathology

Formatted like a pathology slide, so compatible with WSI scanners

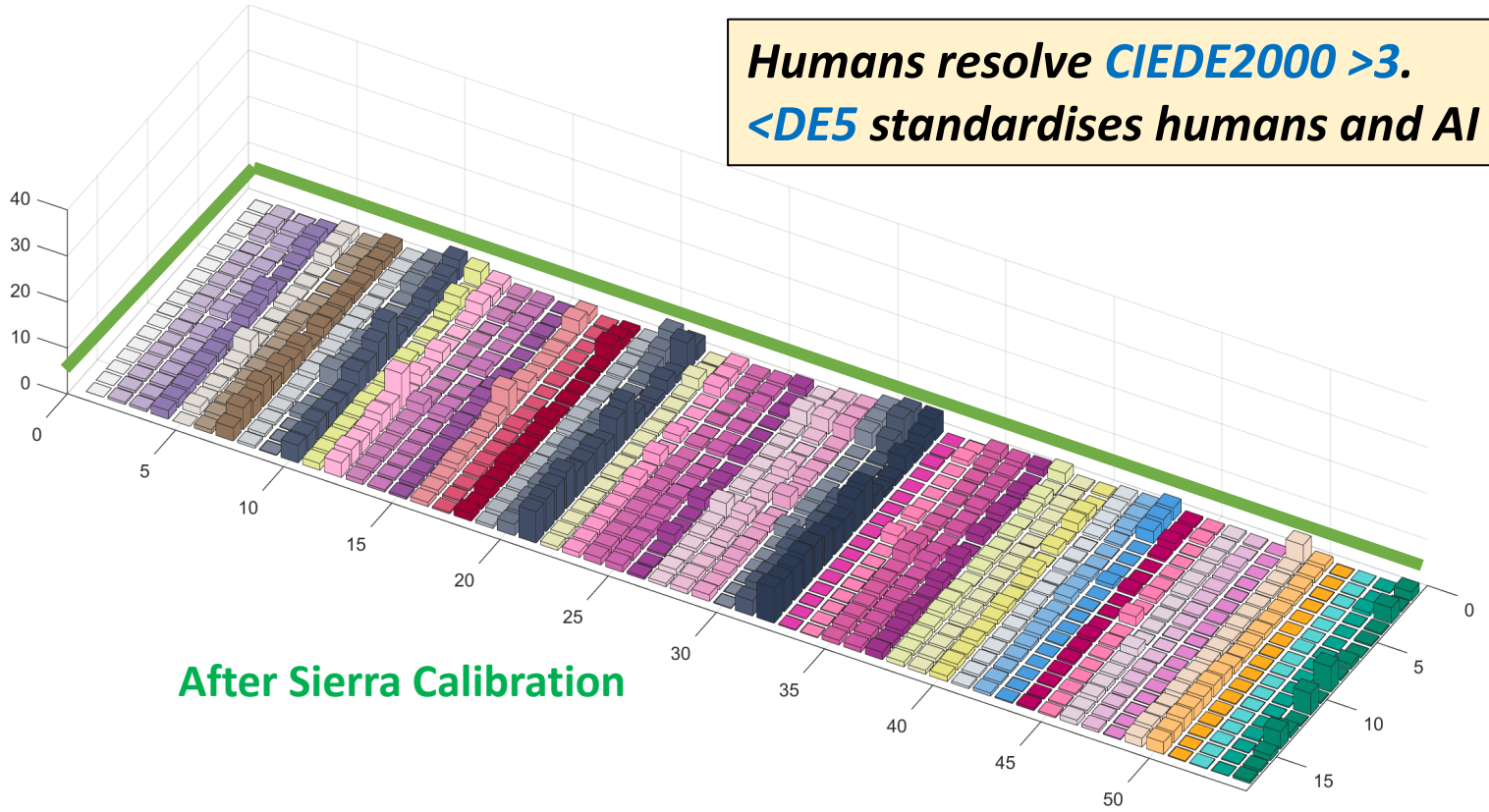
Complements FDA guidelines and promotes **interoperability** and simple adoption

Creative Imaging Technology

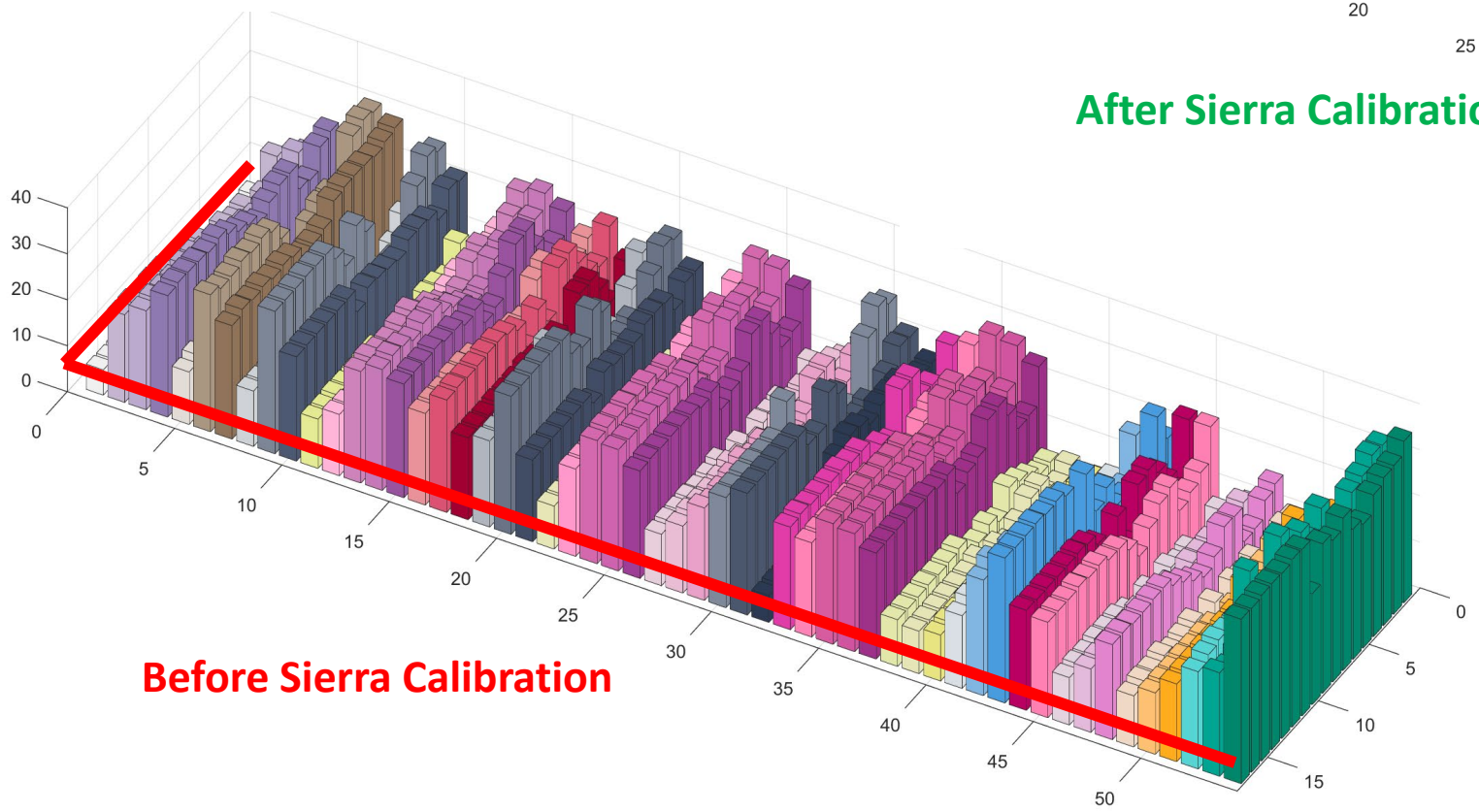
Industry-wide metrics for QA & GLP are **Accessible**

Calibration to meet stringent QA & GLP is **Achievable**

Humans resolve CIEDE2000 >3.
<DE5 standardises humans and AI

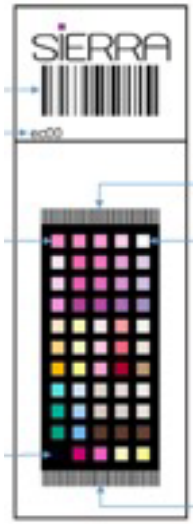


After Sierra Calibration



Before Sierra Calibration

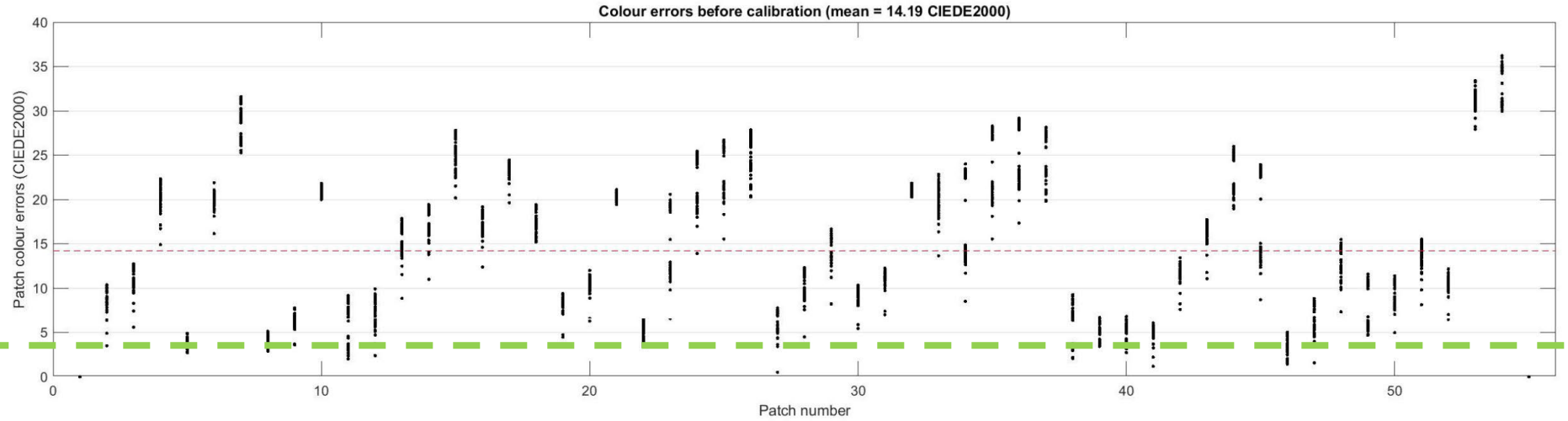
18 scanners
6 vendors
4 industries
8 projects
14 locations



System Colour Error Within 11 Identical Scanners – One Scanner Model is Not Enough for Fidelity and QA

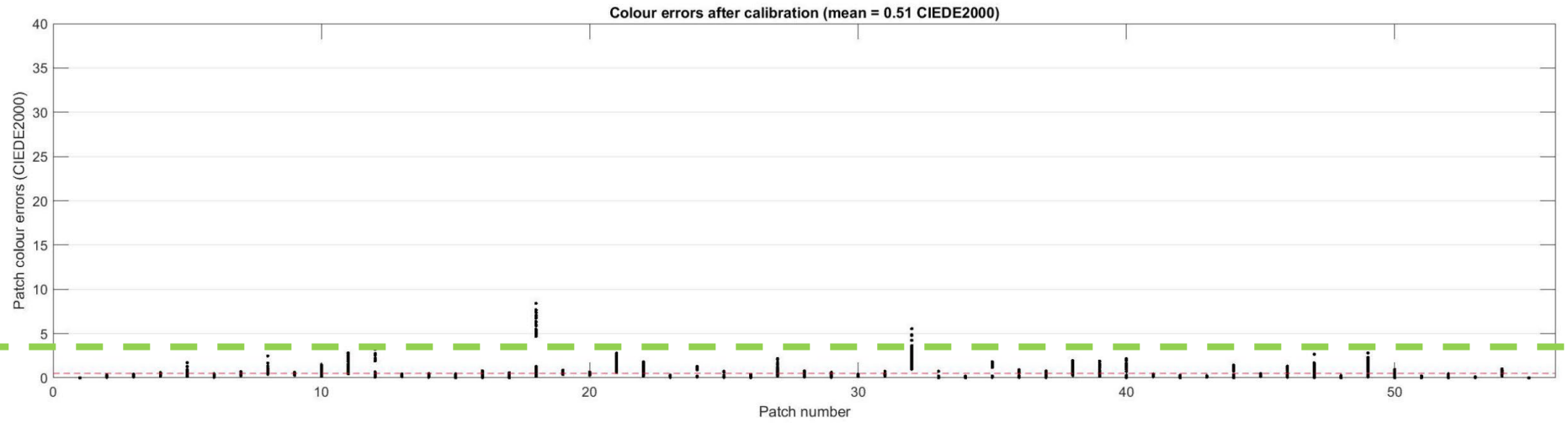
Av. error = 14.9

Av. variation = 2.93



This is an industry-wide occurrence

Variance x 8.5 reduced



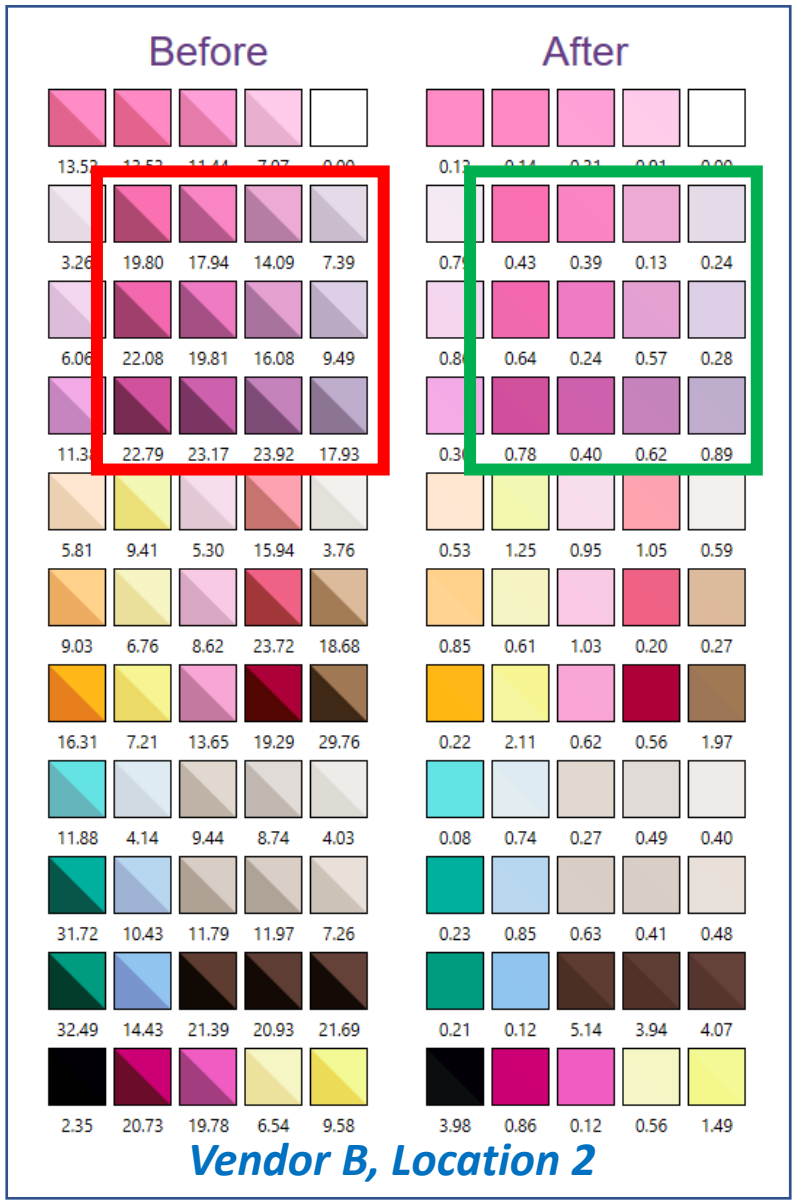
Av. error = 0.51

Av. variation = 0.34

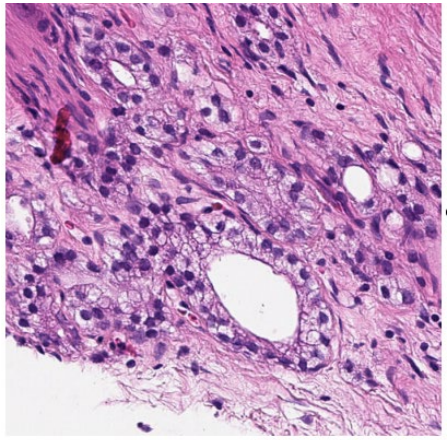
Human resolution

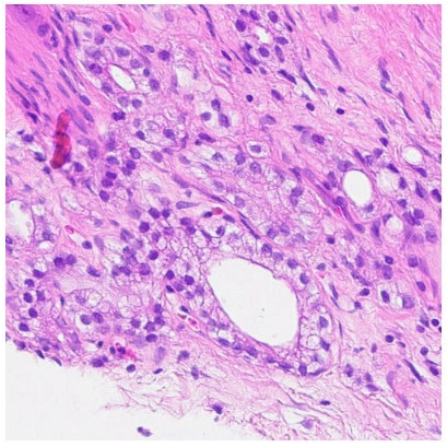
Physical Calibration Can Improve AI Accuracy & Reliability

Vendor A, Location 1



Vendor B, Location 2



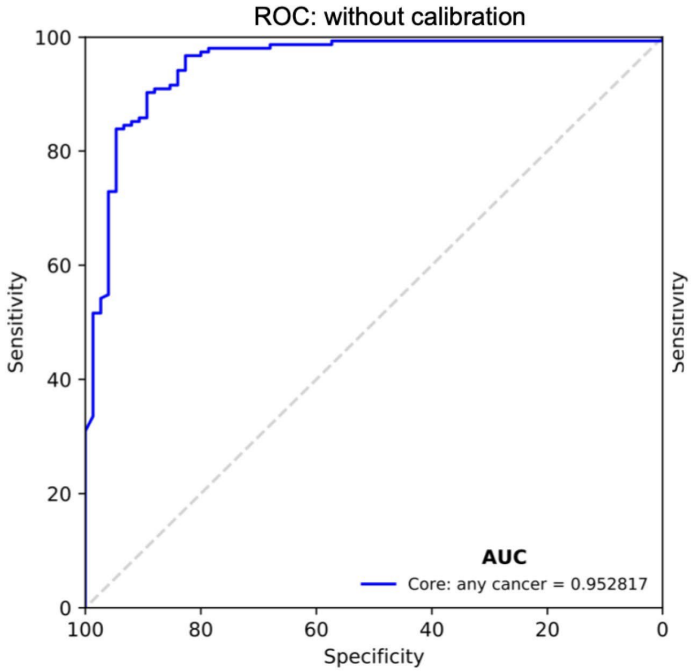


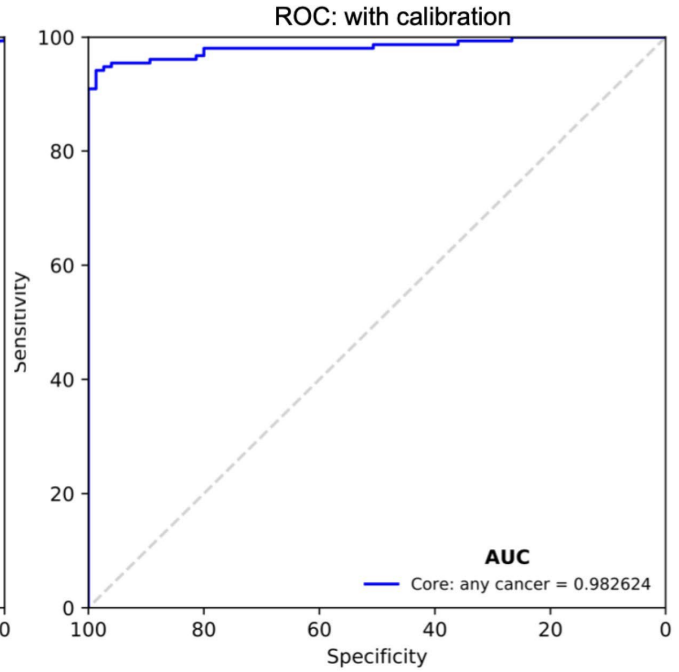
Karolinska Institutet

Prostate Centres Across:

Sweden
Finland
Norway
Denmark

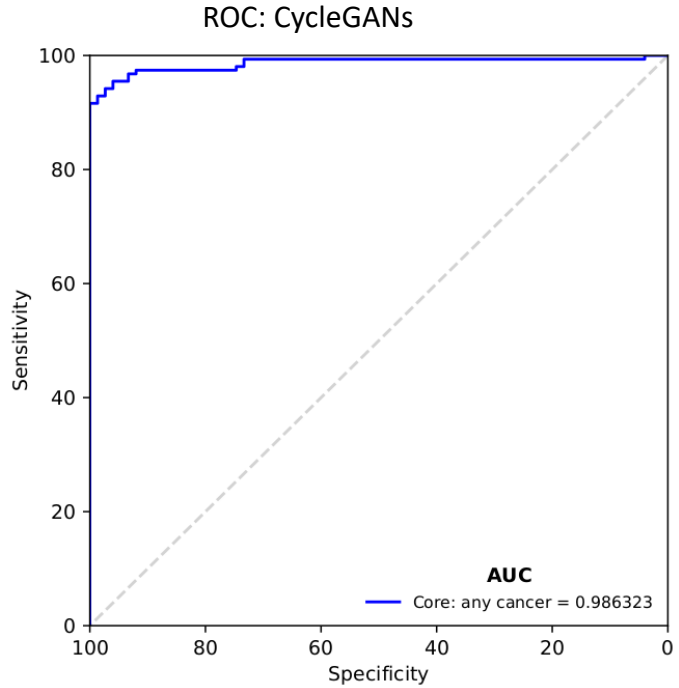
Prostate AI already very accurate (95%)

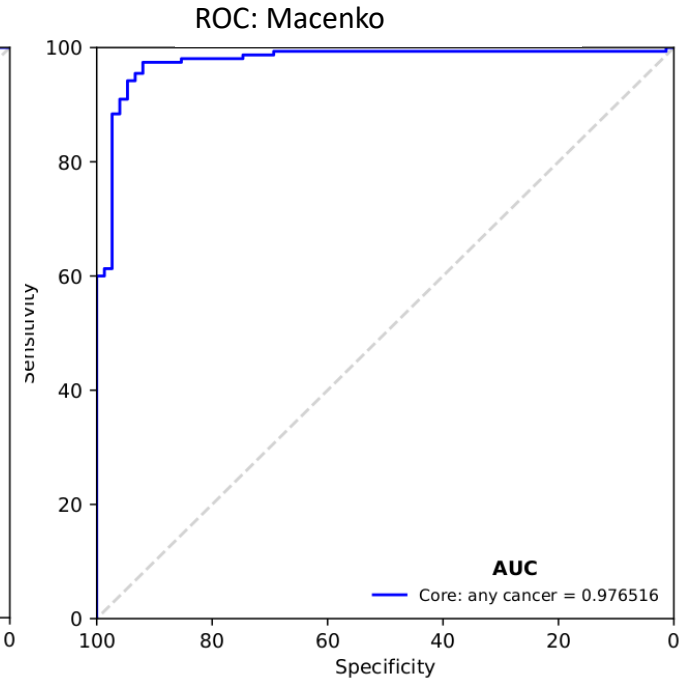




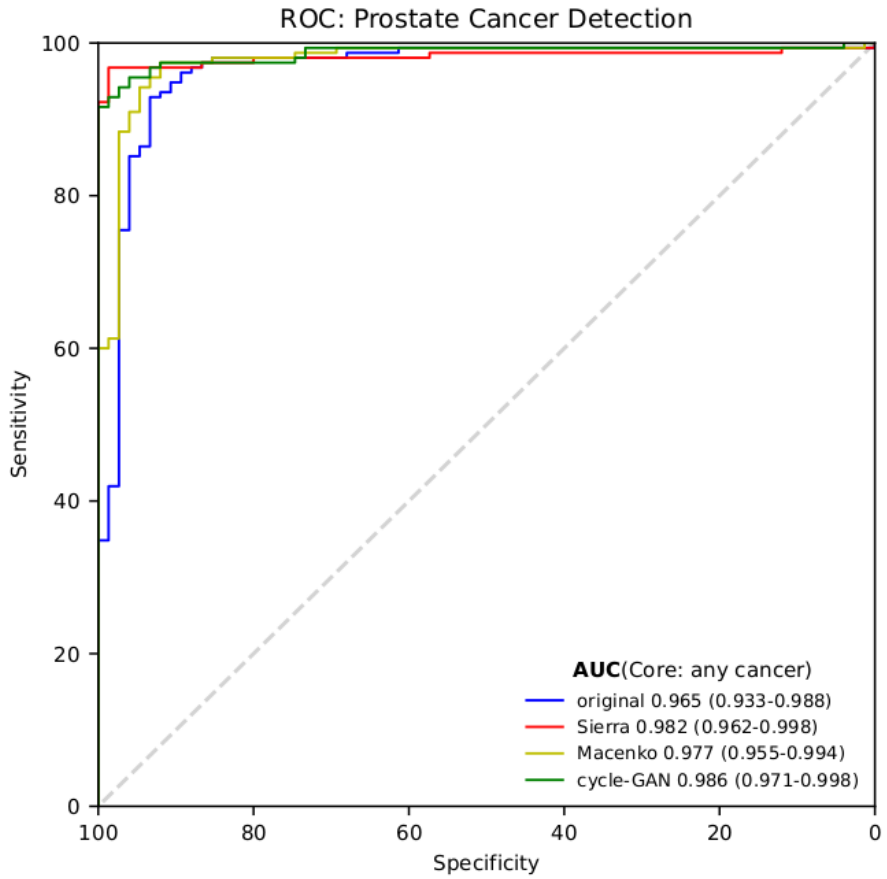
Detection accuracy increased 3% when Sierra standardised colour

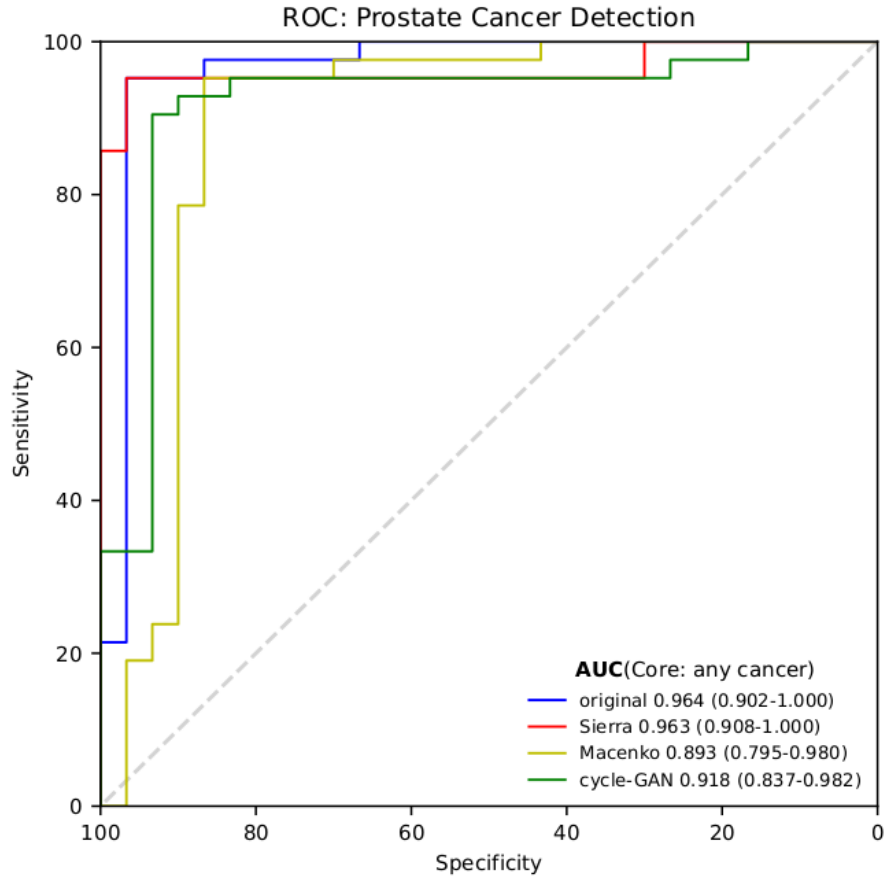
CycleGANs comparable, outcompetes Macenko





Method	Cohen's κ
Original	0.35
Sierra	**0.74**
Macenko	0.65
Cycle-GAN	0.65





When AI was run on independent hospital cohorts, **Macenko** dropped -9% and **cycle-GAN** -7% at a new site (above right)

Sierra – ***RELIABLE*** as standardises each image 1:1 – each image is independently corrected by an ***EXPLAINABLE*** method

Normalisation needs big data for statistical relevance (cycleGAN) and or tuning to local lab differences (Macenko)

Summary

- Scanner-induced domain shift is a digital QA issue
- An independent colour standard can provide quantitative metrics for QA/GLP reporting
- Domain shift can be scanner-agnostically corrected, no augmentation needed - all digital colour is simply the truth of real input tissue, a universal standard.
- Enhanced QA can even be achieved on scanners of the same model
- AI benefits with accuracy and increased reliability for variable deployments on all dataset sizes
- Colour calibration to an independent standard has a potential role in DP and AI regulation

Acknowledgements

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Kimmo Kartasalo
Xiaoyi Ji
Martin Eklund

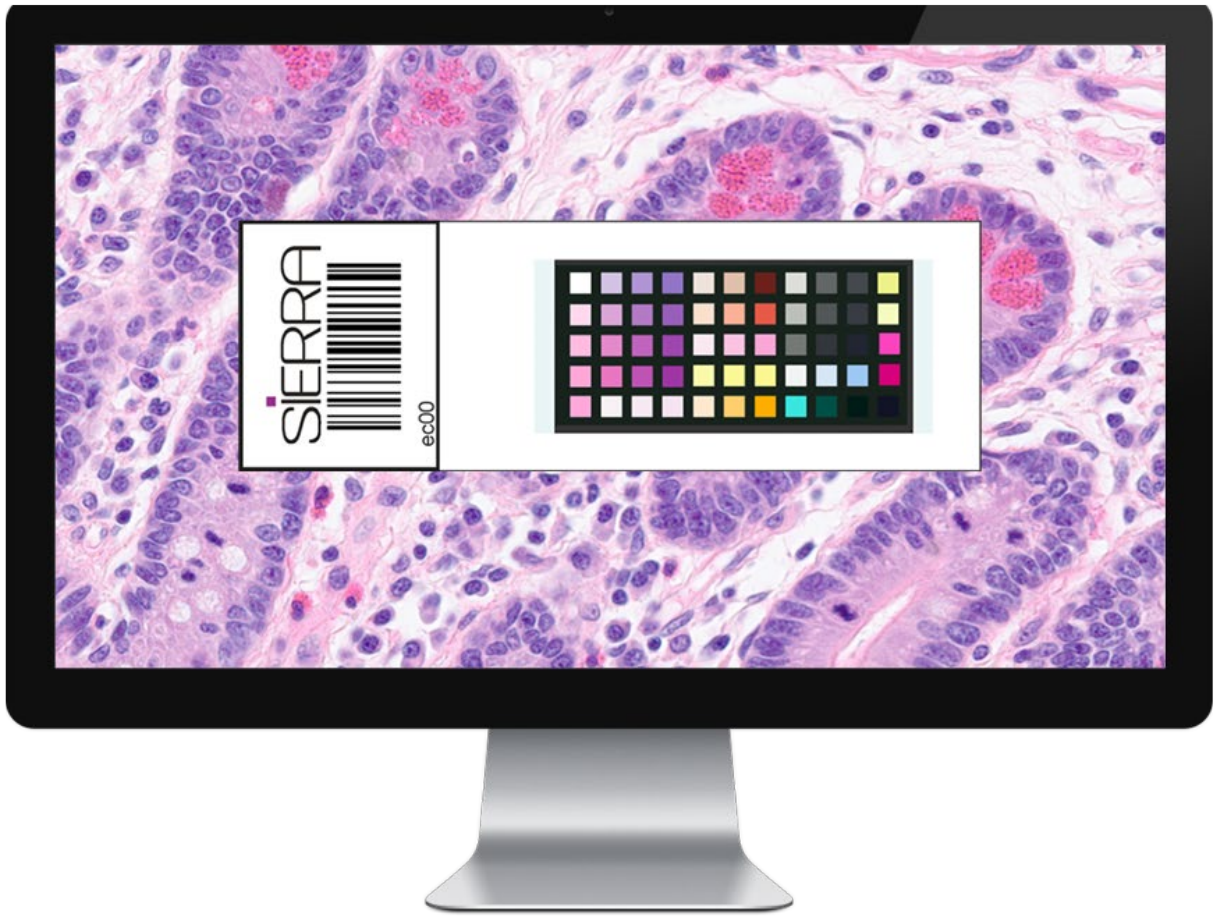
International Color Consortium®

INDUSTRIAL STRATEGY | UK Research and Innovation

UKRI Future Leaders Fellowships

Rick Salmon is an Innovate UK FLF Fellow

Creative Imaging Technology



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www.ffei.ai