Leveraging the HALO Link Collaborative Image Management Platform at a Contract Research Organization

HALO Link is a collaborative image management system that enables users to remotely access and share study data, slides, and analysis results in an intuitive, browser-based platform. HALO Link is a highly flexible platform where metadata fields and workflows are customizable on a per-study basis in the user defined study architecture **(Figure 1)**.

The interactive, web-based slide viewer grants users the ability to review analysis markups, create annotations, and leave comments for collaborators. In addition to image management functionality, HALO Link seamlessly integrates with the HALO® image analysis platform and HALO AI allowing users to launch analysis jobs from within HALO Link with previously saved settings. HALO Link is currently used in organizations as diverse as academia, biotech, pharma, and contract research organizations (CROs). Deployments vary in size from five users to enterprise-wide deployments, such as at the National Cancer Institute (NCI)[1].

In this white paper, we highlight how the Pharma Services team at Indica Labs collaborates with customers using HALO Link, as they function as an independent CRO that provides digital pathology services for their customers.

Indica Labs' Pharma Services collaborates with customers using HALO Link

The Pharma Services team at Indica Labs is a multidisciplinary group with PhD-level imaging scientists, image analysts and pathologists with expertise in many research areas including image analysis, artificial intelligence (AI), oncology, immuno-oncology, GI pathology, and dermatology. The team is growing rapidly and has completed over 245 projects that span the gamut of biomarker assays including chromogenic, single-plex fluorescence, multi-plex fluorescence, and projects requiring AI, spatial analysis, advanced data analysis, and visualizations. Regardless of the scope of the project, the team works collaboratively with their customers to assist in extracting biomarker data from IHC and immunofluorescence studies to inform their customer's decisions on biomarker programs and to help them achieve their research goals.

A cloud-based deployment of HALO Link enables Pharma Services to connect and collaborate with customers and pathologists around the world. Utilizing internet access and a web browser to connect, multidisciplinary biomarker analysis teams can access and interact with the study images, annotations, and results. These highly collaborative teams include

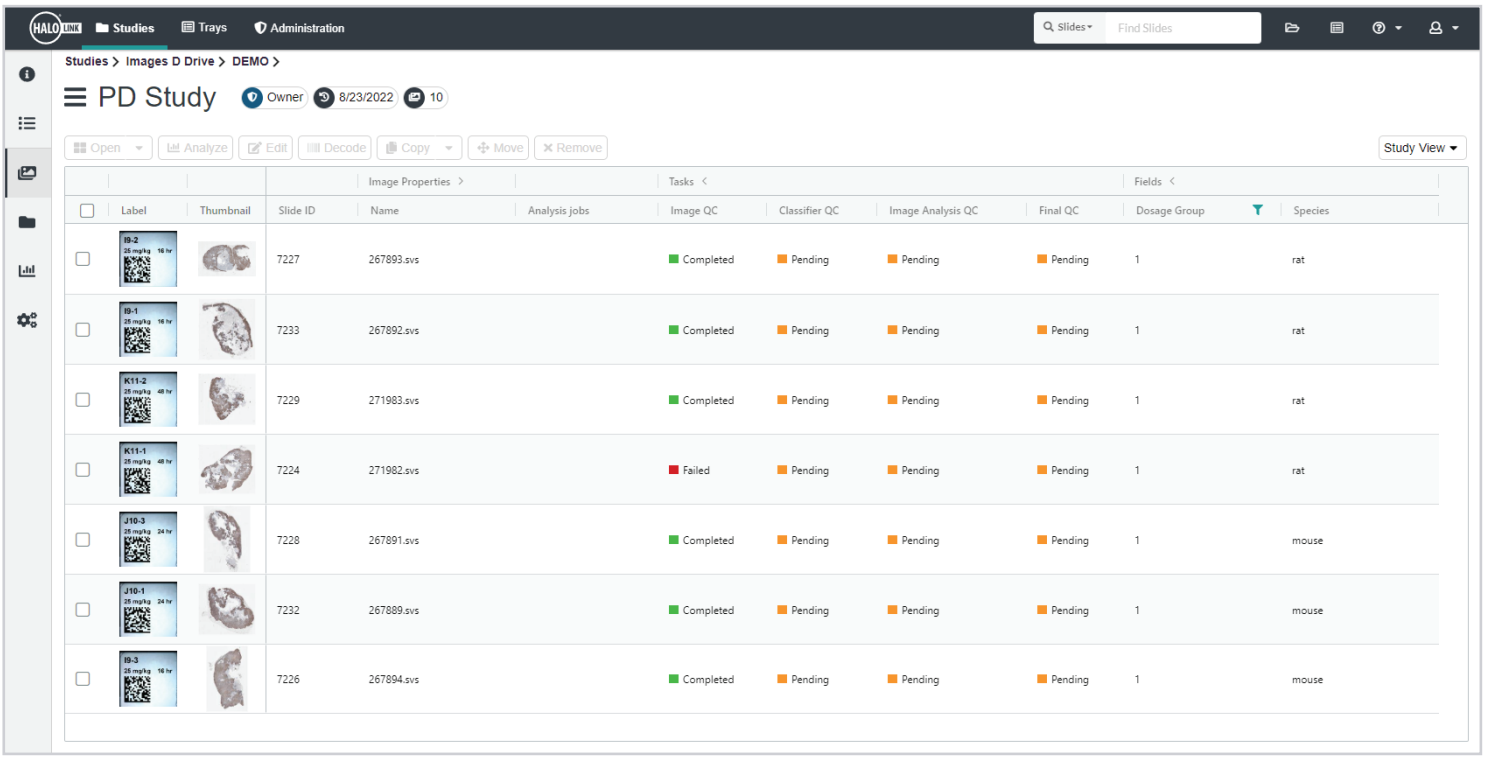


Figure 1. The HALO Link collaborative image management platform. Organize slides into studies, customize metadata and fields, and filter and sort data. Dosage Group and Species are custom fields in this pharmacodynamics study and a filter has been applied to view Dosage Group 1. Tasks can also be customized so that customers can follow progress on their studies. Here, tasks include Image QC, Classifier QC, Image Analysis QC, and Final QC.

pathologists as well as the customer project team, the Indica Labs project team and our respective project team leaders **(Figure 2)**. The customer project team includes the scientific experts looking to interpret the images and study results. The pathologist (from Indica Labs and/or Customer) can access the study to perform various tasks including interpretation, annotations, and quality control. The Pharma Services team includes application expertise and is responsible for HALO and HALO AI image analysis development and secondary data analysis using tools such as TIBCO Spotfire®.

A Flexible Study Architecture Supports CRO Workflows

HALO Link is a flexible image management platform where users can define their unique study architecture. Pharma Services and other CROs choose to create a study hierarchy dependent on the complexity and size of the customer's organization. A smaller organization (Customer 1) can use a simple structure organized by projects while larger organizations (Customer 2) may need to subdivide the studies by departments and then projects **(Figure 3).** In HALO Link, user permissions carry down to studies lower in the hierarchy. If Pharma Services always worked with the same group of people at a customer site, permissions could be extended at the Customer 1 level, and this would ensure that the same group of people have access to Project A and Project B. In the case where there are multiple functional groups at a customer site, a customer could be further subdivided into departments such as Tox Path and Oncology, as shown for Customer 2. User permissions could then be assigned at the departmental level.

Collaborators can be invited to a HALO Link study individually or in the context of a user group. A user group is a defined group of individuals, in some cases from various institutions and organizations, that acts like an email list providing a streamlined invitation workflow. Inviting a user group to a study ensures that every member of the group receives access to the study at the same permission level. A user group could also be created on a departmental basis. For example in Figure 3, the Toxicologic Pathology department could be assigned a user group, enabling access to all projects (Project A and Project B) in that department.

HALO Link offers a simple yet powerful permissions hierarchy **(Table 1)**. User permissions are granted on a per study basis by either the system administrator or the study owner. At the lowest level, a viewer can only

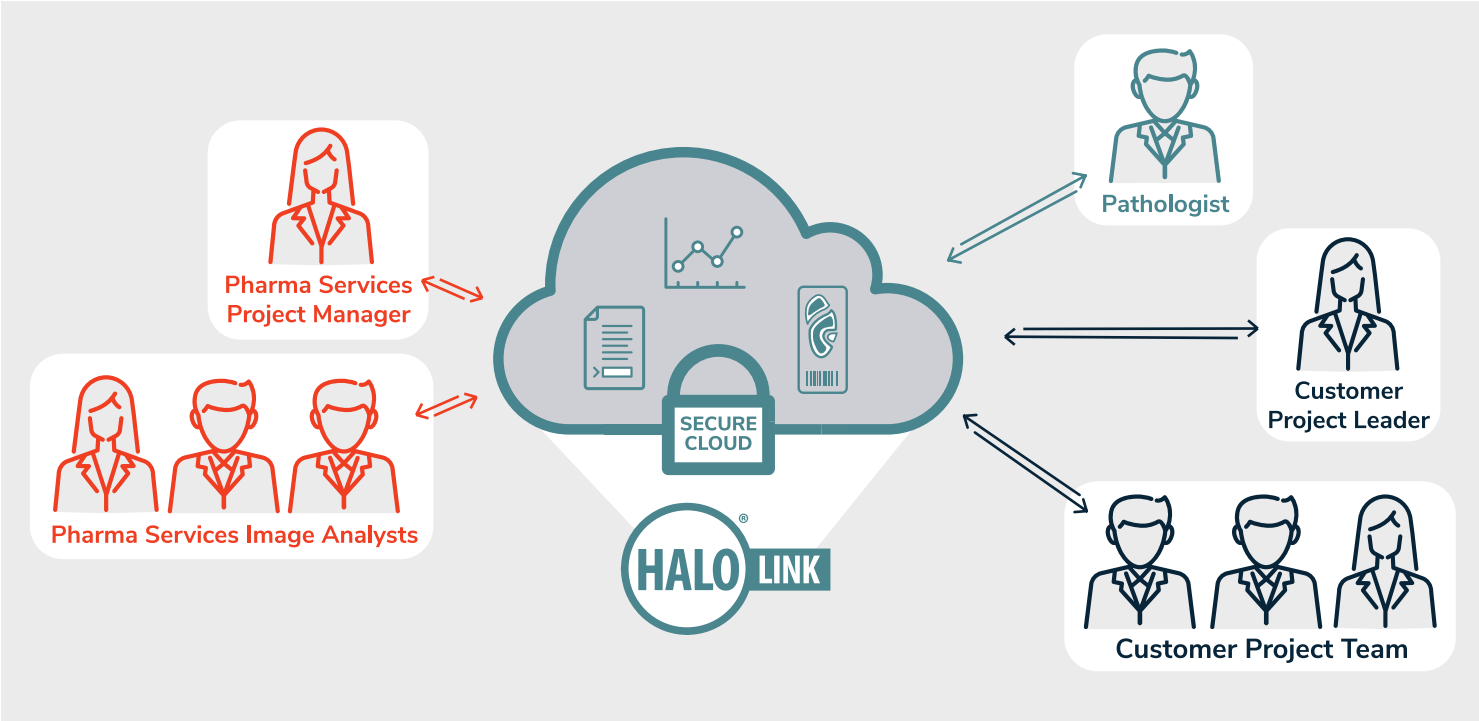


Figure 2. Schematic of how a cloud-based deployment of HALO Link enables international collaborations between organizations. HALO Link serves as a hub or central repository for Pharma Services data which facilitates sharing of images, annotations, and analysis data with customers and external collaborators, such as pathologists.

view the slides, metadata, image analysis results, plots, and attached files of a study. In a CRO environment such as Pharma Services, the end customer would most often be provided with the viewer permission level. A collaborating pathologist would typically be given an annotator permission level, enabling them to create annotations on slides. The next level up is the editor level, which additionally grants users the ability to edit metadata, run analysis, and to move or copy images. At the top of the hierarchy is the study owner, who in addition to editor privileges, also can delete images and invite collaborators. Image analysts in Pharma Services have owner permissions.

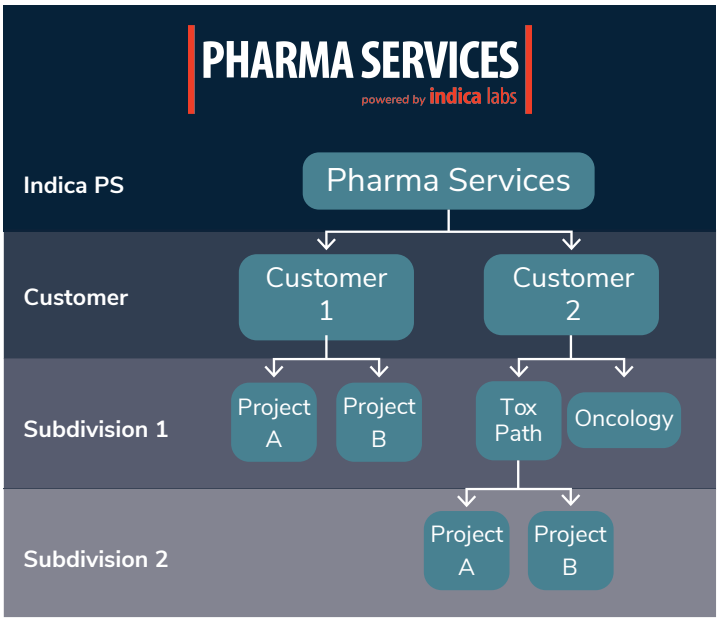


Figure 3. High level organization of Pharma Services' studies in their HALO Link deployment.

Interacting with Customers Over the Course of a Project

Transparency and a close collaborative relationship with the customer are essential for success on a Pharma Services image analysis project. Customers are involved throughout the duration of the project through a series of touchpoints to review results and progress in HALO Link. A typical project includes four stages: Initial Study Review, Region-of-Interest (ROI) Classification, Cellular Analysis, and Project Completion **(Figure 4).** In addition, there are key quality control (QC) checkpoints including Image QC, Classifier QC, Image Analysis QC, and Final QC.

At the beginning of the project, the Pharma Services team creates the study and uploads all images and metadata to HALO Link. The study is shared with the customer team and collaborators, and each are given appropriate access permissions depending on their role. A series of HALO Link tasks are created to

Permission Levels	View	Annotate	Analyze	Move/Copy Images	Delete Images	Invite Collaborators
Owner	✓	✓	✓	✓	✓	✓
Editor	✓	✓	✓	✓		
Annotator	✓	✓				
Viewer	✓					

Table 1. HALO Link privileges for each permission level.

match the study workflow, e.g., Image QC, Classifier QC, Image Analysis QC, and Final QC **(Figure 1, Figure 4).** The image tasks allow the customer team to quickly visualize the progression of the study workflow and identify images that may have failed a specific QC checkpoint. For example, an image may have failed during the Image QC phase because the image is out-of-focus. The Image QC task would be marked as "Failed", the customer would be notified, and this slide could be re-scanned. During the ROI/Classification phase, a tissue classifier may require feedback or pathologist annotations, so the pathologist could create and or edit annotations and provide commentary using the slide and annotation comments. During the tissue classifier and cell analysis algorithm development, the customer team and pathologist can review markups to provide feedback and assess accuracy **(Figure 5).** As the project progresses and each of the HALO Link tasks transition to "Completed", the customer can access the images at any point to review the progress of the image analysis workflow.

Since HALO and HALO Link share a database, the project workflow between the customer, pathologist, and image analyst is completely transparent and collaborative. The pathologist can view the preliminary

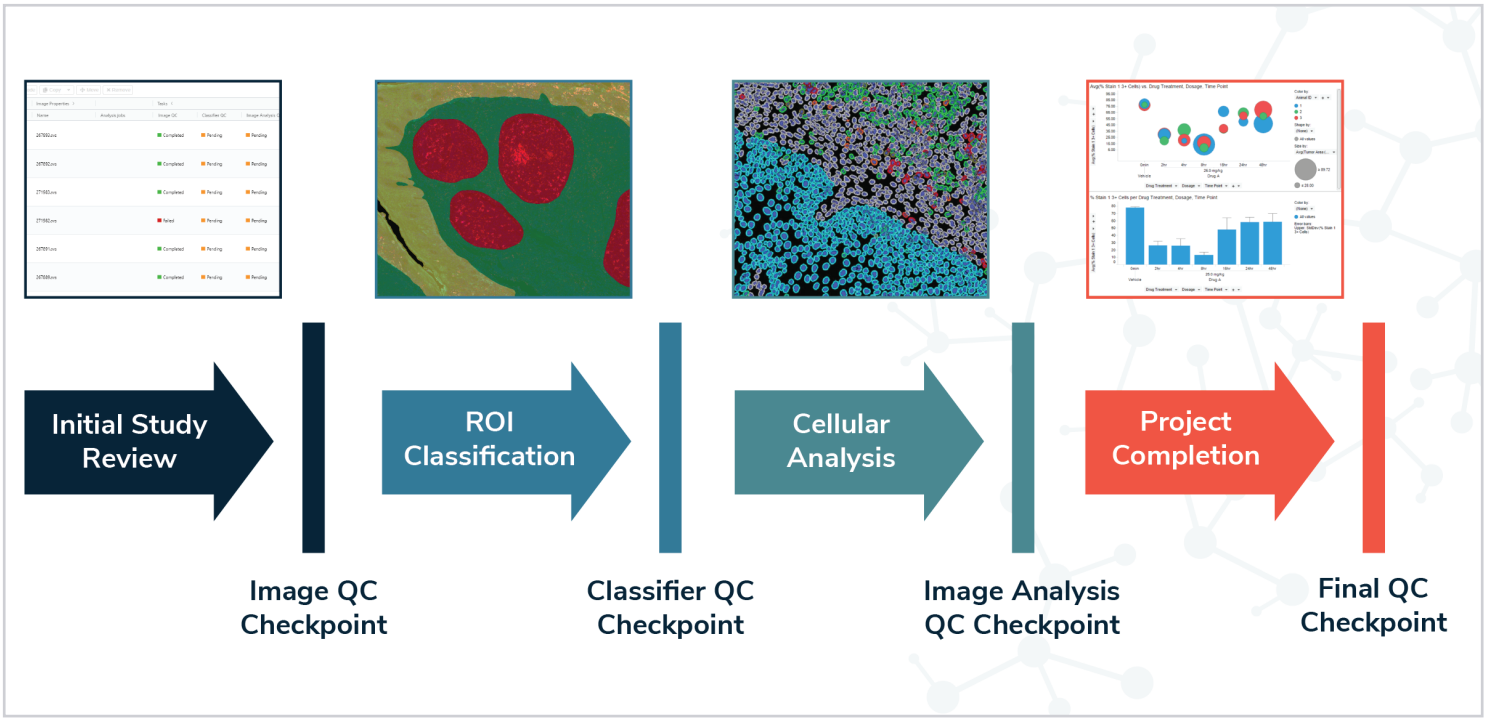


Figure 4. Pharma Services utilize HALO Link extensively in their interactions with customers over the course of a project. Easy remote access is critical to transparency and success as the Pharma Services team interacts with customers throughout the development of complex image analysis workflows. Multiple quality control checkpoints exist for Indica Labs' project lead, image analyst, and pathologist. In the Image QC checkpoint, images and metadata are uploaded to HALO Link and image quality control is performed. In the Classifier QC checkpoint, an ROI for image analysis is defined where the image analyst and pathologist then collaborate on classifier development in HALO Link. In the Image Analysis QC checkpoint, cell and biomarker segmentation parameters are defined and results are reviewed in HALO Link. In the Final QC checkpoint, results, reports, and visualizations are uploaded to HALO Link.

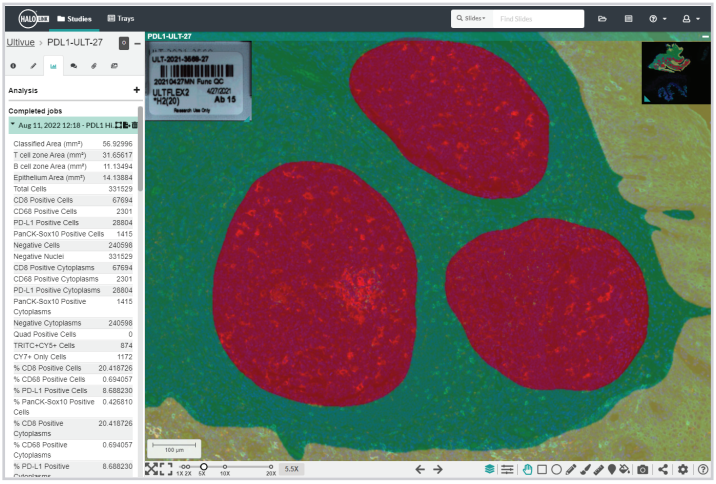
results in HALO Link and provide feedback. In the Image Analysis QC checkpoint, the pathologist and customer review and sign off on the image analysis. Following completion of the Final QC checkpoint, the Pharma Services team uploads all project deliverables to the HALO Link study including HALO object data, summary data, graphs, and visualizations as well as all presentation reports. The ability to quickly and easily upload a wide variety of data types to a study enables Pharma Services to store a complete repository of all data produced during a project in one place and provides a convenient location for customers to access this data. After the Project Completion stage, optional project archiving and image hosting are available services provided by Pharma Services at Indica Labs.

HALO Link trays facilitate collaborative pathology review and QC

Trays in HALO Link can be thought of as a digital version of a physical slide tray where a collection of slides from different studies can be brought together for review and discussion. Prior to a team discussion, pathologists, image analysts, and customers can add comments to slides in a tray facilitating an active dialog regarding classifier performance, image analysis results, or other aspects of the workflow.

In the Pharma Services workflow, trays are a heavily utilized feature during the Classifier QC and the Image Analysis QC checkpoints, where the image analyst, pathologist, and customers can join a conference call to review the tray in HALO Link. Conferencing can be accomplished using the HALO Link Conferencing feature or through a third-party screensharing application. As slides are added to a tray for review, slide metadata, annotations, and analysis results are copied to the tray so that the slide can be reviewed in context. Slides can be added to a tray either from a study or from a search. Trays can house slides from across different studies to create a more robust review of slides pertaining to a specific project if desired. Tray owners and editors can easily drag and drop slides in the viewer slide list to prioritize what is reviewed first. Slides can also be marked as examined in a tray to indicate when they have been reviewed, as are the last slides in **Figure 6**. Following review, a slide can be removed from a tray without deleting the source data in the study, thus providing a temporary repository for discussion of a handful of selected slides that keeps the original study data intact.

A



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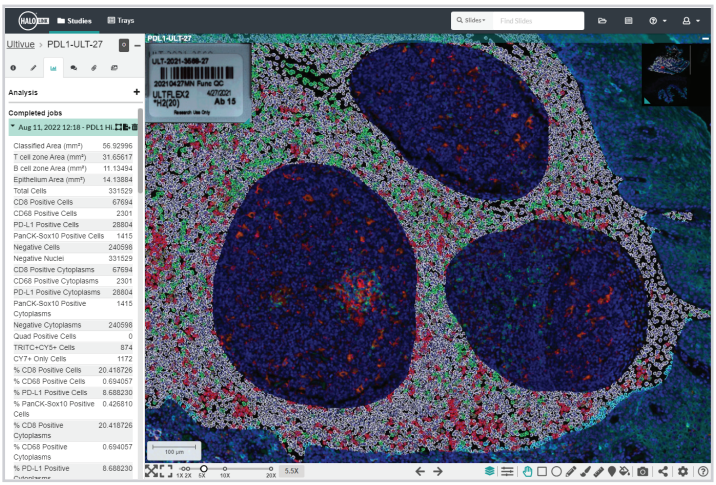

Figure 5. A. HALO AI tissue classifier markup image in HALO Link where B cell zones are red, T cell zones are green, and epithelium is yellow. **B.** Highplex FL analysis of T cell zones is shown in HALO Link.

Summary

The collaborative HALO Link platform is an essential tool for managing successful digital pathology projects from start to finish for the Pharma Services team at Indica Labs and many other CROs offering image analysis services to clients. HALO Link has a flexible and intuitive interface for CROs to customize collaborators, image metadata, study metadata, tasks, and provides tools such as trays for collaborative slide and analysis review.

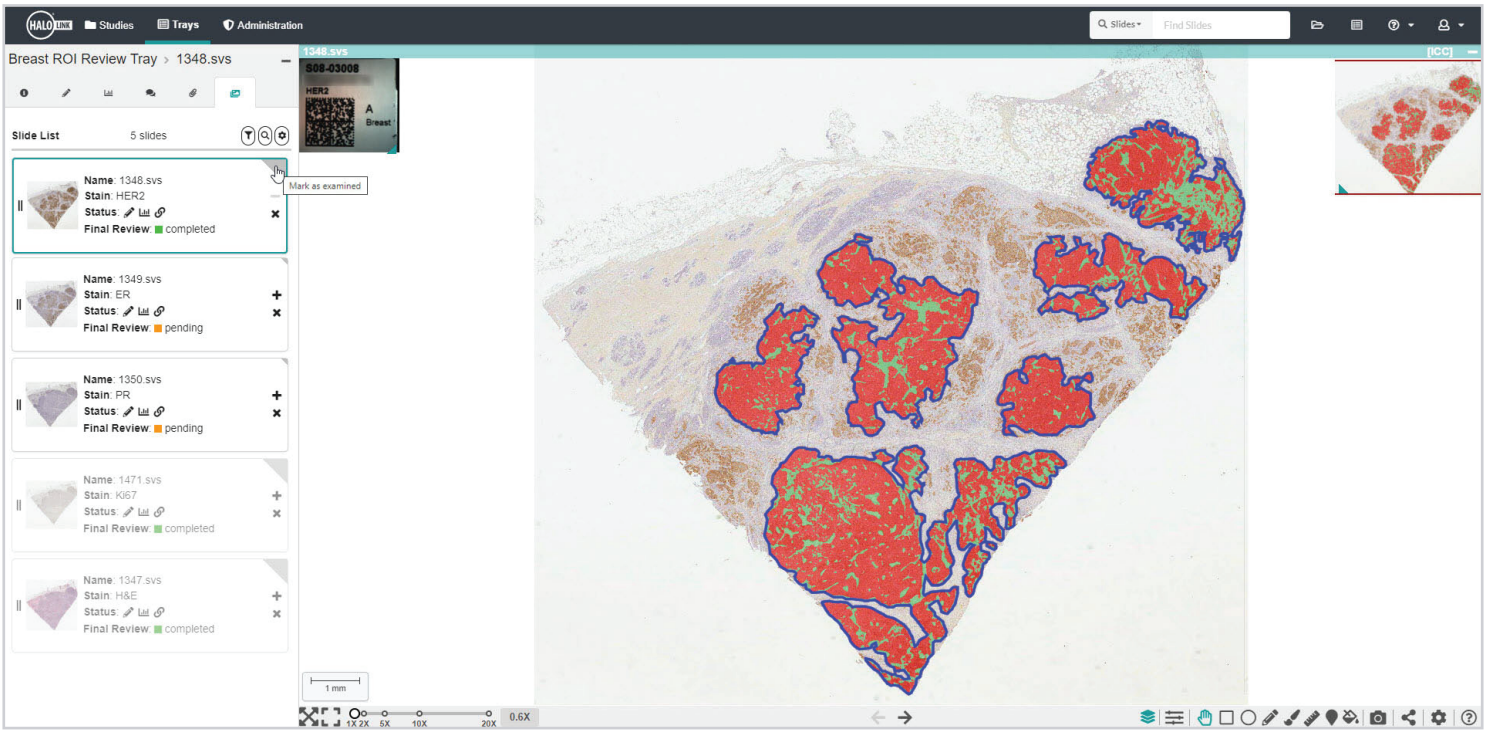

Figure 6. Review select slides from a study in a tray in a collaborative manner. In this Breast ROI Review Tray, the image analyst, customer, and pathologist discuss ROI selection on five sequential sections of a block stained with breast biomarkers. In the HER2 slide, a tumor/stroma classifier has been run on ROIs selected by the pathologist. Tumor is shown in red, and stroma is shown in green. Once reviewed, the user can "Mark as examined" and move on to the remaining slides in the workflow.

References

Cloud Deployment Case Study: Transitioning to the Cloud: Establishing a Collaborative Digital Pathology Platform at the National Cancer Institute – An Enterprise Deployment of HALO, HALO AI, and HALO Link

HALO Link Case Study: COVID-19 Digital Pathology Repository at NCI Delivers Images to Researchers for Real-Time Collaboration

HALO Link Case Study: Ultivue Delivers More Image Analysis Data to Customers Faster with Cloud-Based Image Sharing Software

HALO Link Case Study: Fred Hutch Gives Cancer Researchers Freedom to Explore and Collaborate with Comprehensive Image Management Software

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