MDDT SUMMARY OF EVIDENCE AND BASIS OF QUALIFICATION DECISION FOR IMAGE VIEWER INTEGRITY EVALUATION SYSTEM FOR WHOLE-SLIDE IMAGING DEVICES

BACKGROUND

MDDT Name: Image Viewer Integrity Evaluation System (IVIES)

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Wei-Chung Cheng, PhD
Office of Science and Engineering Laboratories
Center for Devices and Radiological Health
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
Email: Wei-Chung.Cheng@fda.hhs.gov

TOOL DESCRIPTION AND PRINCIPLE OF OPERATION

The *Image Viewer Integrity Evaluation System (IVIES)* for whole-slide imaging devices is a Non-clinical Assessment Model (NAM), software tool that measures the output differences between two pathology whole slide image (WSI) viewing software devices. The IVIES compares the images generated by two devices and reports their pixelwise differences. The IVIES can be used to assist with assessing whether a third-party pathology WSI viewing software device ("third-party viewer") can decode the same input image file and display pixelwise identical images when compared to the predicate WSI device image review manipulation software ("predicate IRMS").

The IVIES analyzes image datasets generated by both devices displaying the same WSI files across multiple regions of interest, magnification levels, and tissue specimens. The IVIES performs colorimetric analysis using standard color space conversions (CIEXYZ and CIELAB) and calculates pixelwise color differences with the CIEDE2000 standard. Based on FDA-established tolerance thresholds, IVIES determines whether images are identical and generates a structured analysis report including dataset table of contents and comparison results.

QUALIFIED CONTEXT OF USE

The Image Viewer Integrity Evaluation System (IVIES) is a software tool qualified to assist with assessing whether a pathology whole slide image viewing software device can decode the same input image file and display pixelwise identical images when compared to the predicate whole slide imaging device image review manipulation software. The IVIES tool quantitatively measures the differences between two images by calculating their colorimetric difference for each pixel. The colorimetric pixel differences can be used as a quantitative measure to compare the performance of two whole slide image viewing software devices and to determine whether additional clinical study data is needed to further characterize the performance of the device. IVIES is not suitable for evaluation of third-party viewers that intentionally alter the image rendering or the downstream components such as the computer environment or the display system.

SUMMARY OF EVIDENCE TO SUPPORT QUALIFICATION

a. Reliable predictions of the device performance using ΔE_{00}

The colorimetric measurement ΔE_{00} used in the MDDT provides reliable predications of any pixel-level differences between the predicate IRMS and the third-party viewer. Consider the 8-bit sRGB color space, which contains $256^3 = 16{,}777{,}216$ distinct RGB datapoints. By exhaustive calculation of color differences between all adjacent datapoints in the three-dimensional sRGB space, the smallest color difference was found to be 0.0064 ΔE_{00}, occurring between the RGB values (0,255,253) and (1,255,253). This finding establishes that the ΔE_{00} metric can successfully differentiate even the most challenging scenario: comparing two images that are identical except for a single pixel pair: (0,255,253) and (1,255,253).

b. Correlation between image quality degradation and ΔE_{00}

To investigate the correlation between image quality degradation and the ΔE_{00} metric, the experiment illustrated in Figure 6 was conducted. In total, 48 images from 8 slides, 3 ROIs per slide, and 2 magnification levels per ROI were prepared to represent the original images generated by the predicate IRMS. The 48 images were compressed using the JPEG compression algorithm with various quality factors (a value, *Q*, between 0 and 100 where 100 is the highest quality) to represent the degraded images. The quality factor was adjusted through 100, 95, 90, 85, 80, and 75 to create 6 datasets. Figure 7 shows the ΔE_{00} results of using the MDDT to compare the 6 datasets with the original images. It can be observed that for each image, the ΔE_{00} and Q show perfect negative concordance. This observation was confirmed by the Kendall's Tau correlation as shown in Figure 8. The result is -1±0, meaning that the two variables have perfect inverse correlation for all 48 images.

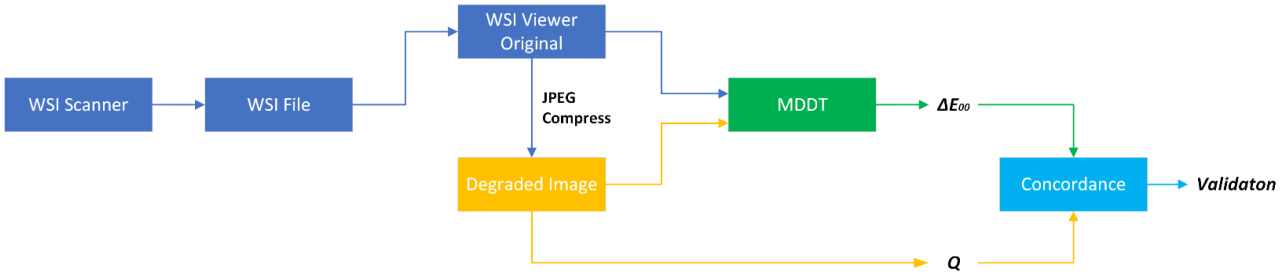

Figure 1: Correlation between image quality degradation and ΔE00.

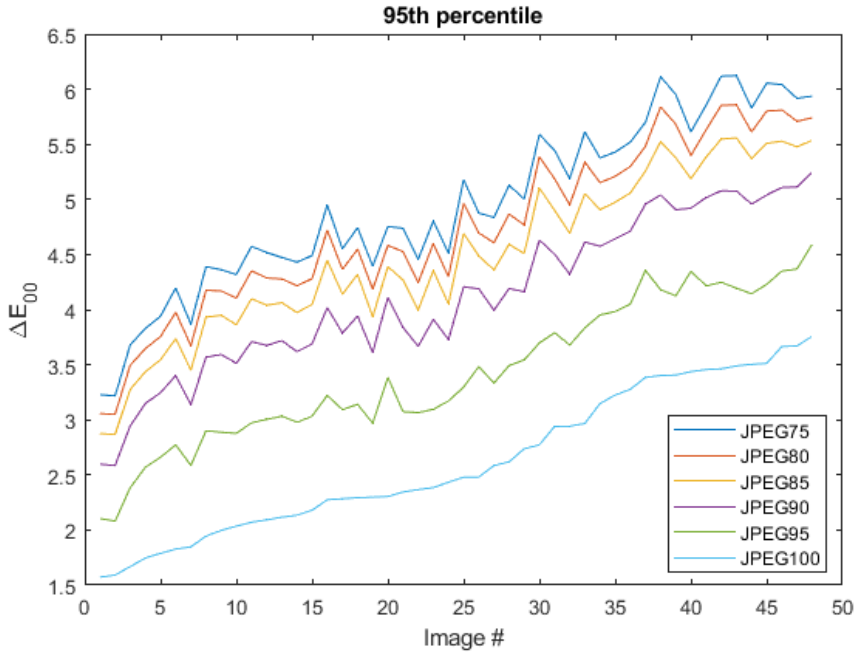

Figure 2: Comparison of the six datasets.

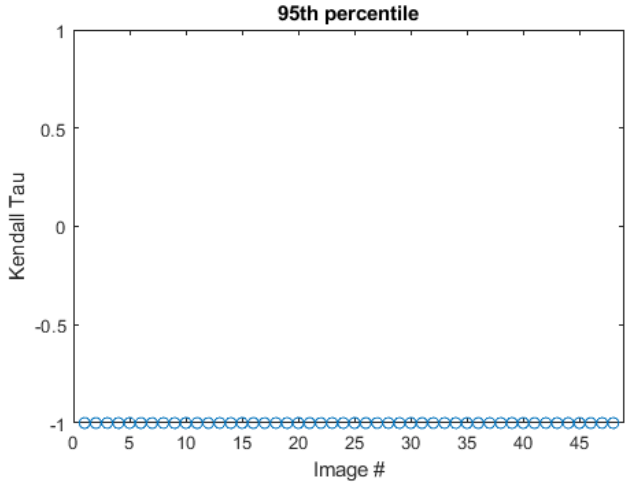

Figure 3: Kendall's Tau correlation coefficients for the 48 images.

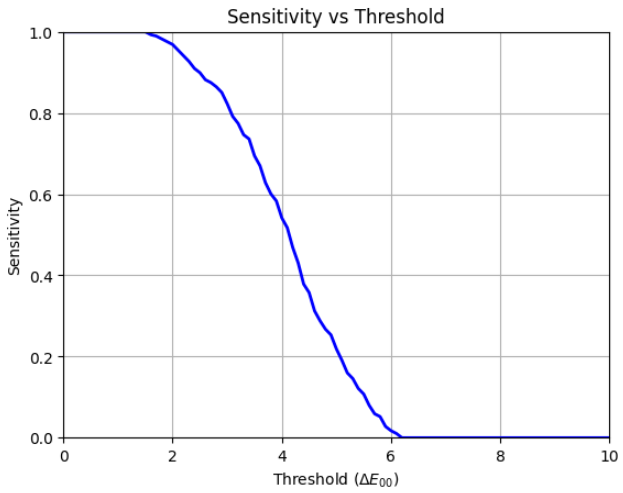

Figure 4: Sensitivity to JPEG compression.

c. Verification of the ΔE_{00} calculation

The correctness of the MATLAB "imcolordiff" function implementing the CIEDE2000 standard had been verified by comparing it with the other tools:

- The MATLAB code shared by the CIEDE2000's creator Prof. Gaurav Sharma[1]
- Bruce Lindbloom's color calculator webpage[2]
- The author's own implementation embedded in the regulatory science tool (RST) published by FDA/CDRH/OSEL[3]

All three comparisons affirmed the correctness of the ΔE_{00} calculation with no errors identified in the calculations.

d. Literature article

The MDDT is partially based on the previous work published in [4, 5].

Discussion of the Evidence Strength to Support Qualification

As shown in Figure 7, if the tolerance is chosen to be 3 ΔE_{00}, all the 6 JPEG-compressed datasets will be classified as "not identical." If the tolerance is increased to 6.3 ΔE_{00}, all the 6 JPEG-compressed datasets will be classified as "identical." In other words, when the tolerance is 6.3 ΔE_{00} or higher, the MDDT cannot detect the JPEG compression anymore. Also note that the smallest ΔE_{00} found in the 6 datasets is 1.6 ΔE_{00}, which is much greater than 0.0064 ΔE_{00}, the smallest color difference in the 8-bit sRGB color space. Figure 9 shows the sensitivity of the MDDT when used to detect JPEG compression in the 6 datasets. In summary, the current evidence demonstrates that the IVIES can determine if images from two whole slide image viewing software are pixelwise identical.

Assessment of Advantages/Disadvantages of Qualification

Assessments of Advantages of Using the MDDT:

- Provide standardized verification/validation tools for devices: The MDDT provides standardized methods for calculating the pixel difference (CIEDE2000) and image difference (95th-percentile) such that performance of different devices can be compared objectively.

[1] https://hajim.rochester.edu/ece/sites/gsharma/ciede2000/
[2] http://www.brucelindbloom.com/
[3] https://github.com/didsr/cpr

- Provide reliable predications about device performance and determine if additional performance studies (e.g. clinical study) is needed: The MDDT provides a well-defined quantitative measure of the pixelwise differences when the third-party viewer cannot reproduce the image identically. Then the sponsor can determine if the pixelwise differences meet FDA expectations, and thus determine if further device development or additional performance studies (e.g., clinical study) is needed. This is expected to reduce the burden of the device development time and cost and on the regulatory review process.

Assessments of Limitations of Using the MDDT:

- Faithful reproduction intent: The MDDT is suitable only for third-party viewers that intend to faithfully reproduce the original whole slide image with respect to the file format specifications or the predicate IRMS. The MDDT is not suitable for evaluating third-party viewers that alter the image rendering for purposes of enhancing the image appearance, reducing storage space, etc. For example, if a third-party viewer intentionally compresses the image using a lossy compression algorithm (e.g., JPEG compression) to reduce file size or data transmission, the third-party viewer may fail the pixelwise comparison test but may still be sufficient for its intended use. In this case, the mitigation is to use other testing methods such as a clinical study to validate the third-party viewer.
- Identical computer environment and display: The MDDT evaluates only the viewer component in the imaging pipeline of a pathology WSI system. The downstream components such as the computer environment and the display are not included in the evaluation. Therefore, the optical image reproduced by the third-party viewer may differ if a different display or computer environment is used. The mitigation is to assure the intended display and computer environment are used with the validated third-party viewer.

CONCLUSION

It is commonly perceived that different WSI viewing software applications should reproduce images in the same file format identically. Consequently, the verification of image reproducibility is frequently overlooked. The MDDT can serve as a validation tool for sponsors to use during their device development phase and assist in preparing performance data for the marketing application submission phase. It also provides a software tool for FDA reviewers to assess the safety and effectiveness of the subject device in faithfully reproducing the original WSI image.

CONTACT INFORMATION FOR ACCESS TO TOOL

The software tool will be available at https://github.com/DIDSR/ivies. Questions or comments concerning this tool may be directed to:

Wei-Chung Cheng, PhD
Office of Science and Engineering Laboratories
Center for Devices and Radiological Health
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
Email: Wei-Chung.Cheng@fda.hhs.gov

REFERENCE

[1] IEC, IEC 61966-2-1: Multimedia systems and equipment-Colour measurement and management-Part 2-1: Colour management-Default RGB colour space-sRGB, 1999.
[2] ISO/CIE, ISO/CIE 11664-4:2019 CIE 1976 L*a*b* colour space, 2019.

[3] ISO/CIE, ISO/CIE 11664-6:2022 CIEDE2000 Colour-difference formula, 2022.
[4] W.-C. Cheng, S. Lam, Q. Gong, P. Lemaillet, Evaluating whole-slide imaging viewers used in digital pathology, Electronic Imaging, 2020 (2020).
[5] W.-C. Cheng, Pixel-wise comparison of whole-slide imaging viewers, Pathology Visions, Oct. 26-29, 2020.