

Pathology Image Informatics Platform (PathIIP)

Year 1 Update





Sunnybrook
HEALTH SCIENCES CENTRE
Pathcore



PIIP
Project
sites

Specific Aims

- **Aim 1:** Development of an improved plugin framework for the existing Sedeen viewer;
- **Aim 2:** Incorporate and evaluate quantitative image analysis algorithms previously developed in the context of DPI as plugins within the PIIP by taking into account a limited but commonly used development-platforms and languages (e.g. Matlab®, C++, Python);
- **Aim 3.** Add image archiving, management and sharing functionality to the platform and create image repositories for two different use cases (breast and prostate cancer);
- **Aim 4:** Perform on site deployment and evaluation of PIIP across multiple clinical, research sites using a field-proven consortia framework. Organize resulting collective as a DPI analysis challenge for further validation.

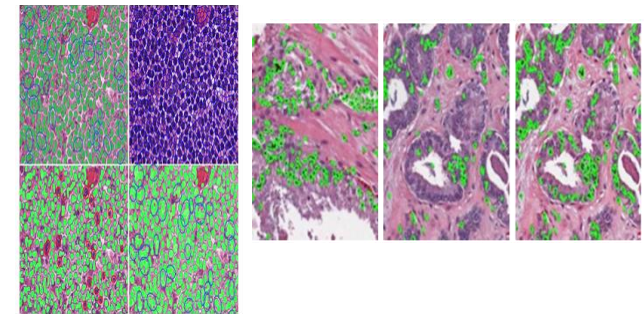
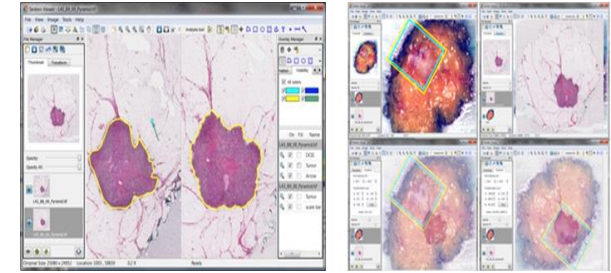
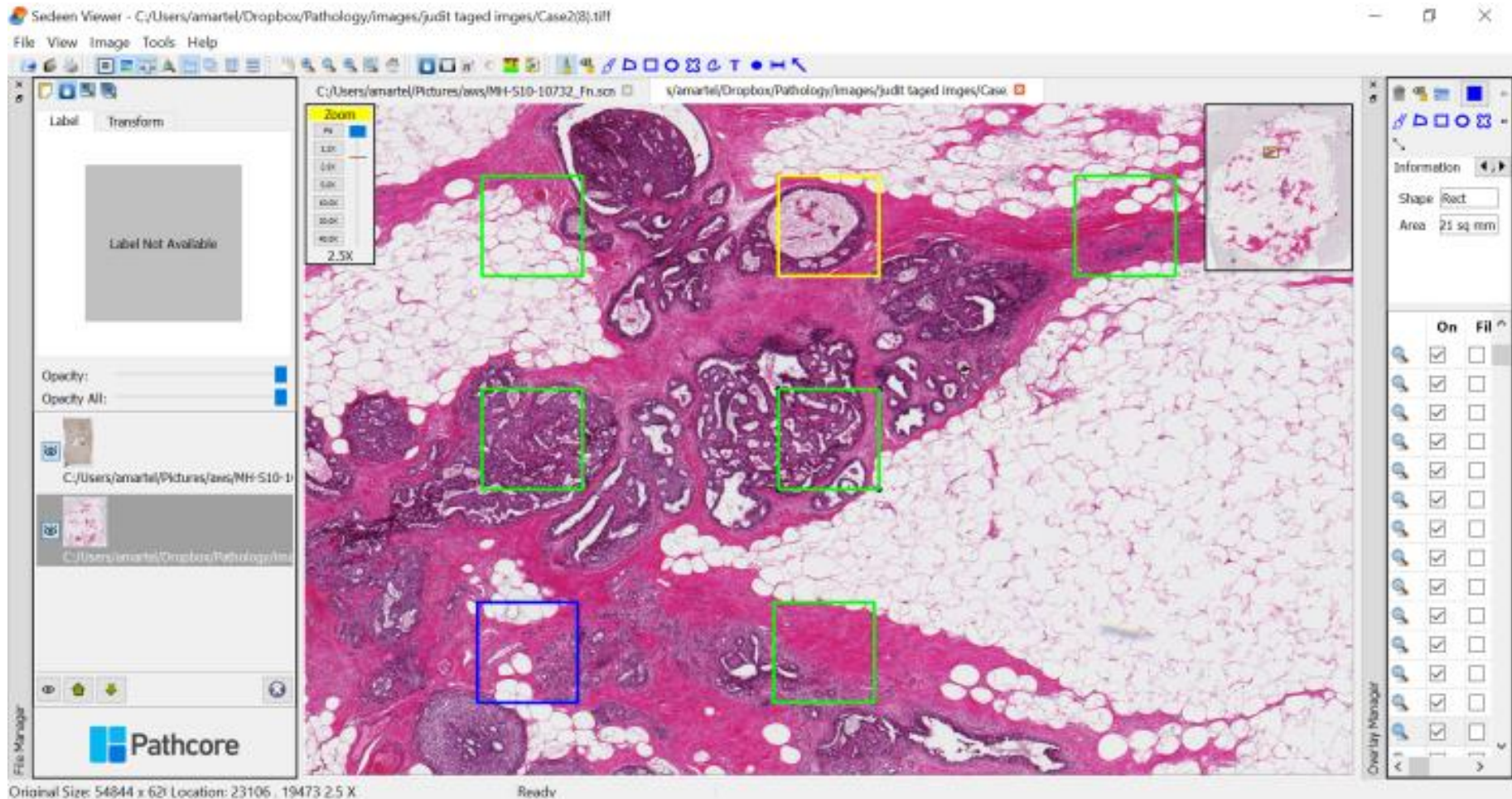


Figure 1. Map showing location of user downloads of Sedeen

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Sedeen Viewer



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Color Normalization

- Employs the color deconvolution algorithm (Ruifrok, Johnston 2001) to separate a color image into three grayscale images based on the actual color present in each type of stain
- The user defines a threshold in the grayscale image to create a binary mask
- Allows for measurement of the ROI for each stain separately

Ruifrok AC, Johnston DA. Quantification of histochemical staining by color deconvolution. Anal Quant Cytol Histol 23: 291-299, 2001.

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Color Normalization

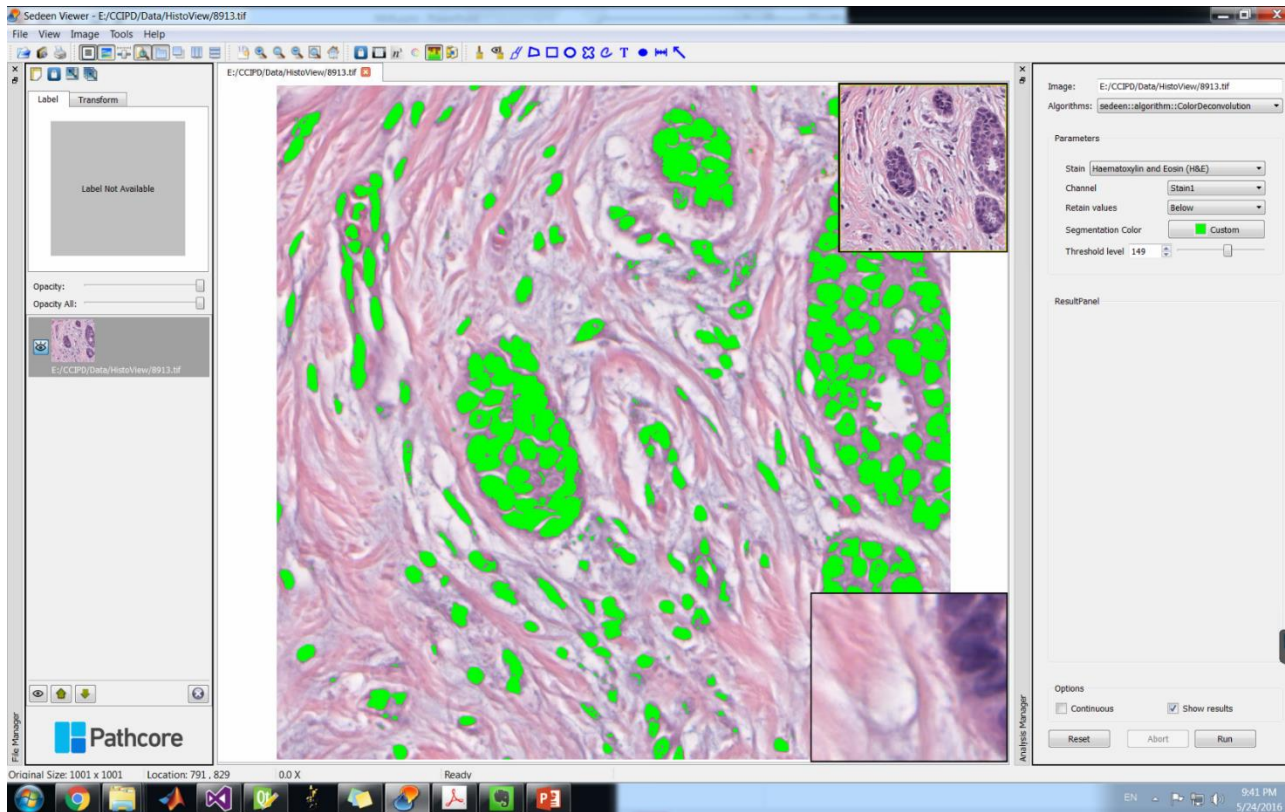


Fig 1. Applying Color deconvolution to H&E stained image.

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Biomarker Quantification

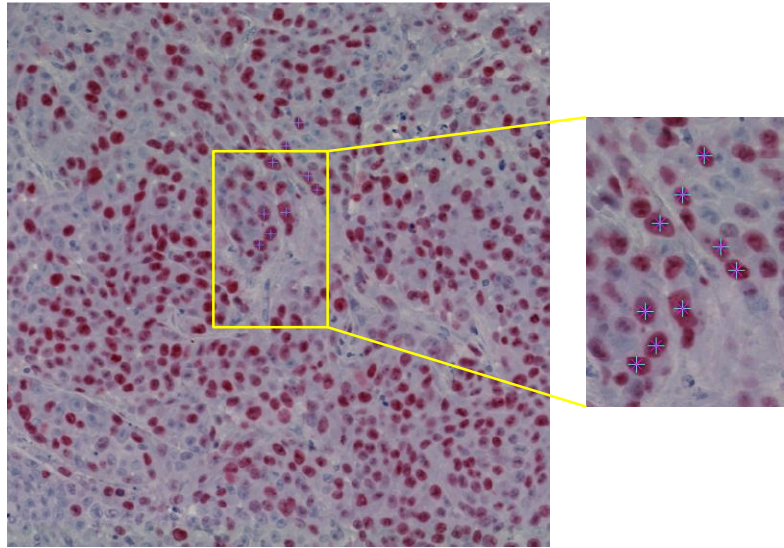
- Employs Hierarchical normalized cuts (HNCut) which combines the normalized cuts algorithm with mean shift clustering (Janowczyk 2012)
- Identifies all pixels that fit within a specific color space
- Minimally interactive, requiring the user to select just a few representative pixels from the color region of interest

Janowczyk, A, Chandran, S, Singh, R, Sasaroli, D, Coukos, G, Feldman, M, Madabhushi, A, “High-Throughput Biomarker Segmentation on Ovarian Cancer Tissue Microarrays via Hierarchical Normalized Cuts”, Institute of Electrical and Electronics Engineers (IEEE) Trans on Biomedical Engineering, vol. 59[5], pp. 1240-1252, 2012 (PMID: 22180503).

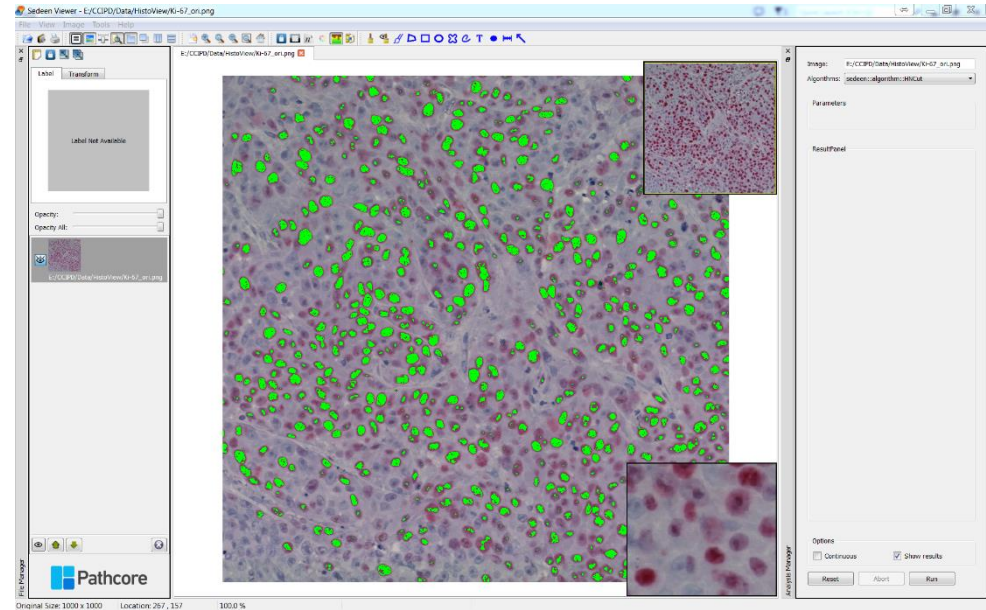
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Biomarker Quantification



a. The user randomly selects a few representative points.



b. HNCut helps to quantify Ki-67 stained tumor nuclei based on the selected points.

Fig 2. Quantifying and annotating immunohistochemically stained slides.

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Nuclei Segmentation

An integrated framework consisting of :

- A novel supervised cell-image segmentation algorithm , which can partition histopathological images as cell regions, background and extra-cellular areas,
- A new touching-cell splitting method.

Implemented with Matlab without graphical user interface.

Kong, Hui, Metin Gurcan, and Kamel Belkacem-Boussaid. "Partitioning histopathological images: an integrated framework for supervised color-texture segmentation and cell splitting." Medical Imaging, IEEE Transactions on 30.9 (2011): 1661-1677.

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Nuclei Segmentation Plugin

How to use an existing Matlab Algorithm as a plugin:

Option 1- Migrate to C++

1. Develop an adapter class in order to use OpenCV API
2. Divide the algorithm into subroutines
3. Re-Implement the functions
4. Use unit tests and validate C++ functions = Matlab functions

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Nuclei Segmentation Plugin

How to use an existing Matlab Algorithm as a plugin:

Option 2- Call a Matlab function

1. Compiled as a standalone executable by using Matlab Compiler Toolbox
2. A plugin is developed in C++, which is an interface between algorithm and PIIP:
 - set algorithm parameters
 - call the standalone executable
 - visualize the results in PIIP user interface

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Nuclei Segmentation Plugin

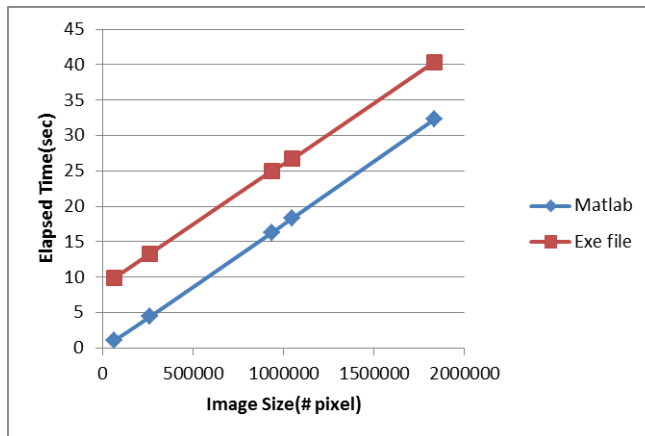
Option 2- Call a Matlab function

Pros

- Easy to share your algorithm
- Do not need a solid C++ background.

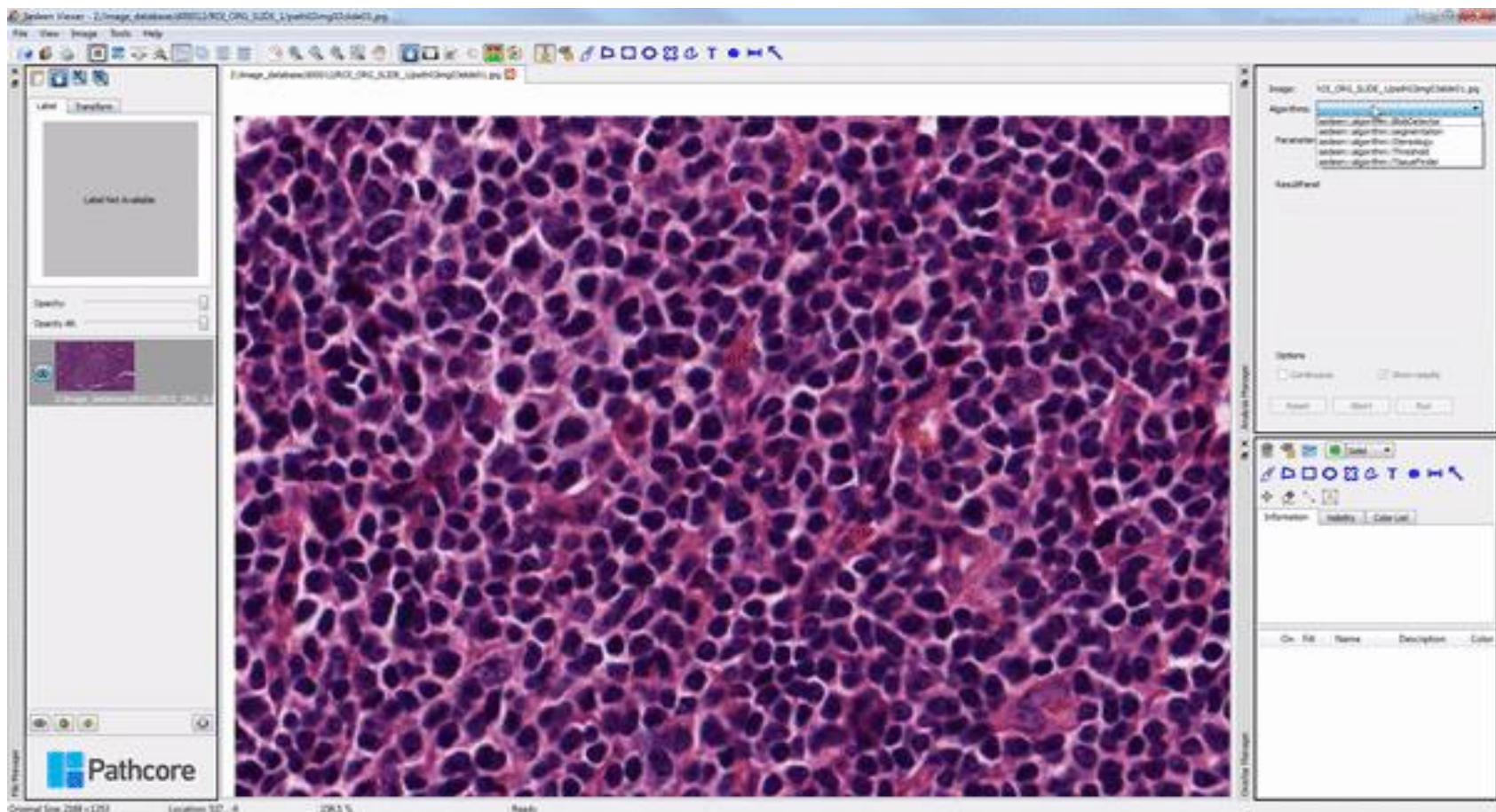
Cons

- Need to initialize Matlab runtime (+8 sec each time)
- Need to write to disk



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Co-registration of IHC slides

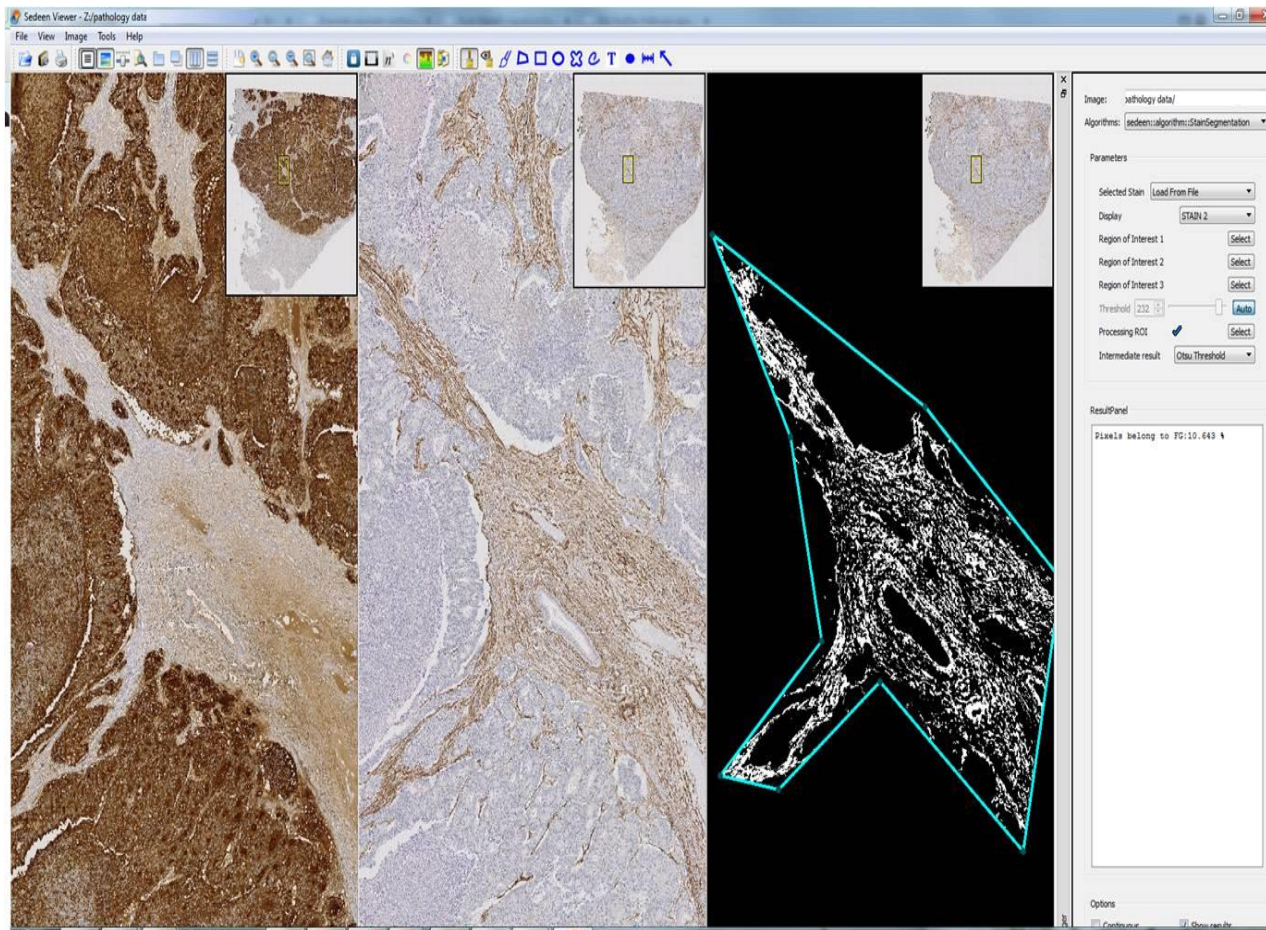
Aims:

- Explore capabilities of Sedeen's manual registration functions
- Implement plugin for comparing IHC stains
- Identify additional functionality required to support registration
- Develop tools for automatic multi-modality registration

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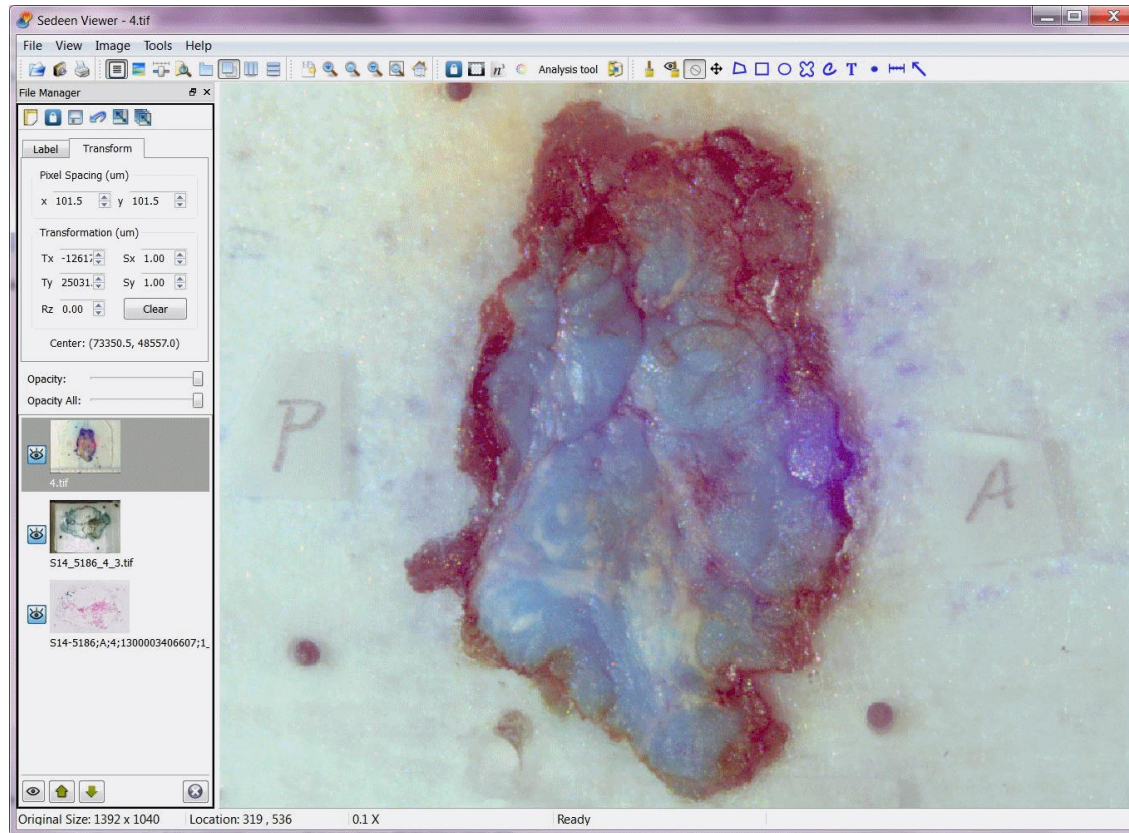
Comparison of multiple IHC stains



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Multimodality Co-registration

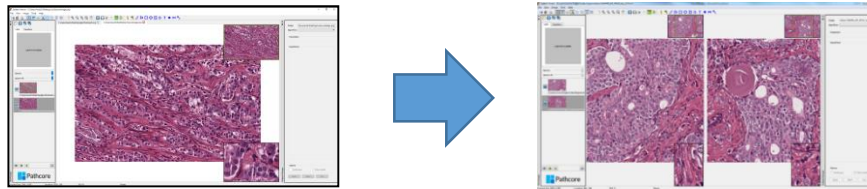


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Human Factors Engineering

- Understanding cognitive challenges informs use cases
 - Example: Compare prior and current image for patient



- Identifying useful leverage points and 'design seeds'
 - Example: Make algorithm automation observable
- Improving usability by modifying interface
 - Example: Modify interaction mechanisms



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Sedeen Updates

SDK Distribution & Documentation

- SDK Distribution
 - Distributed via Dropbox to all participating institutions
 - More flexible system for community to be implemented in the future
- Documentation
 - Training material created and is part of SDK software distribution
 - Contains extensive description of Sedeen framework
 - Provides scenario-based examples for using APIs

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New Features & Support

Year 1 Development Update

- 1st release: February 23rd 2016
- 2nd release: Scheduled for June 2016
- New features and enhancements
 - Improved rendering speed
 - Added new image formats
 - Hamamatsu (.vms, .vmu, .ndpi)
 - Mirax (.mrxs)
 - 12-bit grayscale JPEG images
 - Enhanced annotation functionality
 - Automated updates
 - Dynamic help tool
 - Numerous bug fixes
- See 5.1.0 and 5.1.1 change logs for details

Support

- Pathcore staff provided support via email and Pathcore's support portal
- Improvements to the support portal are planned to enhance the user experience
- Pathcore staff also provides administrative support

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Pathcore



Additional efforts on Sedeen

Sedeen Viewer and SDK framework is being improved in parallel to NCI work

- Adding Aperio XML Support
- Modernizing user interface
- One-button crop from annotations
- Improvements to decoding engines
- Support for more libraries
- Bug fixes
- Etc.

Ongoing improvements are released periodically

- Next release scheduled for June 2016

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Future work

- To provide supervised TMA spot extraction
- To embed nuclei segmentation approach based on marker-controlled watershed algorithm

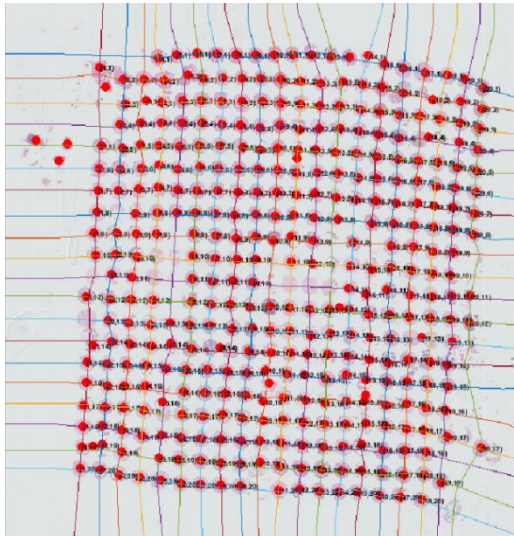


Fig 3. TMA spot extraction

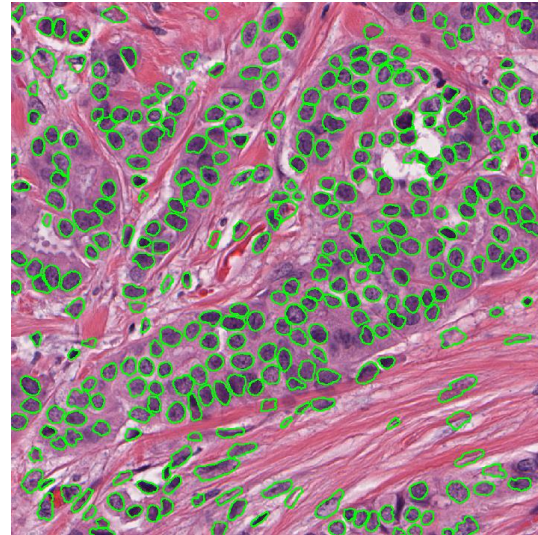


Fig 4. Nuclei segmentation algorithm

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Visit us at: www.pathiip.org





Link to video demo:

https://drive.google.com/a/broadinstitute.org/file/d/0ByJNnq4eaii7QWFQRHY2Nk5wU28/view?usp=sharing_eid&ts=5747b03f

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