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Review

Current Status of Whole Slide Image (WSI) Standardization in Japan

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A whole slide image (WSI) is a digitized microscopic image that is particularly useful in histochemistry and cytochemistry. Several WSI scanners have been introduced in Japan and all use their own native format. Thus, there is basically no interchangeability. However, the Digital Imaging and Communications in Medicine (DICOM) standard format for WSI has been available since 2010. In this review, the configuration and differences among the native WSI and DICOM formats are examined, and the advantages and issues of DICOM standardization are discussed.

Key words: WSI, DICOM, IHE, standardization

I. Introduction

In histochemistry and cytochemistry, many procedures are performed using histology and cytology slides to evaluate the location, expression, and distribution of biological factors. In this context, there is increasing use of digitized microscopic images referred to as whole slide images (WSIs). In pathological diagnosis, use of a WSI has been shown to not be inferior to microscopic diagnosis [3]. Because a WSI is digital data, it has many advantages over glass slides, including ease of handling, quantification and on screen comparison, using commercial image-analysis software. However, all WSI scanner vendors uses their own native formats for WSI files, and there is basically no interchangeability. Most image analysis software also uses a particular WSI native format and cannot be used for other WSI files. Thus, standardization of WSI file format is required, and Digital Imaging and Communications in Medicine (DICOM) was proposed as a standard WSI format in 2010.

Our university opened the new Narita Hospital next to Narita International Airport in March 2020 (Fig. 1). At this hospital, we use a DICOM-based DPS Viewer (Infinitt Healthcare, Seoul, South Korea) for diagnosis (Fig. 2). In this review, differences in WSI format among vendors and DICOM format are discussed, and the possibility of standardization of WSI format is explored, using the DICOM-based DPS viewer as an example.

II. DICOM and Integrating the Healthcare Enterprise (IHE)

DICOM is a standard that was established by the American College of Radiology (ACR) and National Electrical Manufacturers Association (NEMA) in 1985 [1]. DICOM has become popular for radiology images and many other medical images, including those from ultrasound and endoscopy. In Japan, DICOM was officially approved by the Ministry of Health, Labour, and Welfare as a standard in 1999. In DICOM, pathology images are dealt with by Working Group-26 (WG-26; https://www.dicomstandard.org/activity/wgs/wg-26, 2022/4/5), which published Supplement 145 that defines WSI in August 2010. WG-26 then defined an annotation method for WSI in Supplement 222 in 2021. Standardization of the WSI file format was defined by DICOM more than 10 years ago, but this standard has yet to become widely accepted.

Integrating the Healthcare Enterprise (IHE; https://www.ihe-j.org, 2022/4/5) is an international project to establish interoperability among medical information systems. IHE defines guidelines for use of standards such as

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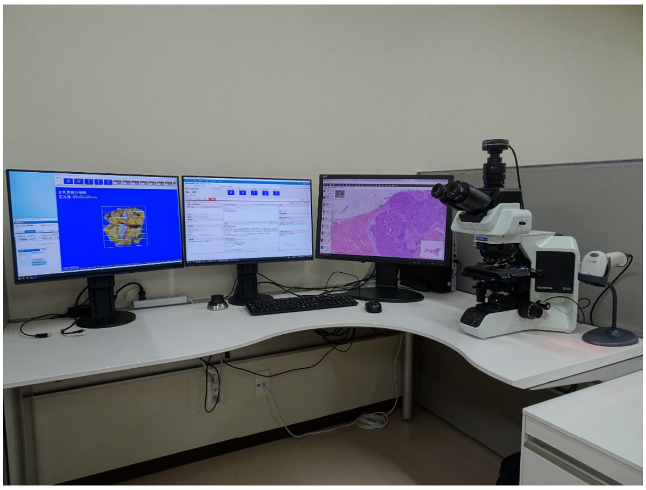

Fig. 1. Pathology diagnosis terminal comprising a microscope and three PC monitors, one of which is a special monitor for pathology images from JVC Kenwood.

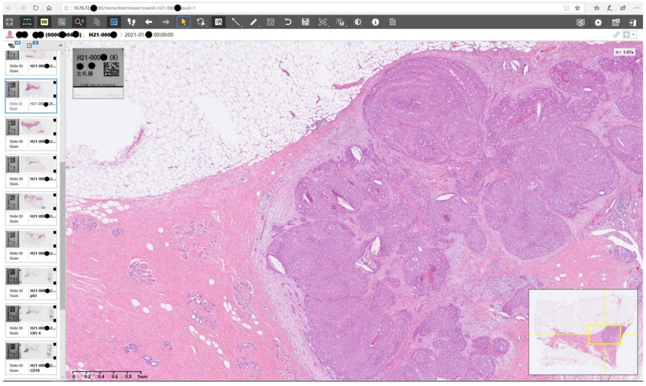

Fig. 2. DPS viewer (Infinitt): a WSI viewer for DICOM format files. We use a Hamamatsu S360 WSI scanner. Infinitt converts Hamamatsu native WSI files to DICOM files that are displayed by the DPS viewer. This software can convert many different WSI files into DICOM files, which enables use of different WSI scanners in the system.

- IHE Cardiology (CARD)
- IHE Dental (DENT)
- IHE Devices (DEV)
- IHE Endoscopy (ENDO)
- IHE Eye Care (EYECARE)
- IHE IT Infrastructure (ITI)
- IHE Pathology and Laboratory Medicine (PaLM)
- IHE Patient Care Coordination (PCC)
- IHE Pharmacy (PHARM)
- IHE Quality, Research and Public Health (QRPH)
- IHE Radiation Oncology (RO)
- IHE Radiology (RAD)
- IHE Surgery (SURG)

Fig. 3. IHE divisions. The purpose of IHE is to drive connectivity of medical information systems, and many divisions are defined. Pathology is included as Pathology and Laboratory Medicine (PaLM).

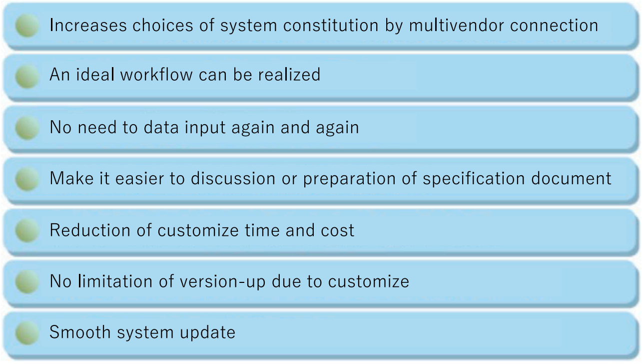

Fig. 4. Probable advantages of IHE introduction through standardization of medical information.

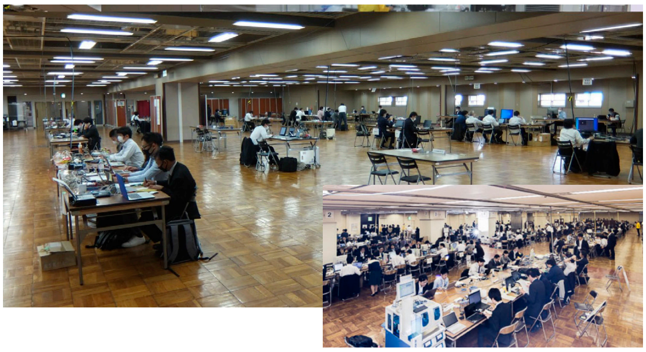

Fig. 5. "Connectathon" from the IHE Japan homepage.

DICOM and Health Level Seven (HL7; a medical information exchange standard). The purpose of IHE is to drive interoperability among medical information systems (https://www.ihe-j.org/basics/, 2022/4/5) by defining pathology and other areas, including cardiology, endoscopy, pharmacy, and patient care (Fig. 3). In IHE, pathology is grouped with laboratory medicine as "Pathology and Laboratory Medicine (PaLM)" [2]. IHE tries to standardize a wide range of healthcare information, and there are many expected advantages if these standards can be introduced (Fig. 4). Similar advantages are likely with introduction of the DICOM standard for WSI. Standardization of information by IHE is necessarily related to communication because it requires bidirectional communication using a standard format. For this purpose, IHE hosts a yearly "Connectathon" [http://www.ihe.net/participate/connectathon/, 2022/4/5], in which vendors bring their own equipment to the venue and try to connect with other systems. Software is modified on site until communication is obtained. This can be difficult and may take several days. Thus, the Connectathon is so named because it is somewhat like a marathon. A photograph of the Connectathon is shown in Figure 5. The results can be found at [https://www.ihe-j.org/basics/, 2022/4/5].

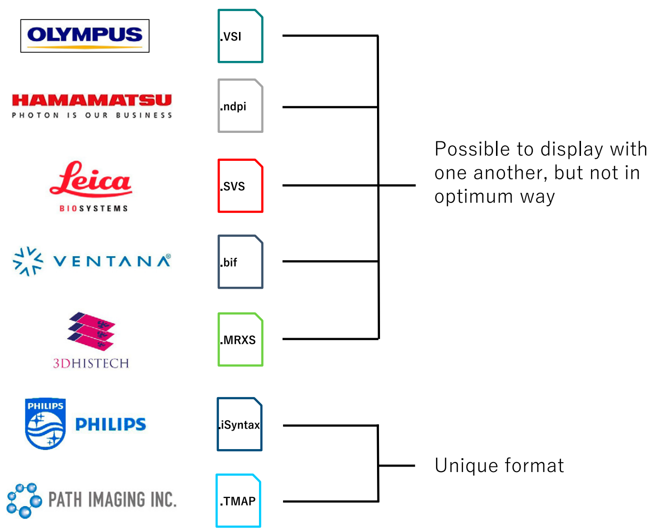

Fig. 6. Extensions of WSI files of WSI scanner vendors: Olympus Evident, Tokyo, Japan; Hamamatsu Photonics, Hamamatsu, Japan; Leica Biosystems, Nussloch, Germany; Roche Diagnostics, Basel, Switzerland; 3DHistech, Budapest, Hungary; Philips, Amsterdam, Netherlands; Path Imaging Inc., Tokyo, Japan.

III. Differences among Native WSI Formats

WSI files are composed of many high magnification microscopic pictures covering every part of a specimen area on a glass slide and connected by software. Extensions of WSI files of WSI scanner vendors are shown in Figure 6. These differ from each other, indicating that the file format is different. To scan the slide, scanners take pictures using their own size tiles. Because tile size is optimized to the objective lens, optical sensor size, and software of each scanner, the tile size differs among the scanners (Fig. 7). Native WSI viewer software is also optimized to the tile size. Moreover, image attribute metadata is added, including image codec, image size, region of interest (ROI), pixel size, and scanner information, and the metadata format also usually differs among vendors. Because the size of the image data is so huge, many WSI scanners use JPEG or JPEG2000 (J2K) to compress the images, while some vendors use their own unique compression format. Interestingly, the upper 5 WSI files in Figure 6 can be displayed by each native viewer, but the operation does not have optimal performance.

Table 1. *Correspondence of vendors to DICOM*

	DICOM file output	Native Viewer
Olympus	○ (Requires option)	×
Hamamatsu Photonics	○ (Requires another software)	×
Leica	×	×
Ventana	○ (Possible as default)	×
3D Histech	○ (License required)	×
Philips	○ (Possible as default)	×
Path Imaging	×	×

The correspondence of WSI scanner vendors to the DICOM standard is shown in Table 1. Many scanners have a function to output WSI files in the DICOM standard or convert native WSI files to DICOM format, but no native WSI viewers can handle DICOM format WSI files. There are several free DICOM viewers, but most are for radiographic images, rather than pathology images. Regarding differences among native WSI files of vendors and DICOM files, some WSI files can be displayed by other native viewers, probably due to use of the same JPEG compression. DICOM also uses JPEG and JPEG2000 compression. In addition to the differences in image parts, image information and metadata, DICOM files have additional information tags for the patient, specimen, clinician, institute, and diagnosis (Fig. 8).

We use a NanoZoomer S360 (Hamamatsu Photonics, Hamamatsu, Japan) for scanning at Narita Hospital. All

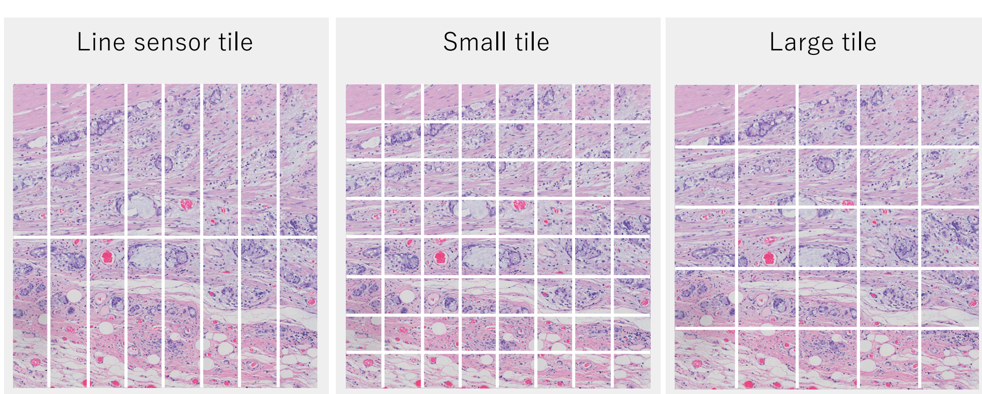

Fig. 7. Differences among WSI files. WSI scanners take pictures as tiles and combine them to form WSI files. The tile size is optimized to each objective lens and sensor, and all are different. Each native viewer is optimized to these tile sizes.

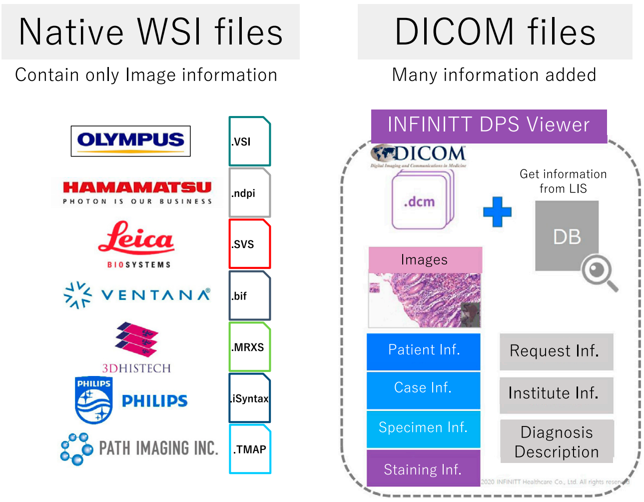

Fig. 8. Differences between native WSI files and DICOM files. Inf.: Information, DB: Database, LIS: Laboratory Information System.

Hamamatsu WSI files are converted to DICOM files using a DICOM converter (Infinitt). This converter can change most vendor WSI files to DICOM format, and this enables addition of different WSI scanners to our system. The tag information added to the Hamamatsu WSI files by our DPS converter is shown in Table 2. This information is text only, but it does increase the DICOM file size; however, the image data are much larger, and thus, the effect of addition of the text on file size can almost be ignored. As shown in Figure 7, WSI scanners take pictures as tiles, and the tile size differs among WSI files. Our DICOM converter first unzips and spreads native WSI files, then carves up the images to the optimum tile size for the Infinitt DPS viewer, and finally recompresses the images to form DICOM files (Fig. 9).

IV. Why use DICOM?

The advantages of standardization suggested by IHE are listed in Figure 4. The advantages of DICOM standardization are similar to those proposed by IHE.

1. Different WSI scanners can be used in the system.
2. Old WSI files or WSI files from other hospitals are available.
3. At the time of equipment renewal, there is no need to convert old WSI files.
4. Possibility of widened selection of image processing and AI software
5. DICOM has good connectivity with the Picture Archiving and Communication System (PACS), which makes it easy to refer to data from a Hospital Information System.

In contrast, the following points are possible disadvantages of DICOM conversion.

1. The image file size may become large.
2. The image quality may decline.
3. Additional time is required for DICOM conversion.
4. There are currently few image-analysis software programs for DICOM image files.
5. DICOM images are assumed to be for reference, rather than for diagnosis.

We evaluated the above issues using our system. The

Table 2. *Example of tag information added to DICOM files*

Data Element JPN	Class	Description
Specimen	Case	Histology, Cytology, or Autopsy
Slide ID	Slide	
Case ID	Case	Same to reception number
Case information	Case	Clinical information
Patient ID	Patient	
Patient Name	Patient	
Patient Name in Japanese	Patient	Patient Name in Japanese
Date of birth	Patient	YYYYMMDD
Sex	Patient	F/M/O
Paraffin block ID	Block	Every slides are displayed according to Paraffin block ID
Paraffin block information	Block	
Organ	Block	
Staining	Slide	
Cut out figure	Slide	The Base64 encoded representation of the JPEG image.
Paraffin block figure	Block	
Macroscopic image	Case	
Number of slides	Case	Number of slides
Number of institution	Case	
Department	Case	
Clinical doctor	Case	Name of the clinical doctor

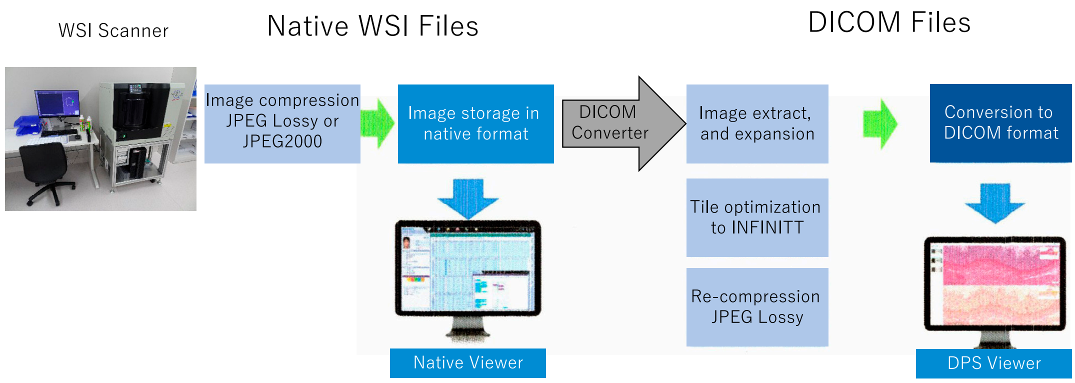

Fig. 9. DICOM conversion by Infinitt. Infinitt first unzips and expands the native WSI file, and then recompresses it at the most suitable tile size for the Infinitt DPS viewer using JPEG lossy. WSI files can be converted without changing the tile size, but this reduces the speed using the current version of the DPS viewer.

Table 3. *Comparison of WSI file size between Hamamatsu and DICOM*

Maker	Specimen	Size of WSI file (MB)	Size of DICOM file (MB)	%
Hamamatsu	Histology	747	251	34%
	Histology	1423	436	31%
	Histology	1229	418	34%
	Cytology	1350	385	29%
	Cytology	1336	357	27%
	Cytology	4030	1371	34%

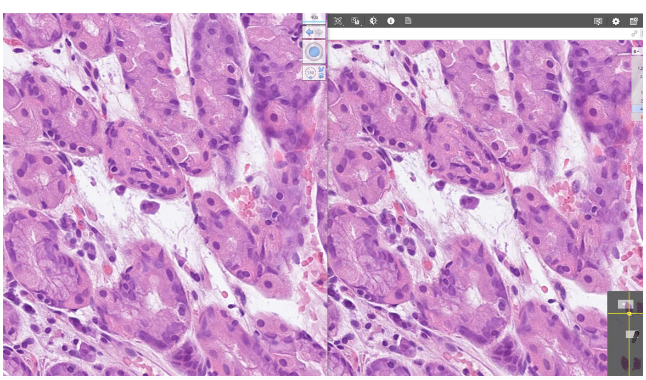

Fig. 10. Comparison of images before and after DICOM conversion. The left image is before conversion (NDP viewer, Hamamatsu) and the right image is after DICOM conversion (DPS viewer, Infinitt). The images are displayed on the same monitor as screen captures.

results for the image file size are shown in Table 3, in which the blue column shows the Hamamatsu native file size, and the green column outlined in red shows the DICOM file size of the same slide after DICOM conversion. DICOM files are about one-third the size of Hamamatsu native files. This does not necessarily make DICOM files superior, but Infinitt clearly compresses files more than Hamamatsu. The image quality is another concern because file conversion and greater compression may reduce the quality of DICOM files. In Figure 10, the left side shows an image in the Hamamatsu NDP viewer, and the right side is after conversion to a DICOM image, shown in the Infinitt DPS viewer. These images are displayed on the same monitor, with screen captures taken for comparison. The image is a 40× magnification of the same area of gastric fundic glands, and no difference was detectable. These trials indicate that there is no problem in file size and image quality caused by DICOM conversion. DICOM conversion may take a few minutes, but this is unlikely to be important. A quick response is needed in use of intraoperative frozen section diagnosis, but a microscope is mainly used in this situation. The FDA permits use of JPEG and DICOM for pathological diagnosis [1]. Overall, there do not seem to be any concerns with DICOM conversion of pathology WSI files.

V. Image Analysis Software

Several image analysis software programs are available. An image analysis utility called QuantCenter (http://www.3dhistech.com/research/quantcenter/, 2022/4/5) from 3DHistech (Budapest, Hungary) is shown in Figure 11. This software converts WSI files from many vendors into a 3DHistech format, and can convert DICOM files to 3DHistech files. The company indicate that they offer ten analysis functions, which seem to be very useful. The image analysis utility Aperio (https://www.leicabiosystems.com/digital-pathology/analyse/, 2022/4/5) from Leica Biosystems (Nussloch, Germany) is shown in Figure 12. This also has many useful analysis functions. In this review, only the 3DHistech and Leica systems are introduced, but most WSI scanner vendors offer their own image analysis software or introduce third party software. The problem is that these software programs are only for the native format of each vendor, and it is not possible to use a DICOM image itself. The 3DHistech system can analyze a DICOM image after conversion, but cannot be described as analysis software for a DICOM image. Most WSI vendors are still trying to advance their own native format, rather than aiming for

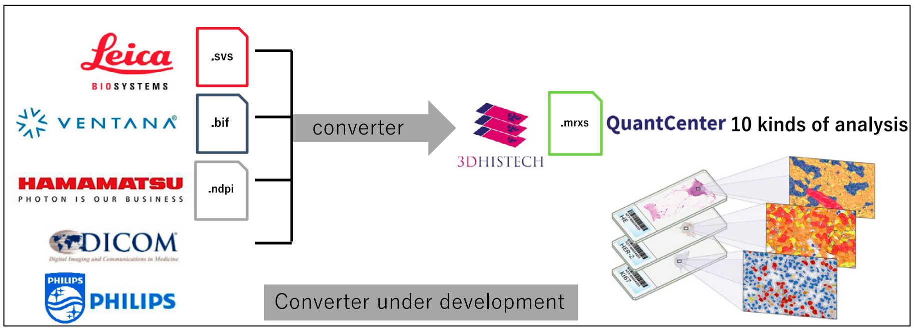

Fig. 11. 3D Histech QuantCenter. This utility converts native WSI files of each vendor to the 3DHistech format, and then analyzes the files using 10 kinds of analysis software. This converter is also suggested to be able to convert DICOM WSI files to the 3DHistech format.

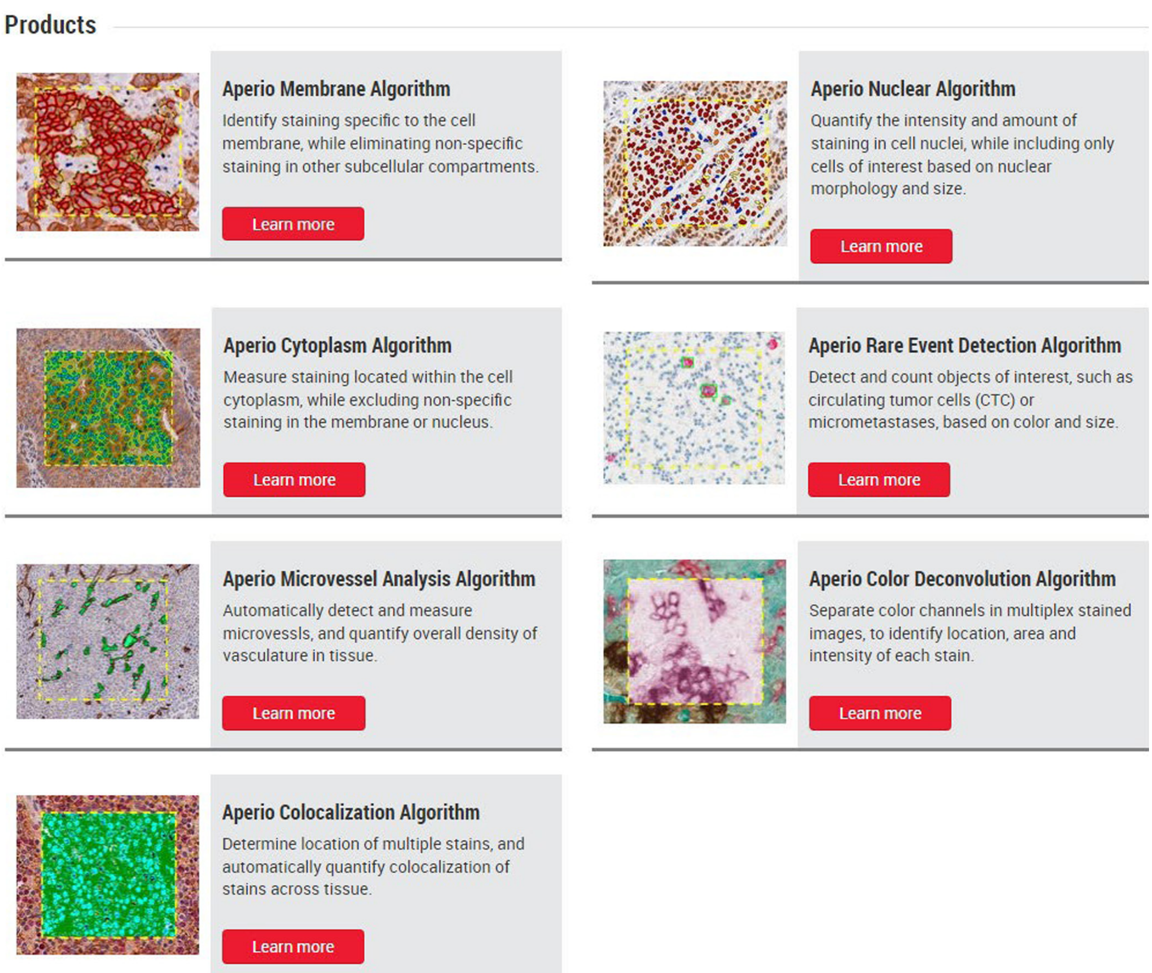

Fig. 12. Image analysis utilities in Aperio from Leica.

DICOM standardization.

Based on all of the information above, the following is a summary of the current situation:

1. A DICOM standard for WSI standardization has been established.

2. DICOM conversion requires additional time, but is relatively fast.

3. DICOM image size and image quality do not seem to be a major problem.

4. Many scanners can output a DICOM image, but few WSI viewers can accept DICOM files.

5. There are currently few image analysis software programs for DICOM images.

This situation is somewhat similar to "which comes first, the chicken or the egg". However, many vendors already have DICOM output function, and this suggests that there will be progress toward WSI standardization. There is also likely to be development of DICOM viewer software for pathology diagnosis and image analysis software for DICOM format WSI files.

VI. Conflicts of Interest

The author declares that there are no conflicts of interest.

VII. References

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