

# QUESTIONS TO ASK DURING THE EVALUATION OF A VIRTUAL MICROSCOPY SYSTEM

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This document identifies key elements of a virtual microscopy system, explains why the element is important, and provides corresponding information on Aperio's ScanScope Systems. It is an invaluable tool in identifying system needs and requirements and framing an effective evaluation process.



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# TABLE OF CONTENTS

Installed Base & Customer Satisfaction .....	1
Digital Slide Image Quality .....	1
Digital Slide Creation Functionality .....	2
Digital Slide File Format .....	3
Open Architecture .....	3
Digital Slide Viewing .....	4
Digital Slide Workflow Management .....	5
Digital Slide Image Analysis .....	5
Intellectual Property .....	7
Notes .....	8

## Questions to Ask During the Evaluation of a Virtual Microscopy System

Virtual Microscopy holds great promise for significantly improving pathology workflow. Correctly implemented, a virtual microscopy solution can improve productivity and accuracy, deliver better interpretations, and enable immediate sharing, consulting, and image analysis. But not all virtual microscopy solutions are created equal, and a substandard system can be worse than no virtual microscopy system at all.

This document provides a series of questions to ask a potential virtual microscopy supplier, for purposes of evaluating the product offering.

### INSTALLED BASE AND CUSTOMER SATISFACTION

Many companies selling virtual microscopy solutions do not have an installed customer base or history of product improvement. A proven track record is a strong indicator of a product's strength.

Question	Comment [Refer to Notes]	Aperio	Other Vendor
How many VM systems have you sold?	Placements do not necessarily mean purchases.	Has sold over 100 systems in 13 countries.	
How many repeat sales do you have?	Repeat sales are an excellent indicator of customer satisfaction.	Approximately 25% of customers have purchased multiple systems.	
How many of your systems are remotely accessible?	IT issues can be a major source of frustration when installing a VM system.	Over 90% of customer systems are remotely accessible via the Internet.	
Do you have a list of references I can contact?		Yes! Please ask your representative for a list of customer references.	
How advanced are your VM systems?	Second, third or later-generation systems are more advanced than first-generation systems.	Aperio's T2 and T3 scanners are 2 <sup>nd</sup> and 3 <sup>rd</sup> generation instruments, respectively.	

### DIGITAL SLIDE IMAGE QUALITY

One of the most important attributes of any virtual microscopy system is digital slide image quality, which should be as good as, if not better than, viewing a glass slide through a microscope. Aperio suggests you scan the same set of glass slides on several candidate scanners *under the same conditions*, and evaluate the digital slide images yourself.

Question	Comment [Refer to Notes]	ScanScope System	Comparative System
What is the scanning resolution in $\mu\text{m}/\text{pixel}$ ?	A higher scanning resolution will generally produce higher quality digital slides.	20x objective: 0.50 $\mu\text{m}/\text{pixel}$ 40x objective: 0.25 $\mu\text{m}/\text{pixel}$	
Does your system use a Bayer mask color CCD?	Bayer mask color interpolation reduces the <i>effective</i> scanning resolution by 40-50%. [1]	No, ScanScope Systems do not use Bayer mask CCD. The tri-linear array measures red, green and blue color at each pixel, without Bayer mask interpolation.	
What objective lenses are supported?	Higher NA objective lenses generally produce higher quality digital slides. [2]	Plan Fluor: 20x/0.5, 40x/0.75 Plan Apo: 20x/0.75, 40x/0.9 (T3)	
How does your system auto-focus?	The goal is an image that is perfectly focused everywhere (uniformly focused); different approaches to auto-focus yield different degrees of focus uniformity. [4]	Focus adjusted on line-by-line basis in accordance with pre-focus map, producing highly uniformly focused digital slides.	
Are your digital slides seamless?	Digital slide images should be free from seams and alignment artifacts.	Yes. There are no optical aberrations along the scanning axis, enabling seamless stripe alignment.	

## Questions to Ask During the Evaluation of a Virtual Microscopy System

Do you change image data during alignment?	Alignment artifacts can be hidden from the human eye, but will cause havoc if digital slides are later analyzed by image analysis	No. Alignment is made without warping or other non-linear algorithms frequently used to “force” alignment.	
Do you provide a quality score to assess image quality?	It is impractical to manually evaluate the image quality of thousands of digital slides	A reliable image quality score is automatically provided for every digital slide.	

### DIGITAL SLIDE CREATION FUNCTIONALITY

In addition to image quality, the ease and speed at which slides are captured are also important considerations.

Question	Comment [Refer to Notes]	ScanScope System	Comparative System
How long does it take to scan a slide?	Scan times can be misleading. Scan time estimates should include time to load/unload, scan, compress, and write the digital slide to disk. Times for post-processing, if required, should be added. [5]	Throughput of < 4 minutes for a 15x15mm area at 0.5 µm/pixel (20x). Includes times for loading and unloading slide from the autoloader; all steps in auto-scanning the slide; image compression; and writing of TIFF digital slide image file to disk.	
Does the system perform entire-slide scans at the highest resolution?	Many systems scan at 2X or 4X resolution, and then require user intervention to manually select regions to be scanned at a higher resolution.	All Aperio systems scan the entire slide at the highest resolution.	
Do you support one-touch walk-away automation?	Auto-scanning without operator intervention should work reliably for well-prepared slides.	Yes. Both the 120-slide T2 and the 5-slide T3 support one-touch automatic scanning.	
What is the capacity of your autoloader?	The capacity should be scaled to support an 8-12 hour unattended run.	At 5 minutes per slide, a 120-slide unattended run with the T2 requires 10 hours.	
What slides does your autoloader accept?	Some autoloaders will only work with special glass slides. Understand any limitations.	Aperio’s Gen-3 autoloader accepts all slide types, including beveled slides.	
Do you have a random-access autoloader?	Random access autoloaders streamline workflow. [6]	Yes, the ScanScope T2 features a 120-slide random-access autoloader.	
Can I manually scan a slide?	Manual scanning is desirable to scan “stat” slides quickly while a batch is being scanned by the autoloader, or for poorly prepared slides, or to scan regions of a slide.	Yes, all ScanScopes support manual scanning during an autoloader batch of the entire slide or selected regions of a slide.	
How do I change scanning resolution?	Environments with multiple scanning resolution requirements, or that have multiple users, need to understand how easily and quickly the scanning resolution can be changed.	Scanning resolution can be changed with the optional 2x Magnification Changer, or by interchanging objective lenses.	
What kind of barcodes do you support?	Barcode support is desirable. Auto-scanning non-barcoded slides should be possible.	Datamatrix (2D) barcodes and many 1D barcodes are supported. Support for other barcodes is possible. Barcodes are not required for auto-scanning.	
Can I scan 2x3-inch slides?	Some scanners cannot handle larger format slides.	Yes, the T3 supports scanning 2x3-inch slides.	

## Questions to Ask During the Evaluation of a Virtual Microscopy System

Question	Comment [Refer to Notes]	ScanScope System	Comparative System
Can I create z-stacks?	Many digital slide applications require quality through-focus (depth) images.	Yes, z-stacks can be created (locally or remotely) directly from within ImageScope with Remote Revisit software (optional).	
Can I remotely interact with a glass slide?	Some telepathology applications require live remote access. Latency in controls is undesirable.	Yes, optional Remote Revisit software facilitates interactive telepathology, with none of the latency hassles inherent in robotic microscopes. [7]	
Can I access and clean the objective lenses?	Some systems do not provide access to the objective lens, making cleaning difficult.	Yes, objective lenses in a ScanScope are readily accessible.	

### DIGITAL SLIDE FILE FORMAT

Digital slide file format is critically important to ensure interoperability, compatibility with image analysis software packages, and optimal performance.

Question	Comment [Refer to Notes]	ScanScope System	Comparative System
What file format do you use to store digital slides?	Standard (open) formats are generally preferred over proprietary formats.	ScanScope .svs files are standard TIFF files that comply with the latest TIFF standard (TIFF 6.0).	
Is the file stored as a single file?	Some digital slide formats store individual tiles separately.	.svs files are stored as singles files.	
What compression types do you support?	JPEG2000 support is desirable. JPEG support is essential. [8]	.svs files support both TIFF/JPEG and TIFF/JPEG2000.	

### OPEN ARCHITECTURE

An open architecture ensures future interoperability of your virtual microscopy system.

Question	Comment [Refer to Notes]	ScanScope System	Comparative System
What elements of your system are "open"	An "open" architecture means adherence to standard and the publication of interfaces for others to use.	Aperio is committed to an open architecture. ScanScope Systems output standard TIFF files which are described in publicly available documents. Aperio publishes programming interfaces (APIs) to its ImageServer software, its Algorithm Framework, and to the Viewport, the heart of the ImageScope viewing software. [9] <a href="http://www.aperio.com/documents/">http://www.aperio.com/documents/</a>	

## Questions to Ask During the Evaluation of a Virtual Microscopy System

### DIGITAL SLIDE VIEWING

The best way to evaluate a viewer solution is to use it in a typical environment.

Question	Comment [Refer to Notes]	ScanScope System	Comparative System
Did you develop your own viewing solution?	Being locked into a third-party viewing solution means that changes cannot be made by the virtual microscopy supplier.	Yes. Aperio's viewing solution was developed by Aperio's engineers.	
Do you offer desktop viewing software?	Desktop viewing software, which is installed on the client computer, generally provides better performance.	Yes. Aperio's ImageScope viewing software is available for PC and Mac. [10]	
Do you offer web-browser based viewing software?	A web-browser based viewer does not require installation of client software, but generally offers fewer features than a desktop viewer.	Yes. Aperio offers a web viewer that is compatible with all popular web browsers on any platform. [11]	
What are the limitations of your viewing software?	Does it work only on a PC? If so, is there a native version for the Apple Macintosh?	Aperio's ImageScope viewer is available for PCs and Macs.	
Do you have a publicly accessible web site with digital slides?	Many virtual microscopy suppliers offer public digital slide galleries. Test the remote viewing performance for yourself.	Yes, visit <a href="http://images2.aperio.com">http://images2.aperio.com</a>	
Can I annotate digital slides?	Annotating digital slides is one of the many benefits of digital slides over glass slides.	Yes, ImageScope supports a rich annotation facility.	
Does your viewing software support conferencing?	A mode in which multiple remote parties can simultaneously view <i>and annotate</i> the same digital slide, synchronously, is desirable.	Yes, ImageScopes supports multi-party conferencing with synchronized viewing, leader-follower control, and real-time annotation sharing capabilities.	
Can I pan and zoom instantly and continuously?	Rapid smooth panning and zooming to <i>any area</i> of a digital slide <i>at any magnification</i> is a minimum requirement of any viewing software.	Yes, ImageScope supports instant pan and zoom to any region and magnification, while maintaining a macroscopic (thumbnail) view of the entire specimen.	
Can I view multiple digital slides side by side?	Comparing two or more digital slides, preferably synchronously, can be helpful.	Yes, ImageScope supports side-by-side coordinated (synchronous) viewing of multiple digital slides.	
Does your viewing software support viewing 3D digital slides?	Viewing 2D digital slides is suitable for most applications. It is desirable for a viewer to also be compatible with 3D image data.	Yes, ImageScope supports viewing 3D digital slides, whether the 3D information is the entire slide or z-stacks from selected regions.	
Can I export a region of a digital slide?	Exporting a user-selected region of a digital slide is useful for publication and reporting.	Yes, in addition to quickly exporting the current screen, Aperio's Digital Slide Studio software provides flexible image adjustment and export capabilities. [12]	
Can I change contrast, brightness and gamma?	The ability to enhance the displayed image supports personal preferences and optimization for different display technologies.	Yes, ImageScope supports real-time contrast, brightness, and gamma adjustments for image enhancement.	

## DIGITAL SLIDE WORKFLOW MANAGEMENT

Simple and efficient tools for managing digital slides are required to fully benefit from the creation of thousands of digital slides.

Question	Comment [Refer to Notes]	ScanScope System	Comparative System
What software do you provide to manage digital slides?	A virtual microscopy system should support managing volumes of digital slides from multiple scanners.	Aperio's Workflow Manager software makes it easy to manage digital slides and associated data from one or multiple ScanScope Systems. [13]	
How can I interface your system to my LIS?	Interfacing to an LIS (Laboratory Information System) should be straightforward.	Interfacing to an LIS is facilitated by Aperio's many open programming interfaces (APIs). Aperio also provides data export via open XML messages and data files.	
What experience do you have interfacing to LIS systems?		Aperio has supported the interface of its ScanScope Systems to an LIS at several customer sites.	

## DIGITAL SLIDE IMAGE ANALYSIS

The analysis of giga-byte sized digital slides using image analysis software is technically challenging, but is critically important to being able to leverage the benefits of a virtual microscopy system.

Question	Comment [Refer to Notes]	ScanScope System	Comparative System
Can I export regions of a digital slide for analysis by third-party software?	While helpful, this capability may not provide meaningful results for many applications.	Yes, using ImageScope's screen export function, or Aperio's Digital Slide Studio software. [14]	
Do you support image analysis of user-selectable regions, or the <i>entire-slide</i> ?	Being able to analyze both user selectable regions and the entire slide is essential for many applications.	Yes. Aperio's Algorithm Framework supports the application of image analysis algorithms to selectable regions of a digital slide, and also to the entire digital slide, <i>directly from within ImageScope</i> . [15]	
Can I exclude regions of a digital slide from analysis?	Excluding regions for analysis (e.g., tissue folds) is often important.	Yes, ImageScope features a "negative" annotation tool to identify regions to be excluded from analysis.	
What image analysis algorithms do you offer?		A simple yet powerful pixel counting algorithm is provided (at no charge). Aperio also offers algorithms for micro-metastasis detection and for quantitative immunohistochemistry. [16]	
Do you support image analysis with third-party algorithms?	Given the wealth of image analysis algorithms available today, being locked into one company's image analysis algorithms is a disadvantage.	Aperio's algorithm framework is available to third parties, and enables the application of third-party algorithms to user selectable regions of a digital slide, or to the entire digital slide.	

## Questions to Ask During the Evaluation of a Virtual Microscopy System

Question	Comment [Refer to Notes]	ScanScope System	Comparative System
What third-party <i>entire-slide</i> image analysis software do you support?		Macros from ImagePro Plus, Media Cybernetics' popular image analysis software, can easily be applied to digital slides, directly from within ImageScope. Aperio's architecture is also compatible with Biomagene's algorithms.	
Can I automatically apply image analysis to <i>entire slides</i> in a batch mode?	Automated image analysis can save hours of labor for high-throughput applications.	Yes. Workflow Manager supports batch-mode processing of any number of algorithms to any number of digital slides.	
How can I view the results of image analysis?		Algorithm results are viewed directly from within ImageScope, and can be exported to Excel for further analysis.	
Do you generate and save a mark-up image?	A mark-up image is a pseudo-color image that provides confidence that the algorithm correctly performed the desired analysis.	Yes, mark-up images can be saved in the same file format (.svs) as digital slides.	
How can I analyze tissue microarrays?	Analyzing TMAs, with their multiple spots per slide, is challenging and time consuming.	Aperio's powerful TMA Lab™ software is specifically designed for the management and analysis of TMA data. [17]	
Does your system support <i>remote</i> image analysis?	The remote analysis of digital slides (e.g., via the Internet) is critically important for telepathology of IHC digital slides	Yes, ScanScope Systems support remote viewing and analysis of digital slides, including by third-party image analysis algorithms.	
Does your system support server-side analysis?	Server-side processing is essential for managing remote analysis by large numbers of remote users.	Yes, ScanScope Systems support server-side processing of digital slides, centralizing image analysis at one secure location and eliminating the need for installing algorithms on remotely located client computers.	
Can I view digital slides from within Matlab?	Matlab is sophisticated mathematical software used by algorithm developers.	Yes, .svs digital slides can be opened and viewed from Matlab. Image data is easily extracted for analysis within the Matlab development environment.	
Is your image analysis solution scalable?	Many software solutions may work well on a few sample images, but become impractical as the volume of images and studies increase	Aperio's Client/Server [18] architecture allows for distributed ("grid") processing. Management of image data, analysis, and results is done from a single database, accessible from anywhere on your network, or even the Internet.	

### INTELLECTUAL PROPERTY

Freedom from fear of litigation is important in the selection of a virtual microscopy system.

Question	Comment [Refer to Notes]	Aperio	Other Vendor
What patents do you have in virtual microscopy?		Two issued patents covering the use of line-scanning in virtual microscopy. Aperio has also filed patents to protect its digital slide <i>viewing</i> and <i>entire-slide image analysis</i> technology.	
Do you have a license to the virtual microscopy patents from Bacus Labs?	Aperio believes that licenses to the Bacus Labs patents are <i>required</i> by anyone operating in the virtual microscopy field.	Aperio is the <i>only</i> virtual microscopy company that is both (i) licensed under Bacus' patents and (ii) not locked into Bacus' proprietary file format that requires the annually licensed WebSlide Server software.	

### NOTES

- [1] **Bayer Mask.** Image tiling systems utilize conventional color CCD cameras, i.e., black and white cameras that have been modified by their manufacturer by placing a Bayer mask in front of the monochrome CCD. A Bayer mask is an array of red, green and blue color filters allows an individual pixels to measure one (and only one) of these three colors. Color values from multiple pixels are averaged to estimate the color at any given pixel.

Bayer mask color interpolation reduces the *effective* scanning resolution of the tiling system by 40-50%. In other words, an image tiling system that quotes a scanning resolution of 0.5  $\mu\text{m}/\text{pixel}$  at 20x has an effective scanning resolution that is only 0.7  $\mu\text{m}/\text{pixel}$ . Alternatively, when compared to a non-Bayer mask system—like Aperio's ScanScope line-scanning system—the scanning resolution of an image tiling system (in  $\mu\text{m}/\text{pixel}$ ) must be considerably higher (0.25  $\mu\text{m}/\text{pixel}$ ) to capture the information captured by a ScanScope at 0.50  $\mu\text{m}/\text{pixel}$ . An additional disadvantage of Bayer mask systems is that the inability to measure all three color channels simultaneously at every pixel results in digital slide image files that are unnecessarily large.

- [2] **Objective Lenses.** Just as in conventional microscopy, image quality is directly related to the quality of the objective lens utilized by a virtual microscopy scanner. Higher numerical aperture (NA) objective lenses (e.g., Plan Apochromats) have smaller depths of focus, and will generally provide crisper image. For some applications (e.g., cytology) the larger depth of field of a lower NA objective lenses may be desirable, provided that the NA of the objective lens does not become the limiting factor in the system. For other applications, the color attributes of a Plan Fluorite objective lens may be preferred over those of a Plan Apochromat. In general, it is desirable for a scanner to support different objective lenses.

- [3] **Number of Tiles/ Stripes.** Assuming tiling with a 1,000 pixel x 1,000 pixel CCD at a scanning resolution 0.25  $\mu\text{m}/\text{pixel}$ , the dimensions of a single image tile are 0.25 mm x 0.25 mm. The digitization of a 20mm x 30mm area would require the capture of 9,600 image tiles (assuming no overlap). If captured with a Bayer mask CCD nearly four times as many tiles (38,400) must be captured—resulting in an image that is 4 times larger—in order to achieve an *effective* scanning resolution of 0.25  $\mu\text{m}/\text{pixel}$ . Compare this to 80 stripes from a ScanScope (using narrow stripes mode).

- [4] **Uniform Focus.** While effective scanning resolution is critically important when evaluating the image quality of a virtual microscopy system, uniform focus is equally important. Image tiling systems are constrained to one focal position for every image tile that is captured. This limitation is often problematic when higher NA objective lenses are used because the narrow depth of field of these objective lenses causes individual image tiles to be out of focus at the edges. Line-scanning systems have the advantage of being able to adjust focus several orders of magnitude more frequently than tiling systems, generally providing a more uniformly focused digital slide. The final evaluation of the focus uniformity achieved by different virtual microscopy system is best made by scanning the same set of glass slides on several candidate scanners.

- [5] **Scan Times / Sustained Throughput.** For systems without an autoloader, scan time should measure the elapsed time beginning with placing a slide on the stage until the resulting digital slide can be accessed remotely from a server. For system with an autoloader, sustained throughput is a more appropriate measure.

Aperio's ScanScope T2 instrument is equipped with a fully automated slide loader capable of scanning up to 120 barcoded slides in a single run. The < 4 minute per slide sustained throughput includes slide loading and unloading, tissue finding, auto-focusing, automated scanning, image compression [JPEG or wavelet (JPEG2000)] and slide quality assessment. Automatic scanning also includes decoding of datamatrix (2D) barcodes or, in the event that a barcode is not present, the capture of an image of the slide label. All relevant image capture parameters (e.g., file name, ScanScope ID, scan time, barcode, quality score, the directory path to the digital slide image, etc.) are stored in a database that is readily accessible using Aperio's Workflow Manager software.

- [6] **Random Access Autoloader.** A random access autoloader, in contrast to a stacked-slide autoloader, has the benefit that any slide can be accessed at any time. This capability supports reloading slides from the loader onto the stage, for example, to facilitate manual rescanning of poorly prepared specimens, or replacing or interchanging glass slides scheduled for scanning. Stacked-slide autoloaders do not support reloading arbitrary slides.

- [7] **Interactive Telepathology / Remote Revisit.** Interactive telepathology using virtual microscopy eliminates the hassles encountered with remotely controlled microscopes. It provides more information, faster than conventional

## Questions to Ask During the Evaluation of a Virtual Microscopy System

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telepathology approaches. Using Remote Revisit, users can create digital slides with high resolution (through-focus) details for all specimen types, including cytology, hematopathology and frozen sections.

- [8] **Digital Slide File Format.** ScanScope's .svs files are standard TIFF files that comply with the latest TIFF standard (TIFF 6.0). TIFF supports the pyramid type data structure that Aperio uses to enable rapid zooming to and from any magnification. TIFF also supports different types of compression. Aperio currently supports JPG and JPEG2000 compression in its TIFF (svs) files, in accordance with the selections made by a ScanScope user. The selection of compression type should be matched to the codec (compression / decompression) module that is built into the viewing software, and should be selected based on the advantages and disadvantages of each. JPG compression (compression using Fourier transforms) is computationally faster and the images are larger (when compared to JPEG2000 at the same compression ratio. JPEG is required for web browser based viewers like Internet Explorer that do not currently support JPEG2000. JPEG2000 (compression using wavelets) achieves higher compression ratios than JPG, resulting in smaller image files and faster remote viewing, but at the expense of computational complexity (compression takes longer).
- [9] **Open Architecture.** Aperio's Chief Technology Officer, Ole Eichhorn, is chair of the file format committee for LDIP (Laboratory Digital Imaging Project), a joint academic/industry effort by the Association for Pathology (API) to establish "DICOM" like standards for ensuring compatibility and interoperability in the field of virtual microscopy. Aperio is committed to continuing to lead the industry by promoting the importance of standards. Aperio publishes many of its software interfaces on its web site (<http://www.aperio.com/documents/>).
- [10] **ImageScope Viewing Software.** Aperio's ImageScope™ viewing software enables access to digital slides anywhere (locally and remotely) and anytime, while providing capabilities not available with microscope viewing, such as annotation sharing, location referencing, and side-by-side viewing of multiple slides. The ImageScope viewer provides the following capabilities (i) instantly pan and zoom to any region and magnification, while maintaining a macroscopic (thumbnail) view of the entire specimen, (ii) integrated multi-party conferencing with synchronized viewing, leader-follower control, and real-time annotation sharing capabilities, (iii) side-by-side coordinated viewing of multiple slides, (iv) real-time contrast, brightness, and gamma adjustments for image enhancement, (v) linked graphical and textual annotations - clicking one concurrently accesses the other, (vi) built-in ruler, (vii) easy exporting of sub-regions in TIFF format, and (viii) viewing of z-stacks captured by a ScanScope in coordination with the corresponding digital slide.
- [11] **Web Viewing Software.** Aperio offers web viewer software that, in conjunction with its ImageServer software, facilitates the viewing of ScanScope digital slides directly from a web browser; without the need to recompress digital slides into the types of proprietary formats supported by third-party viewing solutions from companies like Zoomify, Xippix and Flashpix. The ImageServer software is at the heart of Aperio's remote viewing. This software is deployed in more than 50 customer sites and has been thoroughly tested in environments where large numbers of users have simultaneously accessed hundreds of digital slides. A report of Aperio's remote viewing performance testing can be found on Aperio's web site at <http://www.aperio.com/Documents/>.
- [12] **Digital Slide Studio.** Aperio's Digital Slide Studio module provides flexible image adjustment and export capabilities. Zoom, crop, rotate, scale, adjust brightness and contrast, apply digital filters, add/delete thumbnail and label images, and re-compress images into other common file formats with ease. Insert portions of digital slides that highlight specific areas of interest into reports, books, or articles; or e-mail them to colleagues. Include annotated images in presentations. With Digital Slide Studio, there's no limit to what can be done with ScanScope-created digital slides.
- [13] **Workflow Manager.** The Workflow Manager software displays the label image (or barcode) and a thumbnail image for each digital slide in the database. 2-D Datamatrix barcodes are automatically decoded and associated with digital slide images and their corresponding slide-specific (textual) information. This software provides sorting, grouping, and filtering by any field, and enables secure access to multiple local or remote digital slide databases, as well as multi-party local or remote access to the same database.
- [14] **Exporting a Region for Analysis.** ImageScope allows exporting the current screen of image data as a TIFF file, which can be imported into a third party image analysis program. Another approach is to use Digital Slide Studio

## Questions to Ask During the Evaluation of a Virtual Microscopy System

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software to crop and/or scale a digital slide to create a TIFF file corresponding to a user-selectable region of a digital slide which can then be imported into a third-party image analysis program.

- [15] **Algorithm Framework.** Existing image analysis algorithm can be integrated into Aperio's Algorithm Framework using Aperio's software development kit. This approach has the benefit of enabling the application of existing image analysis algorithms to user-selectable regions or sub-regions of a digital slide, and also to the entire digital slide, without having to address the complexities of managing large amounts of data and computer memory.
- [16] **Aperio Image Analysis Algorithms.** The ScanScope System's open architecture supports use of Aperio or third-party algorithms to perform integrated image analysis. Aperio offers the following IHC image analysis algorithms: (i) nuclear scoring algorithms for ER and PR, and (ii) membrane scoring algorithms for Her-2. In addition, Aperio offers a rare-event detection algorithm for detection micrometastasis clusters, which when applied to an entire digital slide solves the "needle in the haystack" problem by automatically identifying a small number of cells of interest from among thousands. Other algorithms can readily be integrated into Aperio's algorithm framework.
- [17] **TMA Lab.** Aperio's TMA Lab™ software is an important research application for Virtual Microscopy. High-density tissue microarrays (TMAs) allow researchers to validate new biomarkers or to discover and dissect molecular pathways, simultaneously, in hundreds of tissue samples. But TMAs, with their multiple "spots" per slide, are challenging and time-consuming to analyze. TMA Lab provides powerful management capabilities of TMA slides and their individual spots and enables manual or automatic scoring through application of image analysis algorithms.
- [18] **Client/Server Analysis.** Aperio's Client/Server architecture allows for the efficient management of your analysis workload. Any number of workstations may be configured as Clients and receive analysis jobs from the server. As your analysis workload grows, additional Client machines can be added to give you the turn-around time you desire. The Client/Server architecture also allows for batch analysis and the automatic analysis of image data as part of the scanning process. All analysis results are recorded in a central database, so that this information is managed and accessible from anywhere on your network.