

Aperio Release 6 Notes & News

February 24, 2005

Welcome to Aperio's Release 6!

This document tells you everything you need to know about this release, including installation instructions, new features, fixed bugs, and helpful hints. We suggest you read through it completely before installing any of the software, but if you are too anxious you may choose to follow just the “Installation” instructions for the software. (We've added a single-page New Feature Summary on page 4 just for you.)

The Overview section describes each component of the software, and *where* it is installed. If you have questions about which components you have and/or where each component is located, please contact us.

The Installation section describes how each component is installed. With the exception of the ScanScope Controller software, all software can be downloaded and installed by customers without Aperio assistance (although we will be happy to help).

The New Features and Notes section describes changes to the software, new features, bugs which have been fixed, and gives considerations for running the software. If you have questions about new features or these considerations please contact us.

All Aperio documentation has been updated. You may find the latest documentation at <http://www.aperio.com/documents>. Additionally, all desktop programs have online help pages. The online help pages for each program have been updated to correspond to the software.

Contact Us

Please let us know if you have questions or comments, email to support@aperio.com or call us at (760) 539-1100. European customers may send email to europesupport@aperio.com or call our European (London) office at +44 (0) 1420 540 271.

You might also just warn us when you're planning to install upgrades, just in case you'll need us. And we strongly recommend you contact us and allow us to help you upgrade the Controller software on your ScanScope(s), as this installation/upgrade process is the most likely to require our assistance.

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New Features Summary

We know you're anxious to find out what's new in Release 6, so here's a summary:

General Capabilities

- Improved facilities for third-party integration with digital slides and program APIs.
- User-level digital slide access authorization.
- Storage and display of slide macro images¹ in digital slide files (SVS).
- Expanded support for JPEG2000 compression.

ScanScope Console and Controller

- Support for T3 ScanScopes.
- High-resolution macro camera and area camera support (T3 ScanScopes).
- Manual macro focus for slides with faint tissue areas.
- High-resolution macro image option for slides with faint tissue areas.
- Automatic light source failure detection.
- Automatic light intensity gain adjustment.

ImageScope

- “Smart sync” to align two or more images when viewing side-by-side.
- All digital slides open in one instance of ImageScope.
- Workstation-specific default gamma files.
- Initial magnification and maximum magnification options.
- Support for rulers as a new kind of annotation.
- Image navigation enhancements: forward/back buttons, “joystick mode”.
- Windows extension to display digital slide thumbnails in Explorer and open dialogs.

Analysis Algorithms

- Algorithm “markup images” to show analysis results visually.
- Support for “negative annotations” to deselect subregions for analysis processing.
- Implementation of server-side analysis algorithm batch processing.

ImageServer and WebViewer

- WebViewer now integrated into ImageServer.
- RSS feeds for image directories.
- ImageServer now runs as a service.
- Linux support.

TMALab

- Interactive analysis algorithm support in TMALab (like ImageScope).

Workflow Manager (formerly Virtual Slide Manager)

- Integrated support for server-side algorithm batch processing.
- Automatic export of analysis results to Excel.
- Capability to upload, edit, and delete macros for server-side algorithm processing.
- Support for *printing* Datamatrix 2D barcode labels.

¹ A slide macro image is a low-resolution snapshot taken of the entire slide area at the start of a scan.

Overview

All of the Aperio software has been updated for Release 6. Some of these programs are provided free of charge, such as the ImageScope viewer. Others are included with ScanScope systems, and still others are licensed for one or more users. If you have questions about the software you are licensed to use, please let us know.

For Release 6 we've created an extensive demo / tutorial using ImageScope. This is a script which walks you through opening images, creating and viewing annotations, running analysis algorithms, and using Slide Conferencing. If you are curious about the new features of Release 6 this is a great place to start. The demo may be downloaded from the Aperio website at <http://www.aperio.com/documents>.

Aperio now has a marketing department! Yippee. And as a result, we've changed several *names* of programs. The name changes are noted in the list below. Additionally, we no longer refer to "virtual slides". Instead, we call them "digital slides". The server machine which stores ~~virtual~~ digital slides is now called a DSR (digital slide repository). Don't worry, you'll get used to it. We did :)

The list which follows describes all Aperio software. Programs listed with an asterisk* are free to all users. Programs listed with a bayonet† are included in all ScanScope systems. (If you own a ScanScope, you are automatically licensed to use this software.) We now refer to this software in aggregate as our Digital Slide Information Management System, aka DSIMS. All other software is licensed separately.

Controller†	Software which runs on the ScanScope machine itself, controlling the operations of the device ² .
Console†	Desktop program which runs on a DSR ³ , system console, or any other Windows PC; provides the user interface for an operator to control operations of ScanScope devices.
ImageServer†	Software which runs on a DSR providing a high-speed network interface to stored digital slides; communicates with the ImageScope viewer and WebViewer, as well as second- and third- party software via an open message API ⁴ .
Database schema and intercepts†.....	Software which runs on a DSR providing the interface to the digital slide database.

² The Release 6 version of the controller supports T2 machines with or without an autoloader, and T3 machines. T108 machines are not supported by the Release 6 version of the Controller. Aperio will continue to support (but not enhance) the current T108 Controller software.

³ In this document the acronym DSR is used for Digital Slide Repository, the server machine on which digital slides are stored. All T2 systems have a DSR. T3 ScanScopes may or may not have a separate DSR, if they don't, the T3 ScanScope *itself* has this function.

⁴ API is an acronym for Application Program Interface; several APIs within a ScanScope system provide "open" interfaces for second- and third- party software.

WebViewer	Software which runs on a DSR <i>as part of ImageServer</i> which provides a platform-independent capability to display digital slides in a standard web-browser ⁵ .
Digital Slide Conferencing (DSC)† .	{Formerly known as Virtual Slide Conferencing , or VSC} Software which runs on a DSR or other networked server which provides digital slide conferencing capabilities; communicates with the ImageScope viewer.
Workflow Manager†	{Formerly known as Virtual Slide Manager , or VSM} Desktop program which runs on a DSR, system console, or any other Windows PC for displaying and managing scanned digital slides. Enables display and maintenance of digital slide metadata and provides a simple interface to ImageScope for slide viewing. In this release a simple but powerful mechanism for running analysis algorithms in a batch processing mode has been added.
Security Manager†	A new desktop program in release 6 which runs on a DSR, system console, or any other Windows PC for maintaining user access settings for digital slides.
ImageScope*	Desktop program which runs on a DSR, system console, or any other Windows PC for viewing digital slides. Includes the capability to display and author annotations, to run analysis algorithms, and to join virtual conferencing sessions.
TMALab	Desktop program which runs on a DSR, system console, or any other Windows PC for segmenting and viewing TMA digital slides, and for managing their associated data. Includes the capability to run analysis algorithms.
ImageBatcher†	Utility program which enables one or more “batches” of digital slides to be compressed after scanning.
Digital Slide Studio†	{Formerly known as ImageCompressor } Utility program which enables digital slides to be cropped, scaled, adjusted, and rotated, and which enables their format and compression type to be changed.
System Information*	Utility program which displays system information and software versions; useful for problem determination.
Algorithm Framework* ⁶	Software which runs on a DSR or other server machine to enable analysis algorithms to be run on digital slides in client / server fashion. A version of AAF ⁷ is included in ImageScope and TMALab to enable analysis algorithms to be run directly on a workstation.

⁵ The WebViewer software no longer requires a separate webserver; please refer to the notes below for details.

⁶ The workstation-only version of AAF is free and is included in the ImageScope and TMALab programs. The client/server version of AAF is licensed separately on a per-server-machine basis.

⁷ The Aperio Algorithm Framework is often abbreviated as AAF.

- Positive Pixel Count Algorithm* A simple algorithm which demonstrates the capabilities of the AAF; bundled with ImageScope and TMA Lab. This algorithm provides quantitative measurements of stain densities of designated colors, as a way to identify “positive” and “negative” tissue. The source code for this algorithm is available as part of the Algorithm Framework SDK as an example for algorithm developers.
- Nuclear IHC Algorithm Algorithm software which analyzes nuclear IHC stained digital slides such as ER and PR, provides quantitative measurements of nuclear staining⁸.
- Membrane IHC Algorithm..... Algorithm software which analyzes membrane IHC stained digital slides such as Her2, provides quantitative measurements of membrane staining⁸.
- Micrometastasis Algorithm..... Algorithm software which analyzes micrometastasis stained digital slides, performs rare event detection and quantitative measurements of micrometastasis staining⁸.
- Algorithm Framework SDK* A Software Development Kit which enables second- or third- parties to develop algorithms which run in Aperio’s Algorithm Framework. Includes C++ source code and header files, examples, and documentation⁹.

⁸ This algorithm has not been approved for clinical use.

⁹ This software and documentation is now FREE to all customers, and to third-parties which wish to develop analysis algorithms for ScanScope digital slides. Please contact Aperio for more information.

Installation Instructions

All software is distributed as a single self-installing executable. If older versions of any software are already present they will be automatically updated; there is no need to uninstall any software first¹⁰. With the exception of the ScanScope Controller, all software can be downloaded and installed by customers without Aperio assistance (although we will be happy to help).

All Aperio software may be downloaded from <http://www.aperio.com/download>. For currently registered users, there will be a list of your Release 6 installers. For new customers, please register and contact us so that the proper items can be listed for download. If desired you may contact us to obtain CD-media with the software installers.

Many Aperio programs contain an integrated auto-update capability. During installation you may be asked whether you wish to check for software updates; if the machine on which you are installing has internet connectivity we suggest you do so. This way you can be sure you are running the latest versions. Additionally, such programs have a “Check for Updates...” feature in their Help menus. You may wish to select this feature from time to time to make sure you have all the latest fixes and enhancements.

The table below summarizes all the software which comprises Release 6:

Installer	location	license	comments
Controller_v6.s.0.b.exe	ScanScope	w/ SS	Coordinate with Aperio
Console_ v6.s.0.b.exe	Desktop (including DSR)	w/ SS	
ImageServer_ v6.s.0.b.exe	DSR	w/ SS	
DatabaseSchema_ v6.s.0.b.exe	DSR	w/ SS	MSDE should be running
DBIntercept_ v6.s.0.b.exe	DSR	w/ SS	
WebViewer_ v6.s.0.b.exe	DSR		Optional
DSCServer_ v6.s.0.b.exe	DSR	w/SS	
WorkflowManager_ v6.s.0.b.exe	Desktop (including DSR)	w/ SS	
SecurityManager_ v6.s.0.b.exe	Desktop (including DSR)	w/SS	New in release 6
ImageScope_ v6.s.0.b.exe	Desktop (including DSR)	free	
TMALab_ v6.s.0.b.exe	Desktop (including DSR)		
ImageBatcher_ v6.s.0.b.exe	Desktop (including DSR)	w/ SS	
DSStudio_ v6.s.0.b.exe	Desktop (including DSR)	w/ SS	
SysInfo_ v6.s.0.b.exe	(all)	free	
AAF_Server_ v6.s.0.b.exe	AAF server (DSR or other)		
AAF_Client_ v6.s.0.b.exe	AAF client (desktop or DSR)		w/ ImageScope & TMALab
Positive_ v6.s.0.b.exe	AAF client (desktop or DSR)	free	w/ ImageScope & TMALab
Nuclear_ v6.s.0.b.exe	AAF client (desktop or DSR)		Requires AAF
Membrane_ v6.s.0.b.exe	AAF client (desktop or DSR)		Requires AAF
Micromet_ v6.s.0.b.exe	AAF client (desktop or DSR)		Requires AAF
AAF_SDK_ v6.s.0.b.exe	Algorithm developer machine	free	Contact Aperio for details

¹⁰ All Aperio software is installed in the directory **C:\Program Files\ScanScope** by default. If you have older versions of software which are installed in a different directory, we recommend uninstalling it explicitly first. Please contact us if you have questions about this.

The following sections briefly describe the installation of each component. We suggest you read through all sections before installing any software as there are some inter-dependencies. If you have any questions about installing software or possible inter-dependencies please contact us.

In general the components of Release 6 have been designed so you do not have to worry about the order in which you install software. However, we do recommend you install software in the following sequence:

- All software on your DSR:
 - Console
 - Database Schema and Intercepts
 - ImageServer
 - WebViewer
 - Digital Slide Conferencing Server (DSC)
 - Workflow Manager
 - Security Manager
 - ImageScope
 - TMA Lab
 - Digital Slide Studio
 - ImageBatcher (only if still needed)
 - System Information
 - Algorithm Framework Client and/or Server
 - Algorithms

- All software on your system console machine:
 - Console
 - Workflow Manager
 - Security Manager
 - ImageScope
 - TMA Lab
 - Digital Slide Studio
 - System Information

- All software on your ScanScope machine(s)¹¹ – please contact Aperio for assistance:
 - Controller
 - Console
 - ImageScope
 - System Information

¹¹ T3 machines may serve as their own DSR, in which case all “DSR” software is installed on the T3 machine.

- All other desktop machines, as appropriate:
 - Console
 - Workflow Manager
 - Security Manager
 - ImageScope
 - TMA Lab
 - Digital Slide Studio
 - System Information
 - Algorithm Framework Client
 - Algorithms

We recommend that your installer files should be placed in the “C:\AperioInstall” directory of your DSR or ScanScope machine. This is a good way of keeping track of which versions of the software have been installed on your system. You can simply copy them from the CD you received from us or save them to this location from the download site.

Controller

The ScanScope **Controller** is the software which runs on the ScanScope machine itself, controlling the operations of the device. The Release 6 version of the Controller supports T2 machines with or without an autoloader, and T3 machines. T108 machines are not supported by the Release 6 version of the Controller¹².

Installing a new version of the Controller is a bit complicated; therefore we strongly recommend that you call Aperio technical support and have us help you with this upgrade.

The Controller runs on the ScanScope machine itself, and must be installed there. To access T2 machines, it is necessary to use Timbuktu or Windows Remote Desktop from another computer to access the T2 directly.

The following steps should be performed:

- Scan one or more typical slides with the old Controller to use as a baseline for comparison. Note the scan times and examine the images for quality.
- If installing on a T2, copy the Release 6 Controller installer to the ScanScope machine into the **C:\AperioInstalls** directory. This is typically done from the DSR or system console machine used for Timbuktu or Remote Desktop access to the ScanScope.
- Stop the Controller if it is running. Double-click the “Stop ScanScope” or “Stop ApService” icon on the desktop to stop it.
- Make a backup copy of the existing Controller folder and rename it using the date, e.g. “Controller 02-29-05”. This is a precautionary measure in case of problems.
- Double-click the Controller installer to initiate the upgrade. You must select “Repair” not “Modify”, on the first screen. In most situations all defaults can be accepted to upgrade the Controller software. A utility program named XMLUpdater will be run as part of the installation to update the Controller parameter file. It is not necessary to re-align the ScanScope after installing the Controller.

¹² Aperio will continue to support (but not enhance) the current T108 Controller software.

- Start the new Controller by double-clicking the “Start ScanScope” or “Start ApService” icon on the desktop.
- Scan the same slides as you scanned before performing the upgrade with the new Controller. Note the scan times and examine the images for quality.

After installing the Controller software we recommend you perform a number of test scans before placing the ScanScope back “in production”.

Console

The ScanScope **Console** is a desktop program which runs on a DSR, system console computer, or any other Windows PC; it provides the user interface for an operator to control operations of ScanScope devices.

A newer Console can communicate with an older Controller, so generally you should upgrade your DSR and other computers which are running the ScanScope Console *before* you upgrade the ScanScope Controller itself. Nothing bad happens if you upgrade the Controller first, but this is not recommended.

Installation is straightforward; simply double-click the installer to run it. Please select “repair” on the first screen. In most situations all defaults can be accepted to upgrade the Console.

ImageServer

ImageServer is software which runs on a DSR, providing a high-speed network interface to stored digital slides. It communicates with the ImageScope viewer and WebViewer, as well as second- and third- party software via an open message API. Communication with ImageServer is backward-compatible, so that older clients can communicate with a new server and vice-versa. In general we recommend updating the software on your DSR first, then updating the various machines which communicate with it.

Installation is straightforward; simply double-click the installer to run it. In most situations all defaults can be accepted to upgrade ImageServer. You should make sure that ImageServer is not running during the installation; if it is you can simply close the ImageServer window to take it down.

Important: If this is the first time you have installed a version of ImageServer which supports JPEG2000 compression, you will be asked to reboot following the installation. It is not necessary to reboot immediately following the installation, but a reboot will be necessary before ImageServer can serve JPEG2000-compressed images.

ImageServer supports a significant number of new options, available via command lines flags, set by editing the C:\Program Files\ScanScope\ImageServer\ImageServer.ini file. These options are discussed in the ImageServer documentation. As noted previously for release 5, ImageServer now has a “-label” parameter which *enables* serving of slide label images. If this flag is not present, label images will not be served. This is to enable compliance with HIPAA in situations

where slide labels contain live patient data and image access is not restricted. If you wish to view slide label images, you should set the “-label” parameter.

One of the new capabilities in Release 6 is user-level authentication for access to digital slides. If you desire to use this capability you must update the ImageServer configuration to use the database on the DSR for authentication, via the “-authip” and “-authprt” parameters. Additionally, another capability in Release 6 is storing annotations and digital slide metadata in the DSR database so they can be shared among multiple users. If you desire to use this capability you must update the ImageServer configuration by specifying the “-dbip” and “-dbprt” parameters. Please refer to the ImageServer documentation for details or contact us for more information.

Database Schema and Intercepts

The **Database Schema** and **Database Intercepts** are software which runs on a DSR providing the interface to the digital slide database. These two components are provided as separate installers, but should be upgraded together.

Installation/upgrade of the database schema should be performed *while the MSDE database is running*. This will typically be the case on your DSR. Simply double-click the installer and accept the default settings to perform the database schema upgrade.

Installation/upgrade of the database intercepts should be performed after the database schema has been updated. Simply double-click the installer and accept the default settings.

WebViewer

The **WebViewer** is software which runs on a DSR, integrated with ImageServer, which provides a platform-independent capability to display digital slides in a standard web-browser.

Installation/upgrade of the WebViewer is straightforward; simply double-click the installer and accept the default settings.

For release 6 the WebViewer has been completely rewritten to use ImageServer’s new APML template facility. This makes it easy for you to customize WebViewer pages and/or integrate them into your web applications. Please see the notes below and refer to the documentation for the WebViewer posted at <http://www.aperio.com/documents>.

Digital Slide Conferencing Server (DSC)

The **Digital Slide Conferencing Server** is software which runs on a DSR or other networked server which provides digital slide conferencing capabilities. It communicates with the ImageScope viewer.

In previous releases this software was named **Virtual Slide Conferencing Server**, or VSC. When you install the new version the name will be changed.

Installation/upgrade of the DSC server software is straightforward; simply double-click the installer and accept the default settings. You should make sure that DSC server is not running during the installation; if it is you can simply close the DSC server window to take it down.

Workflow Manager

The **Workflow Manager** is a desktop program which runs on a DSR, system console machine, or any other Windows PC for displaying and managing scanned digital slides. It enables display and maintenance of digital slide metadata and provides a simple interface to ImageScope for slide viewing.

In previous releases this software was named **Virtual Slide Manager**, or VSM. When you install the new version the name will be changed.

It is recommended that you update your database schema and intercepts (on your DSR machine) *before* installing the new version of Workflow Manager.

Installation/upgrade of the Workflow Manager software is straightforward; simply double-click the installer and accept the default settings. Workflow Manager shares modules with ImageScope and TMA Lab, so we recommend you update all Aperio software on a machine at the same time.

If you are installing a barcode label printer for use with Workflow Manager please verify that you have a Zebra Technologies T402 printer or a TLP 2844-Z printer (or equivalent). These printers are built for the ZPL printer language that is used by Workflow Manager and do not use the EPL language that is used by some other software applications. When installing the printer, you simply need to attach the device to your DSR or workstation using a parallel cable attached to the computer's LPT1 printer port. It is not necessary to install the Windows drivers for the printer; in fact, the Windows drivers can cause barcode printing to fail.

Workflow Manager is designed to print on custom slide labels that can be ordered through Aperio. Follow the printer instructions (in the user guide) for setting the print width to match the width of the custom slide labels. After this step, you should be ready to print 2D barcodes from Workflow Manager.

Security Manager

Security Manager is a new program in release 6 which runs on a DSR, system console machine, or any other Windows PC for maintaining user access settings for digital slides. It is not necessary to set any user access settings; this capability is provided for customers who require it.

Security Manager communicates with the database on your DSR machine. It is important to update your database schema and intercepts (on your DSR machine) *before* installing or using Security Manager.

Installation of Security Manager is straightforward; simply double-click the installer and accept the default settings. Security Manager shares modules with Workflow Manager, ImageScope, and TMA Lab, so we recommend you update all Aperio software on a machine at the same time.

ImageScope

ImageScope is a desktop program which runs on a DSR, system console machine, or any other Windows PC for viewing digital slides. It includes the capability to display and author annotations, to run analysis algorithms, and to join virtual conferencing sessions.

ImageScope is forward- and backward- compatible between releases. At many sites it may be difficult to determine all the machines which are running ImageScope, and this is okay; it is not necessary to upgrade all machines at once. ImageScope includes an auto-update facility, so eventually all copies will be updated. Of course to use new features a new version must be installed.

Installation/upgrade of ImageScope is straightforward; simply double-click the installer and accept the default settings.

Important: If this is the first time you have installed a version of ImageScope which supports JPEG2000 compression, you will be asked to reboot following the installation. It is not necessary to reboot immediately following the installation, but a reboot will be necessary before ImageScope can display JPEG2000-compressed images.

If you use analysis algorithms it is especially important that you upgrade ImageScope, as there are many new features. Server-side batch processing of analysis algorithms requires the new versions of Workflow Manager and ImageScope.

TMA Lab

TMA Lab is a desktop program which runs on a DSR, system console machine, or any other Windows PC for segmenting and viewing TMA digital slides, and managing the associated data. It includes the capability to run analysis algorithms just like ImageScope.

TMA Lab is forward- and backward- compatible between releases. At many sites it may be difficult to determine all the machines which are running TMA Lab, and this is okay; it is not necessary to upgrade all machines at once. TMA Lab includes an auto-update facility, so eventually all copies will be updated. It is important to upgrade ImageScope at the same time as TMA Lab on any one machine, since they share components.

Installation/upgrade of TMA Lab is straightforward; simply double-click the installer and accept the default settings.

The TMA Lab installer does not install JPEG2000 support. However, if the Release 6 version of ImageScope is installed on the same machine it *will* install JPEG2000 support, which can then be used by TMA Lab to process and display JPEG2000-compressed virtual TMA slides.

ImageBatcher

ImageBatcher is a utility program which enables one or more “batches” of digital slides to be compressed after scanning. The on-the-fly compression feature of the ScanScope Controller makes this program unnecessary in most configurations but it is provided for backward compatibility.

Installation/upgrade of ImageBatcher is straightforward; simply double-click the installer and accept the default settings. The ImageBatcher installer does not install JPEG2000 support. However, if the Release 6 version of Digital Slide Studio is installed on the same machine it *will* install JPEG2000 support, which can then be used by ImageBatcher to create JPEG2000-compressed digital slides.

Digital Slide Studio

Digital Slide Studio is a utility program which enables digital slides to be cropped, scaled, adjusted, and rotated, and which enables their format and compression type to be changed.

In previous releases this software was named **ImageCompressor**. When you install the new version the name will be changed.

Installation/upgrade of Digital Slide Studio is straightforward; simply double-click the installer and accept the default settings.

Digital Slide Studio shares components with ImageScope and TMA Lab, so it is recommended to upgrade all Aperio software on any one machine at the same time.

Important: If this is the first time you have installed Aperio software which supports JPEG2000 compression, you will be asked to reboot following the installation. It is not necessary to reboot immediately following the installation, but a reboot will be necessary before Digital Slide Studio can process or create JPEG2000-compressed images.

In release 6 we've included a *command line version* of Digital Slide Studio named **icomp**. This program is installed in the **C:\Program Files\ScanScope\Digital Slide Studio** directory. **icomp** may be scripted easily to automate digital slide transformation or extract tasks.

System Information

System Information is a utility program which displays system information and software versions. It is useful for determining the Aperio software installed on any particular machine,

and for problem determination. System Information is backward- and forward- compatible, but should be updated on all machines at the same time as other Aperio software.

We recommend System Information be installed on all ScanScopes, your DSR, and your system console machine (if any). For problem determination purposes it may be useful to install it on other machines as well.

Algorithm Framework (Client / Server)

The Aperio Algorithm Framework (AAF) is software which runs on a DSR or other server machine to enable analysis algorithms to be run on digital slides in client / server fashion. A client-only version of AAF is included in ImageScope and TMA Lab to enable analysis algorithms to be run directly on a client computer.

There are two separate parts to the AAF; the client and the server. The AAF server should always be installed first, and is installed on the DSR machine. The AAF client is installed on the DSR machine and any other machines in the network which are to be used for algorithm processing (AAF enables distributed processing by multiple servers on a network). We recommend upgrading AAF first, then installing updated versions of algorithms.

To install/upgrade the AAF server, simply double-click the installer, accepting the defaults.

To install/upgrade any/all AAF clients, simply double-click the installer, accepting the defaults.

We recommend testing with the client and server on the same machine first (typically your DSR). Later you can install the AAF client on other machines in your network to distribute algorithm processing. Please contact us for more information.

Algorithms

With Release 6 the format of algorithm processing routines which run under AAF has changed. If you have pre-existing algorithm software you should obtain new versions (from Aperio or a third-party algorithm vendor) which are compatible with the Release 6 Algorithm Framework.

Aperio provides the following algorithm routines:

- Positive Pixel Count Algorithm – quantifies the amount(s) of specific stain(s) present in a digital slide by quantifying pixel densities of designated colors, as a way to identify “positive” and “negative” tissue. This algorithm is provided free by Aperio as part of ImageScope and TMA Lab (client-only), and with the Algorithm Framework (client/server). Additionally, the *source code* of this algorithm is provided as an example with the Algorithm Framework SDK. For more information about this algorithm please see the documentation posted at <http://www.aperio.com/documents>.

- Nuclear IHC Algorithm – segments nuclei and measures quantity of stained vs. unstained nuclei and staining density on digital slides stained with Nuclear IHC stains, such as ER and PR. Please contact us for more details¹³.
- Membrane IHC Algorithm – segments cell membranes and measures quantity and degree of stained membranes and staining density on digital slides stained with Membrane IHC stains, such as Her2. Please contact us for more details¹³.
- Micrometastasis Algorithm – locates and quantifies micro-metastasizing cell clusters in digital slides. This algorithm typifies rare-event finding processing for digital slides. Please contact us for more details¹³.

Algorithm Framework Software Development Kit (SDK)

The Aperio Algorithm Framework SDK has been updated for Release 6, but a description of the changes as well as the installation instructions are beyond the scope of this document. If you are an algorithm developer and/or have an interest in potentially developing algorithms to run under the Aperio Algorithm Framework, please contact us for more information.

Note: as of Release 6 the Algorithm Framework SDK is FREE for development use by all customers and interested third-parties.

¹³ This algorithm is not approved for clinical use.

New Features and Notes

The following sections describe the new features and enhancements made to each component of a ScanScope system. In addition, significant bug fixes, operational considerations, and notes are also given. This is not exhaustive – we've tried to be brief here and highlight only the most significant changes.

If you have questions or comments about any of these features, fixes, or notes, please let us know. Additionally we are in active development of Release 7, so if you have input for new features or favorite bugs you'd like to see corrected, please tell us that too!

Third-party interface and digital slides files

The Aperio software creates, processes, and displays digital slides using the SVS file extension. (SVS = ScanScope Virtual Slide¹⁴.) Aperio has created a white paper which describes interfacing digital slides to third-party software in general and the SVS file format in particular. Please visit <http://ww.aperio.com/documents> to download this document.

These files are actually written according to the TIFF standard, using one of several types of image compression: none, LZW [lossless], JPEG [lossy, quality selectable], or JPEG2000 [lossy, quality selectable]. SVS files contain several separate images in one file: the "base" image, a full resolution image of the entire slide; a thumbnail image, the entire slide scaled to about 1000 x 500 pixels; the label image, a picture taken of the slide's label; and one or more "pyramid" images, which are progressively lower resolution versions of the base image.

Although SVS files are fully-compliant TIFF files, they often cannot be processed by third-party software directly, due to their large size, tiled organization, the compression type, and the presence of multiple images within the file. For this reason we chose a unique file extension. It is possible to create "vanilla" TIFF files for processing by third-party software using the Digital Slide Studio, which enables images to be cropped, scaled, and formatted differently (e.g. without tiling or compression). Digital Slide Studio also enables you to extract files in standard JPEG format. If you have questions about extracting standard TIFF or JPEG files from SVS files please contact us.

User-level digital slide access authorization

In release 6 there is an optional capability to restrict access to digital slides by user. Authorization for digital slides and users is managed by the new Security Manager program, and is enforced by ImageServer. Authorization for slides is managed at the directory level, and is supported by both ImageScope and WebViewer. Directories containing digital slides can be designated as "public" (accessible by anyone) or "private" (accessible only by authenticated users). For any given user access to a private directory can be read-only or full. Read-only

¹⁴ In keeping with our nomenclature change these files really should be called SDS, ScanScope Digital Slides. However customers have created thousands of virtual digital slides, so we decided not to change this extension.

access entitles a user to view the slide but not to update slide metadata or associated information such as annotations. Full access enables slide updates, and enables the ability to rename or delete the files¹⁵ as well.

By default ImageServer uses the database on the DSR to store user authentication information. If desired customers may interface ImageServer to an external authentication source. The message API for doing this is described in the ImageServer documentation. If you are interested in doing this please contact us for more information.

Macro images in digital slides

With Release 6 the macro image obtained at the start of a scan is now stored in the digital slide file (SVS), and may be displayed in the ImageScope viewer and on WebViewer pages. The macro image includes the entire slide area, regardless of the scan area determined by tissue finder or designated manually.

JPEG2000 compression

As with release 5, the software in Release 6 supports JPEG2000 compression. This type of compression yields files which are much smaller than JPEG for the same quality level, or much higher quality for the same file size (depending upon the quality setting). This is especially advantageous when *zooming beyond 100%*. (See the discussion of this under ImageScope below).

If you have a significant library of existing digital slides, we recommend you experiment with JPEG2000 compression before switching over all scanning. **All your existing digital slides will always be supported by Aperio software.** We are providing JPEG2000 compression because it has significant benefits but it will never be a requirement.

When digital slides are compressed with JPEG2000, a quality factor is specified. The range of quality is 1-100, with a default value of 30. In our testing we have determined that JPEG2000 with a quality factor of 30 results in *slightly better* image quality than JPEG with the same quality factor. We have also determined that JPEG2000 with a quality factor of 70 results in files which are *slightly smaller* than JPEG at a quality factor of 30, but with fewer compression artifacts. You can experiment with different quality factors using the Digital Slide Studio program.

Please note that existing digital slides should not be recompressed in most cases, because the secondary compression may result in some image degradation.

JPEG2000 compression requires significantly more computation, and hence takes longer. Scanning or compressing digital slides with JPEG2000 may take up to 50% longer than before. This is particularly evident when scanning with on-the-fly compression at 20X. For this reason the system default as installed for compression when scanning at 20X is JPEG (type=2) with a

¹⁵ The capabilities to rename and/or delete slides must be explicitly enabled via ImageServer parameters.

quality factor of 30. There are other factors involved when scanning at 40X, so the compression time is usually not rate-limiting. Therefore the system default as installed for compression when scanning at 40X scanning is JPEG2000 (type=3) with a quality factor of 70.

The compression type and compression quality level used when compressing on-the-fly can be changed easily in the ScanScope controller. It is also easy to make “Parameter Sets” so that switching both compression type and quality together can be done easily. Please contact Aperio support if you have any questions about this.

As an option, Aperio now makes available a hardware compression board made by Matrox Imaging, which accelerates JPEG2000 compression by about 50%. This board is typically installed in a ScanScope T2 in conjunction with on-the-fly compression. It may also be installed in a DSR or other Windows machine for use by Digital Slide Studio if on-the-fly compression is not being used. Please contact us for more information.

ScanScope Console and Controller

For Release 6 many changes have been made to the ScanScope **Console** and **Controller** software. T2 ScanScopes (with or without autoloaders) and T3 ScanScopes are supported by the Release 6 Controller.

Here is a list of the most significant changes to the ScanScope Console and Controller:

- **High resolution macro camera support.** The Console and Controller now support high resolution macro cameras in T3 machines, enabling better tissue finder operation and more accurate focus point placement.
- **Manual macro focus.** The Console and Controller now support manual macro focus for digital slides with faint tissue areas or sparse distributions. This capability can be used on an exception basis when required.
- **High-resolution macro images.** The Console and Controller now support high-resolution macro images. This is an optional mode where a low-resolution scan is performed to obtain a macro image, rather than a snapshot taken using the macro camera. This enables more accurate tissue finding and focus point placing for slides with faint tissue areas or sparse distributions such as cytology samples. It takes approximately two minutes to obtain a high-resolution macro image. High-res macro mode may be selected via controller parameters and/or via Parameter Sets. This capability can be used on an exception basis when required.
- **Automatic light source failure detection.** A burnt out light bulb or other light source failure is now automatically detected and scanning is aborted.
- **Automatic light source gain adjustment.** The Controller now performs automatic light source gain adjustment following bulb replacement or other activities which change the light source intensity.
- **Default for scanning at 40X is now JPEG2000 at quality 70.** The default for scanning at 20X remains JPEG at quality 30. Please see the JPEG2000 compression section above on page 19 for details.
- **Enhancements to tissue finder logic.** The algorithms used to determine the scan area from the macro image and to automatically place focus points have been refined. With

this release there are fewer cases where tissue areas and focus points have to be determined manually.

- **Improved handling of disk space errors.** The Controller now reports and gracefully recovers from conditions where the ScanScope disks are full. This typically occurs when there is a network communication error between the ScanScope and the DSR, such that scanned slides are stored locally instead of on the DSR disks.
- **Improved gripper logic to detected missing or dropped slides.** The logic for managing the slide gripper in the T2 autoloader has been enhanced to detect missing or dropped slides, or cases where the slide “sticks” in the slide rack. This typically occurs when the slide is wet or sticky, or when a slide label protrudes over the edge of a slide.
- **Numerous changes to improve diagnostics and logging.**

ImageScope

The ImageScope viewer has been significantly enhanced for Release 6. Older versions of ImageScope still may be used to view slides created with Release 6, and conversely the new version of ImageScope fully supports slides created with previously releases.

For Release 6 we've created an extensive demo / tutorial using ImageScope. This is a script which walks you through opening images, creating and viewing annotations, running analysis algorithms, and using Slide Conferencing. If you are curious about the new features of ImageScope for Release 6 this is a great place to start. The demo may be downloaded from the Aperio website at <http://www.aperio.com/documents>.

Here is a list of the most significant changes to ImageScope:

- **Smart sync.** When two or more digital slides are opened for viewing this capability enables them to be synchronized automatically, even if they are not identical. (This means the images are aligned so that the same region of each image is displayed, at the same resolution.) For example, this may be used to synchronize an H&E slide and IHC slide made from consecutive slices of the same tissue block.
- **All digital slides open together in ImageScope instance.** In previous releases each digital slide opened in a separate copy of ImageScope, and separate window; now all open in one copy, with windows side-by-side. This enables multiple slides to be compared easily, and avoids an accidental proliferation of instances of ImageScope. It also enables ImageScope to manage cache memory more efficiently.
- **Default gamma file.** ImageScope now enables a default gamma file with image adjustments to be specified for a particular workstation. This allows you to compensate for a particular monitor, ambient lighting conditions, etc. It is still possible to load other designated gamma files which may have corrections for slide types or stains. Under all circumstances gamma files only affect how a digital slide is viewed, they never alter the contents of the digital slide itself.
- **Navigation improvements.** ImageScope has a number of navigation improvements, including forward and back buttons (to enable revisiting previous views, much like a web browsers), and “joystick mode” (which enables you to pan continuously through an image in any direction).
- **Support markup images and interactive/batch analysis modes.** See the Analysis Algorithms section below

- **Rulers as annotations.** For Release 6 ImageScope now treats rulers as a new kind of annotation. Multiple rulers can be created for any digital slide, and stored for later recall. Rulers are also now printed in “snapshots” (like other annotations).
- **Support for macro images.** As noted above, in Release 6 ScanScope systems now store a “macro image” for each slide in the digital slide file. This is a low resolution snapshot of the entire slide area. ImageScope enables macro images to be displayed in the Image Information dialog box.
- **Initial magnification option.** ImageScope now provides an initial magnification option, which enables you to specify the default magnification to use when a digital slide file is opened (as a percentage). A value of zero means “fit the slide into the window”.
- **Maximum magnification option.** ImageScope now provides an option to specify the maximum magnification for viewing. This allows you to change the maximum magnification from 100% to a *larger value*, so that you can “zoom in” further. This doesn’t actually increase the resolution of the image, but it does enable the human eye to see more detail, especially when using monitors with a small dot pitch such as laptop screens and very high-resolution monitors.
- **Maximum cache size option.** ImageScope now provides an option to specify the maximum amount of memory allocated toward digital slide caching. This is useful on workstations which are running a lot of other software, enabling ImageScope to cooperatively share the machine’s memory.
- **Use registry rather than INI file for storing program settings.** ImageScope now stores workstation options in the computer registry rather than a local INI file.
- **Windows extension to display digital slide thumbnails.** When ImageScope is installed, it now installs a small extension to Windows which enables digital slides to be displayed as thumbnails in the Windows Explorer and Windows dialog boxes. After ImageScope has been installed this capability is present regardless of whether ImageScope is running or not.

Analysis Algorithms

The capability of running analysis algorithms on *entire* digital slides is one of the unique features of Aperio’s ScanScope systems, and in Release 6 we’ve made a number of significant improvements to this capability.

Here is a list of the most significant changes to algorithm processing:

- **Support markup images.** All analysis algorithms now have the ability to [optionally] create “markup images” which show the results of the algorithm processing visually. For example, an algorithm which segments cell nuclei can display the segmentation results by outlining positively stained nuclei in green and negatively stained nuclei in red. Markup images are associated with an annotation layer. This layer also contains algorithm results and the quantitative measurements computed by the algorithms. All algorithms results are stored as an annotation layer for the digital slide, and in Release 6 these layers are stored in the DSR database. This enables algorithm results to be viewed by multiple users from different locations.
- **Support batch mode analysis.** Analysis algorithms can be run “client-side”, interactively, as part of ImageScope and TMALab. With Release 6 they can also be run “server-side”, in batch mode. Workflow Manager has been enhanced to enable

submitting algorithm processing jobs, editing them, and monitoring their progress. Workflow Manager enables sets of algorithm parameters to be stored as “macros” for batch mode processing. Finally, Workflow Manager enables algorithm results for one or more slides, or all slides in batch, to be exported directly into Microsoft Excel.

The Aperio Algorithm processing facility enables an entire digital slide to be analyzed, or a selected region of analysis (ROA). An ROA is designated using annotation tools, and may be discontinuous (that is, it may consist of multiple regions). In Release 6 we’ve added support for “negative annotations” in an ROA. A negative annotation is a region which is *to be excluded* from algorithm processing. If an ROA consists only of negative annotations, then an algorithm will run on the entire slide except for the designated regions. Any combination of normal and negative annotations may be authored to precisely define the regions of a digital slide to be analyzed. In Release 6 support for negative annotations is carried throughout the ScanScope system; ImageScope provides the capability to author them, and the algorithm processing routines support them when algorithms are run “client-side” as part of ImageScope or TMA Lab, and “server-side” via the Workflow Manager’s batch processing capabilities.

ImageServer and WebViewer

In Release 6 ImageServer has been enhanced significantly, including the addition of a web page template facility which has enabled the WebViewer to be integrated directly into ImageServer.

Here is a list of the most significant changes to ImageServer:

- **ImageServer now runs as a service.** By default, ImageServer now runs as a Windows service rather than a stand-alone program¹⁶. The service includes a “heartbeat” capability which automatically restarts ImageServer in the event of any failures. It is now no longer necessary to sign on to a DSR for ImageServer to be available.
- **User-level authentication.** As noted above, Release 6 supports user-level authentication; please see the section on page 18 for details.
- **Annotation sharing.** ImageServer now stores annotations for “remote” digital slides in the DSR database. All users which access ImageServer can view all annotations stored for digital slides, including algorithm results.
- **APML template support.** ImageServer now provides the capability to generate HTML pages from directory and image file information using a simple template language called APML (Aperio Markup Language). This facility was used to rewrite the WebViewer application, and makes it much easier for you to customize WebViewer pages. Please see the documentation at <http://www.aperio.com/documents> for details.
- **Linux support.** ImageServer is now available to run on Linux as well as Windows. We have tested with RedHat versions 7, 8, and 9 on single-processor machines, but by design ImageServer should run on any Linux distribution and on multi-processor machines. Please contact Aperio if you are interested in running ImageServer on Linux.

The Aperio **WebViewer** has been rewritten in Release 6 to use ImageServer’s APML template facility. This change has several benefits:

¹⁶ In most circumstances running ImageServer as a service is desirable. It is still possible to run ImageServer as a stand-alone program if this is required; please contact Aperio support for details.

- **A separate webserver is no longer required for WebViewer.** ImageServer now provides viewer HTML pages as well as image data.
- **A single port can now be used for WebViewer and image access.**
- **Enhanced performance.** This change is architecturally simpler and faster than using a separate webserver for generating pages, and WebViewer page performance is now faster.
- **User-level authentication.** As noted above, Release 6 supports user-level authentication; please see the section on page 18 for details. Having WebViewer integrated into ImageServer enabled a simple implementation of authentication which uses standard web browser mechanisms.

There are several other **WebViewer** enhancements in Release 6:

- **Current Magnification.** The current magnification is now displayed in the WebViewer.
- **Image information.** WebViewer now includes an Image information display box which “pops up” in a separate window to display digital slide attributes, the image’s label image (if any), and the image’s macro camera image (if any).
- **RSS feeds¹⁷.** WebViewer now generates RSS feeds when displaying image directories. These feeds may be used with any RSS reader to enable users to “subscribe” to directories of images, and easily view updates to the directories.

Additionally, new features have been added to the open ImageServer API, which supports HTTP requests. Detailed documentation for the ImageServer API is contained in the ImageServer documentation. For Release 6 there are three documents which describe these programs; the ImageServer documentation describes the ImageServer program itself, along with the parameters it supports and its API. This document may be found at:

http://aperio.com/documents/Aperio_ImageServer.pdf

A separate document describes the WebViewer and especially how it may be easily customized and/or integrated into second- and third- party websites. This document may be found at:

http://aperio.com/documents/Aperio_WebViewer.pdf

As noted, ImageServer now supports a simple template language called Aperio Markup Language (APML). Customers wishing to customize the WebViewer templates and/or create their own web applications using this facility can find a description of the APML language in the following document:

http://aperio.com/documents/Aperio_Markup_Language.pdf

For Release 6 several performance improvements have been made to **ImageServer**. As before, details from our performance testing are posted on the Aperio website at:

http://aperio.com/documents/Aperio_ImageServer_performance_measurements.pdf.

¹⁷ RSS is an acronym for Real Simple Syndication; this is a standard mechanism for providing a “table of contents” for a website or group of data. RSS feeds contain XML data and are displayed by desktop programs called “Feed readers” in a manner similar to email.

Included in the performance improvements is the capability for ImageServer to cache directories as well as image data, speeding access to directories which contain many digital slides.

TMALab

For Release 6 TMALab has been enhanced significantly with the ability to run analysis algorithms interactively, just like ImageScope, except for TMA cells. One or more or all TMA cells can be analyzed using the same algorithms as used with ImageScope.

As with ImageScope, in Release 6 TMALab now has the ability to display algorithm results visually via “markup images” as well as quantitatively.

Digital Slide Studio

(This program was named **ImageCompressor** in prior releases.)

In release 6 we’ve included a *command line version* of Digital Slide Studio named **icomp**. This program is installed in the **C:\Program Files\ScanScope\Digital Slide Studio** directory. **icomp** may be scripted easily to automate digital slide transformation or extract tasks.

Running **icomp** with no parameters generates the following help text:

```
usage: icomp <source> <dest> (<options...>)
  -d<description> description included in output file
  -b<blocksize>   output block size, 0 = stripped (default = cAOC)
  -t<thumb>       0 or 1 - whether to generate thumbnail (default = 1)
  -tw<width>      thumbnail width (default = computed)
  -th<height>     thumbnail height (default = computed)
  -p<levels>      pyramid levels (default = computed)
  -c<comptype>    0=none, 1=LZW, 2=J2K/WIS, 3=J2K/MIL, 8=JPEG
  -ct<threads>   number of compression threads (default = computed)
  -cp<prio>       compression thread priority (default = computed)
  -q<quality>     compression quality (1-99, default = 30)
  -il<left>       cropping: left offset
  -it<top>        .         top offset
  -iw<width>      .         width
  -ih<height>     .         height
  -ow<width>      output width (default = same as input)
  -oh<height>     output height (default = same as input)
  -s<scale%>     scale percent (both X and Y)
  -sx<scaleX%>   scale percent (X only)
  -sy<scaleY%>   scale percent (Y only)
  -r<rotation>   orthogonal rotation (0-7)
  -x<excelfile> write stats into specified excel file (CSV)
  -v(1)          display informational messages (1 = more)
```

The <source> and <dest> parameters are required and specify the input image file and output image file, respectively. All other parameters are optional and may be used to control the processing. Please contact Aperio if you have any questions about using **icomp**.

Workflow Manager

The **Workflow Manager** has been extensively updated for Release 6. (This program was named **Virtual Slide Manager** in release 5.)

This program displays a list of all slides scanned within a system (including by multiple ScanScope machines), and allows them to be sorted and filtered by case, date, type, and other attributes. In addition slide metadata may be defined and maintained.

Workflow Manager provides a simple interface for launching the ImageScope viewer for individual slides or for all slides in a case. Slide thumbnails and label images are displayed for easy reference, along with accession numbers or other data decoded from barcodes¹⁸. All scan data are displayed such as ScanScope machine id, date/time of scan, focus quality value, etc. A facility is provided to “QA” slides prior to releasing for further processing.

In Release 6 Workflow Manager has been enhanced to support running analysis algorithms server-side in a batch processing mode. Users may sequentially view digital slides, annotating regions of analysis as desired, and then queue them up for analysis processing. Workflow Manager provides the ability to view the queue of jobs awaiting processing, and to delete jobs from the queue. It also enables sets of algorithm parameters to be stored as “macros” for use by batch processing runs.

After algorithm processing is complete, users may view results interactively using ImageScope. In addition, a simple facility enables one or more slides’ algorithm results to be exported directly into Microsoft Excel for further analysis, graphing, etc.

Workflow Manager now enables Datamatrix 2D barcode labels to be printed, using a Zebra barcode printer. In a typical workflow process labels are printed as the slides are prepared, and affixed to slides to unambiguously identify them. Slide metadata information is entered into Workflow manager at the same time, reducing the chance of mis-associating the data with the scanned slide. When slides are scanned the ScanScope controller decodes the barcode values, and the scanned image is associated automatically back to the metadata entered when the label was printed. The digital slide can then be viewed or processed further by analysis algorithms.

¹⁸ The ScanScope Controller can decode a variety of commonly used barcode types.