



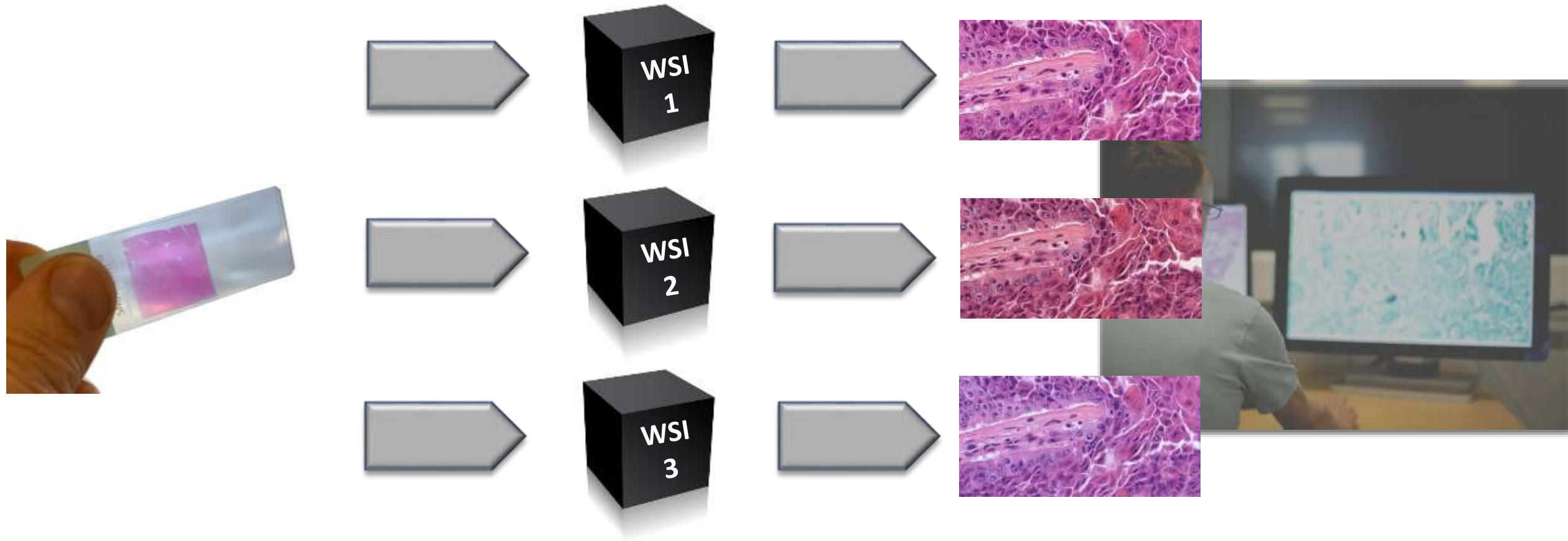
A Pathology of Digitisation in Digital Pathology

Scanner Colour Standardisation and QA

Rick Salmon, PhD

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

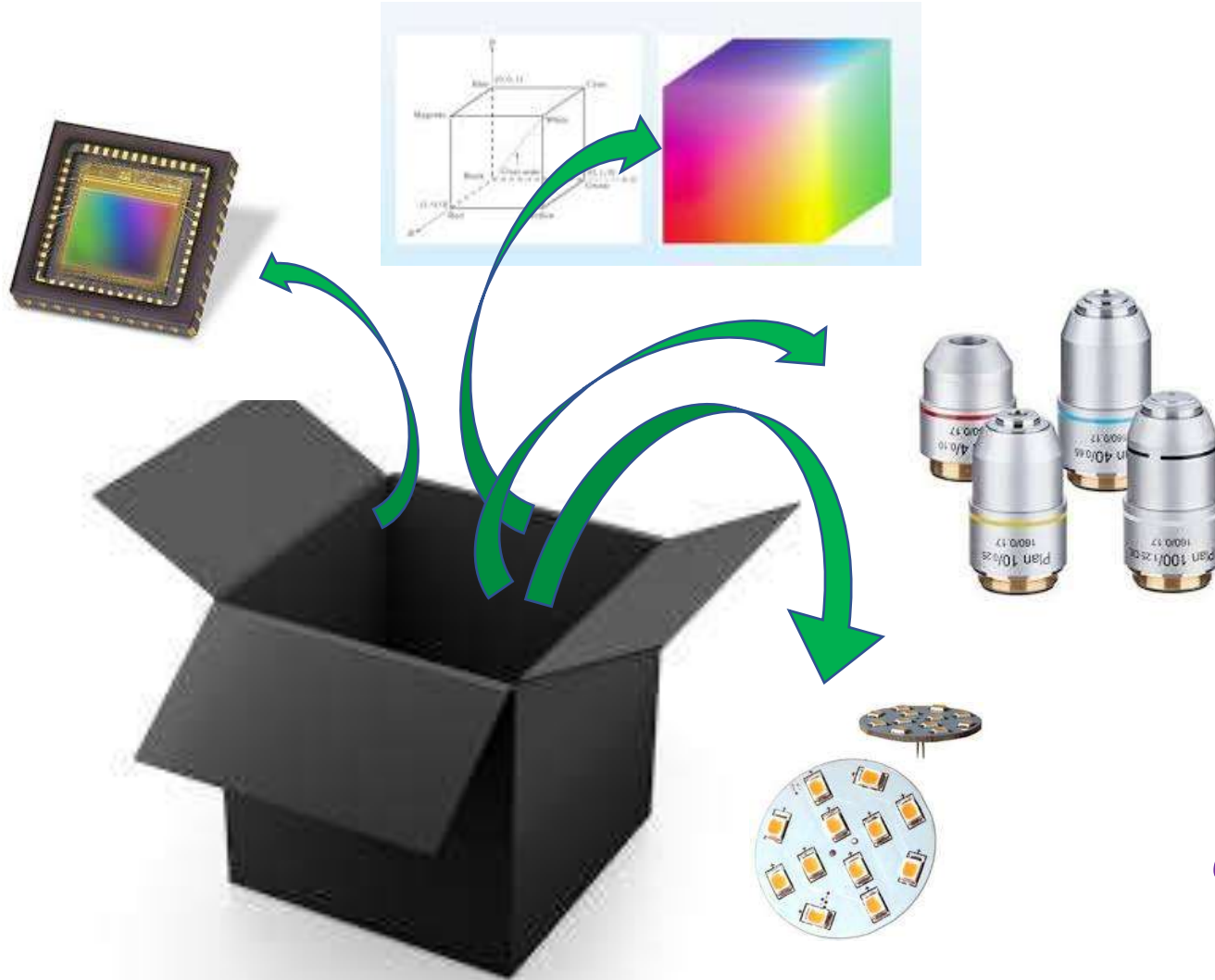


- ***Digital scanner colour variation*** – errors in the pixel pathway induced by accuracy of digital imagers



Both are incredibly important 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:

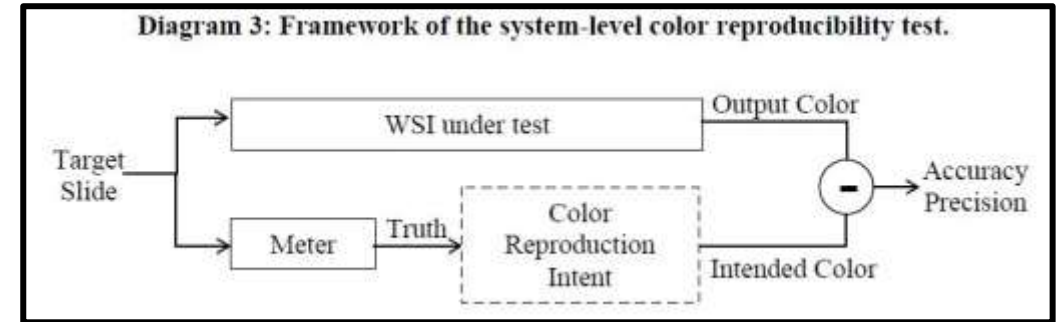
Sensors
Lenses
Illumination
Image processing

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

The 'Black Box' of Digital Pathology

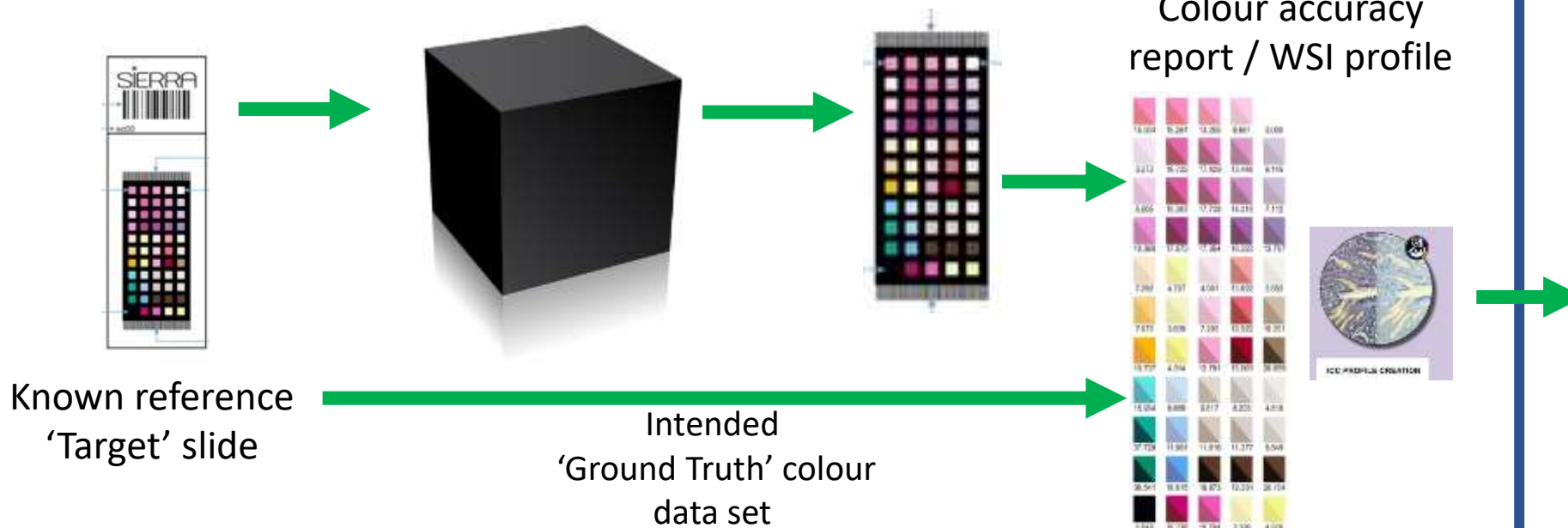
...What Can Be Done About Colour Variation?

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



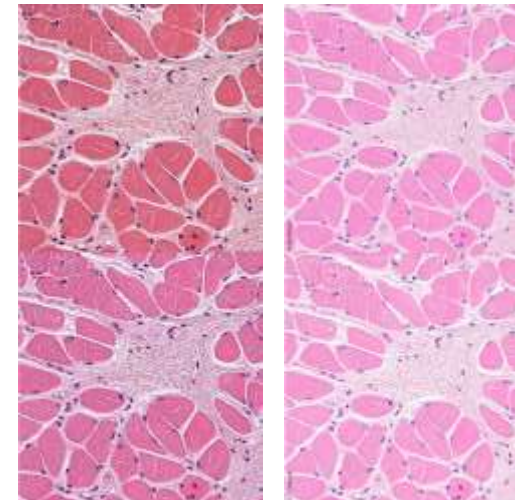
Reference: FDA 2016 Guidance

How this works in the real world

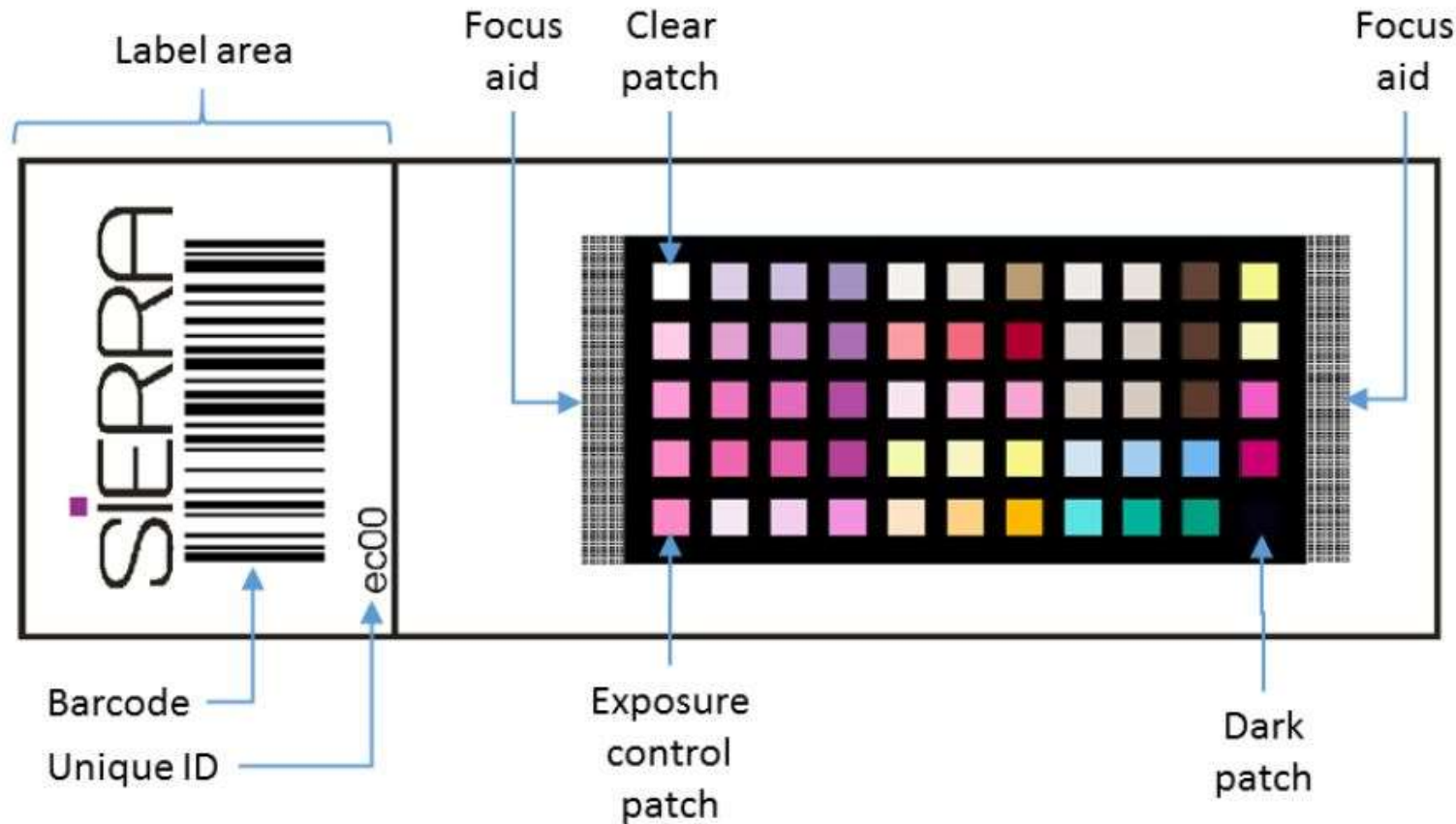


Before ICC

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

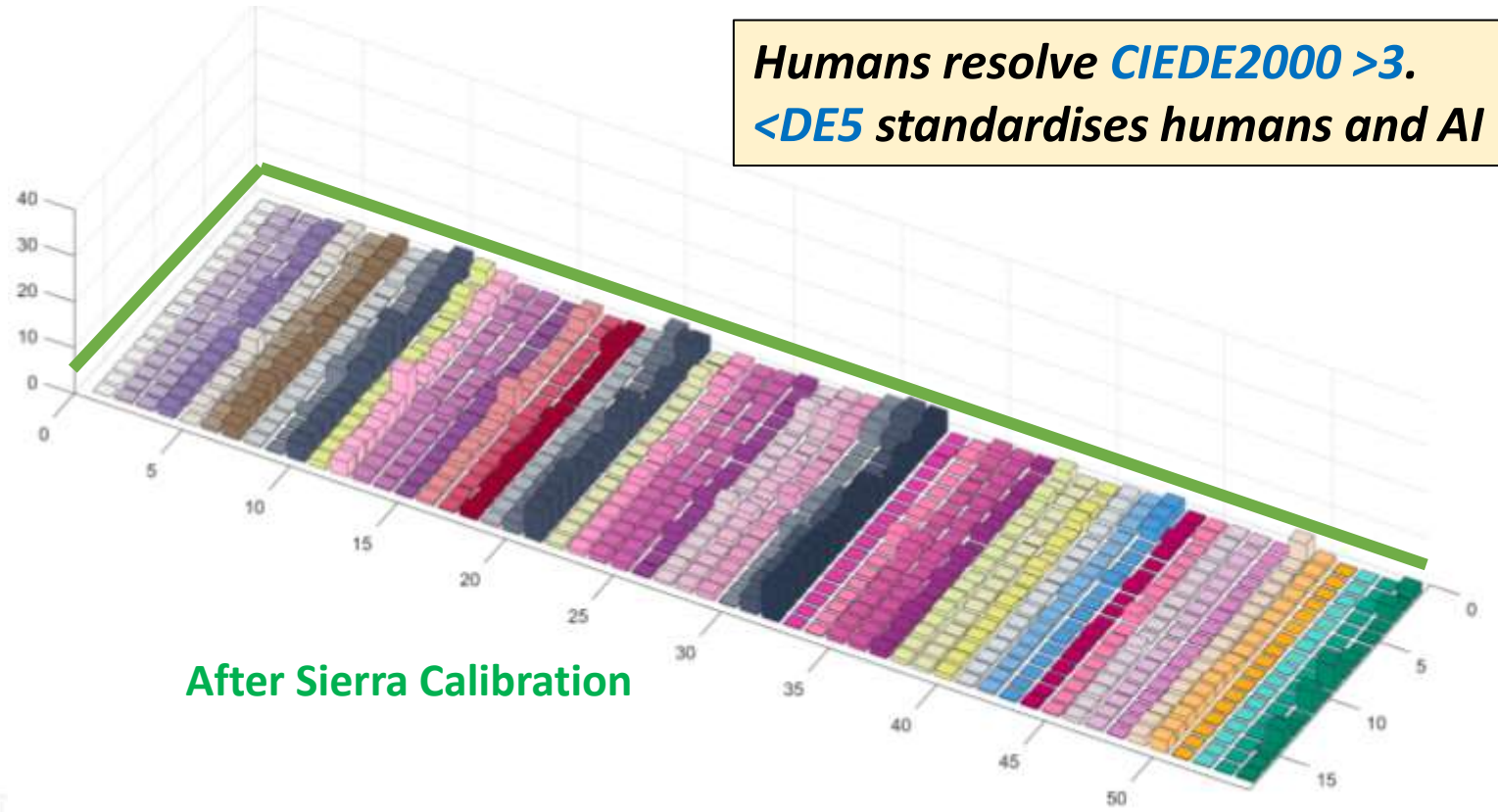
Formatted like a pathology slide, so compatible with WSI scanners

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

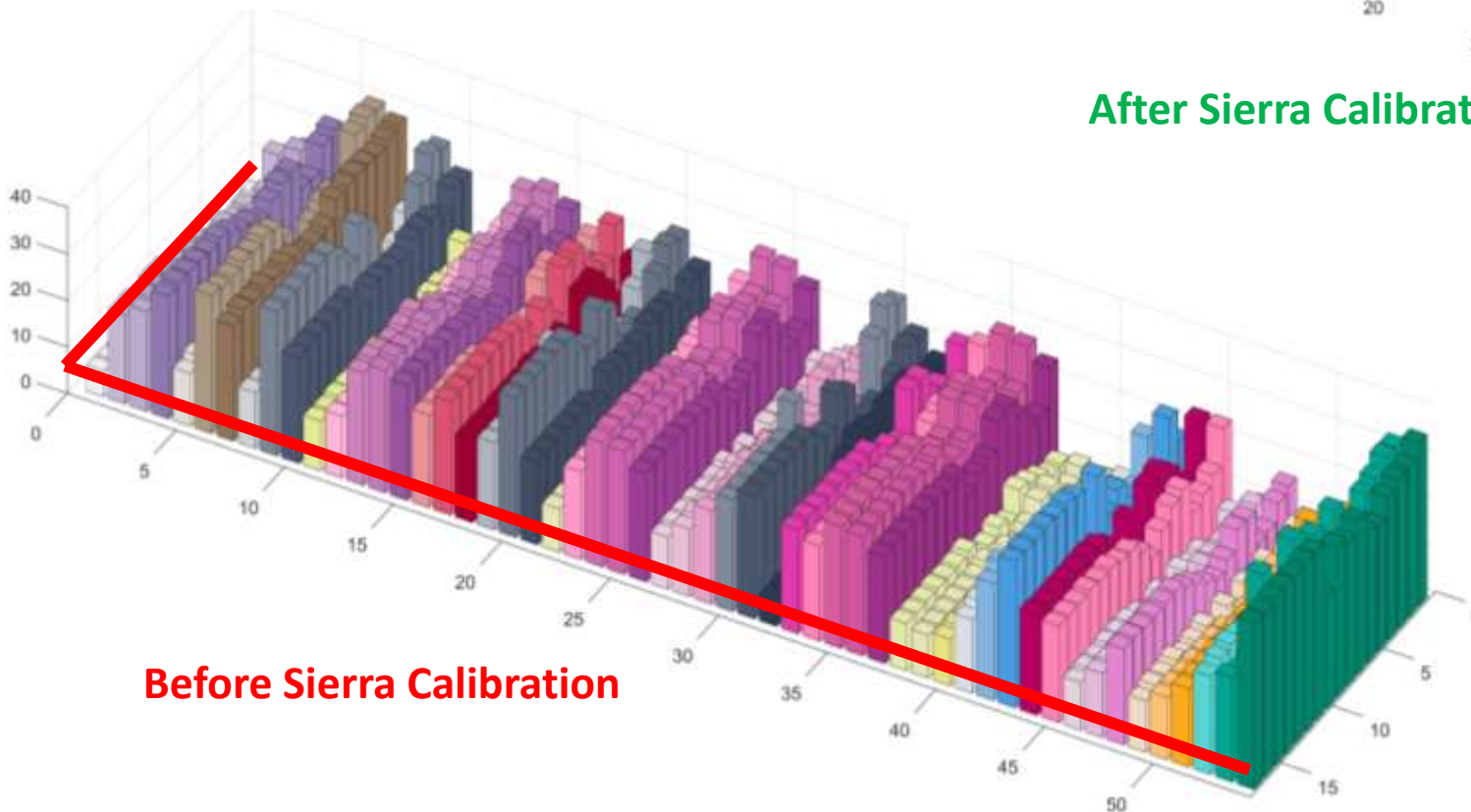
Industry-wide metrics for QA
& GLP are **Accessible**

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

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

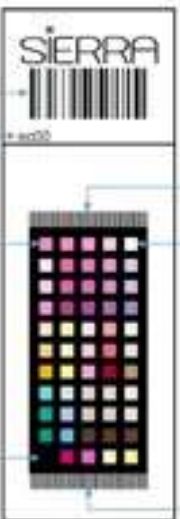


After Sierra Calibration



Before Sierra Calibration

18 scanners
6 vendors
4 industries
8 projects
14 locations



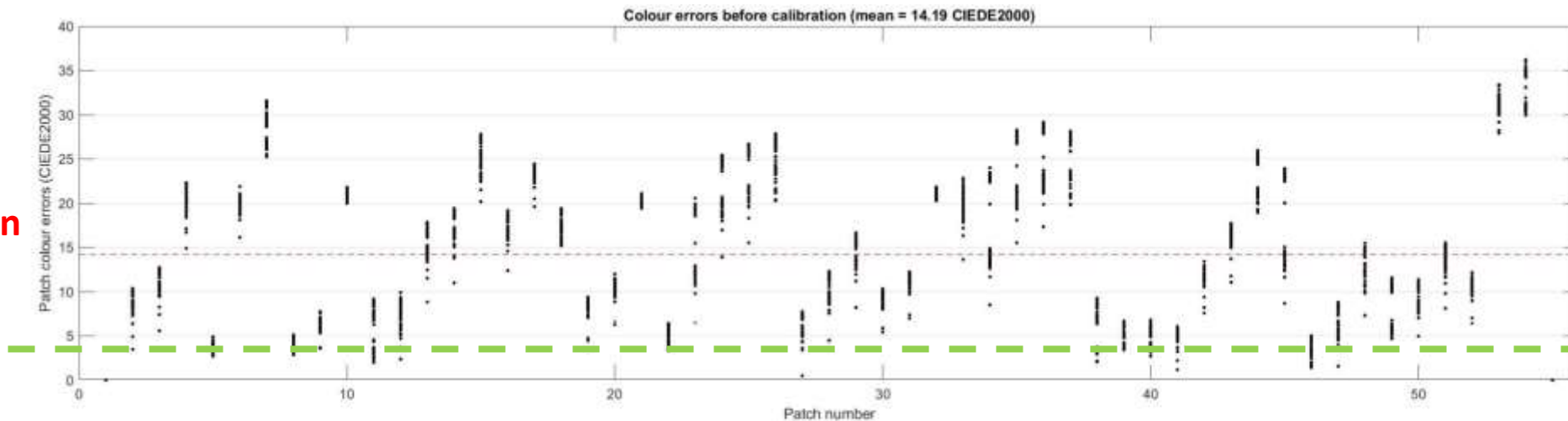
System Colour Error Within 11 Identical Scanners

– One Scanner Model is Not Enough for Fidelity and QA

Av. error =
14.9

Av. variation
= 2.93

*This is an
industry-wide
occurrence*

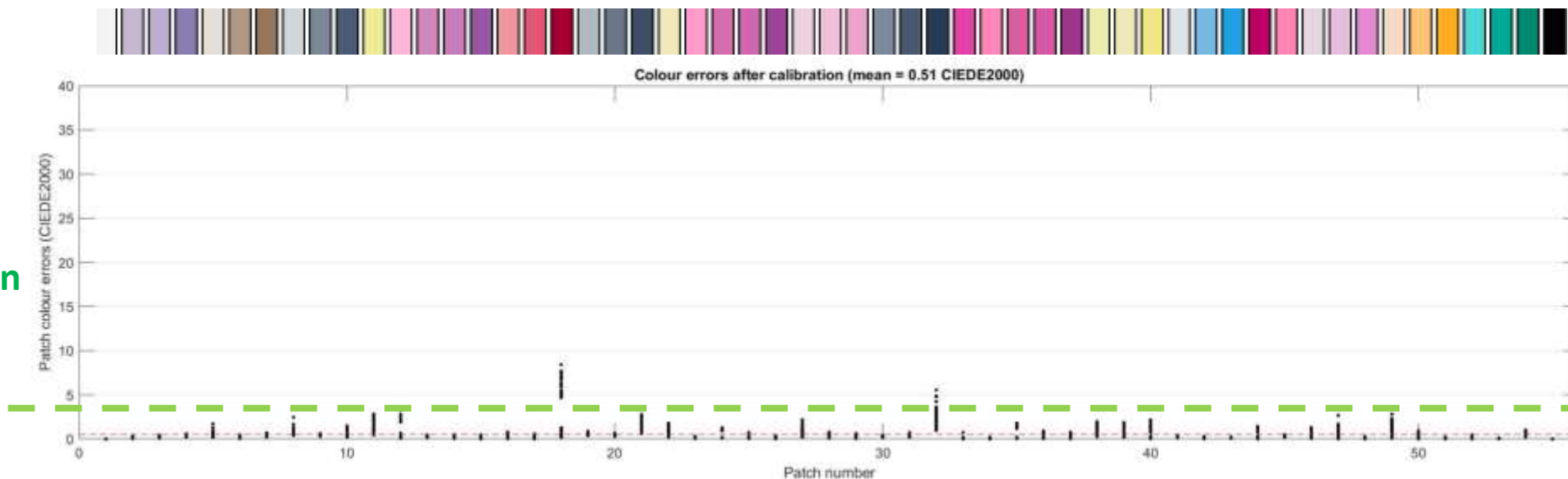


Av. error
= 0.51

Av. variation
= 0.34

Variance
x 8.5 reduced

Human
resolution



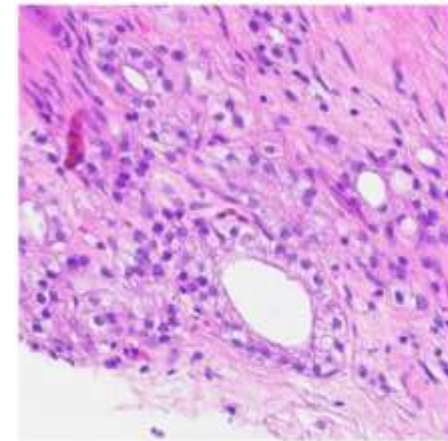
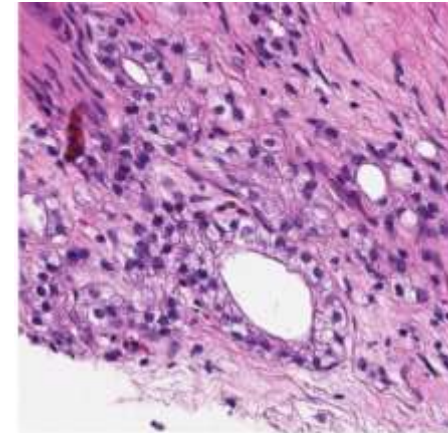
Physical Calibration Can Improve AI Accuracy & Reliability



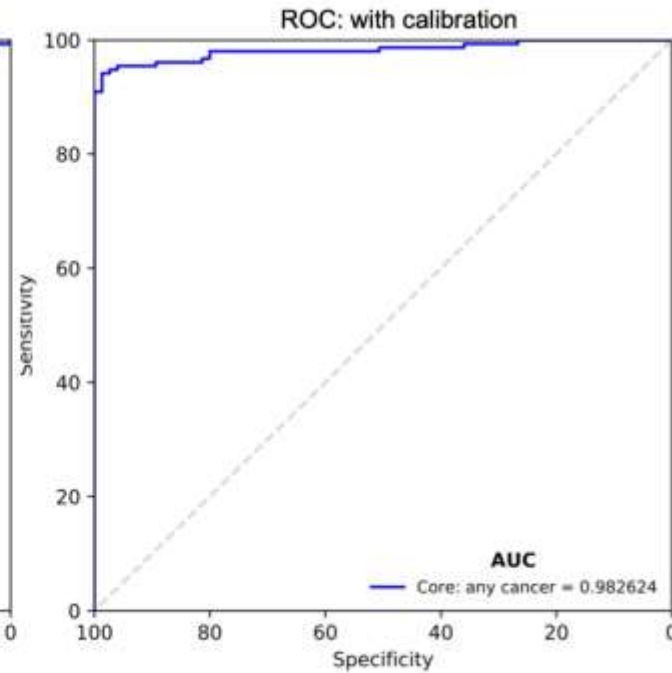
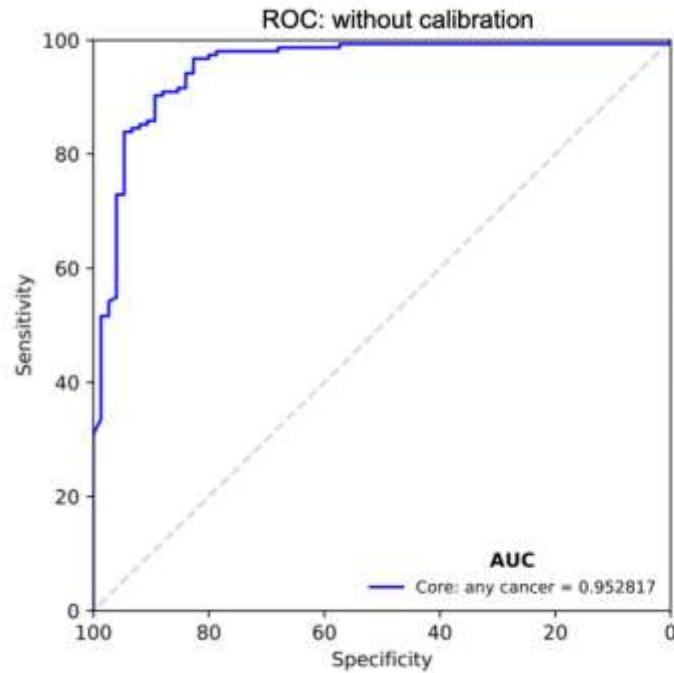
**Karolinska
Institutet**

Prostate
Centres
Across:

Sweden
Finland
Norway
Denmark

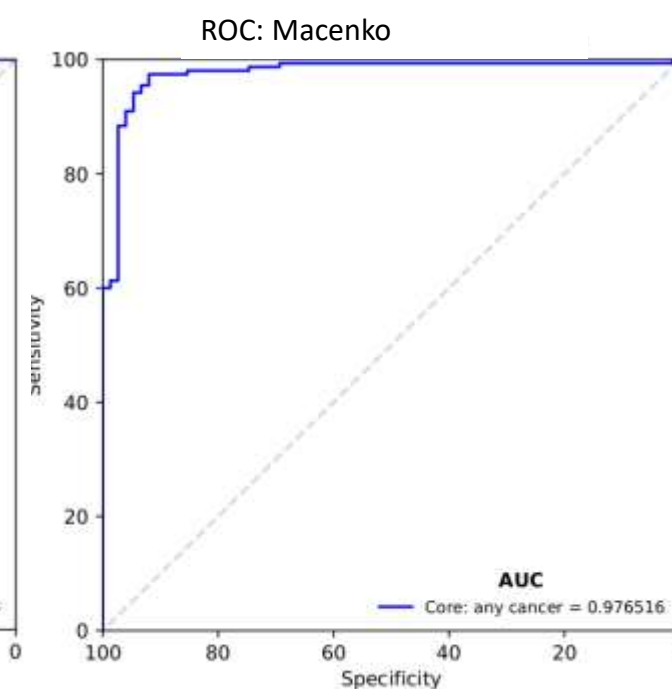
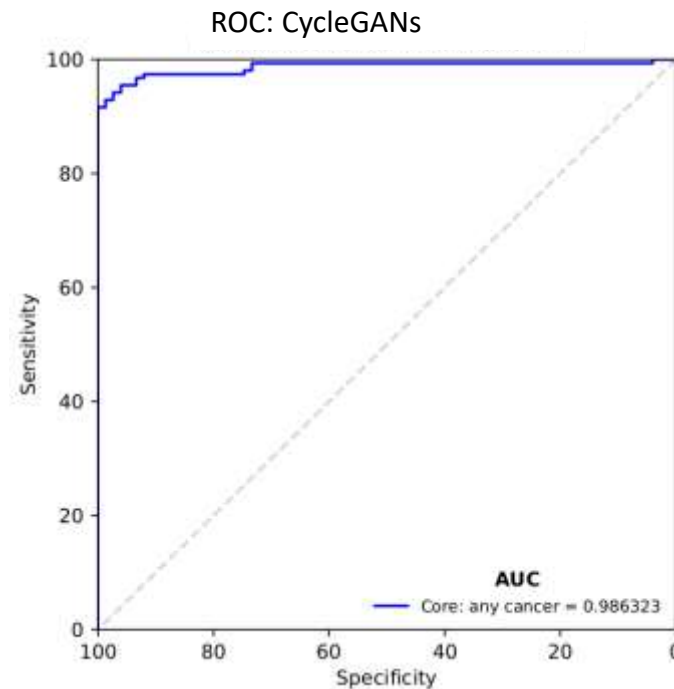


Prostate AI already
very accurate (95%)

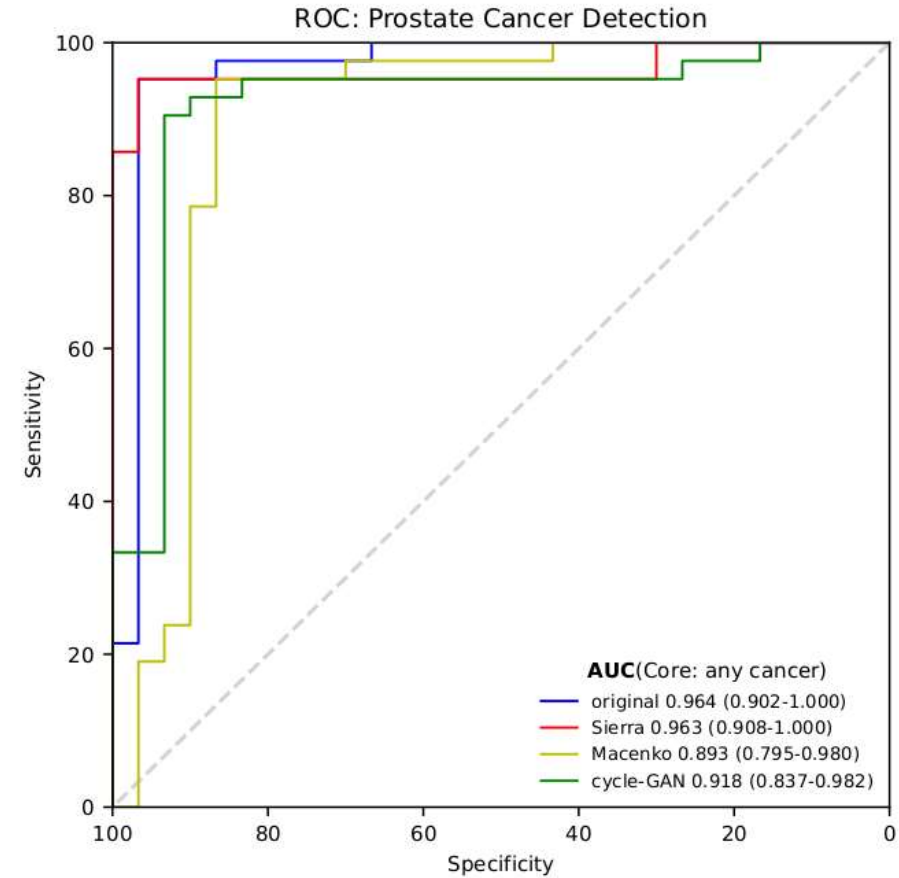
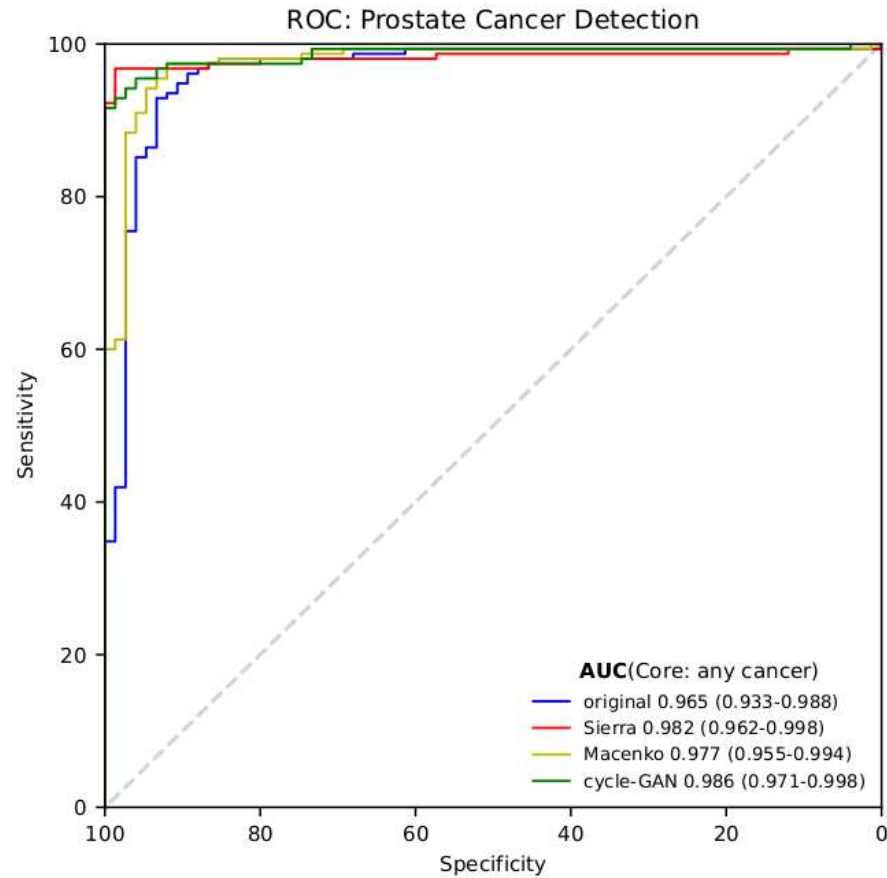


Detection accuracy
increased 3% when Sierra
standardised colour

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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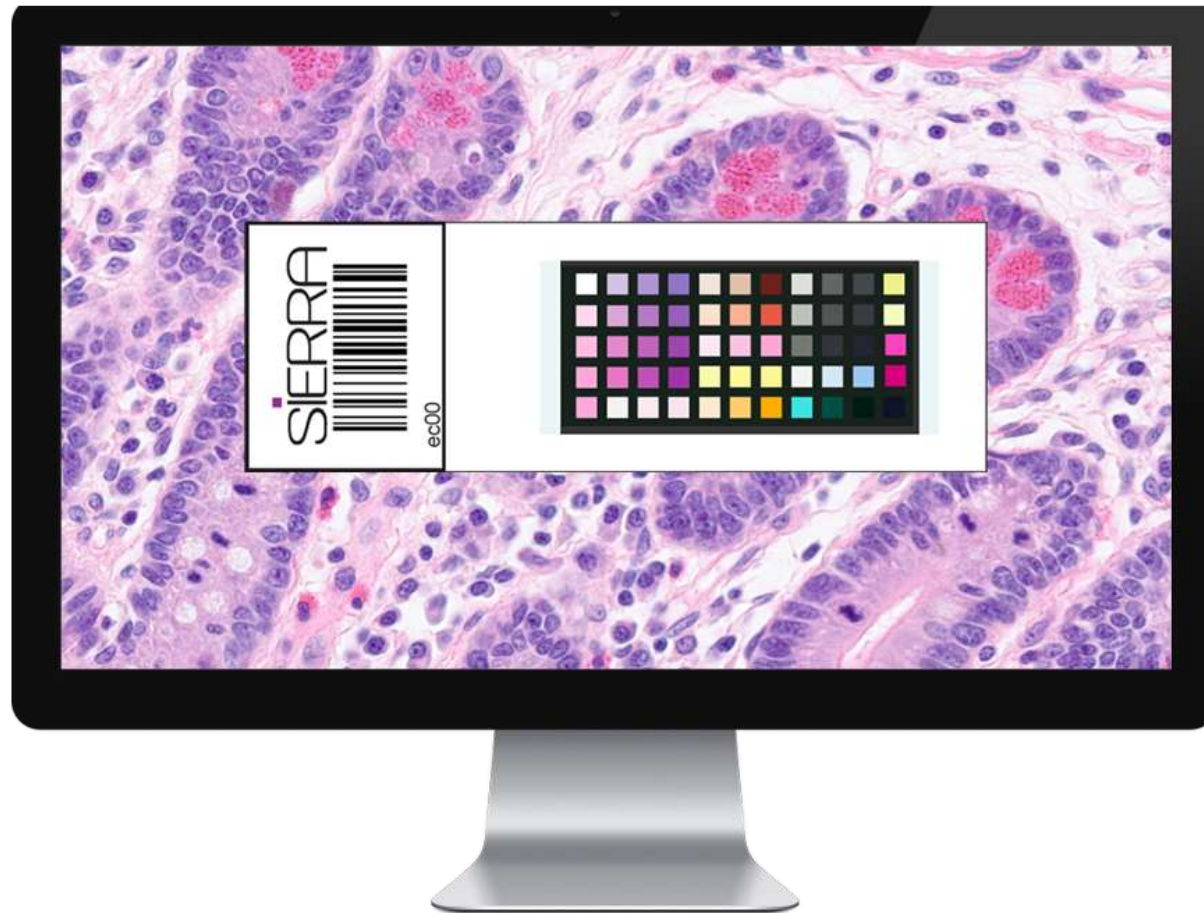
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Rick Salmon is an
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Get in contact to discover how Sierra helps your AI and WSI applications

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