ICC Working Group Meetings
Eastman Kodak Company
4225 Kincaid Street
Burnaby BC V5G 4P5
Canada

Medical Imaging Working Group minutes
18 November 2013

Mr Craig Revie, chair of the Medical Imaging Working Group, opened the meeting at 8.30am. Those present at the meeting and calling in remotely introduced themselves.

Mr Revie and Mr Aldo Badano welcomed the attendees to the first meeting of the Medical Imaging Working Group and introduced the session. Mr Revie introduced the Medical Imaging area of the ICC web site at http://www.color.org/groups/medical/medical_imaging_wg.xalter. He indicated that meeting records were archived on the web site. The meeting was being recorded and could be listened to after the meeting at http://www.npes.org/Portals/0/standards/2013-11-18%2011.52%20Medical%20Imaging%20Working%20Group.wmv

Before starting the business of the meeting, Mr Revie drew attention to the ICC IP policy, which is on the ICC web site at http://www.color.org/iccip.xalter.

The agenda for the meeting was presented as follows: [see attached]

Calibration slide for pathology

1. Colour calibration of digital pathology systems (Yukako Yagi)
2. GE/Omnyx calibration proposal (Vipul Baxi)
3. Calibration of Leica ScanScope AT2 (Allen Olson)
4. Calibration based on IT8.7/2 (Viktor Vargo)
5. Philips digital microscope calibration (Bas Hulsken)
6. Contents and structure of calibration materials and test methods (Craig Revie)
7. Discussion of next steps

Display calibration

8. Review of mRGB proposed standard (Michael Flynn)
9. Proposal for calibration target for medical color display systems (Tom Kimpe)
10. Research proposal to assess the impact of colour calibration on diagnostic accuracy (Elizabeth Krupinski)

11. Requirements and overview of current state-of-the-art colour calibration for mobile devices (Andy Masia)

Medical photography

12. Best practices for digital photography in medicine (John Penczek)
13. Calibration standard for ophthalmology (Christye Sisson)
14. Requirements for dental photography (Andrew Casertano / Francisco Imai)
15. Discussion of next steps

Other topics

16. Evaluation of DICOM greyscale display function (Phil Green)
17. Multispectral imaging extensions (Max Derhak)
18. Review of ICC usage by DICOM [Phil Green / David Clunie]

David Clunie was unable to attend the meeting and it was decided to defer the last topic to the Architecture Working Group meeting on 20 November.

Calibration slide for pathology

Aldo Badano noted that if this project is successful, the group will need to look at channels for standardization. The need for consistency and support for auto detection were emphasized as motivators for this work

1. Colour calibration of digital pathology systems

Dr Yukiko Yagi of Massachusetts General Hospital Pathology Imaging & Communication Technology Center presented some work on color standardization in digital microscopy [see attached]. She showed a range of stain images resulting from different protocols and stains, and compared original images with those standardized by normalization. She also considered the effect of scanner and viewer. In her view the main problem resulting from the lack of standardization was uncertainty around the accuracy of the colour images, effectively reducing confidence in diagnosis.

Dr Yagi showed a number of approaches to standardization, including a calibration slide image on the Harvard University web site. She demonstrated how colour correction improves consistency between scanners using a 9-patch slide calibration target she had developed.

Mr Revie summarized the Yagi calibration method, which has been circulated as a draft ICC White Paper and posted on the MIWG web site.

Mr David McDowell noted that ISO TC130 and TC42 have developed a number of standards relevant to calibration of captured images and subsequent display, and **will provide a summary to the group**.

Dr Yagi clarified that the slide calibration target she had developed was based on Rosco filters, and their spectral transmission is published as part of the manufacturer specification data. Experience has shown the material has good reproducibility.

She also noted that the display and slide white point are matched, and that the slide white point is assumed to be sRGB.

2. GE/Omnyx calibration proposal

Dr Vipul Baxi of Omnyx presented a description of the Onmyx calibration procedure [see attached]. The aim was to get the display to match what the user sees under the microscope. An individually measured film calibration slide based on the Macbeth ColorChecker had been developed and a 3x3 correction matrix generated from the microscope RGB and the measurement data. The mean colour error was 5.7 ΔE 94. A measurement of the blank film was taken as the slide white point.

It was pointed out that the calibration is based on a film dye set, which will not necessarily give good performance with a stain, depending on the sensor sensitivities. The display calibration was performed with a Spyder 4 Pro, and final measurements of the end to end system with an Ocean Optics USB4000.

Dr Michael Brill noted that guidelines for display measurement had been published by the Society for Information Display, and could be downloaded from http://www.sid.org/ICDM/IDMSLicenseDownload.aspx

Following calibration, a psychophysical evaluation was performed, using a simultaneous comparison and a categorical judgement scale. Mr John Dalrymple suggested that it might be better to separate the slide scan and display components, as in a typical ICC workflow, rather than an end to end calibration.

The meeting discussed the spectral transmittance of stains. It was suggested that this data could be combined and published as a journal article. Some stains (notably eosin) have colours outside the sRGB gamut.

While the majority of stains follow Beer's Law, so that the stain film thickness is linearly related to the transmittance, some have significant scattering and shifts of the spectral peak. There is no interaction between tissue and stain colour, but crystallization can be present unless there is something for the stain to bind to.

Stephen Hewitt has worked with the Biological Stains Commission in the US to understand the behaviour of stains better, and expects to publish this work shortly.

X-Rite delegates Tom Lianza and Andy Masia observed that modern scanners tend to have broader spectral sensitivities than traditional graphic arts scanners. Sensitivities that are linearly related to human colour matching functions have increased noise; the broader

sensitivity in modern scanners increases the signal to noise ratio but reduces accuracy, especially in the blue region.

3. Calibration of Leica ScanScope AT2

Dr Allen Olsen of Aperio ePathology, Leica Biosystems presented a description of work done to calibrate the Leica ScanScope microscope [see attached]. He emphasized a component-wise approach to the calibration, leaving display calibration to a separate step.

He had used an IT8.7/2 (ISO 12641) photographic slide to verify the characterization. Channels were independently white balanced to the clear patch on the slide, and individual regression equations derived.

The meeting asked whether fluorescence had any effect. Dr Olsen stated that eosin is quite fluorescent with both the fluorescent excitation and fluorescent emission in the visible range of the spectrum but as the emission occurs in all directions the effect on the calibration was small. He had compared published data on spectral transmittance of stains, and his observation was that most disagreement was at the spectrum edges, where the visual impact is very small. It was noted that in the DAB stain, peak absorbance changes with stain density and in general the density of stain alone does not predict the colour since the dyes used in stains also vary.

From the measurement data and the microscope RGB Dr Olsen had generated a look-up table, extrapolating by regression to obtain output values for the outer values in the LUT, such as the RGB primaries. sRGB had been assumed for the display, and ICC profiles had been generated with the LUTs. With the profiles the results were generally lighter and slightly more magenta. The results were generally good, the largest errors being found closest to the white point.

Dr Olsen suggested that spectral characterization methods could be developed, using the scanner spectral sensitivity, and potentially leading to a stain-specific profile for which the system would need to provide a way of identifying the stain type, possibly by bar-coding. Generic profiles had worked well, but stain-specific calibration might be expected to give better results.

Dr Po-Chieh Hung of Konica Minolta asked if the LUT smoothness had been evaluated. Mr Olsen replied that only primaries had been used, which he hoped combined smoothly. There were some residual non-linearities. Dr Brill noted that noise had a significant impact at the dark end when using density.

Mr Revie noted that there were 15 different staining protocols in common use with a maximum of three stains used at one time.

4. Calibration based on IT8.7/2 (Viktor Vargo)

Dr Viktor Varga of 3DHistech presented an outline of his experience of calibrating a scanner using an IT8.7/2 test target [see attached]. He had based the work on existing technology, including the sRGB standard for displays. He noted that the uniformity and consistency of displays is also of importance when standardizing scanner calibration. He considered that it was of prime importance to address developing country markets, mobile displays etc, where displays cannot readily be calibrated.

5. Philips digital microscope calibration (Bas Hulsken)

Dr Bas Hulsken of Philips presented work on microscope calibration using an IT8.7/2 target [see attached]. He compared errors using different modeling techniques, and also compare these with results on tissue. There was considerable variation between results on different scanners – for example closer fitting of the IT8.7/2 target was usually associated with worse results on tissues.

The LUT used is optimized for the calibration target. A linear 3x3 matrix had performed better than a matrix/tone reproduction curve or LUT approach. Dr Hulsken had also compare rendering intents, and found that Media-Relative Colorimetric introduced more variation.

Dr Hulsken showed the effect of focus and resolution on the modulation transfer function (MTF) of the system It was noted that ISO 12233 defines the slanted edge method for MTF measurement.

Dr Hulsken had made custom targets, and found small differences between them. He had also used IT8.7/2 test targets from Kodak.

The meeting noted some issues about measurement procedures, which used a directional geometry. Mr David McDowell undertook to **circulate a list of relevant ISO TC42 standards** on measurement of photographic test targets.

6. Contents and structure of calibration materials and test methods (Craig Revie)

Craig Revie introduced the draft document on slide calibration (see http://www.color.org/groups/medical/Digital_microscope_test_materials_and_test_methods-v2.pdf). He emphasized that he wanted to leave the actual calibration procedure to vendors, and in the document define the test methods. He hoped the group would provide input on the document to arrive at a set of agreed tests, and invited companies to contribute based on their experience.

In overview, the proposed system consists of:

A. A reference slide with associated spectral measurements, ideally using stain protocols.
B. An image file that can be analyzed to determine colours of scanned image.
C. Display signal measurement, possibly evaluating the data sent to the display rather than measure the display.

In this overview, the first part A is spectral while from B onwards is colorimetric. A standard file format (B), such as DICOM is required, such that there is a colorimetric interpretation of the image data e.g. using an ICC profile. The test procedure does not specify what methods should be used for the calibration, just how to evaluate it.

7. Discussion of next steps

In discussing the document, it was noted that Dr Wei-Chung Chang of the FDA had proposed using a field-programmable gate array to capture the RGB values sent to the display. It was noted that in modern displays the actual data sent to the display is hashed, so would need to be sampled before it is sent to the DVI output.

The meeting agreed that generic acceptance criteria were not needed in the document. For regulatory approval, a 'safe and effective' threshold is required. This threshold could be dependent on the modality or application.

It was agreed that **the group would contribute to the document**.

Display calibration

8. Review of mRGB proposed standard

Dr Michael Flynn of Henry Ford Health System introduced the mRGB colour space proposal (see attached). This is a draft report of AAPM Task Group 196.mRGB is based on a set of primaries and the Gray Scale Display Function (GSDF) in neutrals.

The proposed specification does not define ambient illuminance or chromaticity, but is intended to support a wide range of end use viewing conditions. The GSDF Lmax, Lmin and Lambient are dependent on the actual display and viewing conditions. The reflectance of a panel when off is defined to be ¼ of the black point Lmin. The white point can be 250, 350 or 420 cd m^{-2}. This would make it possible to have pre-computed profiles, or firmware that allows selection from preinstalled tables.

In response to the discussion, Dr Flynn stated that the adaptive dynamic range is specified because the human visual system is unable to distinguish dark colours at higher dynamic range levels. In principle the DICOM file format permits storage of metadata or an ICC profile defining the intended viewing condition, and the display in a DICOM system should adapt for the GSDF in an image. The image can then be re-rendered to the display.

In some modalities such as radiology it is already assumed that the display is calibrated to the GSDF. The goal of the mRGB work is to extend this to colour in such a way as will allow monochrome and colour images to be displayed together.

The AAPM task force / IEC TG196 will meet in Chicago on 1st December, and anyone interested in this work is invited to contact Dr Flynn for details.

9. Proposal for calibration target for medical color display systems

Mr Albert Xthona of Barco Healthcare presented a summary of the need for display calibration in medical imaging and a proposed calibration target [see attached].

It was emphasized that in medical imaging it is important to show differences between things, rather than absolute colours. Any calibration system needs to allow for future improvements in technology, such as display gamut and image capture systems.

Mr Xthona outlined requirements for a display calibration target. In practice it is possible to make simultaneously viewed displays match each other, although this implies calibrating to the lower dynamic range and gamut of the two. He showed the workflow, and noted that one goal was that the system should be scalable.

The meeting discussed the use of colour difference metrics to evaluate calibration accuracy. Dr Brill observed that Riemannization of CIELAB-based colour difference metrics allows creation of a uniform space from such a metric (e,g, see http://www.ansatt.hig.no/ivarf/publications/Pant_11_cra.pdf).

Mr Xthona also reported that work is being done at Barco to improve the angle-dependency of their medical displays. They try to ensure the display is 'well-behaved', for example losing contrast and saturation slowly. The meeting also noted that modern displays were designed to work better at higher viewing angles (i.e. elevations above the normal) than lower ones, since displays are more commonly looked at from above.

Mr McDowell recommended referring to ISO TC130 standards that provide display measurement and setup parameters, such as ISO 12646.

10. Research proposal to assess the impact of colour calibration on diagnostic accuracy

Professor Elizabeth Krupinski presented a summary of proposed research [see attached]. Her previous study had showed that diagnostic accuracy is not affected by display setup, but efficiency is. She now wishes to find out whether having user preferences for display parameters will affect diagnostic accuracy or efficiency.

Professor Krupinski has identified 10 common stains for the experiment. The aim will be to determine whether an individually calibrated display, where the system learns the user preferences, or a more perceptually uniform, universally applicable system is better. To do this she will determine which calibration method works best, and then compare with preference-driven, tailored displays.

The project is proposed as a 5-year study, with preference data generated by 2016.

11. Requirements and overview of current state-of-the-art colour calibration for mobile devices

Mr Andy Masia presented a summary of colour calibration for mobile devices [see attached]. He emphasized that the use of mobile devices for viewing medical images is a reality, regardless of the difficulties of calibrating or colour managing such systems. Practitioners currently want to see on screen what they see on a microscope, even though this may not be optimal for diagnosis.

Mr Masia identified some of the problems with control of colour on mobile systems, such as:

- There is no registry infrastructure, e.g. to store the system profile
- Some systems have Dynamic Contrast Control which adjusts the display according to the ambient illumination (this can sometimes be turned off in user preferences)
- Display measurement is constrained by the lack of USB power on most devices; WiFi and Bluetooth are possible options but would add cost

The two potential approaches to colour management for mobile systems are server-based (where the server is responsible for the colour management but needs to know the calibration state of the device) and client-based (where the device is responsible for its calibration state). To develop suitable systems the use cases need to be determined, e.g. whether gamut scalability is needed. The architecture does not necessarily have to be standardized, as the system integrator could select this.

Mr Masia invited delegates to **participate in developing use cases and systems**.

Medical photography

12. Best practices for digital photography in medicine

Dr John Penczek presented work on medical photography best practices [see attached]. The work arose from the ICC/FDA Summit on Color in Medical Imaging held in May 2013. He had found the largest characterization errors on capture, so wanted to work to minimize these.

Dr Penczek showed the draft document outline, listed suggested contributors and **invited participation**. He emphasized the need to build on existing information where possible, and not duplicate or reinvent.

The meeting discussed where the document should be published. Dr Brill proposed an initial journal article, followed by an ICC White Paper, and then to collaborate with other organizations to develop standards. Mr Revie suggested each topic could potentially be a journal article.

It was felt that targeting areas where colour accuracy is important, such as telemedicine, should be a priority.

13. Calibration standard for ophthalmology

Ms Christye Sisson provided a presentation on ophthalmic imaging standards, focusing on calibration of retinal images [see attached]. She showed examples of uncalibrated images of a single retina on different capture devices, and the result of applying a calibration.

In the discussion it was noted that dermatoscopy has similar requirements, and in this field methods of colorimetric imaging have been published. It was agreed to provide a link to this publication. The problem is also similar to that of whole-slide imaging (WSI), where there is a need to calibrate for a particular type of material with spectral reflectances/transmittances which differ from photographic dye sets. Dr Brill noted that there was a need to define performance levels for the fundus cameras, as some may fail to give adequate results even after calibration.

14. Requirements for dental photography

The meeting discussed the particular requirements in dental photography, which involve precise recording and colour matching of prosthodontic materials including teeth and bridges, both for making new prosthodontics and for archiving patient records. Francisco Imai of Canon noted that there were a number of publications in this area, and a Society for Color Appearance in Dentistry has been established.

The meeting agreed that the capture of appearance in dentistry is as yet an unsolved problem. Matching colours in prosthodontics is not a simple formulation problem, as ceramic materials such as zinc dioxide are heated to very high temperatures and inevitably this involves a change in colour. Shade guides are widely used, but these are not stable over time.

Dr Brill undertook to **provide links to current ASTM standards in this area** to David McDowell, who will collect these and report to the group.

15. Discussion of next steps

This was deferred to the end of the meeting.

Other topics

16. Evaluation of DICOM greyscale display function

Dr Phil Green of Gjøvik University College, Norway presented some work undertaken recently by his PhD student Kwame Baah to derive just-noticeable differences in neutrals

on a display, and compare these with the predictions of the DICOM GSDF and the function being considered by CIE TC1-93 for defining self-luminous grayscales under different conditions [see attached]. The initial results suggest that both functions predict the experimental JNDs reasonably well.

17. Multispectral imaging extensions

Mr Max Derhak of Onyx Graphics presented a summary of multispectral imaging in IccLabs [see attached]. This is based on new features planned for ICC v5, and will allow a variety of workflows using spectral image data and spectrally defined viewing conditions.

In the discussion it was suggested that software needs to have intelligence to prevent the wrong processing being applied. This intelligence will need to be in the CMM. Additional work will be needed to define specifications for different application areas and modalities, and it is not possible to make assumptions about what these will be at this stage.

Summary and next steps

Mr Craig Revie briefly summarized the meeting and thanked the presenters and the audience for their participation. The meeting proceeded to discuss possible next steps.

There were possibilities of meetings held in conjunction with regular ICC meetings in Tokyo in early March and Heidelberg in mid-June. Another option would be to hold a meeting in conjunction with a meeting of the Radiological Society of N America. Mr Matsui-san suggested working with Professor Yamaguchi to investigate the possibility of meeting in Tokyo, where a number of the vendors are located.

Although the remote participation for the meeting had worked adequately, the meeting felt that it could be difficult to participate in this way. It would be better to hold such meetings with a specific topic focus, for 1-2 hours depending on the topic. It was agreed to hold meetings on the third Thursday of every month at 10:00am EST, with the following schedule:

19 Dec: Medical Photography

16 Jan: Displays

20 Feb: WSI

20 Mar: Dental

17 Apr: Mobile

Additional teleconferences can be arranged as needed (contact Debbie Orf at NPES to set up). Mr Revie will also set up a meeting for the calibration slide by Doodle poll – at this stage just bullet points for content are needed.

The meeting closed at 5:30pm.

Action Items

Colour calibration of digital pathology systems

1. Provide a summary of relevant ISO TC130 and TC42 standards to the WG members (David McDowell)
2. Coordinate an email discussion regarding the development of a white paper (Craig Revie)

Contents and structure of calibration materials and test methods

3. Contribute to document (WG members)

Best practices for digital photography in medicine

4. Participate in developing document (WG members)

Requirements for dental photography

5. Provide links to current ASTM standards in this area to David McDowell (Michael Brill)

International Color Consortium

Medical Imaging Working Group agenda

Vancouver, 18th November 2013

Agenda - calibration slide for pathology

08:30 (**15**)	Introduction	Craig Revie / Aldo Badano
08:45 (**20**+10)	Colour calibration of digital pathology systems	Yukako Yagi
09:15 (**20**+10)	GE/Omnyx calibration proposal	Vipul Baxi
09:45 (**20**+10)	Calibration of Leica ScanScope AT2	Allen Olson
10:15 (**20**+10)	Calibration based on IT8.7/2	Viktor Vargo
10:45	Coffee break	
11:00 (**20**+10)	Philips digital microscope calibration	Bas Hulsken
11:30 (**15**+45)	Contents and structure of calibration materials and test methods *Discussion of next steps (one hour minimum)*	Craig Revie
12:30	Lunch break	

Agenda - display calibration

13:30	Introduction	Craig Revie
13:30 (**15**+5)	Review of mRGB proposed standard	Michael Flynn
13:50 (**15**+5)	Proposal for calibration target for medical color display systems	Tom Kimpe
14:10 (**15**+5)	Research proposal to assess the impact of colour calibration on diagnostic accuracy	Elizabeth Krupinski
14:30	Coffee break	
14:45 (**20**+10)	Requirements and overview of current state-of-the-art colour calibration for mobile devices	Andy Masia

Agenda – medical photography

	Medical photography	
15:15 (**15**)	Best practices for digital photography in medicine	John Penczek
15:30 (**15**)	Calibration standard for ophthalmology	Christye Sisson
15:45 (**15**)	Requirements for dental photography	Andrew Casertano / Francisco Imai
16:00 (15)	*Discussion of next steps*	
	Other topics	
16:15 (**15**+5)	Evaluation of DICOM greyscale display function	Phil Green
16:35 (**15**+10)	Multispectral imaging extensions	Max Derhak
	Review of ICC usage by DICOM	[Phil Green / David Clunie]
17:00	Evening reception	

Why standard methodologies for the assessment of the color transfer properties in digital microscopy?

1. **Evidence of color performance of slide scanners will facilitate technology comparisons (not only with the optical microscope) and provide an approach to the bench test requisites for the regulatory review of such devices.**
2. **A methodology for measuring would allow for consistency within and among systems/vendors which is required to allow the development of robust computer-assisted detection and diagnosis approaches.**
3. **In addition, the methodology could be part of procedures for system and component QC/QA.**

Aldo Badano, FDA Laboratory of Imaging Physics

Why standard methodologies for the assessment of the color transfer properties in digital microscopy?

4. **Such a test might increase opportunities for innovation at all levels of the imaging chain by providing a standard methodology to identify components with improved performance.**
5. **The use of the methodology will contribute to the understanding of the limitations of digital systems in terms of color performance.**
6. **A standard methodology will be useful for other areas of digital microscopy including novel stains/techniques (eg, multispectral).**

Color aspects and Color Standardization in Digital Microscopy

Yukako Yagi, PhD
yyagi@partners.org
Director of the MGH Pathology Imaging & Communication Technology Center
Assistant Professor of Pathology, Harvard Medical School
Affiliate Faculty, Wellman Center for Photomedicine, MGH

MASSACHUSETTS GENERAL HOSPITAL
PATHOLOGY

HARVARD MEDICAL SCHOOL

Today's Topics

- Towards Standardization
- Color Aspects
- Types of Color Issues in WSI
- Color Standardization

Towards Standardization

Standardization in Digital Microscopy

Standardization of the image quality and the color displayed are important aspects of digital pathology implementation. While the most common reason for the variations of color and image quality is the variance in the protocols and practices in the histology lab, the image displayed can also be affected by variation in capture parameters, image processing and display factors in the digital systems themselves. It is difficult to identify which exactly causes the problem.

Steps: Towards Color and Image Quality Standardization

1. To Notice
   - To realize the image quality and color issues are often present in the images we use
2. To Identify
   - To identify the causes of issues in WSI
3. To Solve
   - To develop the methodologies to improve the color and image quality of WS images
4. To Promote
   - To introduce the methods solutions to the public

Standardization

Today, we focus on "color" in Whole Slide Imaging (WSI)

Color Aspects

Color Aspects in Digital Pathology

- Thickness of Specimen
- Staining
- Scanner or Scanning process
- Viewer Software
- Display

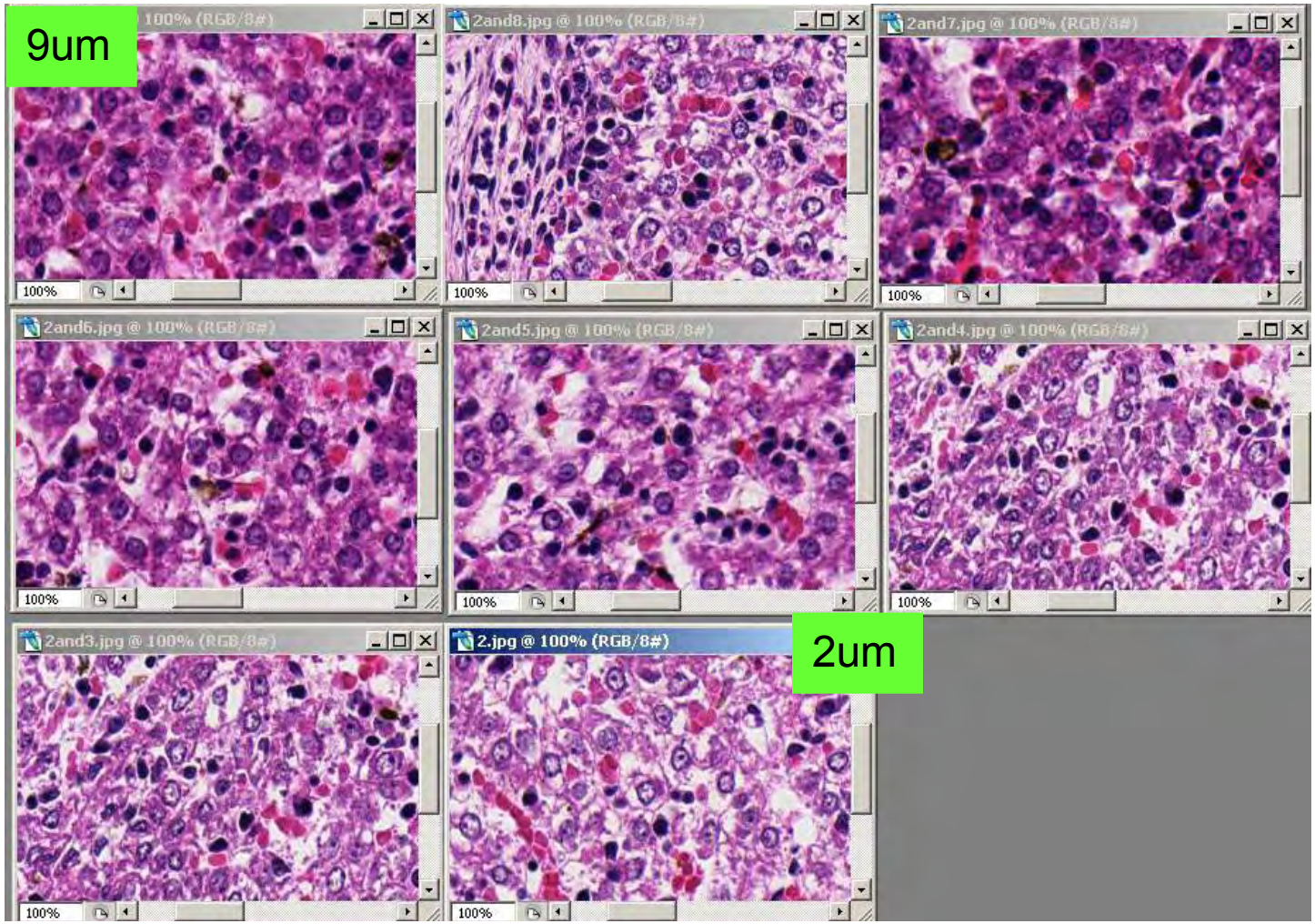
Color Aspects in Digital Pathology

- Thickness of Specimen
- Staining
- Scanner or Scanning process
- Viewer Software
- Display

Thickness of Specimen & Staining

Thicker sections are stained more by the automated staining machine

Thickness of Specimen & Staining



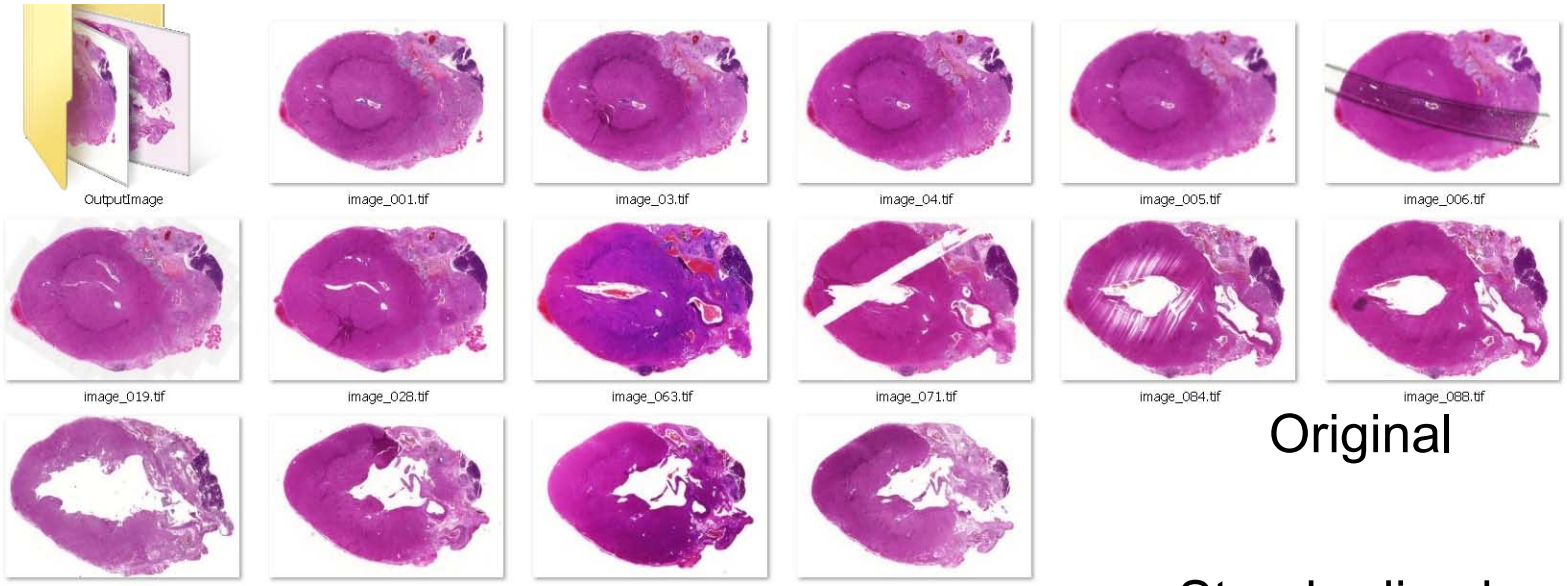
More details can be seen on slides of thinner sections

Thickness of Specimen & Staining

The appearance of stained slide varies between laboratories or institutions

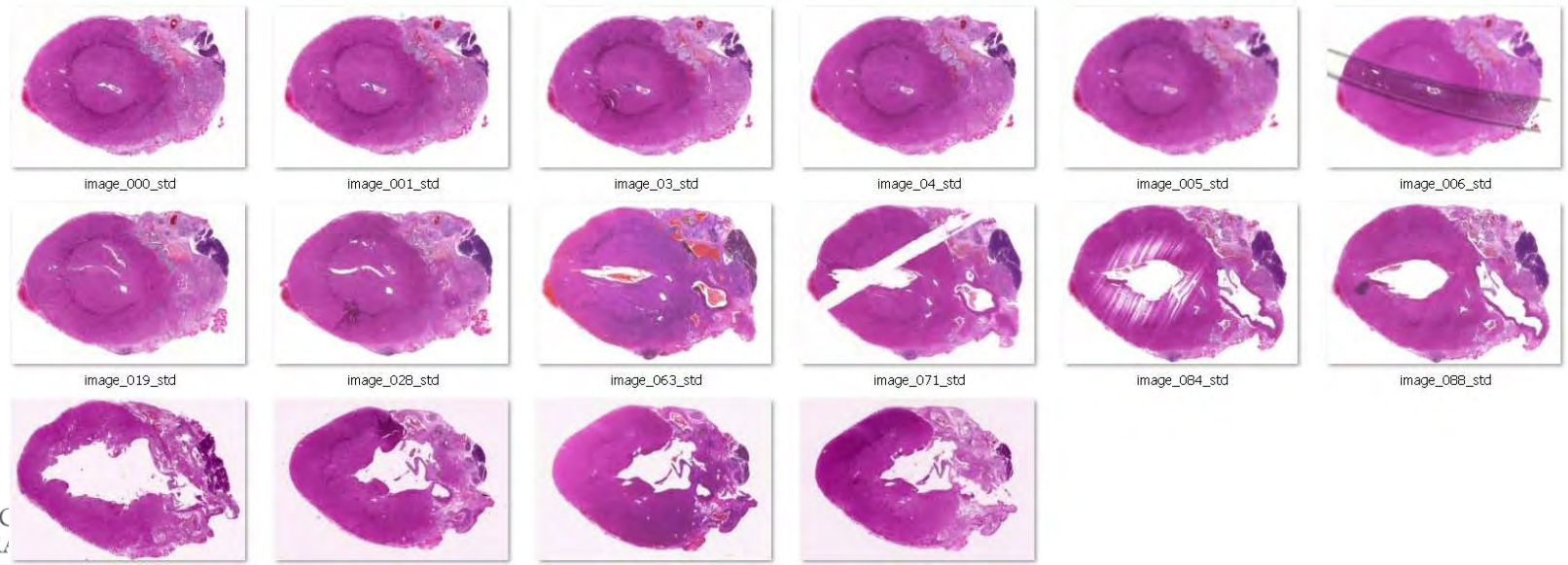
Examples of H&E stained variations caused by variations in staining protocols

Color issues in WSI 3D (Staining)

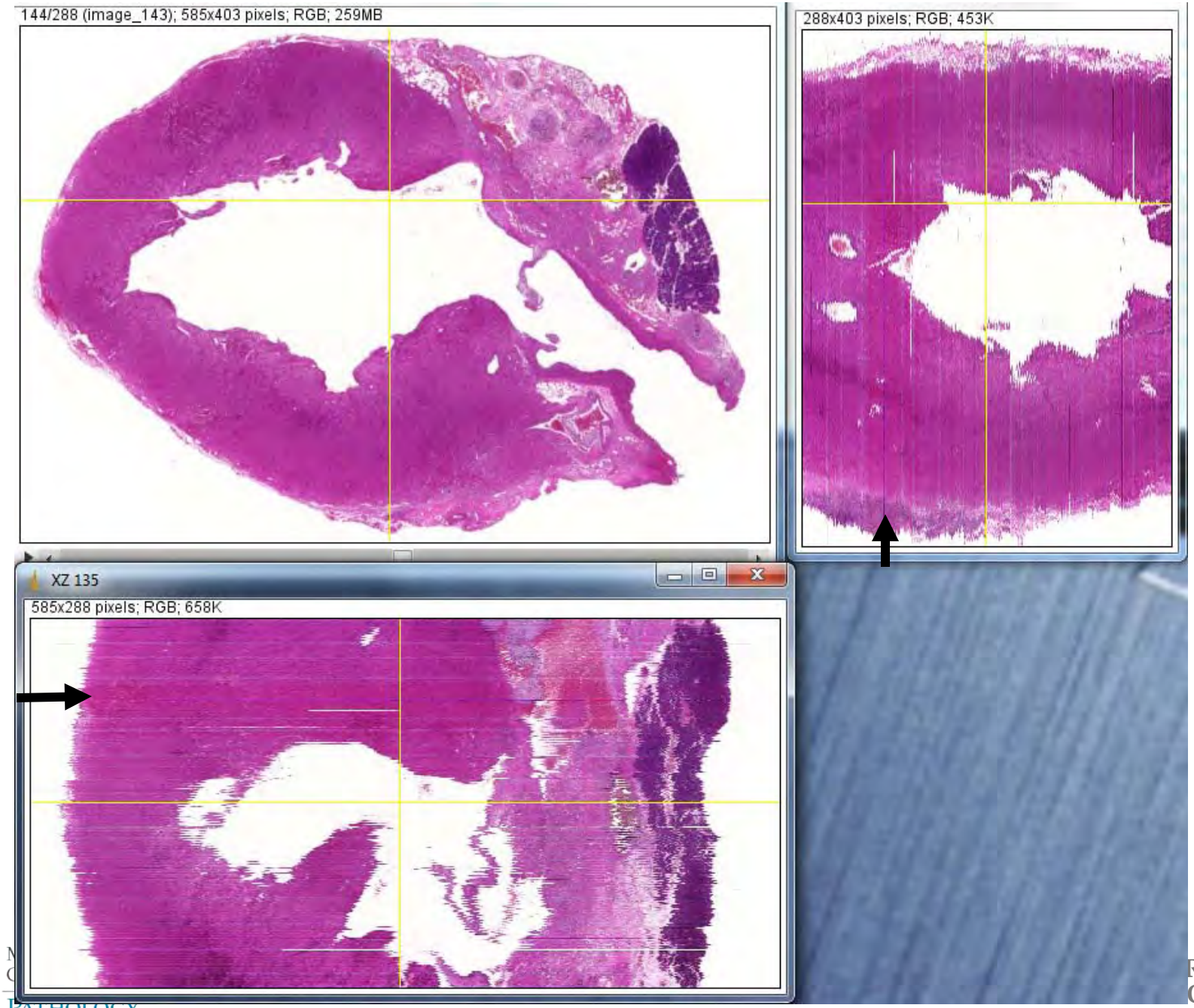


Original

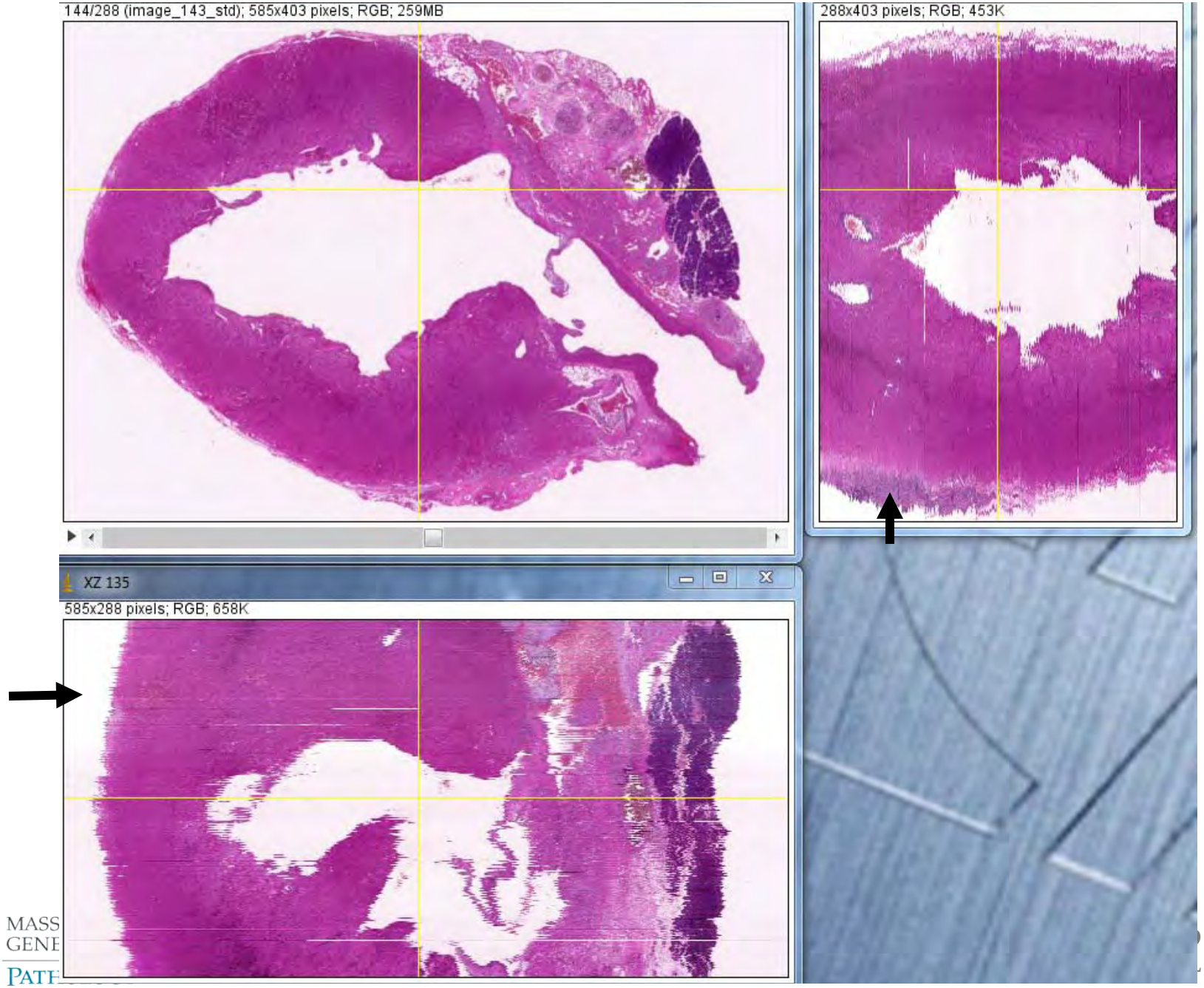
Standardized



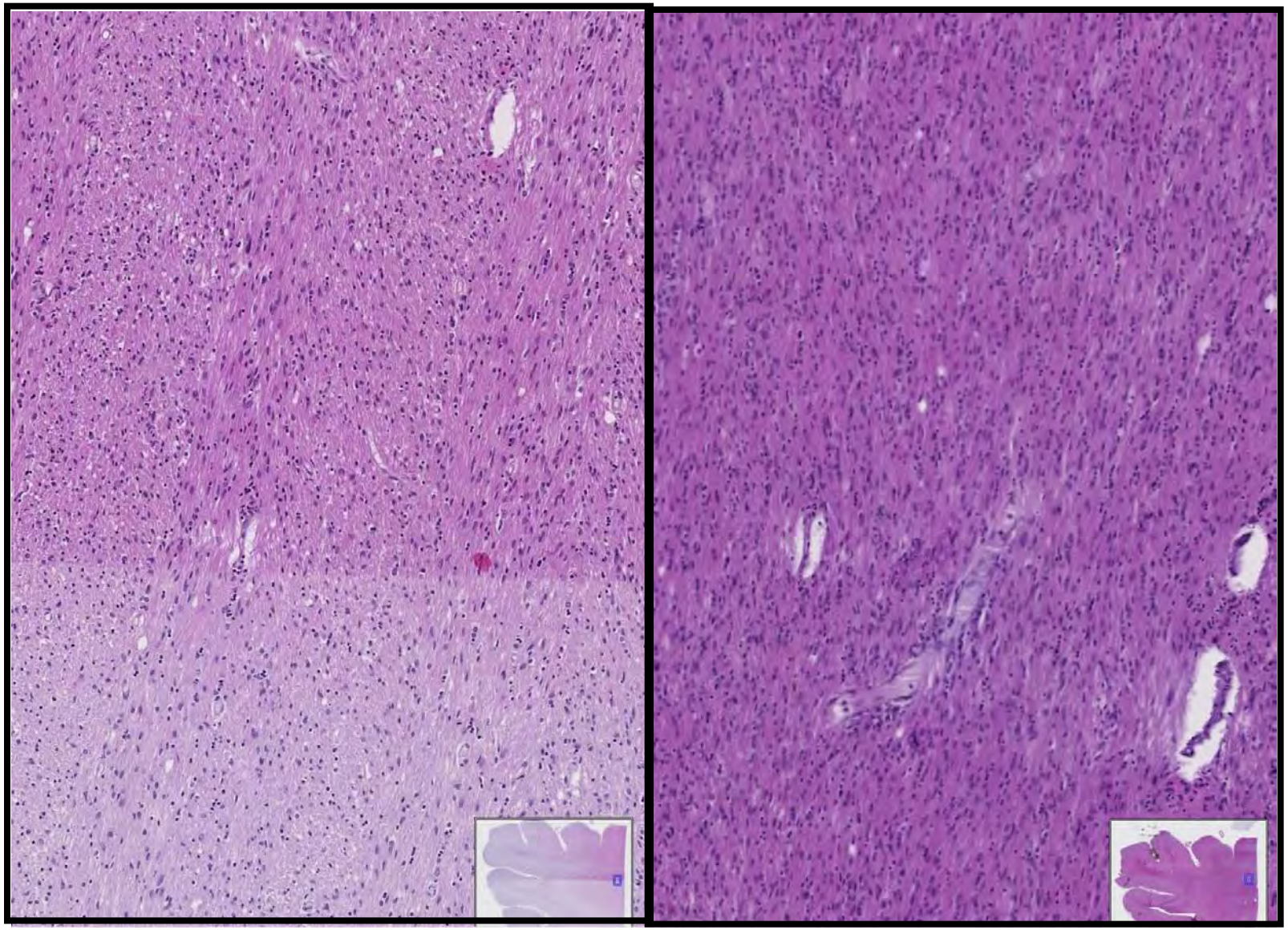
Before color normalization



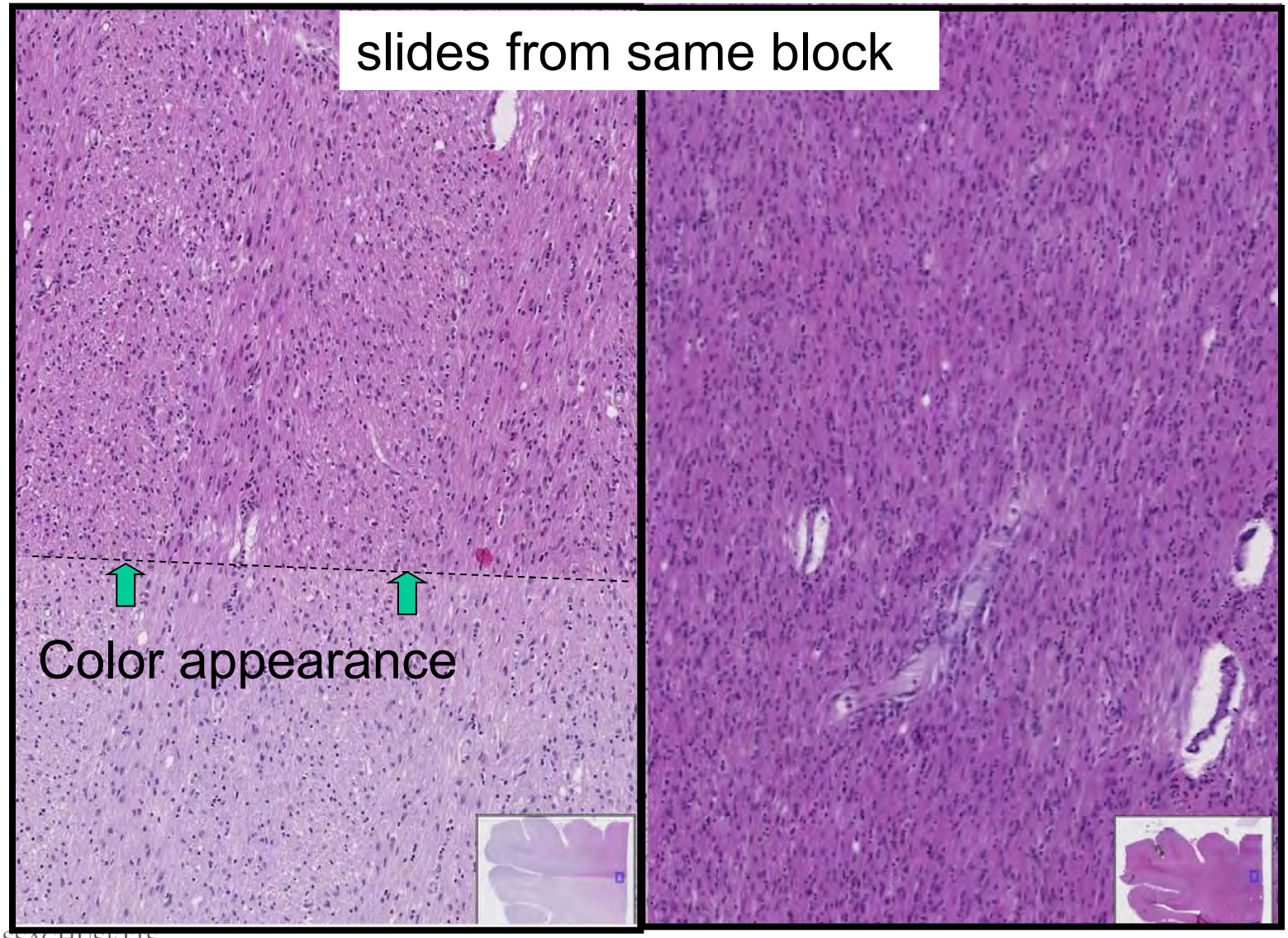
After color normalization



Thickness of Specimen & Staining issues in serial sections of WSI



Thickness of Specimen & Staining issues in serial sections of WSI

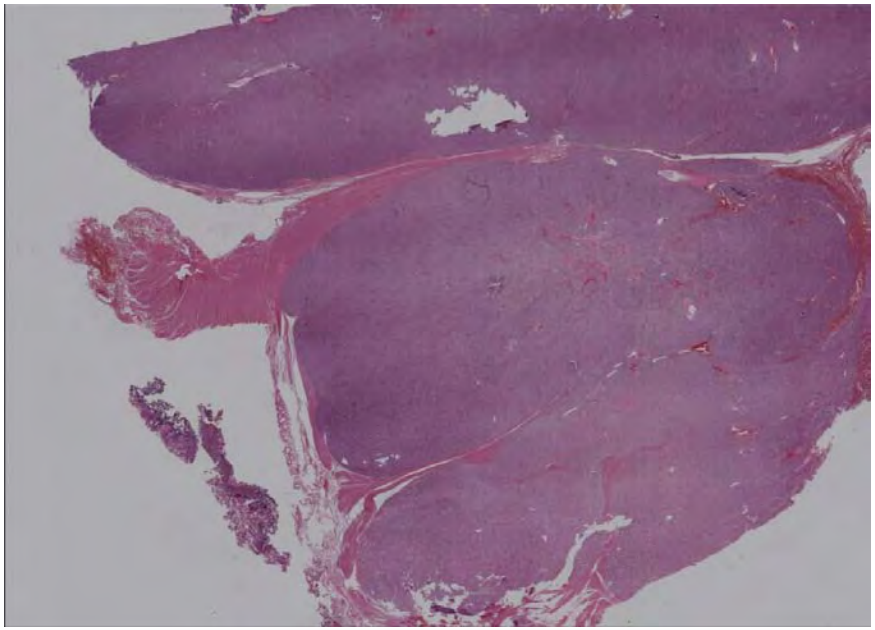


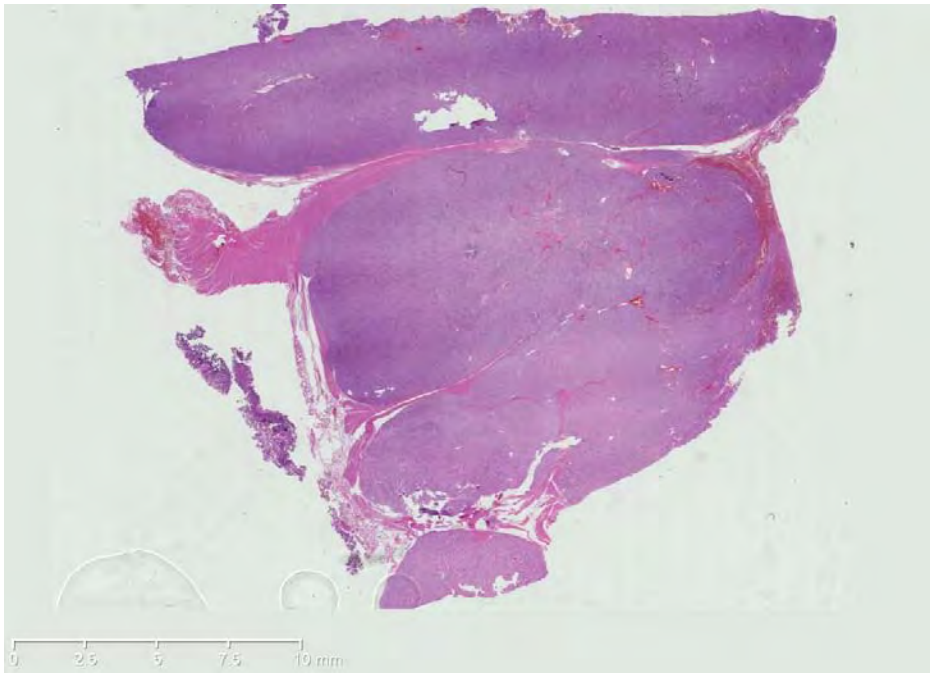
Color Aspects in Digital Pathology

- Thickness of Specimen
- Staining
- Scanner or Scanning process
- Viewer Software
- Display

Scanner or Scanning Process

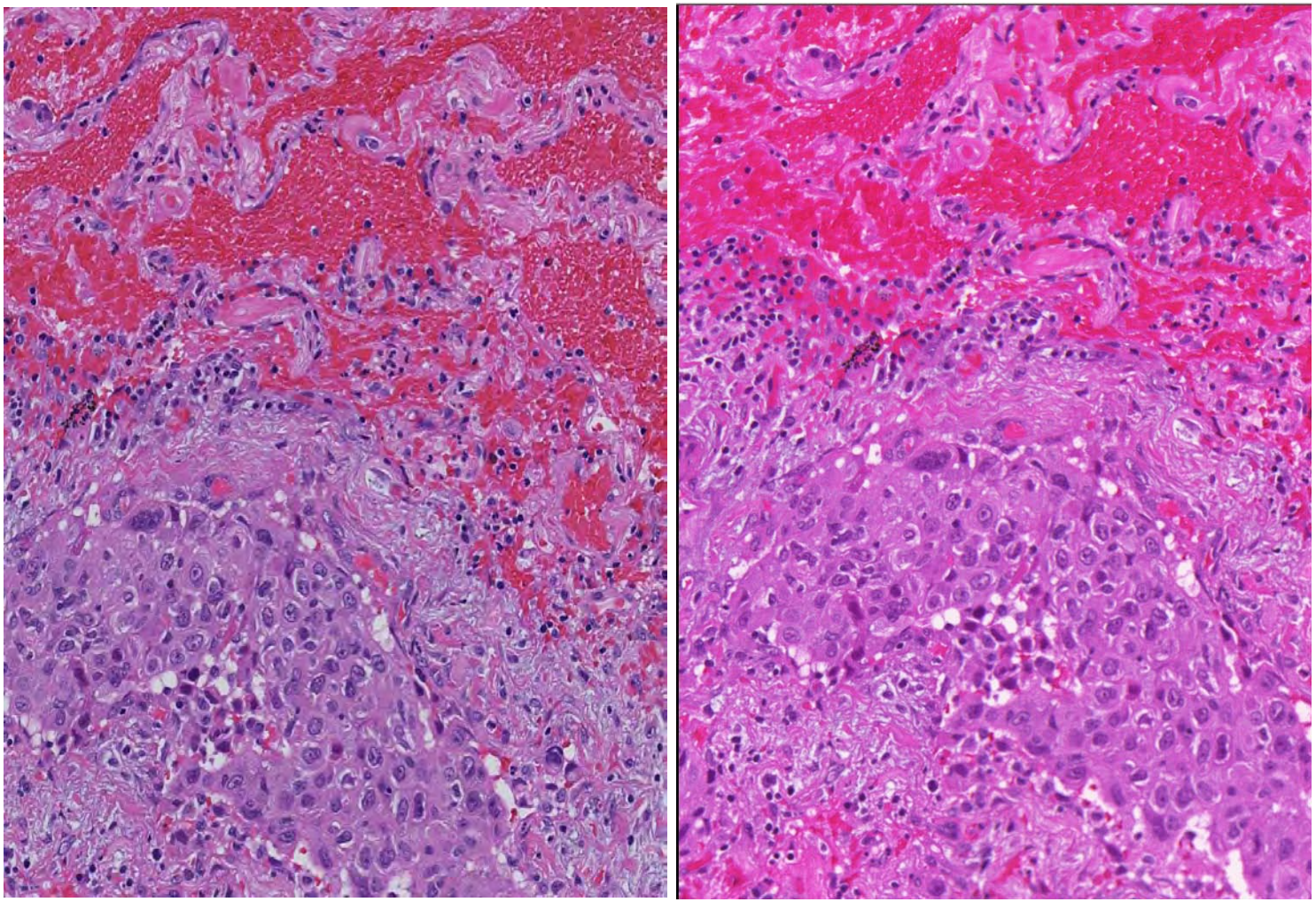
Same slide, different scanners



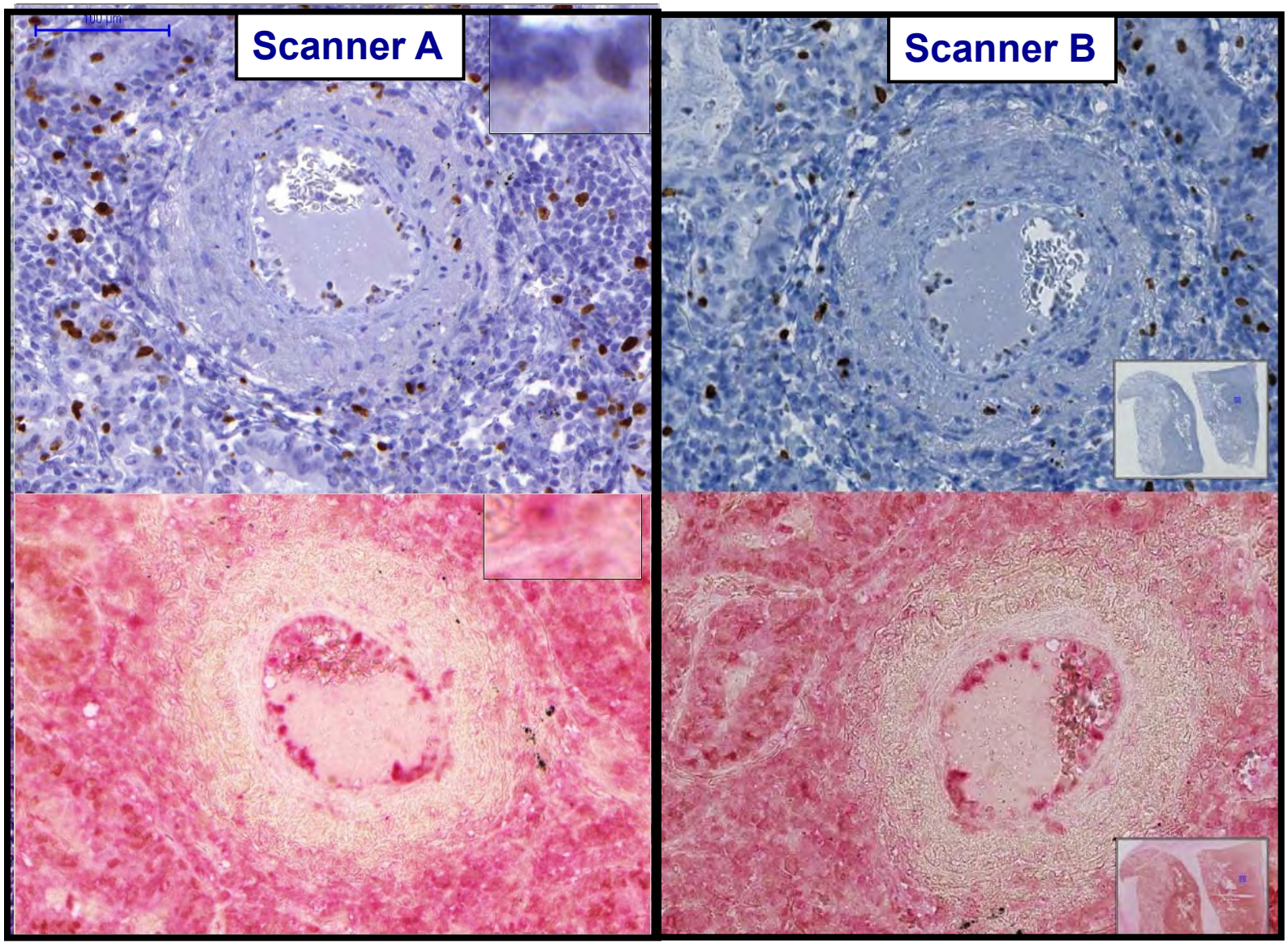


Scanner or Scanning Process

Same slide, different scanners



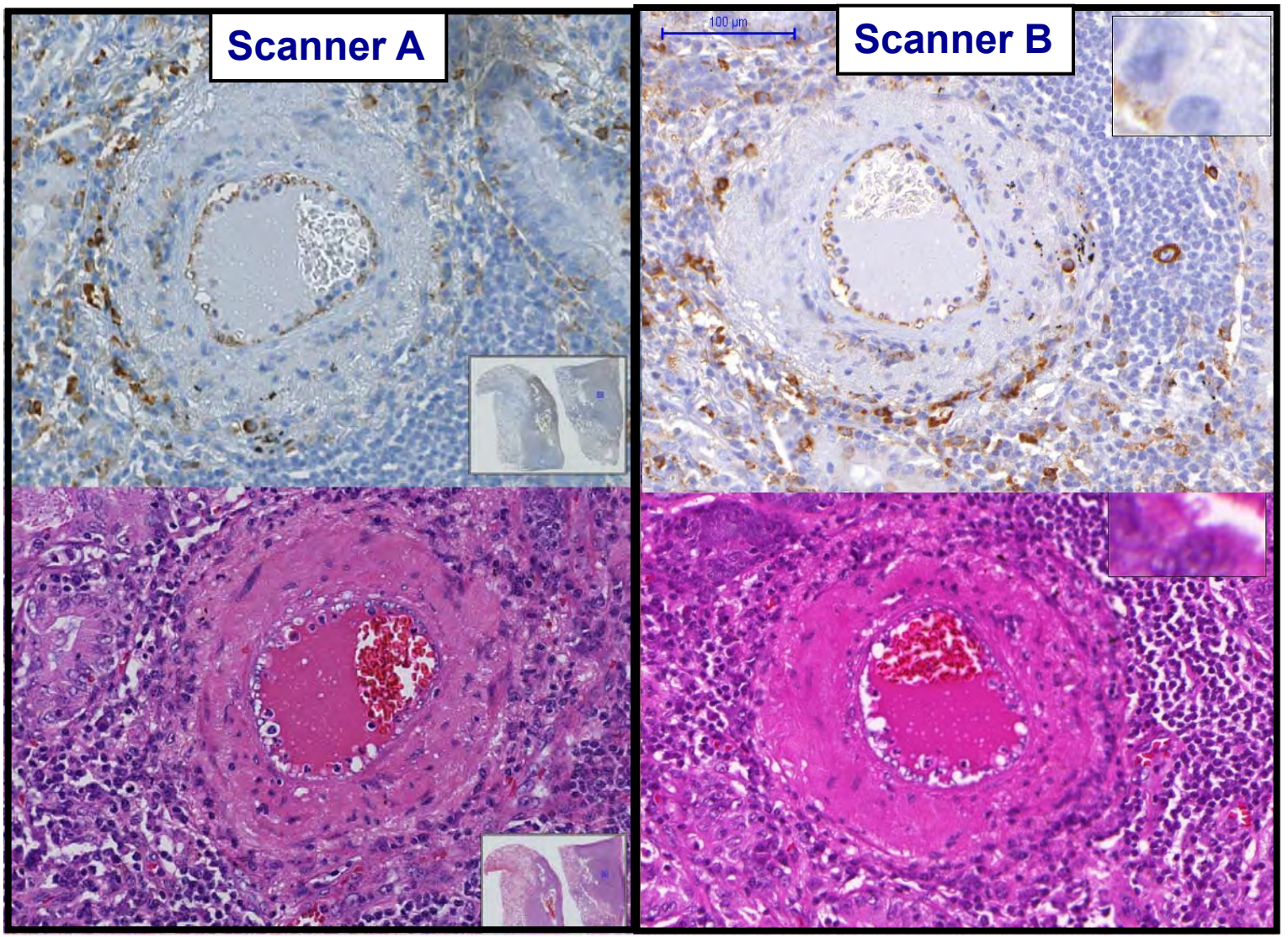
Scanner or Scanning Process



IHC

IHC Double Stains

Scanner or Scanning Process

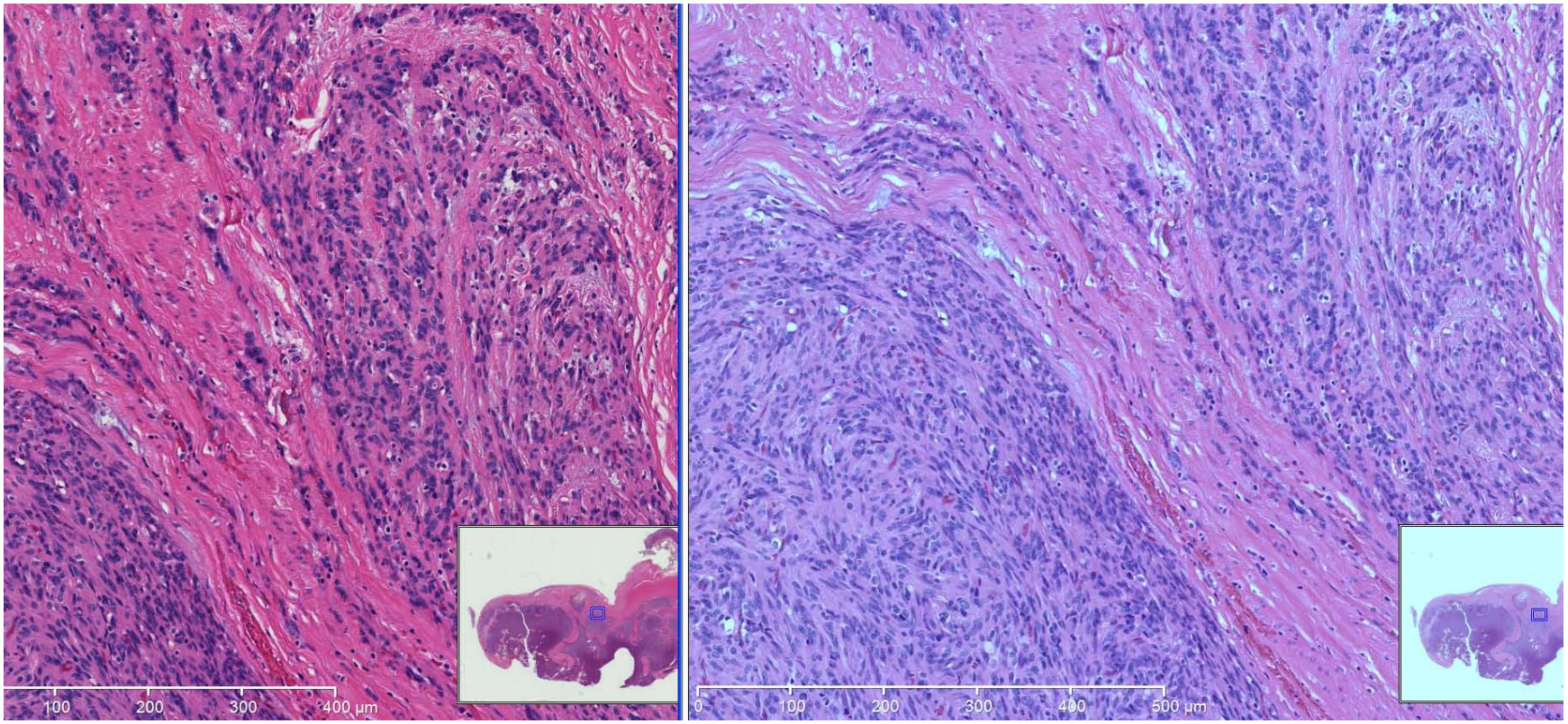


Color Aspects in Digital Pathology

- Thickness of Specimen
- Staining
- Scanner or Scanning process
- Viewer Software
- Display

Viewer Software

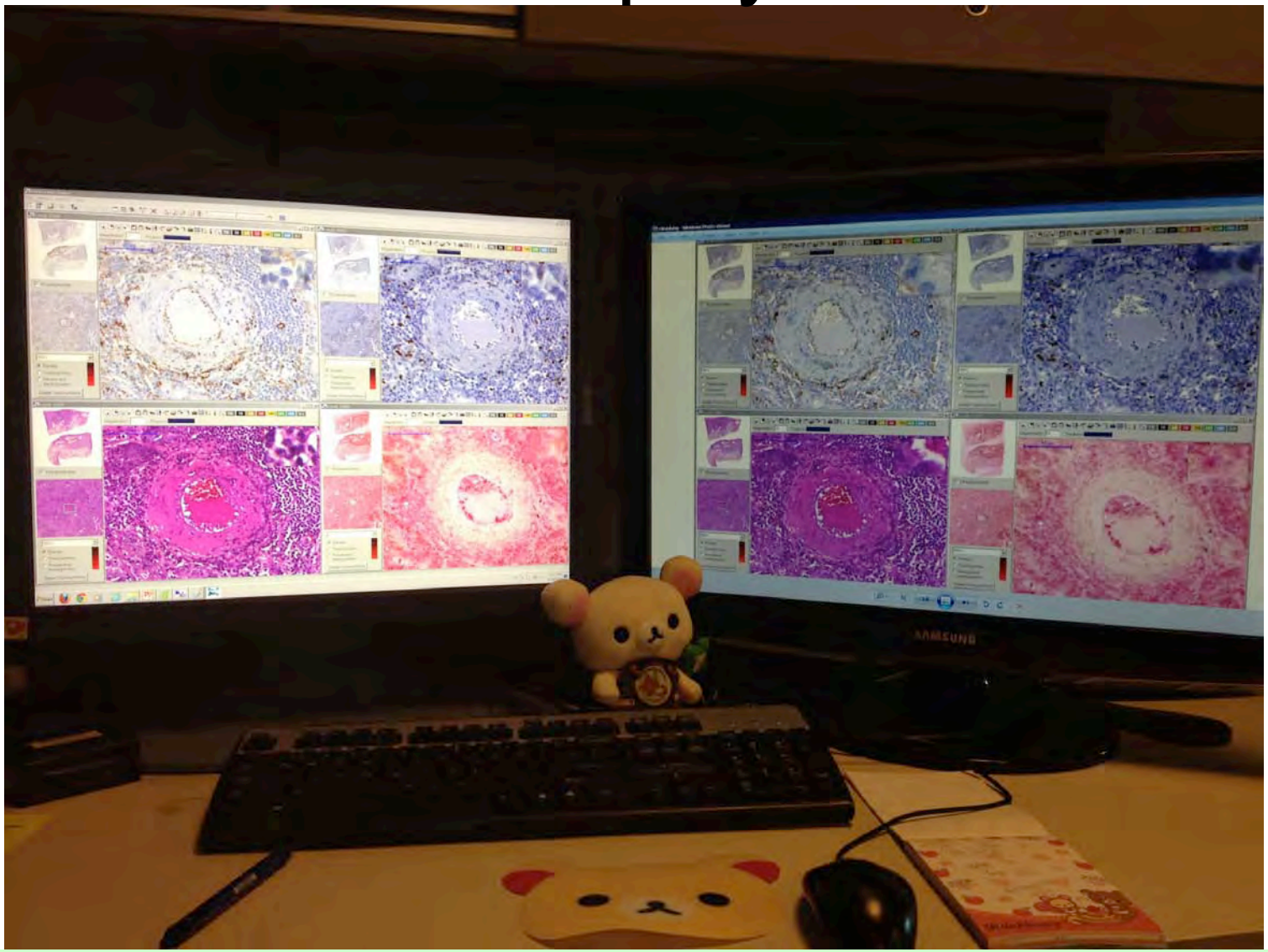
Same scanner, same slide, two different viewers



Color Aspects in Digital Pathology

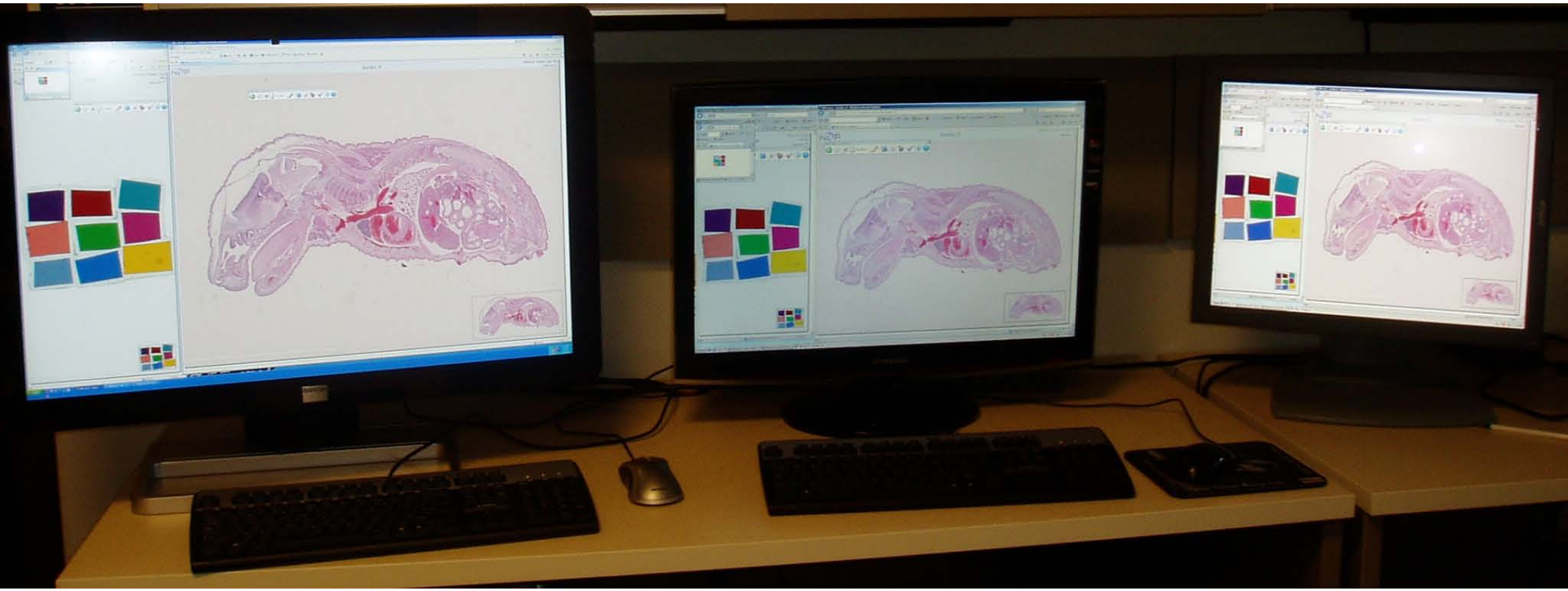
- Thickness of Specimen
- Staining
- Scanner or Scanning process
- Viewer Software
- Display

Display



Same images in same PC were viewed by 2 different displays

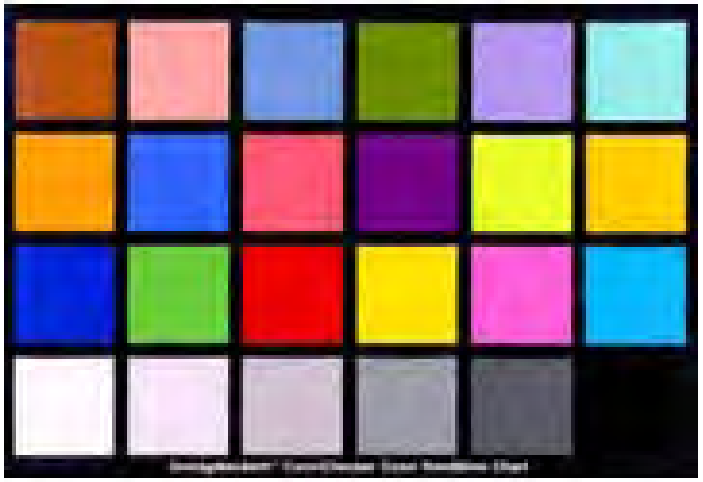
Display



Same image in same PC was viewed by 3 different displays

Example Experiment: Color of Display

Macbeth Color Chart



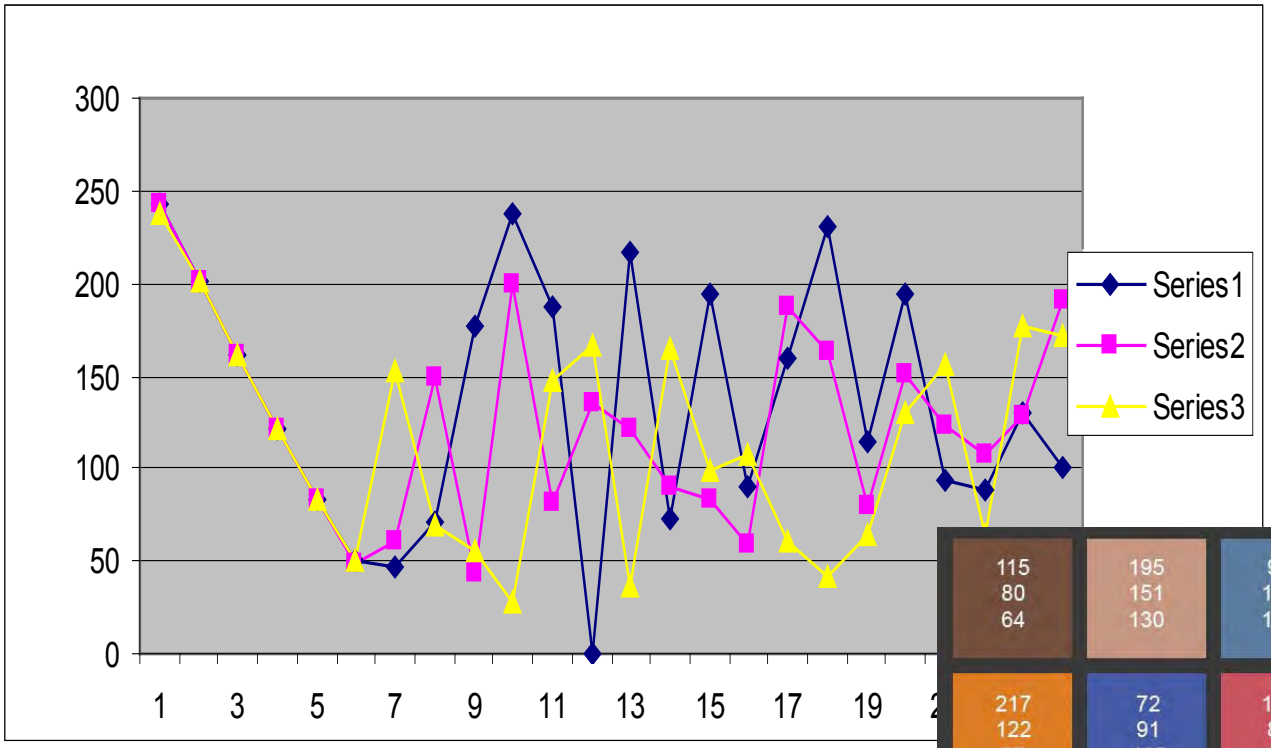
In color-related fields, a color chart is a physical arrangement of standardized color samples, used for color comparisons and measurements such as in checking the color reproduction of an imaging system. Color charts are used to calibrate and to profile graphic devices, such as digital cameras and scanners. Therefore standardized IT8 targets are made by several companies.

Display
Experiment with Macbeth Color Chart at the Department of Pathology in MGH

The standard displays of our Department are of 2 different models. We randomly selected 23 standard displays from one of the two models for this experiment.
All driver software and display settings were exactly the same for all the 23 displays.

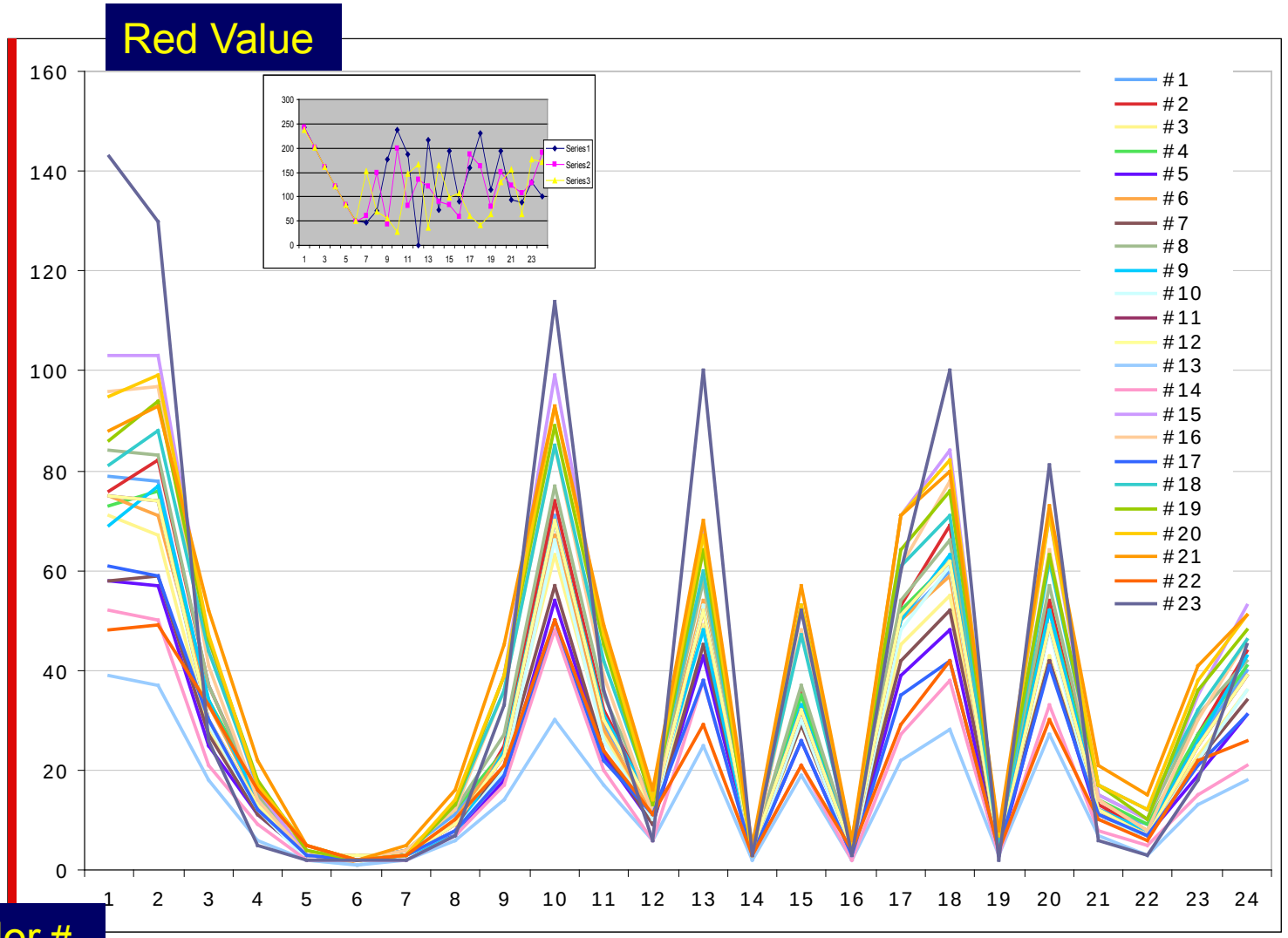
We measured the each color on each display by Display Analyzer.
If the data is too offset, we calibrated using Monitor Calibration tool

Macbeth Color Chart RGB Value

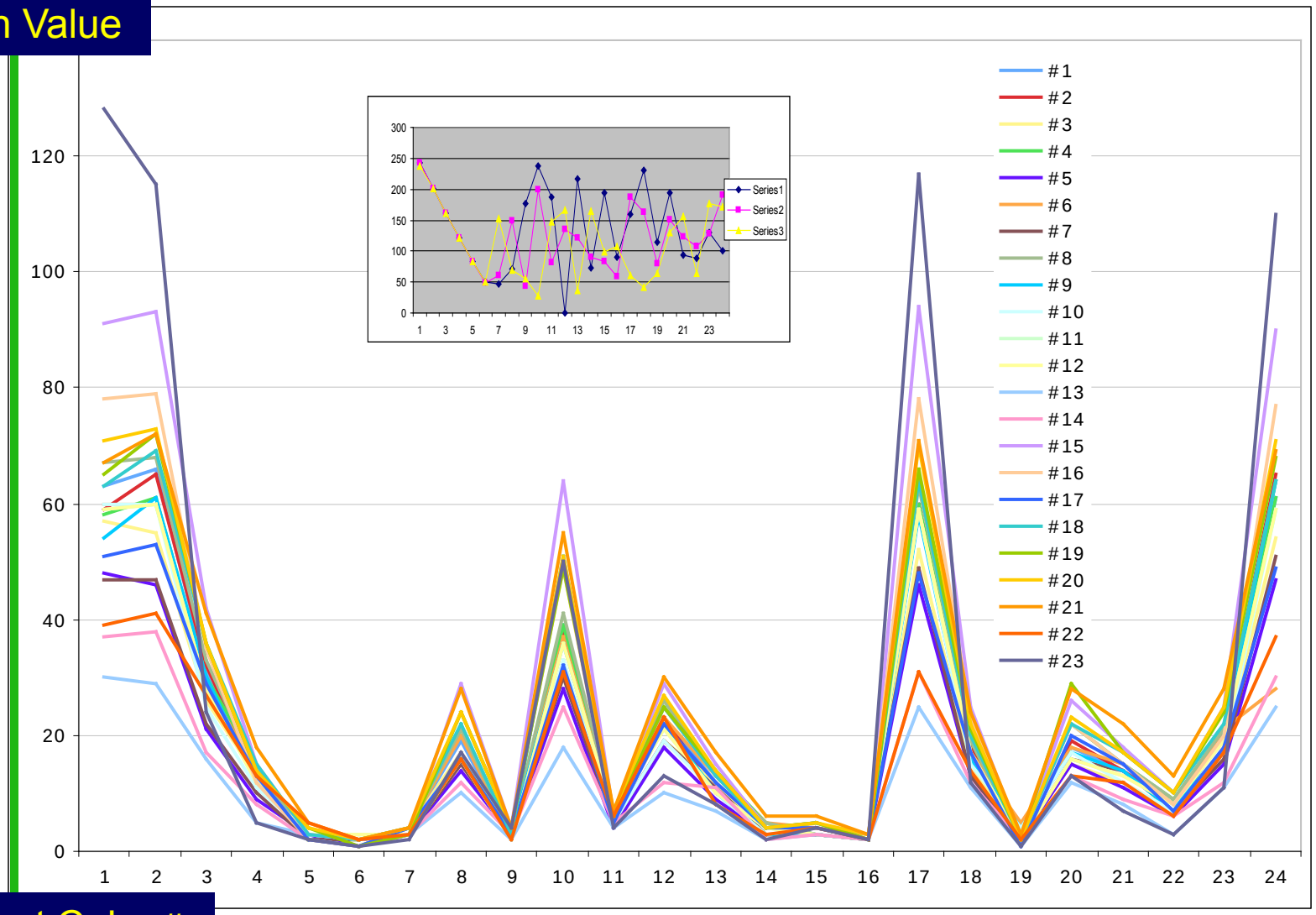


115 80 64	195 151 130	94 123 156	88 108 65	130 129 177	100 190 171
217 122 37	72 91 165	194 84 98	91 59 107	160 188 60	230 163 42
46 60 153	71 150 69	177 44 56	238 200 27	187 82 148	0 135 166
243 242 237	201 201 201	161 161 161	122 122 121	83 83 83	50 49 50

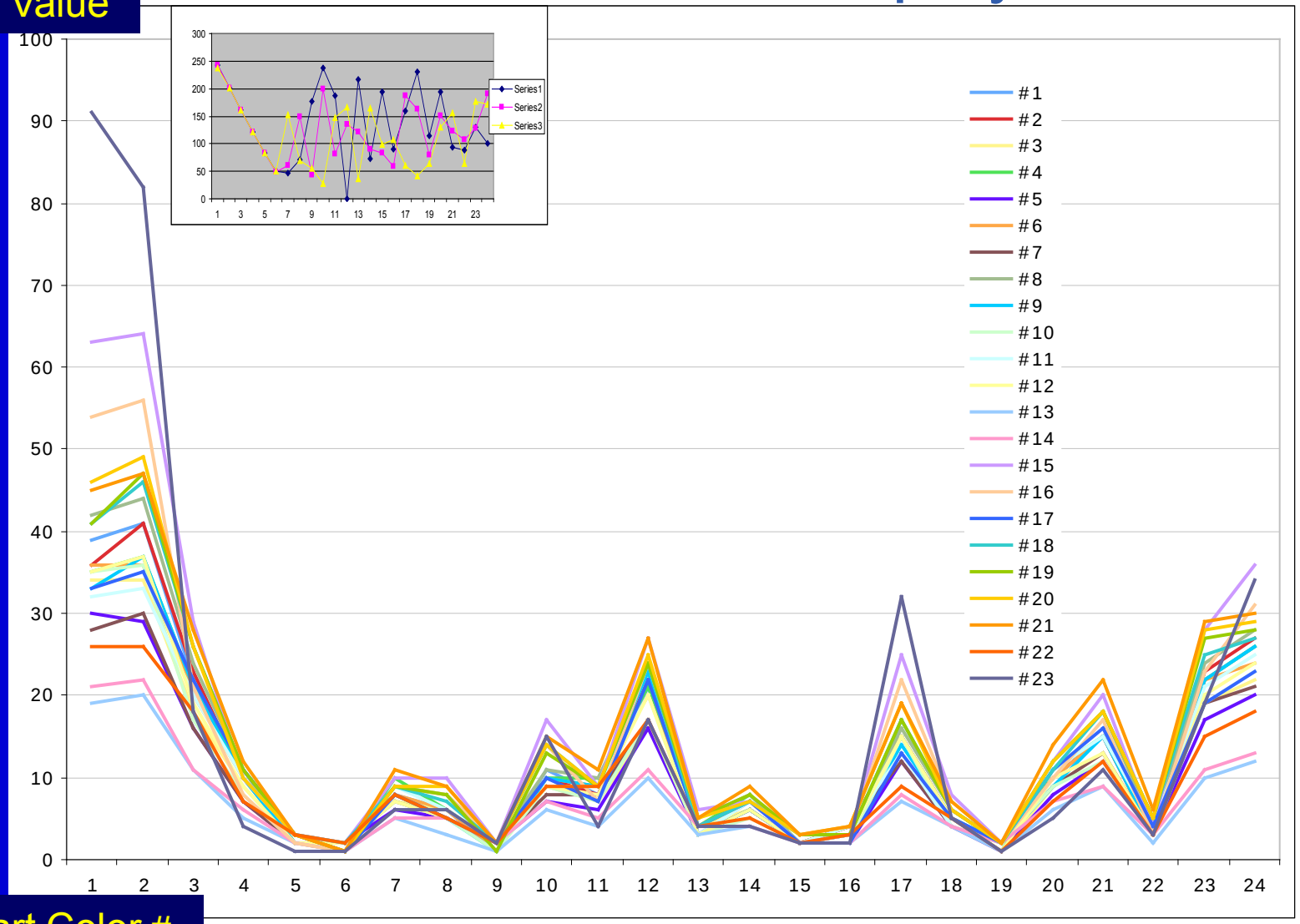
Red Value 23 Displays



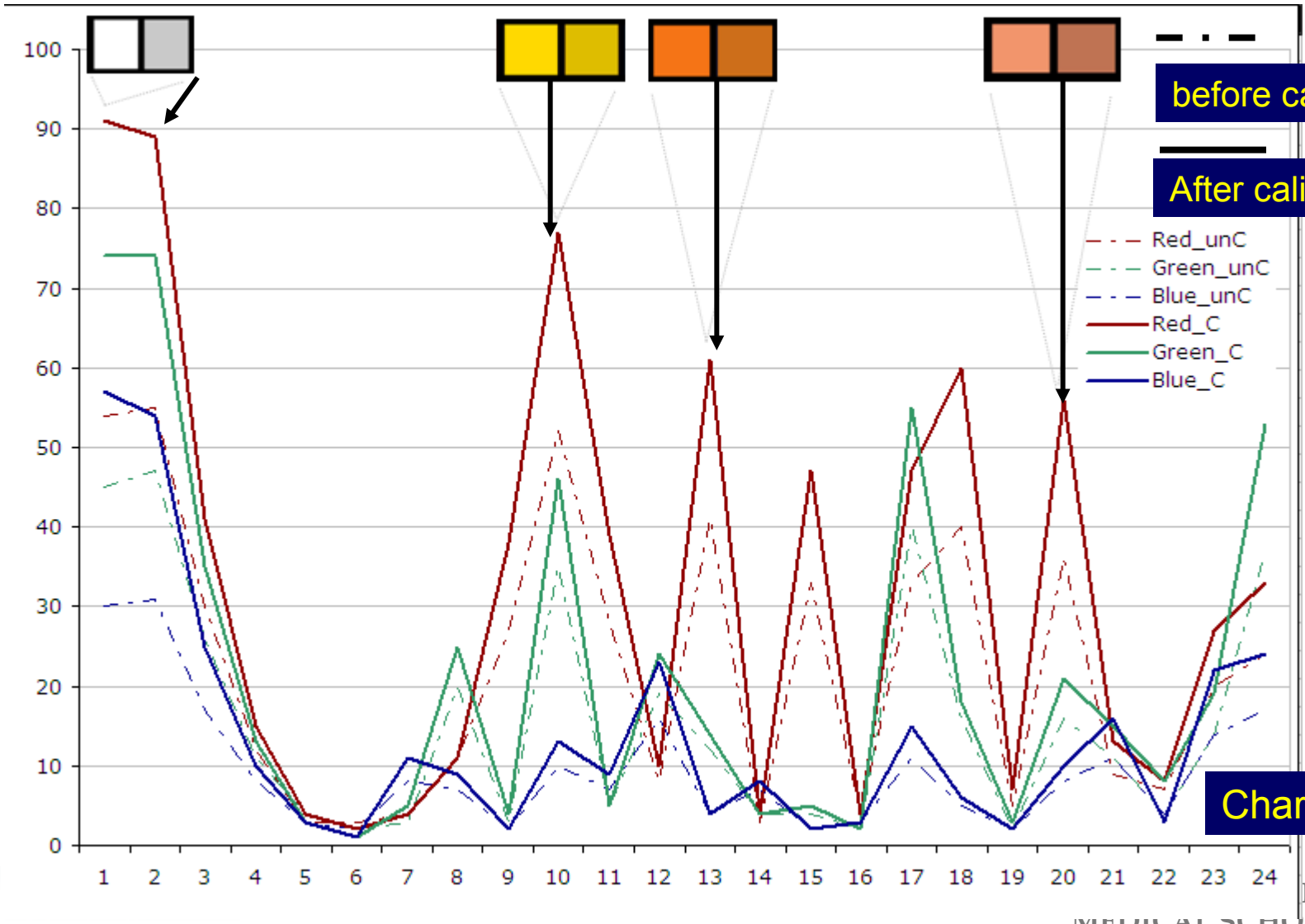
Green Value 23 Displays



Blue Value 23 Displays

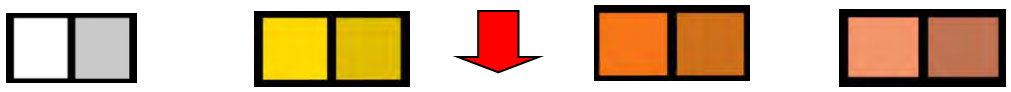


Example of Color differences: before calibration and after calibration



Results: Experiment with Macbeth Color Chart at Dept of Pathology, MGH

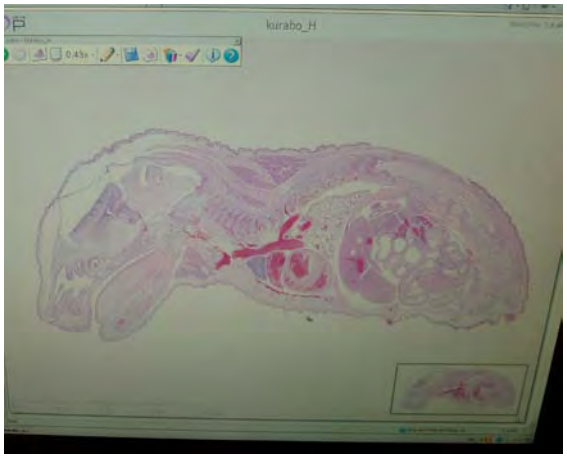
Pathologists were looking at same image without noticing the differences in color. After the calibration, the color differences were clearer.



Probably, it is not good to use the WSI ??
User should be able to notice the color shift of his own display

Until we showed the result, no one noticed how bad our displays were

Why is it problem?

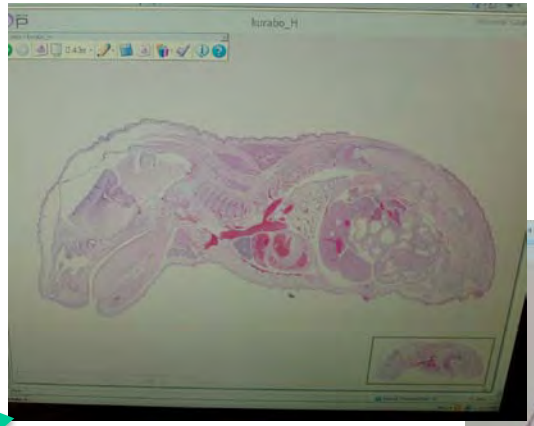


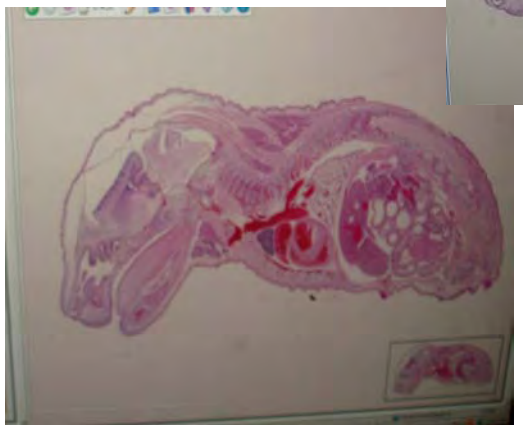
Is it problem?

Staining

Scanning

Display





Is it problem?

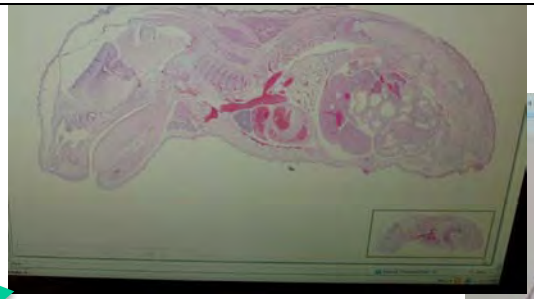
Yes

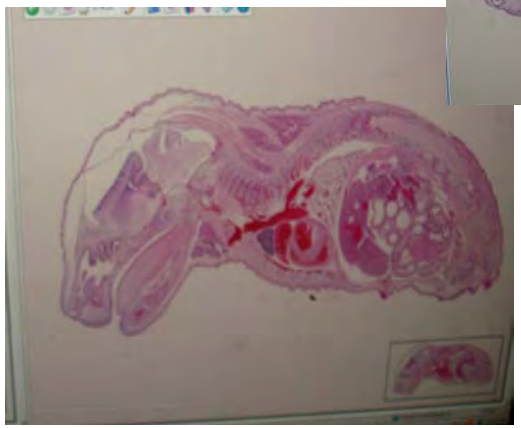
Staining

Display

Pathologist looks at an actual slide under the microscope

Scanning





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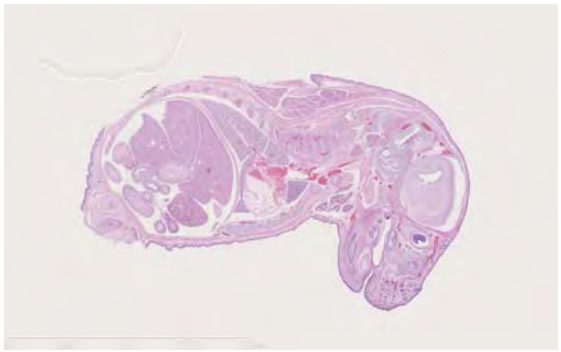
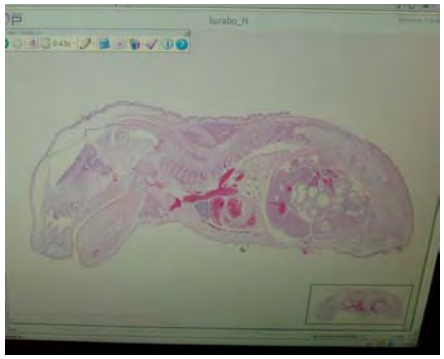
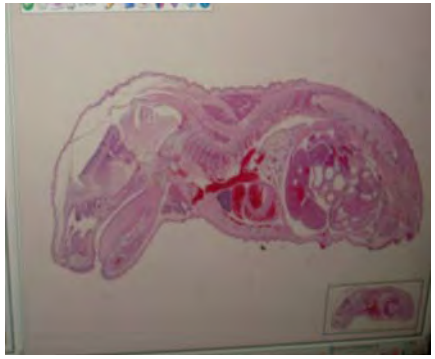
HARVARD MEDICAL SCHOOL

Is it problem?

Yes



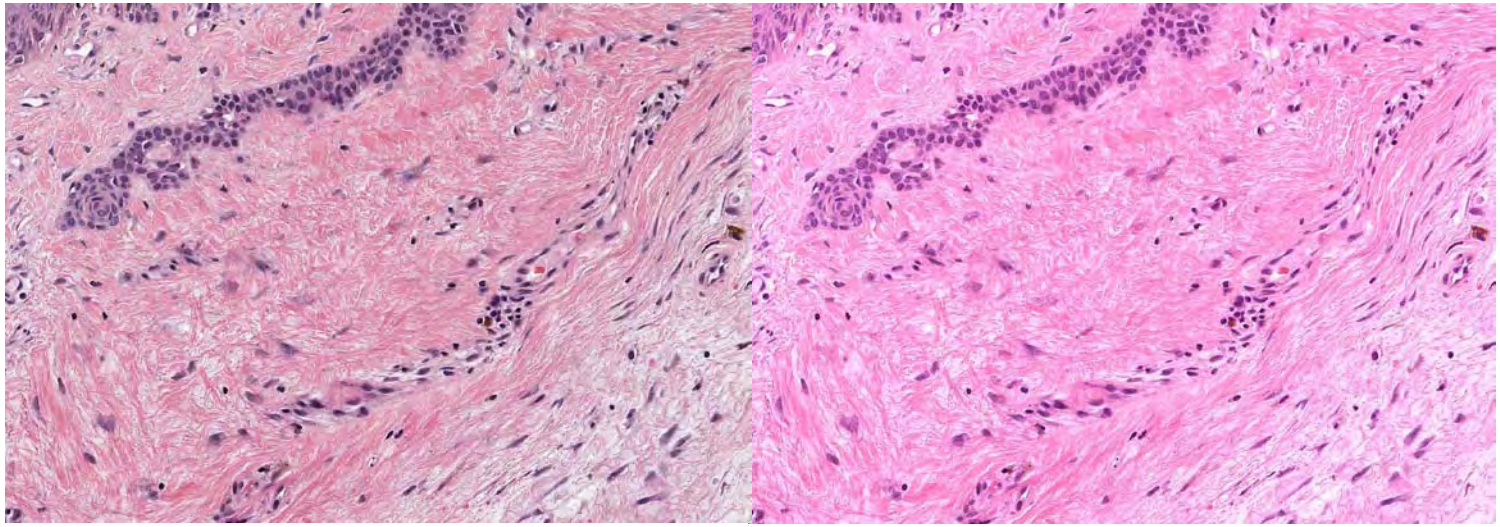




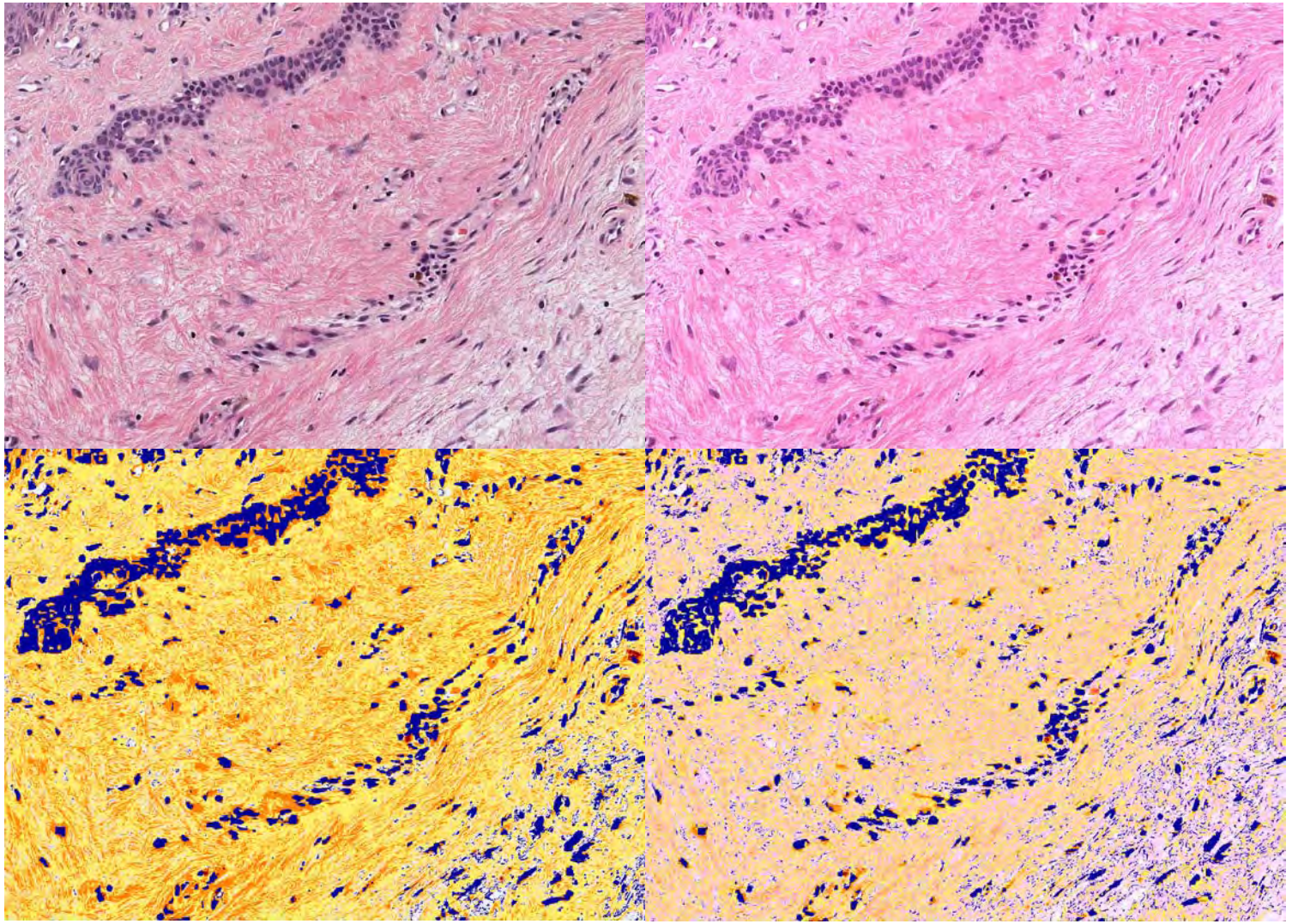
When a pathologist looks at the image on the monitor without a glass slide, it is difficult to know if the color of the image is accurate or not.

It may cause diagnostic error; or pathologists may be uncomfortable to make a diagnosis.

Is it problem?



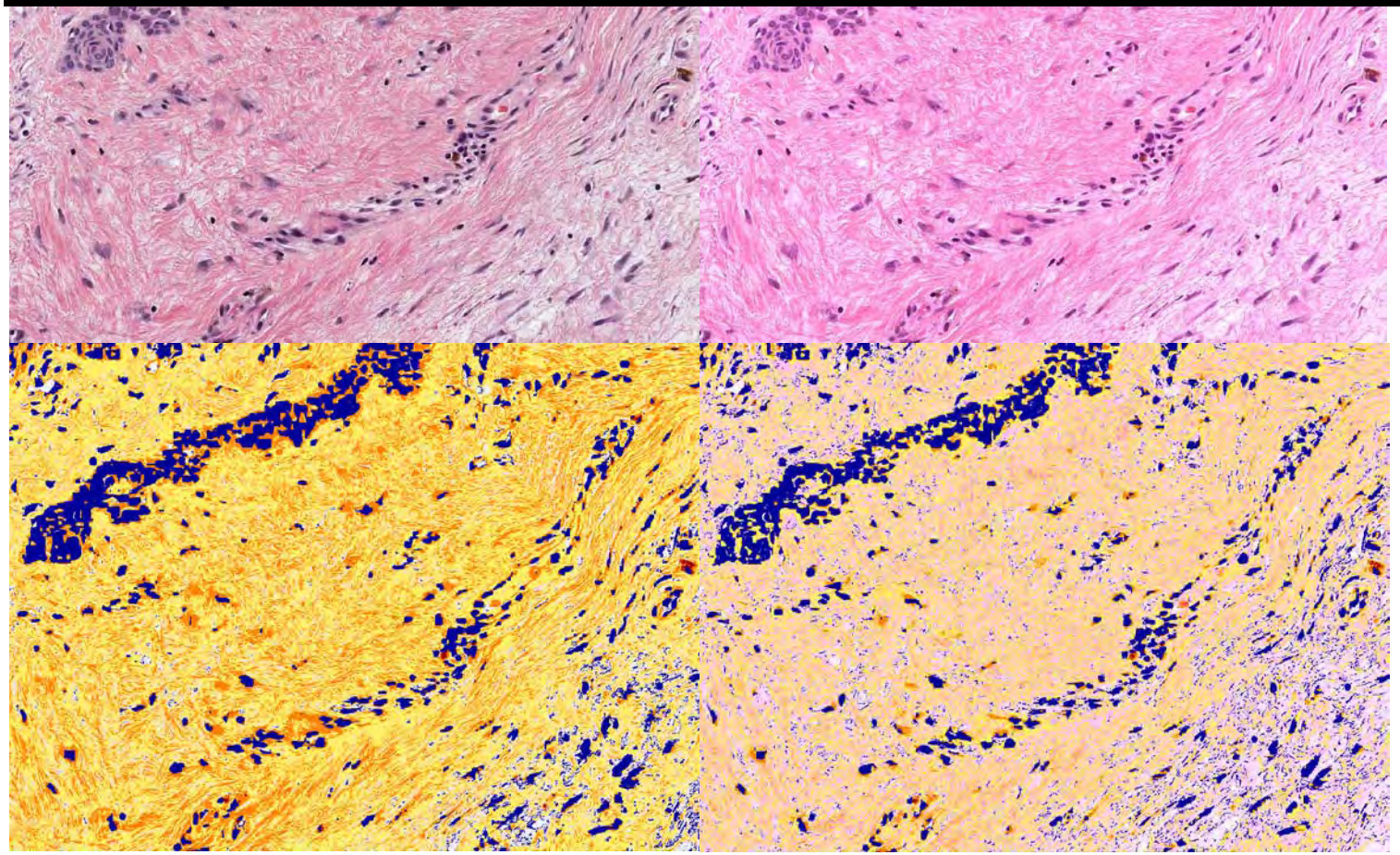
Is it problem? Yes



8.8% 7.9%

Is it problem? Yes

- When we use it for Computer Aided Diagnostic System or image analysis



8.8% 7.9%

Color Standardization in WSI

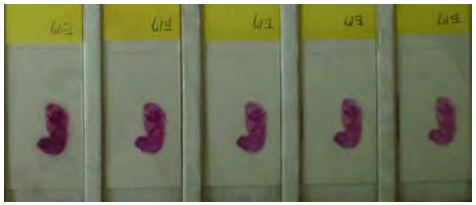
- To prevent diagnostic errors
- To use WSI for Computer Aided Diagnostic System

The reason of Color Standardization for us

- Between scanners
- To make sure the color (WSI) is safe to use before showing pathologists or using for analysis

Color Standardization in WSI

From Staining to Display

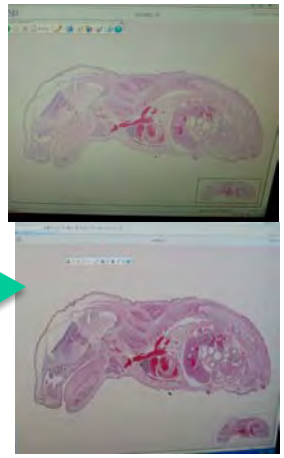


Staining

Scanning

Viewer software

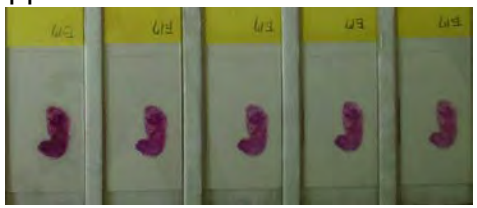
Display



Color Standardization in WSI: From Staining to Display

Staining

Multispectral Imaging application



Today's topics

Scanning

Display

How can we identify the cause of the difference in color and standardize?

To identify the causes of issues in WSI

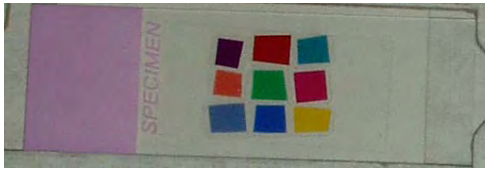
We have developed a slide set at MGH

Calibration Slides for Scanner

Image Quality & color

Color

Calibration Slides for Pathologist (Display)



Color

Color Calibration Slide

(Overview of telepathology, virtual microscopy, and whole slide imaging: prospects for the future, Ronald Weinstein et al. In Human Pathology, 2009)

Original Slide for Microscope

9 color filters were selected for Histology Stained Slides, which especially works best with H&E stained slides. The filter selection was based on spectral information of each color. Previously, a research study was conducted.

Image Quality Slide

15-day old or older mouse embryo paraffin block is sectioned by automated sectioning machine with 3um/section. (100 slides at a time)

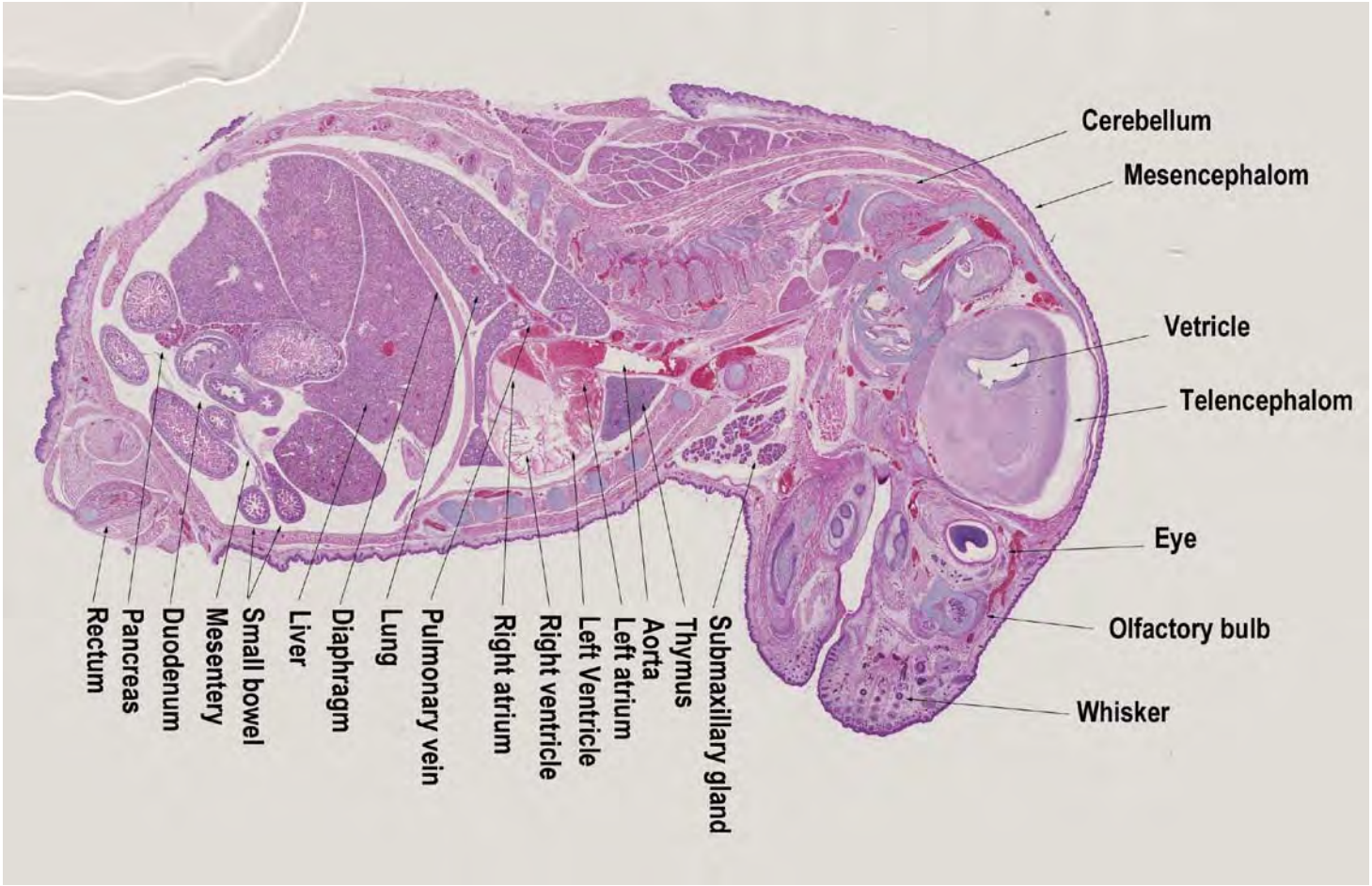
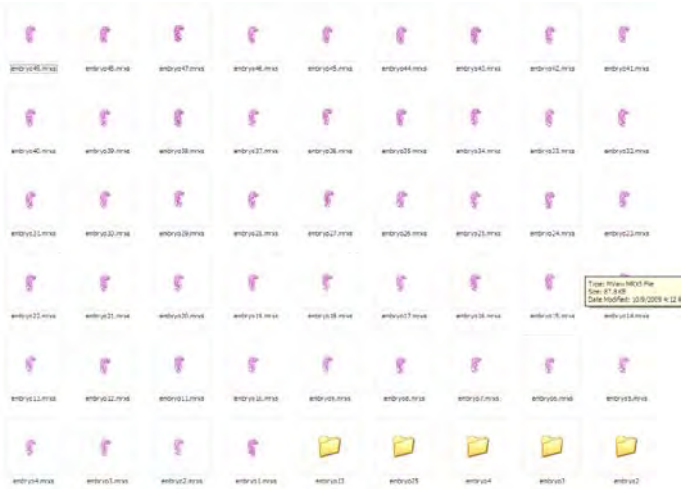


Image Quality Slide

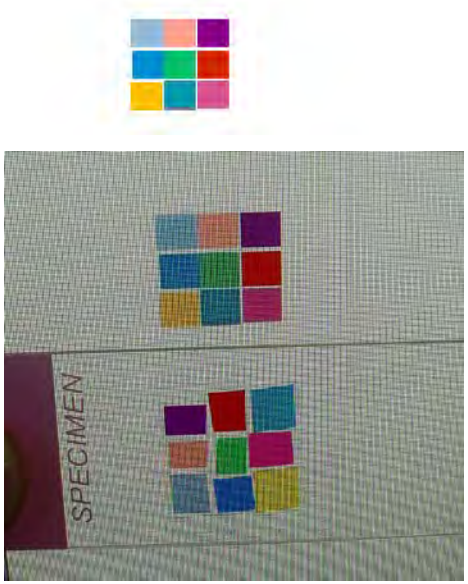
•H&E stain is performed with an automated staining machine at the same time.

•All Slides are scanned with one of the scanner in the lab and scanned images are posted on the web site.



Display for the Viewer

Go to Calibration slide web of PICT Center, MGH

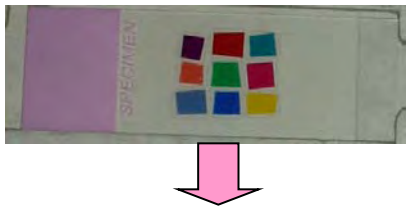


Compare the color of calibration slide vs calibration slide on the display. If it is too far, contact HELP DESK

This Slide is hand made in the lab. The cost is very close to 0. It can be given to all pathologists

Scanner

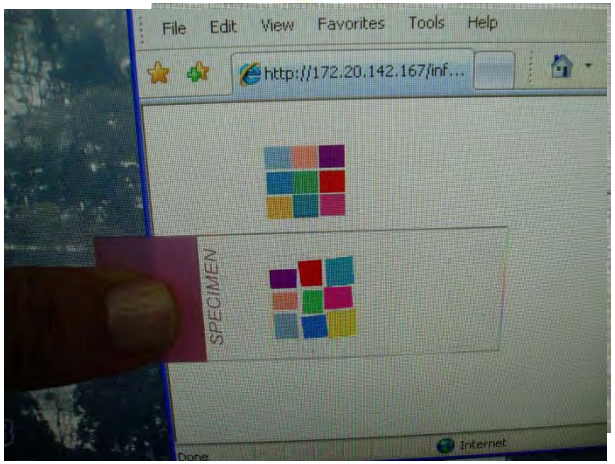
Scanning



VS

Review Display

The Imaging web site has the colors of the Calibration slide.



Compare the displayed colors of the calibration slide to their actual colors to understand the difference

The Imaging web site has Calibration slide.

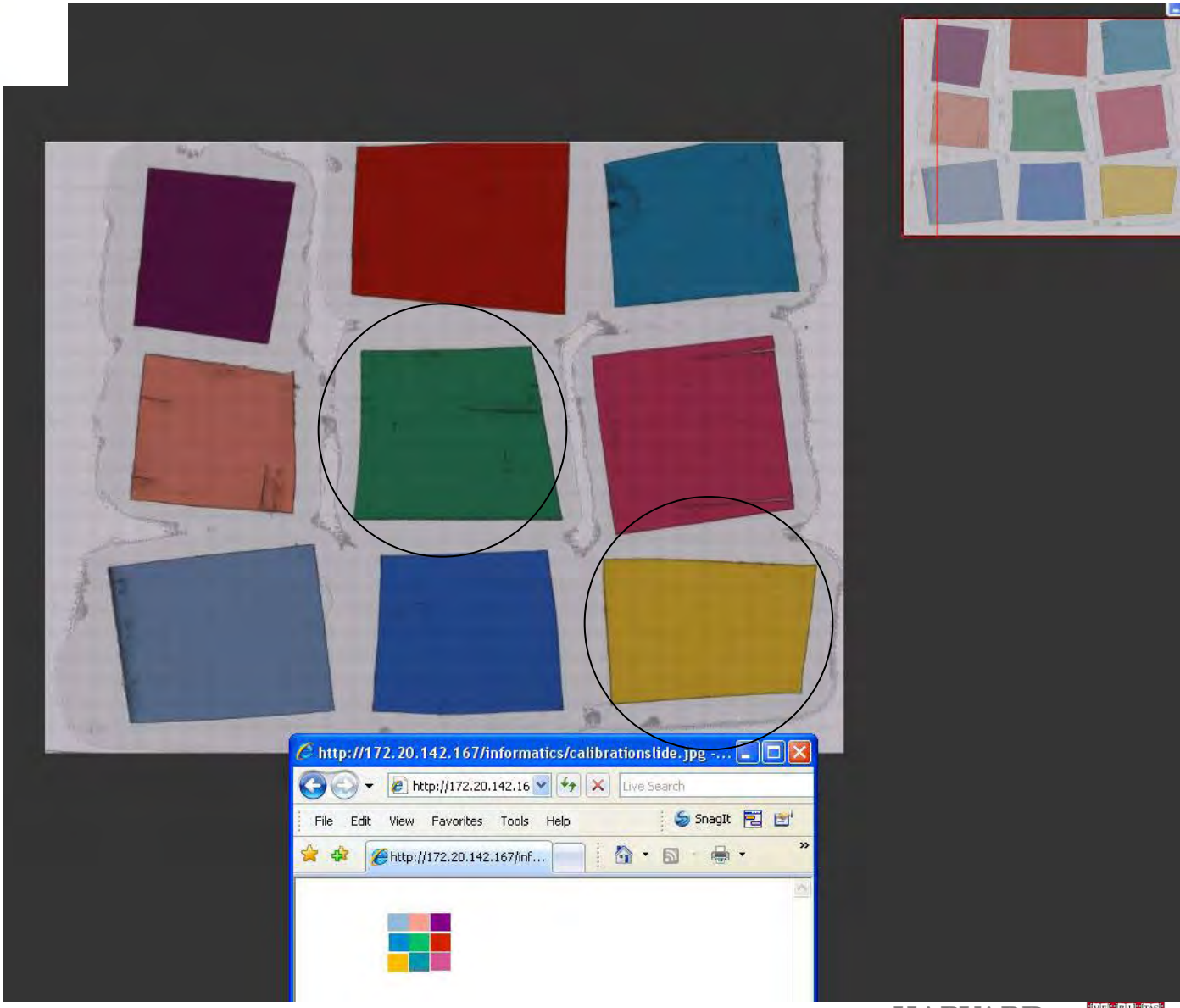
Results: Scanner 1

Almost all colors are wrong

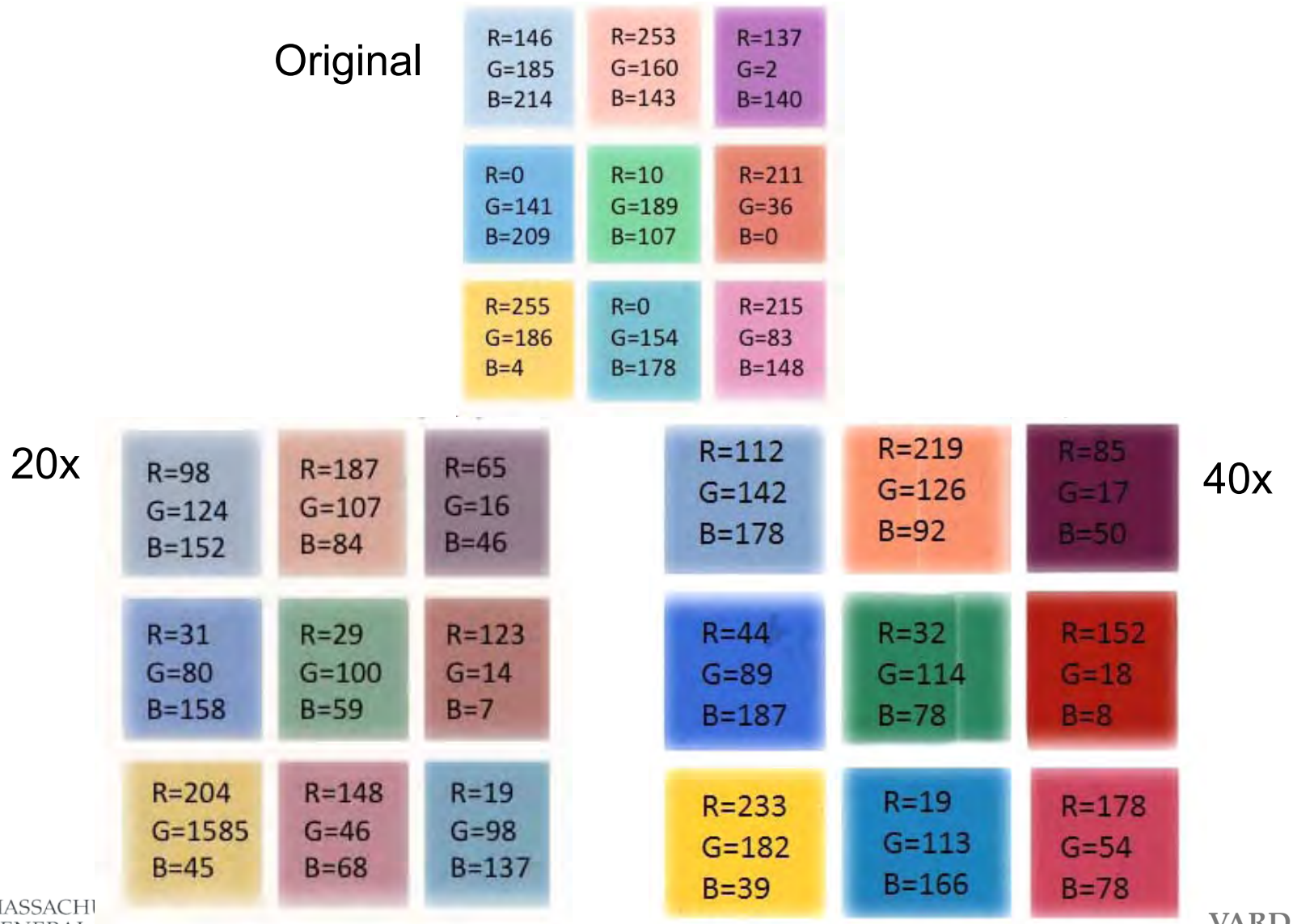
Results: Scanner 2

Better than Scanner 1. Especially Pink and Blue are wrong

Results: Scanner 3



Results 20x vs 40x of the scanner 1



Results

We have tested 5 different scanners with the calibration slides. No scanner produced exactly same color with the original even after the adjustment of the error of each Display

Image Quality Evaluation & Color Standardization

Color Standardization

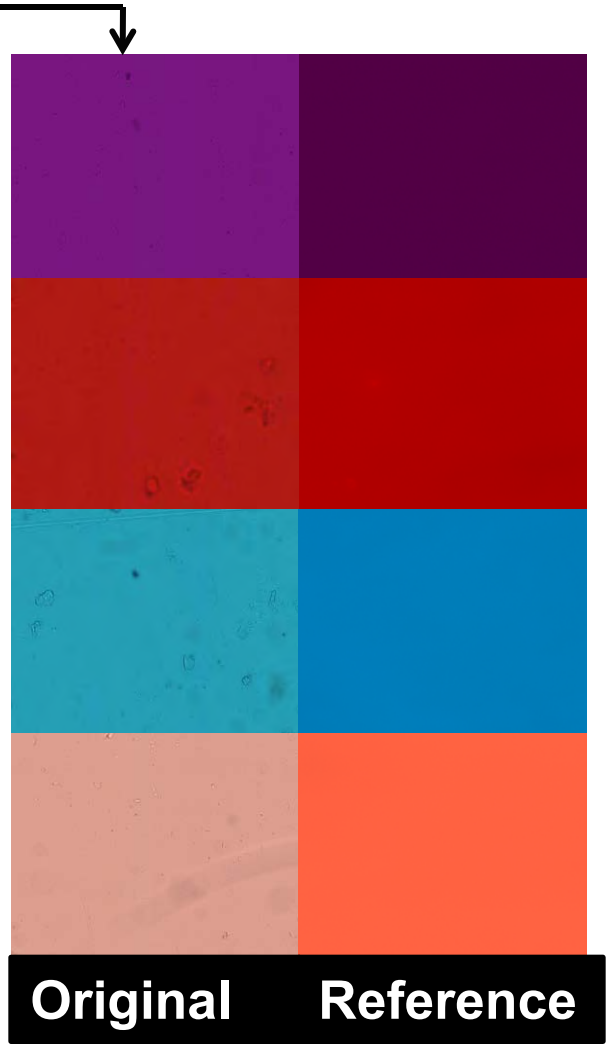
Color patches

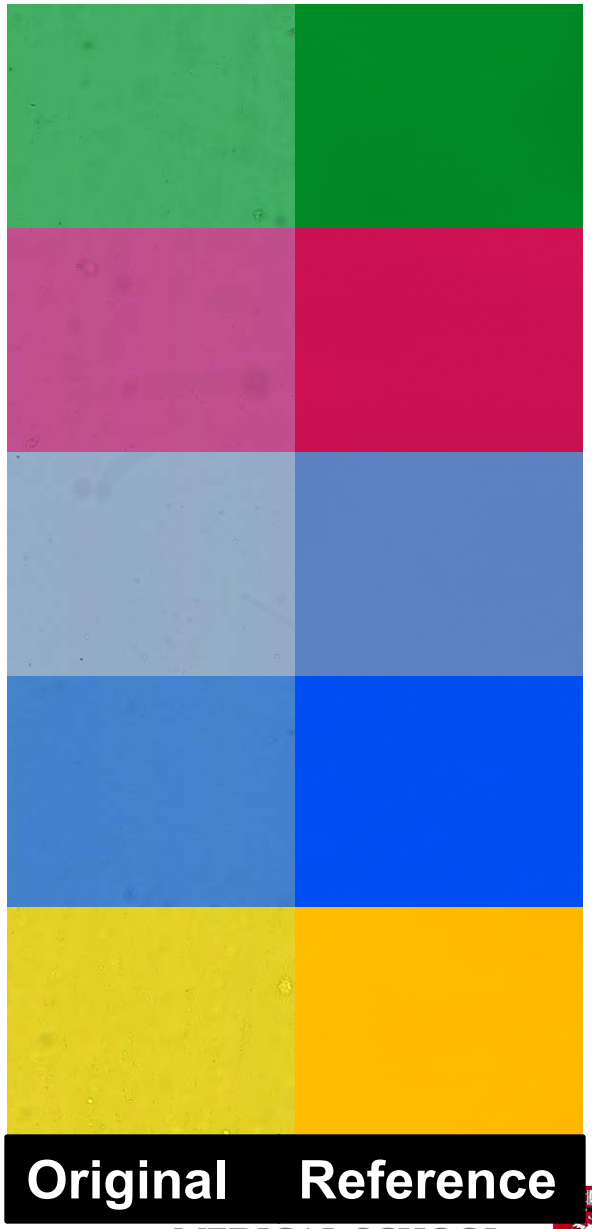
- **Colors are not accurate enough**

- Standardize using the original and reference color patches

Original - Produced by a whole slide scanner

Reference - Produced by using spectral information of the patches





Polynomial transformation

$$\begin{pmatrix} R \\ G \\ B \end{pmatrix} = \begin{pmatrix} a_{1,R} \ldots . a_{m,R} \\ a_{1,G} \ldots . a_{m,G} \\ a_{1,B} \ldots . a_{m,R} \end{pmatrix} \left[\theta_m \begin{pmatrix} R \\ G \\ B \end{pmatrix} \right]$$

Color of the patches as produced by a particular scanner

Reference color of the color patches

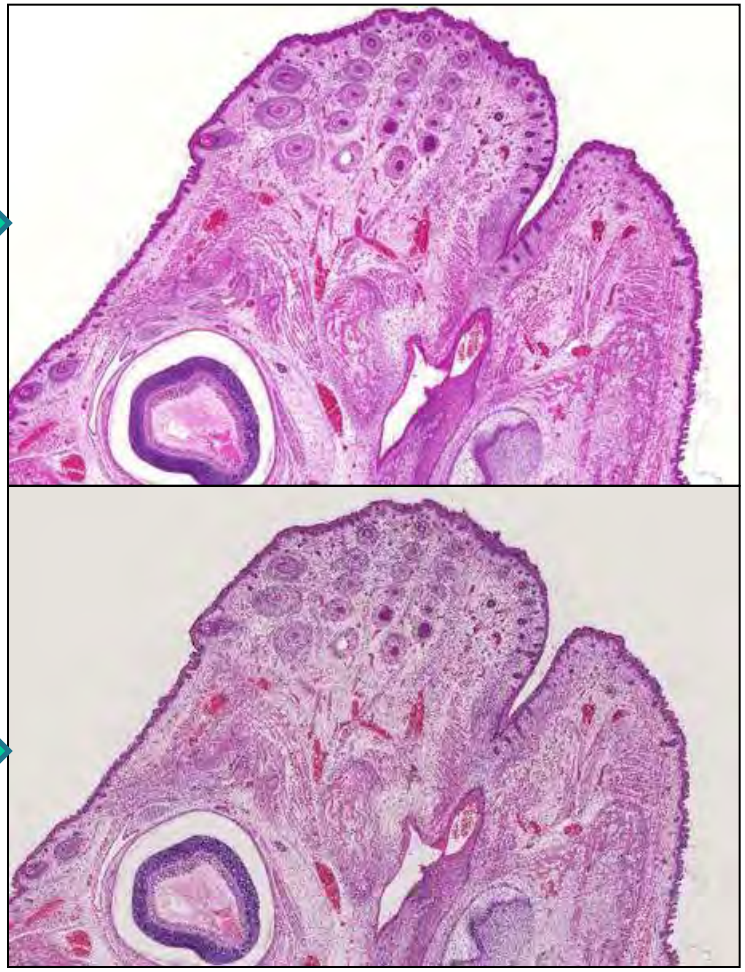
Color transformation matrix will be stored for used in color standardization

Each scanner will have its own Color transformation matrix

Whole slide scanners and Color Imaging

Whole slide scanner 1 (WSI 1)

Whole slide scanner 2 (WSI 2)

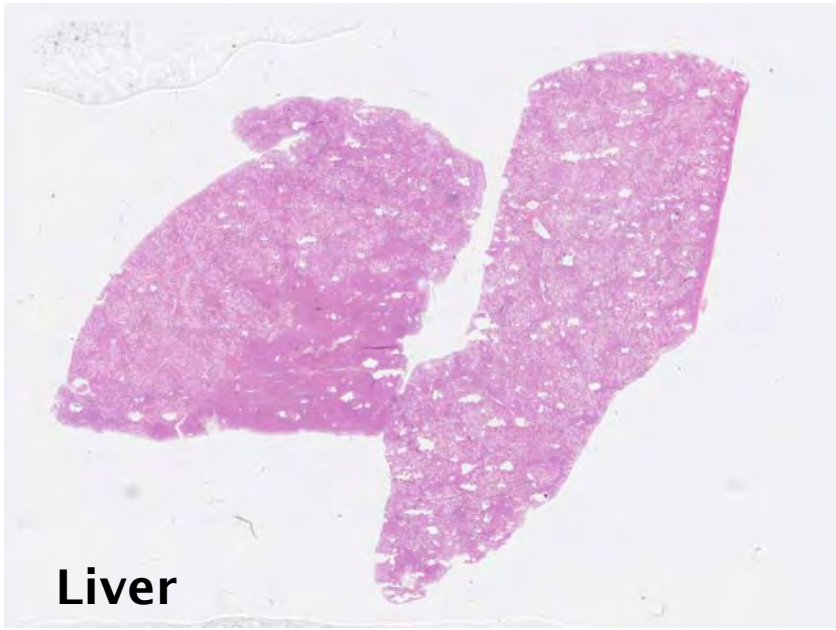


Use the mouse embryo slide to confirm the color transformation matrix

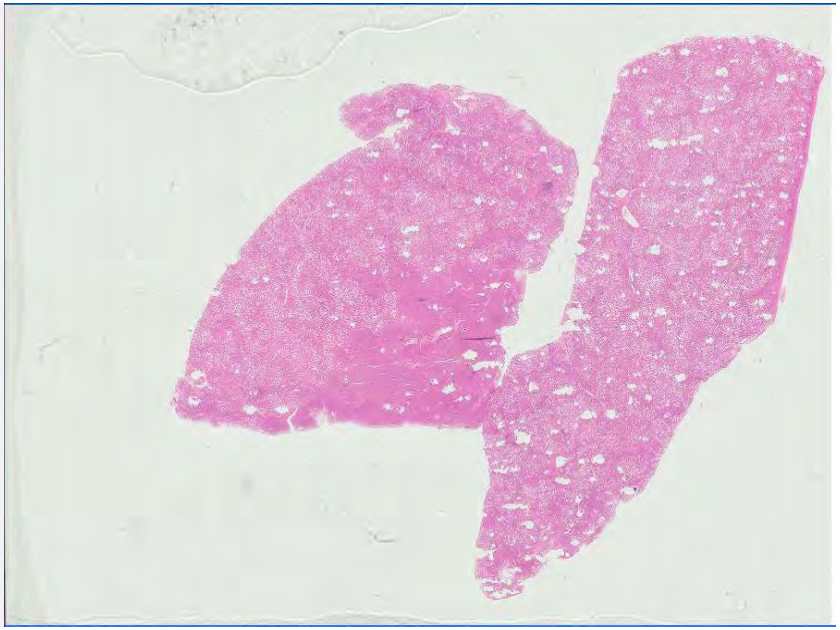
Results in Liver

Thumbnail images of the original whole slide images

Scanner A



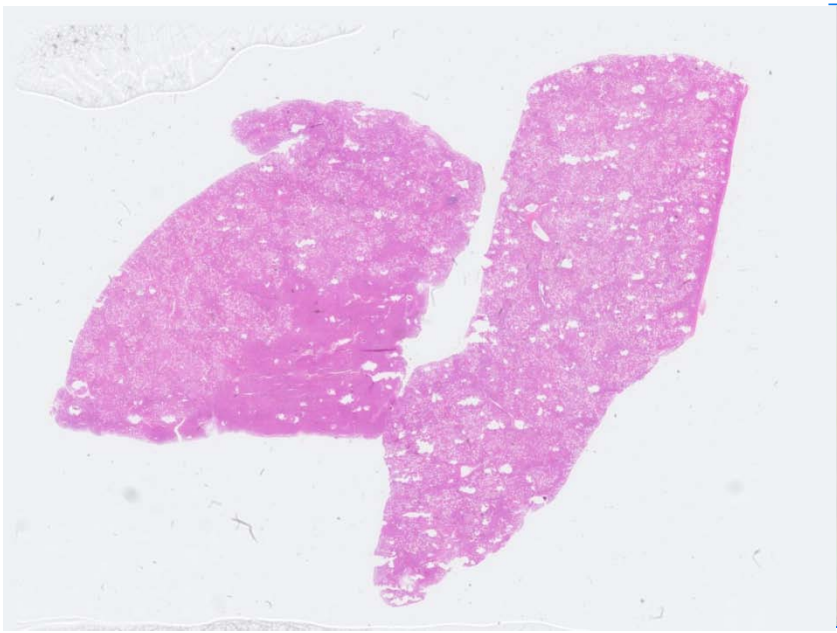
Scanner B



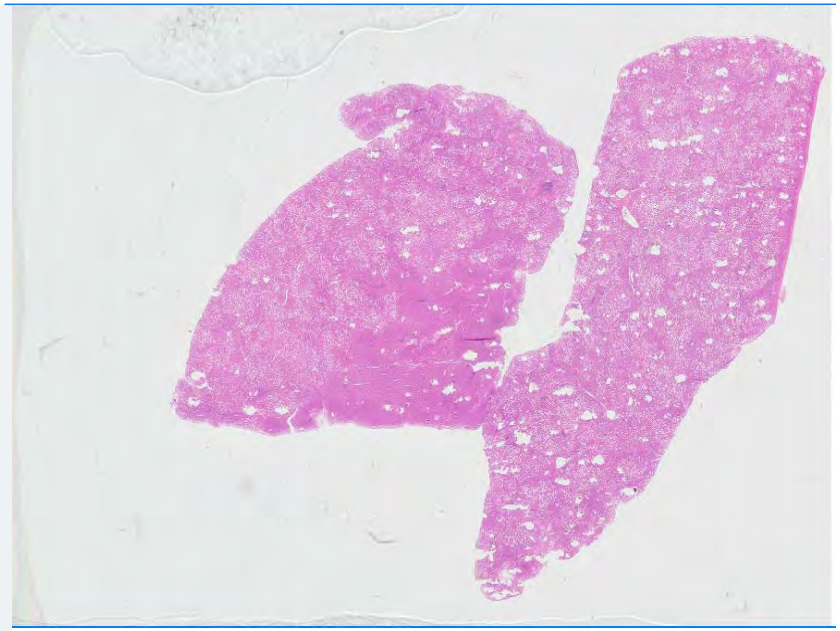
There is color variation….

Thumbnail images of the standardized whole slide images

Scanner A



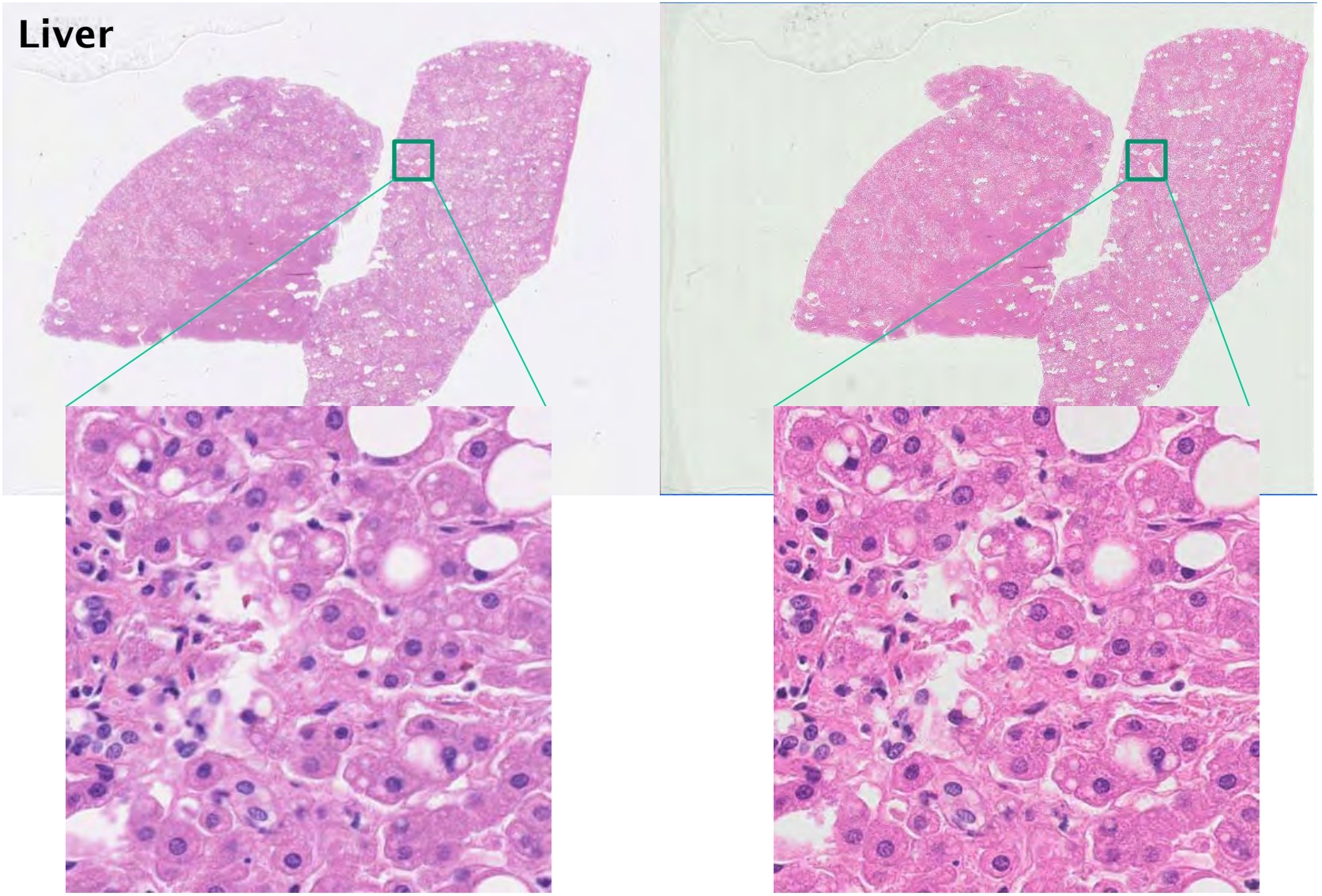
Scanner B



Application of color correction minimizes the color differences…..

Scanner A

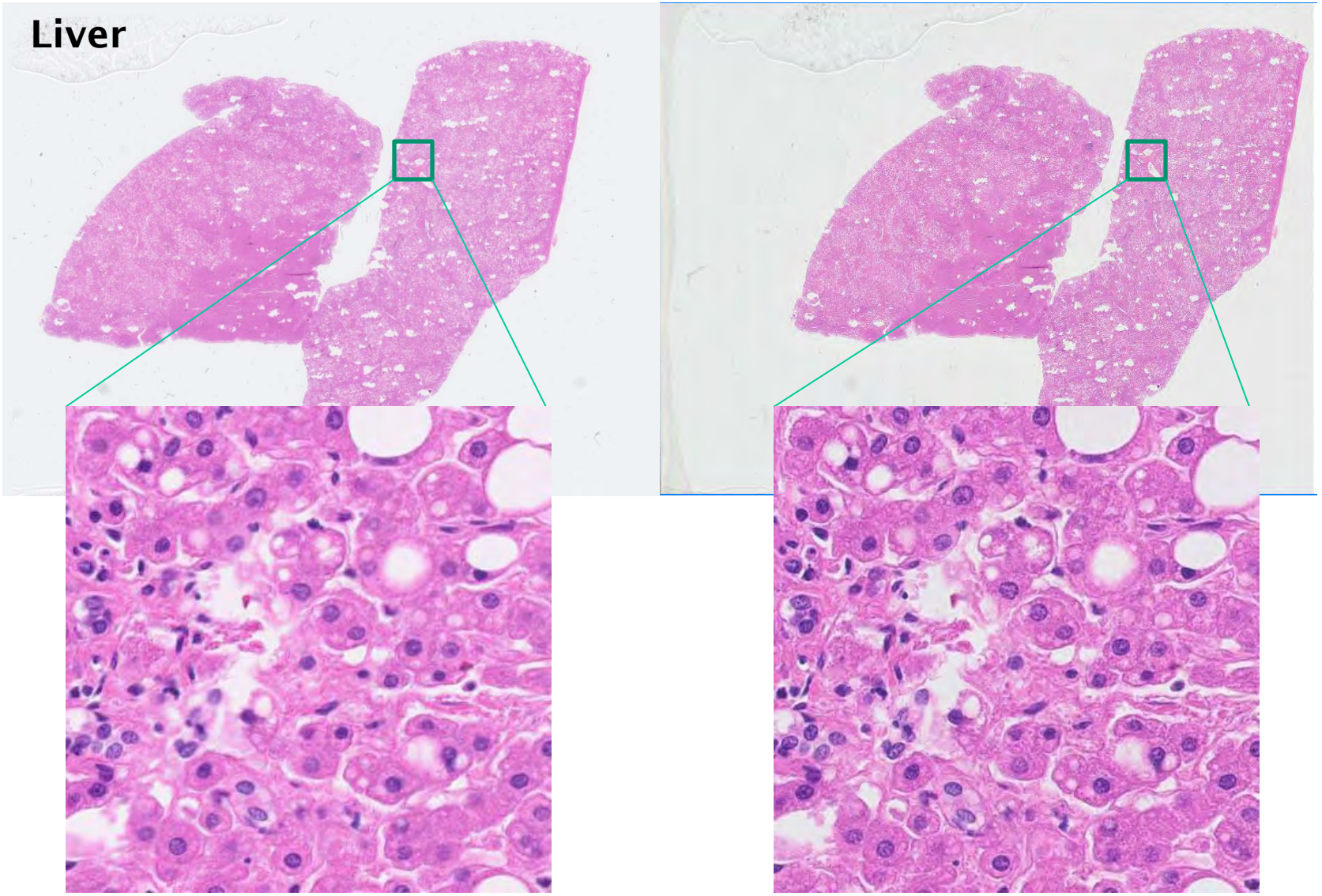
Scanner B



Without color correction...

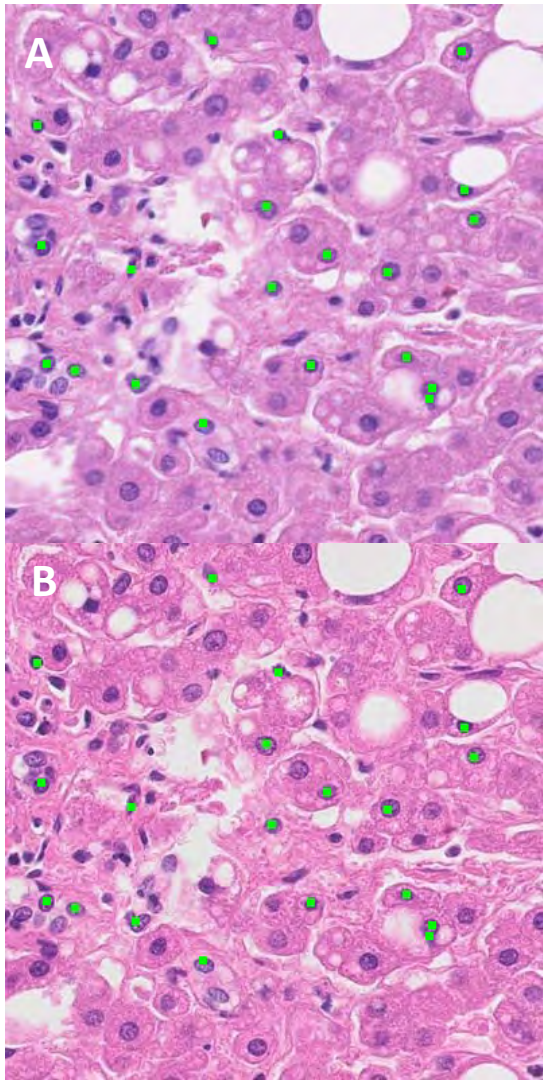
Scanner A

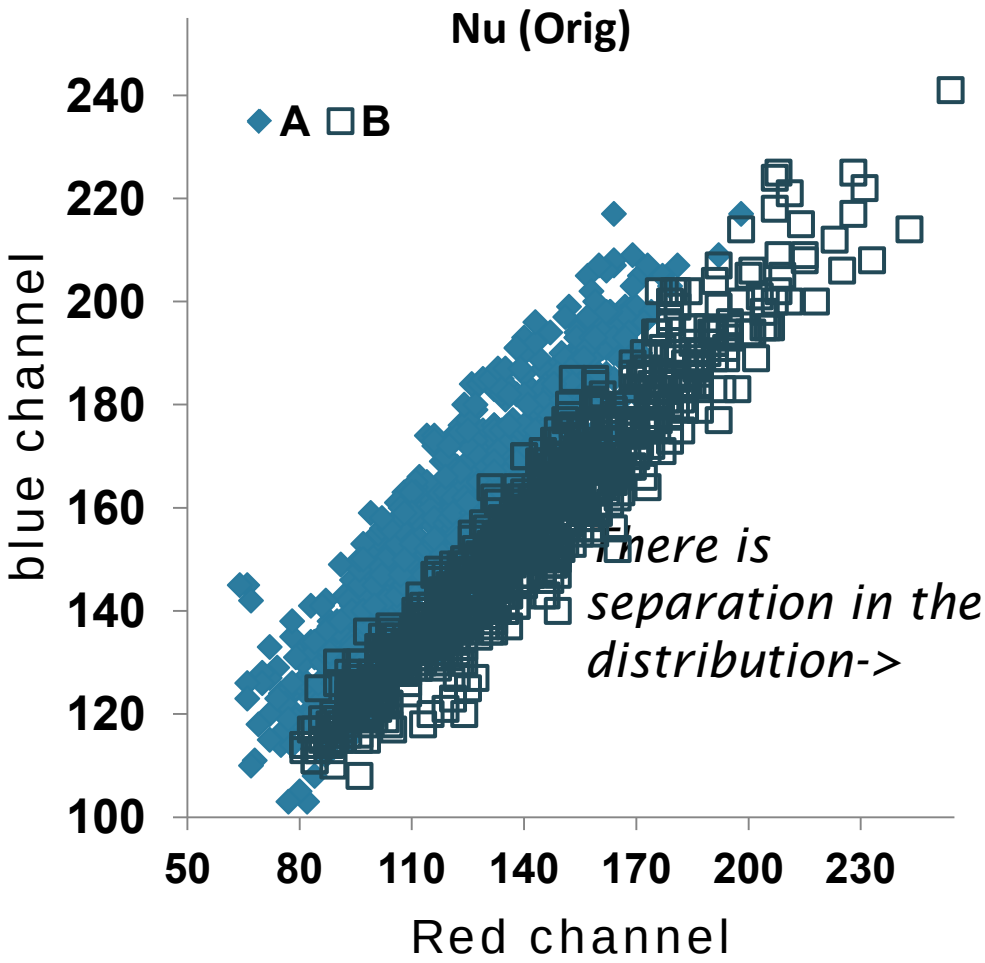
Scanner B



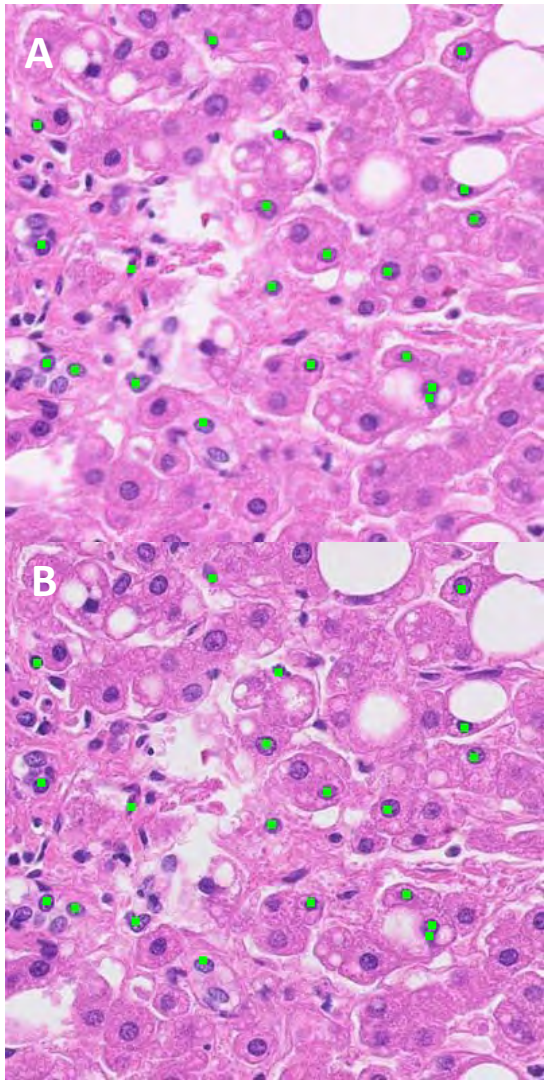
Result of color correction...

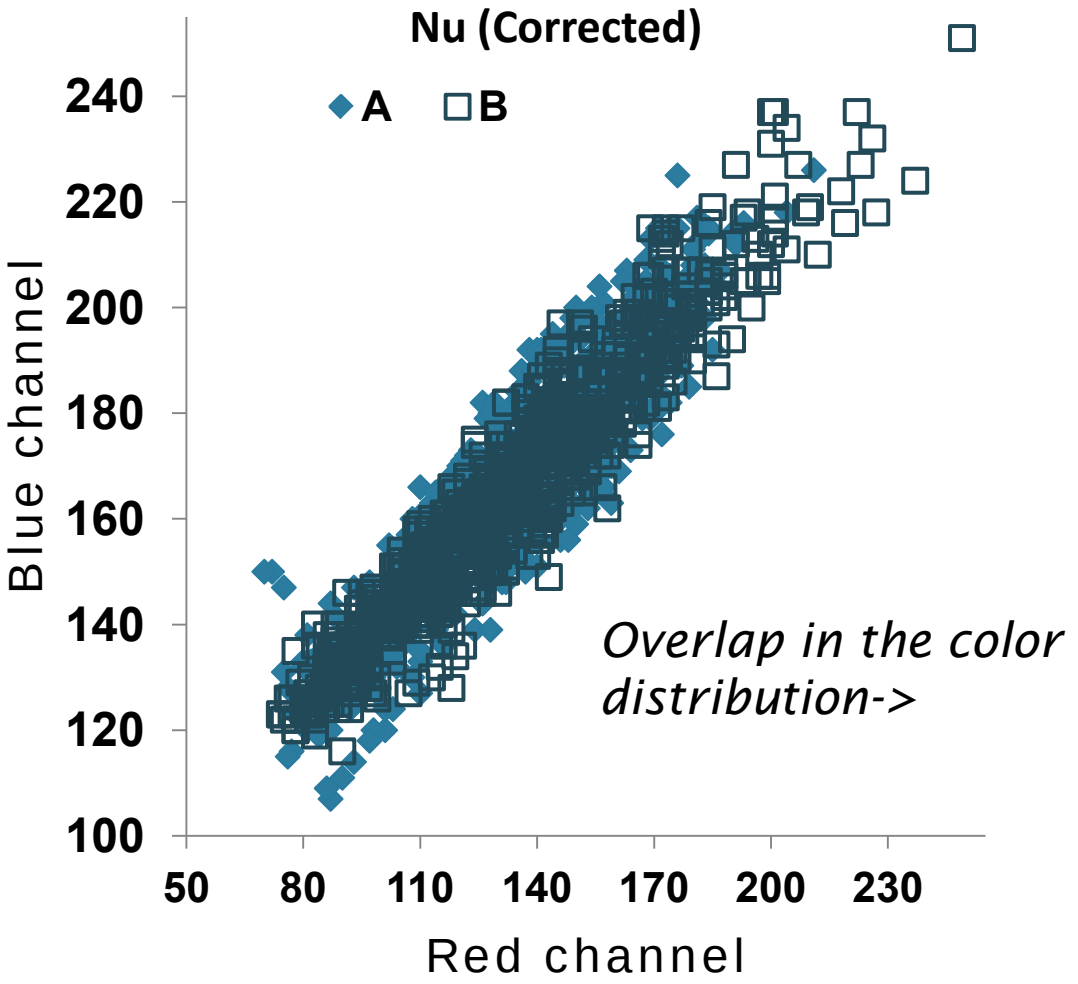
Original


A
B

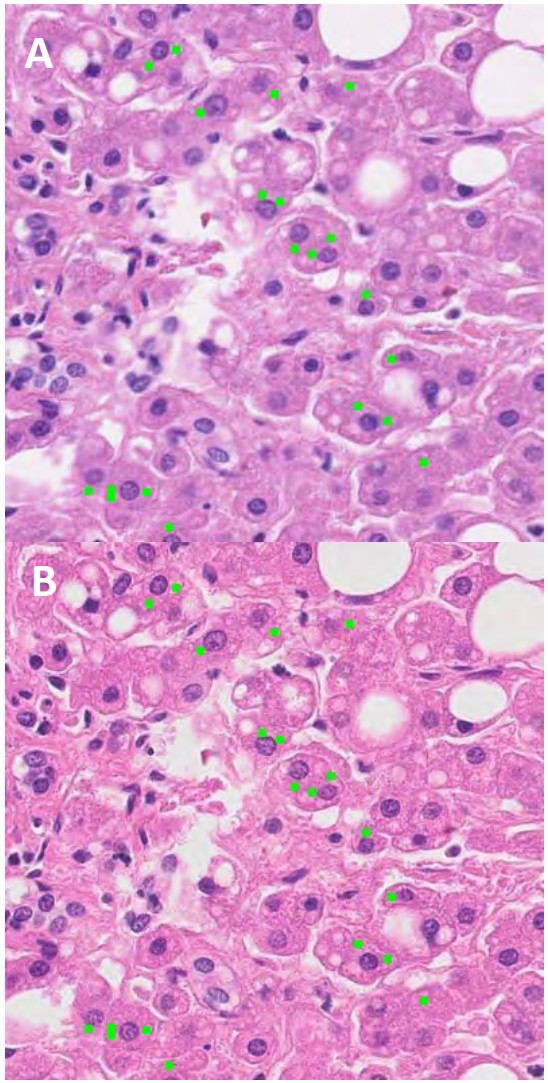

Nu (Orig)
A
B
240
220
200
180
160
140
120
100
blue channel
50
80
110
140
170
200
230
Red channel
There is separation in the distribution->

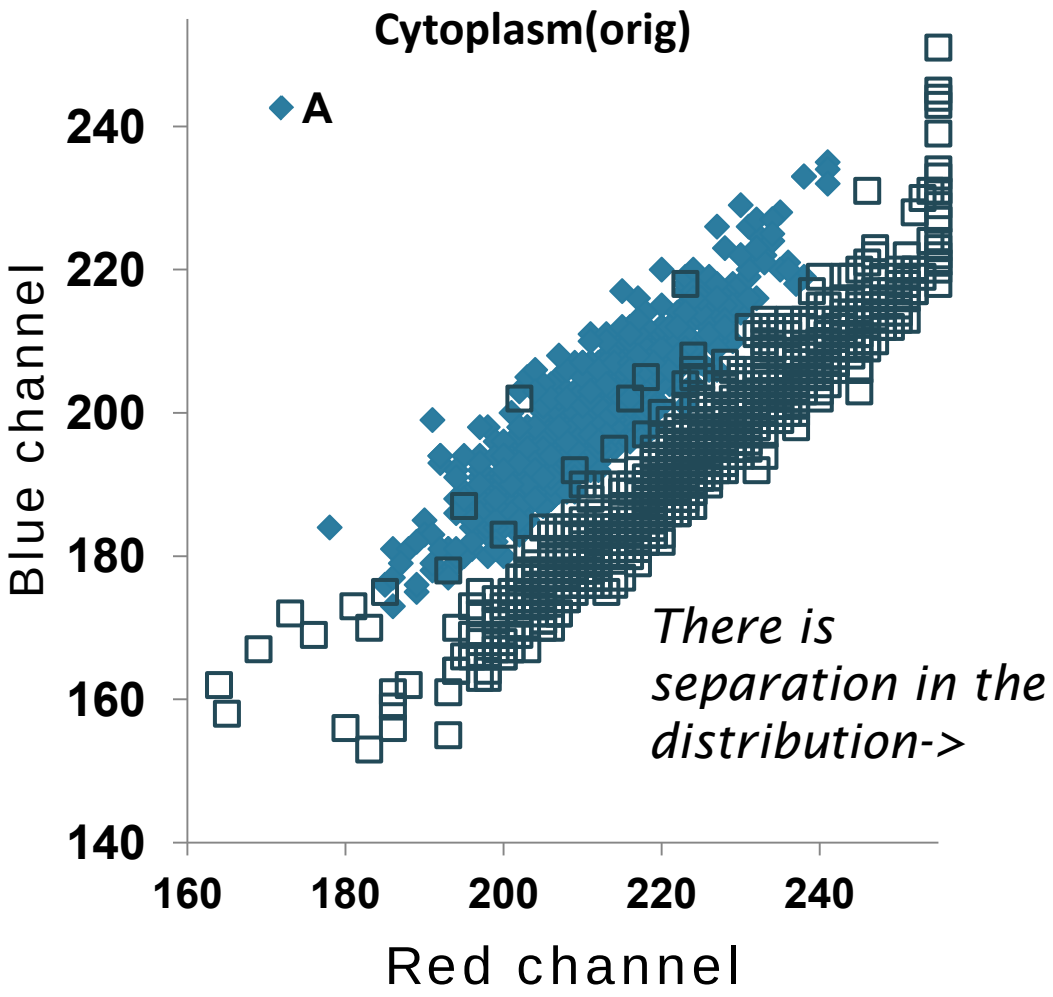
Corrected


A
B

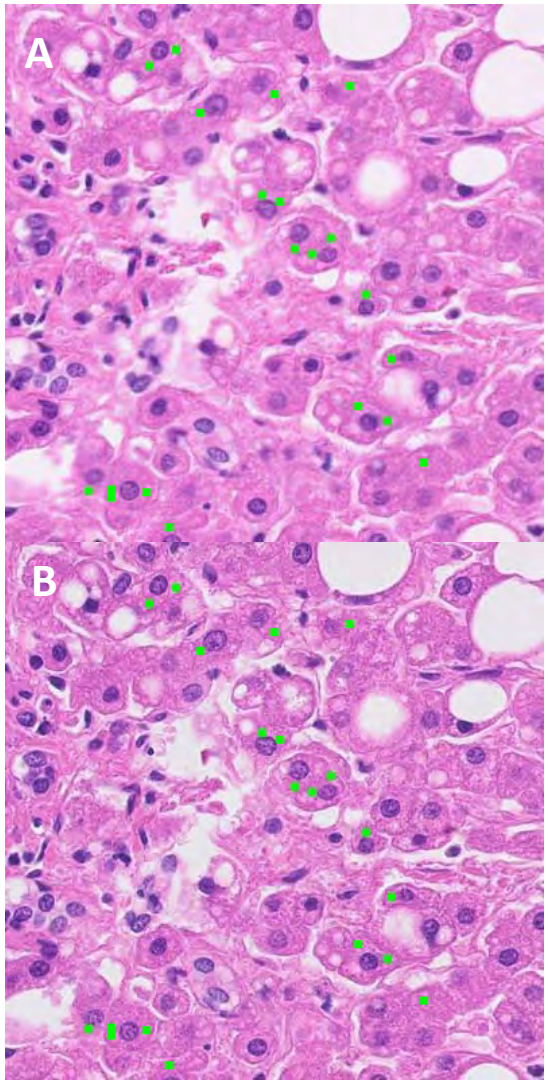

Nu (Corrected)
A
B
Blue channel
240
220
200
180
160
140
120
100
50
80
110
140
170
200
230
Red channel
Overlap in the color distribution->>

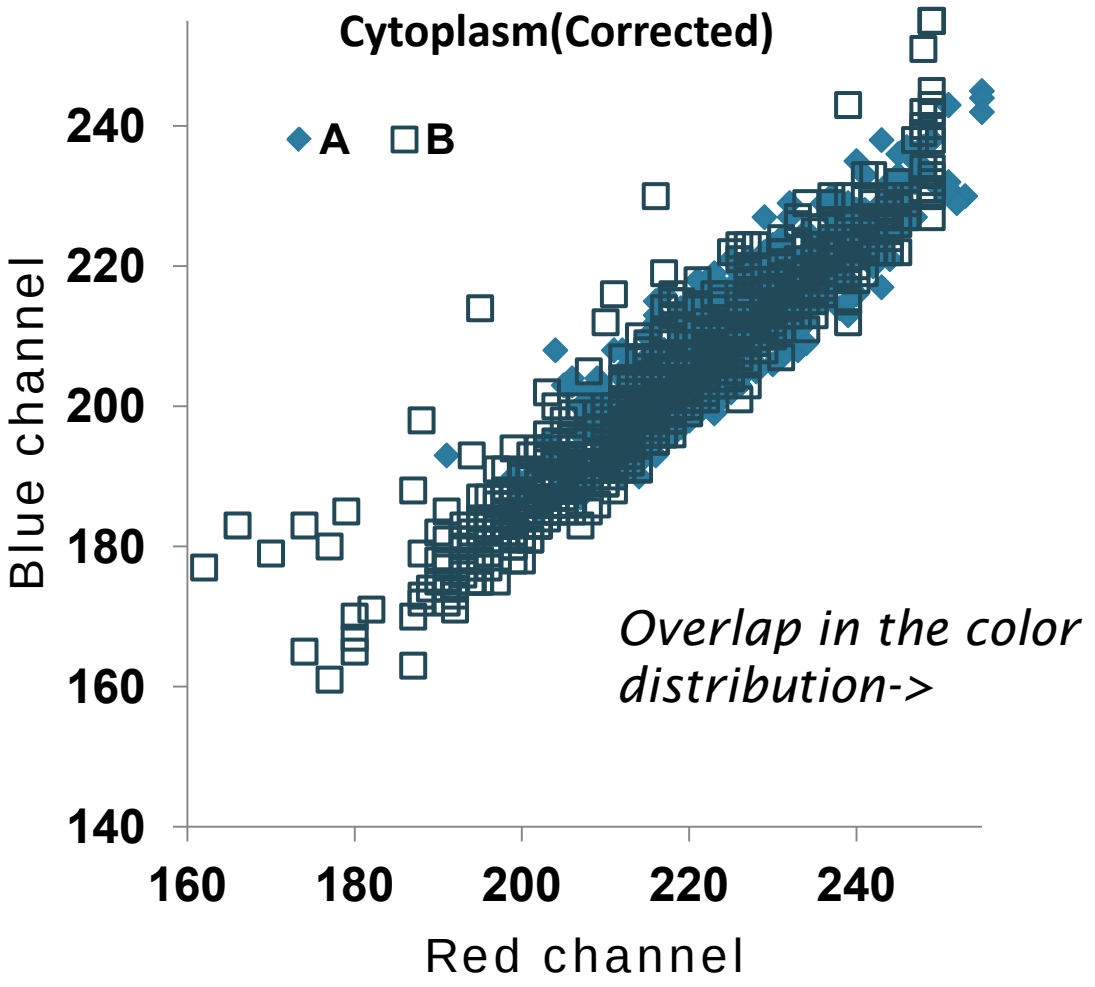
Original


A
B


Cytoplasm(orig)
A
240
220
200
180
160
140
Blue channel
160
180
200
220
240
Red channel
There is separation in the distribution->

Corrected

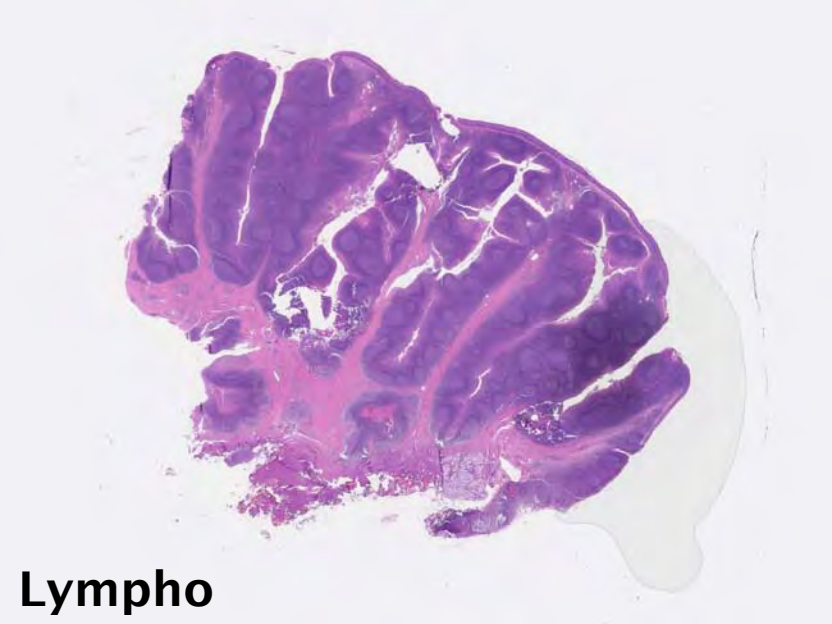

A
B


Cytoplasm(Corrected)
A
B
240
220
200
180
160
140
Blue channel
160
180
200
220
240
Red channel
Overlap in the color distribution->>

Results in Lymphoma

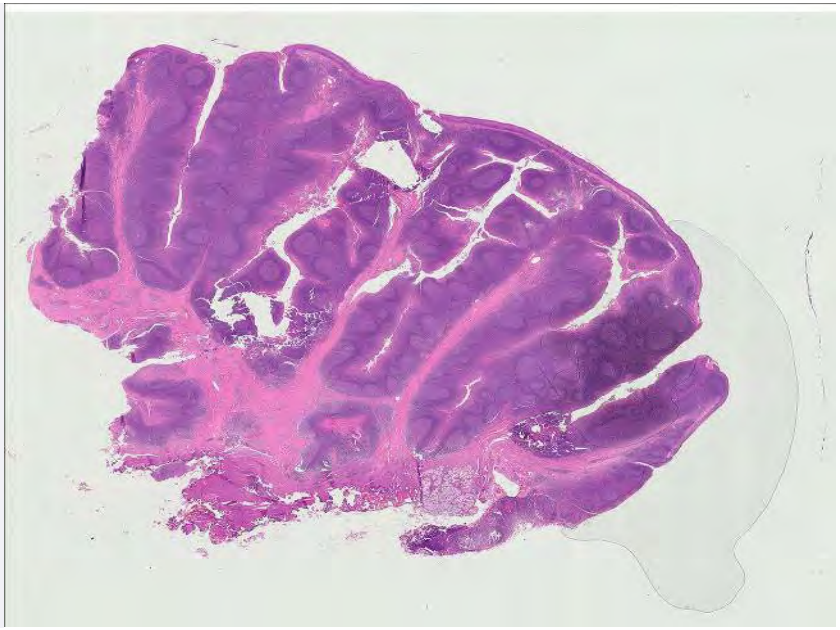
Thumbnail images of the original whole slide images

Scanner A



Lympho ma

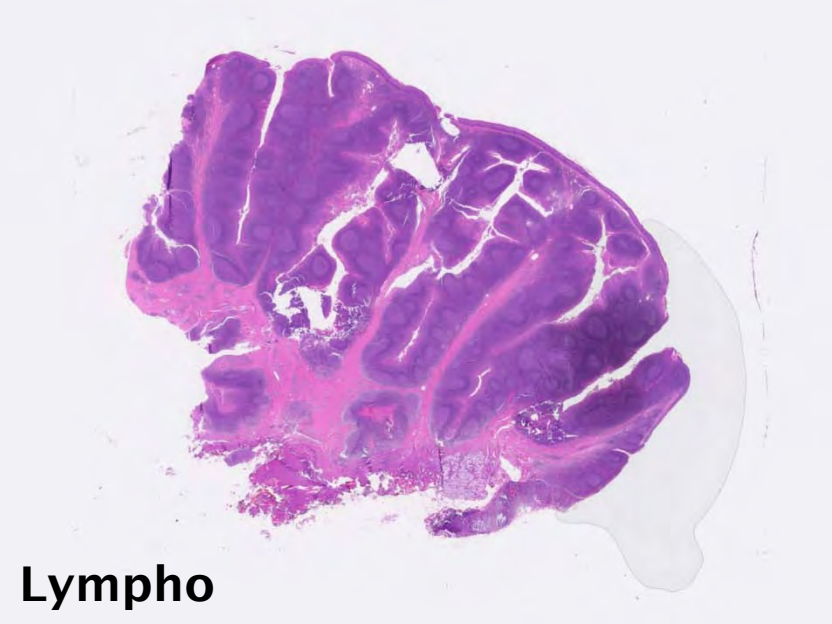
Scanner B



There is color variation….

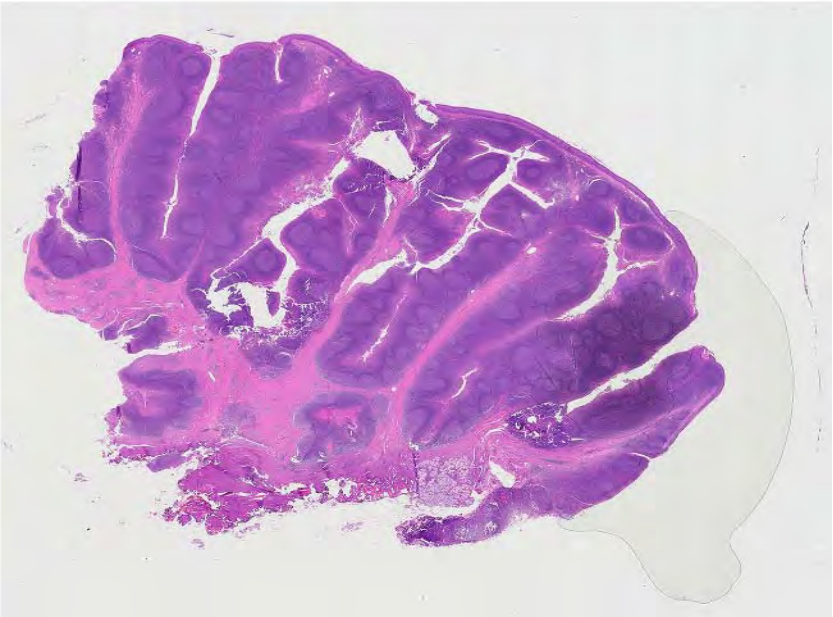
Thumbnail images of the standardized whole slide images

Scanner A



Lymphoma

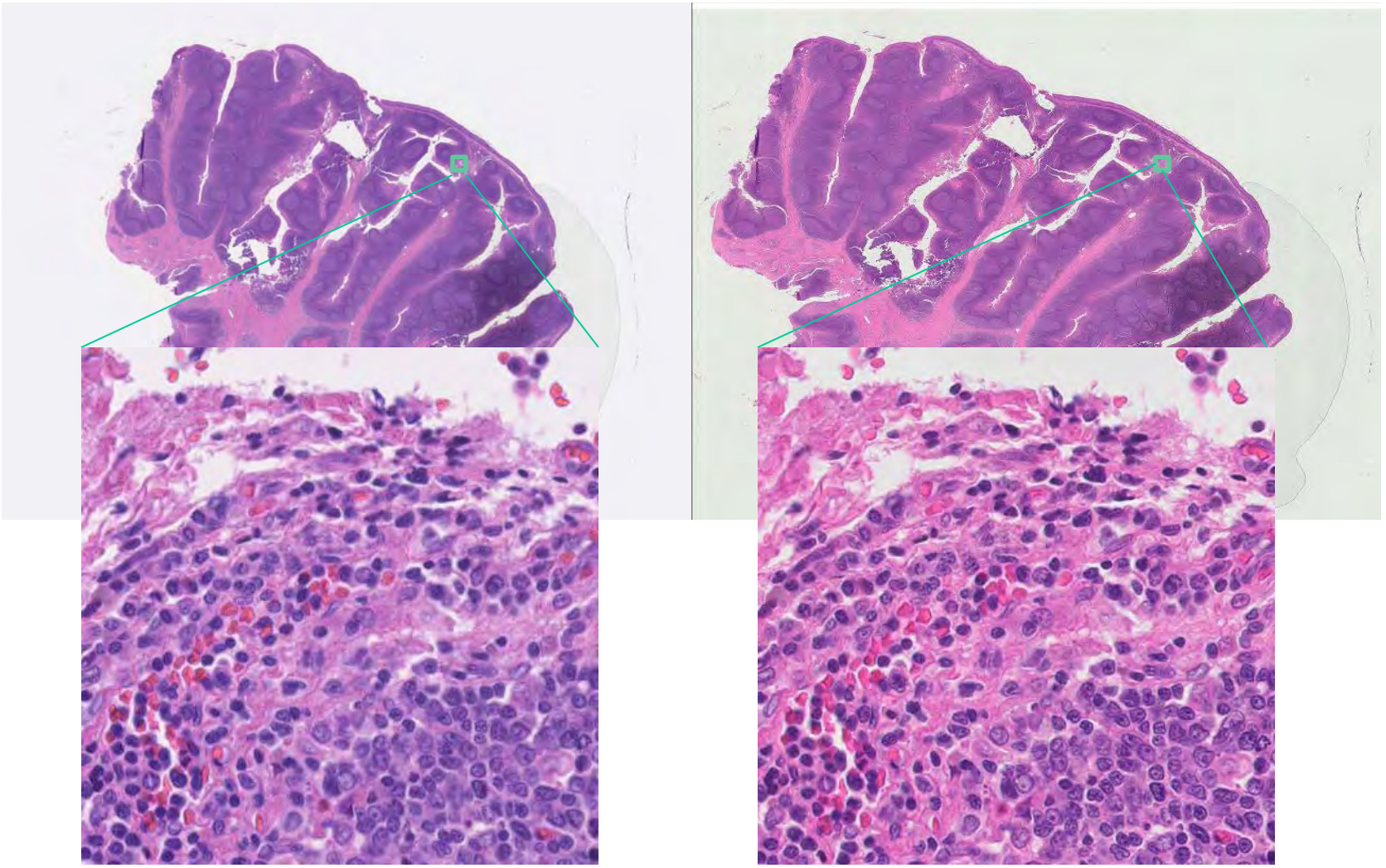
Scanner B



Application of color correction minimizes the color differences…..

Scanner A

Scanner B

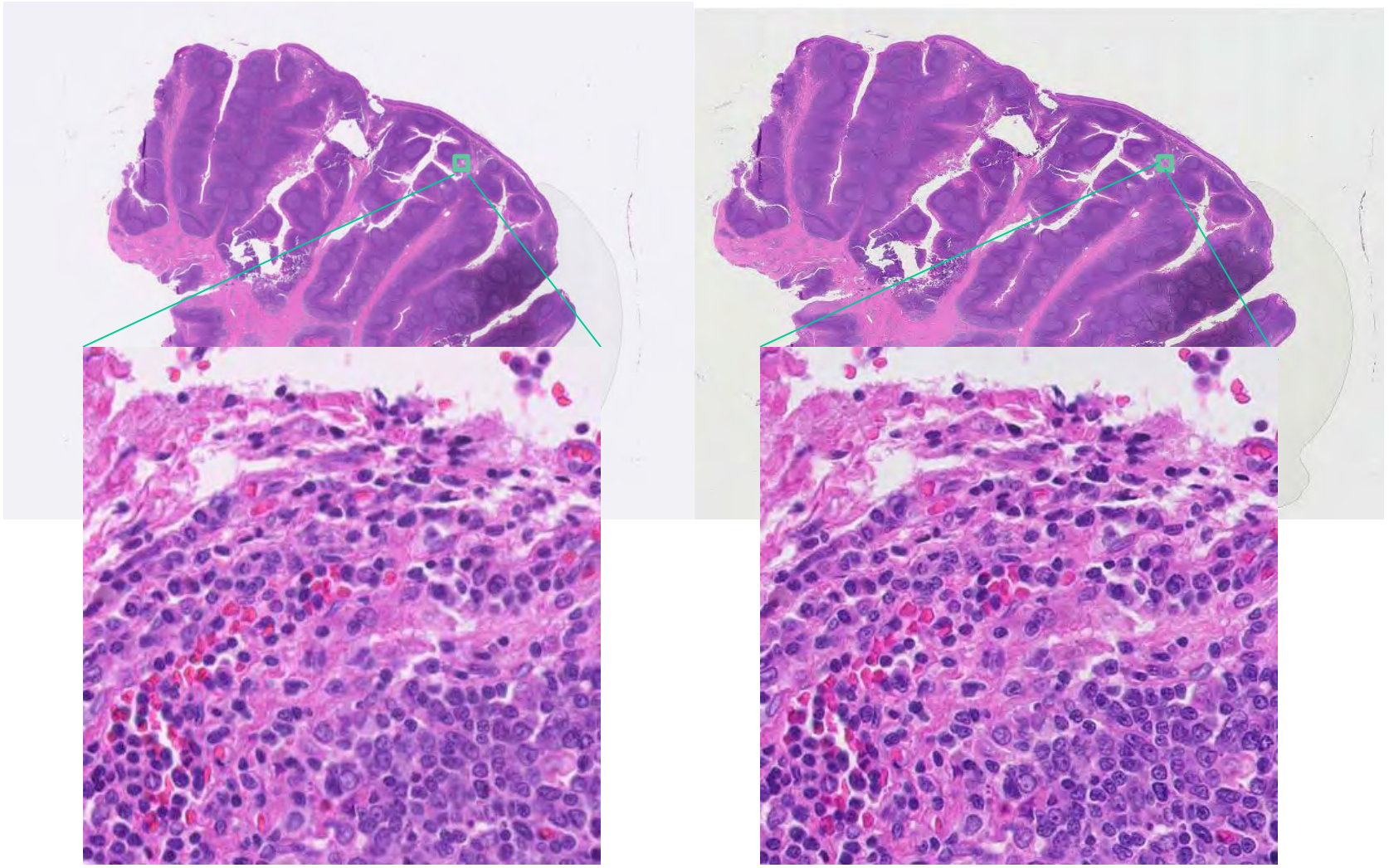


There is color variation....

(no correction)

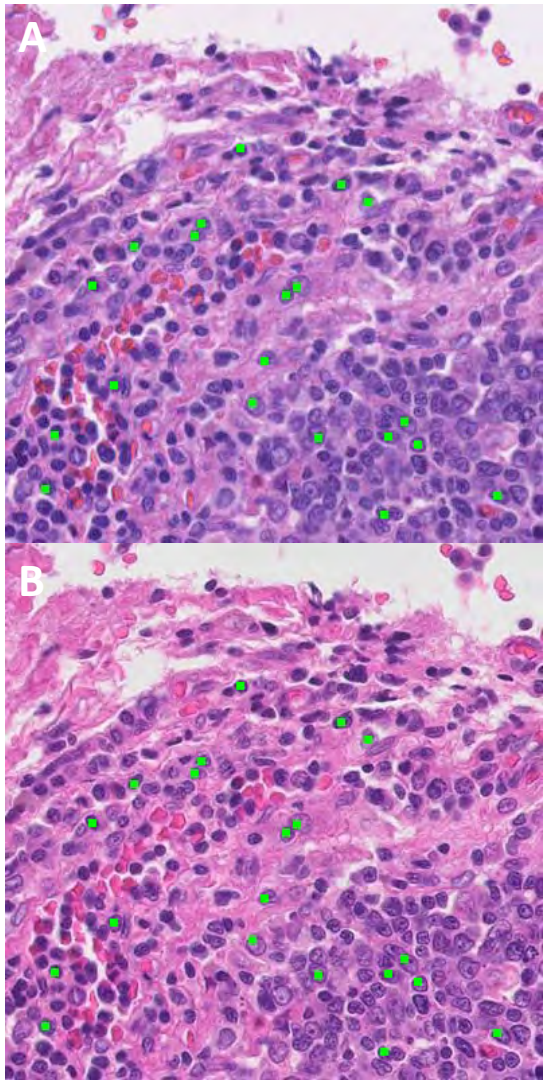
Scanner A

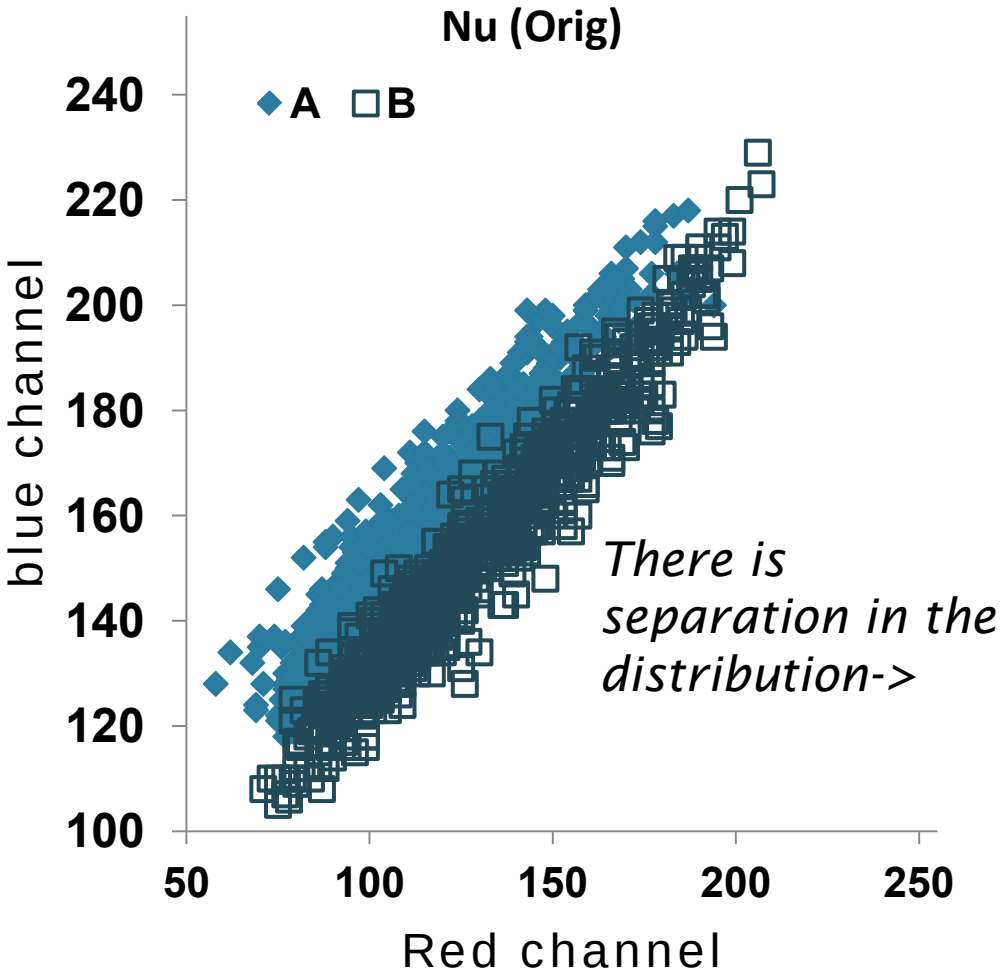
Scanner B



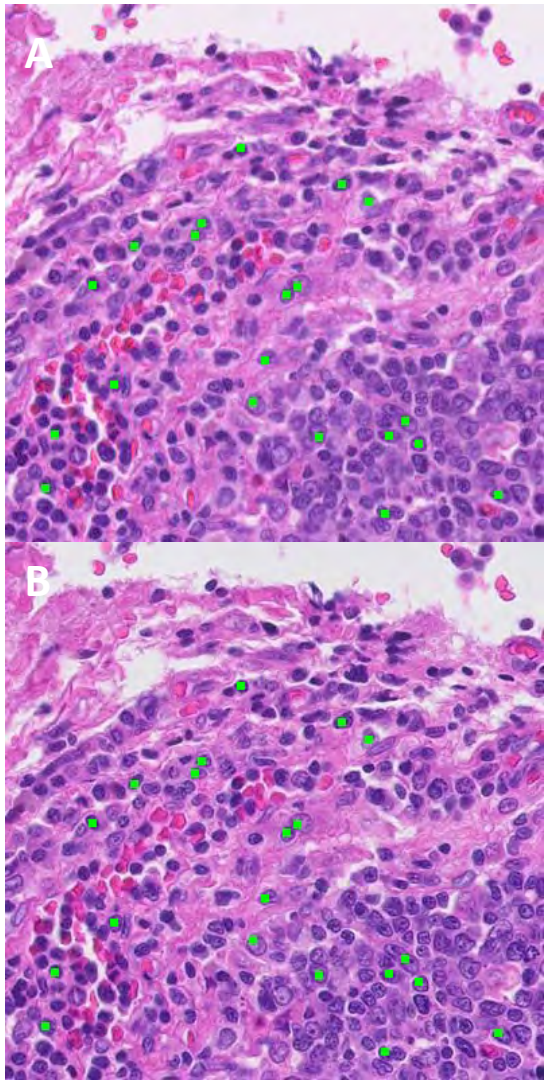
Application of color correction minimizes the color differences.....

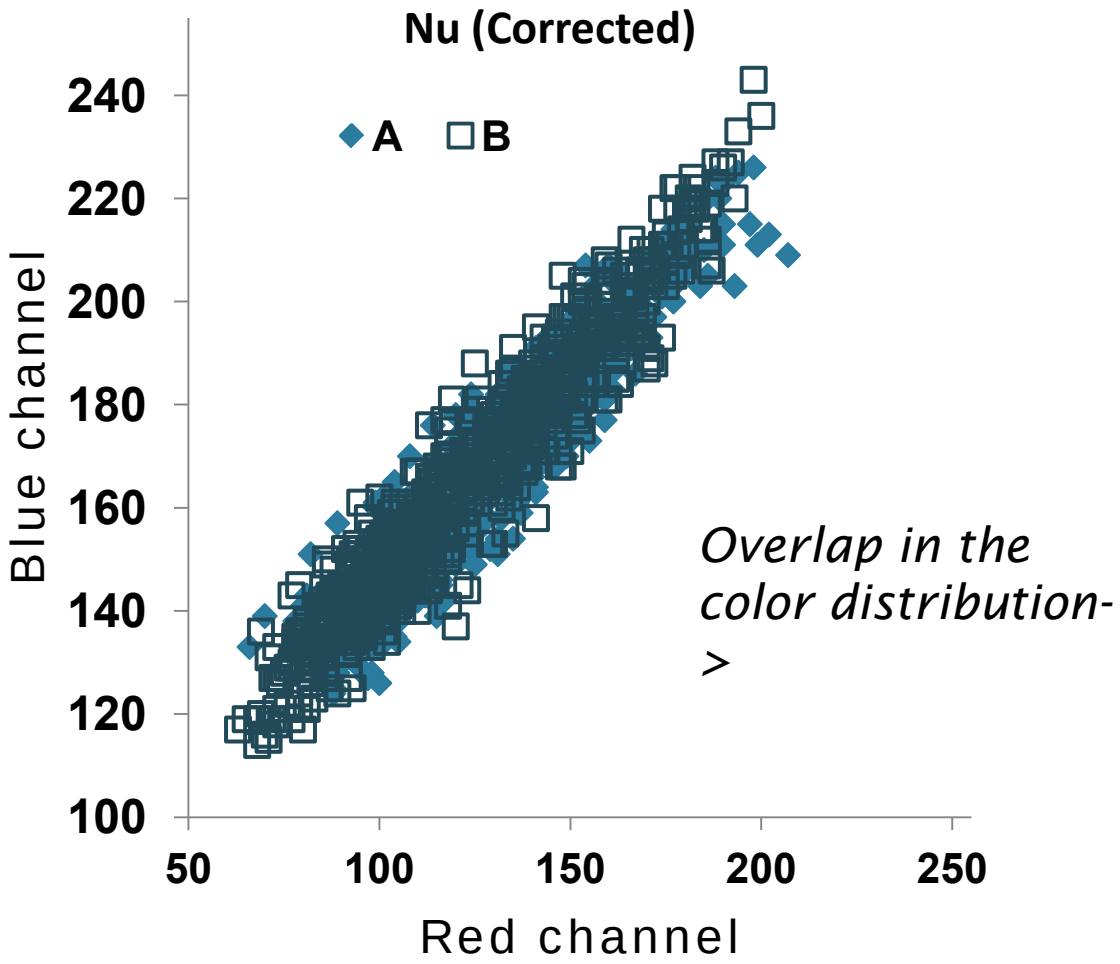
Original


A
B

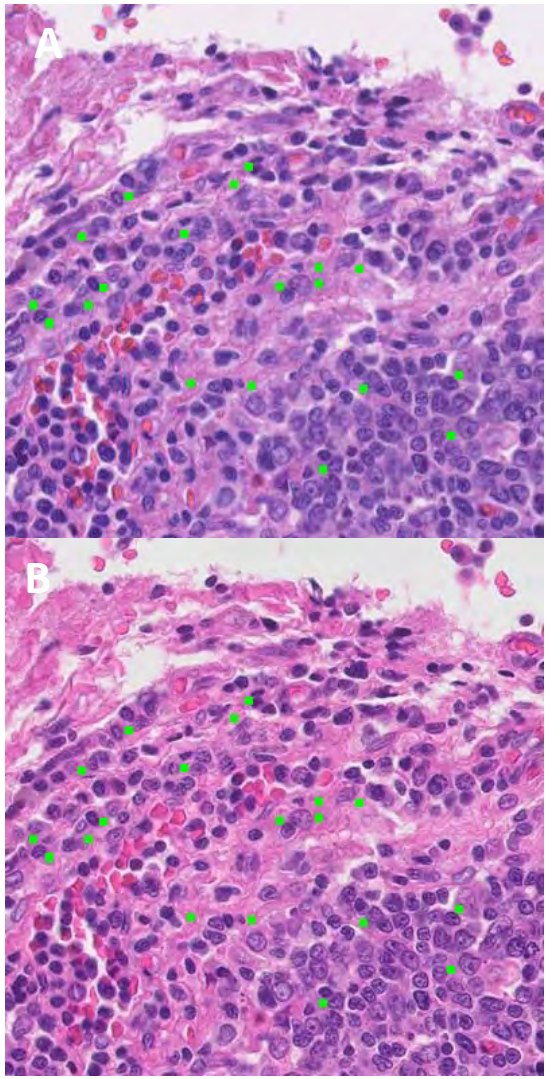

Nu (Orig)
A
B
240
220
200
180
160
140
120
100
blue channel
50
100
150
200
250
Red channel
There is separation in the distribution->

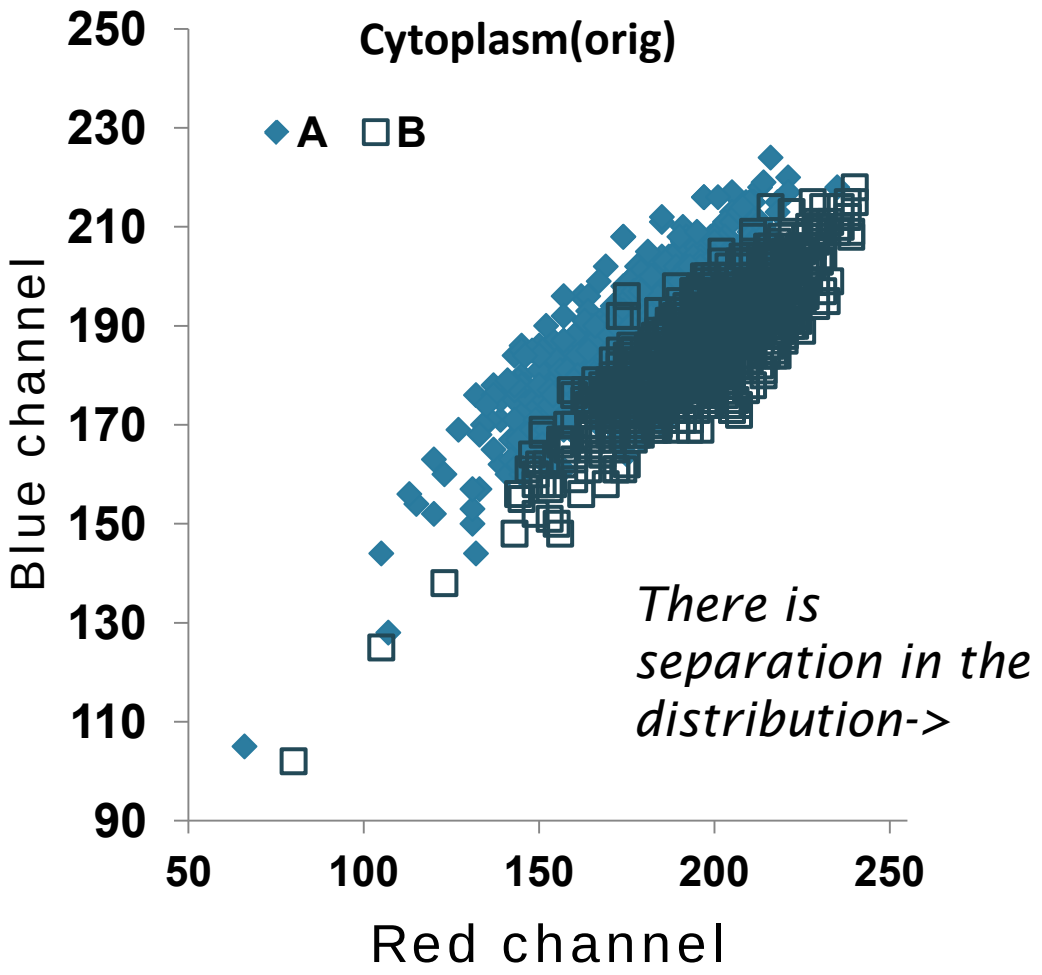
Corrected


A
B

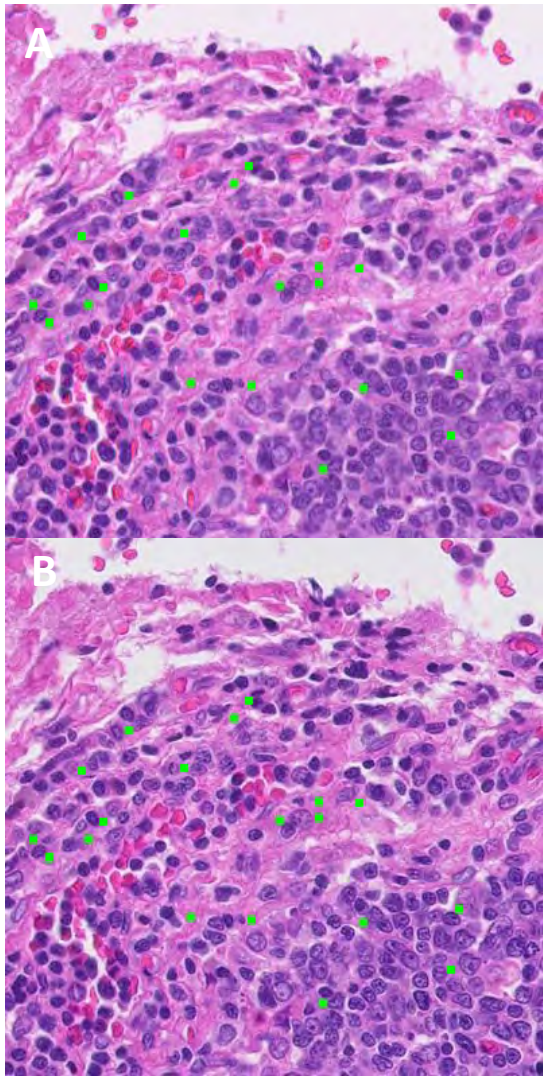

Nu (Corrected)
A
B
Blue channel
240
220
200
180
160
140
120
100
50
100
150
200
250
Red channel
Overlap in the color distribution->>

Original


A
B


Cytoplasm(orig)
A
B
Blue channel
250
230
210
190
170
150
130
110
90
50
100
150
200
250
Red channel
There is separation in the distribution->
MASSACHUSETTS GENERAL HOSPITAL
PATHOLOGY
HARVARD MEDICAL SCHOOL

Corrected


A
B

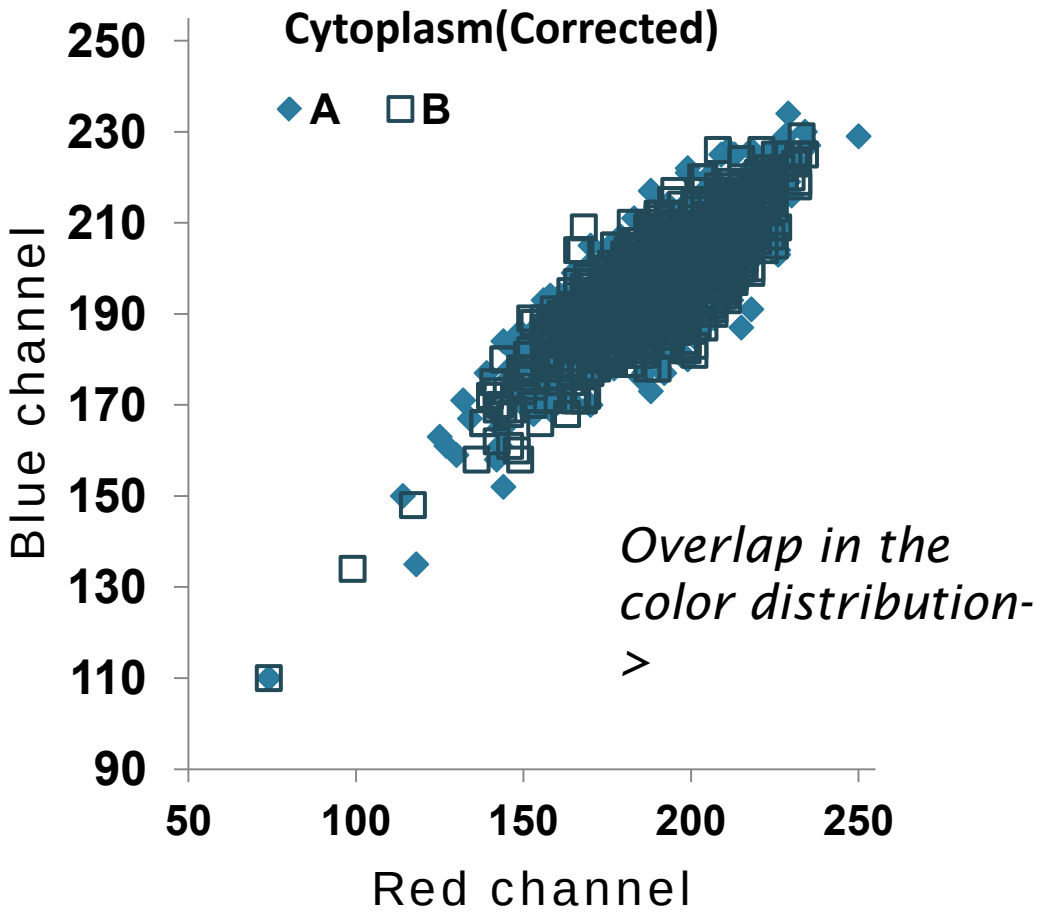

Cytoplasm(Corrected)
A
B
Blue channel
250
230
210
190
170
150
130
110
90
50
100
150
200
250
Red channel
Overlap in the color distribution->>

Image Quality Evaluation

Image Quality Evaluation Algorithm

Image Quality Multiple regression analysis

Definitive evaluation index q, is calculated by $q = \alpha + \beta s + \gamma n$

α, β, γ are derived from training data.

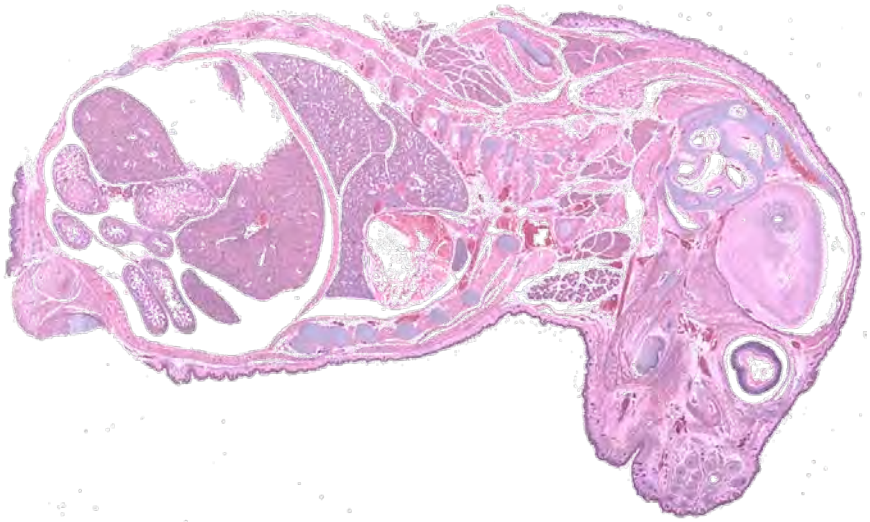


Image Quality Evaluation Method for Whole Slide Scanning

MASSACHUSETTS GENERAL HOSPITAL PATHOLOGY

Noriaki Hashimoto[1], Pinky A. Bautista[2,3], Masahiro Yamaguchi[1], Nagaaki Ohyama[1], Yukako Yagi[2,3]

[1]Tokyo Institute of Technology, [2]Massachusetts General Hospital, [3]Harvard Medical School

HARVARD MEDICAL SCHOOL

Introduction

What is whole slide imaging (WSI)?

- WSI means to transform a conventional glass tissue slide into a digital image so users can access the image remotely on a computer monitor as if they are using a microscope

Issues with WSI

- WSI has to provide consistent high-quality images
- The images need good color representation
- Image data needs a standard format for storage

A high image quality is fundamental to perform an accurate image analysis and to provide a correct diagnosis. Also an improved image quality can help to improve the efficiency of a WSI scanner.

The purpose of this study

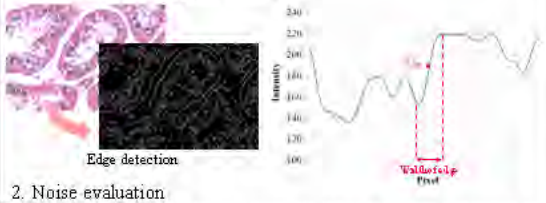
1. To develop an image quality evaluation algorithm for whole slide scanning
2. To determine the appropriate image quality parameter values
3. To investigate how to implement the algorithm in whole slide scanners

Evaluation Algorithm

Evaluation method is based on sharpness (focus) and noise

1. Sharpness evaluation

a. The edges in the image are detected using the Canny algorithm.
b. Pixel-widths of the detected edges are determined and the average value is used as the sharpness index,[5].



2. Noise evaluation

a. A unsharp masking technique is used to detect the edges and noises in the image.
b. The center pixel (3x3-pixel window) is replaced with the minimum difference between its surrounding pixels in order to leave only the noises. The mean-square of replaced pixel values is used as the noise

Unsharp masking (Edge and noise detection)

Calculate the minimum difference within 3x3 pixels (Edge reduction)

Multiple regression analysis

Definitive evaluation index q, is calculated by

$$q = \alpha + \beta s + \gamma n$$

α, β, γ are derived from training data.

We can choose the arbitrary index for multiple regression depending on the requirement of user's application. If we use the subjective evaluation values, the image quality for diagnostic application is calculated. Otherwise, using the objective evaluation values allows the result to show the image quality required for image analysis.

Experiments

1. Evaluation of the algorithm

50 images were captured from the various types of slides scanned by NanoZoomer 2.0HT (HAMAMATSU), and trimmed into 400x400 pixels.
We conducted a survey to get the subjective scores of pathologists, technicians, and image specialists. The images were rated on a scale of one to five, i.e., 5 was the best quality and 1 was the worst. The average scores of each image were used for multiple regression analysis, in which we investigated the correlation between the computed results using our algorithm and the subjective scores. From the regression analysis results, we determined the appropriate image quality parameter value, i.e., threshold value between good and bad quality image.

The screenshots of the survey

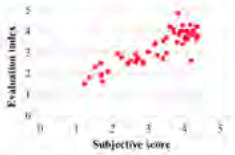
2. Application to WSI

We applied the proposed image quality evaluation method to the WSI of an H&E stained mouse embryo. Its image size was 36,000x24,000 pixels.
The entire image was divided to 400x400-pixel blocks, and the evaluation algorithm was applied to all blocks. The equation derived by multiple regression analysis was used to evaluate the image quality of each block.
In this experiment, the block, whose evaluation index was greater than the threshold value based on the results of the subjective experiment, was visualized with the original color. Otherwise, each block was shaded depending on the evaluation index. The blocks, which had more white pixels than 75% of the block, were regarded as background and also visualized with the original color.

Results

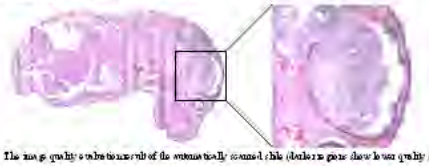
1. Evaluation of the algorithm

In the result of multiple regression analysis, the correlation coefficient was 0.869.
This confirms the evaluation indices are highly correlated to the subjective scores. In this case, we defined 3.5 as the threshold for the good-quality image.



2. Application to WSI

We scanned the mouse embryo slide in automatic focusing mode and applied the proposed image quality evaluation method.



The image quality evaluation result of the automatically scanned slide (darker area show lower quality)

Some regions of the evaluating result indicated the low image quality. We specified a focus point on such region manually and the mouse embryo slide was re-scanned. Then, the image quality evaluation method was applied to the re-scanned image.

The image quality evaluation result of the re-scanned slide (darker area show lower quality)

Stitched image where the re-scanned region was pasted into the original image

The image qualities of the regions, which had low-quality indices in the original image, were improved. By integrating improved regions of the re-scanned image into the original image, the image quality of the entire image improves.

Discussion

We performed a simulation on the application of image quality evaluation in whole slide scanning. In the simulation a slide was first scanned in automatic focusing mode. Then, the image quality of the scanned image (WSI) was evaluated using our proposed method. The slide was re-scanned wherein a focus point was specified on regions in the whole slide image which exhibited low image quality values. These regions were replaced with their counterparts from the re-scanned image. In the actual implementation however, the scanner's protocol could be configured such that only the regions with low image quality values will be re-scanned. The results presented above show the effectiveness of the present image quality evaluation method in identifying the quality of the image.
The current scanner that we used in our experiment implements line scanning. So that, the shaded strips present in the whole slide images correspond to edges of the line. It is part of our future work to investigate the performance of the present image quality evaluation on other scanners with different scanning method.

Conclusion

The image quality evaluation algorithm is extremely important for WSI. Results of our experiments show that by incorporating the proposed image quality evaluation method, the quality of whole slide images is improved. The image quality evaluation method that we presented could be integrated to the scanning procedure of digital slides. The effectiveness of the evaluation indices used in our experiments were confirmed through linear regression analysis.

Discussions

- The two types of calibration slides helped users to improve the color accuracy of the images they are looking at.
- Two algorithms for color and quality are working well for 5 scanners
- We have developed additional calibration slides to improve the reliability of WSI system 
- Many pathologists have started to realize that accurate color and image quality are important in WSI.

Summary : Standardization

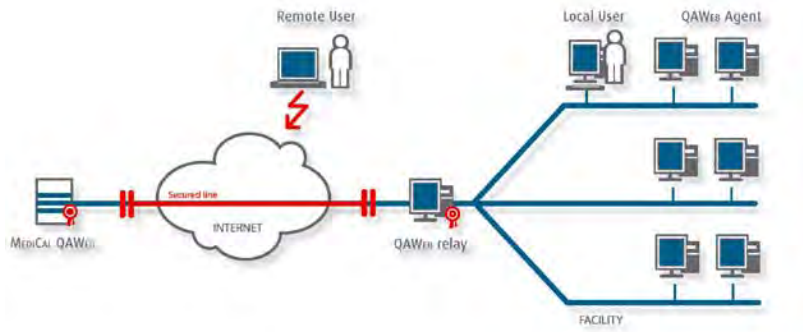
Scanning

Color Standardization Algorithm

Image Quality Evaluation Algorithm

Display

Online Management System is available



Staining

Digital Staining Standardization is available

Acknowledgements

• This research was partially supported by Olympus, Canon, 3DHISTECH, Kurabo.
• Authors acknowledge to PICT Lab, Pathology Informatics, Department of Pathology at MGH

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Thank You!

Omnyx

TRANSFORMING THE SCOPE OF PATHOLOGY

Omnyx/GE Healthcare
Color Calibration Procedure

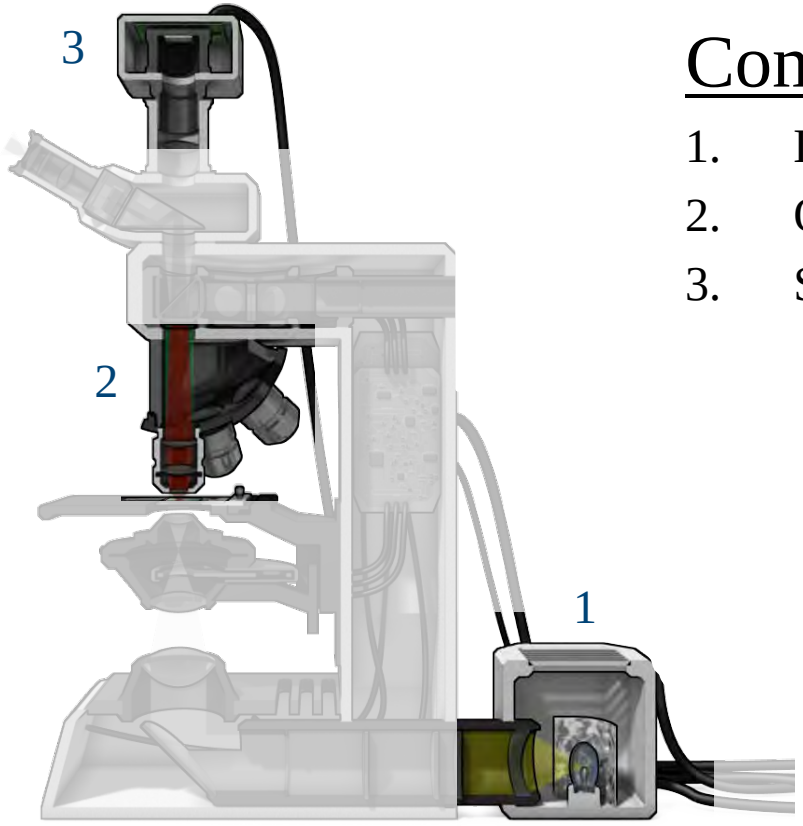
Vipul Baxi, Lead Scientist

Tyler Keay, Research Scientist

UPMC

A joint venture of GE Healthcare and UPMC

Digital Pathology Imaging System



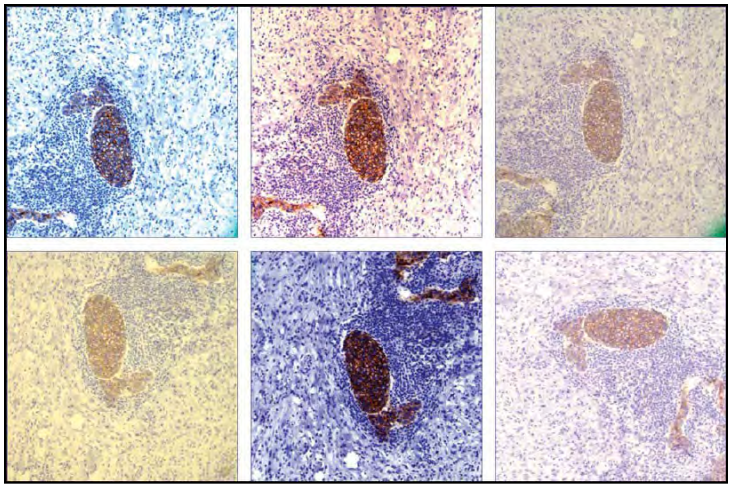
http://www.richardwheeler.net/contentpages/image.php?gallery=Scientific_Illustration&img=Epifluorescence_Microscope&type=jpg

Components affecting Color

1. Light Source
2. Objective Lens
3. Sensor

Importance of Color Calibration

- Provide Standardization
  - Amongst digital scanners produced by the same manufacturer
  - Amongst digital scanners with diverse technology and scanning components
  - Consistency and Accuracy of CAD algorithms
- Transition and adoption of digital pathology
  - Pathologists get the same view of the sample as they would under a microscope
  - Prevent possible misdiagnosis due to color inaccuracy

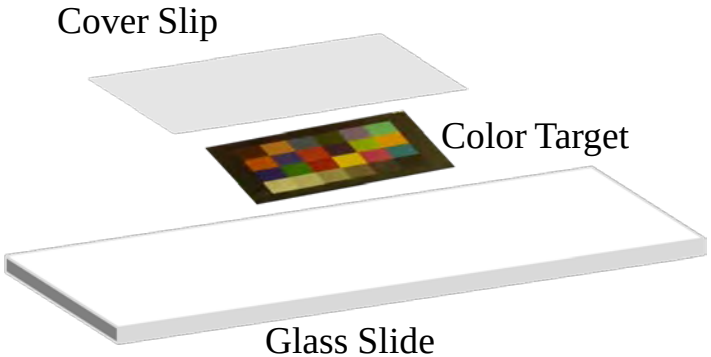


Pantanowitz, L. (2010). "Digital images and the future of digital pathology." Journal of Pathology Informatics **1**(1): 15-15

Color Target Slide for Microscopy

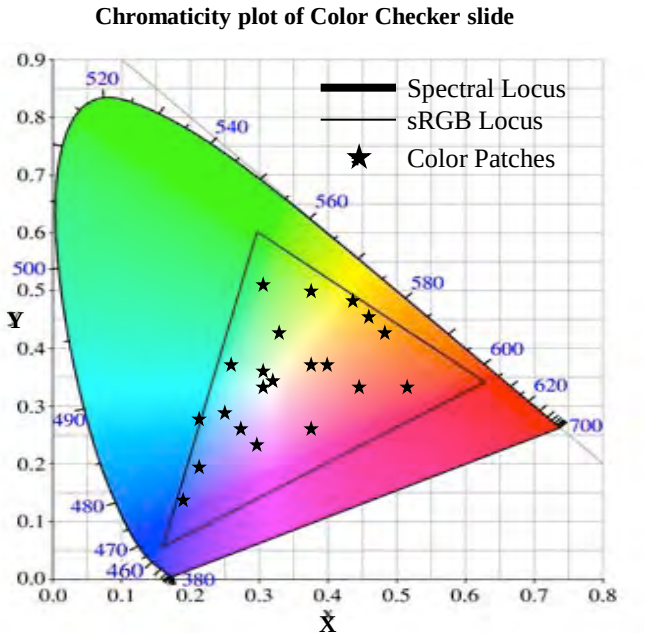
Color Target Film

Target Slide Assembly

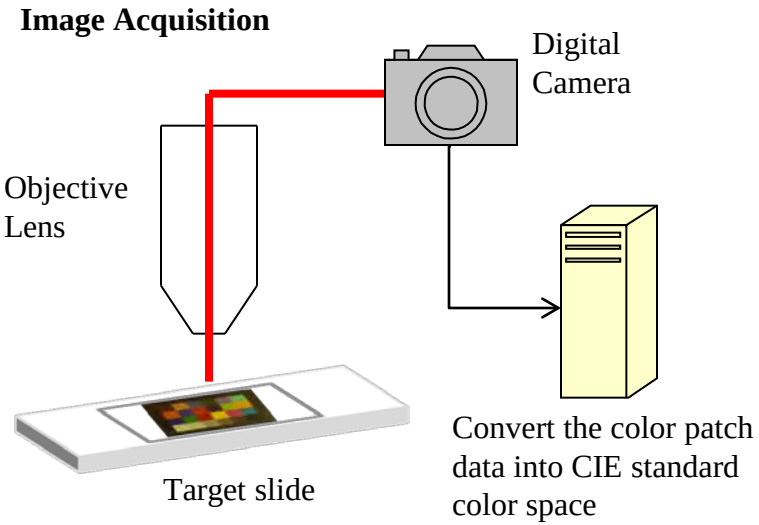


Reference Values

Measure (NIST) and plot reference values of each color patch



Calibration Procedure



Transformation to Reference Values

Color Calibration Matrix

R_1	G_1	B_1
R_2	G_2	B_2
R_3	G_3	B_3

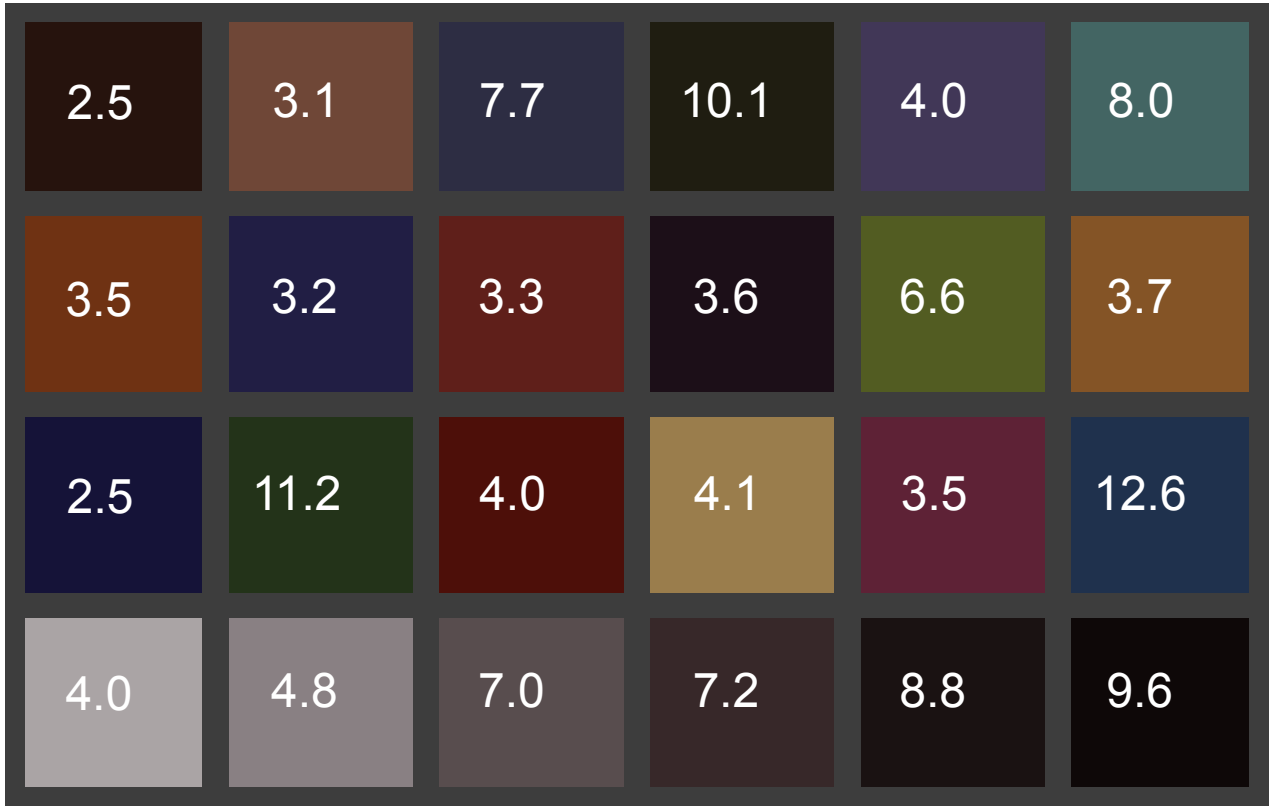
$$R_{out} = R_{in} * R_1 + G_{in} * R_2 + B_{in} * R_3$$
$$G_{out} = R_{in} * G_1 + G_{in} * G_2 + B_{in} * G_3$$
$$B_{out} = R_{in} * B_1 + G_{in} * B_2 + B_{in} * B_3$$

1. Acquire image of each patch
2. Calculate CIE Color Space values

1. Compare to Reference values and obtain best transformation

The transformation matrix can be applied to input color patches and objectively measure the color difference

Correction of Color Patches



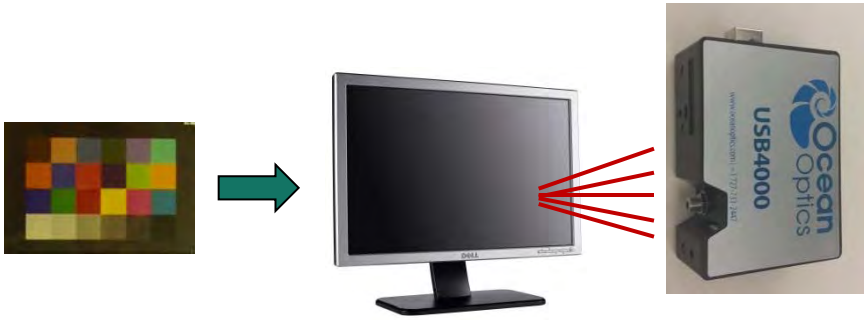
Mean dE94 = 5.7

Color Evaluation At The Display

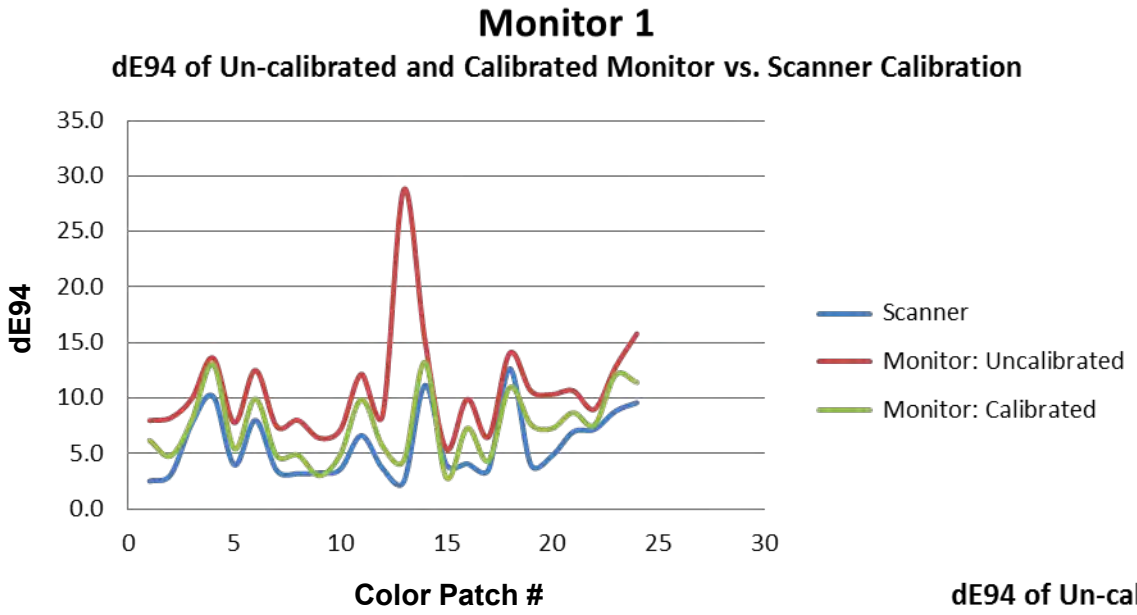
- To understand the impact of color calibration the final end point (the display) must be considered

Measurement Procedure

- Target → Digital Pathology Software → Display → Spectrophotometer
- Display : HP ZR2440W
- Spyder 4 Pro
- Ocean Optics USB 4000
  - 2 sec integration
  - 5 scans averaged

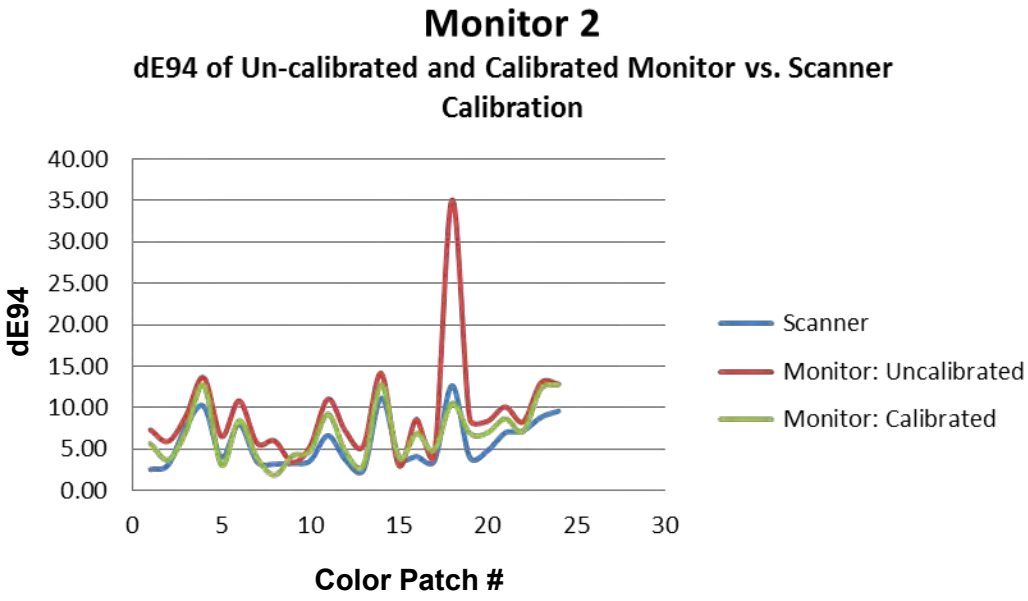


Scanner vs. Display Color Difference



Color Target scanned on a calibrated scanner and displayed on 2 monitors (un-calibrated & calibrated)

dE94	Scanner	Monitor: Un-calibrated	Monitor: Calibrated
Monitor 1	5.7	*10.8* (Δ**4.9**)	*7.4* (Δ**1.7**)
Monitor 2	5.7	*9.3* (Δ**3.6**)	*6.9* (Δ**1.2**)



Setup Measurement Accuracy

- A set of 24 homogeneous color images were created (500 x 500 pixels) with user defined color values
- Images were individually displayed on each of the monitor and the spectral response was measured (Ocean Optics)
- dE94 values for each color image was calculated using the known value as the reference.

Monitor 1

Mean dE94: **2.83** (+/- 1.53)

Monitor 2

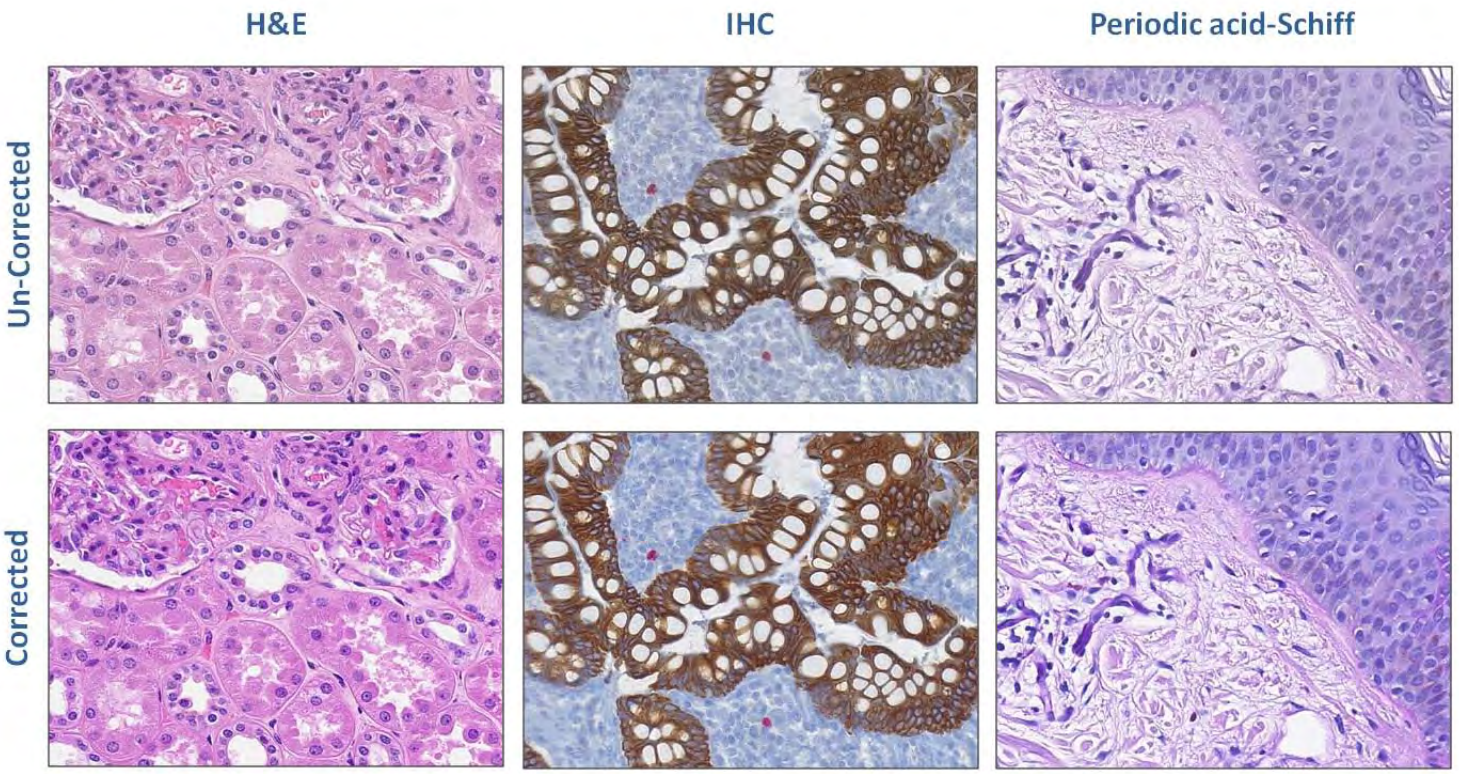
Mean dE94: **3.28** (+/- 1.34)

Review of Whole Slide Images

- Scan Whole Slide images and correct them with the color correction matrix
  - 5 H&E, 2 IHC, 3 Special Stains (PAS, GMS, Colloidal Iron)
- Simultaneously,
  - View the physical slide under a microscope and
  - The digital image (corrected and uncorrected) on a calibrated monitor
- Score each image on the following likert scale:

5: Identical – There is no noticeable difference in color between the glass and digital image
4: Similar – The color is very close, with subtle differences in certain features
3: Noticeably Different – The color is noticeably different, but should not affect diagnosis
2: Significantly Different – The color is extremely different, and may possibly affect diagnosis
1: Misrepresentation – The color is completely wrong

Whole Slide Image Scoring



Avg Score = 3.8
~**Similar**

Avg Score = 4.8
~**Identical**

Conclusion

1. Color calibration is a necessary step to produce WSI that are consistent with optical microscope AND create standardization amongst the different scanners
2. For total color management, the color fidelity of the WSI needs to be maintained by a separate calibration of the monitor.
3. The described calibration method does bring the WSI color closer to the optical microscope.

Next Steps:

1. Develop a robust measurement setup that accurately measures the color response on the monitor.
2. Evaluate the color difference using a color patches different than the Macbeth color checker (ex. IT8.7)
3. Larger scale study evaluating color difference between digital and glass (simultaneous viewing)

References

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2. Al-Janabi, S., Huisman, A., et al. (2011). "Digital pathology: current status and future perspectives." Histopathology: 1-9
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4. Koren, N. "Imatest - Color Correction Matrix." *Imatest*. Imatest, 2009. Web. 08 Sept. 2011. <http://www.imatest.com/docs/colormatrix.html>.
5. Lindstrom, P. (2008). "Delta E Blues: The Science of Color Perception." Seybold Report: Analyzing Publishing Technologies **8**(3): 13
6. Yagi, Y., Gilbertson, J. R. (2005). "Digital Imaging in Pathology: the case for standardization." J Telemed Telecare **11**(3): 109-116
7. Hubel, P. M., Finlayson, G. D., et al. (1997). "Matrix Calculations for Digital Photography." Fifth Color Imaging Conference: Color Science, Systems and Applications: 105-111
8. Yagi, Y. (2011). "Color Standardization and Optimization in Whole Slide Imaging." Diagnostic Pathology **6**(Suppl 1): 1-15

Questions?

Calibration of Leica Scanscope AT2

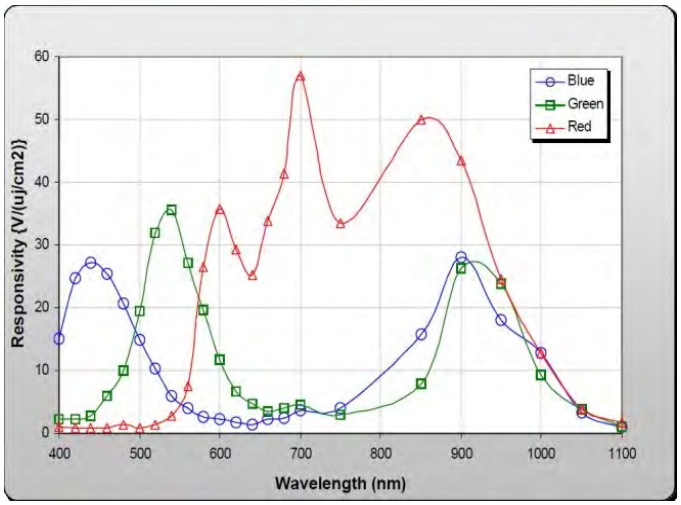
Allen H. Olson, PhD
Aperio ePathology, Leica Biosystems

ICC Medical Imaging Working Group – 18 Nov 2013

Overview

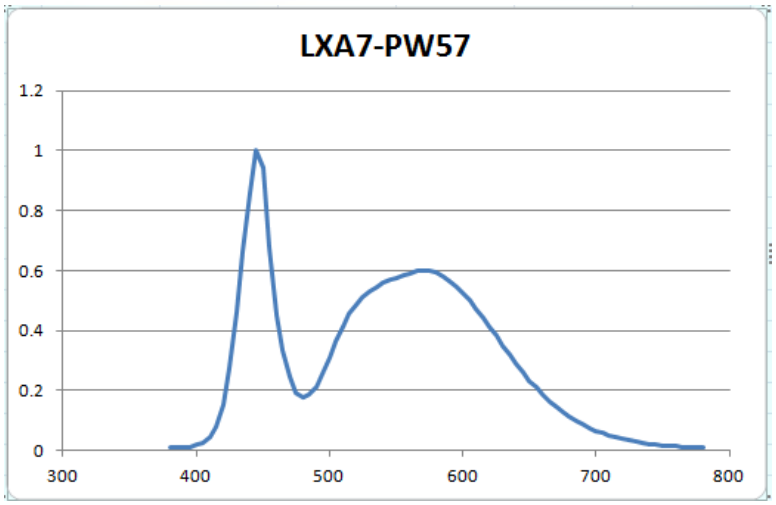
- Spectral Models for Scanner and Microscope
- Histological Stain Spectra (examples from literature)
- Construction of Color Transform
- Viewing of Digital Slides (ICC Profile using 3D LUT)
- Validation of Spectral Models (IT8.7 Film Target)
- Measuring Scanner Spectral Response
- Slide-Specific Color Profiling

Spectral Model for Scanner



Dalsa Piranha PC-30 Camera

$< \bar{r}(f), \bar{g}(f), \bar{b}(f) >$



LED Light Source

$L_S(f)$

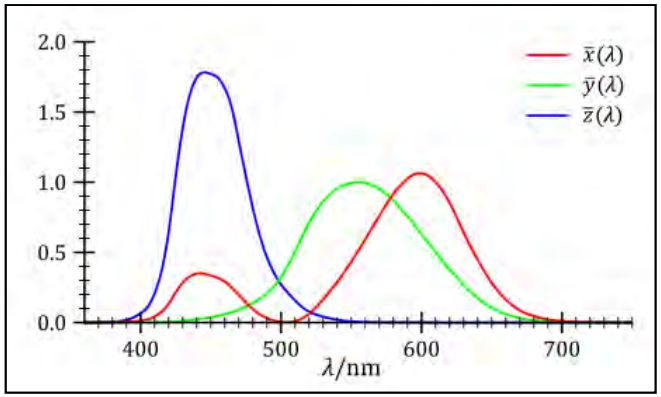
$$< R, G, B > = \frac{1}{< W_r,\ W_g,\ W_b >} \int < \bar{r}(f), \bar{g}(f), \bar{b}(f) > L_s(f)\, T(f)\, df$$

$< R, G, B >$
Scanner Output

$< W >$
White Balance
$[T = 1.0]$

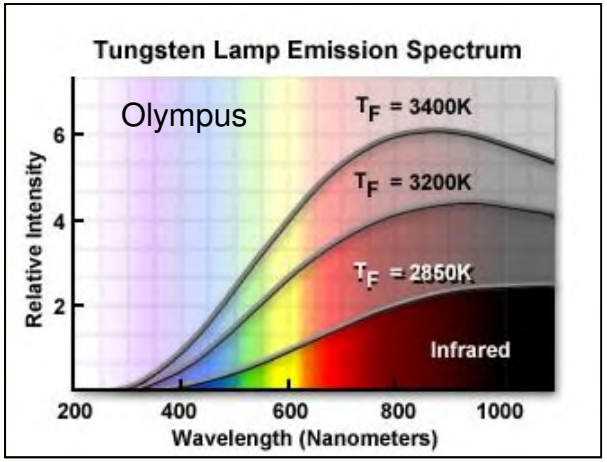
$T(f)$
Stain Transmission Spectra

Spectral Model for Microscope



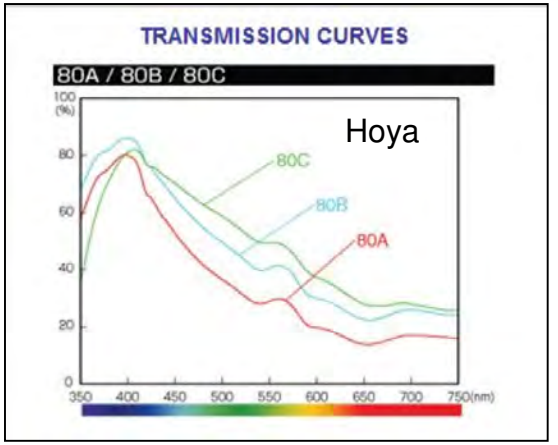
CIE Standard Observer

$< \bar{x}(f), \bar{y}(f), \bar{z}(f) >$



Tungsten Lamp

$L_m(f)$



Daylight Filter

$F(f)$

$$< X, Y, Z > = \frac{1}{W_y} \int < \bar{x}(f), \bar{y}(f), \bar{z}(f) > L_m(f)\, F(f)\, T(f)\, df$$

$< X, Y, Z >$

CIE Tristimulus Values

W_y

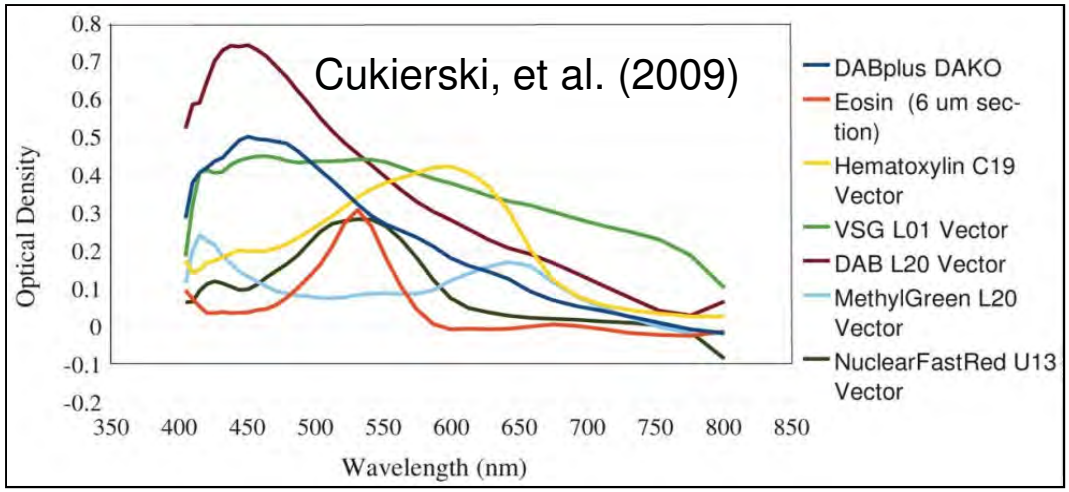
Normalization

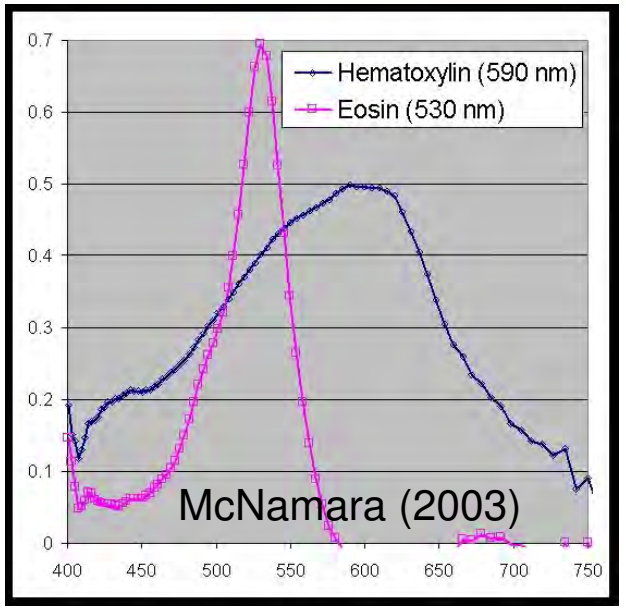
$(Y_{max} = 1)$

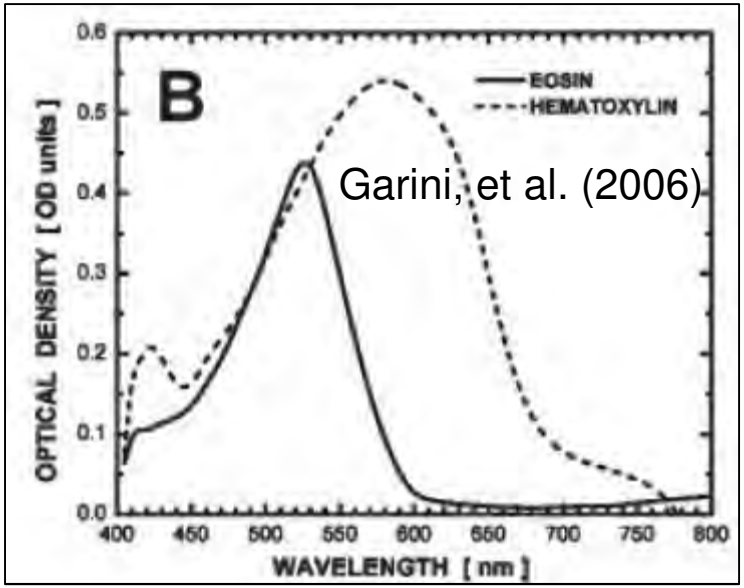
$T(f)$

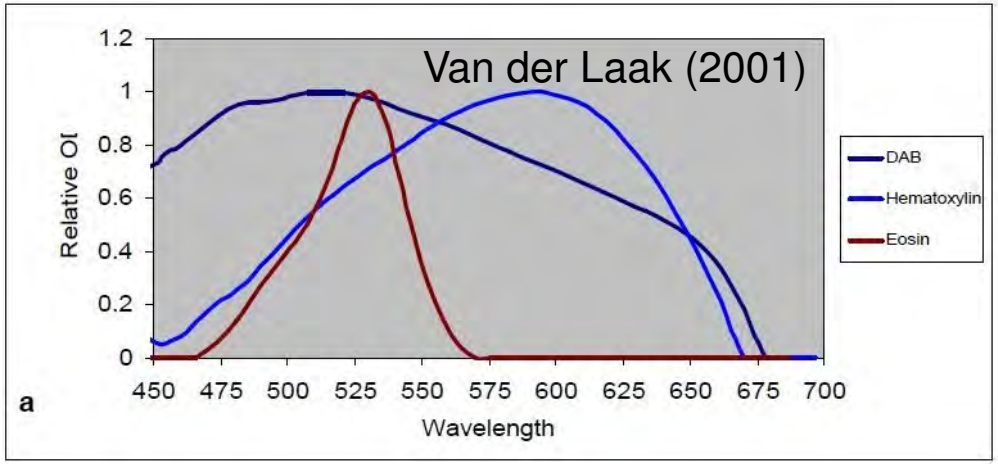
Stain Transmission Spectra

Histological Stain Spectra $T(f)$







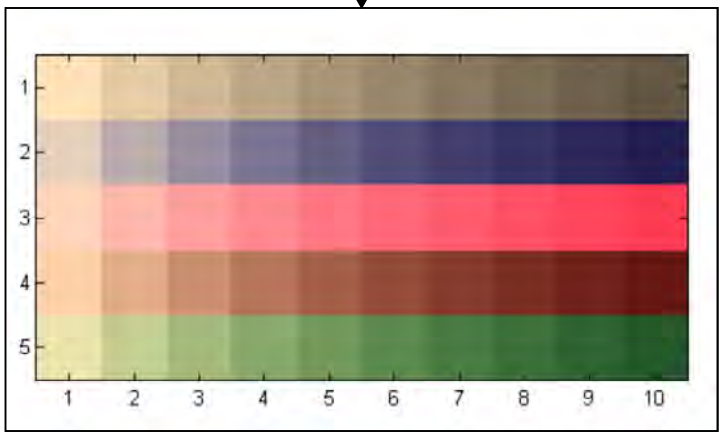


International Color Consortium

Construction of Color Transform

Stain Spectra $T(f)$
Neutral Gray
Hematoxylin Eosin
DAB
Methyl Green

Target Spectra
$[T_k(f)]^{\gamma}$ x $[T_l(f)]^{\alpha}$



Scanner Model

$< R_i , G_i , B_i >$

Microscope Model

$< X_i , Y_i , Z_i >$

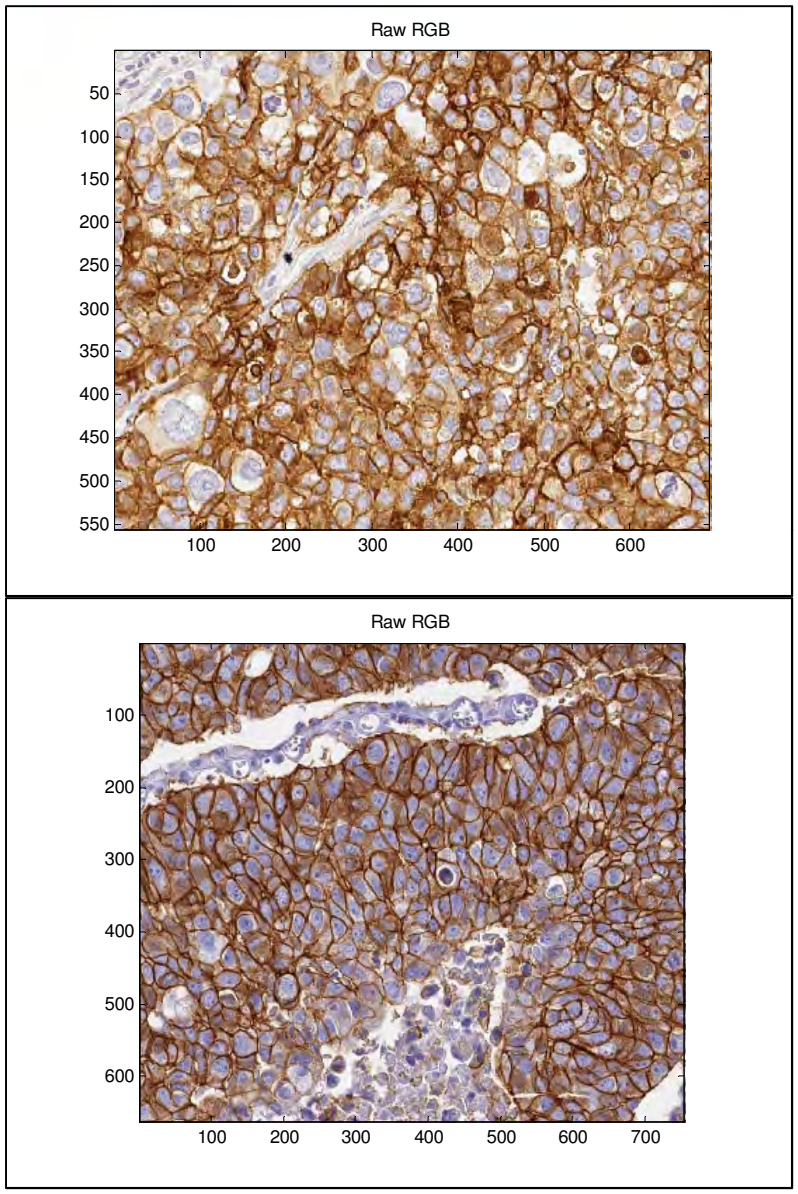
Interpolator

3D LUT
$< X, Y, Z > = LUT(< R, G , B >)$

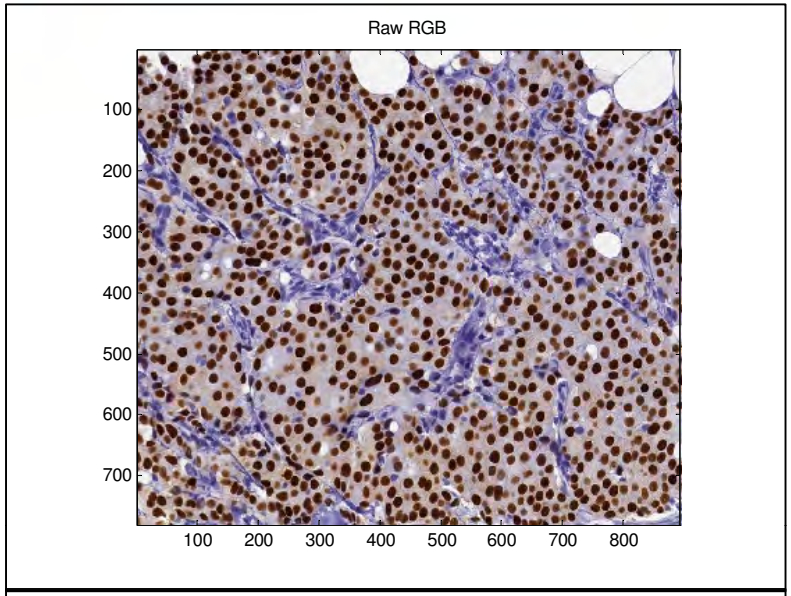
Viewing of Digital Slides

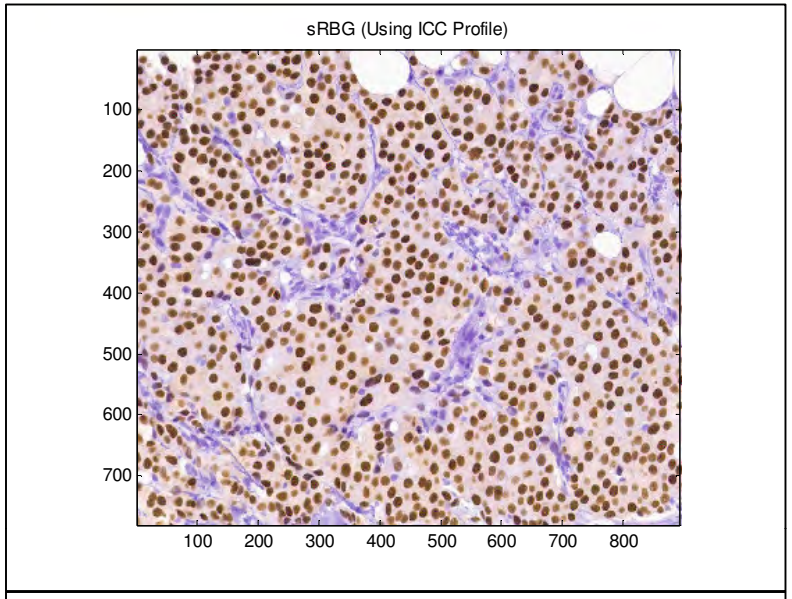
- Color Management – ICC Profile Workflow
- Digital Slide ICC Profile
  - Use “create_CLUT_profile” application (ICC website)
    - Chromatic Adaptation to D50 connection space
    - Microscope White Point = (0.9984, 1.0000, 0.5423)
- Monitor ICC Profile
  - sRGB mode for monitor
  - Use generic sRGB profile
- Viewing Software
  - Aperio ImageScope – LCMS library
- Microscopic Viewing
  - Nikon Eclipse E400 with Hoya 80A filter

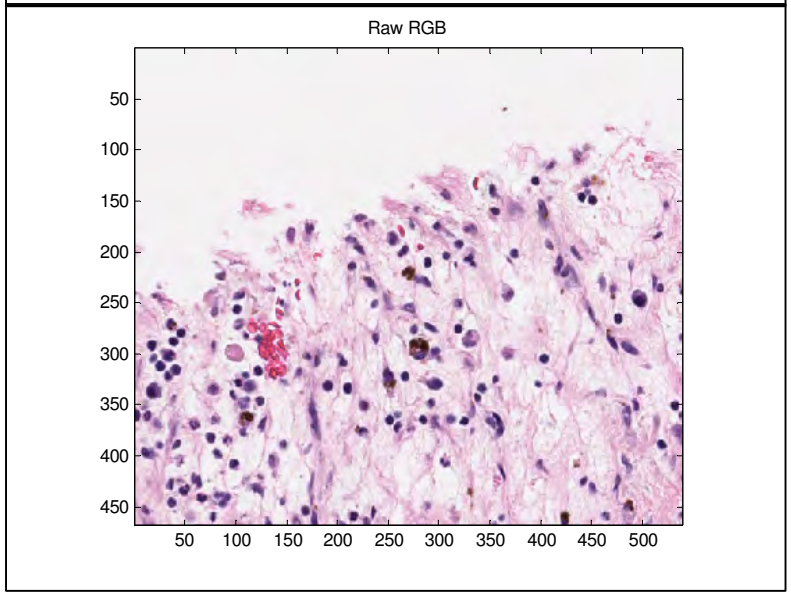
Viewing of Digital Slides

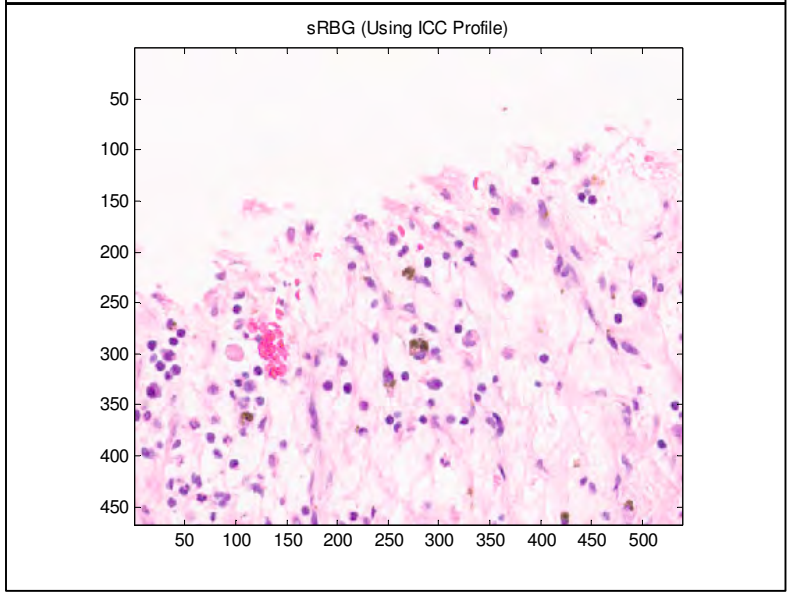


Viewing of Digital Slides

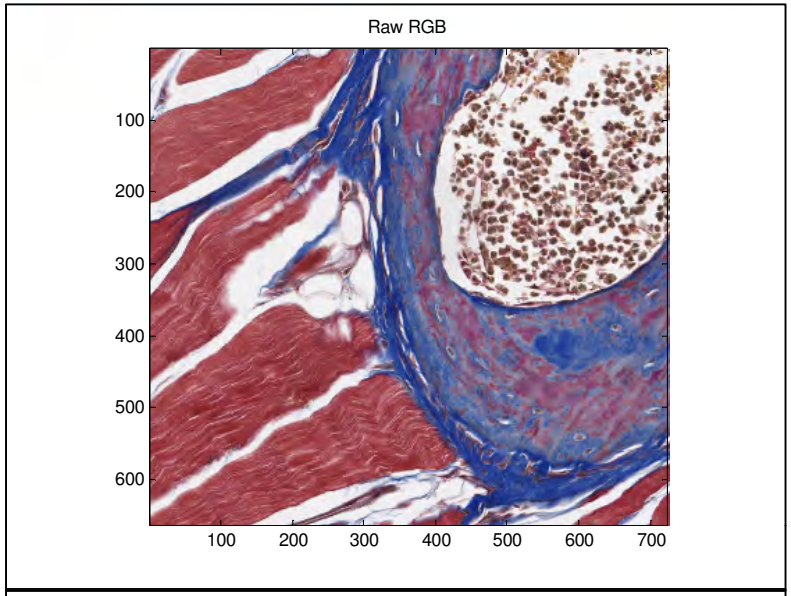


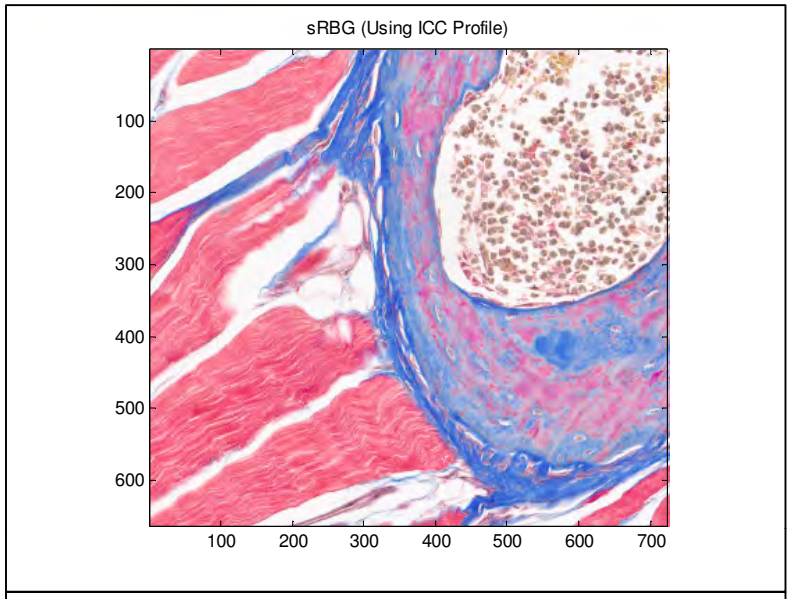


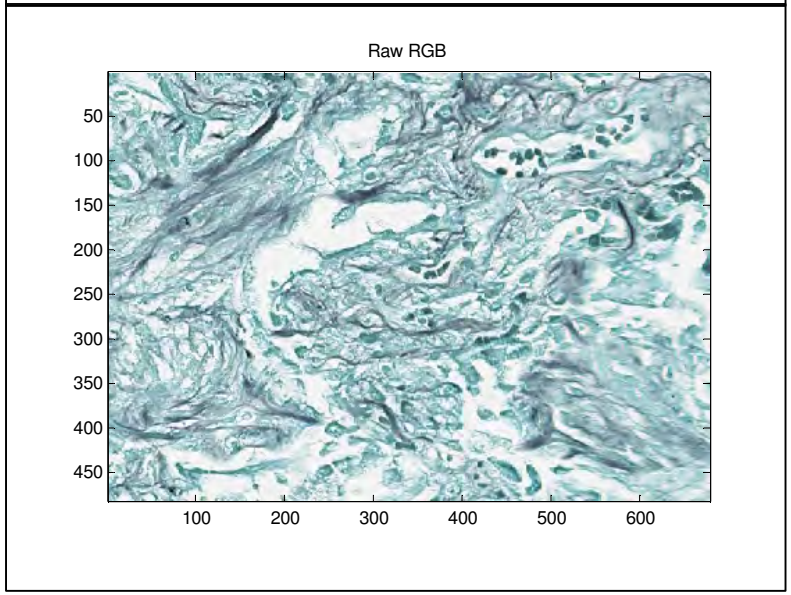


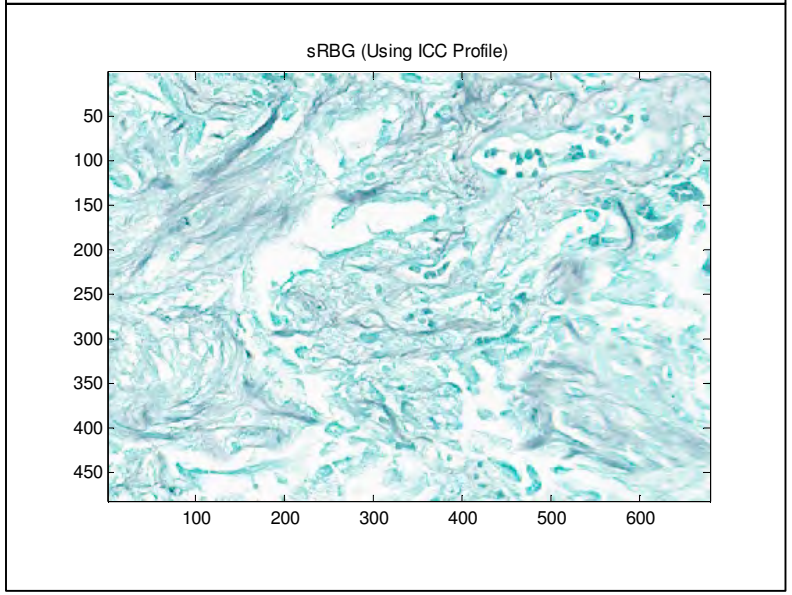


Viewing of Digital Slides

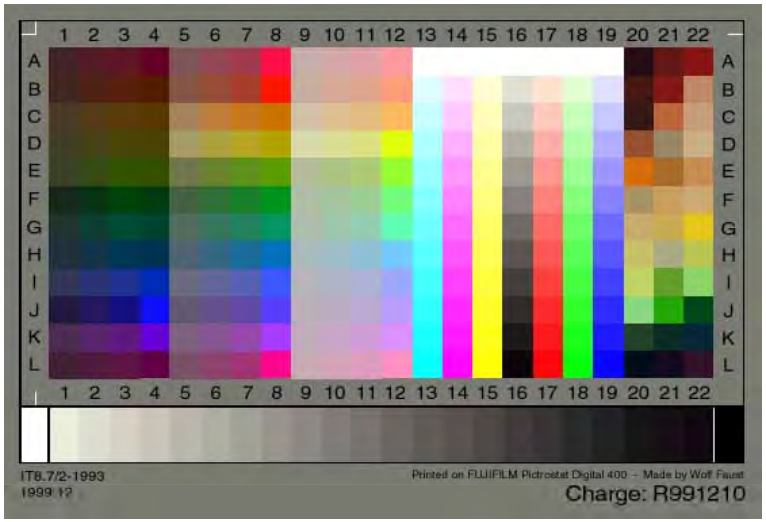








Validation of Spectral Models

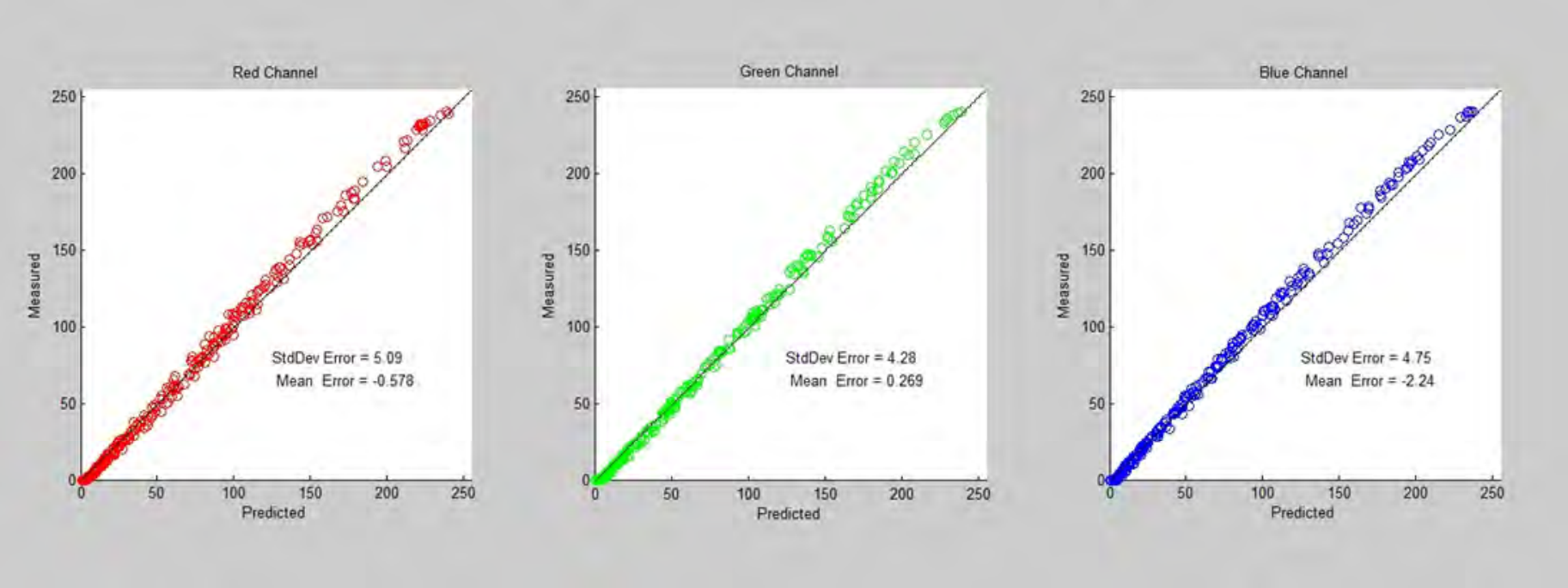


- IT8.7 Ektachrome Film Target
  (Wolf Faust)

- Calibration File
  XYZ (D50)
  Spectral Transmittance
  380-780nm (10nm)

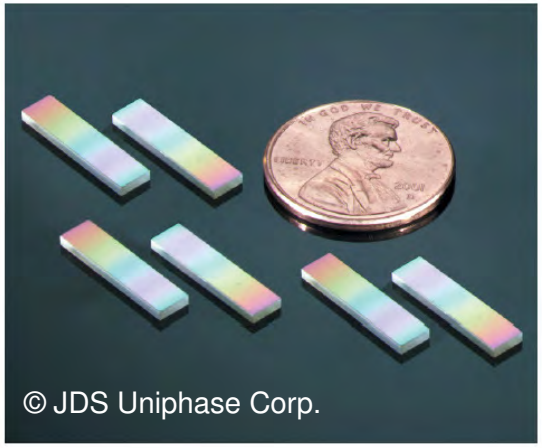
- Scanner Model Validation
  - Scan/Measure Target RGB values
  - Calculate Model-Predicted RGB values
  - Compare Measured vs Predicted values
- Microscope Model Validation
  - Change Lamp to D50 (no filter)
  - Calculate Model XYZ values
  - Compare with calibration XYZ values

Validation of Spectral Models

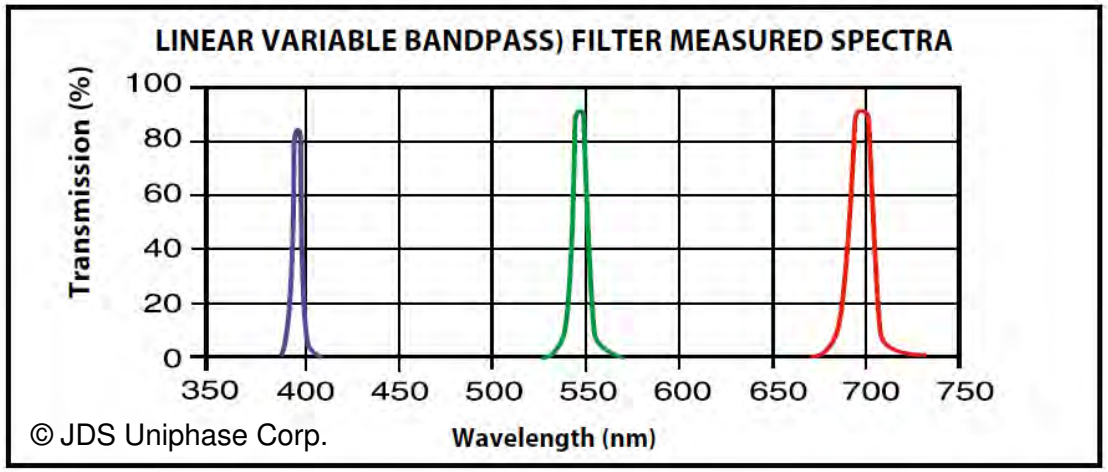


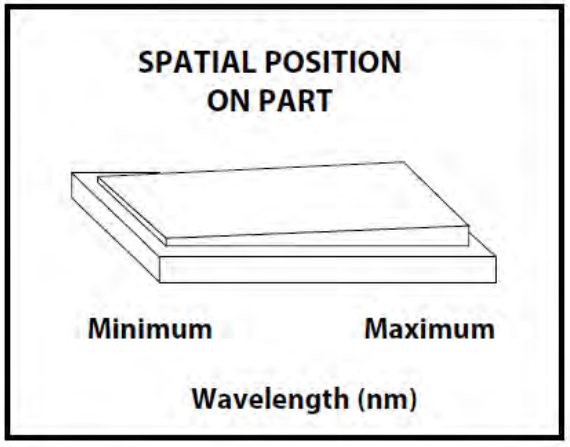
- Scanner Model
  - Standard Error 4-5 counts (shown above)
  - All Model data based upon manufacturer data sheets
- Microscope Model
  - D50 values agree to 10^{-4} (precision of spectral data)
  - Obviously manufacturer calculated these too

Measuring Scanner Spectral Response



Linear Variable Filter

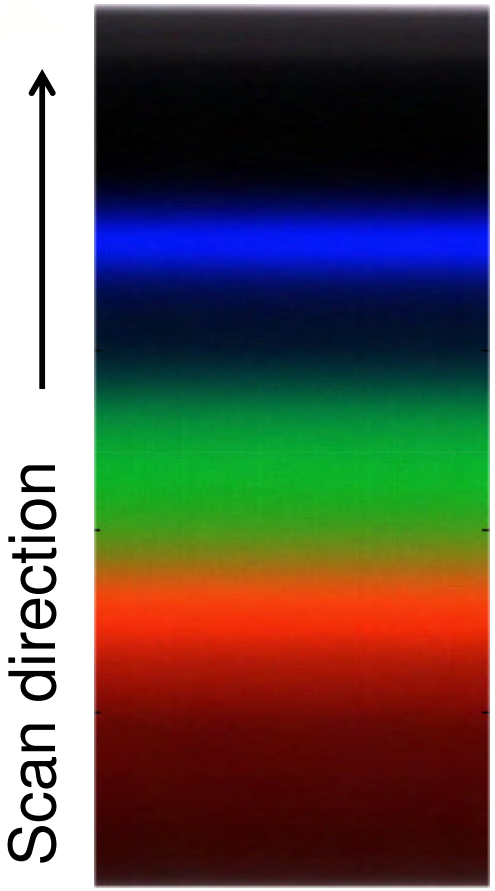


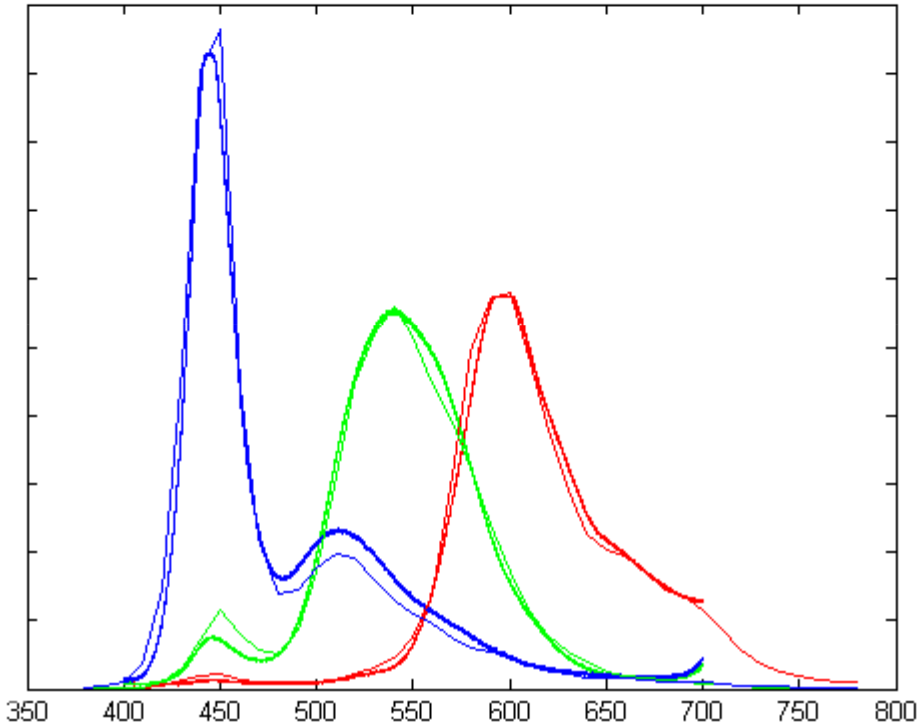


© JDS Uniphase Corp.

1. Scan along length of filter
2. Spectral response $R(f)$, $G(f)$, $B(f)$
3. Compare to model camera/light response

Measuring Scanner Spectral Response

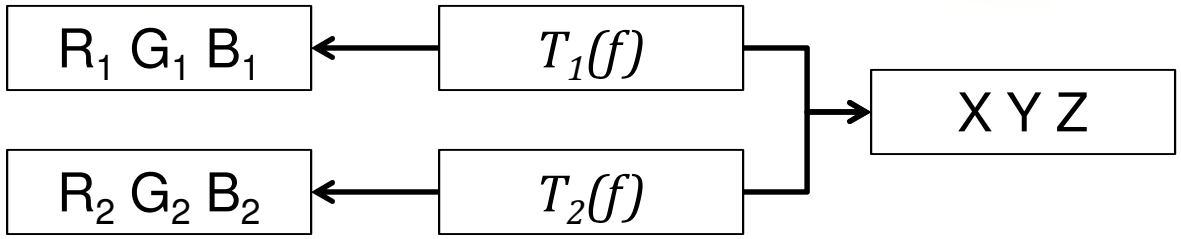




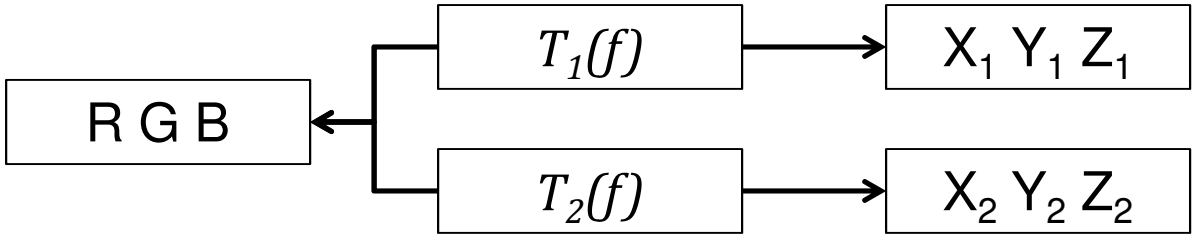
❖ Semrock Quad Band Filter: FF01-440/521/607/700 used for referencing the scan axis to nm.

Slide-Specific Color Profiling

Observer Metamerism



Device Metamerism



- This problem can be avoided altogether for histology.
- Histology slides mostly have two or three stains, designed to not be observer metameric – likely not device metameric either.
- A color transform can be calculated for each slide, based upon the specific stains and their spectral properties.

Conclusions / Questions

- Spectral models for scanner and microscope were combined to generate a color transform based upon manufacturer data specs and stain transmittance spectra from published literature.
- Significantly, the color transform was calculated without actually scanning a target slide.
- The models were then validated using an IT8.7 film target, having known spectral transmittance.
- Calibration of the scanner's transfer function was also performed using a Linear Variable Filter (LVF) and compared favorably to the generic model.
- This approach suggests the possibility of generating slide-specific profiles for each digital slide, based upon pre-calibrated spectral properties of the actual stains.

3DHISTECH

Calibration based on IT8.7/1

Viktor Sebestyén Varga Ph.D.

November 18 2013, Vancouver

Current position of whole slide imaging in pathology

- Many studies show that digital pathology is useful for making diagnosis.

- Technology is ready. There are several vendors making scanners with sufficient quality, speed etc.

3DHISTECH

Current position of whole slide imaging in pathology

- The pathology community would like to use whole slide imaging, but they are uncomfortable without FDA approval.

- FDA understandably requires standardization for the systems.

3DHISTECH

Current position of whole slide imaging in pathology

- Current monitor and camera technology can produce satisfactory results.

- That’s why we have those successful studies and pathologist waiting to use the systems routinely.

Current position of whole slide imaging in pathology

- By any delay we are holding back the availability of the technology to patients!

- The development of the industry has slowed down!

3DHISTECH

What to do?

- As the currently available technologies showed sufficient results we should use them in the first place.

- Later we can develop a 2nd generation standard if it becomes necessary.

Monitors

- We recommend to use the sRGB color space as this is the most widespread color standard for monitors.

- If we would create a special color space which is larger than sRGB then we radiacally limit the number of available display devices.

Monitors

- If we would create a special color space when and for what price would be monitors available?

- Many institutions can’t afford 10K+ USD display devices in quantities.

Monitors

3DHISTECH

- **Some mobile devices and applications are already FDA approved**

FDA NEWS RELEASE

For Immediate Release: Feb. 4, 2011
Media Inquiries: Erica Jefferson, 301-796-4988, erica.jefferson@fda.hhs.gov
Consumer Inquiries: 888-INFO-FDA

FDA clears first diagnostic radiology application for mobile devices
Provides wireless access to medical images for iPhone, iPad users

- **http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm242295.htm**

Monitors

- We should not limit the possibility of remote diagnosis on mobile devices due to a requirement on a special color space.

Available calibration targets

- We bought from Charité in Berlin, Germany a calibrated microscope glass slide.

- This type of slide was used on the 2nd International Scanner Contest to assess scanner color quality.

- The slide is openly available to anybody for a reasonable price.

Available calibration targets

- The slide has a photographic film on it and it is calibrated to the IT8.7/1 standard.

- IT8.7/1 - 1993 (R2003) - Graphic technology - Color transmission target for input scanner calibration

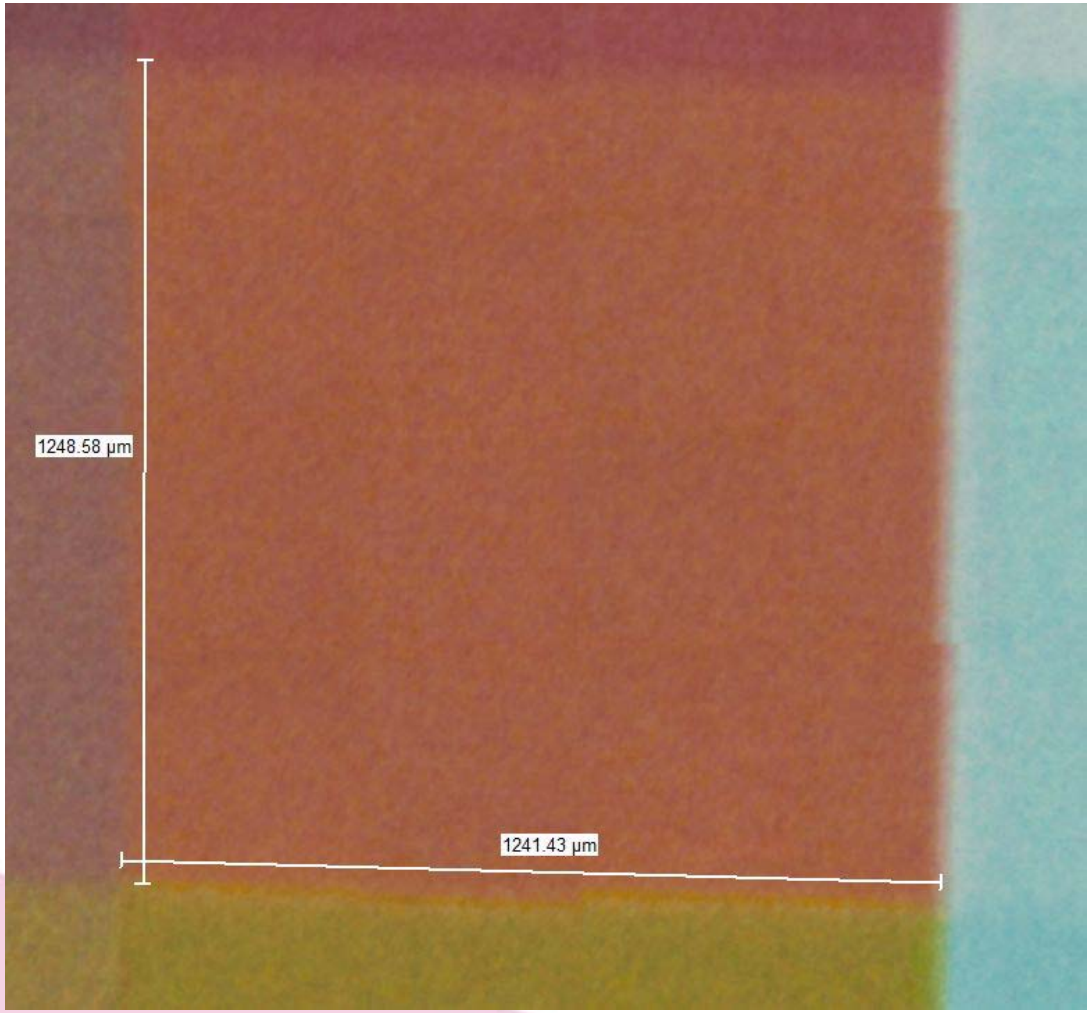
Available calibration targets

3DHISTECH

- One color patch is 1.2 x 1.2 mm
- With a typical 0.25 um / pixel scanner resolution 1 path is 4800 x 4800 pixels
- 23 megapixel, this is more than enough to average out any errors.

Available calibration targets

- **One color patch**



3DHISTECH

Available calibration targets

- **The slide came with detailed individual measurment data**
- **Spotes are measured in standard color spaces**

```
IT8.7/1
DESCRIPTOR "Velvia 100, 100F, Astia 100F, Provia 400X and Sensia 100 (Emul. 687 or
higher), Type 3, L* a* b* (light D50, viewing angle 2)"
CREATED "December 07, 2011"
PROD_DATE "2011:12"
SERIAL "N111203 Batch Average Data"
MATERIAL "Fujichrome Velvia 100 (RVP 100)"
NUMBER_OF_FIELDS 9
BEGIN_DATA_FORMAT
SAMPLE_ID  XYZ_X   XYZ_Y   XYZ_Z          LAB_L   LAB_A   LAB_B          LAB_C   LAB_H
END_DATA_FORMAT
NUMBER_OF_SETS 288
BEGIN_DATA
A1          1.69    1.48    1.08          12.50    6.98    2.00           7.26   15.97
A2          2.06    1.39    0.86          11.92   18.44    4.45          18.97   13.55
A3          2.62    1.46    0.71          12.34   28.15    7.97          29.26   15.79
A4          3.51    1.59    0.58          13.14   40.08   11.70          41.75   16.27
A5          8.22    7.20    5.32          32.26   11.99    2.99          12.36   14.03
```

Available calibration targets

- **Spectroscopic data for each spot with 10 nm precision is also included**

380nm	390nm	400nm	410nm	420nm	430nm	440nm
0.00091824	0.00176521	0.00949385	0.01578880	0.01268378	0.00882265	0.00700251
0.00078407	0.00165351	0.00892271	0.01453170	0.01139506	0.00773698	0.00596058
0.00058924	0.00129804	0.00852275	0.01381671	0.01065996	0.00709638	0.00535962
0.00037871	0.00131613	0.00925115	0.01550941	0.01233086	0.00824112	0.00605750
0.00203092	0.00537091	0.03245061	0.06256583	0.06103052	0.05091783	0.04485548
0.00156014	0.00483033	0.02956906	0.05602203	0.05310111	0.04299920	0.03705385
0.00100718	0.00427990	0.02818066	0.05292655	0.04943358	0.03933310	0.03330519
0.00044349	0.00370273	0.02734909	0.05173849	0.04812323	0.03772201	0.03121903
0.00729106	0.01429436	0.08350096	0.18283713	0.21157364	0.20706955	0.20119433
0.00638787	0.01377743	0.08166103	0.17770098	0.20339274	0.19694950	0.18993581

Available calibration targets

- The IT 8.7/1 standard is based on 5000k or D50 white point.
- We shifted this to 6500K / D65 to provide a white background on the sRGB monitor.

Calibration process

- For an initial standard we would recommend that color fidelity of the scanner should be checked by the pixel values in a scanned digital slide of a calibration target.

- The monitors should be calibrated with off the shelf monitor calibration products.

Calibration process

- The IT 8.7/1 standard has no particular advantage over other standards.

- If there are other available standardized and calibrated slides those could be used as well.

3DHISTECH

Thank you for your attention!

PHILIPS

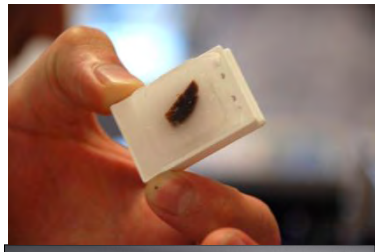
sense and simplicity

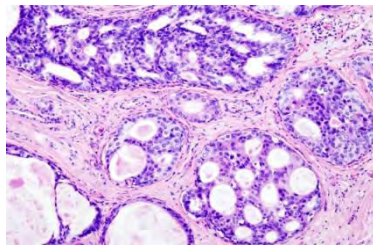
Calibrating the Philips Slide Scanner

Bas Hulsken, PhD
Philips Digital Pathology
November 12, 2013

Contents

- Calibrating a Slide Scanner:
  - Scanner description: sources of variation
  - Color calibration method
  - How to make a color calibration slide
  - What affects color reproduction
  - Other calibrations: Resolution
- Lessons Learned



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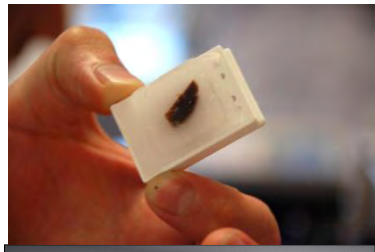
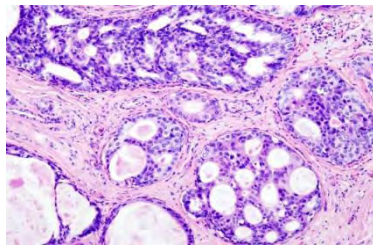
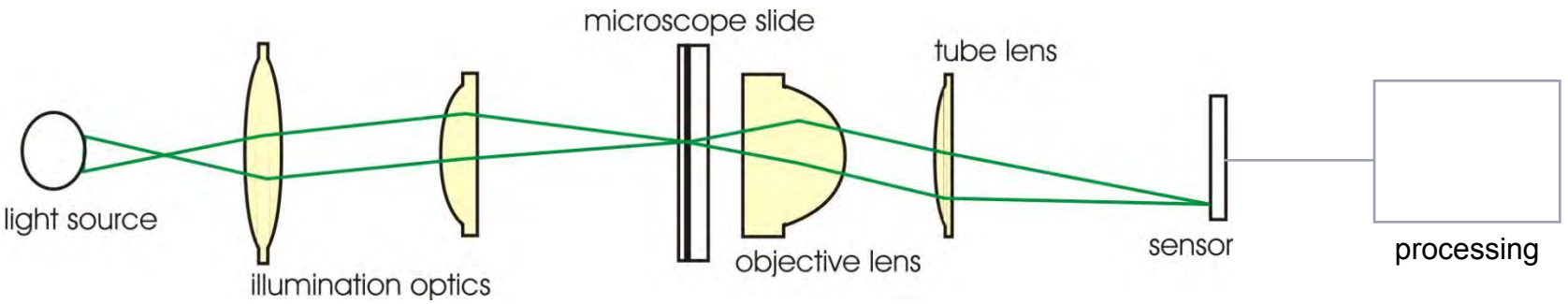


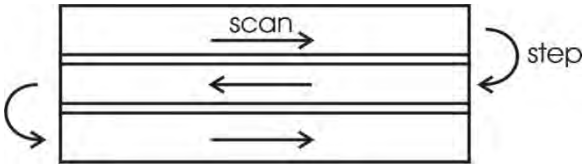


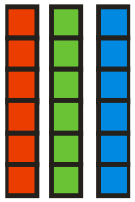
Our Product: The Philips Ultra Fast Scanner

- 30 sec scan time
- 50 sec total time
- 300 slide loader
- Random access
- 40x magnification
- Continuous autofocus
- Philips PACS compatible
- >400MB per second data transfer

How to build a slide scanner







Illumination:
- White LED

Scanner:
- Constant velocity translation

Sensor:
- 3 separate TDI linescan camera's for R,G and B

Processing:
- compression
- storage

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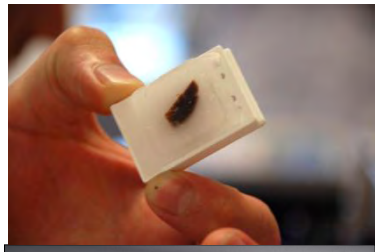

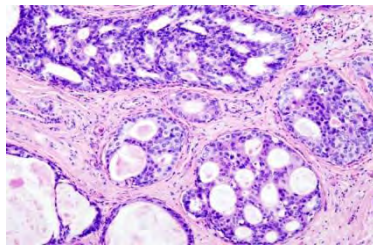

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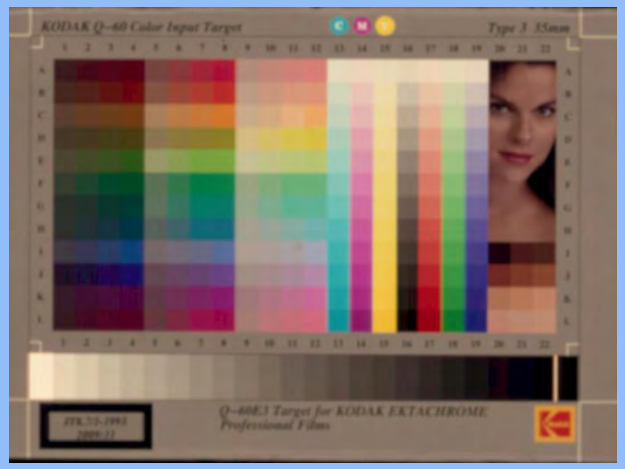
Color Calibration



Standarized Color Target

Scanner

Color Profiler

Residual Error (ΔE)

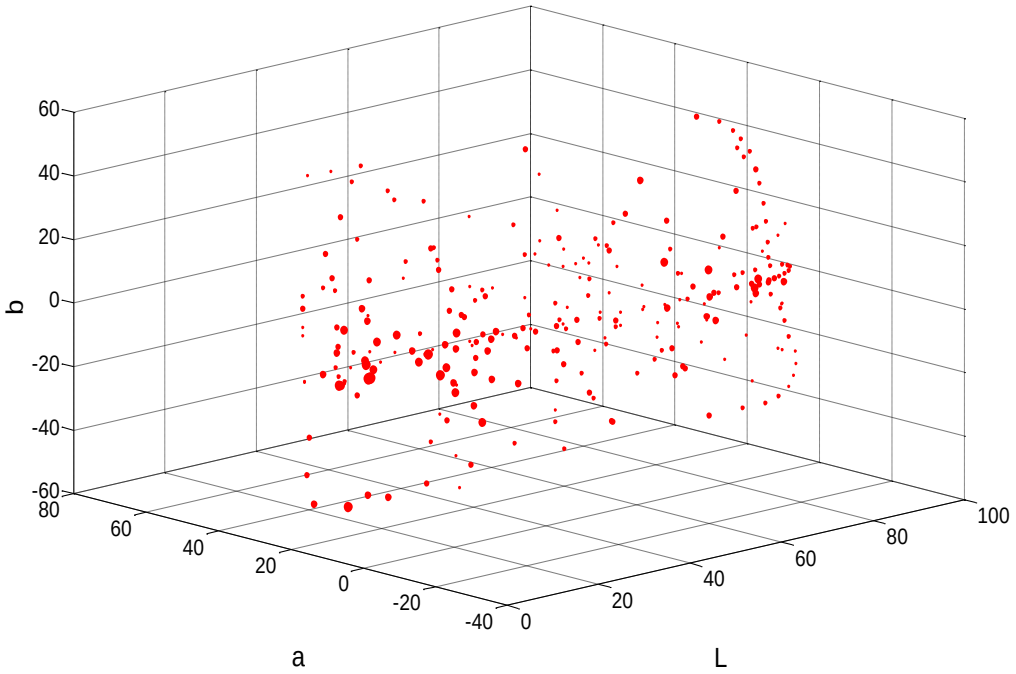
Correction Matrix

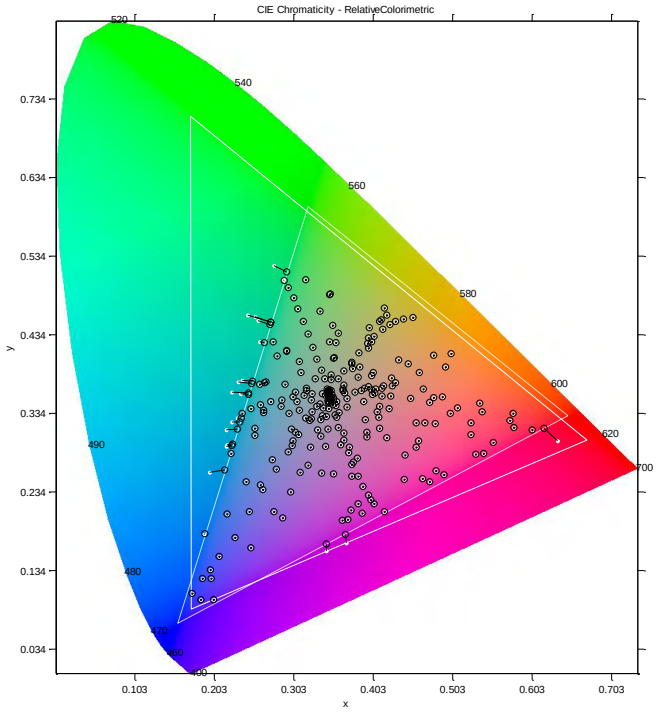
Reference

Color difference: ΔE CIE2000

$$\Delta E_{00}^{12} = \Delta E_{00}(L_1^*, a_1^*, b_1^*; L_2^*, a_2^*, b_2^*)$$

$$= \sqrt{\left(\frac{\Delta L'}{k_L S_L}\right)^2 + \left(\frac{\Delta C'}{k_C S_C}\right)^2 + \left(\frac{\Delta H'}{k_H S_H}\right)^2 + R_T \left(\frac{\Delta C'}{k_C S_C}\right)\left(\frac{\Delta H'}{k_H S_H}\right)}$$





ΔE between a scanner colors and a reference colors represented by the size of a circle

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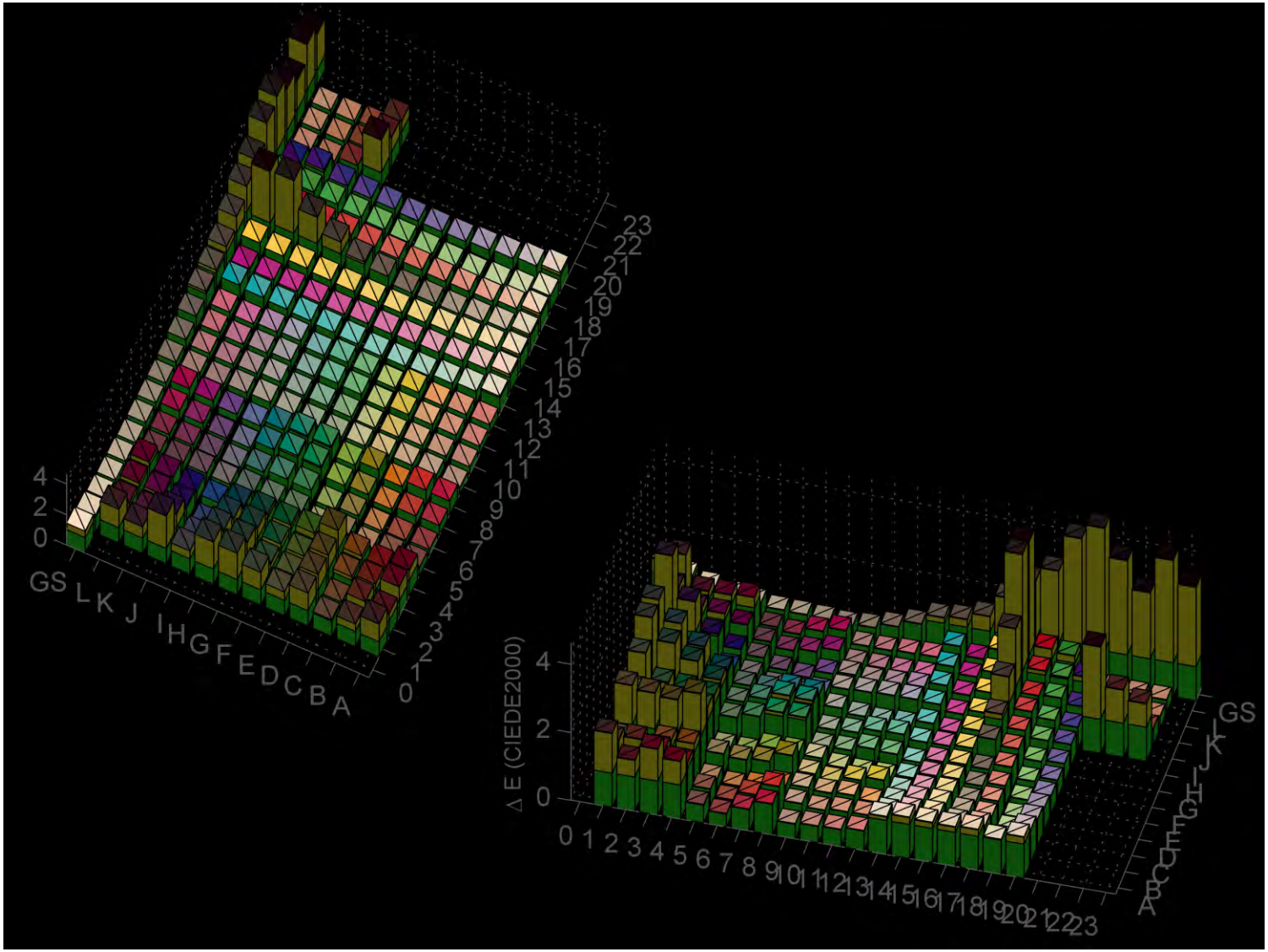
Color Calibration, same colors on all scanners



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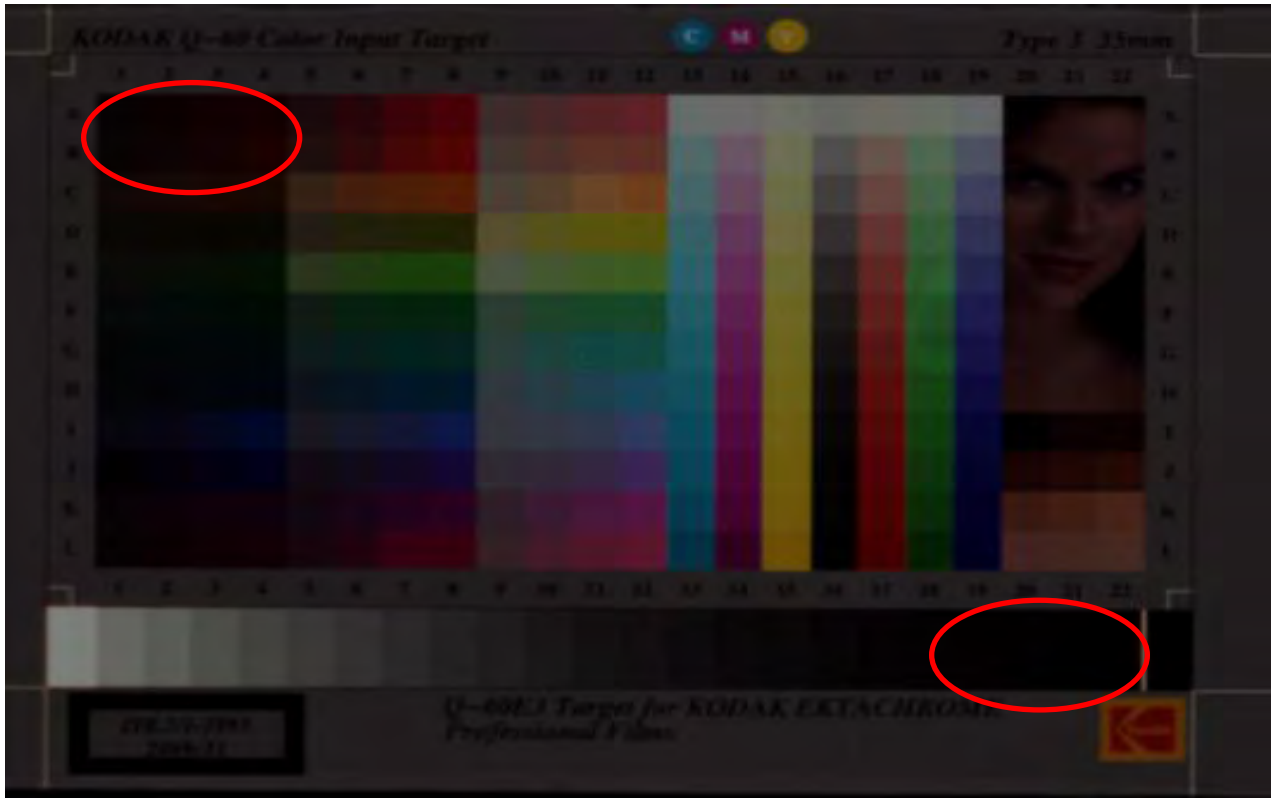
First problem, dark patches

ΔEs are consistently high in the darker color regions.



Film based targets are darker than tissue slides!

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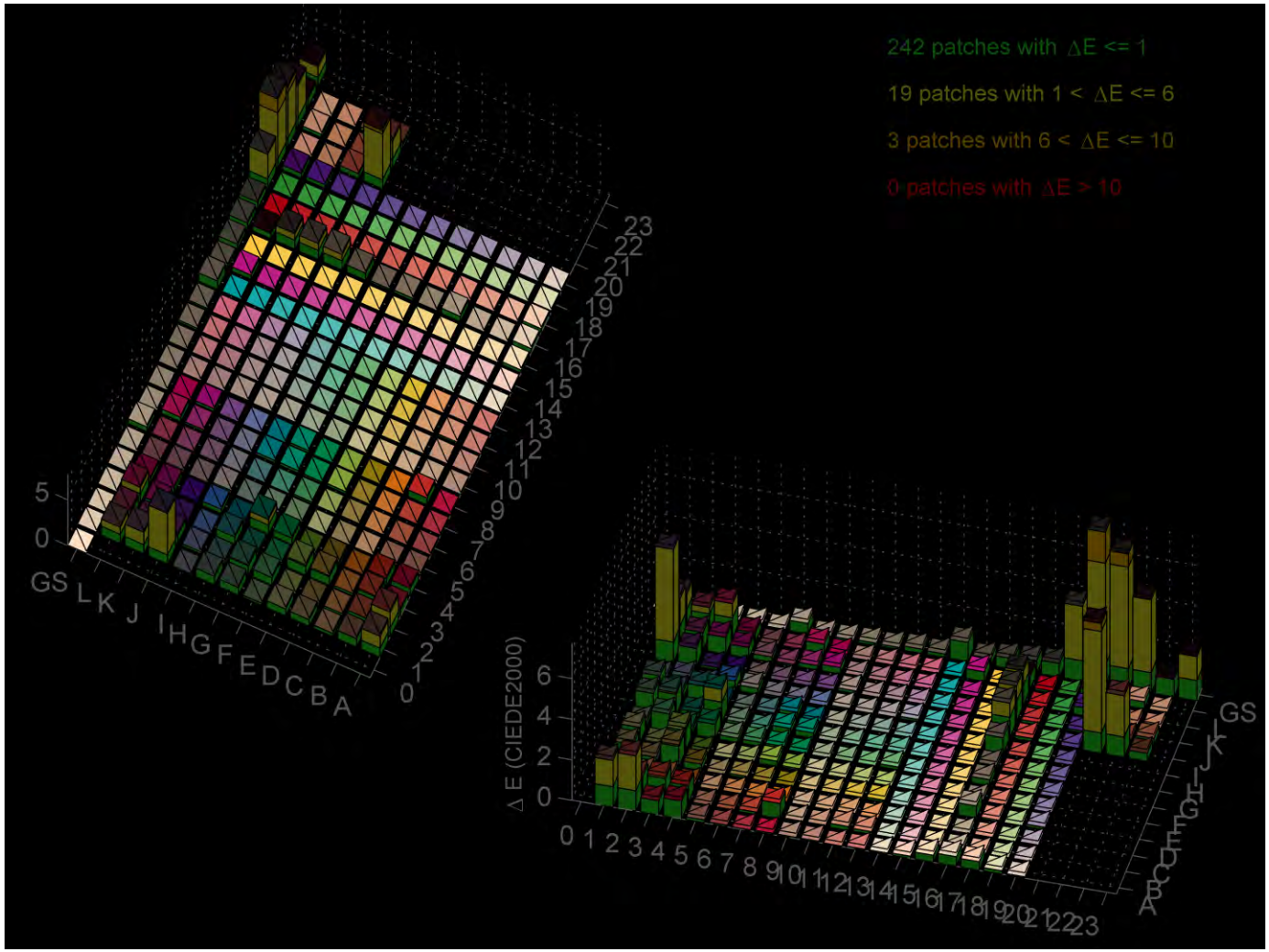
Correction Method



3x3 Matrix

3D LUT

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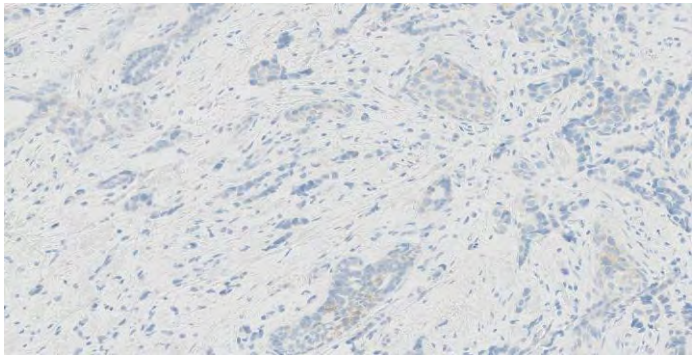
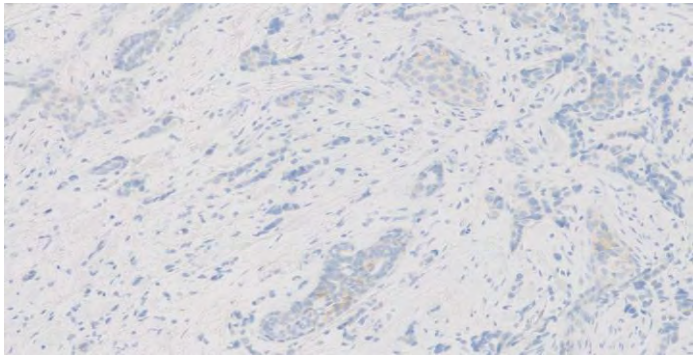
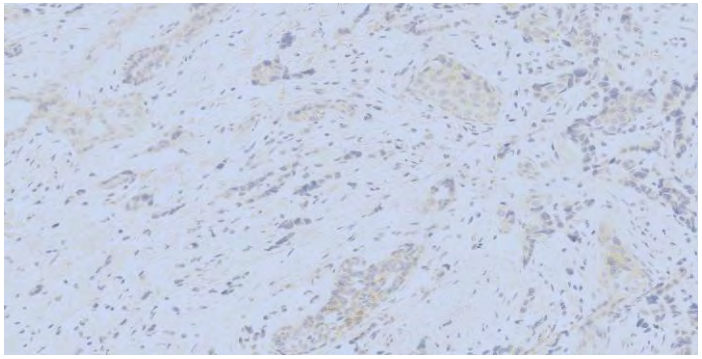
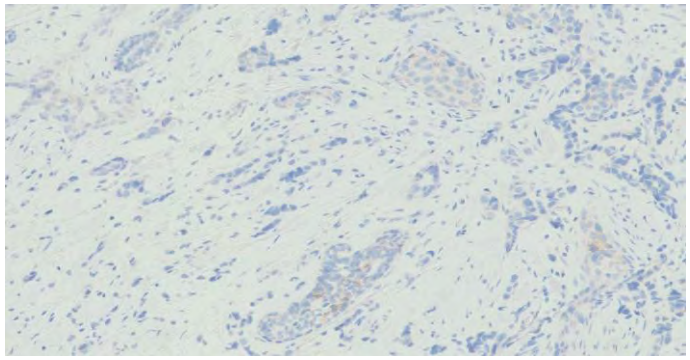
Results on Tissue



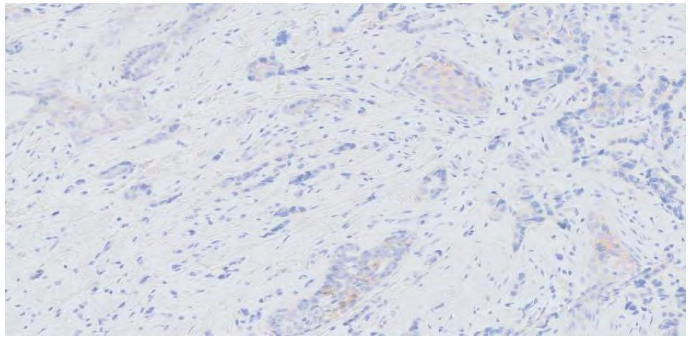


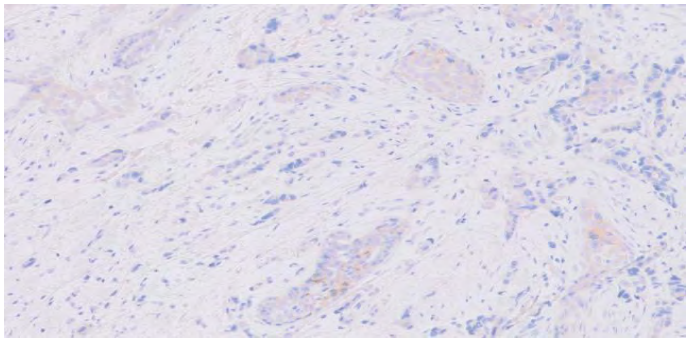
3x3 Matrix





Shaper+ Matrix





3D LUT

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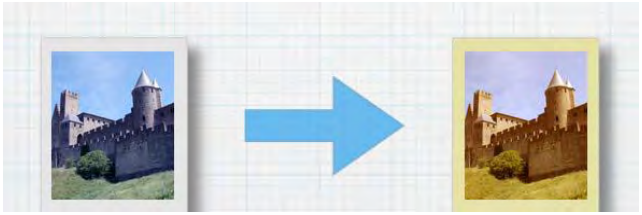
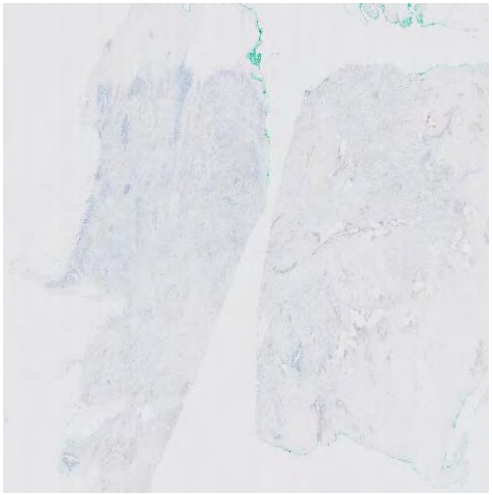
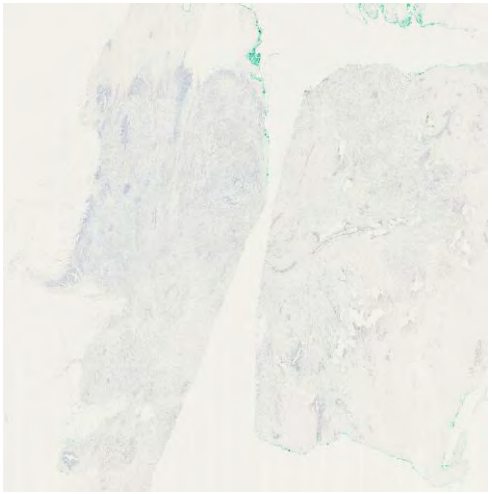
Absolute versus Relative Rendering Intent



relative



absolute



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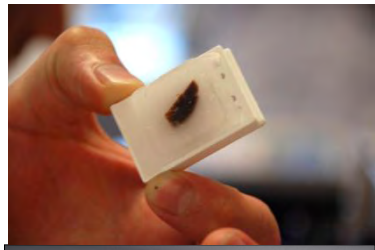

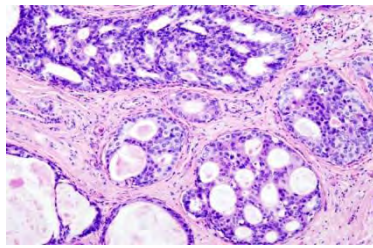

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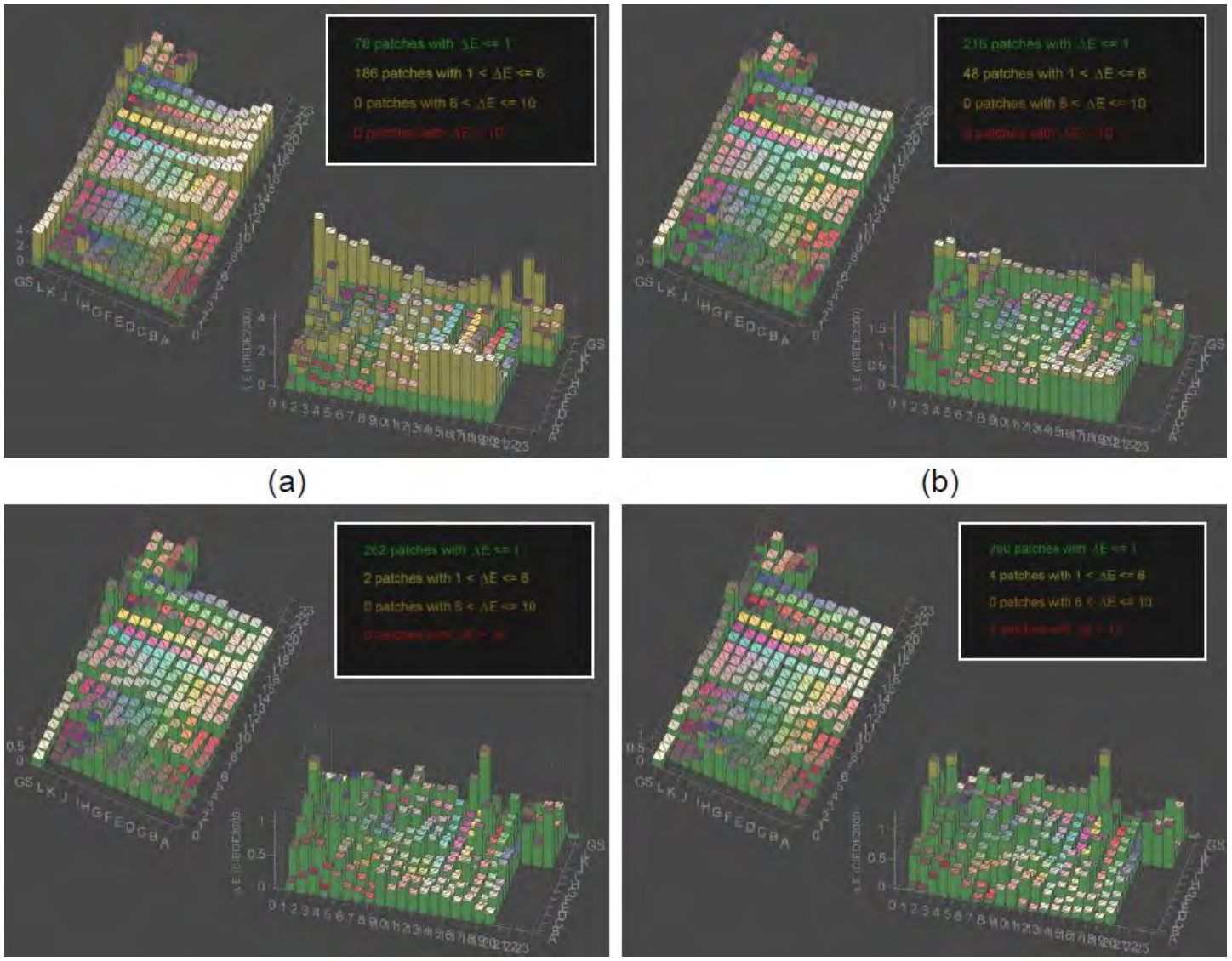
How similar are calibration targets?



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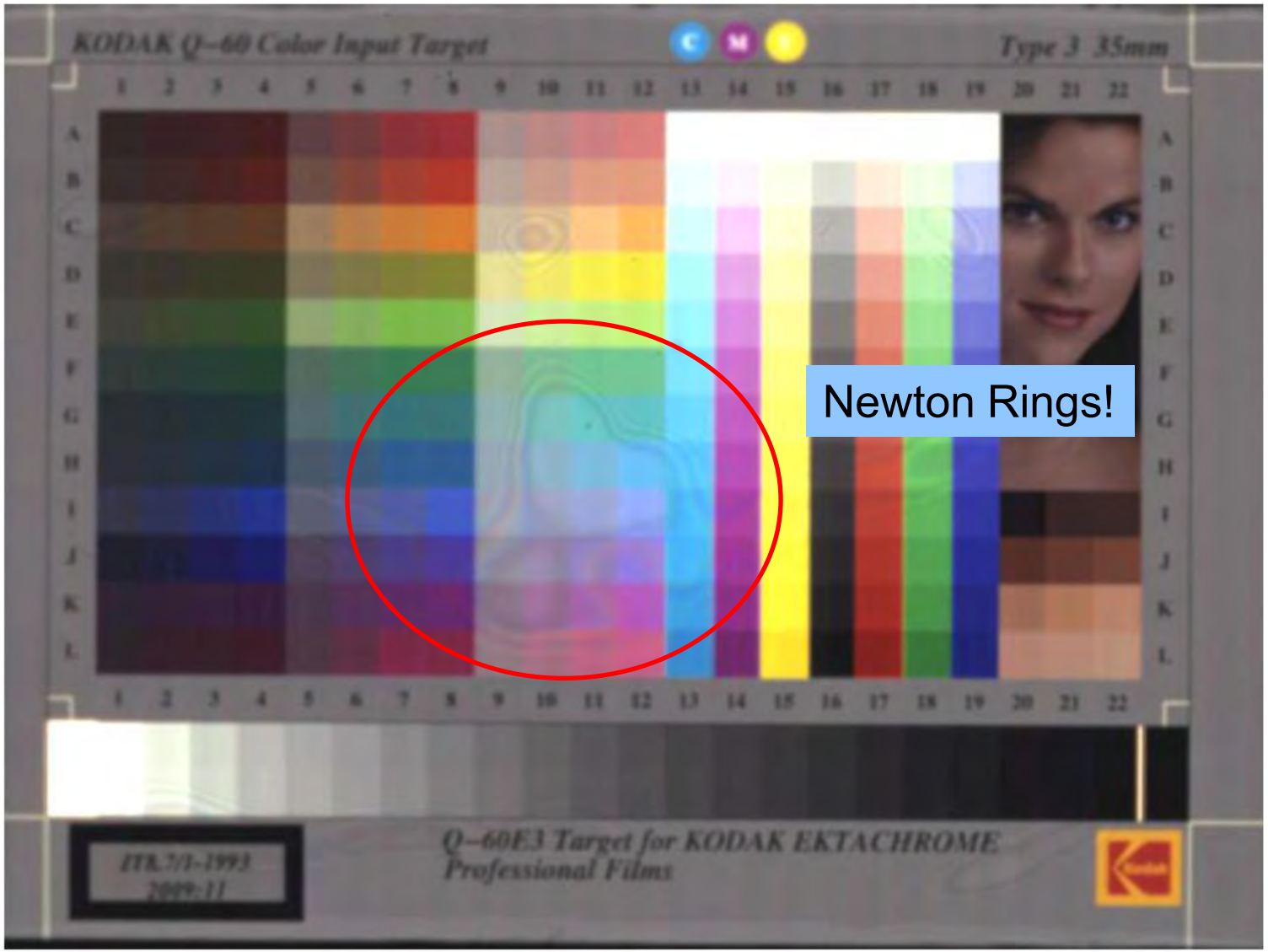
How similar are calibration targets?

Table 7 Number of patches with E > 1 for several calibration targets, with ΔE relative to all other targets.

		Calibration target				
		Orig.	13	16	17	19
Calibration target	Orig.	0	161	171	167	186
	13	161	0	58	44	48
	16	170	56	0	0	2
	17	165	44	0	0	4
	19	182	46	2	4	0

Good targets!

How to manufacture a color target



Color target with index matching fluid

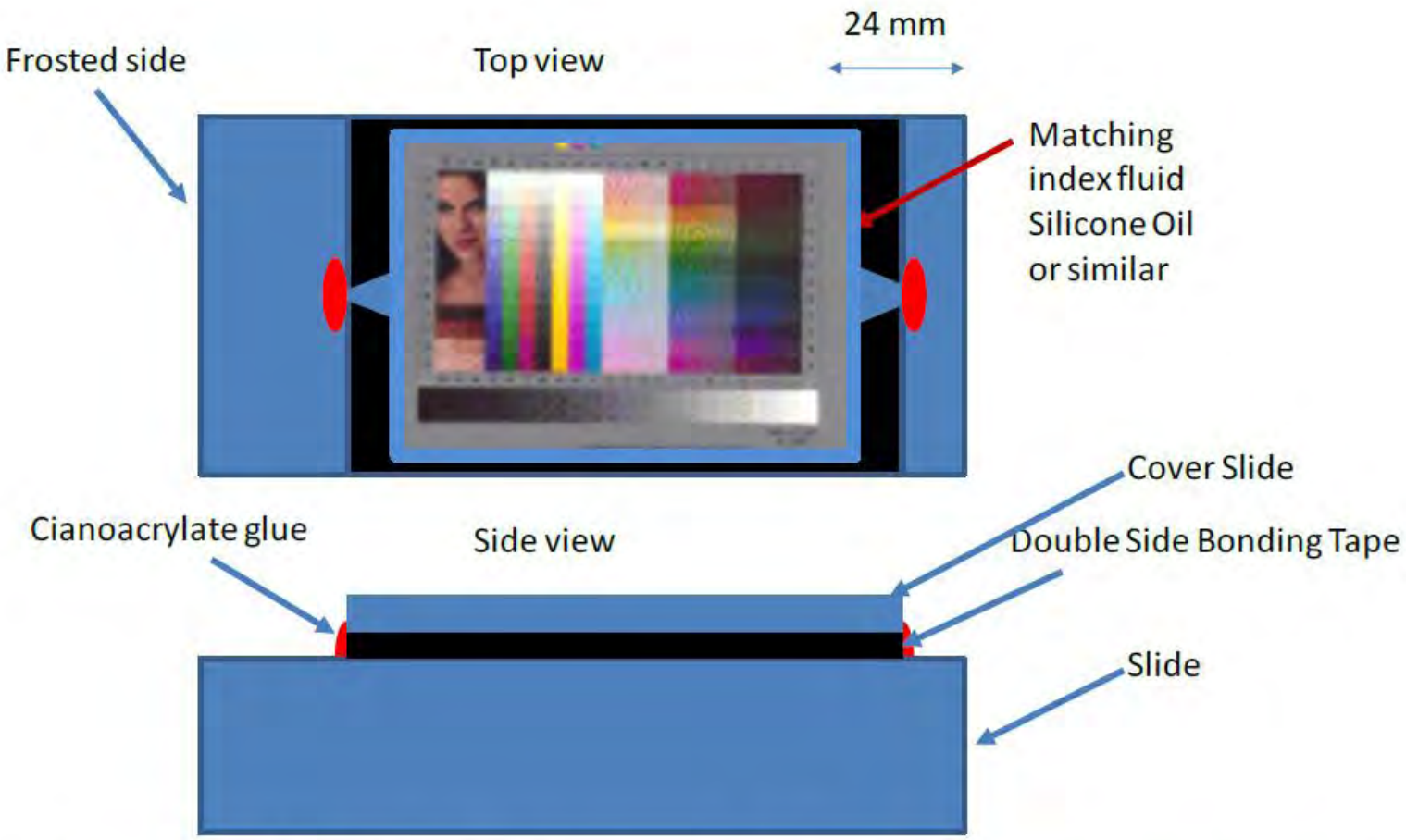


Figure 46 Color Calibration Target manufacturing with double side tape and index matching fluid.

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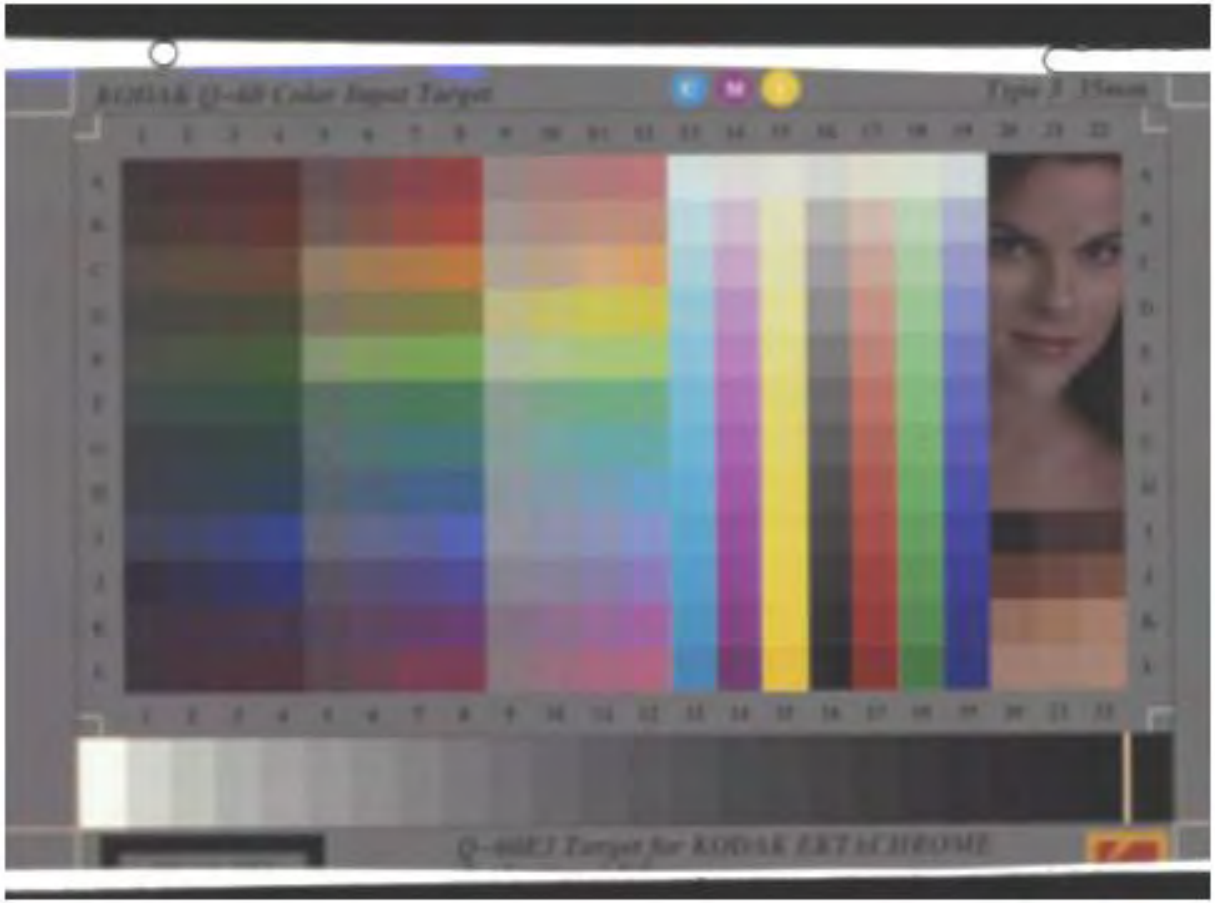
Color target with index matching fluid



- Better transmission
- No Newton Rings
- Scratches less visible

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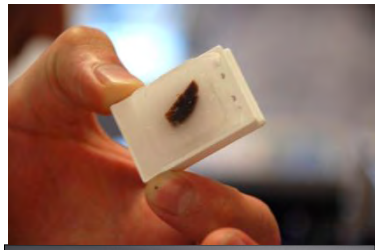


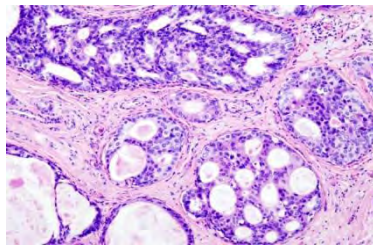

Effect of temperature on colors

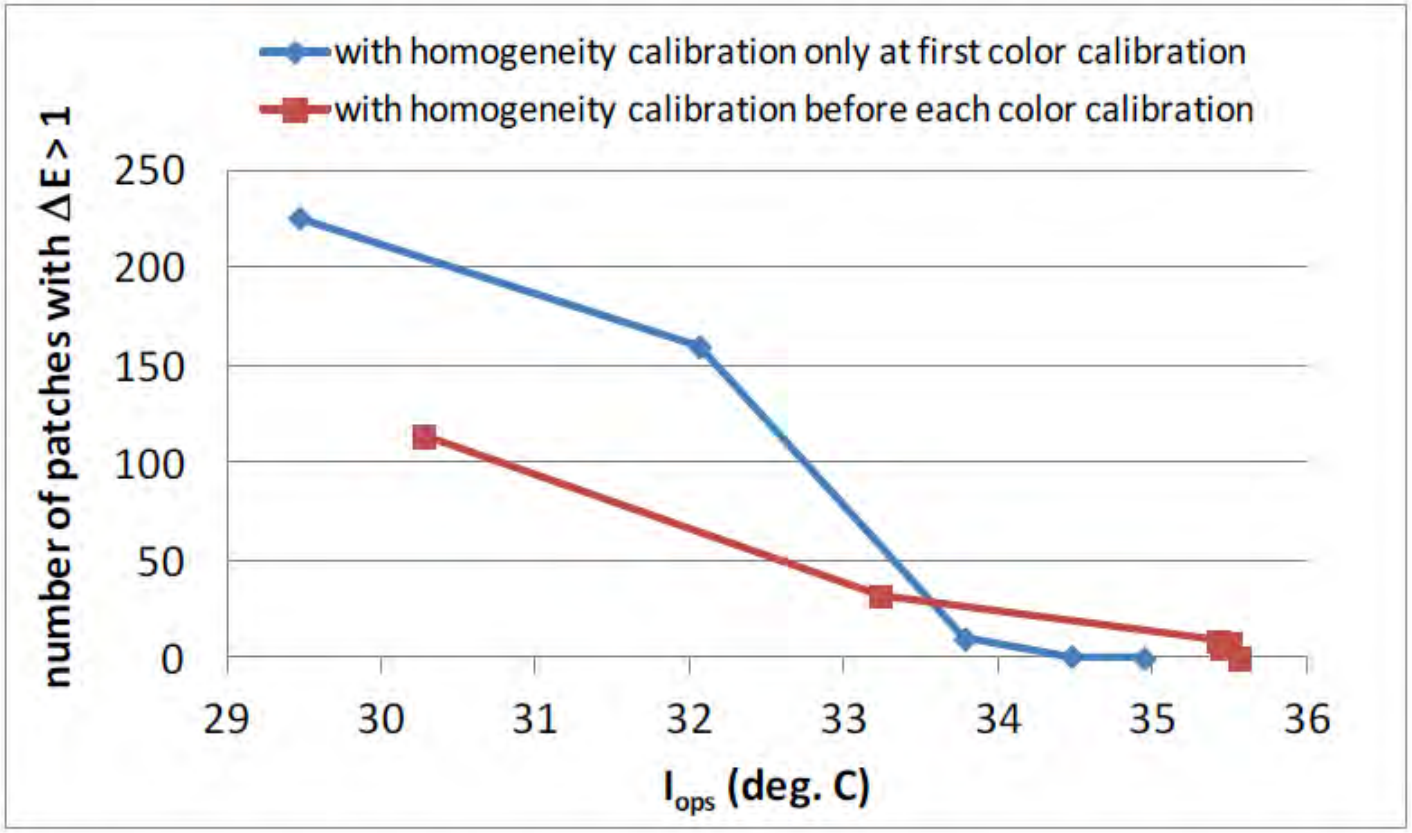

Figure 30 Number of patches with $\Delta E > 1$ when comparing with the stabilized end situation, as function of the temperature I_{ops}, for the cases of homogeneity calibration only before the first color calibration and homogeneity calibration before each color calibration.

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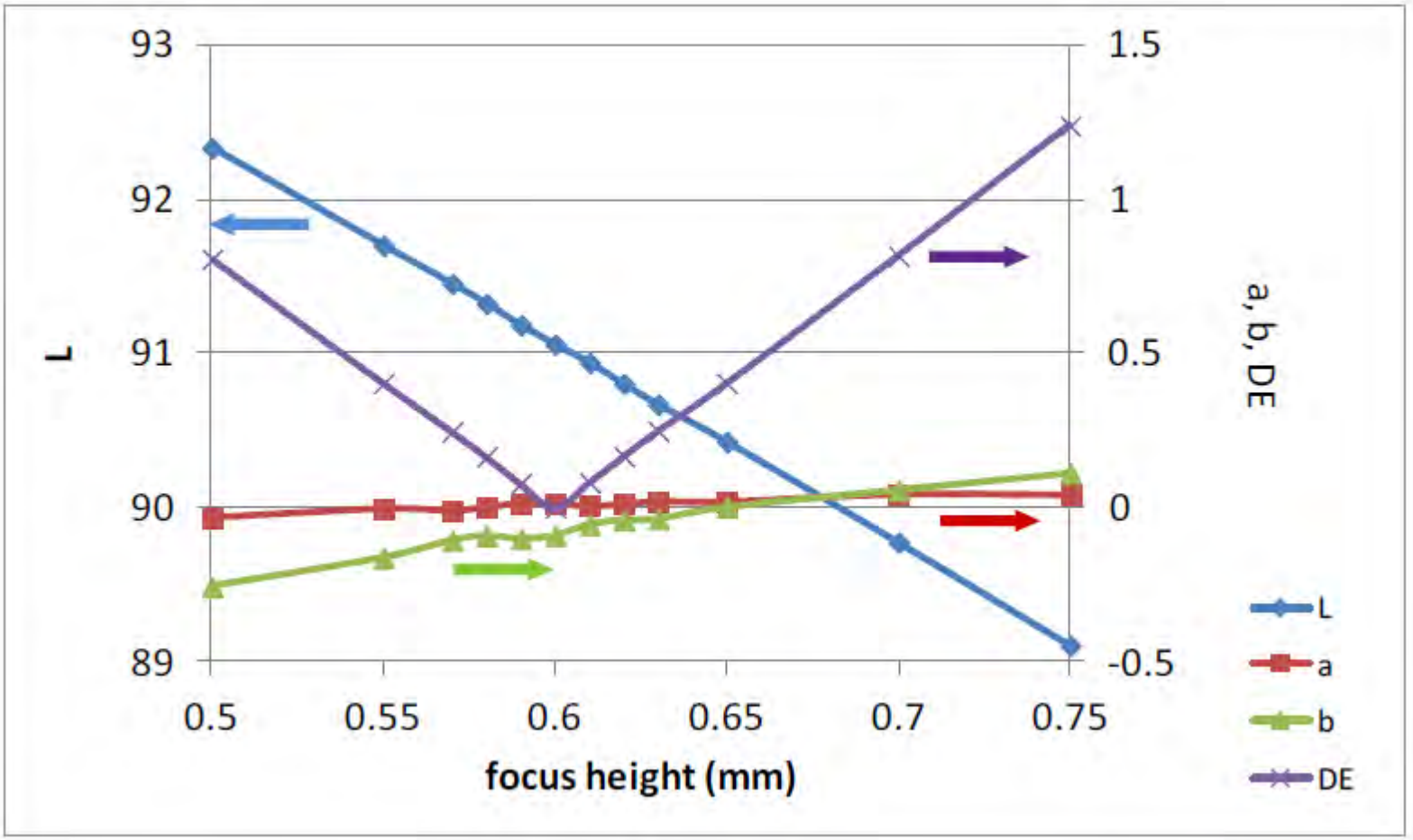
Effect of focus position on color



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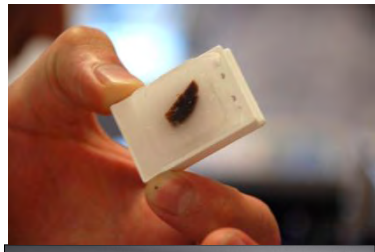


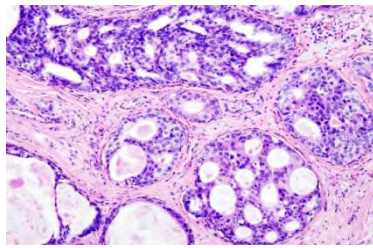

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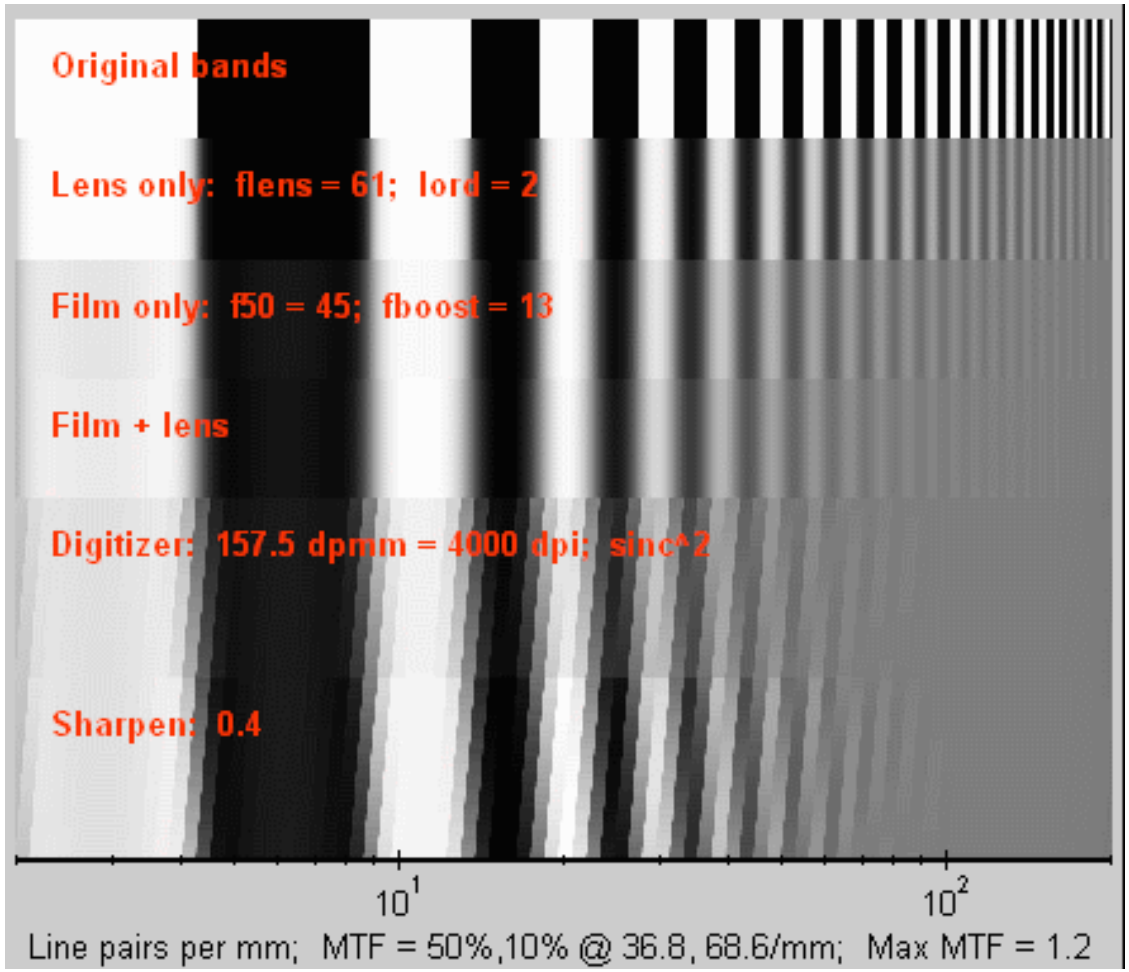
Resolution = Modulation Transfer Function (MTF)



source: www.normankoren.com

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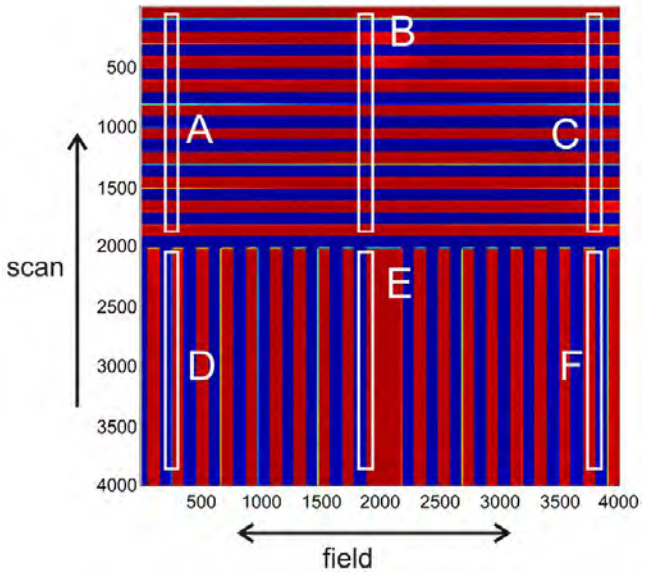
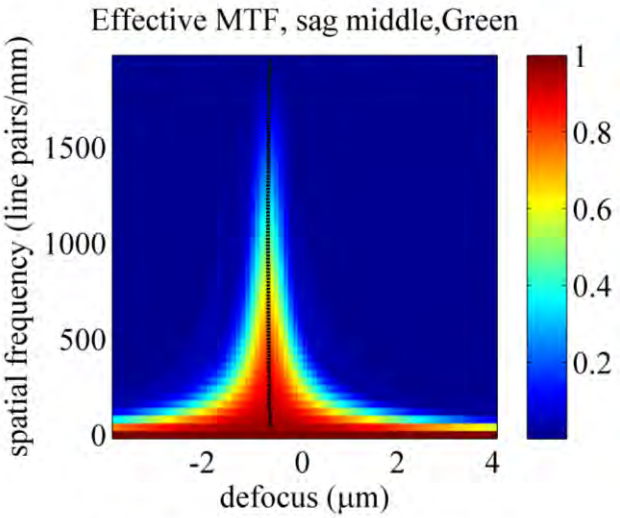
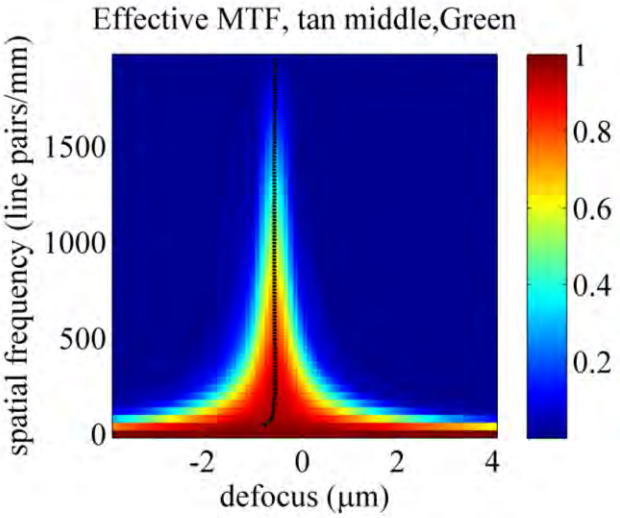
Measuring scanner resolution







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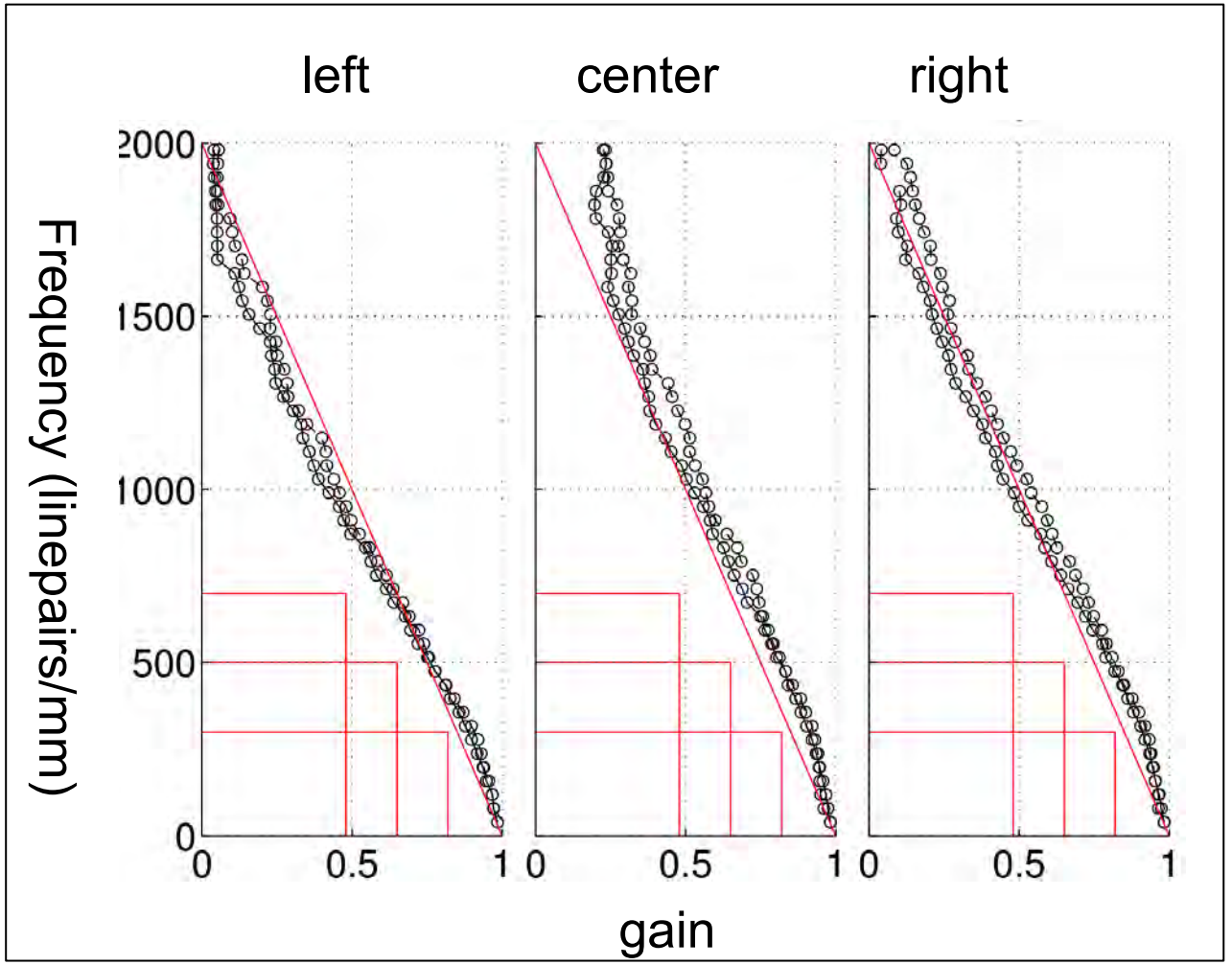
Monitoring Resolution, MTF target in Scanner



Lessons Learned

- Existing color targets are Film
  - You need to make a microscope slide from it
    - Substrate, Cover Slip, Index matching mounting medium
  - Film is less transparent than a tissue slide
  - Trying too hard to make Film targets look similar over your devices might make tissue slides look less similar
  - Film dyes are not the same (spectrally) as histopathology dyes
- Reproducibility
  - Film based targets reproduce well, but you need a test in your quality system to validate manufactures calibration slides.
  - May aspects in a scanner system influence color reproduction, you need continuous monitoring and calibration in your scanner
- Non color aspects that do influence color perception
  - Resolution and contrast and noise influence color perception (and overall image quality perception) even if they don't quantitatively influence color.

2013 ICC Meeting
Medical Imaging Working Group
Nov 18, 2013

mRGB

AAPM TG196 Progress

Michael Flynn
Radiology Research
Henry Ford Health System
Detroit, MI

sRGB: IEC 61966-2-1

- sRGB is a standard RGB color space created cooperatively by HP and Microsoft in 1996 for use on monitors, printers and the Internet.
- the sRGB gamma cannot be expressed as a single numerical value. The overall gamma is approximately 2.2, consisting of a linear (gamma 1.0) section near black, and a non-linear section elsewhere
- IEC 61966-2-1:1999 is the official specification of sRGB. It provides viewing environment, encoding, and colorimetric details.

IEC 61966-2-1
Colour Measurement and Management
in Multimedia Systems and Equipment
Part 2-1: Default RGB Colour Space – sRGB

http://en.wikipedia.org/wiki/SRGB

aRGB: Adobe RGB (1998)

- The Adobe RGB color space is an RGB color space developed by Adobe Systems in 1998.
- It was designed to encompass most of the colors achievable on CMYK color printers, but by using RGB primary colors on a computer display.
- A gamma of 2.2 is assumed.
- The color space encompasses roughly 50% of the visible colors specified by the Lab color space, improving upon the gamut of the sRGB color space primarily in cyan-greens.

Adobe RGB (1998)

Color Image Encoding

Version 2005-05, May 2005

http://http://en.wikipedia.org/wiki/Adobe_RGB_color_space
http://www.adobe.com/digitalimag/pdfs/AdobeRGB1998.pdf

ACR-AAPM-SIIM standard

- The ACR-AAPM-SIIM technical guideline for electronic imaging was recently revised with participation by three professional Radiology organizations:
  - The American College of Radiology (ACR),
  - The American Association of Physicists in Medicine (AAPM),
  - The Society for Imaging Informatics in Medicine (SIIM).
- The recently published guidelines contain specific recommendations for viewing conditions and display characteristics.
  - DICOM Grayscale with defined L_{max} and L_{min} .
  - D65 white point.
  - Undefined color gamut.

ACR–AAPM–SIIM Technical Standard for Electronic Practice of Medical Imaging

JT Norweck, JA Seibert, KP Andriole,
DA Clunie, BH Curran, MJ Flynn,
E Krupinski, RP Lieto, DJ Peck, TAMian

…

Display

1. Workstation Characteristics
   - f. Ergonomic factors
     2. Viewing Conditions
2. Display characteristics
   - a. Luminance response
     1. Ambient Luminance, L_{amb}
     2. Minimum Luminance, L_{min}
     3. Maximum Luminance, L_{max}
     4. Luminance Ratio, LR
     5. L_{max} for Diagnostic & other
     6. Luminance vs Gray Level
     7. Calibration
     8. Quality Control
     9. White Point.
   - b. Pixel Pitch and Display Size

…

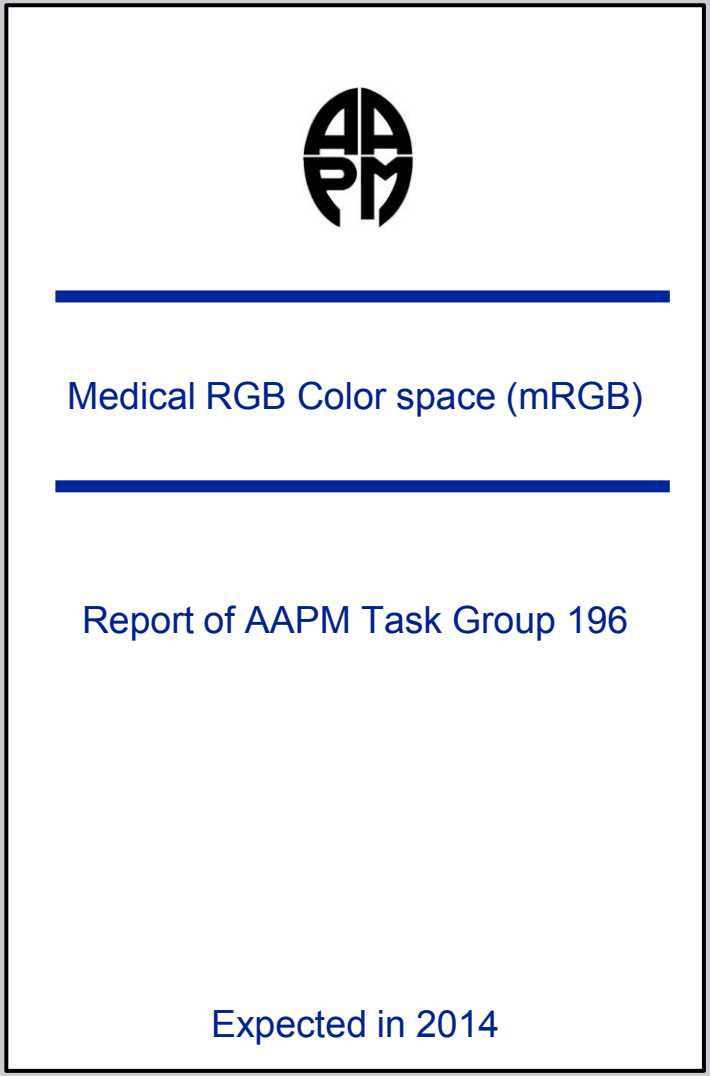
J Digit Imaging (2013) 26:38–52

http://link.springer.com/article/10.1007%2Fs10278-012-9522-2

AAPM TG196: mRGB

AAPM Task Group No. 196
Requirements and methods for color displays in medicine.

Aldo Badano, PhD
Paul Boynton
Wei-Chung Cheng
Danny Deroo
Michael Flynn
Patrick Le Callet
Takashi Matsui
John Penczek
Craig Revie
Hans Roehrig
Ehsan Samei
Peter Steven
Stan Swiderski
Gert Van Hoey
Masahiro Yamaguchi



http://www.aapm.org/pubs/reports/

http://www.aapm.org/org/structure/default.asp?committee_code=TG196

Color spaces compared

* IEC 62563 terminology

Specification*	sRGB	aRGB	ACR	mRGB
Luminance Response	~2.2 power function	2.199 power function	DICOM GSDF	DICOM GSDF
Color Gamut	HDTV based ITU-R BT.709-5	'Wide' (extended G)	-nd-	sRGB (aRGB option ?)
L_{max} , cd/m^2	80	160 (125-200)	350/420/250	350/420/250
L_{min} , cd/m^2	-nd-	0.56	L_{max} / LR	L_{max} / LR
Luminance Ratio (LR)	-nd-	287.9 (230-400)	350 (> 250)	350
White Point	D65	D65	D65	D65
Gray tracking	-nd-	-nd-	-nd-	IEC MT51
Surround	20% refl. lx	Gray < 20% L_{max}	-nd-	20% L_{max}
Ambient Illumination, lx	64 (D50)	32	20-40	-nd-
Veiling Glare	1.0%	accounted	-nd-	-nd-
L_{amb} , cd/m^2	-nd-	-nd-	$L_{amb} < L_{min}/4$	$L_{amb} < L_{min}/4$

Proposal for calibration target for medical color display systems

Tom Kimpe [1], **Albert Xthona** [2]

[1] Barco Healthcare, Kortrijk, Belgium
[2] Barco Healthcare, Beaverton OR, USA

tom.kimpe@barco.com
albert.xthona@barco.com

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Why calibration?

Stability of state-of-the-art display systems

- A lot of effort is being spent on guaranteeing stability and quality of digital pathology scanners (and other modalities or image processing algorithms that produce color medical images)

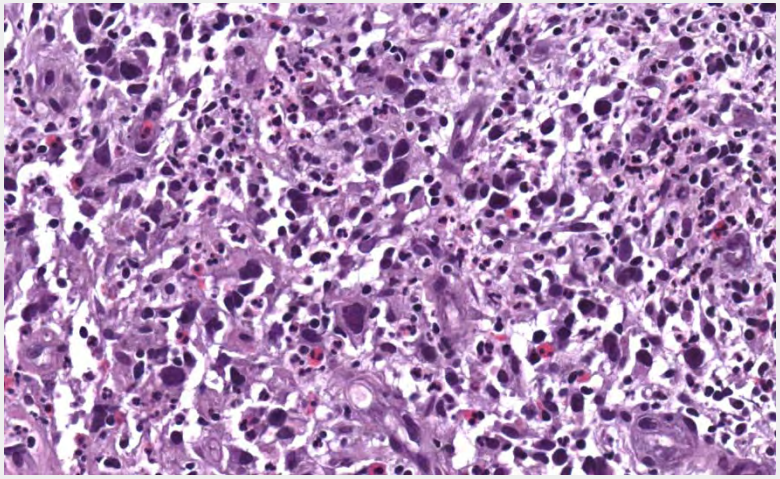
- However, today's (consumer) display systems suffer from substantial instabilities and inconsistencies over time and display area

  - Uniformity center to corner
  - Luminance change with aging
  - White point variation
  - Color shift with aging
  - Different distribution of colors

Non-Uniformity of Display Degrades Image

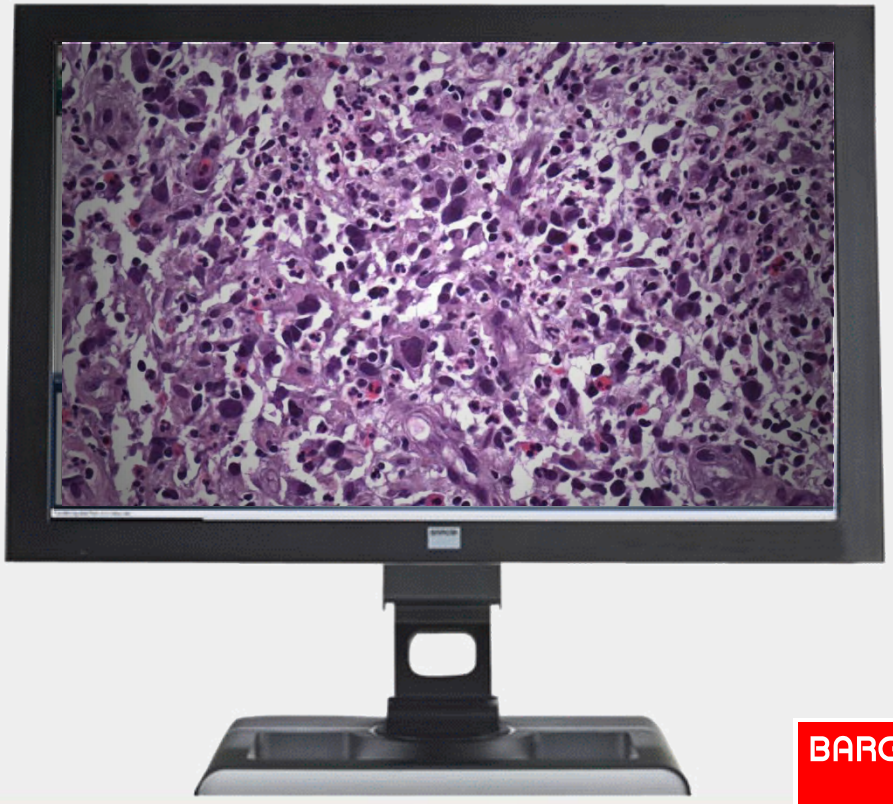
uniformity

(scanner image even corner to corner)



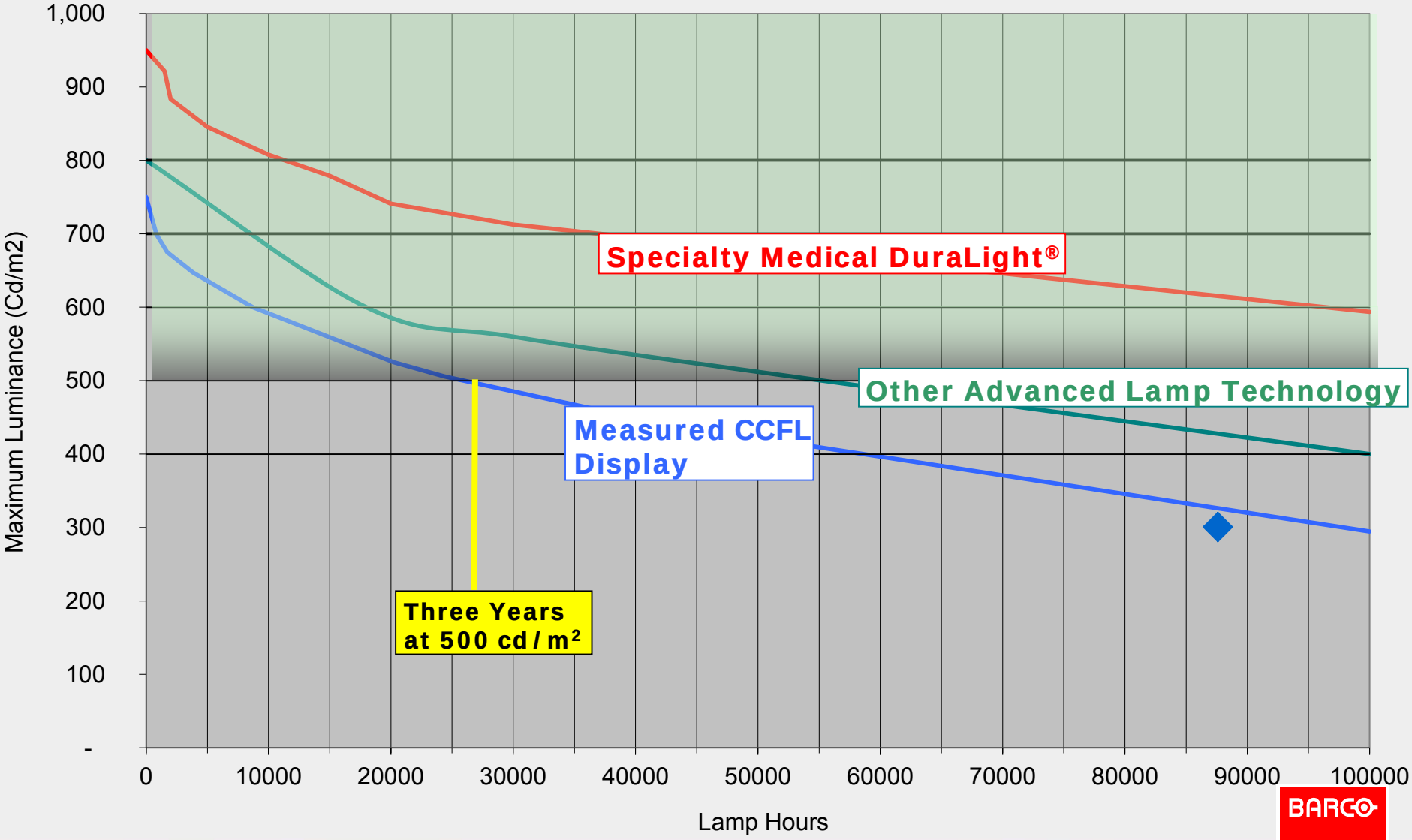
non-uniformity

(center brighter & corners darker)



Images Courtesy of Dr. Cucoranu, UPMC

Display's maximum luminance declines. Unless stabilized, older displays will be dimmer



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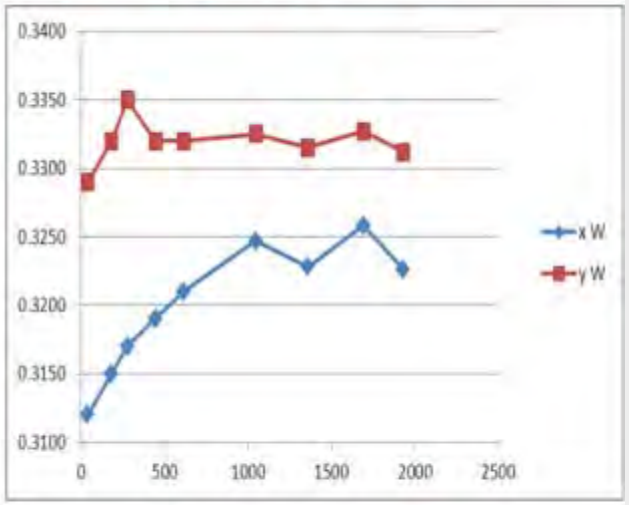
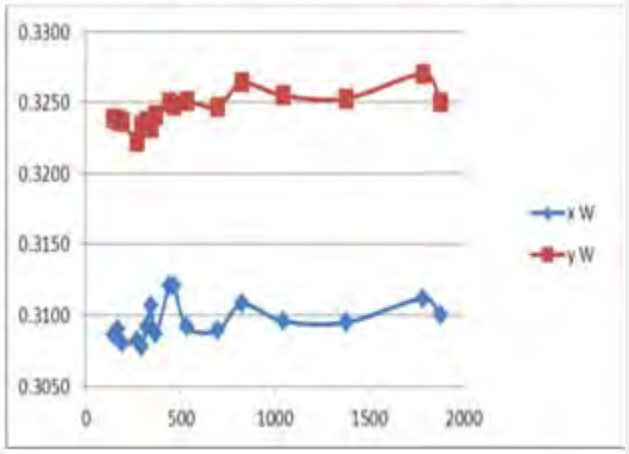
Color point stability of displays over time

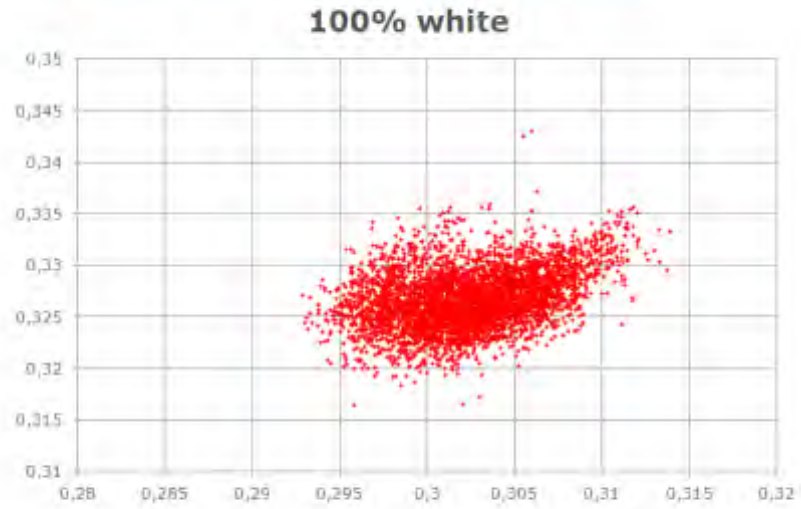
CCFL backlight



LED backlight



White point variation of color displays

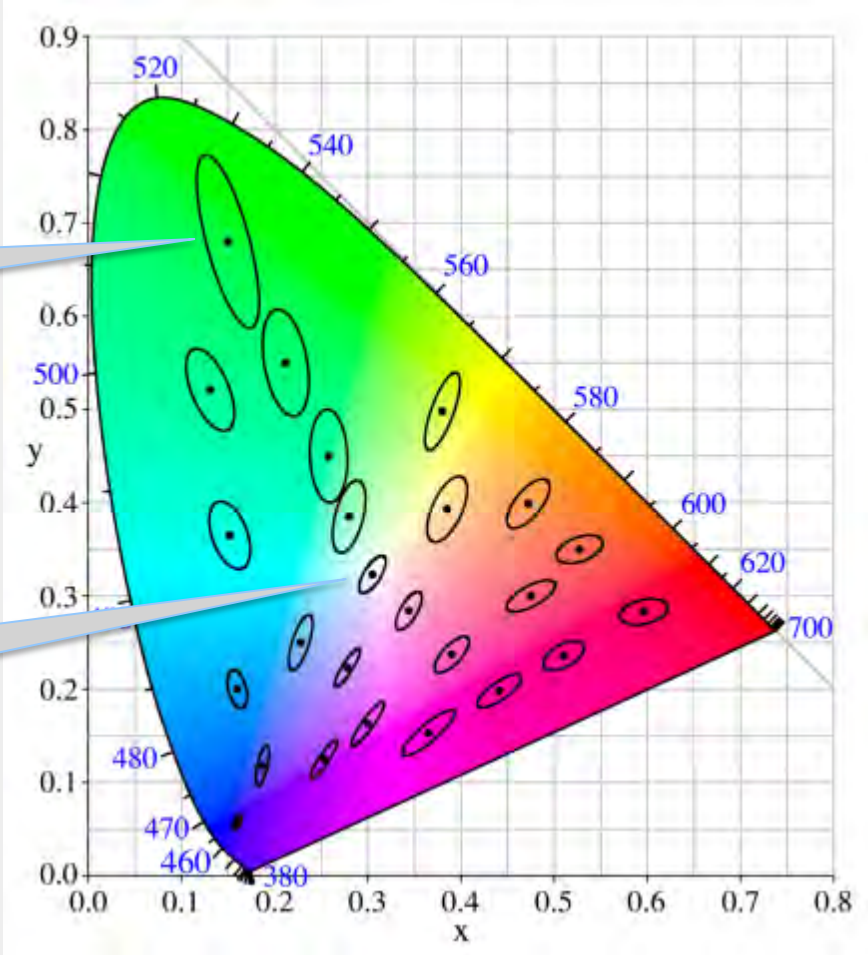


(x,y)-coordinates of 4355 color displays during manufacturing measured with Minolta CA-210

Displays choose how to arrange colors: How should colors be arranged?

Some differences need to be quite large to be noticed

Our eye more readily discerns other differences



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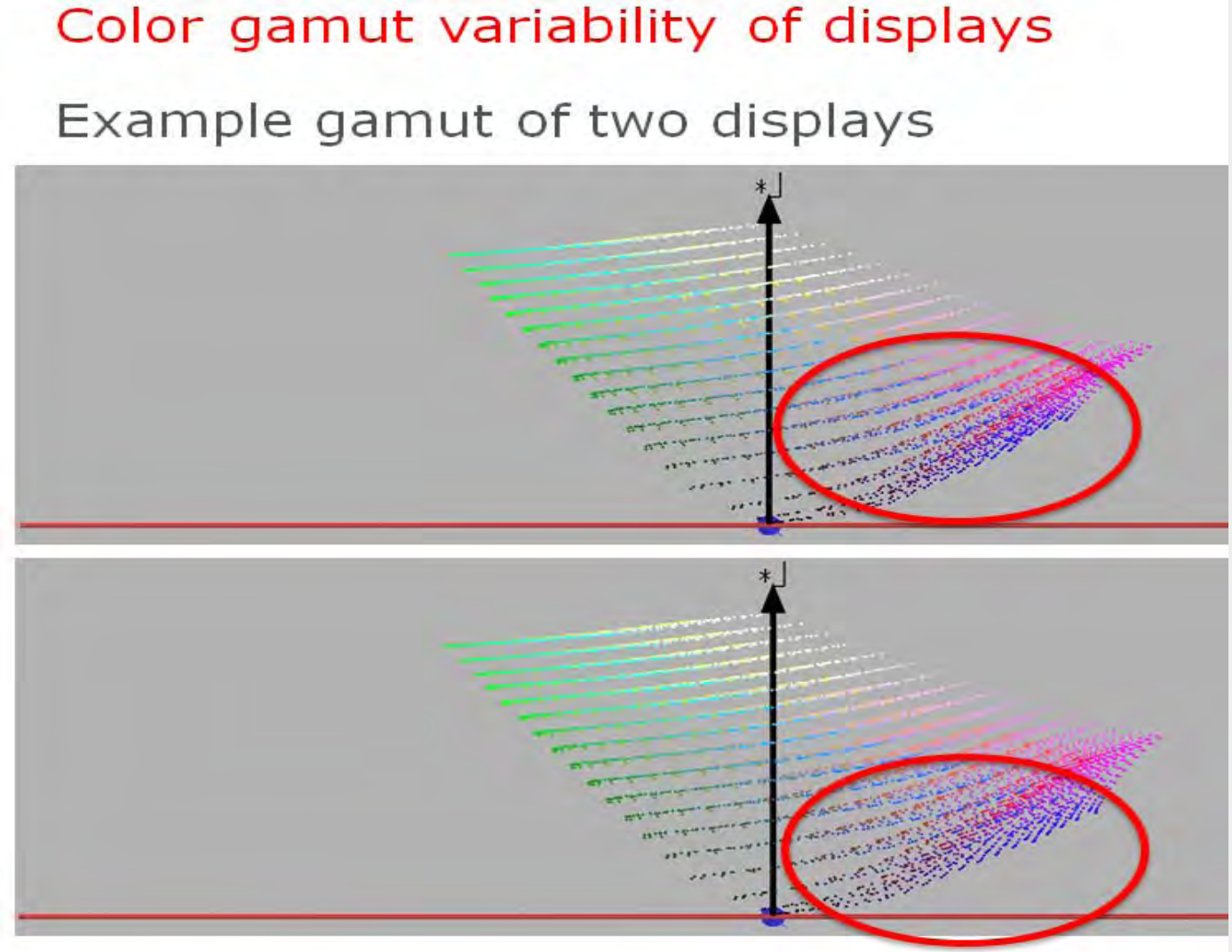
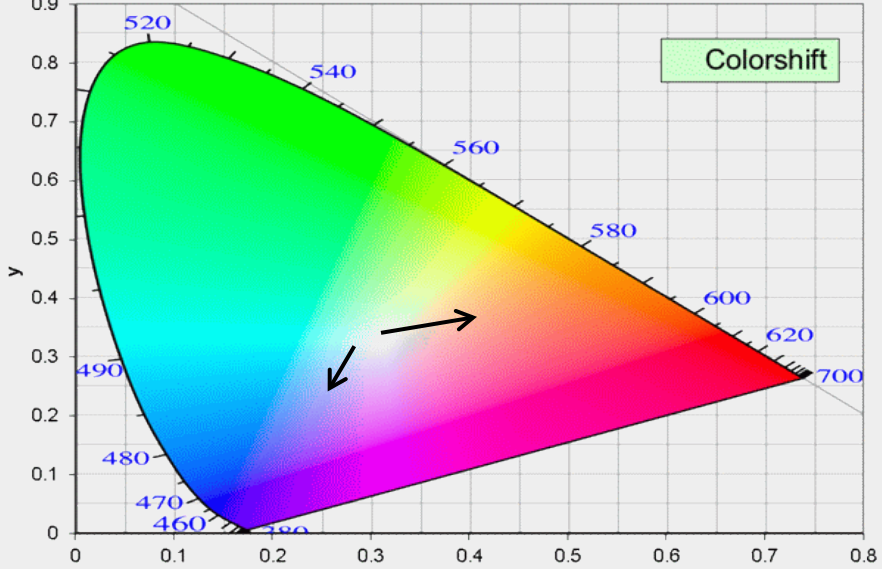
Arrange colors in consistent fashion spread out colors in useful way



Color shift of display: aging light source, optics



new display

Aged LED
(less red&green)

Aged CCFL
(less blue)

Expectations of a medical display

- After some variation has been compensated, and some remains

- Good clinical performance must still be possible:
  On the same display over time
    - Eg. one could see a pathology today on a particular display, but not anymore six months from now.
  - In between display systems of the same type or of other type
    - Eg. in a reading room full of display systems one could see a subtle pathology on one display but not on another display.

Proposal for calibration target for color medical displays

Color Calibration proposed based on perceptual optimization, not absolute

- Key points:

  - Absolute calibration does not allow for technical advances and limits every display to the worst display that can be accepted

  - Different (color) modalities seem to have different (clinical) requirements

  - spacing things evenly *gives applications best palette*
  - visibility of image value differences independent of location in gamut

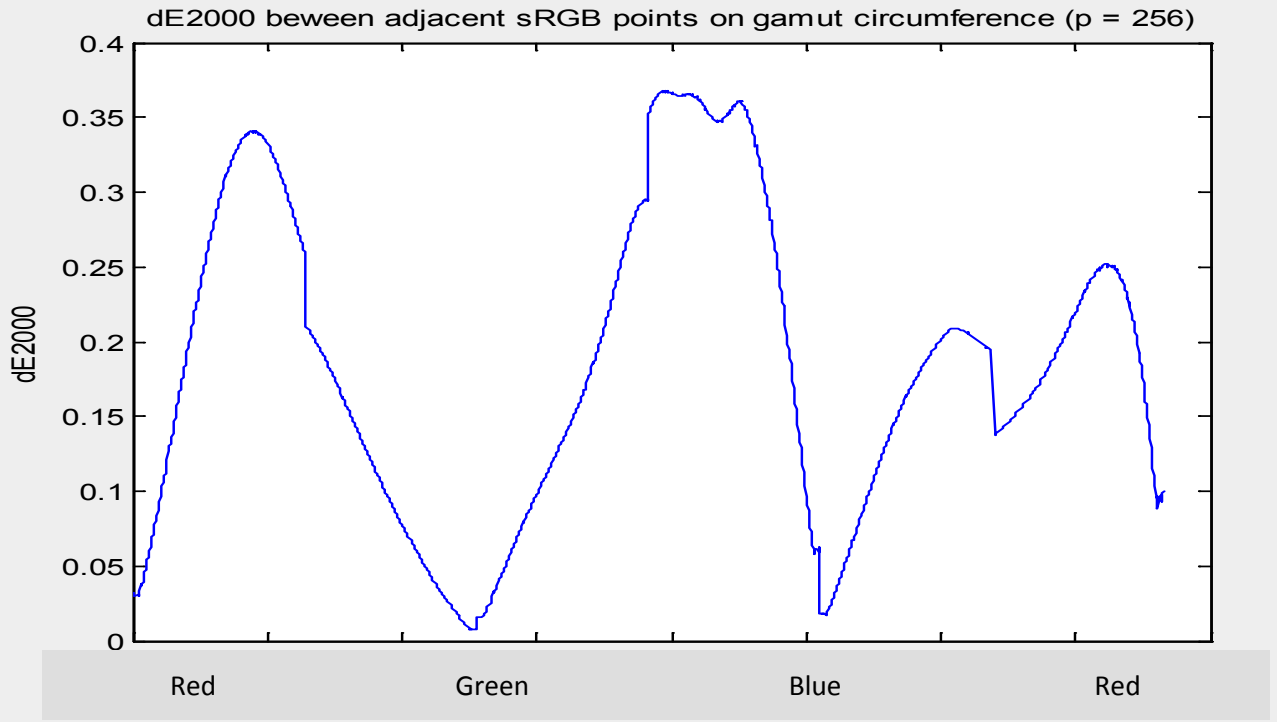
  - Therefore making sure that the display behaves perceptually linear both for greyscale and color seems a good choice.

Proposed calibration target

- Complying with DICOM GSDF for greyscale curve
  - permit simultaneous or sequential use with radiology images
  - accomodate large range of luminances (100-2000 nit)
- Not reducing the native luminance, contrast and color gamut of the display
- Aiming for DeltaE2000 perceptual (color) uniformity for the color behavior within the gamut
  - make differences equally important
  - promote efficient storage of images
- We have the intention to work towards an open industry standard as we have done with DICOM GSDF.

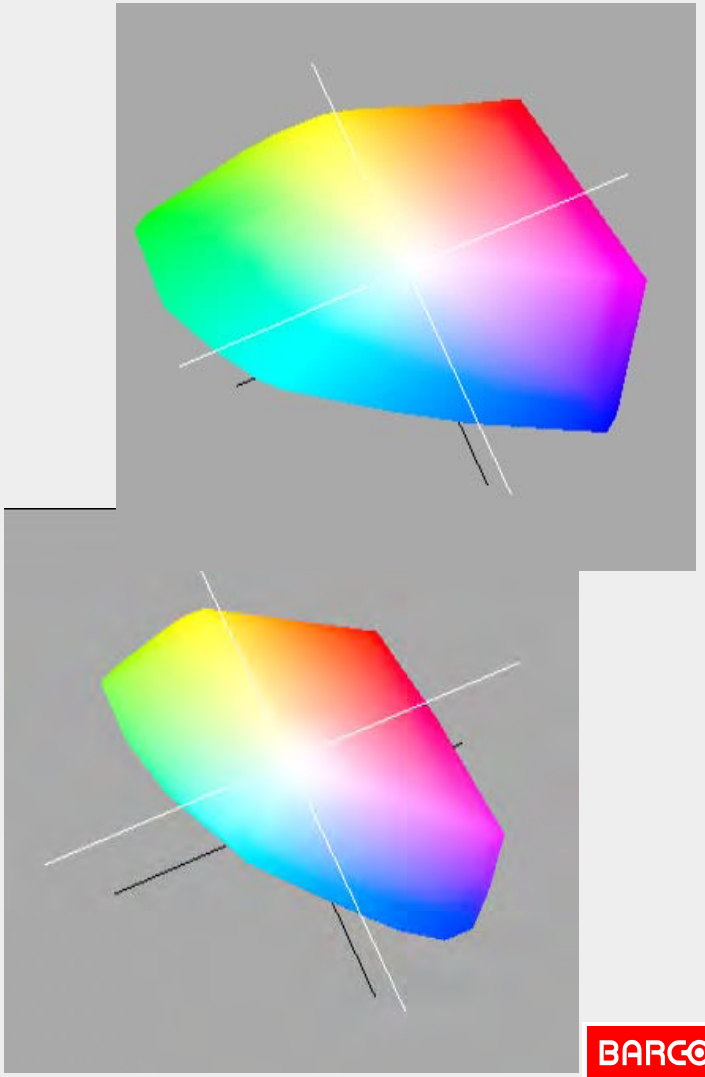
Why not sRGB?

- sRGB is very limiting {80 cd/m2, not in line with evolution of primaries expected soon} and not perceptually uniform
- difference between adjacent hues more or less noticeable as measured by delta-E
- more useful steps available if steps are similar size



Correctly utilize wider gamuts

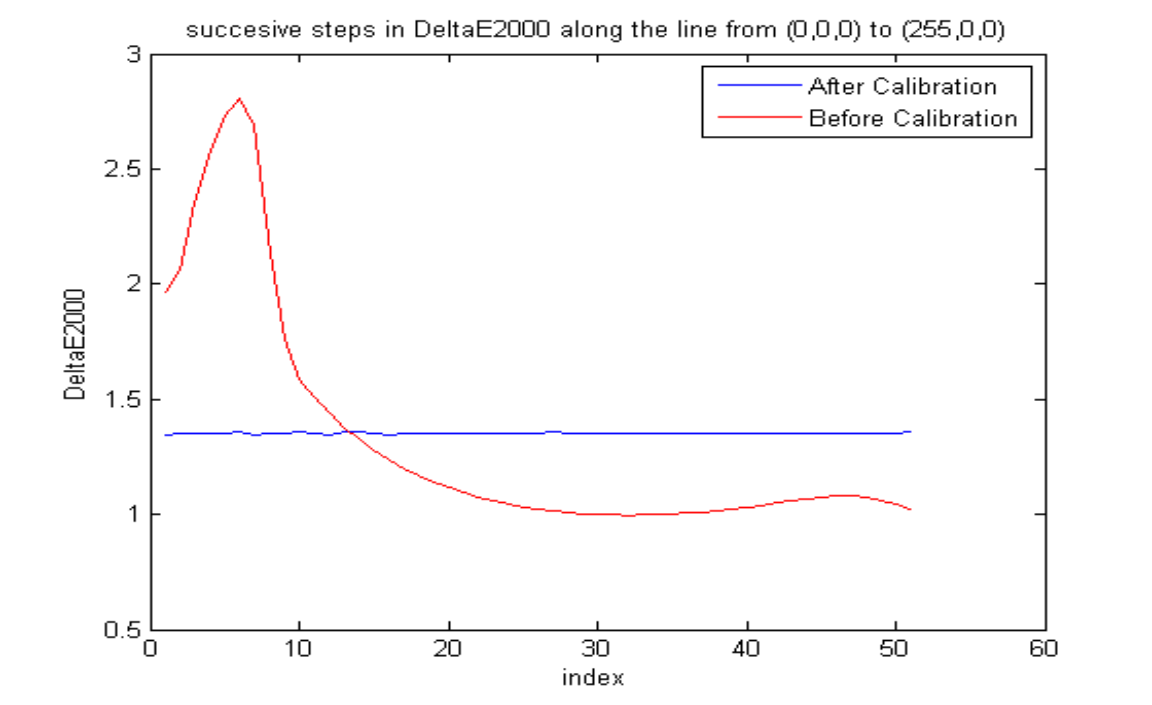
- Large increase in gamut only slightly increases number of perceived shades of saturation
- Handle individual variation and aging
- Different display designs may have only wide gamut in red or green
- DeltaE2000 perceptual approach optimally distributes colors so as to equally value all image color differences



Results that can be achieved

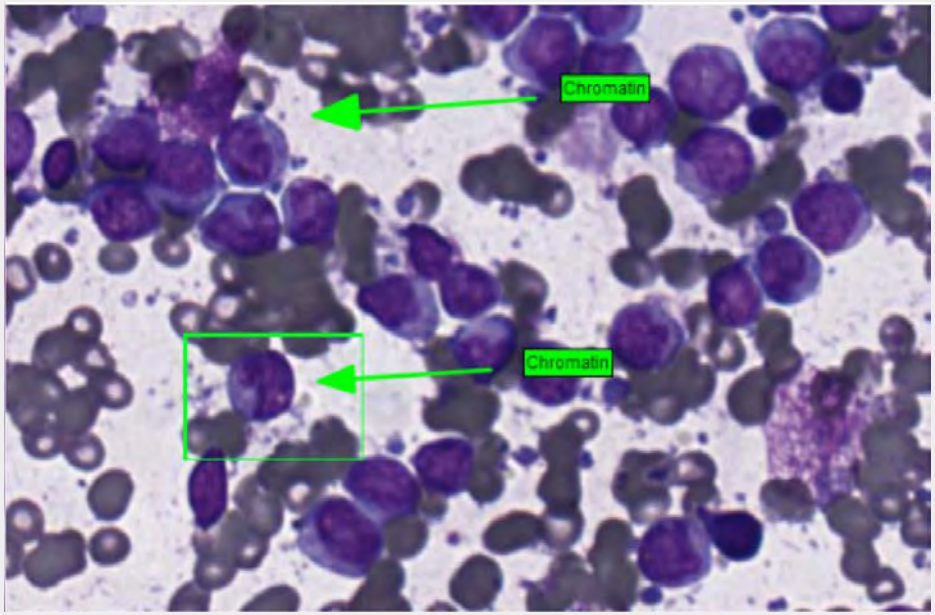
Calibration results (1)

- Subtle color tint targets are much better visible on calibrated display vs. a standard sRGB or DICOM GSDF calibrated display
- Calculations of deltaE2000 confirm improved uniformity of the display



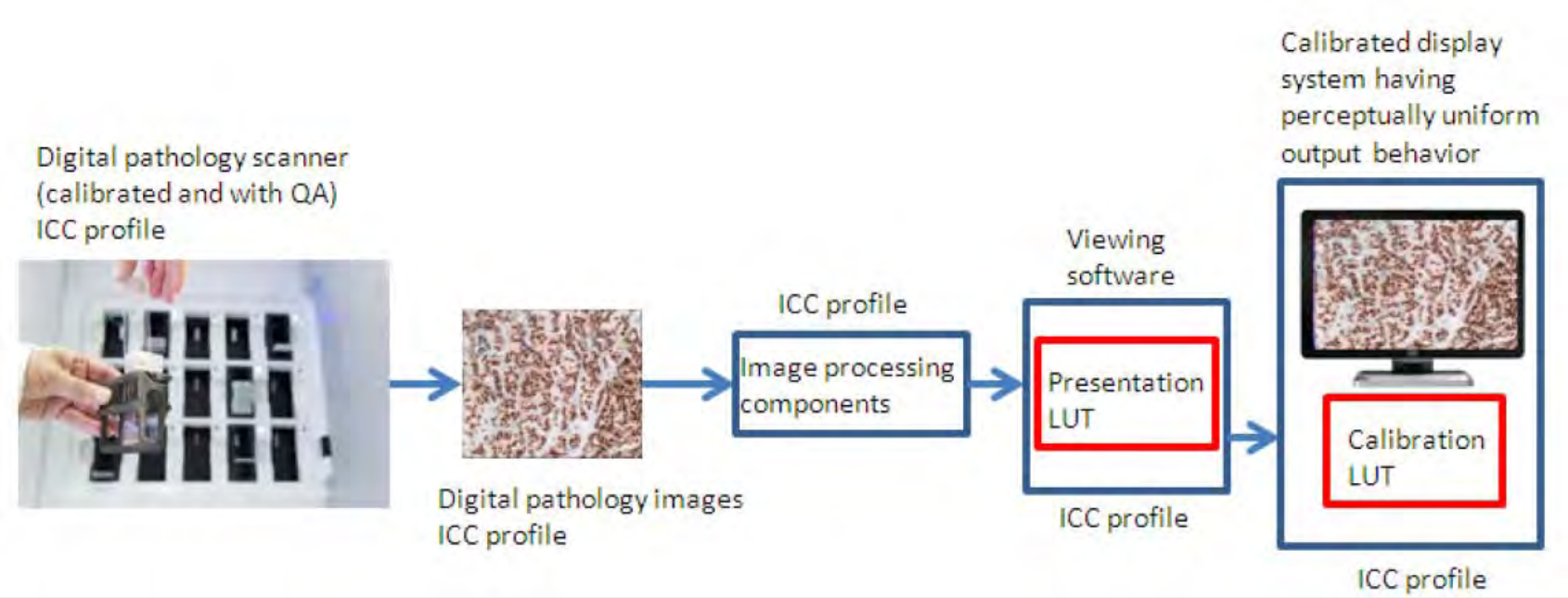
Calibration results (2)

- Visual inspection of pathology images shows that details such as cell core and chromatin are better visible on calibrated displays
- Calculations confirm that indeed these features have higher perceived contrast

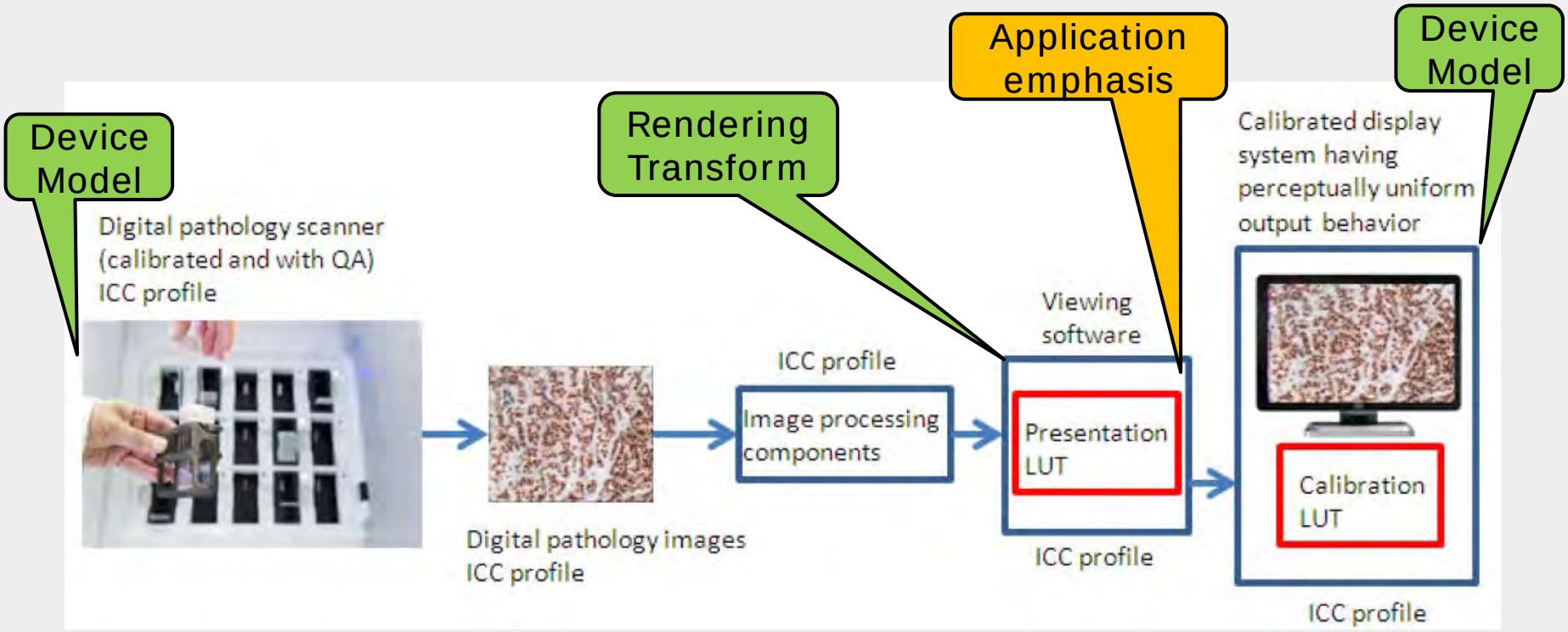


Discussion

- We would appreciate a discussion about how such a calibration practically could be integrated in the ICC platform
- Would this color workflow require a new rendering intent?



Discussion



-> Barco would like to work together to prepare a *flexible* imaging chain that enables *interchangeable* and *unequal* components

tom.kimpe@barco.com

albert.xthona@barco.com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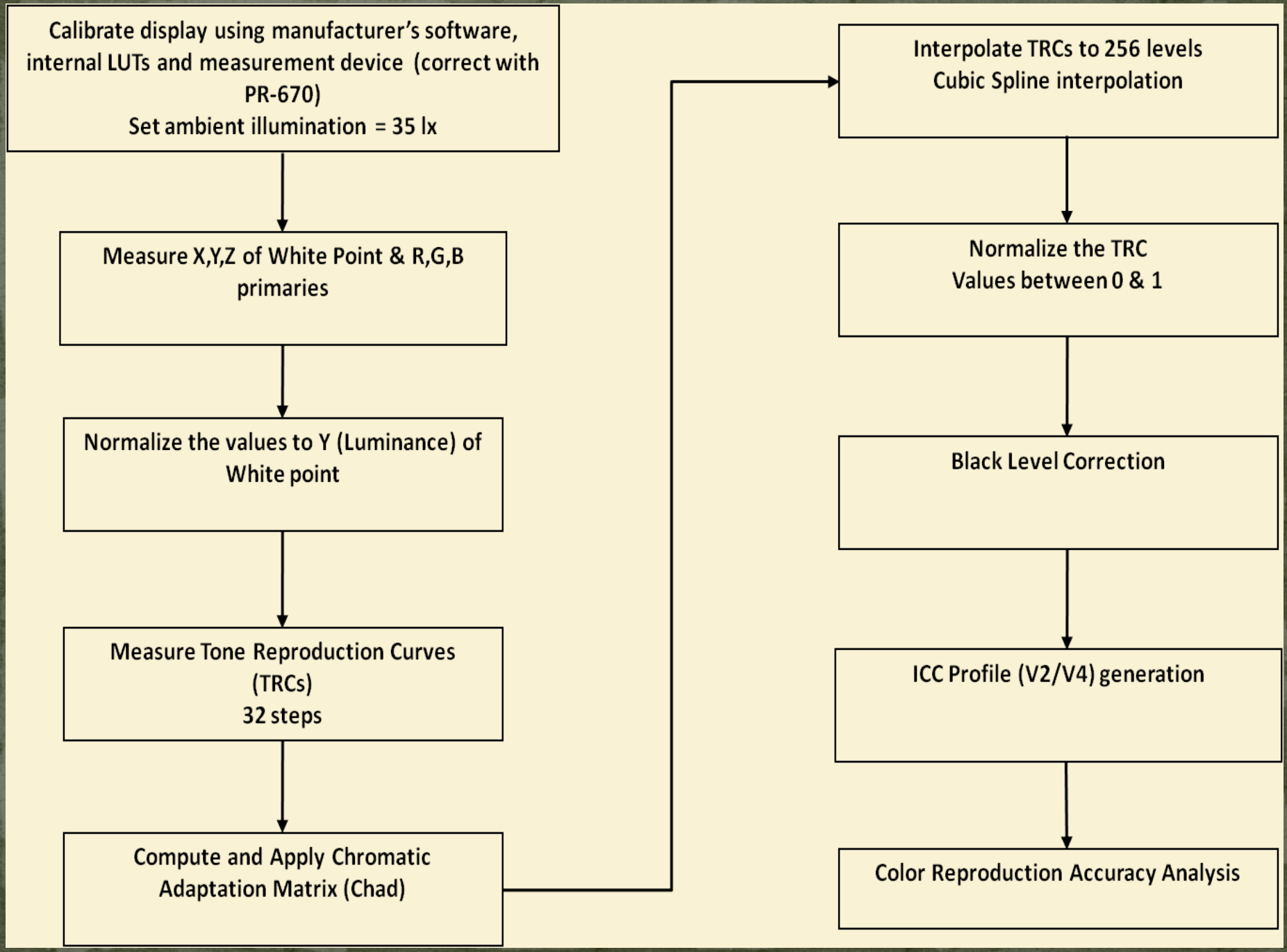
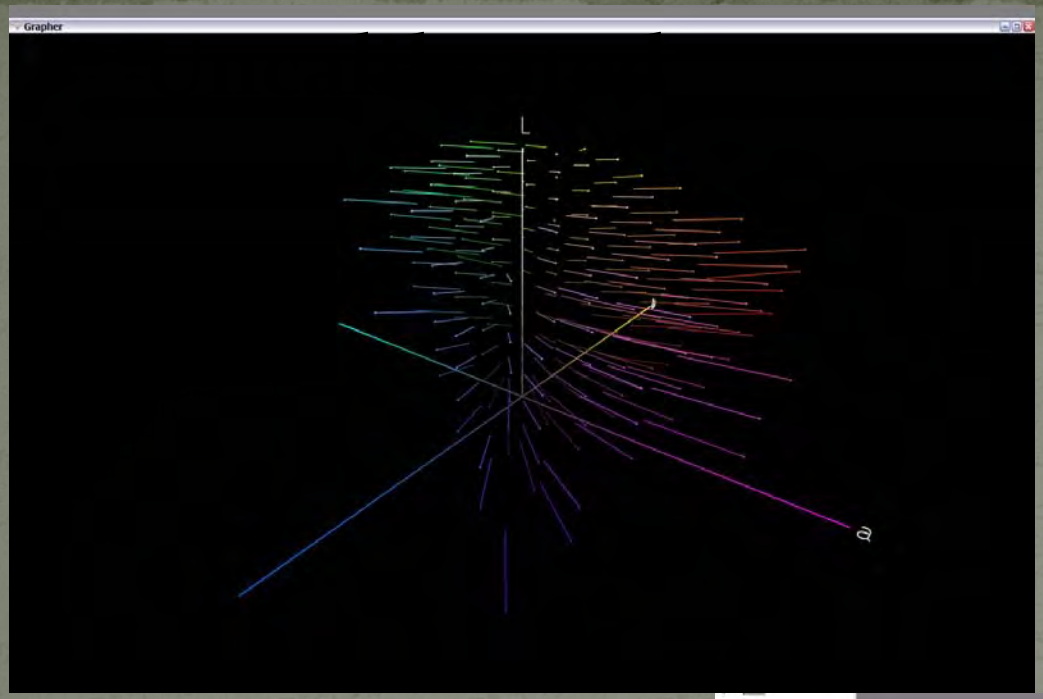
Research Proposal to Assess the Impact of Color Calibration on Diagnostic Accuracy

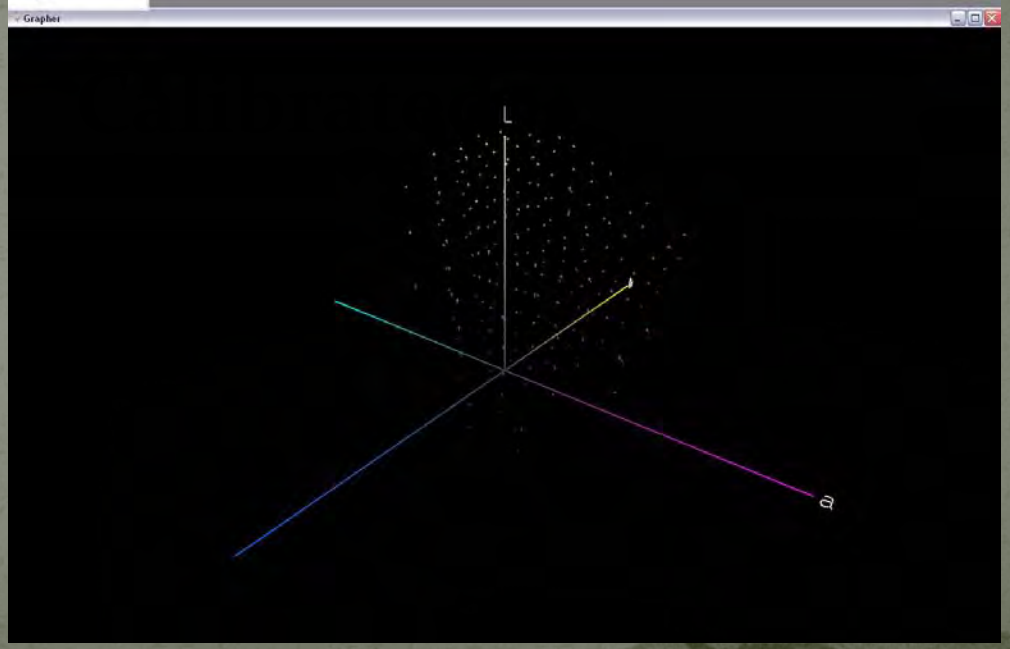
Elizabeth Krupinski, PhD
University of Arizona

Silverstein et al. Achieving High Color Reproduction Accuracy in LCDs for Color-Critical Applications. JSID 2012;20:53-62

Experimental Setup

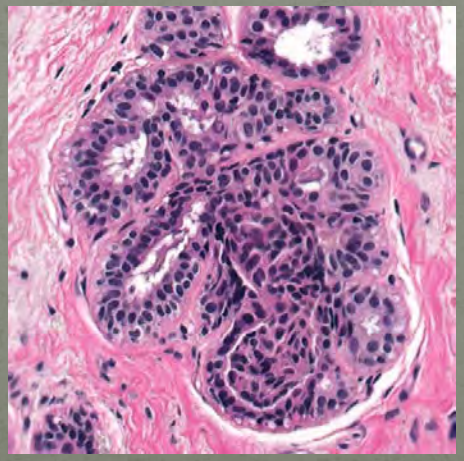

Calibrate display using manufacturer's software, internal LUTs and measurement device (correct with PR-670)
Set ambient illumination = 35 lx
Measure X,Y,Z of White Point & R,G,B primaries
Normalize the values to Y (Luminance) of White point
Measure Tone Reproduction Curves (TRCs)
32 steps
Compute and Apply Chromatic Adaptation Matrix (Chad)
Interpolate TRCs to 256 levels
Cubic Spline interpolation
Normalize the TRC
Values between 0 & 1
Black Level Correction
ICC Profile (V2/V4) generation
Color Reproduction Accuracy Analysis

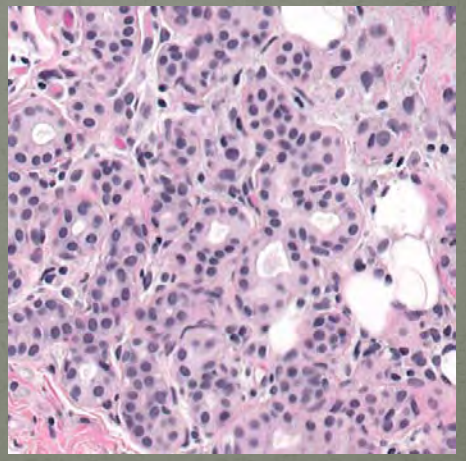

Grapher
L
a


Grapher
L
a

Images

- Whole slide images DMetrix scanner
- Breast biopsy specimens
- 250 ROIs selected by expert pathologist
  - ½ malignant & ½ benign
- Independently graded 2nd pathologist excellent or good quality





Study Methods

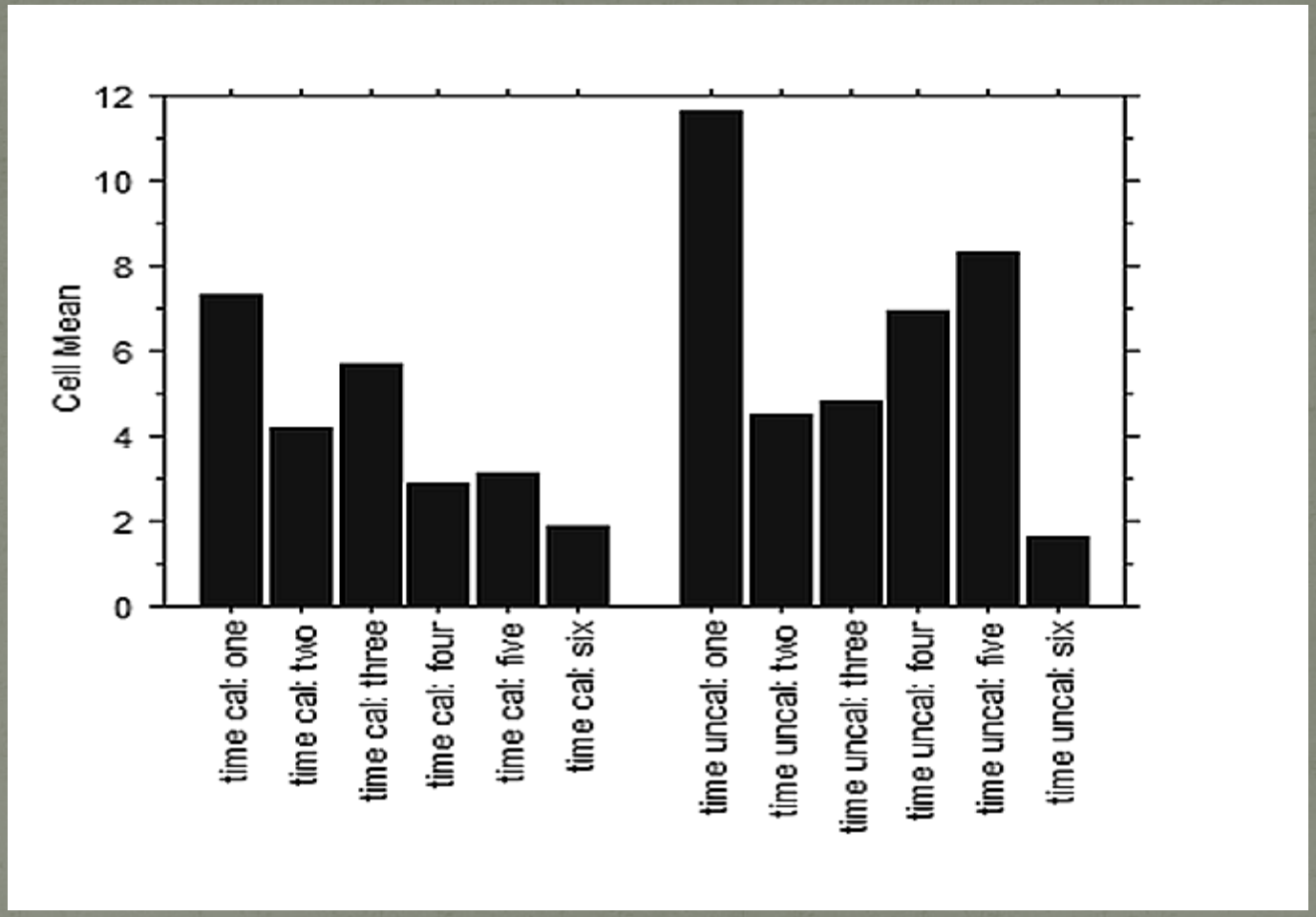
- 6 pathologists – 2 Board certified, 4 residents
- NEC 2690 Color LCD
  - 1920 x 1200
  - Lmax = 320 cd/m^2
  - Contrast ratio = 1000:1
  - Wide gamut
  - Calibrated/color managed & off-the-shelf
- Counterbalanced min 3 weeks between
- Rate benign vs malignant
- Trials timed automatically

MRMC ROC Az

Reader	Uncalibrated Az	Calibrated Az
1	0.9003	0.9142
2	0.9747	0.9856
3	0.8235	0.8586
4	0.7827	0.7884
5	0.8098	0.7889
6	0.8015	0.8062
Mean	0.8488	0.8570

$F = 0.71 \quad p = 0.4112$

Timing Results



Average 4.895 sec vs 6.304 sec p = 0.0460

Proposed Project

- Methods for developing color calibration & processing solutions for diagnostically-optimized color space (e.g. perceptually uniform) that combine info about display with interactive tools & a priori knowledge from user experience, image content (spectral characterization), & acquisition system (spectral detector characterization)
- Calibrate *based on individual preferences* for display parameters (hue, saturation, contrast, dynamic range) & determine if will yieldhigher diagnostic accuracy & efficiency

Perceptually Uniform Color Space Compared to sRGB

- Perceptual uniformity allows equipment vary in absolute capability while retaining familiar look
- Retains interoperability between displays installed years apart
- Silverstein method based on matrix-based ICC profiles with simple 1D characterization display's primaries = only first order approximation more general ICC profiling based on 3D LUTs with 3D characterization display's gamut
- Plan use displays calibrated to perceptually uniform color space in lieu of sRGB to which Silverstein displays were approximations
- In perceptually uniform space colors evenly distributed across gamut so all mutually distinguishable colors expressed with min # bits/channel => less error (due to quantization), on average, in reproduction of arbitrary color in perceptually uniform color space than in sRGB assuming same bit depth both color spaces

Preferences

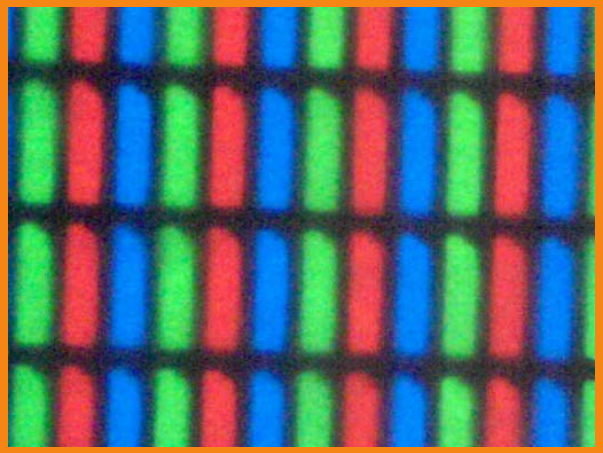
- Images presented MG 6 MP color LCD calibrated sRGB or perceptually uniform color space based on full 3D characterization display & implemented using 3D
- Zoom ROI preferred diagnostic viewing point & set preferred hue, saturation, contrast, dynamic range.
- Will have preferred hue, saturation, contrast, dynamic range settings for min 15 pathologists on 100 images

Final Observer Study

- i & ii will be tested first determine which (sRGB vs perceptually uniform) calibration method yields highest performance
  - sRGB calibrated using 3D LUT calibration preceded by adaptive 3D characterization
  - Perceptually uniform calibration using 3D LUT calibration preceded by adaptive 3D characterization
- i or ii used to compare iii & iv (tailored displays)
  - Behavior individual pathologist from Aim 1 fed to intelligent display settings recommender & tailored settings generated for specific pathologist
  - Behavior all pathologists in Aim1 fed to IDSR & average preference setting generated

MOBILE FOR MEDICAL

DISPLAY CALIBRATION CHALLENGES



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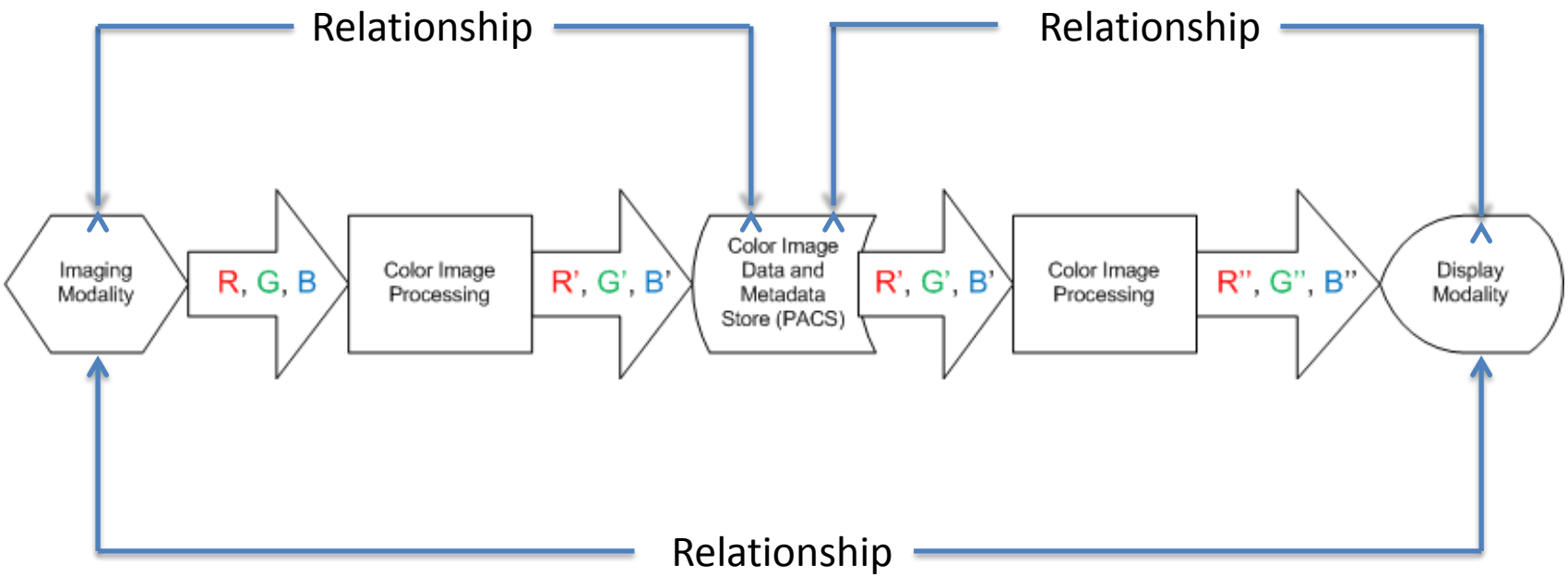
INTRODUCTION

- **Practitioners use mobile devices (tablets, phones) for a wide range of functions including**
  - access to patient records
  - ordering procedures
  - viewing medical images from numerous imaging modalities
  - …

PROBLEMS STATEMENTS

- **Mobile display devices vary significantly with regard to**
  - Image quality
  - Color rendering characteristics
- **No standard color image data processing pipeline across mobile devices**
- **Display and platform technology changes rapidly**
  - Engineering trade offs do not always favor image and color quality and consistency
  - Especially true for mass production – non specialty displays
- **No standard target color rendering condition defined for display modalities used in medical applications**
- **The result:**
  - The same digital data displays differently on different devices
  - Image and color quality is poorly defined and controlled

GENERIC MODEL FOR COLOR CONTROL IN IMAGING



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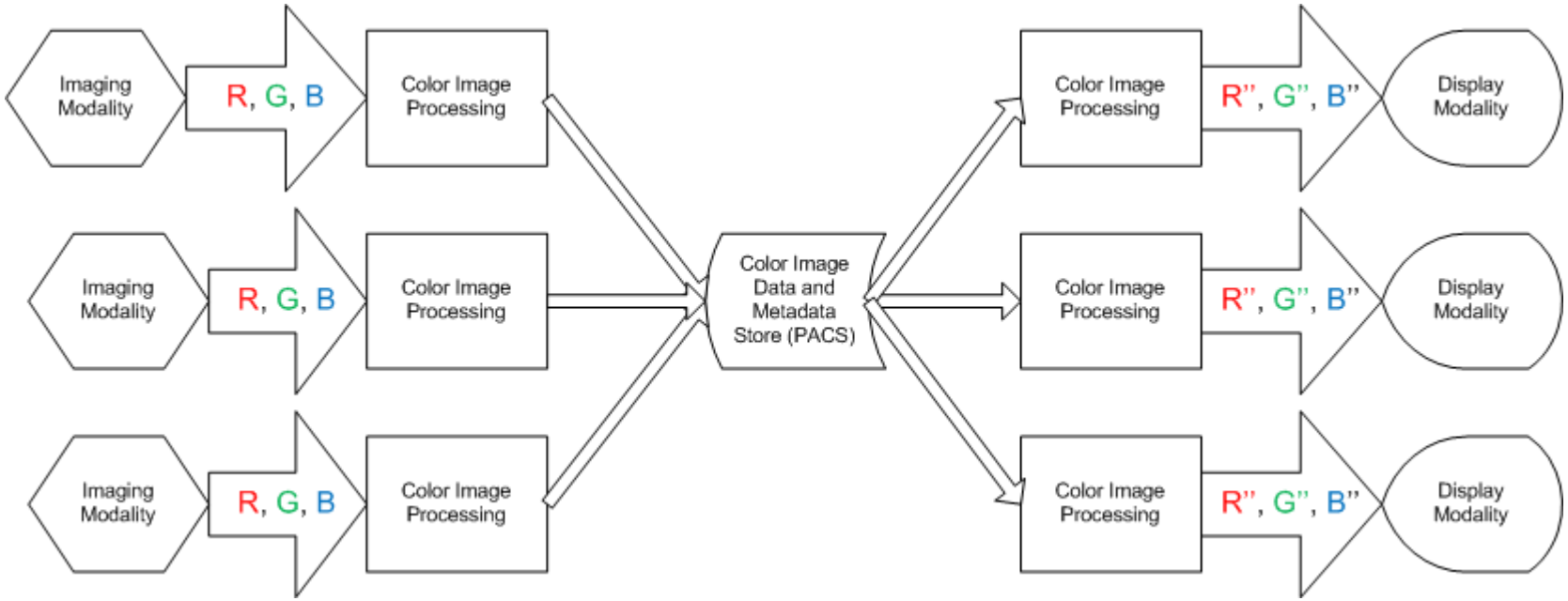
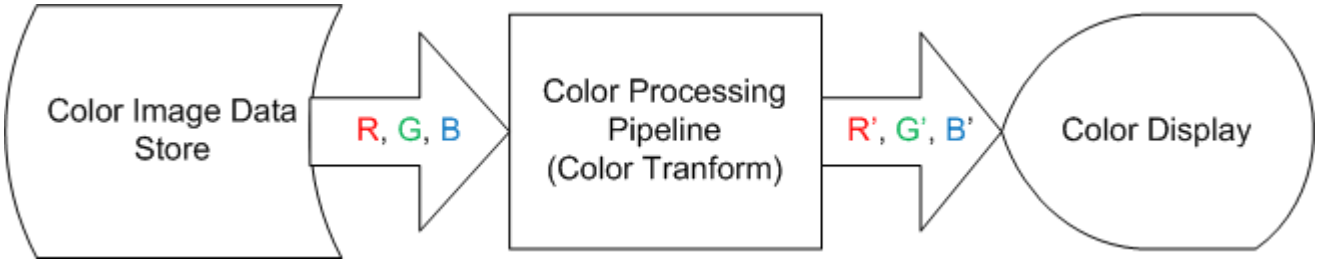
GENERIC MODEL WITH MULTI-MODALITIES



- "Relationship" may be different when Imaging Modalities are of different types
- "Relationship" should be same when Imaging Modalities are different instances of same type
- Definition of data stored on PACS can be different for different types of Imaging Modalities

WORKSTATION DISPLAY CALIBRATION

- **“Back end” processing well understood and well developed**
- **Infrastructures to calibrate the display (color pipeline)**
  - One-dimensional look-up-tables (LUTs)
    - In-workstation (standard OS APIs to write/read)
    - In-display (non-standard APIs and communications protocols)
    - In-display proprietary built-in and “direct connect” sensors with embedded firmware (non-standard APIs and communications protocols)
- **Advanced color transforms (matrix (linear transform) and 3D LUTs) (color pipeline)**
  - In-display scalar hardware (non-standard APIs and communications protocols)



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TWO STAGES

- **Calibrate and profile the display**
  - Set color pipeline to null state
  - Display standard test colors and measure each with a colorimeter
  - Calculate calibration tables
  - Calculate profile
- **Apply corrections based on calibration and profile data to on-screen graphics using s/w or h/w color pipelines**
  - Apply calibration using h/w or s/w LUTs
    - In-display
    - In-video card
    - In-server (calibrate as source)
  - Apply profile using a CMM using CPU or GPU

PROBLEMS UNIQUE TO MOBILE DEVICES

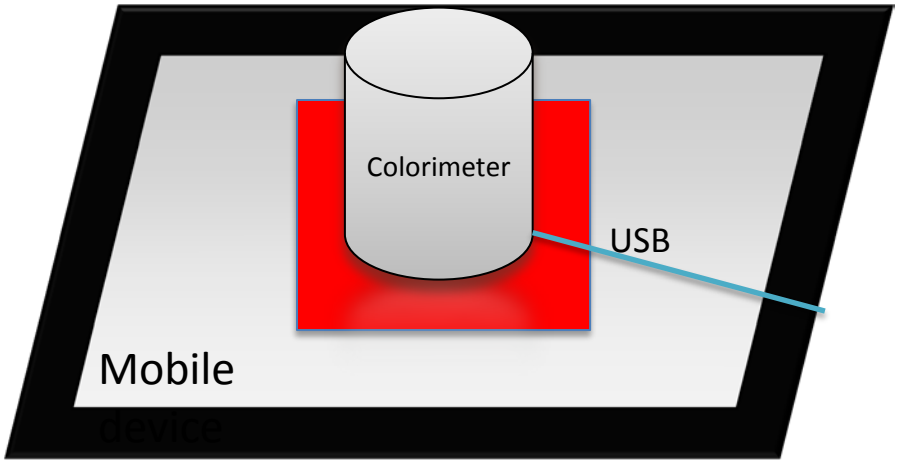
- **No standard color pipeline**
  - Color pipeline must be implemented in software using either CPU or GPU
    - At the server
    - At the App level
    - At the OS level
- **Some platforms do not have USB interface**
  - Client/server architecture required to implement the calibration and characterization function
- **No standard infrastructure to manage profiles**
  - Function must be provided by the application
- **No standard, and highly dynamic, viewing and stray light conditions**
- **Dynamic display settings**
  - Ambient adjustment
  - Power savings
  - DCC

COLOR DATA PIPELINES

Type of process	In Workstation (OS)	In display	In application software	In Mobile
For Cal				
3 by 1-D LUTs	Yes (H/W)	Some	Some	No
LUT-Matrix-LUT	No	Some	Some	No
3-D LUT	No	Some	Some	No
For Characterization				
CMM	Service called by App	No	Yes	No

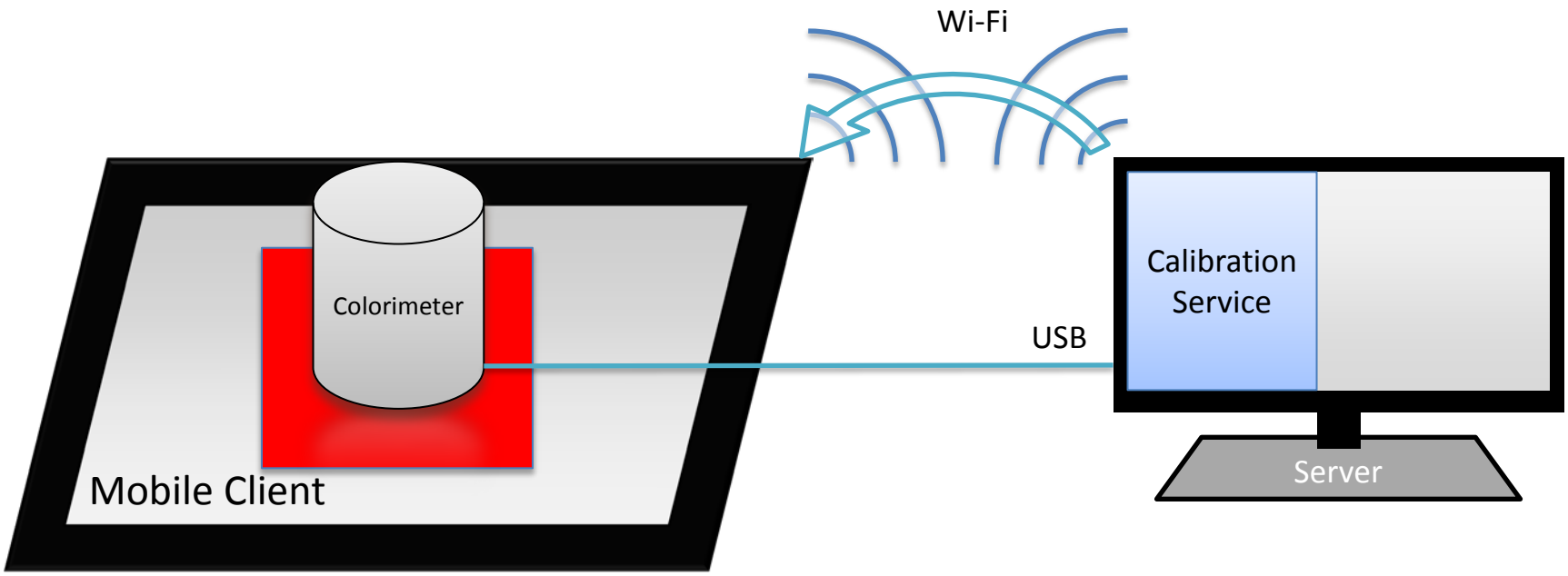
CALIBRATION AND PROFILING WITH USB ENABLED PLATFORM

- Calibration and profiling local to the device
- Systems must support file sharing across applications
- Profile stored locally on the mobile device



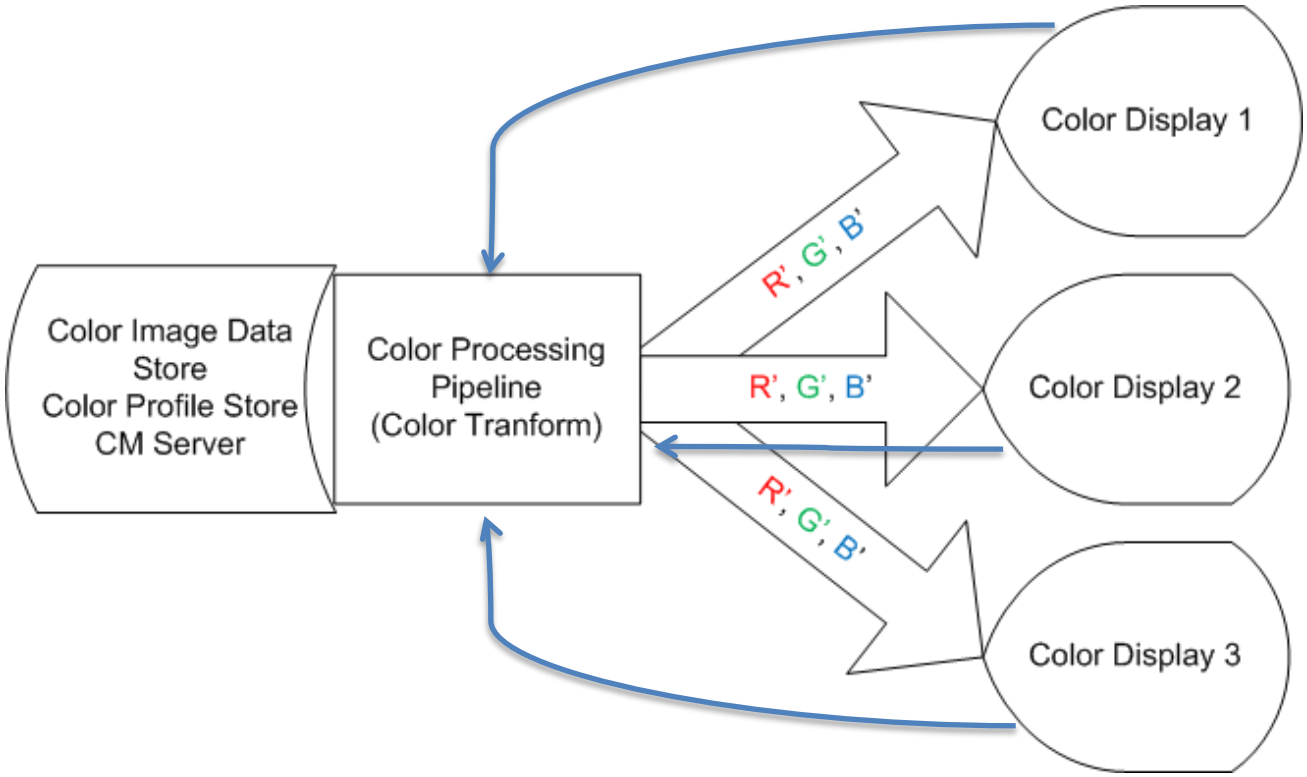
CALIBRATION AND PROFILING NON-USB SUPPORTED DEVICE

- **Client/server architecture is required**
  - Server interfaces to Colorimeter and performs all data analysis
  - Client on mobile device displays test colors
- **If no file system available across apps; the profile is stored on cloud**



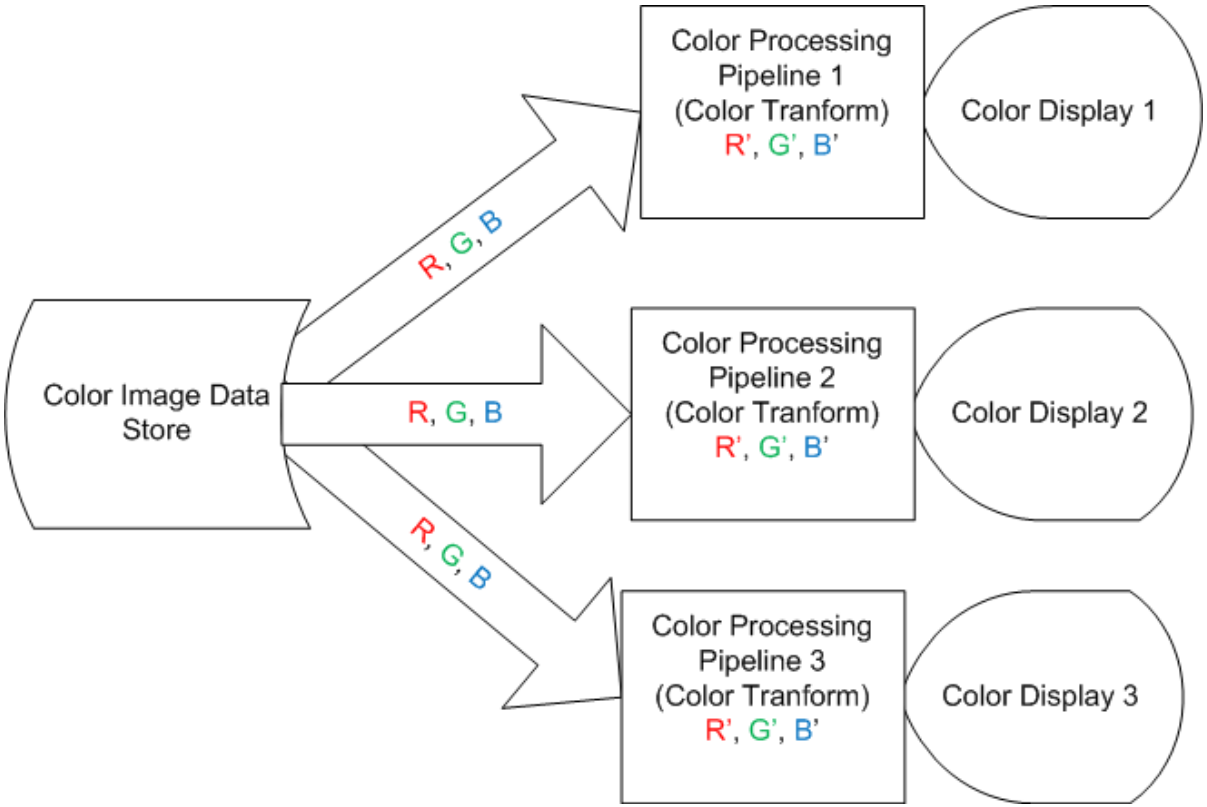
x-rite PANTONE®

SERVER BASED CALIBRATION



x-rite PANTONE®

CLIENT BASED CALIBRATION



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ISSUES AND NEXT STEPS

- **Determine requirements**
  - Taxonomy of uses cases
  - Reproduction Aims
  - Calibration enough?
    - Calibration and characterization both needed?
  - Ambient/stray light compensation required?
  - Dynamic controls to be defeated?
- **Quantify “out of box” mobile display variability**
- **Determine architecture**
  - Server based
  - Client based
  - In-app
  - In-OS
- **Interested parties**
  - Contact amasia@xrite.com

DISCUSSION

Best Practices for Digital Color Photography in Medicine

John Penczek
NIST & Univ. Colorado, Boulder

ICC Medical Imaging Task Force

Vancouver Meeting

Nov. 18, 2013

Mission & Scope

Mission:

Collect industry best practices in the field of digital photography and write a guidance document which can be used by the medical industry to minimize the color errors created during the digital color camera image capture process.

Scope:

This guidance document will apply for a range of digital cameras (from cellphone cameras to scientific grade cameras) and lighting conditions. Recommendations will also be made for camera setup and color correction in post processing.

Contributors

John Penczek, NIST/Univ. of Colorado (project coordinator)

Ives Vander Haeghen, University of Ghent Hospital

Stein Olav Skrovseth, Norwegian Centre for Telemedicine

Elizabeth Krupinski, Arizona State University

Aldo Badano, FDA

Phil Green, ICC

Draft Outline

Introduction and background
Penczek, Krupinski, Skrovseth

Factors that can contribute to color errors
Penczek, Krupinski

Recommended light conditions
Penczek, Krupinski

Recommended camera setup
Penczek, Krupinski, Skrovseth, Vander Haeghen

Use of reference color charts
Penczek, Vander Haeghen

Color correction in post-processing
Skrovseth, Vander Haeghen

Recommendations on color management
Green, Vander Haeghen

Note: Content should expand on or introduce new information to what is already available (e.g. ATA Practice Guidelines for Teledermatology 2007)

Publication

How will this document be published?

- **ICC publication**
- **Journal article**
- **Collaboration with other organizations (e.g. American Telemedicine Association)**

Report: Ophthalmic Imaging Standards

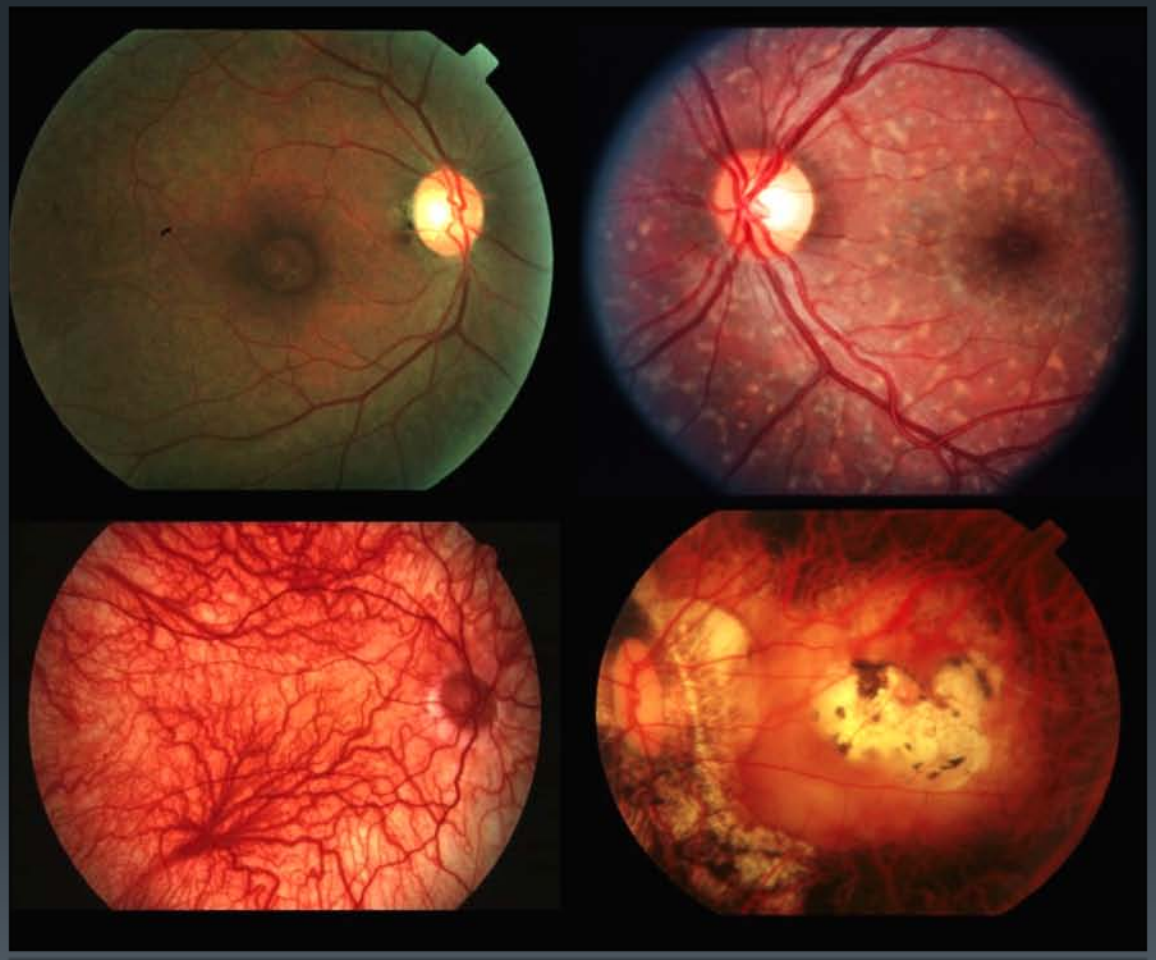
Christye P. Sisson, CRA, MS

Associate Professor, Biomedical Photographic Communications

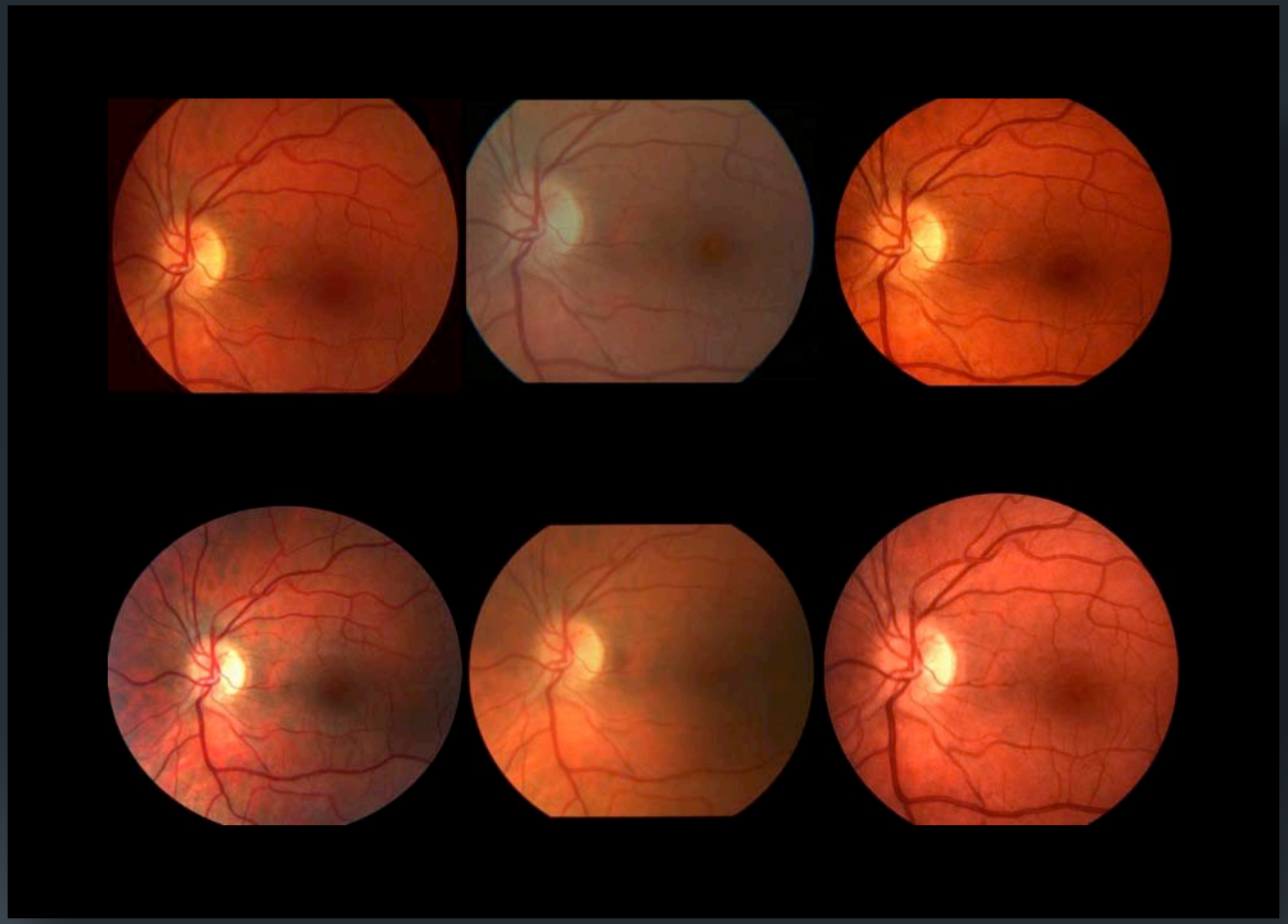
Program Chair, Photographic Sciences, School of Photographic Arts and Sciences

Retinal Color Variation Across Populations

Determined by ethnicity, pigmentation, disease process



Problem Summary: Image Variables

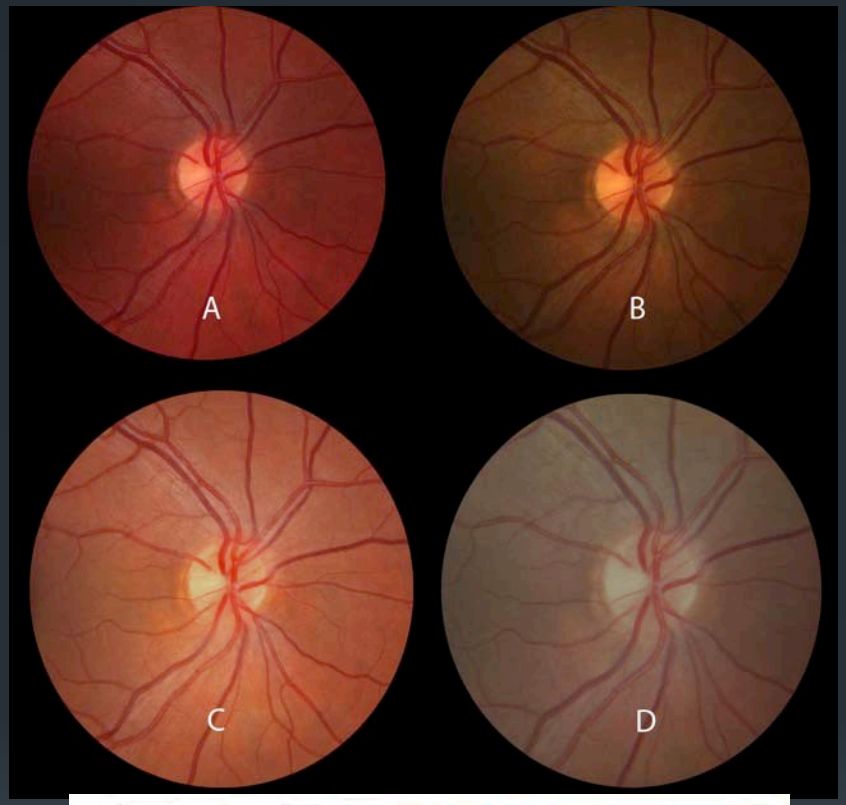


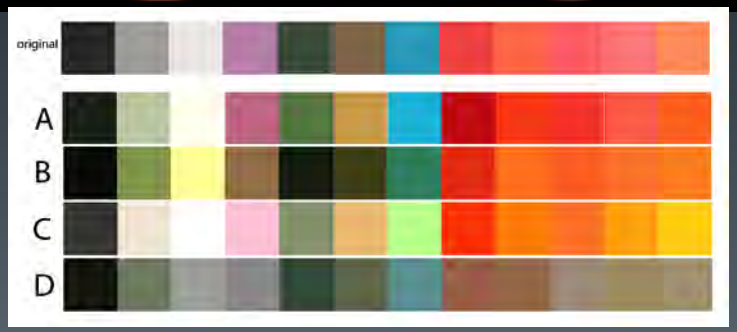
- One reason for the color differences in the appearance of the retina in fundus imaging in ophthalmology is the lack of a suitable calibration method or standard. This causes significant retinal color disparity from camera to camera, even within the same manufacturer for the same patient.

Premise

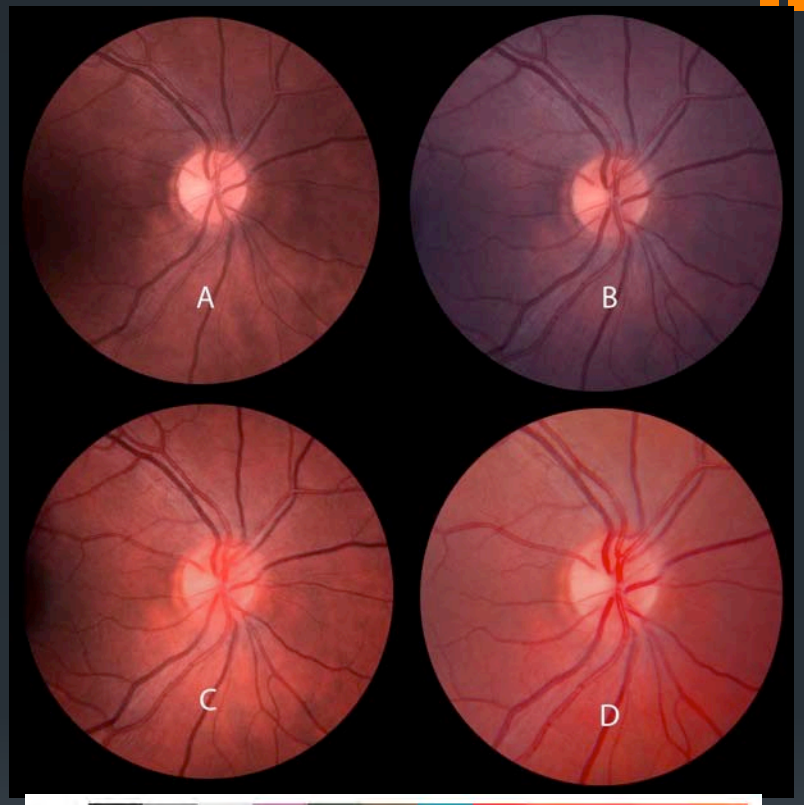
- It is potentially possible to profile a fundus camera, at least individually, to provide for greater camera-to-camera consistency
  - Applying transforms to RAW images in system would be ideal
- What we as ophthalmic imagers and practitioners believe to be “correct” retinal color is not correct at all
- A standard approach to color calibration is needed to begin to regulate input variables

Captured vs. Processed





Before



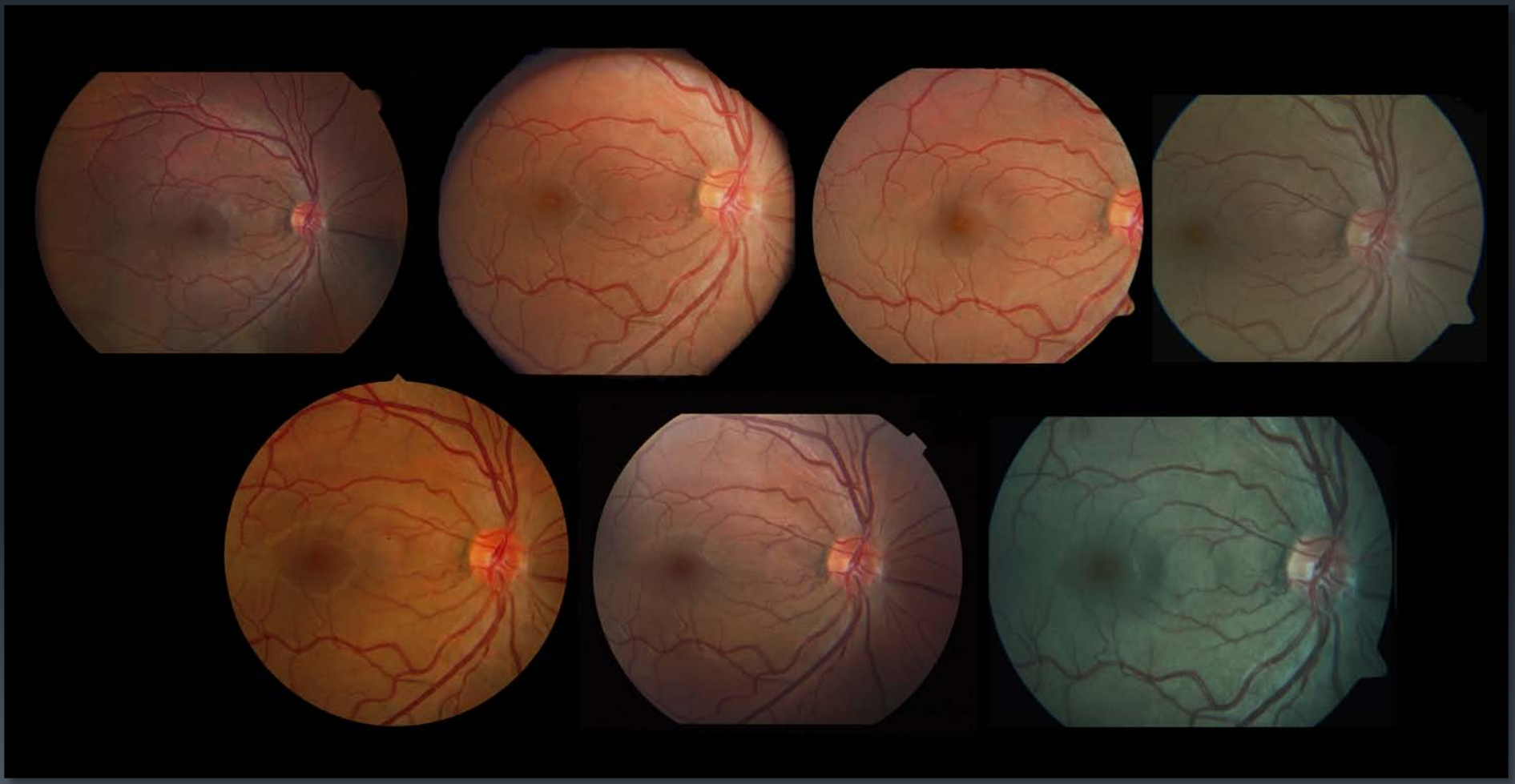
After

Objectives

- Develop a suitable calibration phantom and calibration method, and devise the best working/vendor practices to ensure color consistency across devices and manufacturers.
- To generate a repeatable, reliable method of “profiling” individual fundus camera/ophthalmic digital imaging system combinations, and using that profile to attempt to bring the various systems to a reasonable color standard.
- To work with the main companies that produce these systems to work toward this set of color standards in the interest of longitudinal research and accuracy of imaging in the field at large.

Progress

- Establishment of core participants including: ophthalmic photographers, reading centers, principles in the Ophthalmic Photographer's Society and manufacturers, as well as beta testing sites
- Draft of problem white paper distributed, shared working space online
- Web meeting scheduled for December
  - Preparation
    - Research components of systems, existing color management standards and practices, file type, bit depth and resolution requirements
    - Image objectives/requirements of reading centers
  - Manufacturer's discussion – what can be integrated into the systems as a final goal?
  - Method: color patches, model eye methods, capture methods



Participants:

Christye Sisson
Rochester Institute of Technology, University of Rochester Medical Center

Bill Fischer
Director of Imaging, Flaum Eye Institute, University of Rochester Medical Center

Jim Strong
Ophthalmic Photographer, Penn State Hershey Eye Center

Mark Fairchild
Rochester Institute of Technology, Director, Program of Color Science/Munsell Color Science Laboratory

Tim Bennett
Ophthalmic Photographer, Penn State Hershey Eye Center, OPS past President

Dennis Thayer
Fundus Photography Reading Center, University of Wisconsin

Matt Carnavale
Executive VP and Chief Technical Officer, Sonomed/Escalon

Kevin Langton
Director, Strategic Business Development, Carl Zeiss Meditec

cpspph@rit.edu

Whittle and GSDF Self-luminous Grey Scale JNDs

A psychophysical experiment to evaluate performance of gray scale functions

- **Whittle and Grey Scale Density Function JNDs compared**

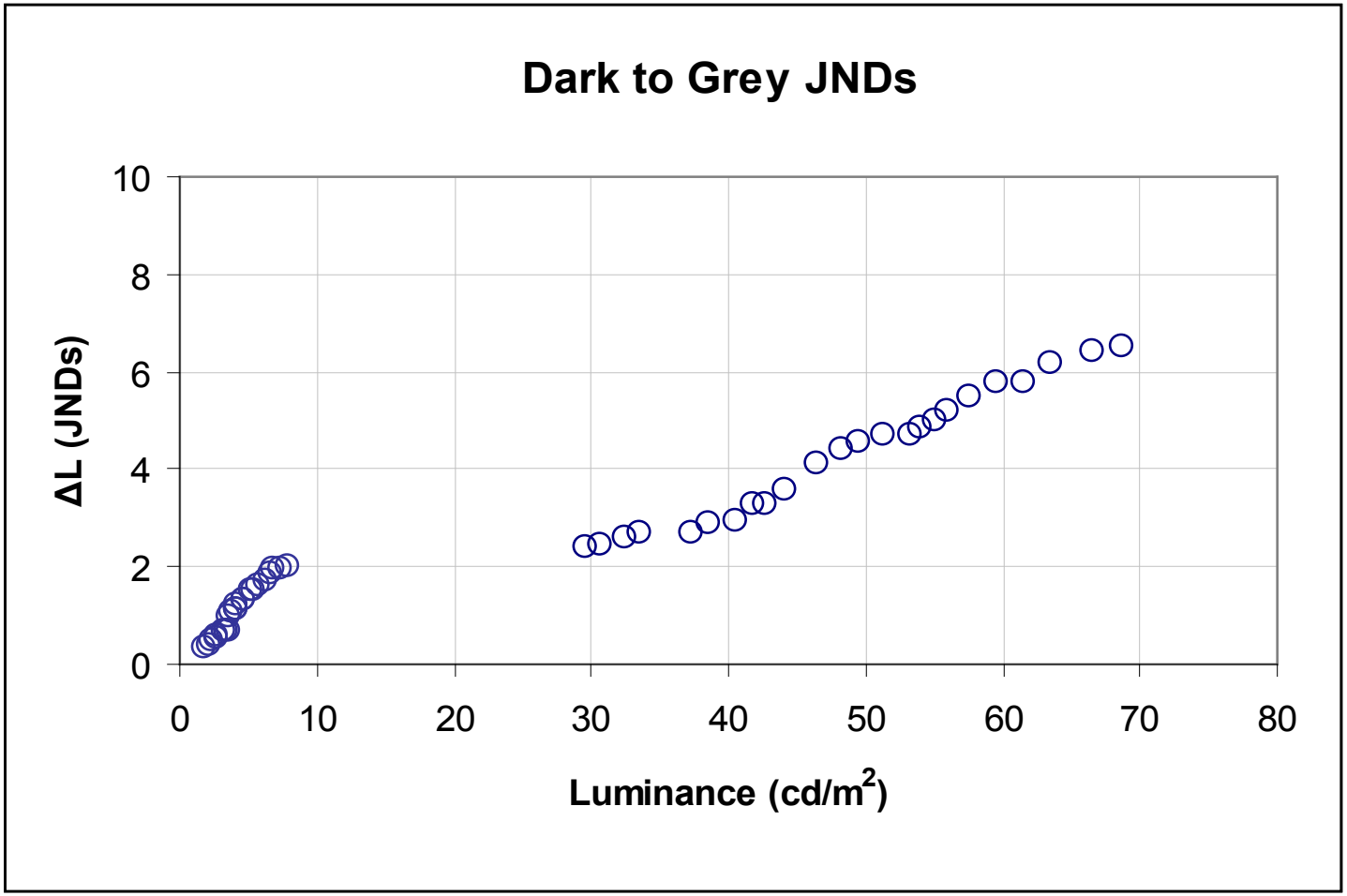
Kwame F. Baah
University of the Arts London, UK

Phil Green
Gjovik University College, Norway

Experiment:

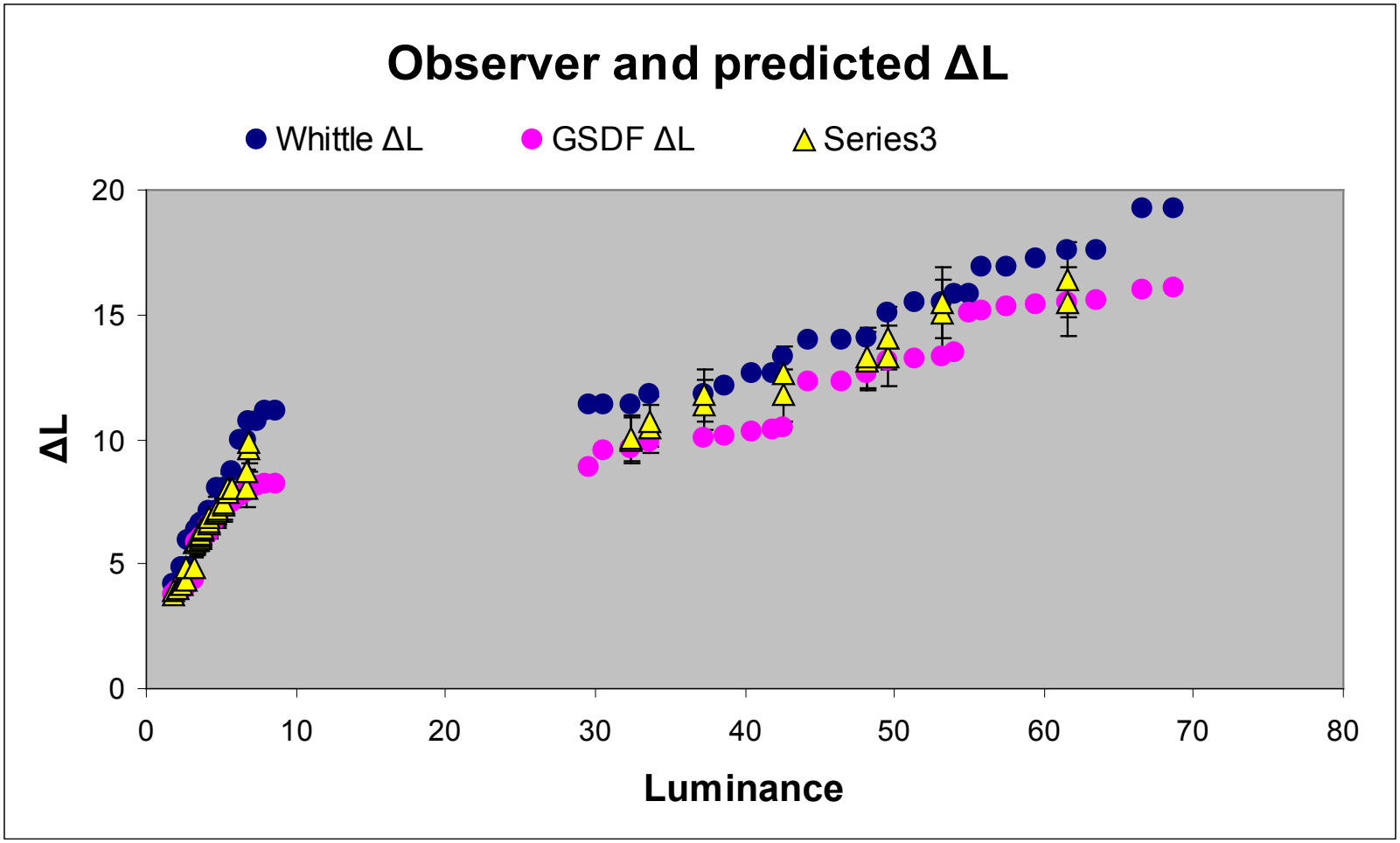
- **EIZO monitor in different white point luminance levels 282-165 cd/m^2**
- **3 reference neutral colours, 24 samples varying in hue, lightness and chroma**
- **23 observers – NHS, Web & Graphic Designers, Colour Science Students.**

Target observation JNDs



Observer detected JNDs for targets in the dark and mid-grey regions for white points of 165.5 - 282.2 cd/m².

Observations compared with predictions of Whittle and GSDF functions



JNDs

DARK TARGETS		
cd/m2	**W**	**GSDF**
282.3	**17.59**	**22.49**
229.2	**6.32**	**8.02**
165.5	**4.85**	**7.33**

STRESS	
W	GSDF
27.7	28.3

GREY TARGETS		
cd/m2	**W**	**GSDF**
282.3	**7.10**	**6.13**
229.2	**6.32**	**6.20**
165.5	**4.85**	**6.41**

STRESS	
W	GSDF
28.1	29.0

International Color Consortium®

Medical Imaging WG

Nov 18, 2013 · Vancouver, BC · Canada

Multispectral Imaging and IccLabs

Max Derhak
Principal Scientist, Onyx Graphics Inc.

Agenda

- Introduction to Multi-Spectral Imaging
- Color Management and some of its Challenges
  - Aspects of Color Science
- Introduction to ICCLabs
  - Touching upon some technical details
- A color managed spectral workflow example
- Conclusion
  - Discussion about benefits and considerations

Multi-spectral Images

- A multi-spectral image is a collection of several monochrome images of the same scene, each of them taken with a different sensor and/or using a different light source.
- Each image is referred to as a *band*.

Uses of Multi-Spectral Images

- An accurate representation of human visual appearance of elements in the scene can be determined
  - *What does it look like when …?*
- Material characteristics of elements in the scene are often determined
  - *How do the materials interact with light?*
  - *What are they or what is the probability that they are …?*
- Traditionally, color management generally considers the first two questions
- For some medical imaging applications the last question is often the most important

ICC Color Management

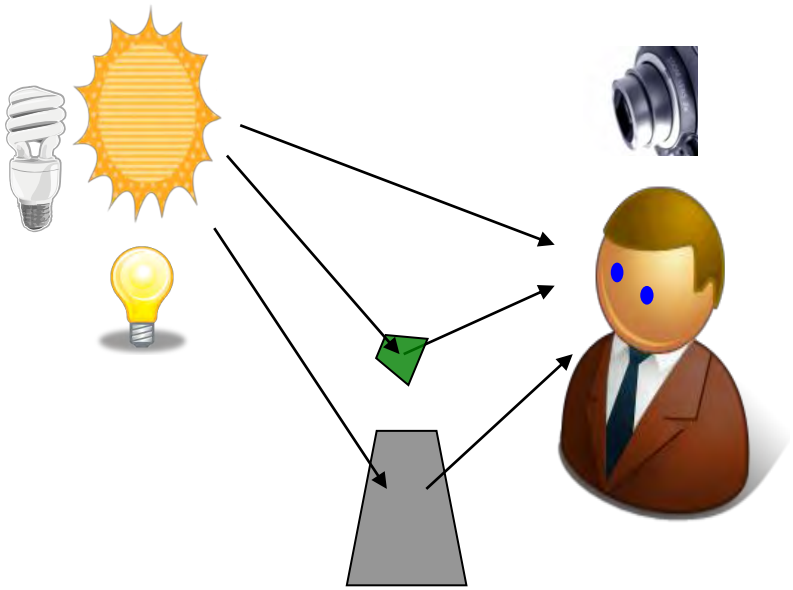
- The purpose of the ICC is to promote the use and adoption of open, vendor-neutral, cross-platform color management systems

- With “Color Management” being defined as the “**communication of** the associated **data** required for unambiguous interpretation of color content data, **and application of** color data **conversions**, as required, **to produce** the **intended reproductions**”

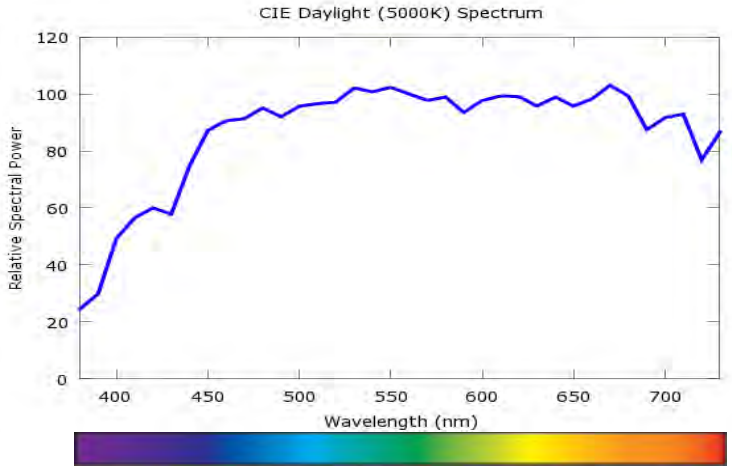
- Its about “communicating color”

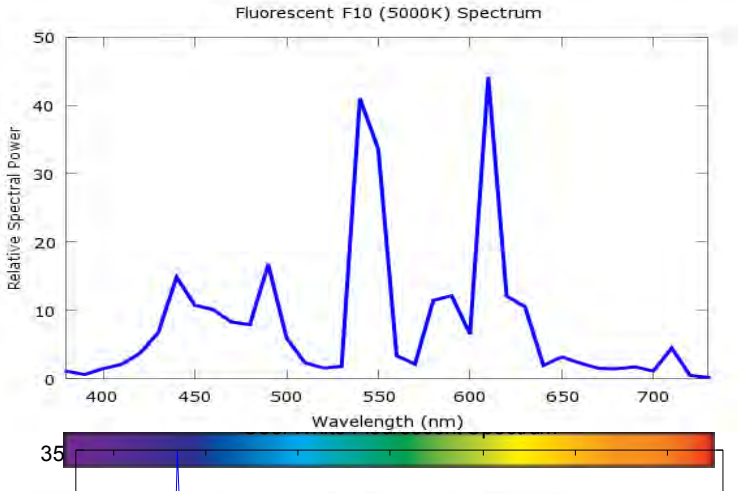
Challenges for Color Management

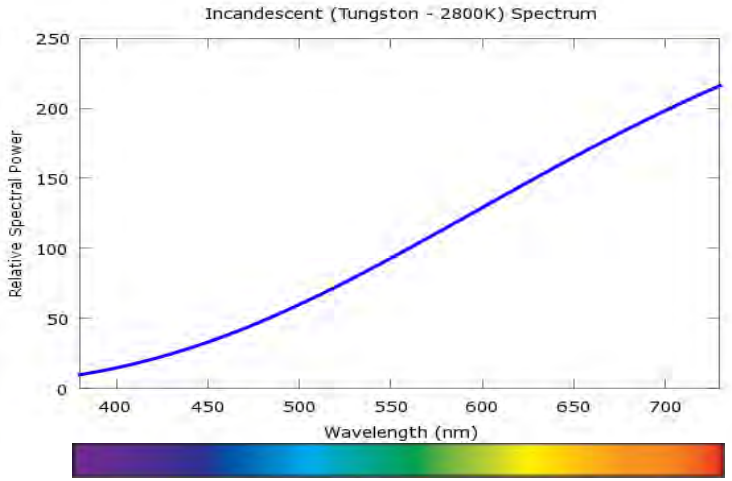
- Different Light Sources
- Characteristics of Surfaces
- Variations in Observer
- Modeling Everything
- Variations in Reproduction Intent

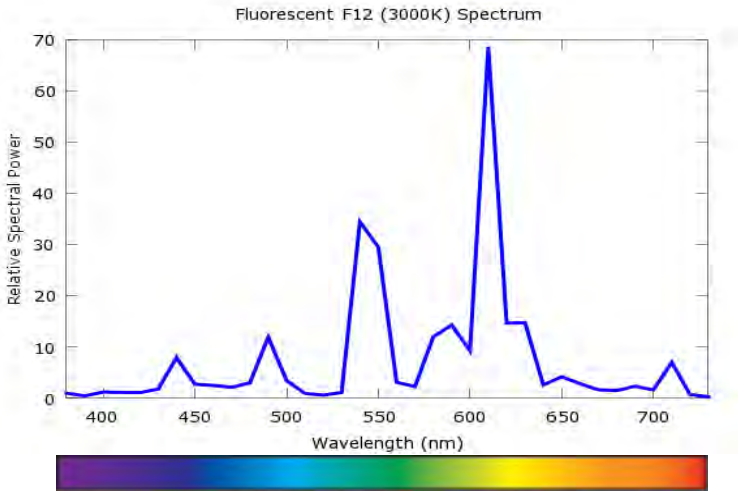


Differences in Light Sources

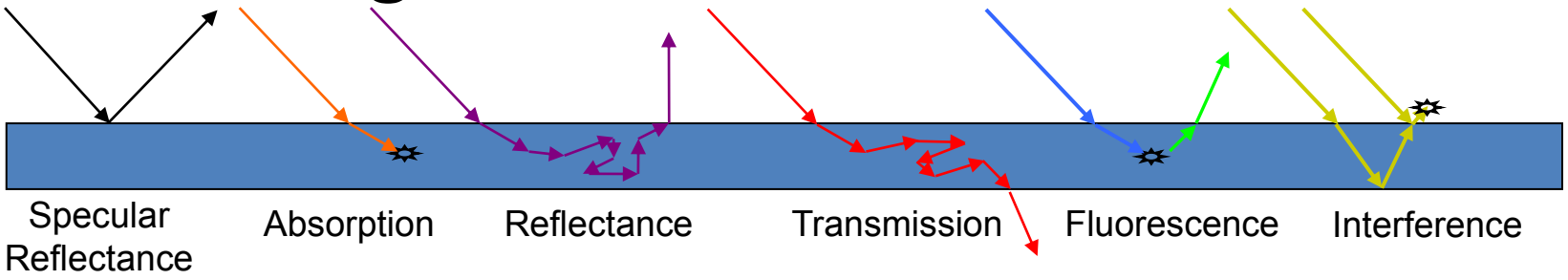








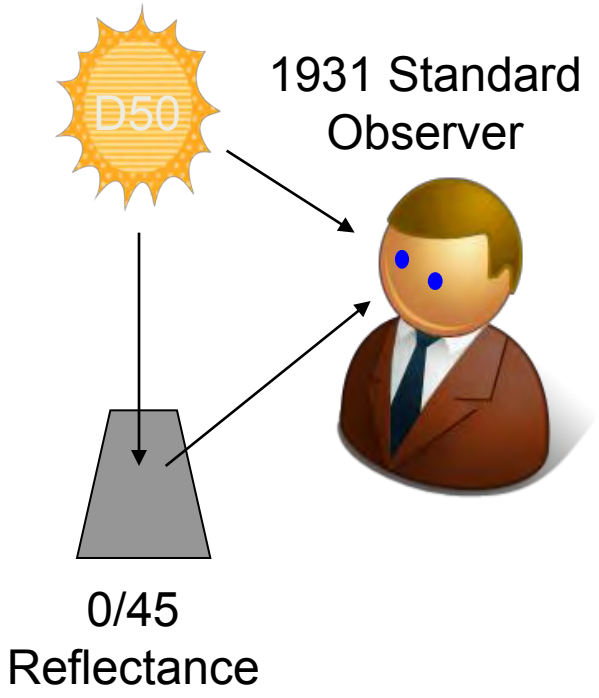
Light-Surface Interactions



- **Specular Reflectance -** light bounces off surface at the opposite angle unchanged (gloss)
- **Absorption** – light enters surface, bounces around and is absorbed – thus raising the energy level of the surface (e.g. thermal heat)
- **Reflectance/Transmission** – light enters surface, bounces around, and eventually leaves surface unchanged at possibly an arbitrary angle
- **Fluorescence** – light enters surface, bounces around, is absorbed and then re-emitted with a longer wavelength (at a lower energy level), bounces around, and eventually leaves (either) surface.
- **Interference** – light enters surface bounces from opposite service where it interferes (constructively or destructively) with light just hitting surface (exhibiting angular dependency)

- **Note***: How a photon interacts with a surface is wavelength dependent*

ICC.1 Color Management Simplifications



- ICC.1 color management simplifications:
  - Fixed Profile Connection Space (PCS) Viewing Conditions
    - D50 Illuminant
    - 500 lx
  - Simple Reflectance Model
    - Flat surface
    - 0/45 geometry
    - No gloss
    - No Fluorescence
  - Standard 1931 Observer
  - Explicit Transforms…

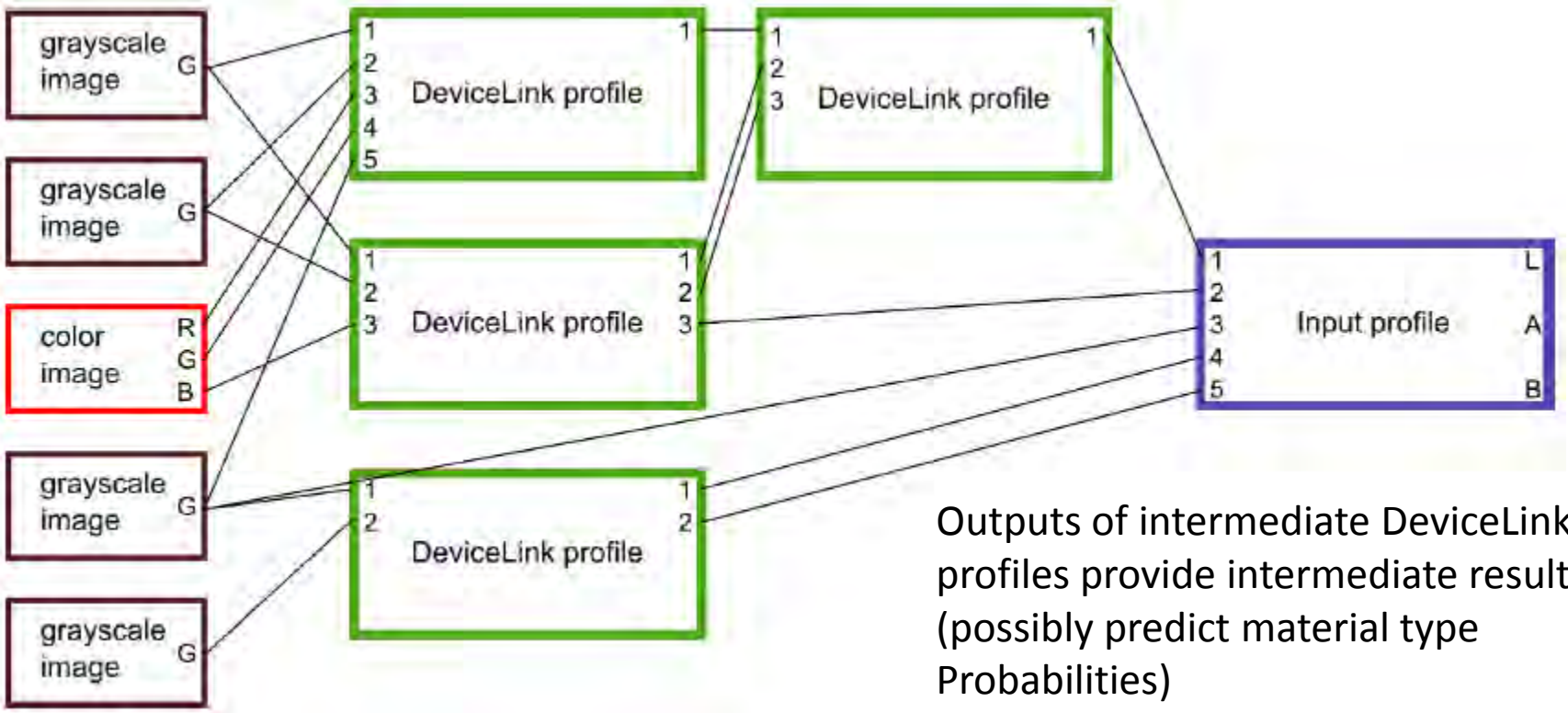
Note: Other Illuminants can be indirectly represented. However, color data in profile MUST always be converted to these viewing conditions for processing by the CMM.

Answering MI Questions with ICC Profiles

Answering these questions using legacy ICC.1 profiles become problematic:

1. What does it look like when…?
   - "Look" is communicated using device independent colorimetric Profile Connection Space (PCS)
   - PCS is limited to D50 illuminant and Standard 1931 2-degree observer
2. How do the materials in the scene interact with light?
   - No spectrally defined PCS
   - No clear/efficient way to encode transforms
   - Limited number of channels can be encoded
3. What are the materials or what is the probability that the materials are …?
   - No PCS needed - can be accomplished using DeviceLink profile
   - Accuracy is limited when input dimensionality is greater than 4 channels

Potential Workflow using ICC.1



Outputs of intermediate DeviceLink profiles provide intermediate results (possibly predict material type Probabilities)

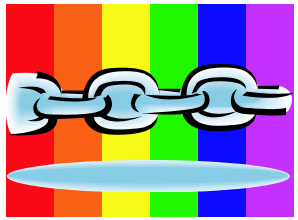
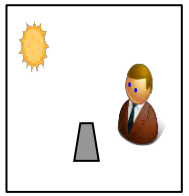
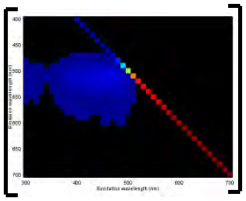
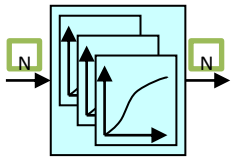
Note: Based on Dicom WG26 multi-spectral state proposal (from Bas Hulsken)

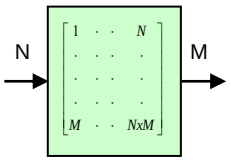
Going Forward with IccLabs

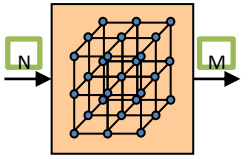
- The main goals of IccLabs address several color management challenges
  - Overcoming limitations of current transforms with D50 colorimetry
  - Adding flexibility and extendibility
- Resulting in a new profile specification and profiles
  - New Color Management Module (CMM) will be backwards compatible with V2 and V4 profiles
  - New profiles (V5) not expected to be compatible with older CMMs
- ICC will provide a reference implementation of an IccLabs based parser and CMM - RefIccLabs

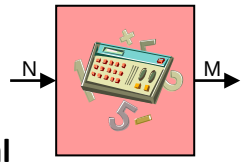
IccLabs – Overview

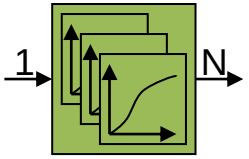
- PCS Extensions
  - **Spectral profile header extensions**
  - **Profile Connection Condition (PCC) tags**
  - **PCS Transforms**
  - **Sparse matrix encoding**
- multiProcessingElements
  - **1-D Look Up Tables (LUTs)**
  - **Matrices**
  - **N-dimensional LUTs**
  - **Calculator element**
  - **ICC Color Appearance Model element**
  - **Tint Array element**
- Hierarchical tag types
  - **Named Color Tag Array**
  - **Support for angular dependencies via Bidirectional Reflectance Distribution Functions (BRDF)**
  - ***Profile Sequence Information***
- Other Extensions
  - **Color Space Encoding profiles**
  - **Gamut Boundary Description encoding**
  - ***Color Measurement (CxF) tag encoding***
  - ***UTF8 text & UTF16 encoding***
  - ***Additional Numeric Array Types***

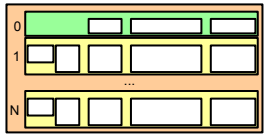





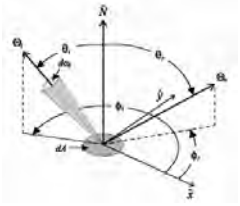
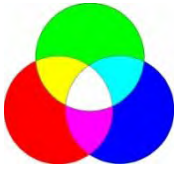
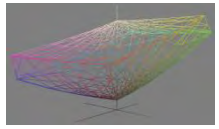






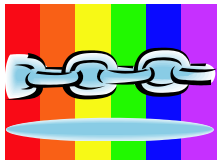




CxF

Flexible PCS Support



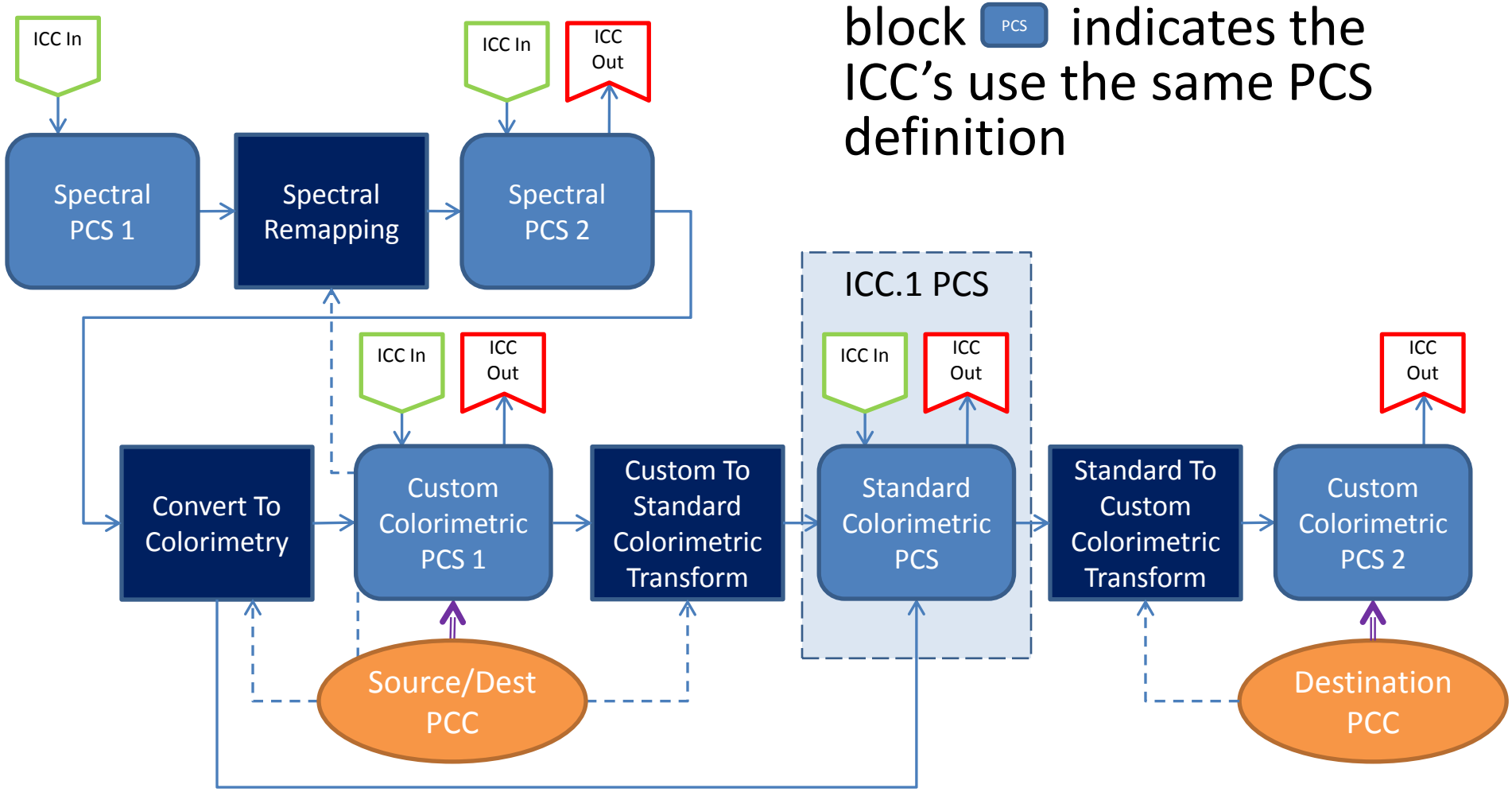
ICC.1 PCS Support

	From Lab	*From XYZ*	*From Reflectance*	*From Transmittance/ Transmissive*	*From Radiant/ Emission*	*From Fluorescence*
To Lab	Yes	Yes	Using PCC	Using PCC	Using PCC	Using PCC
To XYZ	Yes	Yes	Using PCC	Using PCC	Using PCC	Using PCC
To Reflectance	No	No	Yes	Yes	Extract PCC illuminant	Apply then extract PCC illuminant
To Transmittance/ Transmissive	No	No	Yes	Yes	Use PCC illuminant	Apply then extract PCC illuminant
To Radiant / Emission	No	No	Apply PCC Illuminant	Apply PCC illuminant	Yes	Apply PCC illuminant
To Fluorescence	No	No	No	No	No	Exact match required

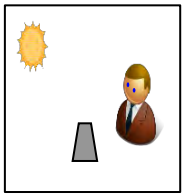
PCC = Profile Connection Conditions

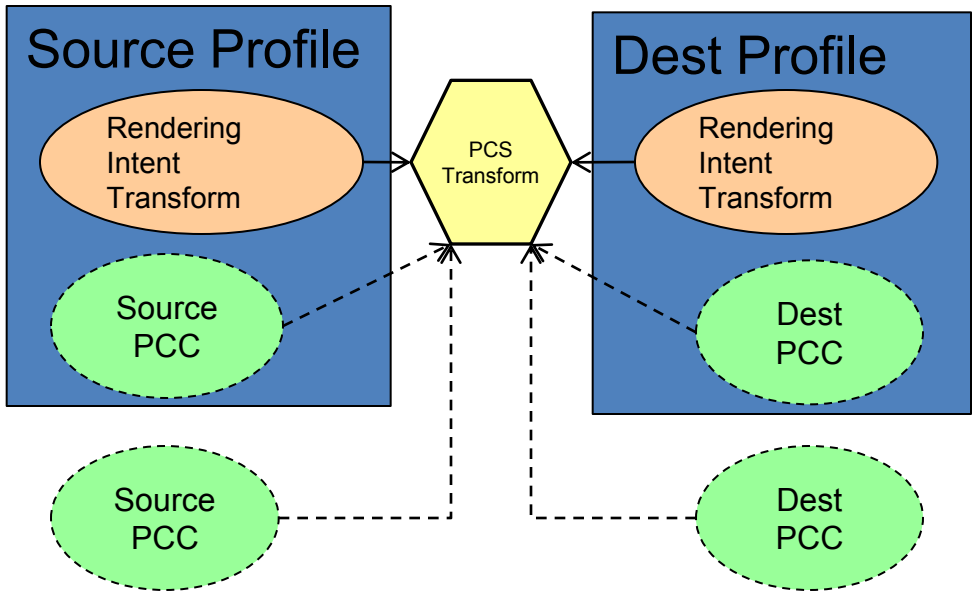
PCS Conversion

- Connect any ICC In to any ICC Out
- Connection to same PCS block PCS indicates the ICC's use the same PCS definition



Profile Connection Conditions





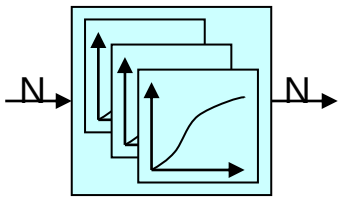
Allows PCS data in profiles to use actual viewing conditions

No need for chromaticAdaptationTag!

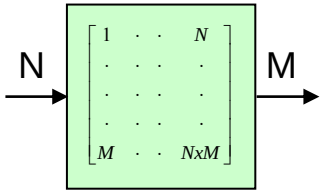
- Profile Connection Conditions comprise of:
  - Color space and spectral PCS metadata in header
  - **spectralViewingConditionsTag**
  - **customToStandardPcsTag**
  - **standardToCustomPcsTag**
- Spectral and custom colorimetric PCS processing is performed using Profile Connection Conditions (PCC)
- PCC information can come from either the profile or externally provided to the Color Management Module (CMM)
- Profile Connection Conditions are NOT required for legacy colorimetric PCS processing

Processing with multiProcessElements

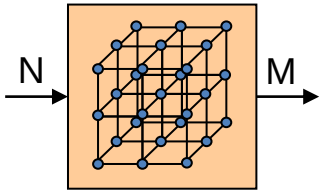
- Allows processing workflows to be defined using an arbitrary order of flexible processing elements with 32-bit floating point processing
- Completely defines transformations from input to output



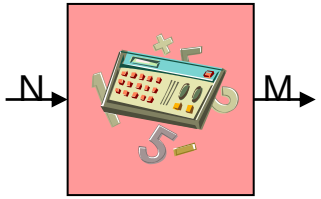
1-D LUTs



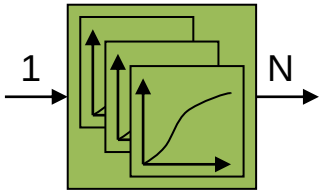
NxM Matrix



Multi-Dimensional LUT



Programmable Calculator



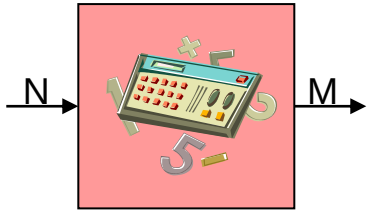
Tint Curves

Color Appearance Model

Placeholder

Programmable Calculator Element

- Provides mechanism for encoding more complex (non-linear) device models
  - Avoids limitations of Color Look-Up Table(CLUT) input channel dimensionality
  - Possible to embed and use other processing elements
  - Results in smaller potentially more accurate profiles



- Defines a script based expression calculator to determine output channels based upon input channels
  - Uses a sequence of operations that apply to an Reverse Polish Notation (RPN) argument stack
  - Finite memory storage for temporary results
  - Nearly all operations are vector based (operating on multiple channels at same time)
  - Secure deterministic behavior

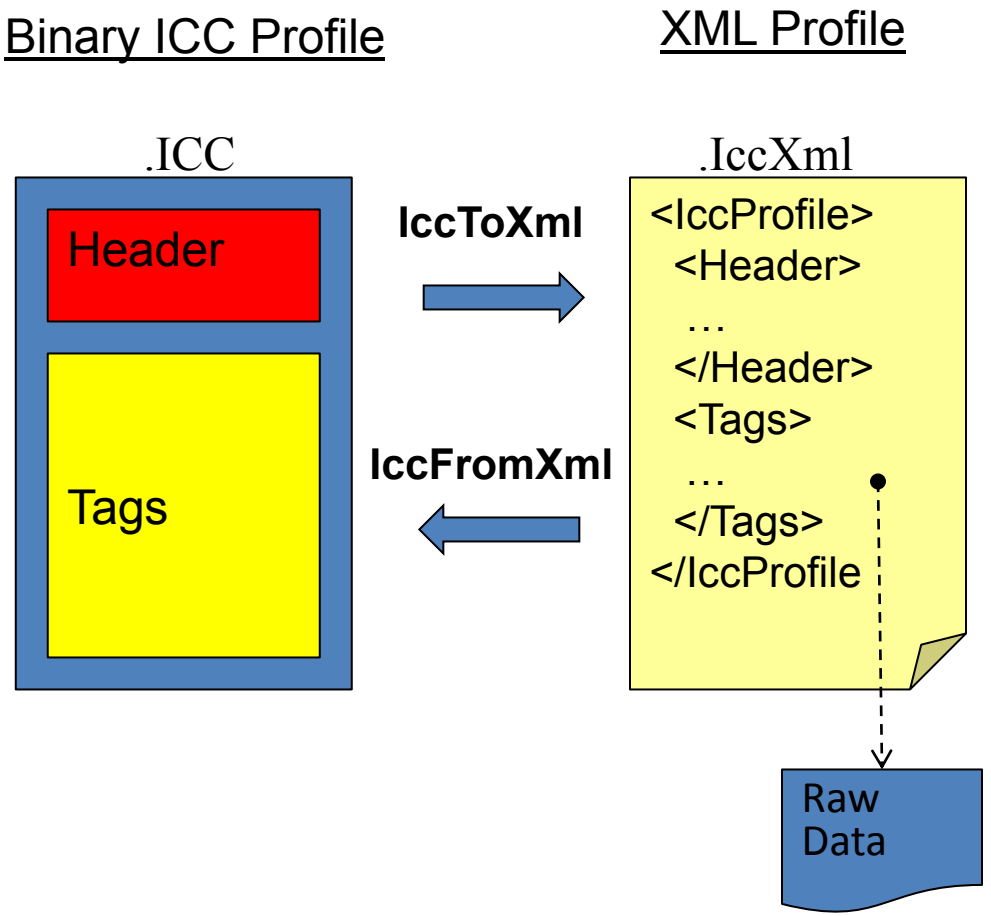
IccLabs General Profile Contents

- Display / Device / Color Space Profiles
  - Header (with spectral PCS)
  - Metadata Tags
  - *Profile Connection Conditions Tags*
  - *Colorimetric Transform Tags*
    - AtoBx / BtoAx : *lut8, lut16, lutAtoB, lutBtoA, multiProcessElementType*
  - *Spectral Transform Tags*
    - DtoBx / BtoDx : *multiProcessElementType*
- *Note 1: PCS and Spectral PCS entries in header determine whether colorimetric and/or spectral transform tags are needed*
- *Note 2: Profiles are valid when only relative or absolute transforms are present*
- Device Link Profiles
  - Header
  - Metadata Tags
  - Transform Tags
    - AtoB0 : *lut8, lut16, lutAtoB, multiProcessElementType*
- *Named Color Profiles*
  - Header (with spectral PCS)
  - Metadata Tags
  - Profile Connection Conditions Tags
  - Transform Tag
    - Named Color Table : *namedColorTagType, tagArrayType(namedColorArray)*
- Stadard Color Space Encoding Profiles
  - Minimal Header
  - Encoding Space Type (and Name)
  - *Optionally override color space encoding parameters : tagStructType*

RefIccLabs

- Provides a C++ reference implementation of profile manipulation and application proposed by IccLabs specifications
- Simultaneously supports both binary and XML representations of profile data

- Libraries and tools
  - IccProfLib (.ICC)
    - IccApplyNamedCMM
    - IccApplyProfiles
    - IccDump
    - wxProfileDump
  - IccLibXml (.IccXml)
    - IccFromXml
    - IccToXml



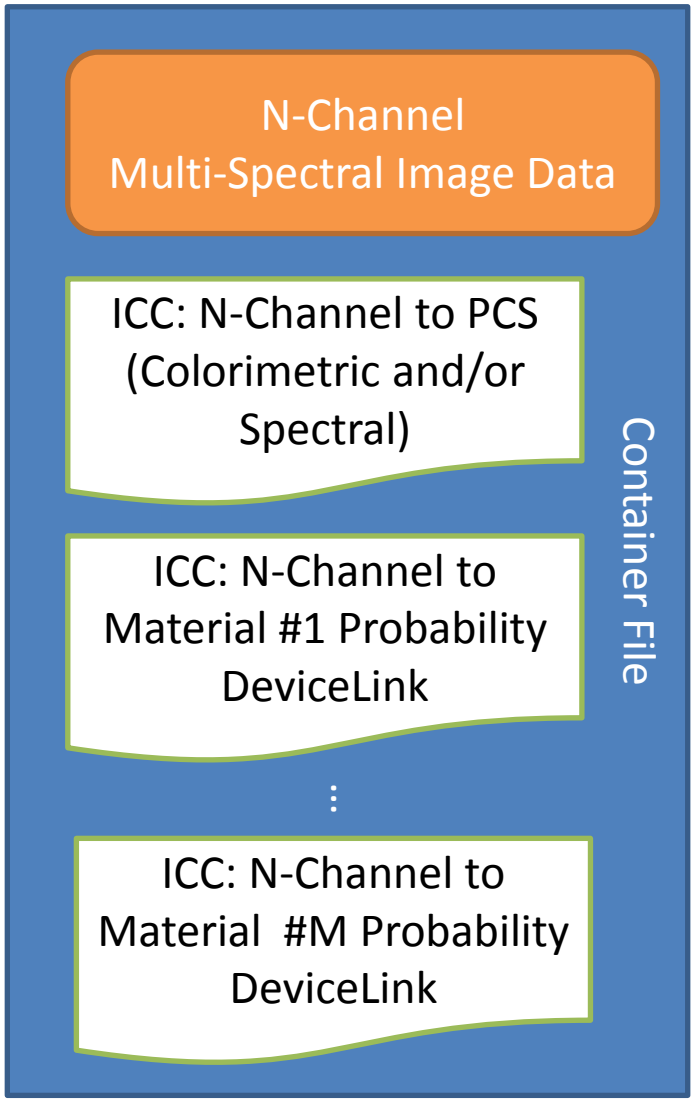
Benefits/Opportunities with IccLabs

- Spectrally based workflows
  - Communicate and account for physical properties of light and surfaces
  - Handle variability in lighting and observer
- Flexible processing elements
  - Enable more complex device models
  - Allow color/vision science to be directly encoded in a profiles
- New data structures, data types and profile class
  - Provide for Named Color specification flexibility
  - Allow for complex data relationships to be easily encoded
  - Allow for easier future extendibility
  - Simplifications for standard color encodings

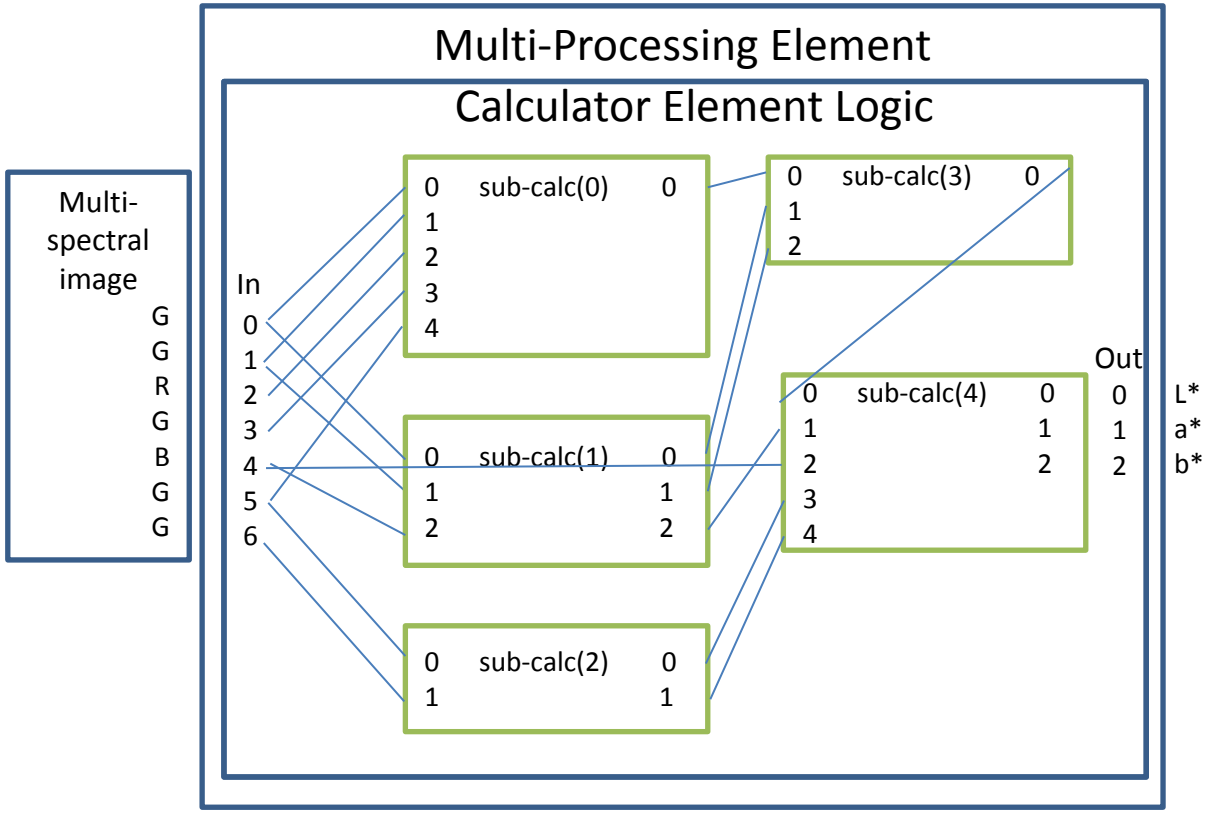
Multi-Spectral Examples

Multi-Use Multi-Spectral Data

- Different questions can be answered by providing different profiles for the same multi-spectral image data
  - All profiles take all same N-Channels as input
  - Output of each profile depends upon use case



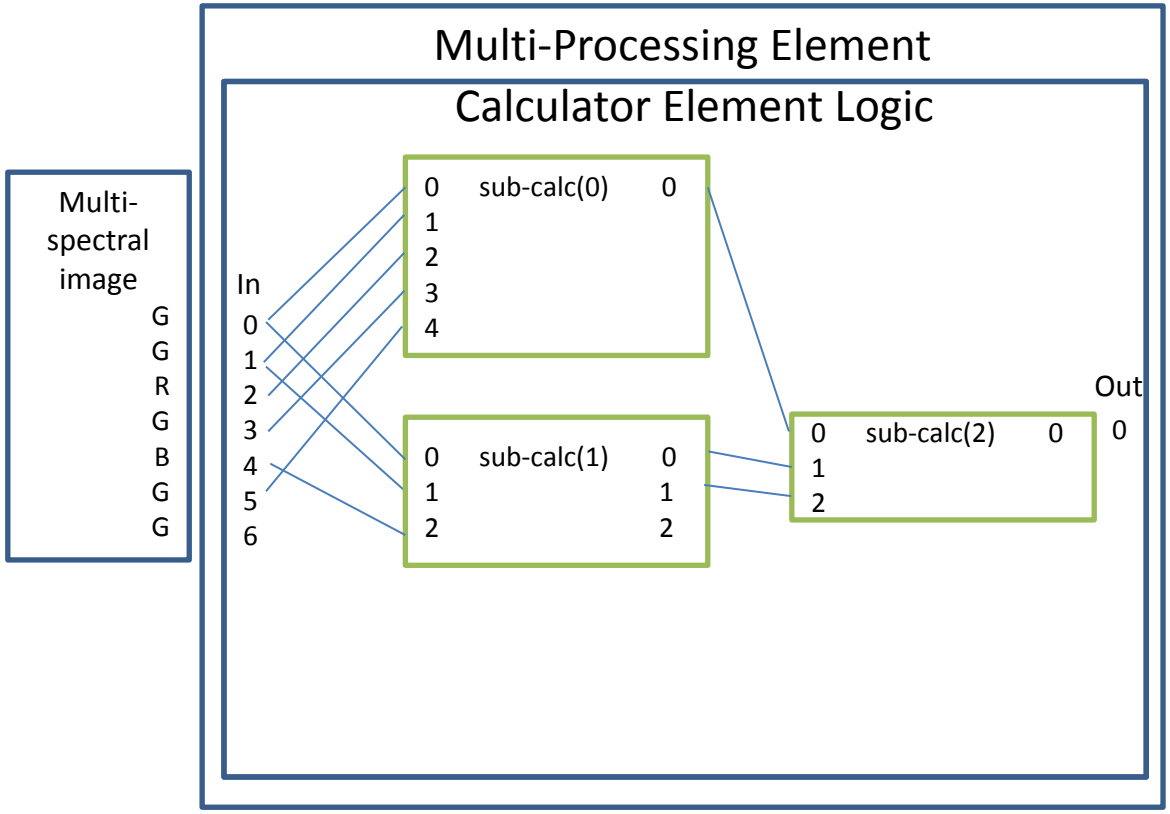
Example Calculator Element Colorimetry



Calculator Element Script

```
in(0,4)
in(5)
calc(0)
tput(0)
in(0,2)
in(4)
calc(1)
tput(1,3)
in(5,2)
calc(2)
tput(4,2)
tget(0,3)
calc(3)
copy
tput(6)
tget(3)
in(5)
tget(4,2)
calc(4)
out(0,3)
```

Example Calculator Element DeviceLink



Calculator Element Script

```
in(0,4)
in(5)
calc(0)
tput(0)
in(0,2)
in(4)
calc(1)
tput(1,3)
tget(0,3)
calc(3)
out(0)
```

Conclusions

Industries that can possibly benefit by ICCLabs

- Medical Imaging
- Fine Art Reproduction
- Motion Picture and Video Industries
- Academic Research
  - Color Science
  - Vision Science
- Industrial Color

Considerations for Medical Imaging

- It should be noted that ICC V2/V4 profiles could work
  - For conventional RGB based imaging workflows
  - Connecting various DeviceLink profiles to process mulit-spectral information (but requires external logic to make connections)
- Possible advantages from IccLabs
  - Colorimetric imaging
    - Use PCS based upon illuminant (actual monitor white point) used by medical industry (other than D50)
  - Spectral imaging
    - Use of Spectral PCS to communicate how light reflects off surfaces
  - New processing elements
    - Direct modeling in profile (possibly smaller more accurate profiles)
    - Use in DeviceLink profile to convert multi-spectral information directly into material type probabilities (No external logic needed)
  - More resources for Smart CMM's to do a better job

Thank You!

Questions?