
FDA Research and Scientific Issues in Digital Pathology

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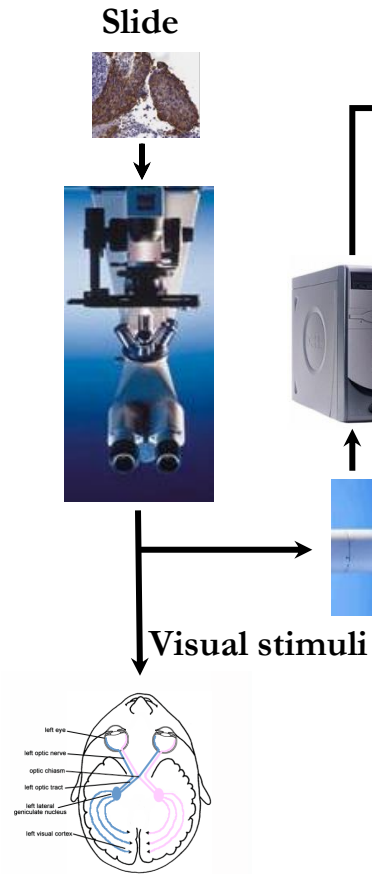
Office of Science and Engineering Laboratories

Center for Devices and Radiological Health, U.S. FDA

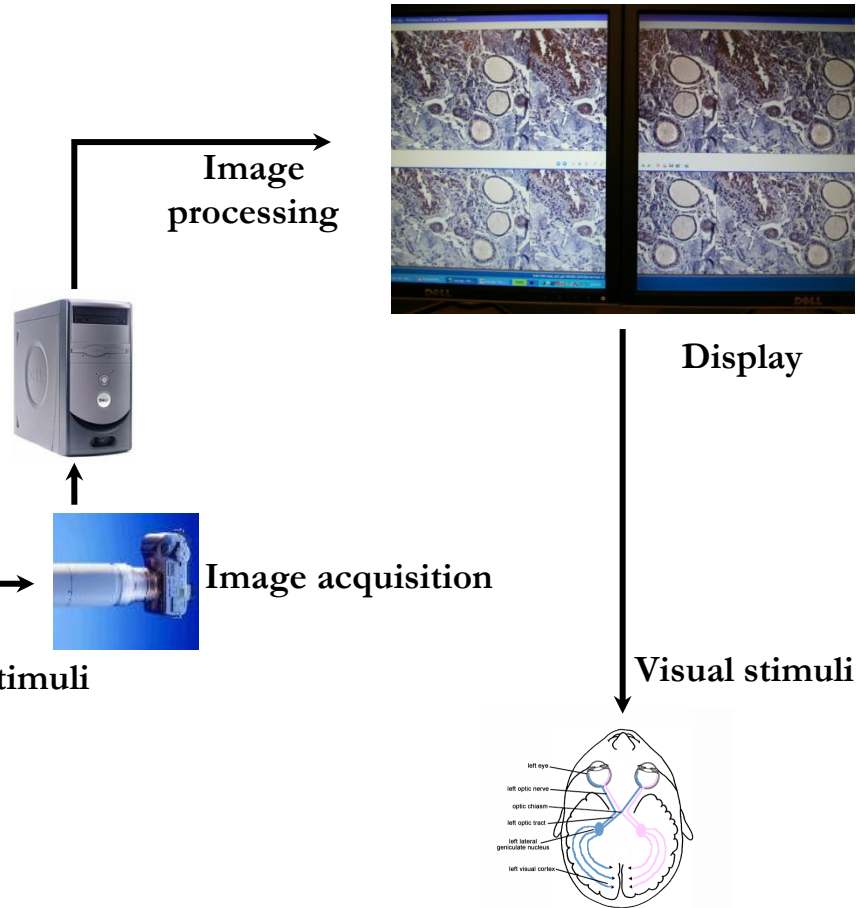
Content

- Challenges in the evaluation of digital pathology systems and hardware.
- From optical to digital: Parallel with migration from analog to digital radiology.
- How to leverage laboratory measurements to ensure the safety and effectiveness of Digital Pathology Whole Slide Imaging (WSI) for routine surgical pathology?
- Current research efforts at CDRH.

Optical Microscopy



Digital Microscopy



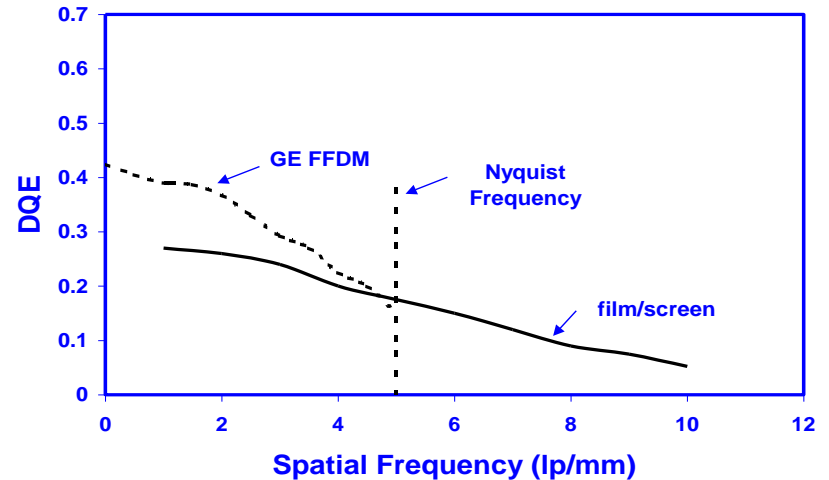
Partial list of technical specifications for a digital WSI surgical pathology system

- Scanning magnification
- Stitching (physical dimensions)
- Resolution and focusing
- Luminance and contrast
- Color Fidelity
- Image Enhancement
- Compression, file format, storage
- Light source (type, auxiliary elements, collection lens, field diaphragm, filters, polarization, diffuser, spectral output)
- Condenser
- Focal length
- Aberrations
- Optical transfer function
- Spectral transmittance
- 3D Positioning (tiling, Z-plane)
- Noise
- Linearity
- Dynamic range
- Spatial resolution
- Spatial uniformity
- White balance
- Exposure/shutter control
- Analog-digital conversion
- Image size/Sub-sampling
- Auto-focusing
- Compression method and ratio
- Color Management
- Display (luminance, contrast, bit-depth, resolution, uniformity, color gamut, angular response, temporal response, environment, calibration/QA/QC)

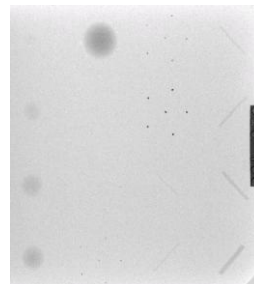
Similarities with transition from analog to digital radiology systems

■ Laboratory measurements

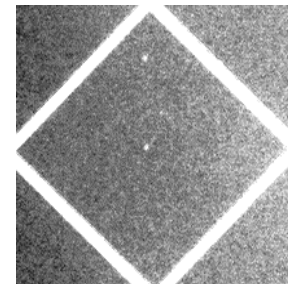
- resolution
- noise
- artifacts



■ Preclinical images (phantoms)



ACR/MAP detectability phantom



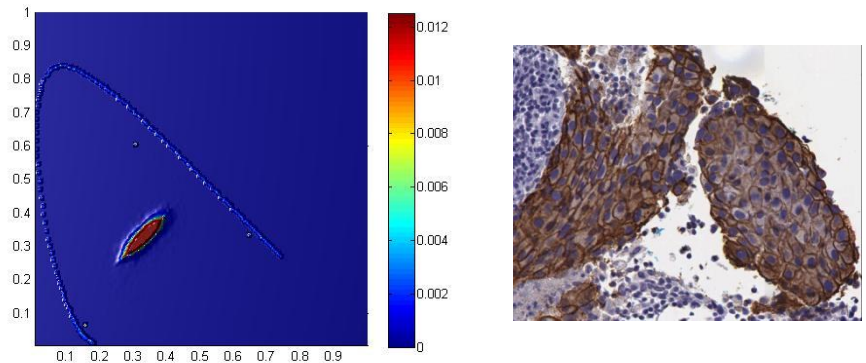
CDMAM contrast detail phantom

Transition from optical to digital WSI surgical pathology system

■ Laboratory measurements

- resolution
- noise
- artifacts
- color
- dynamic range
- Z-axis

■ Preclinical images (phantoms)



Color Statistics of HER2 expression tissue slides as percentage of the CIEXYZ color gamut



Current research efforts and initiatives

- Evaluation methods for medical displays
- Reader studies and variability in digital pathology
- Partnership with stakeholders:
 - American Association of Physicist in Medicine
 - Task Group #196 on “Color Medical Displays”
 - International Electrotechnical Commission
 - Technical Committee 62B “Medical Devices”, Team 51
 - NCI Tissue Array Research Program
 - Variability due to scanner type
 - Biological Stain Commission
 - Variability in staining as seen by WSI systems
 - Hematology Laboratory, NIH Clinical Center
 - Methods for multi-spectral 3D digital pathology for myeloma

Case study: WSI display systems

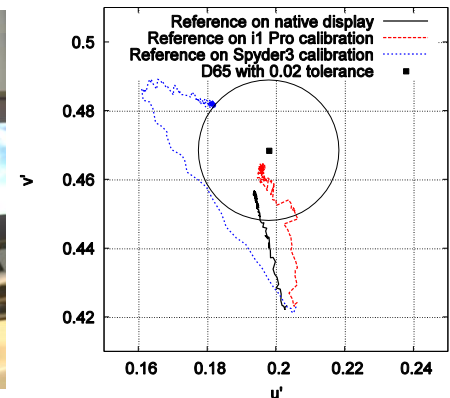
■ Color gamut: accuracy and consistency

- ❑ Gamut is the range of realizable colors by a device
- ❑ Depends on device, acquisition and viewing conditions

■ Calibration color kits (CCK) are used and recommended, but: How to evaluate CCKs?



Three color kits being tested in FDA's display evaluation laboratory (adapted from Cheng and Badano, Proc SID, 2011).



Spectroradiometer and results for grayscale tracking using different color calibration kits (adapted from Suarez et al., Proc Electronic Imaging, SPIE, 2012).

Other issues

- Image size
- Dynamic range
- Z-stack
- Ambient illumination
- Intra-/inter-scanner variability on image quality

Summary

- Need new standard methodologies for assessment.
- Consensus development with stakeholders, professional and standardization organizations.
- Our research informs guidance development process for WSI surgical pathology.
- Similarities with analog-to-digital radiology useful.
- Solid and comprehensive bench test data helps minimize the need for resource-intensive clinical studies.