The Integration of Whole Slide Imaging in the Clinical Anatomic Pathology – Limitations of Laboratory Information Systems, Image Capture Systems and Archives

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Disclosure Page

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I (Yukako Yagi) have been Scientific Advisor for Trestle, DMetrix and Aperio.

Background

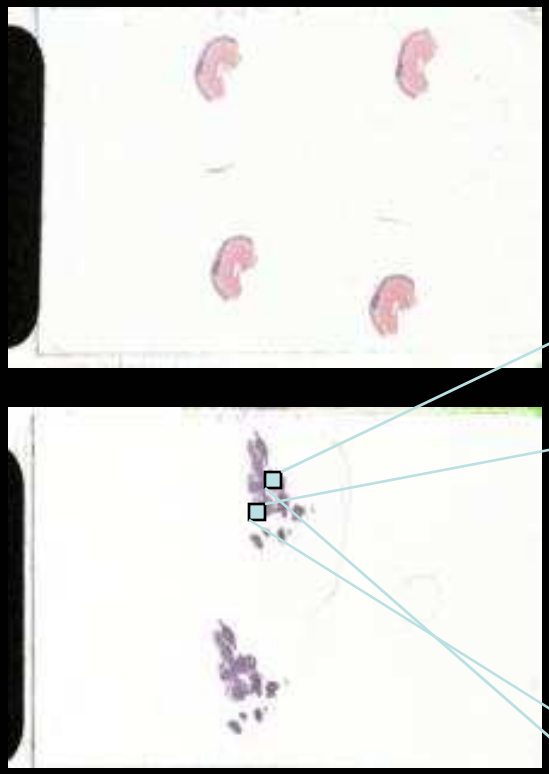
The past five years has seen the emergence of whole slide imaging robots – devices that can automatically image entire microscope slides at high speed and high resolution. A typical device can capture a slide in 5 minutes at tissue sampling rates of 0.3-0.5 microns/pixel, resulting in an uncompressed image file of 5 to 10 GB, and a typical pathology case contains ten slides. Though these “high resolution whole slide images” provide diagnostic information similar to that obtained by direct examination of tissue under the microscope and are proving useful in a variety of clinical activities; their novelty and sheer volume has resulted in a number of image and data management challenges. One of these challenges is that Laboratory Information Systems, which drive workflow and data management in pathology departments, are not well equipped to manage image level information.

What is a whole slide image?

Microscope Imaging

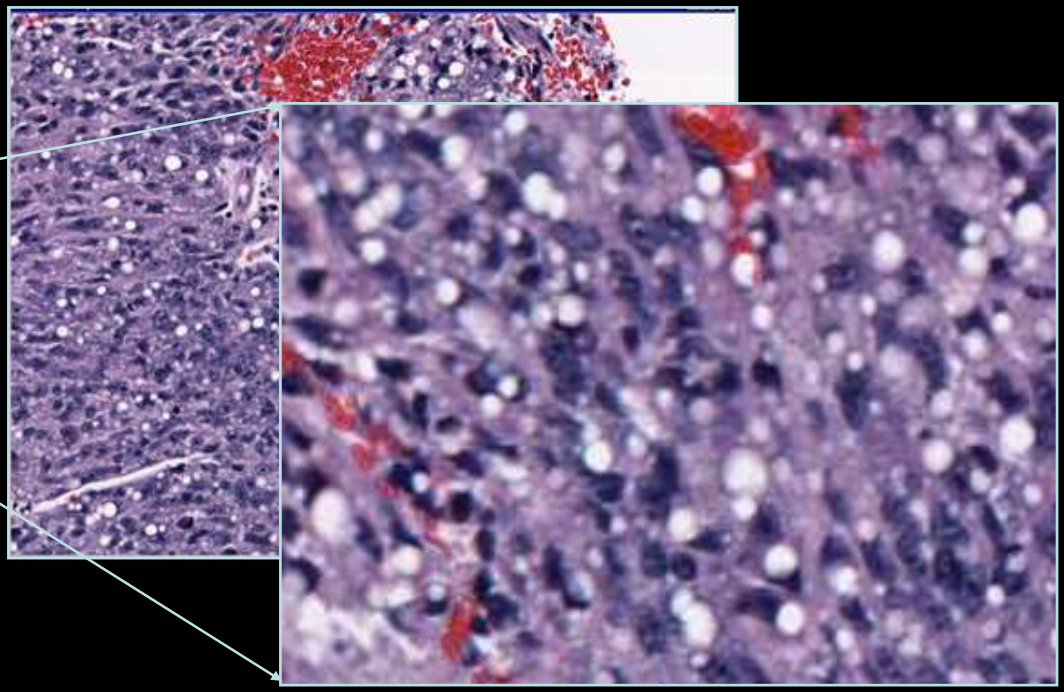
If we try to send all information on a glass slide,
It is more than 2.7GB/slide.

Histology slides

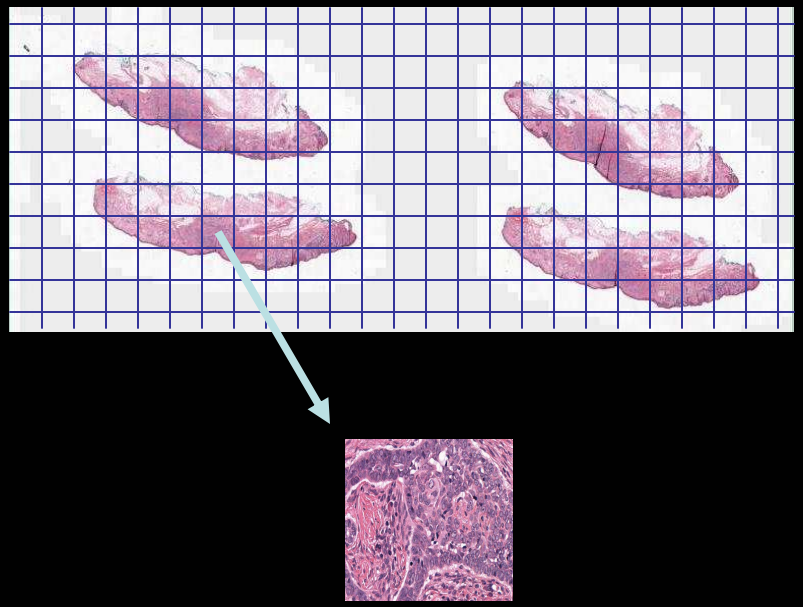


For Static Image Telepathology, a referring pathologist has to be able to select appropriate diagnostic fields. To select suitable fields for consultation requires experience

Needed virtual slide

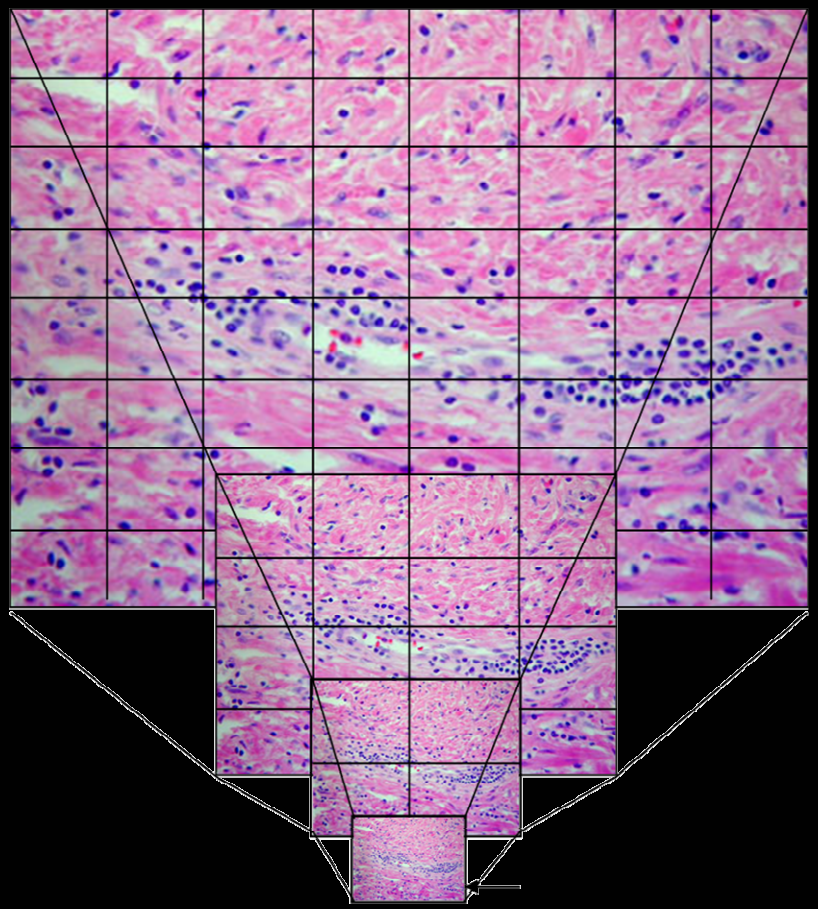


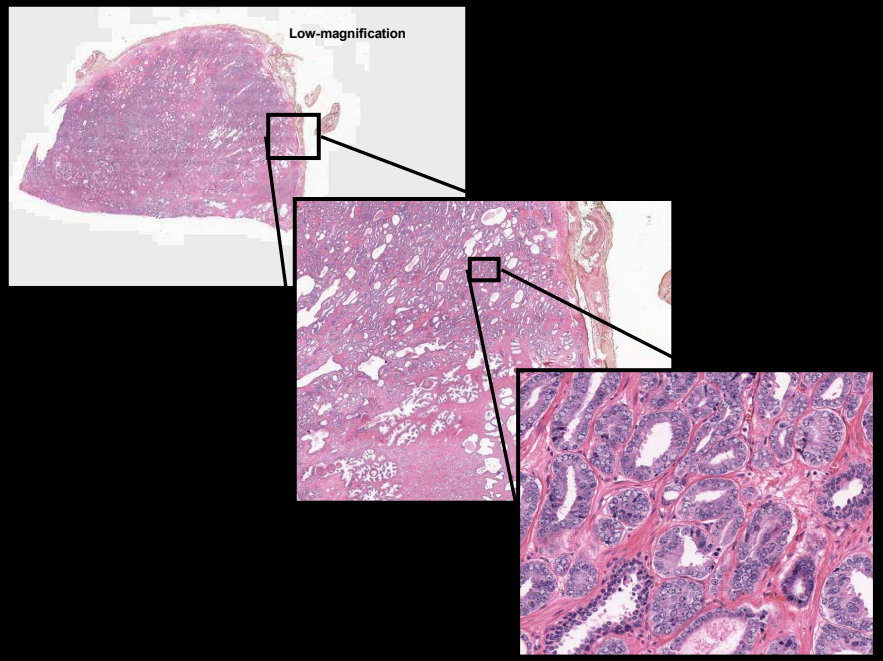
A Digital Slide



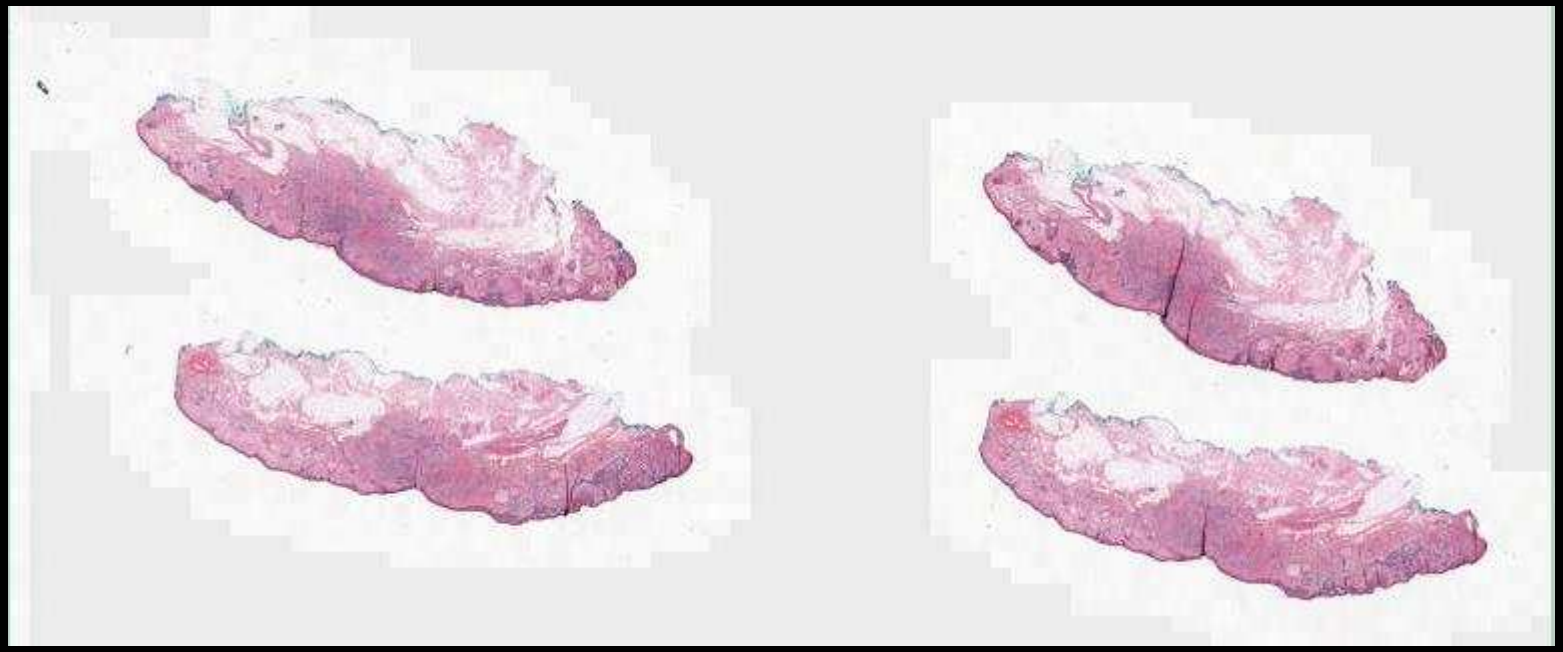
- A classical whole slide image is formed by imaging a entire physical (glass) slide, field by field, and then ‘knitting” these fields together to form a seamless montage
- With some display software, one can pan and zoom around the image set

Pyramid File Structure





- A Digital Slide is a massive data set



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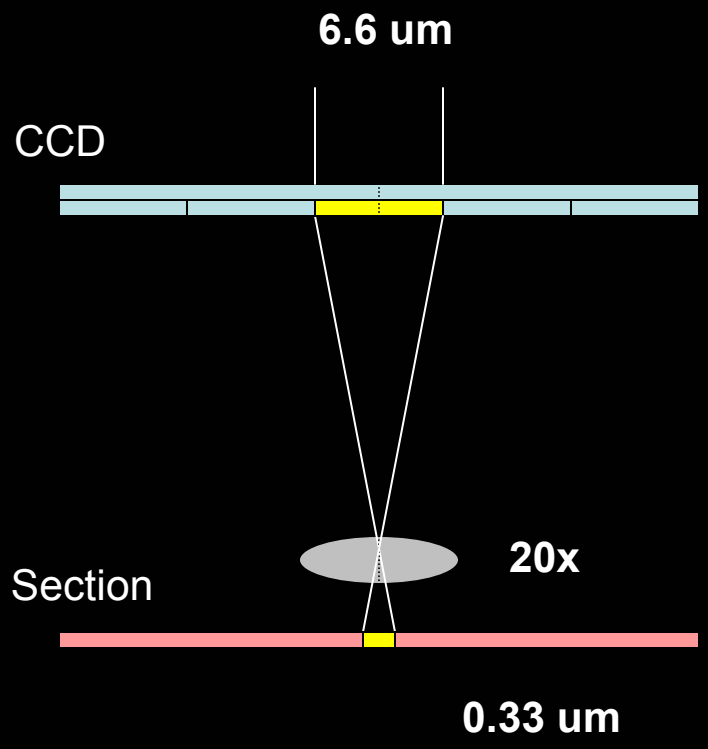
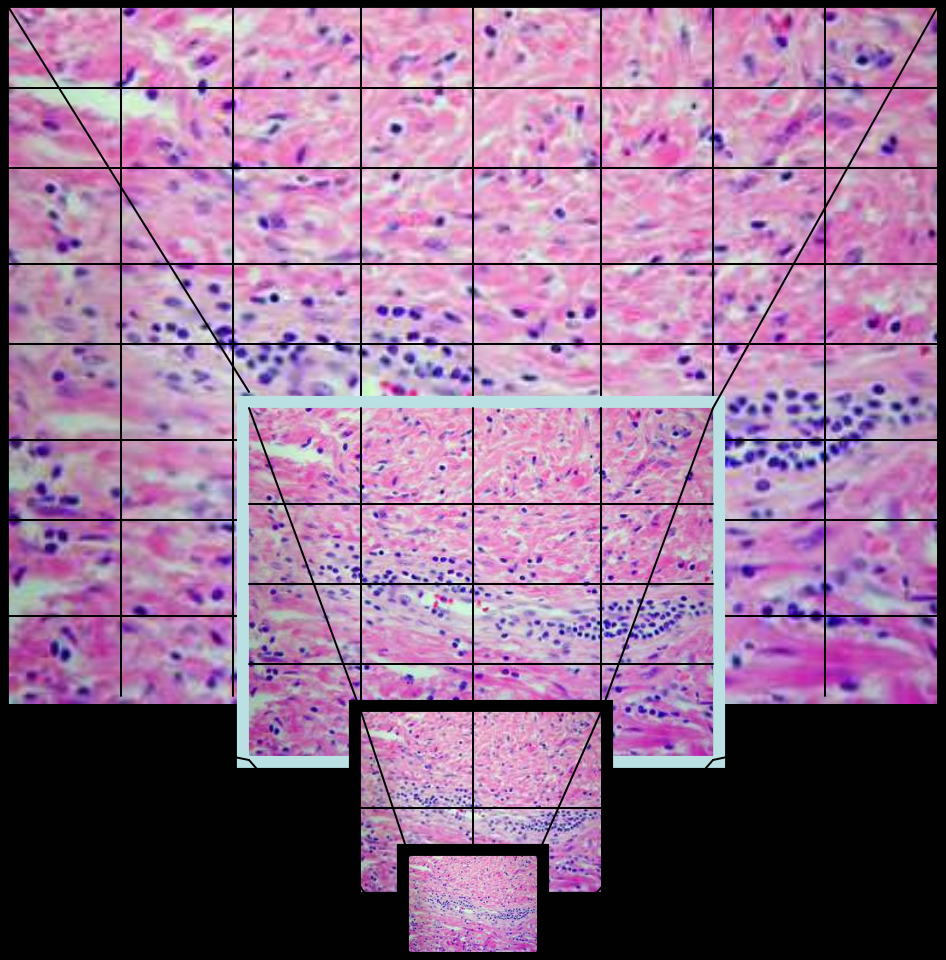


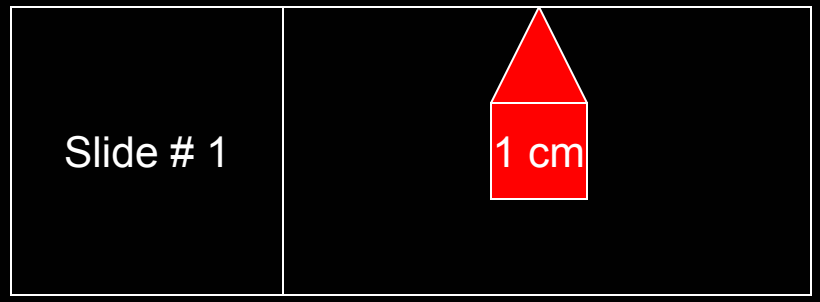
- Consider a WSI system:

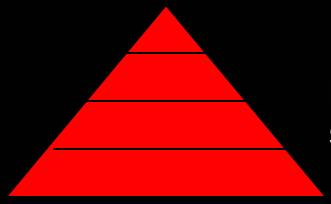
- 0.6 NA, 20x Primary Magnification
- 8.8 x 6.6 mm CCD
- 6.6 um pixels

- 0.33 um/pixel
- 900 million pixels / square cm of tissue
- 3 bytes / pixel (24 bit color)
- 2.7 GB / square centimeter of tissue per focal plane for the base image



Digital Slides have Issues



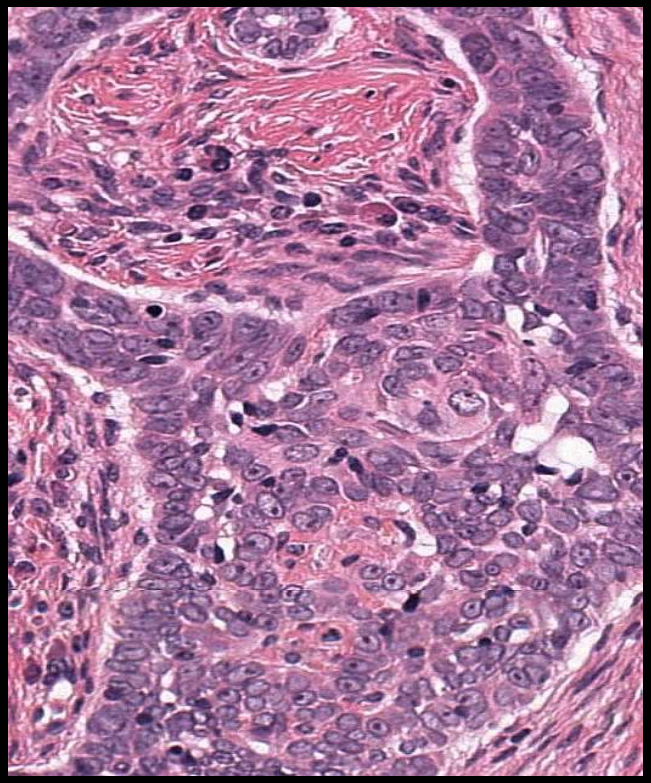


Each level is 1/2 the resolution and 1/4 the size of the one below it

- 2.7 GB/cm is the base image
  - 2.7 + (2.7/4) + ((2.7/4)/4)…
  - 2.7 GB x 1.33 = 3.5 GB per square cm of tissue
- Assume 1.5 square cm per slide, 10 slides per case:
- ~ 52 GB per case!

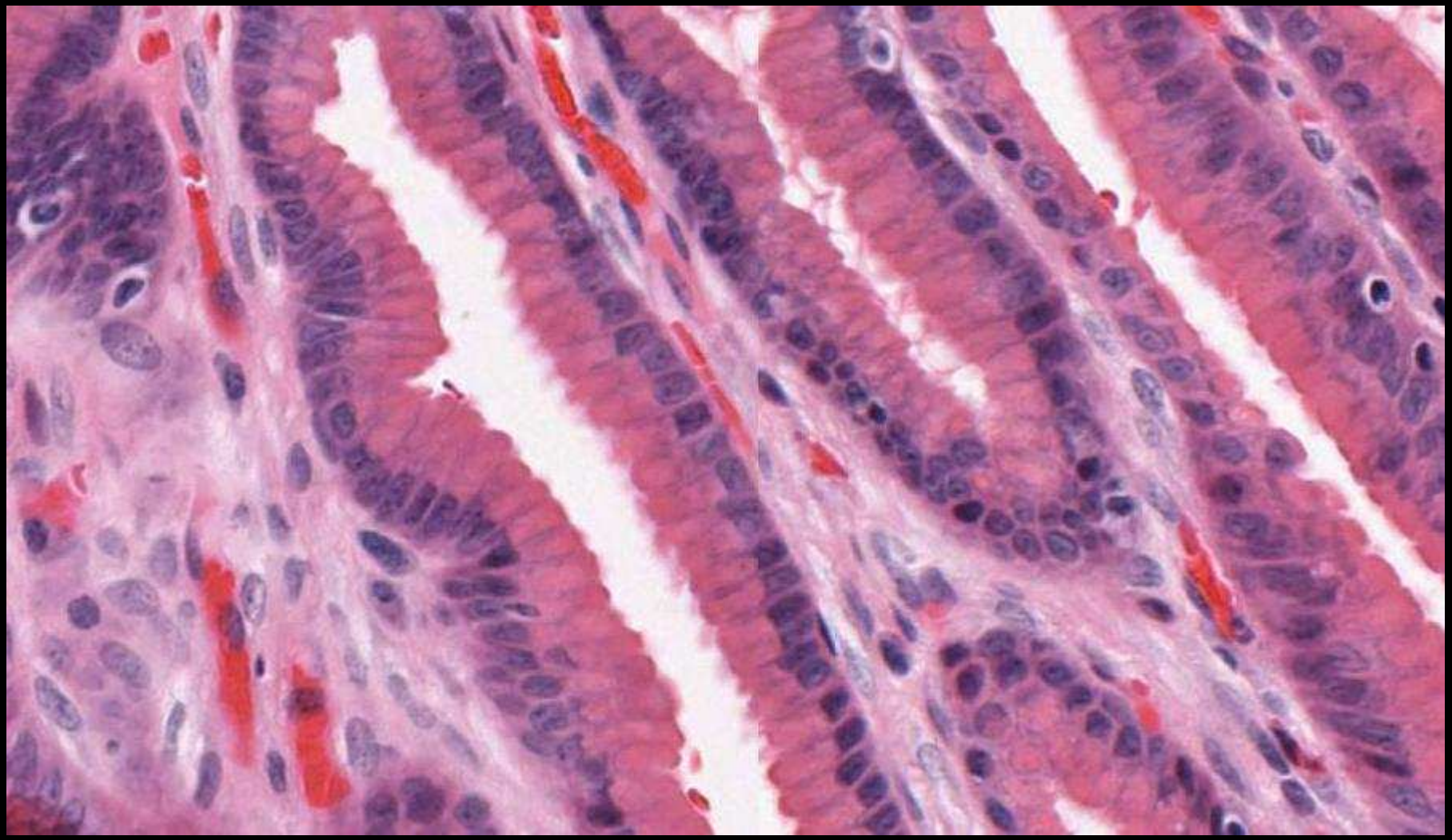
- This is based on 20x optical magnification and one focal plan
- 40x magnification and 5 focal planes ~ 50 GB x 20 = 1 TB

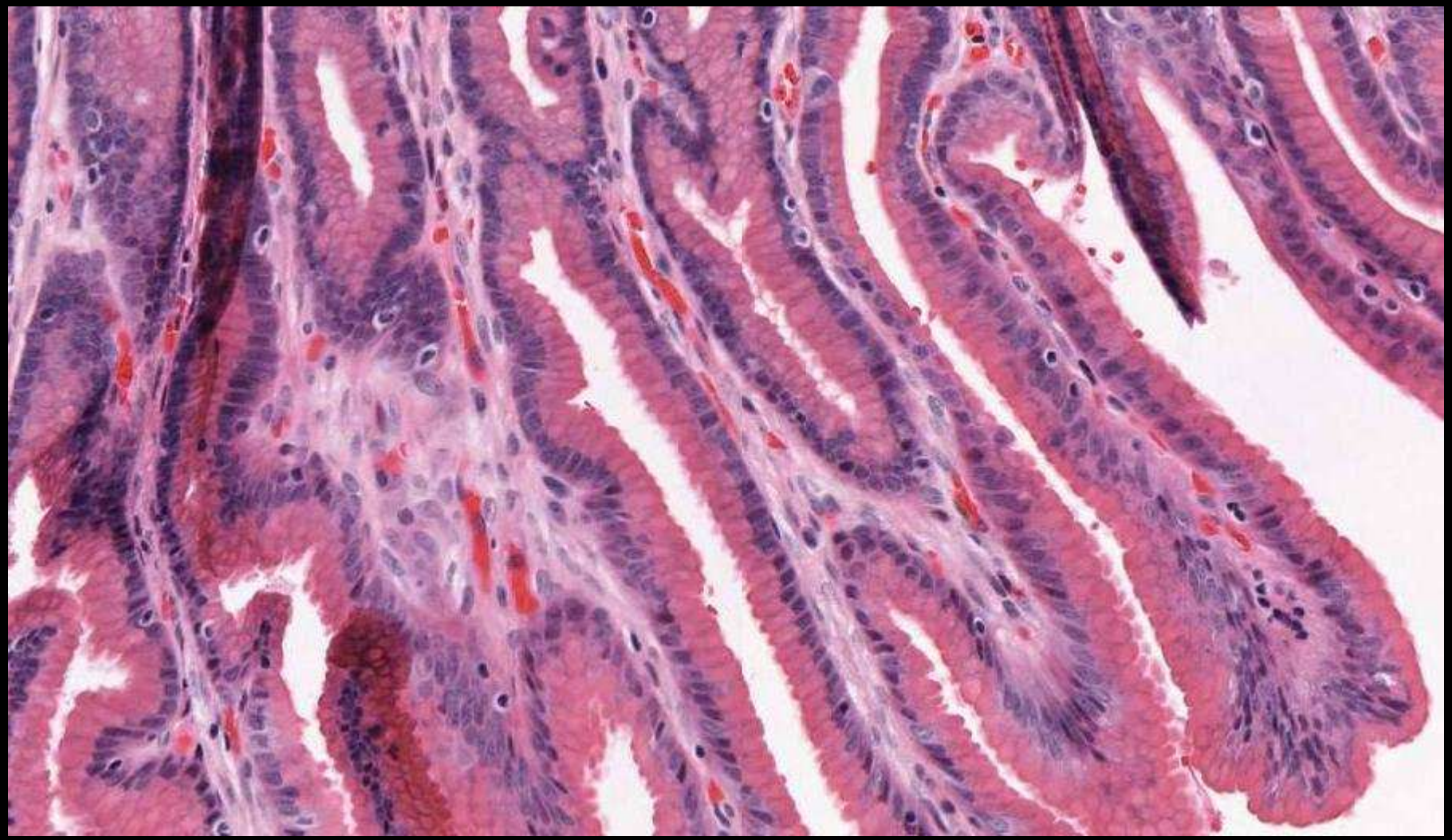
Digital Slides have Issues

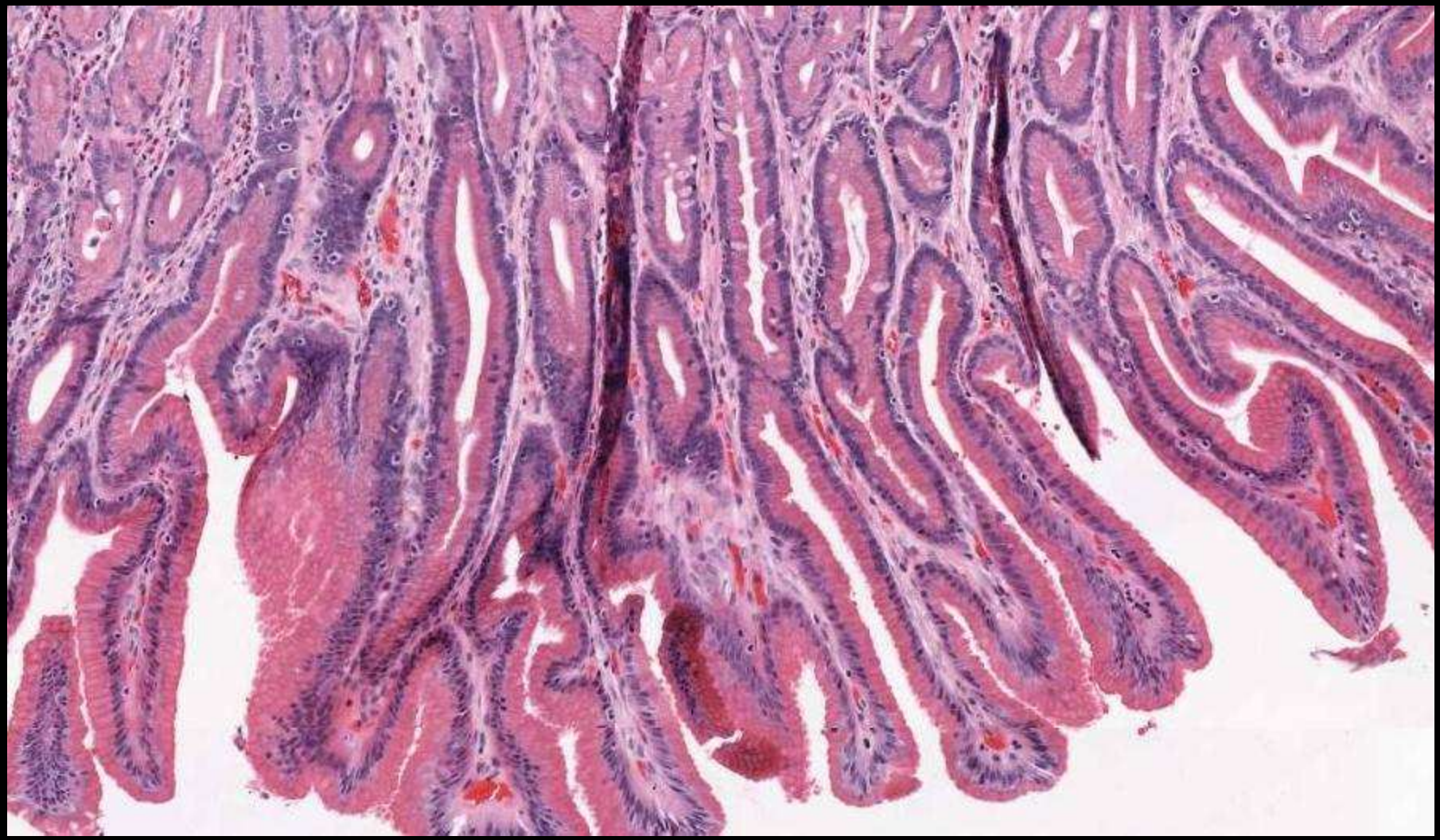


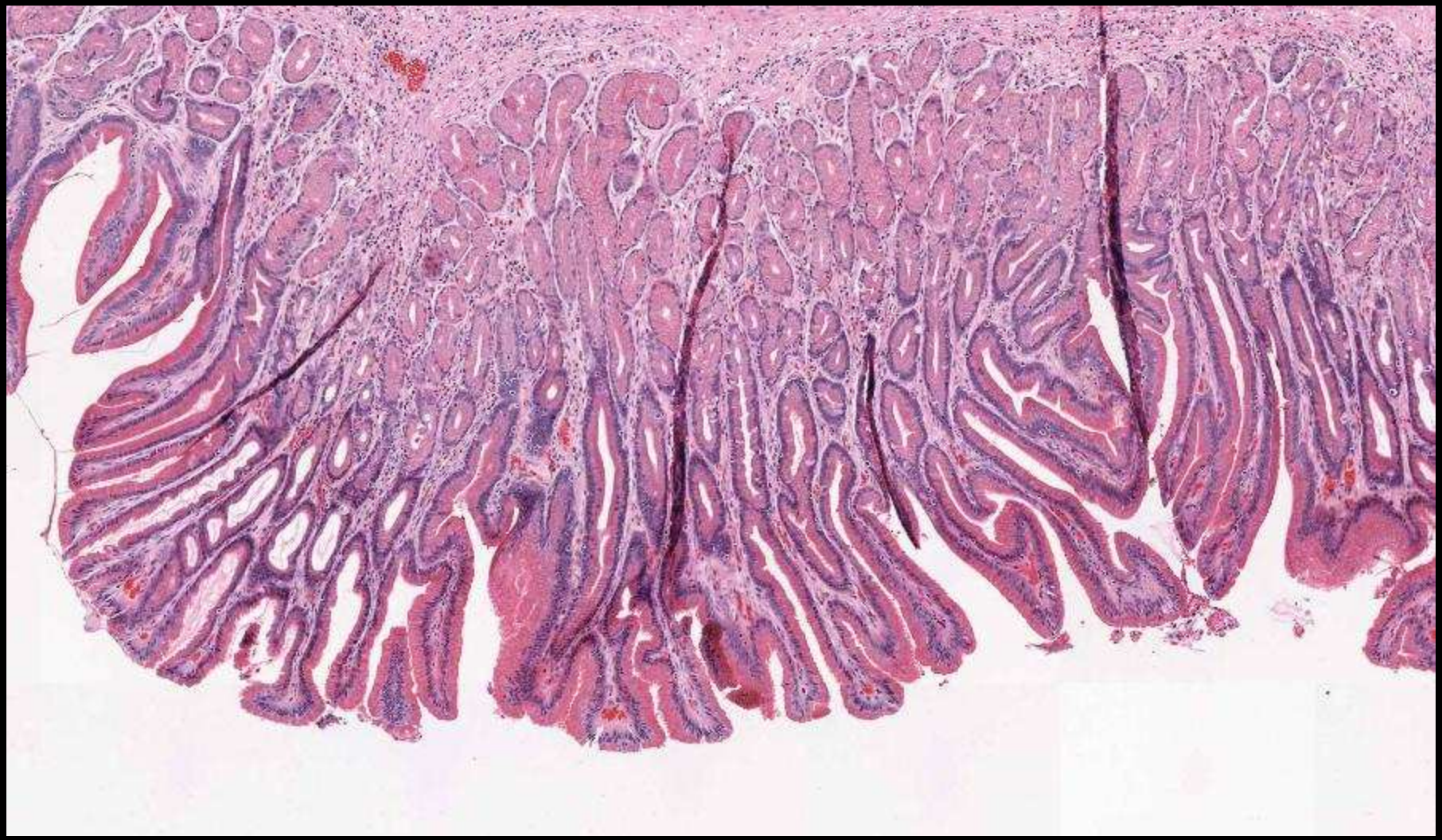
- JPG2000 compression ~ 30:1
- ~ 115 MB per square cm per focal plane…
- 1725 MB per case
- UPMC → 80,000 cases/year
- 138 TB per year
- Is this unreasonable?

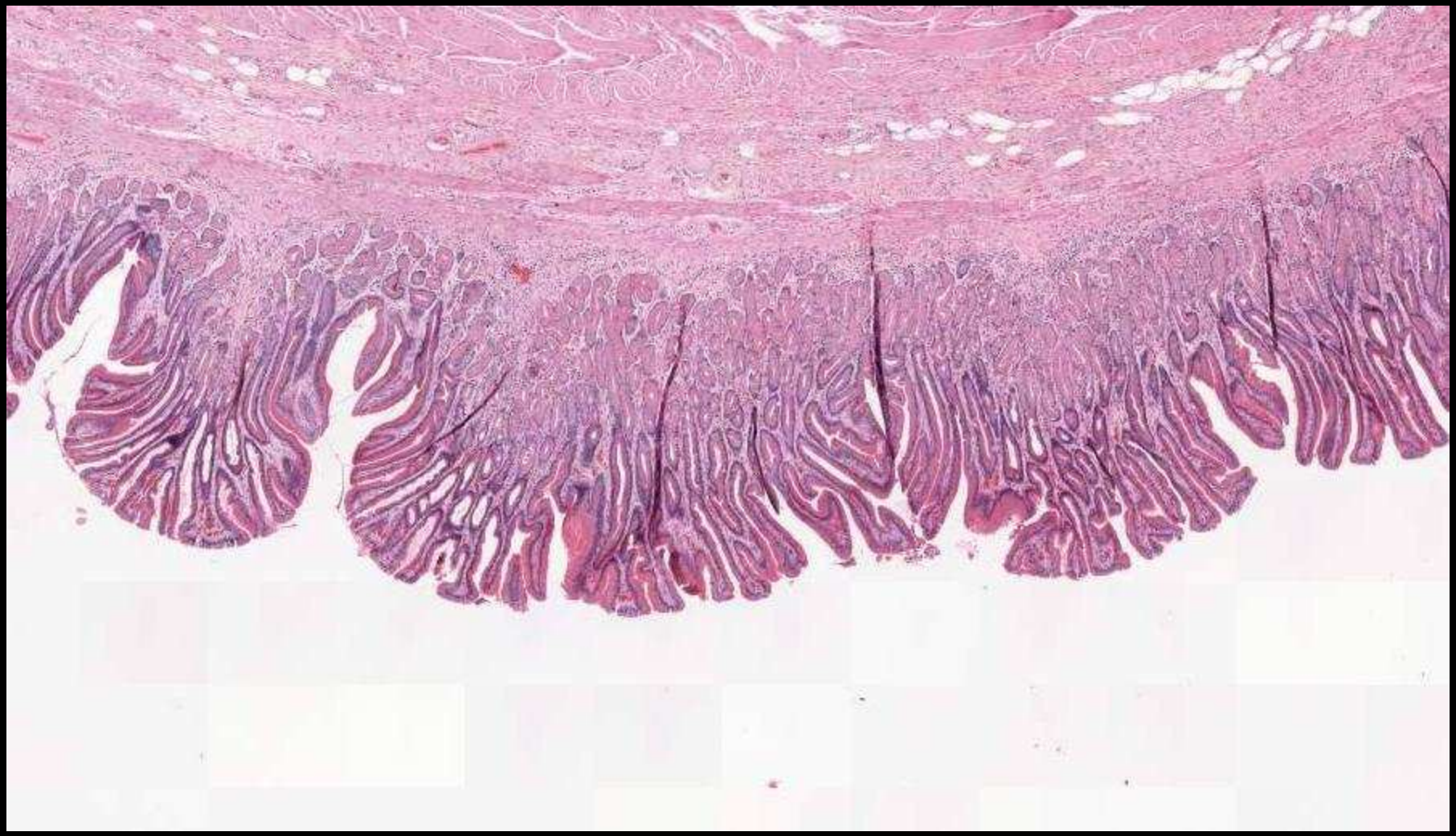
- This is based on 20x optical magnification and one focal plan

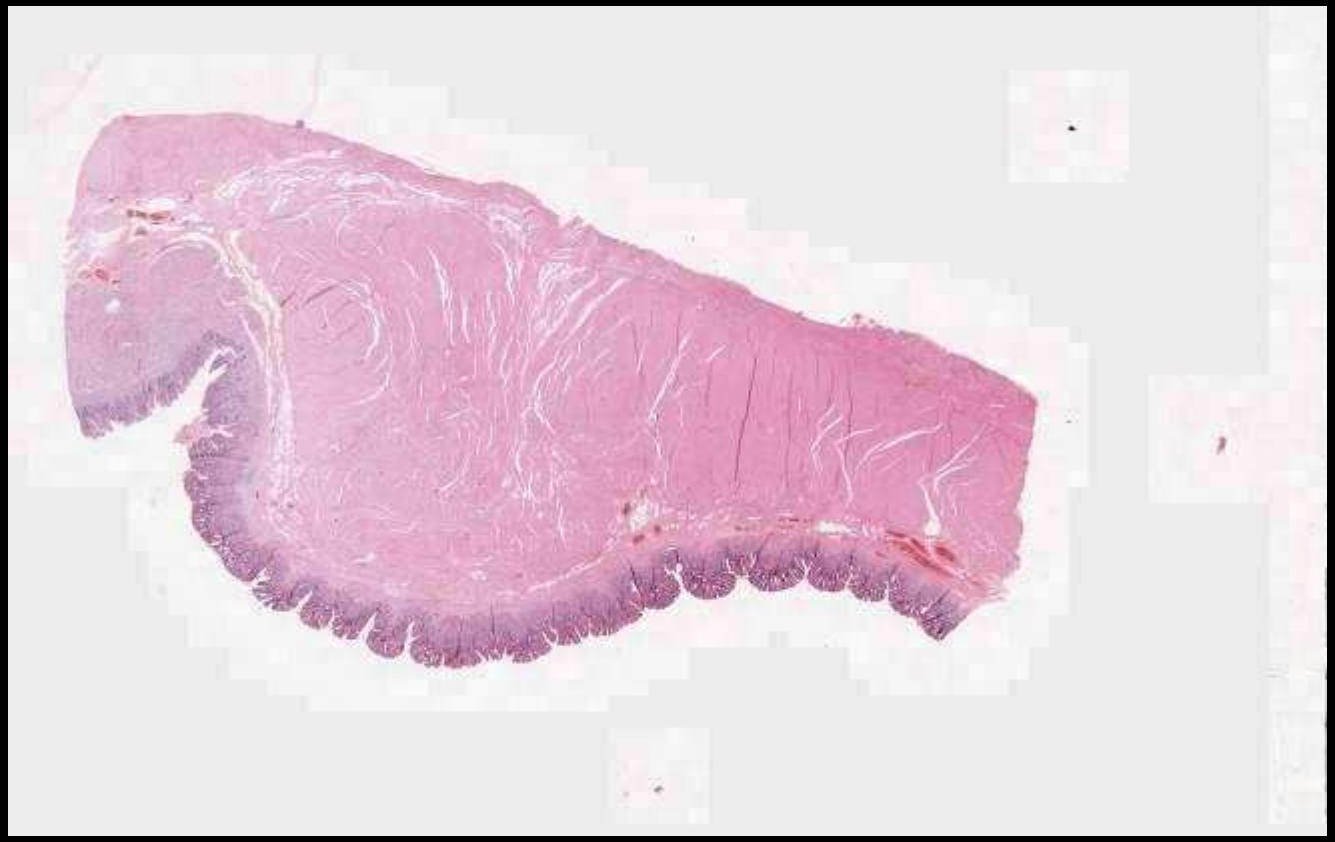










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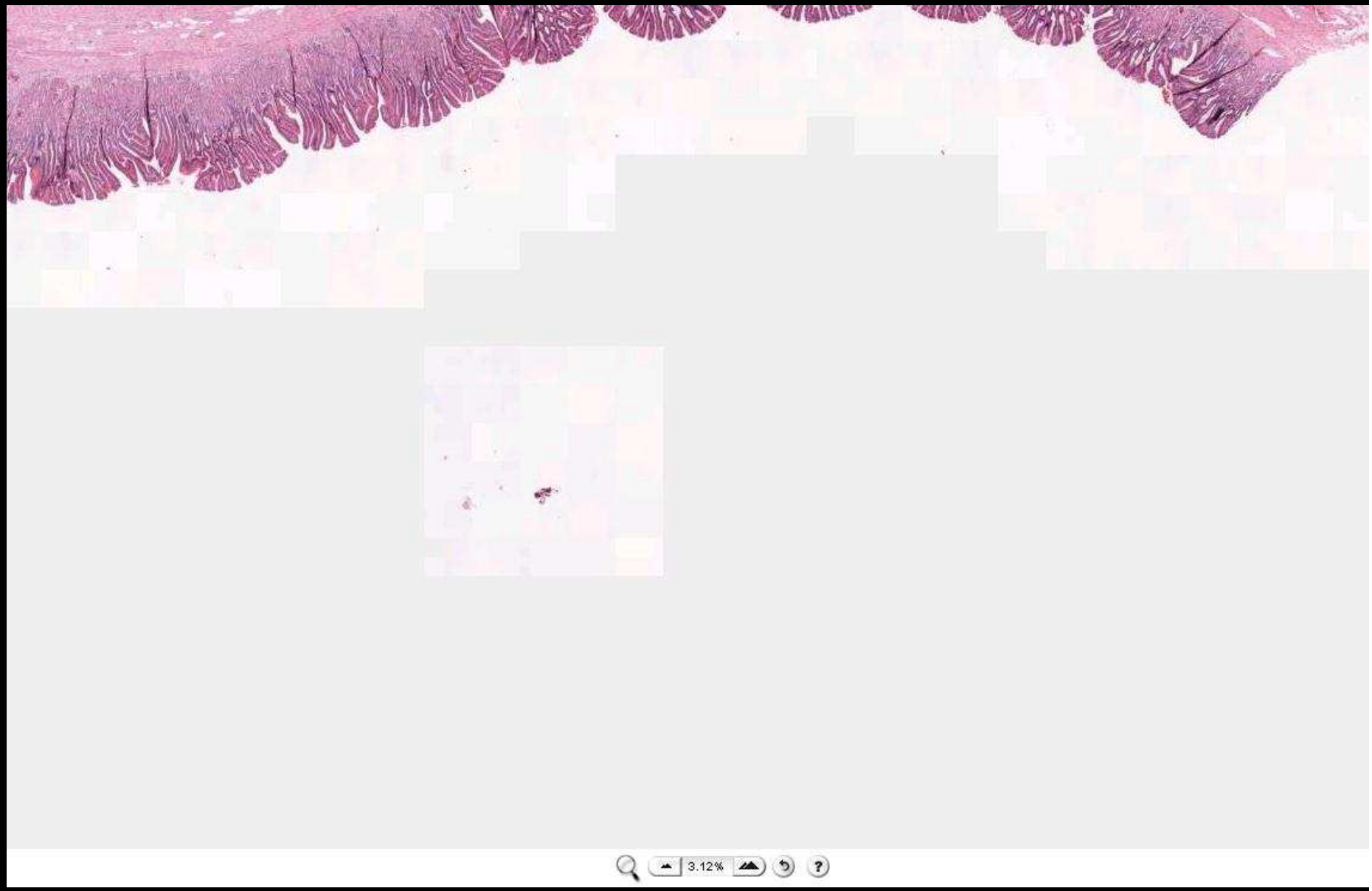
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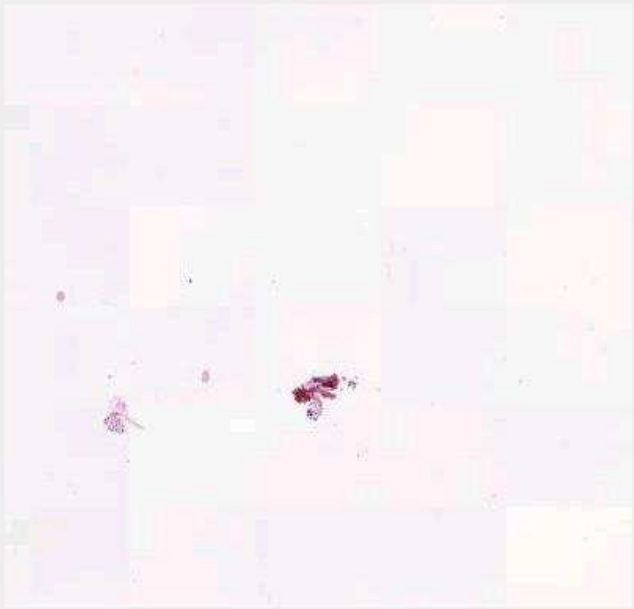


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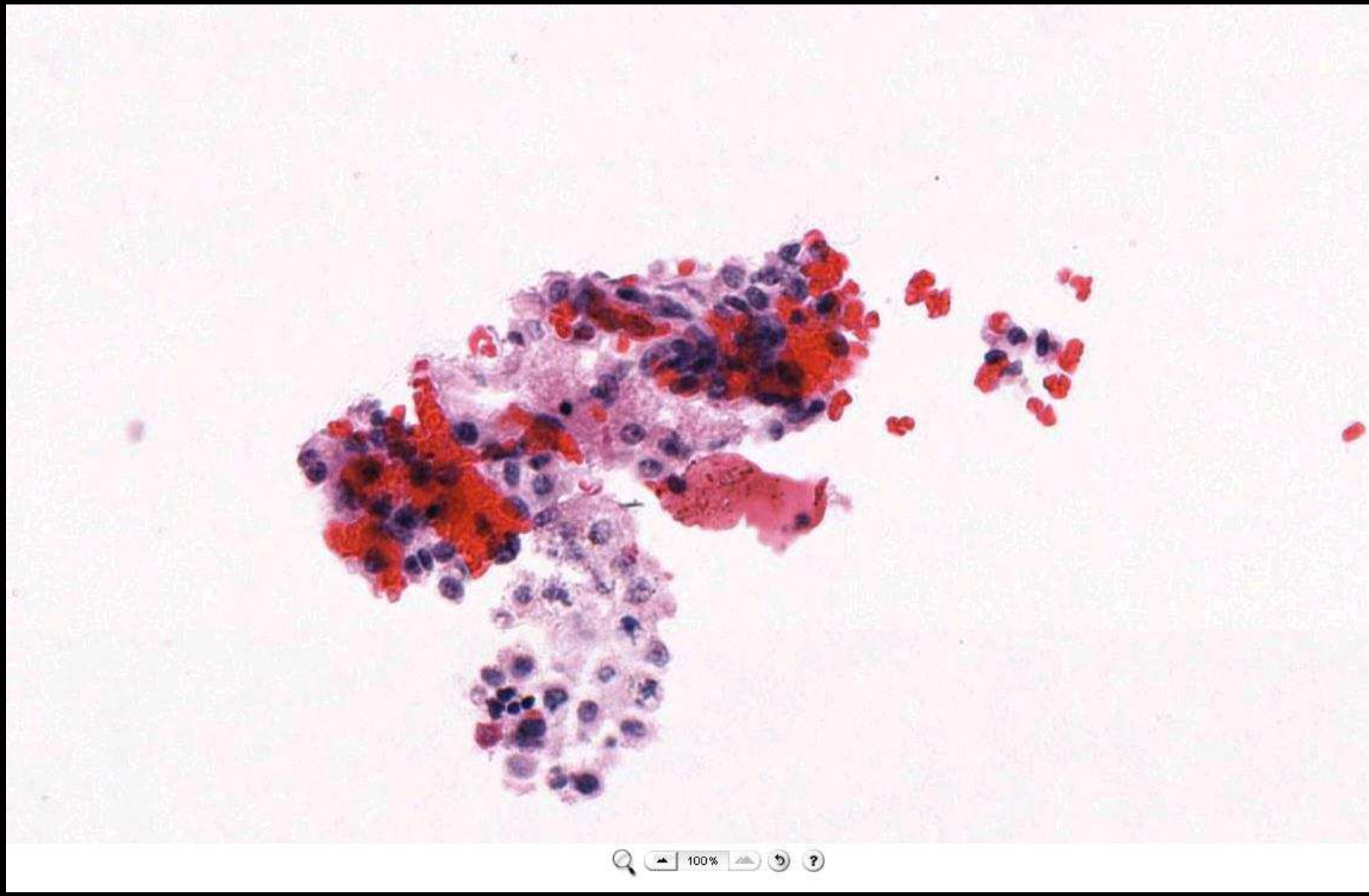
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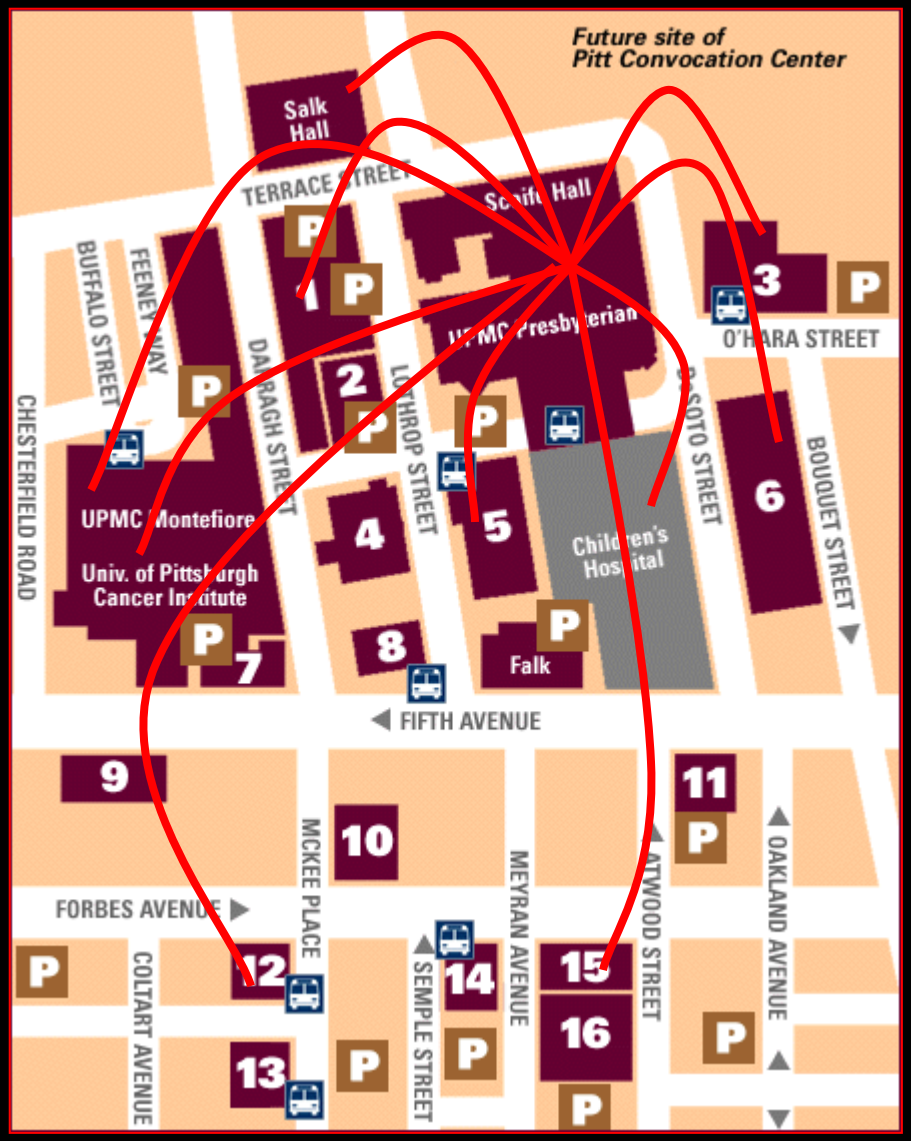
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Univ. of Pittsburgh
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Children's
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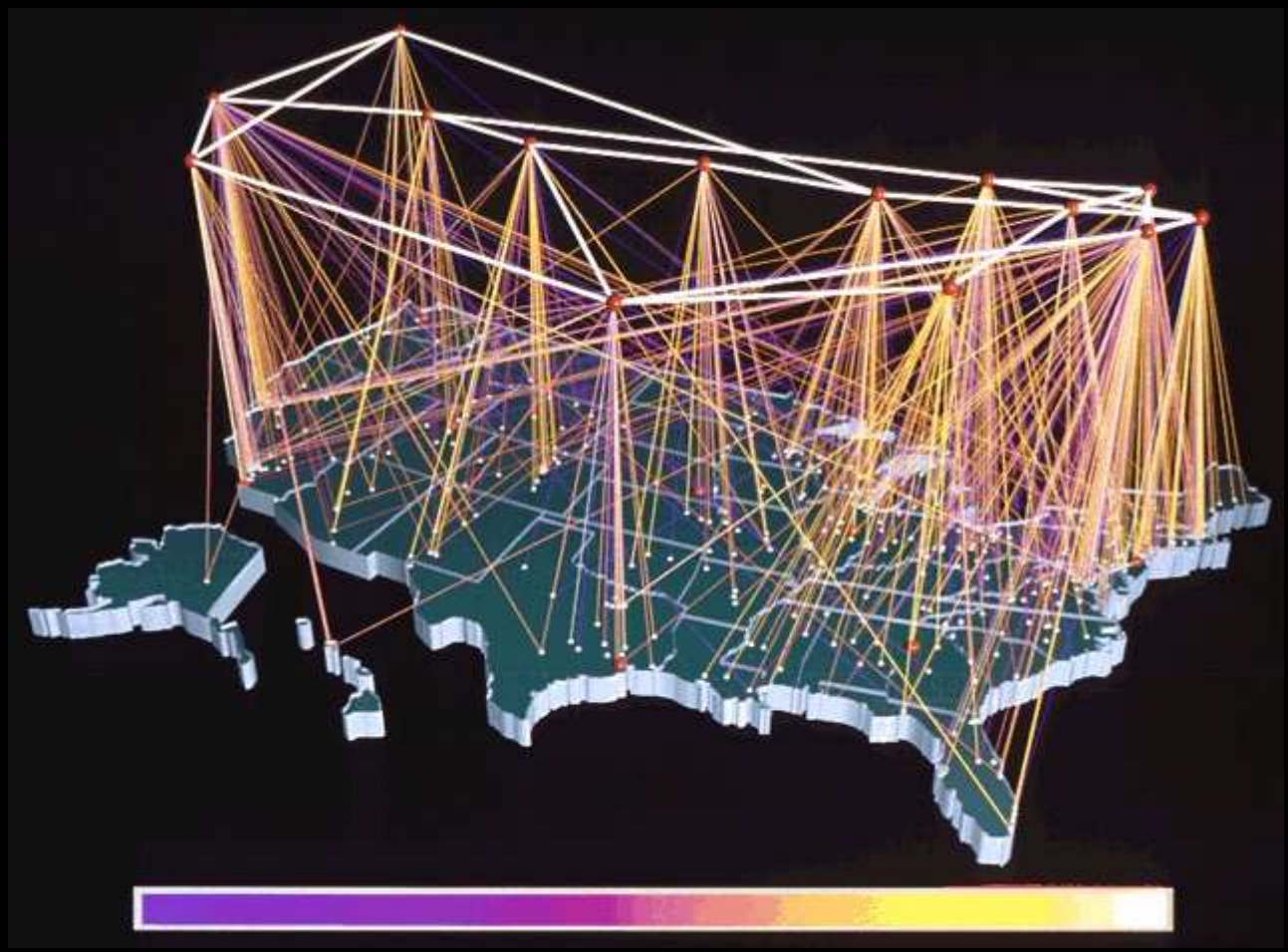
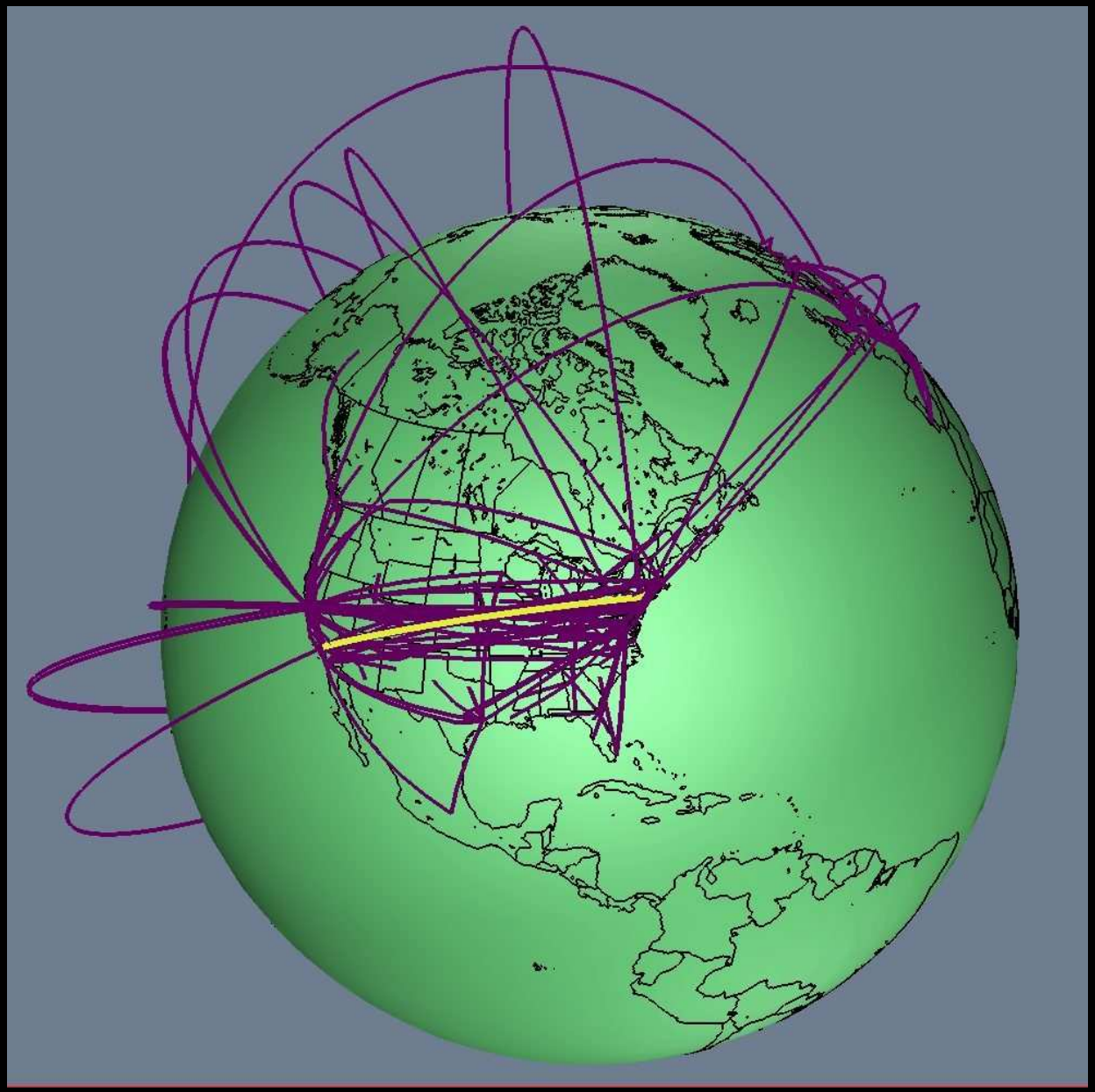




Methods

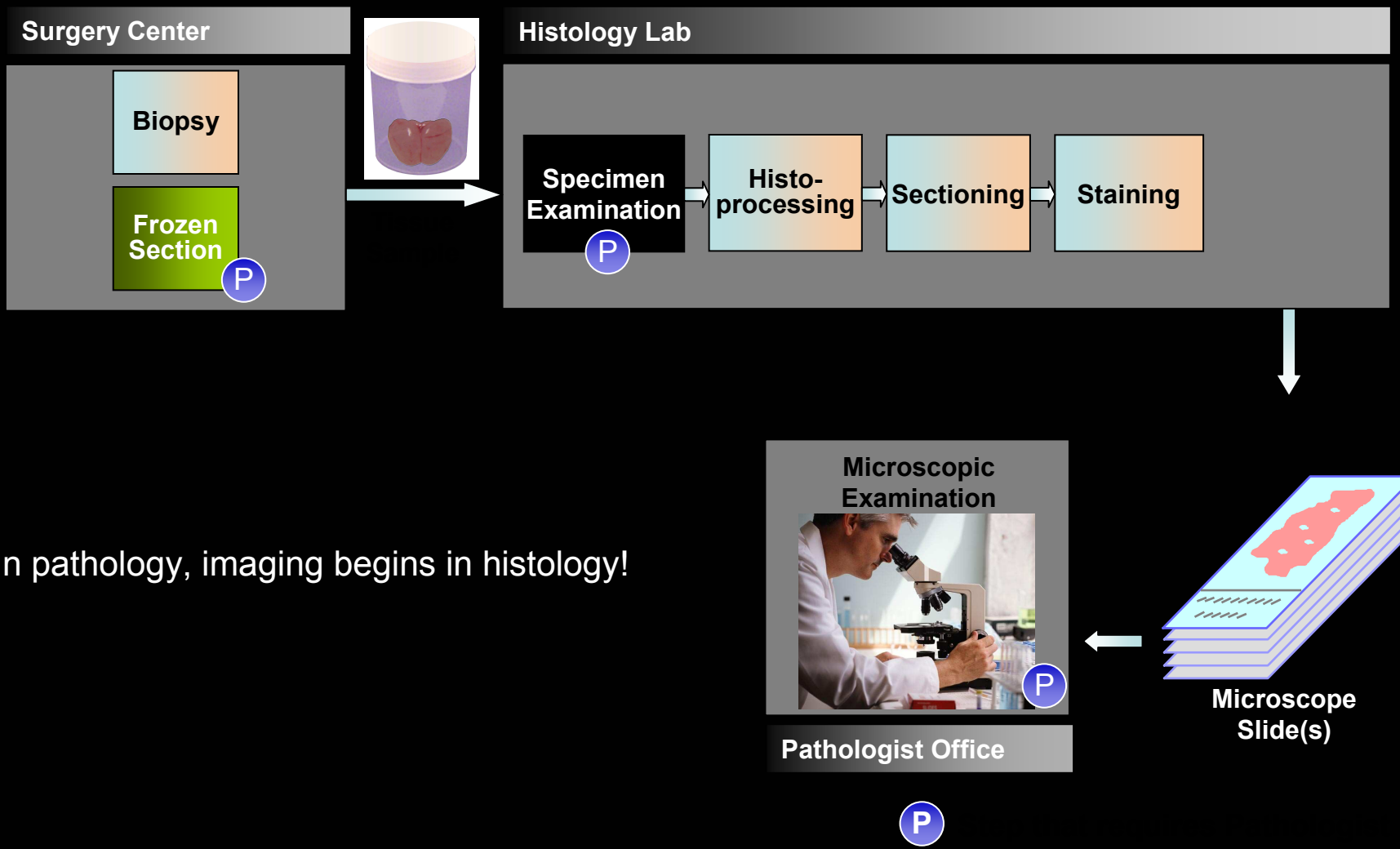
Methods: At the University of Pittsburgh, we have developed an infrastructure for the clinical use of whole slide imaging (WSI) including the implementation of different types of imaging robots, imaging quality assurance protocols, compression and storage mechanisms, mechanisms to serve whole slide images throughout the medical center, slide image viewers and a team of pathologists, imaging scientists and engineers dedicated to the evaluation of whole slide imaging systems in the clinical environment.

It was quickly realized that for the clinical evaluation of WSI to be realistic, images had to be managed (or at least accounted for) within the Laboratory Information System (LIS). The team, assisted by personnel form central IT and Radiology, examined 1) The image information needs of the pathologist, histologist, imager and image data manager and how these needs can be accommodated in with the LIS and Pathology Imaging Systems and 2) Mechanisms by which specific systems – the Copath C/S Laboratory Information System, the Aperio T2 Whole Slide Imager and UPMC's DICOM Compliant Enterprise Image Archive - could share images and image information in support of clinical evaluations.

Why are we implementing a clinical whole slide image delivery system?

Histology Workflow

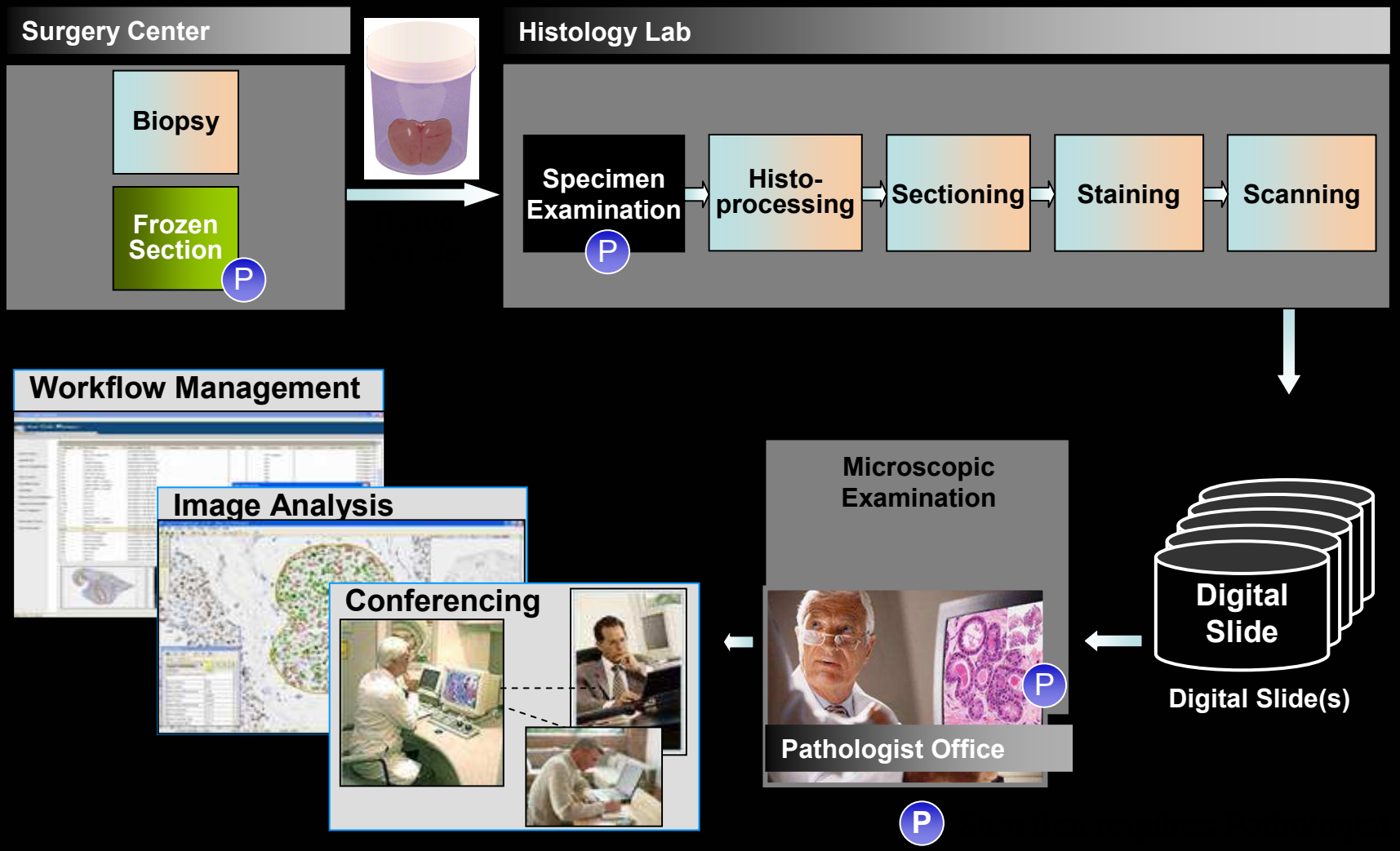
From Tissue Sample to Histological Examination



In pathology, imaging begins in histology!

Virtual Microscopy

Digital Slide Creation, Management & Analysis



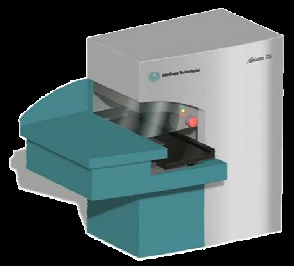
Available systems in US

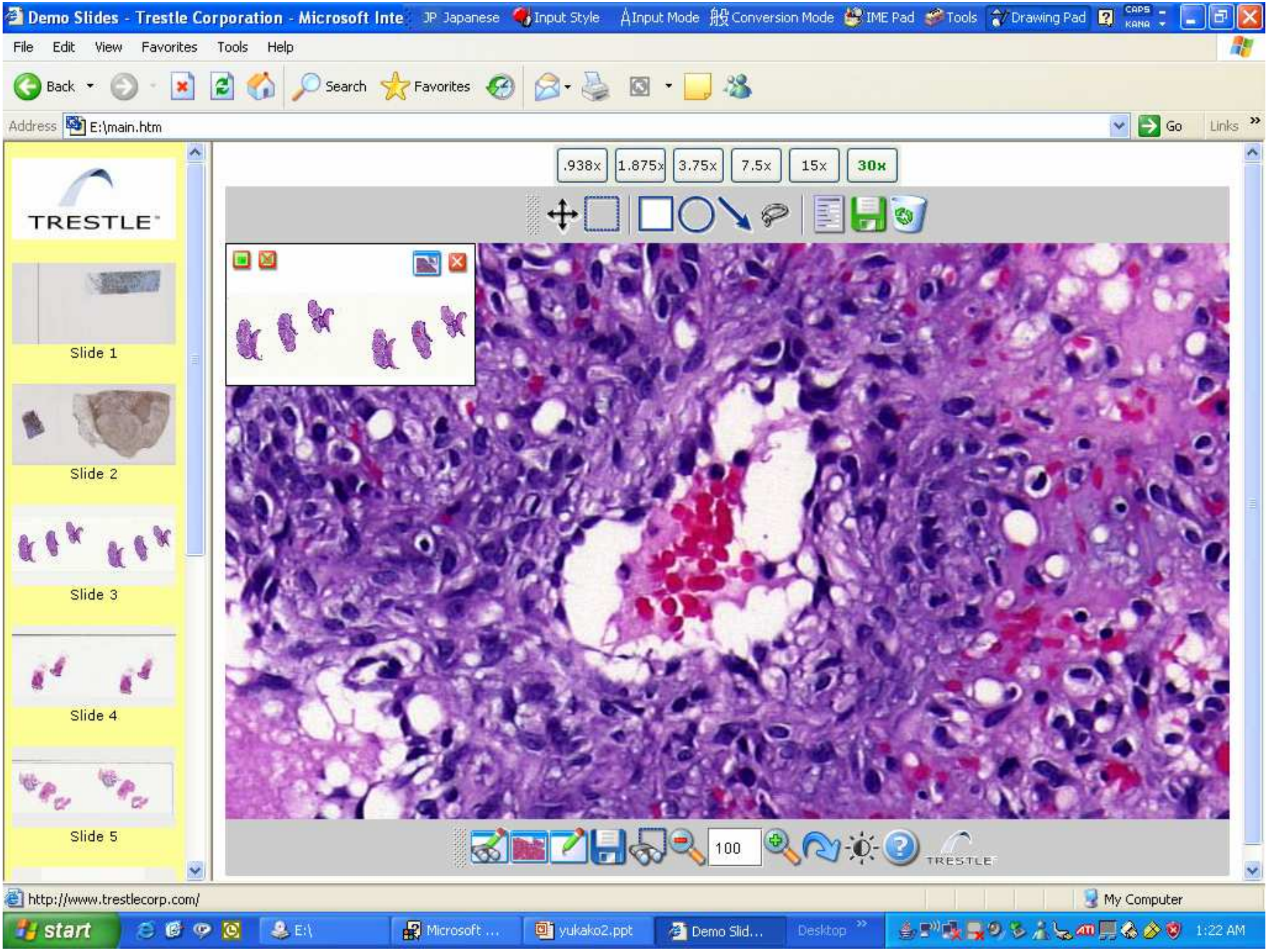
Aperio

Hamamatsu

DMetrix

Trestle

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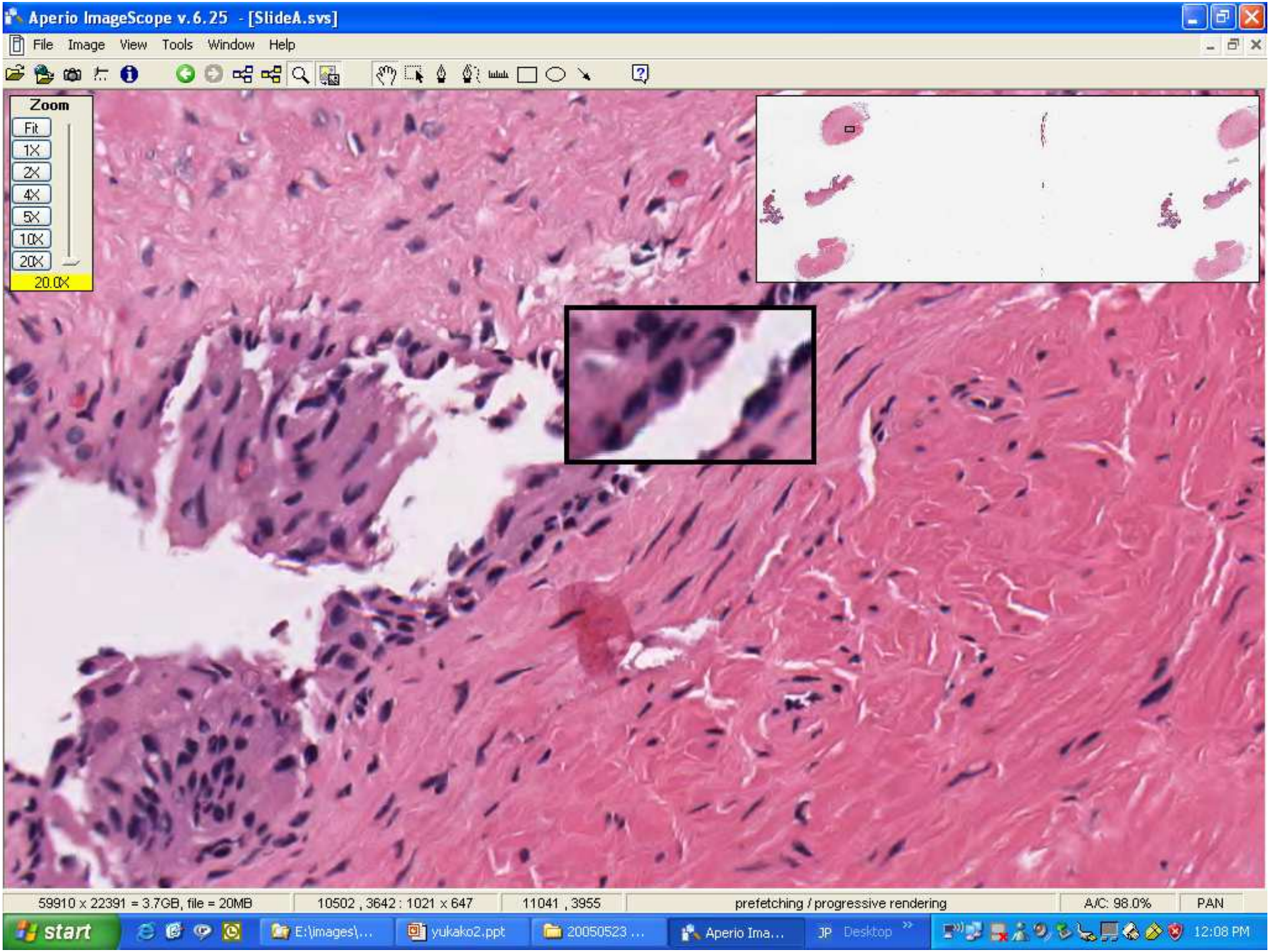
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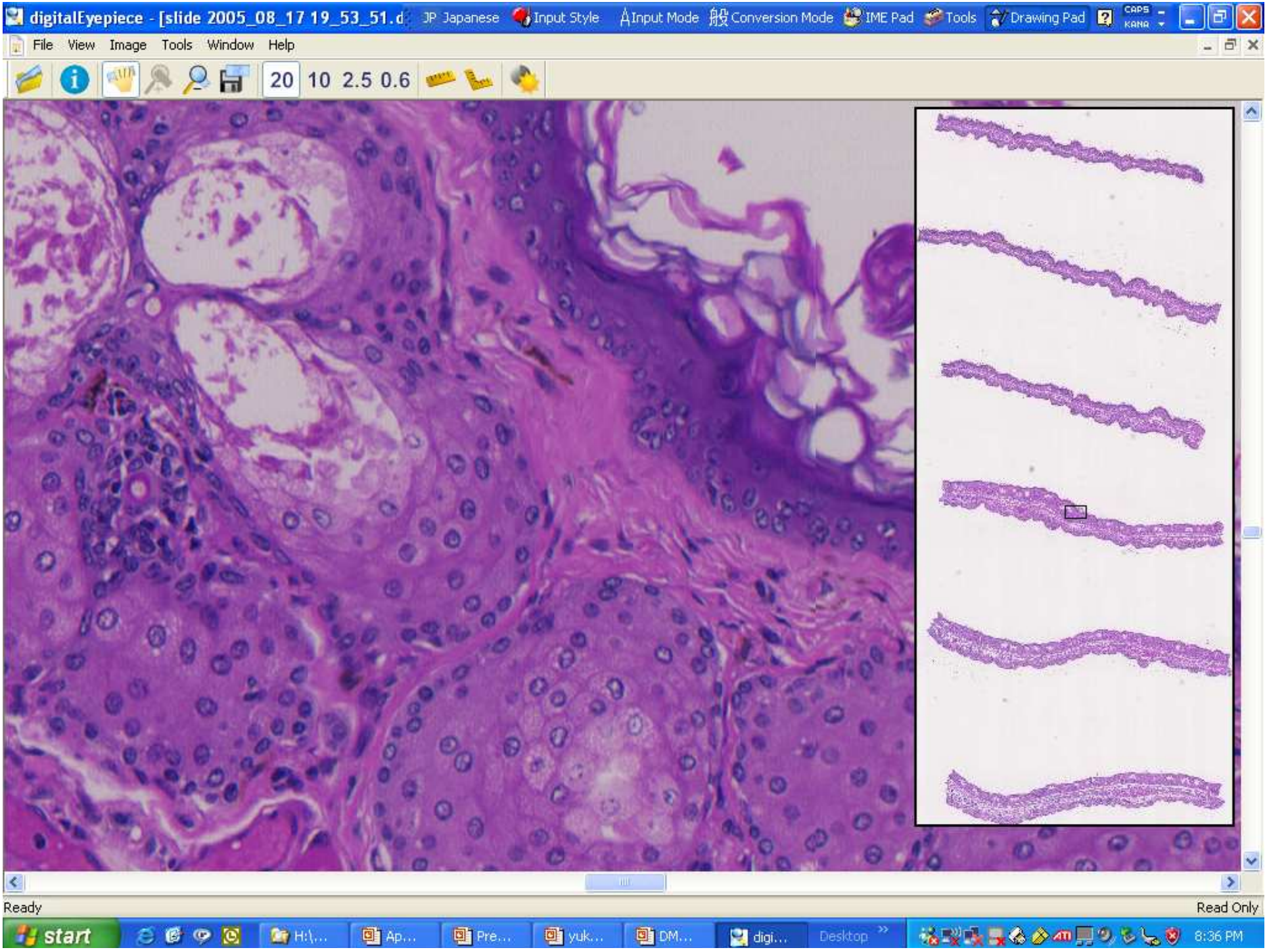
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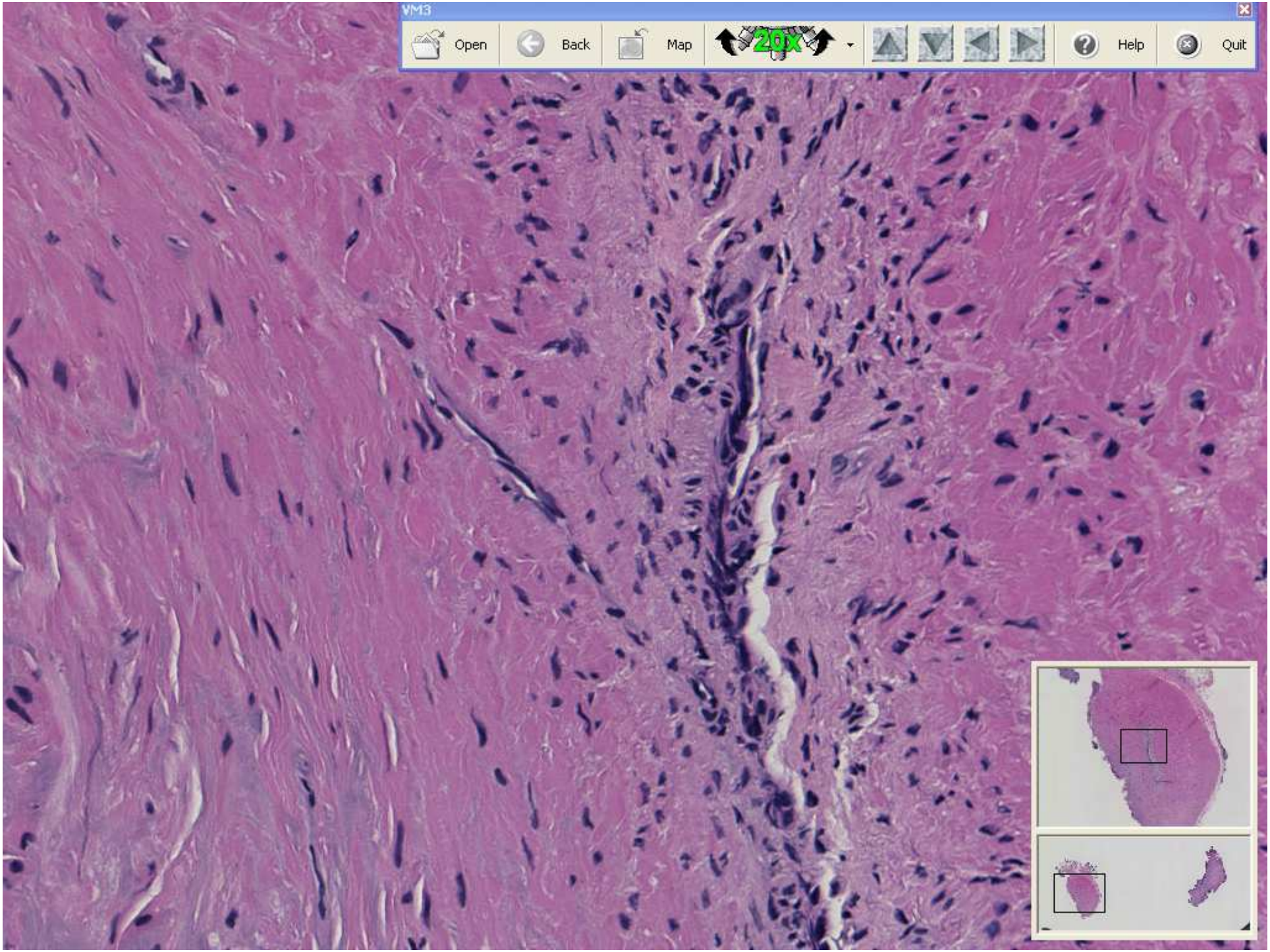
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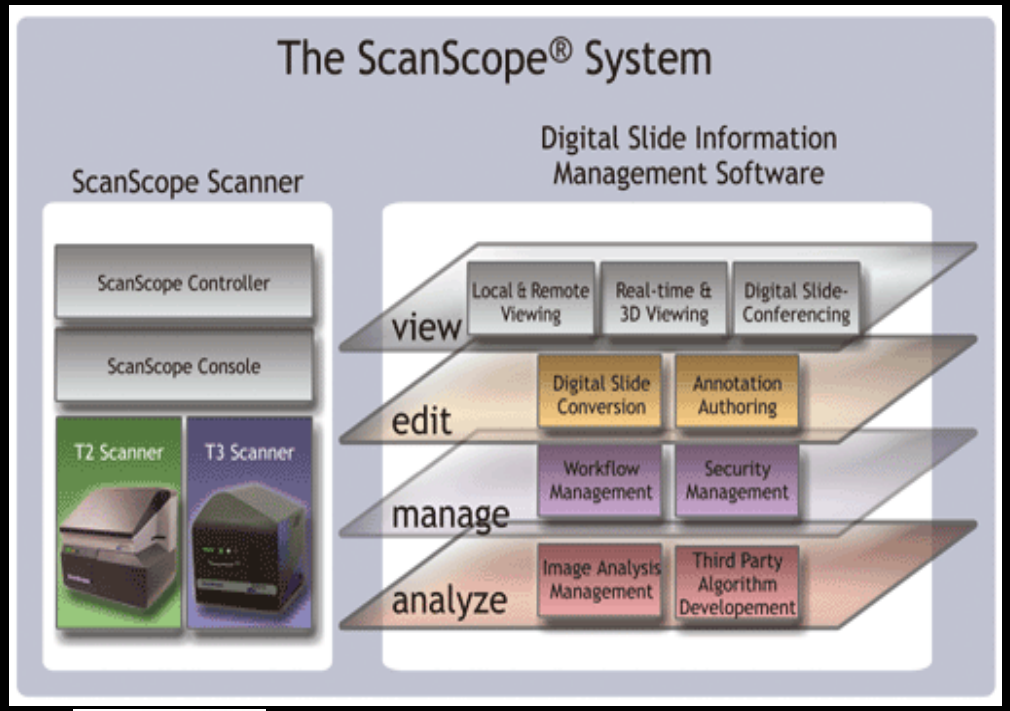
Aperio ScanScope T2/T3/CS



Digital Slide Creation, Management, and Analysis Aperio's ScanScope Systems, comprised of award-winning ScanScope scanners and Digital Slide Information Management Software, deliver integrated digital slide creation, viewing, management, and analysis capabilities for virtual microscopy applications. ScanScope Systems are invaluable to pathologists for a multitude of applications, including education, tissue microarrays, toxicology pathology, telepathology, image analysis and workflow systems (PACS).

Hamamatsu

Adobe Reader - [NDP.pdf]

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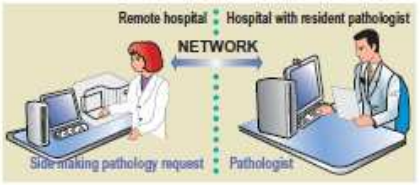
Pages Attachments Comments

NanoZoomer Digital Pathology opens up new applications in pathology

With Hamamatsu Photonics scanning technology, rapid conversion from glass slides into high resolution digital slides become available. The digital slide technology will become indispensable for telepathology to link hospitals through networks and for the development of new diagnostic methods in pathology.

1 Pathological networks not only within a hospital but also among remote hospitals

By applying digital slide technology for telepathology through a network, it is expected to conduct frozen section diagnosis at hospitals with no resident pathologists. In addition, by establishing a network among pathologists, it is expected to conduct consultations quickly and conveniently with remote specialized pathologists for difficult cases. As the result, it is expected to improve the diagnosis accuracy. Furthermore, for pathological diagnosis contract businesses, it is expected to get higher efficiency and increasing turnover by eliminating the process of the slide delivery.



2 Ideal for medical students' education

Since digital slides can be observed from multiple computers, there is no need to prepare individual slides sets for students. In addition, because of simple viewing software, even beginners can concentrate on the essential educational content without complexity of microscope operation.

3 Coordination of Pathological Laboratory Information system and NDP

Through the coordination of Pathological Laboratory Information system and NDP, it is expected to realize the improvement of efficiency and accuracy. Furthermore, digital slides will be shared with other departments, and it will be applicable for conferences.

4 Possibilities for new diagnostic methods using the benefits of new observation methods using PC and digital slide databases

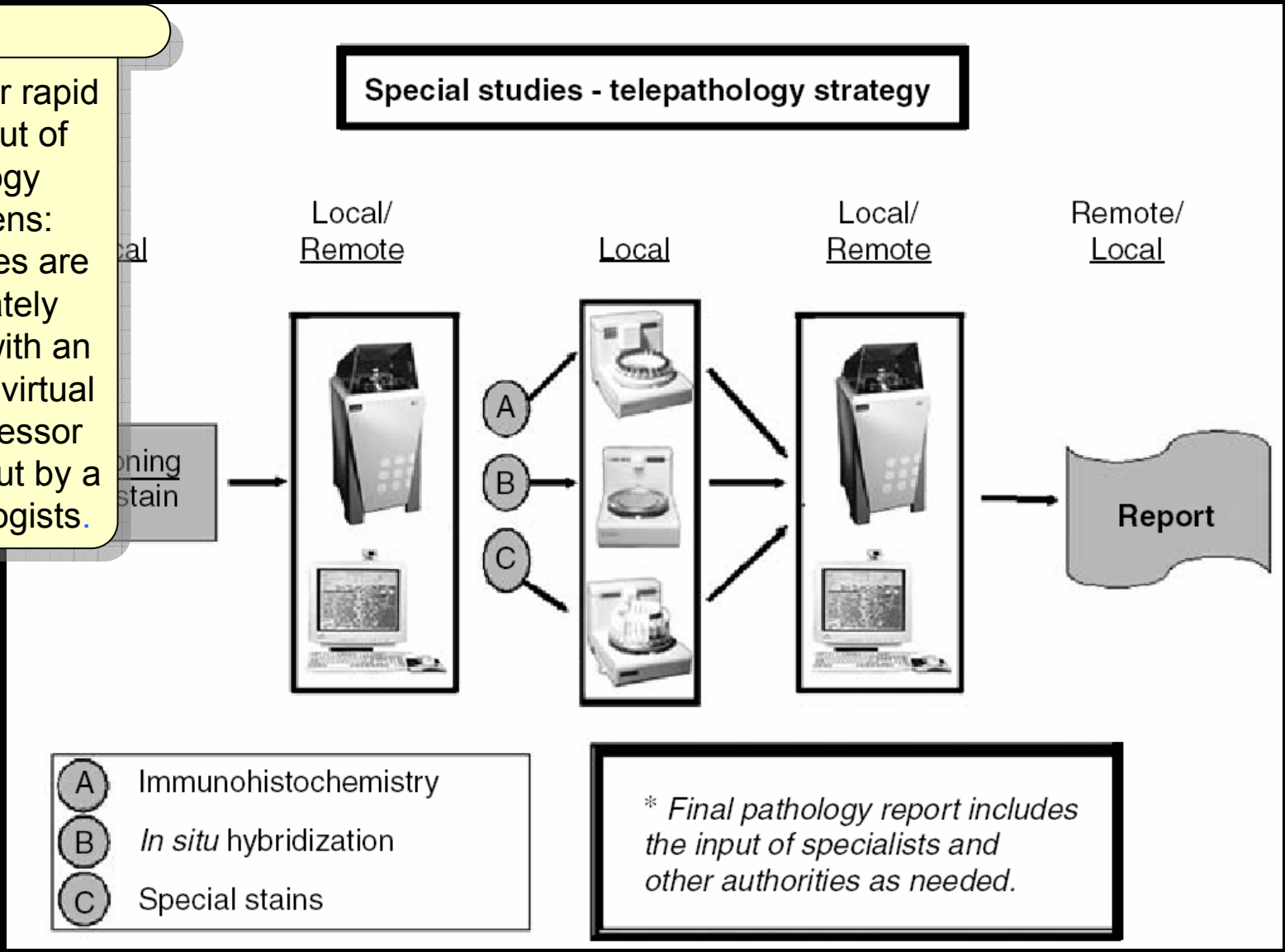
Improvement of diagnosis accuracy is expected through the introduction of new observation methods that were not possible by using conventional microscopes, such as simultaneous observations of details and whole tissues, comparison of pre-treatment and post-treatment and simultaneous observations of multiple slides stained differently such as imunostains and DNA stains. In addition, database of digital slides enables easy search of slides. Furthermore, image analysis, such as the size of nuclei and stain concentration, as well as the creation of case libraries are expected.

3 of 4

start D:\... We... Pre... yuk... ND... Ad... JP Desktop 11:30 AM

DMetrix

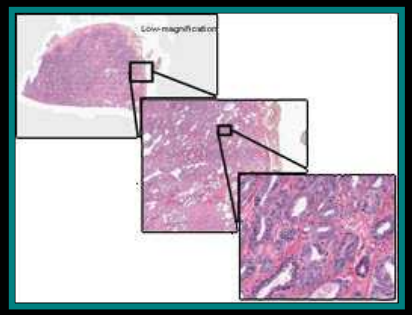
Strategy for rapid throughput of pathology specimens: Glass slides are immediately scanned with an ultra-rapid virtual slide processor and read out by a telepathologists.



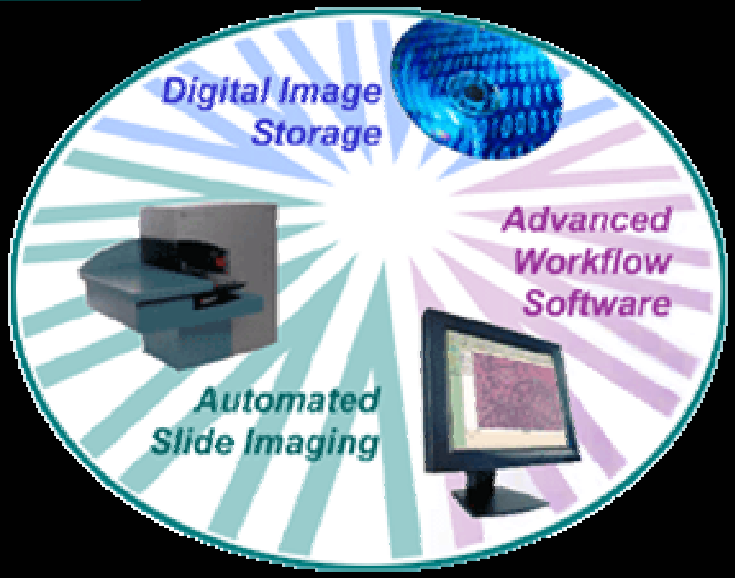
Trestle

We Enhance the Efficiency of Research Operations

Live review of slide over the internet or virtual slide creation



Immediately available for viewing, diagnosis and consults worldwide



Work to be presented

Work to be presented: In this paper we describe the nature of whole slide images and integration of whole slide imaging into the existing workflow of a pathology department. Using an image v glass slide equivalence study in anatomic pathology quality assurance as a context, we will discuss changes required in the Laboratory Information System (LIS) and Histology Laboratory to support image level information, departmental decisions surrounding the dissemination of images, the integration of imaging systems and the LIS and the development of a “DICOM wrapper” to communicate gross and histological images from Pathology to an Enterprise Image Archive.

Whole slide image clinical validation studies

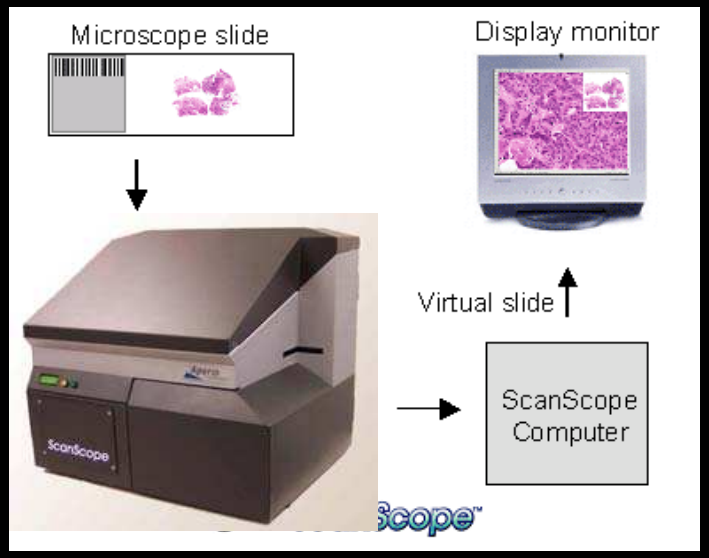
- 3 pathologists
- 25 full cases, same workflow (3-24 slides)
- 200-500 whole slide images per study
- Integration of images with clinical information, histology information (ie staining) and workflow information (ie case status)
- Security issues
- Significant logistical effort

Goal

To create a whole slide image delivery system for pathologists for clinical sign-out responsibilities

**requires AP LIS integration, but workflow will reside in the AP LIS*

Whole Slide Imaging at UPMC



The ability to digitize an entire histologic slide at high resolution and display the resulting image across a broadband network - is becoming an important technology for telepathology and Pathology Imaging

Current Spec

Hardware Specification
Resolution:0.47um/pixel(20x)
0.23um/pixel (40x)
Speed: 40mm2/min
File format: Tiff/Jpeg2000 (Pyramid)
Bar code: 2D
Autoloader: 120 slides

Scanning Process

- Place Slides(120) in Autoloader
- Push “Start” bottom
  - Change slide (30s)
  - Bar Code reading
  - Tissue finding
  - Auto focus
  - Scan (strip)
  - Compression (on board)
  - Stitch
  - Feeding Virtual slide image to the storage

Ave. 3-10 min/slide, about 7 hours for 120 slides

Image size 1-8 GB

File size 20-600 MB

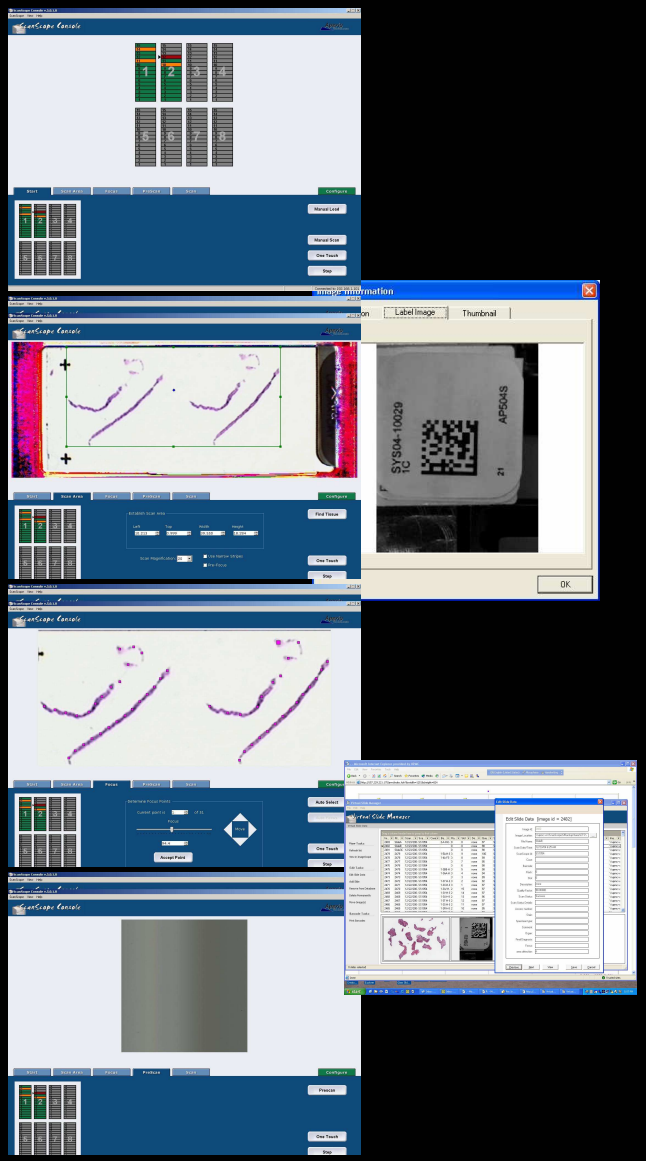
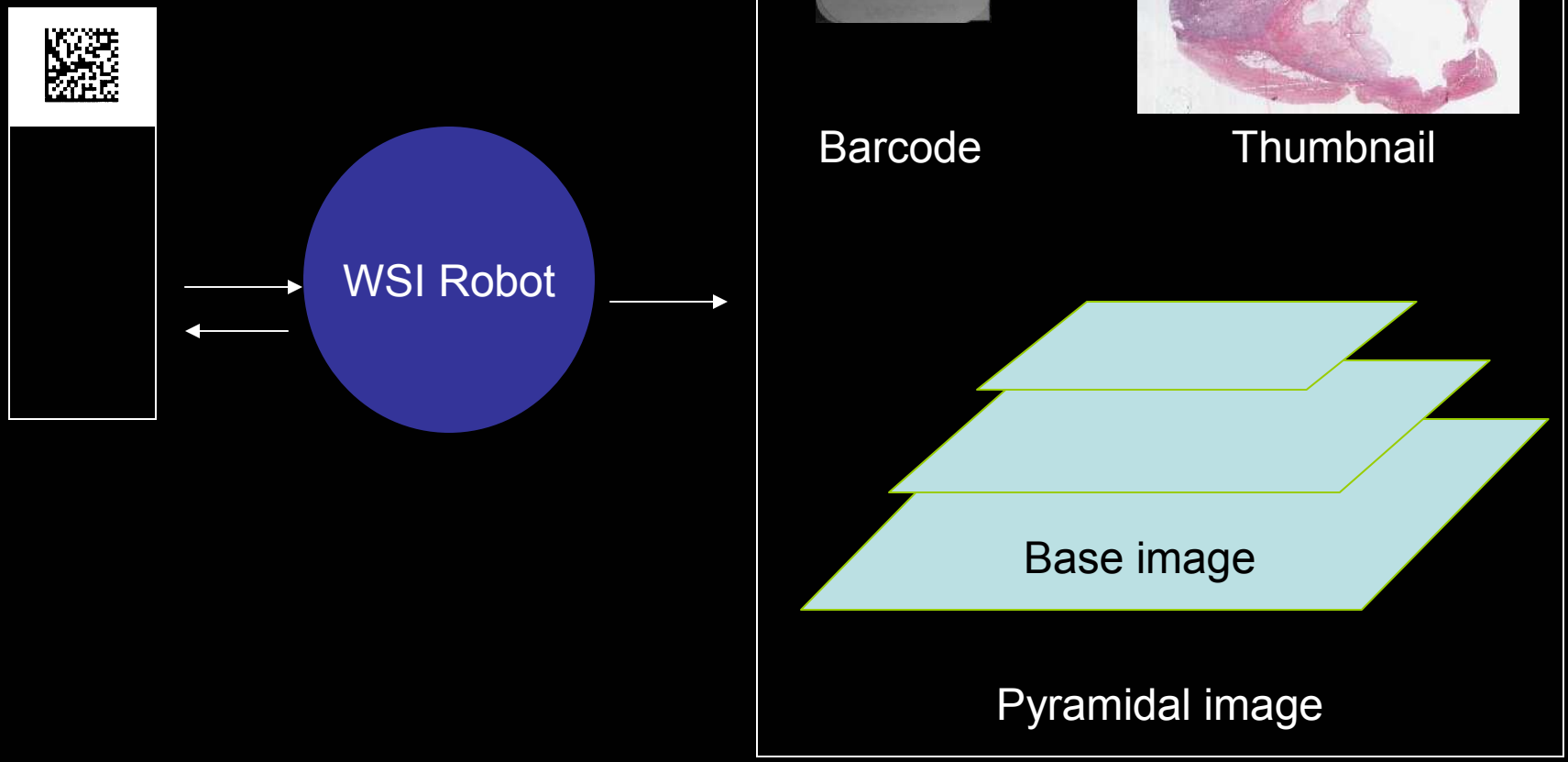
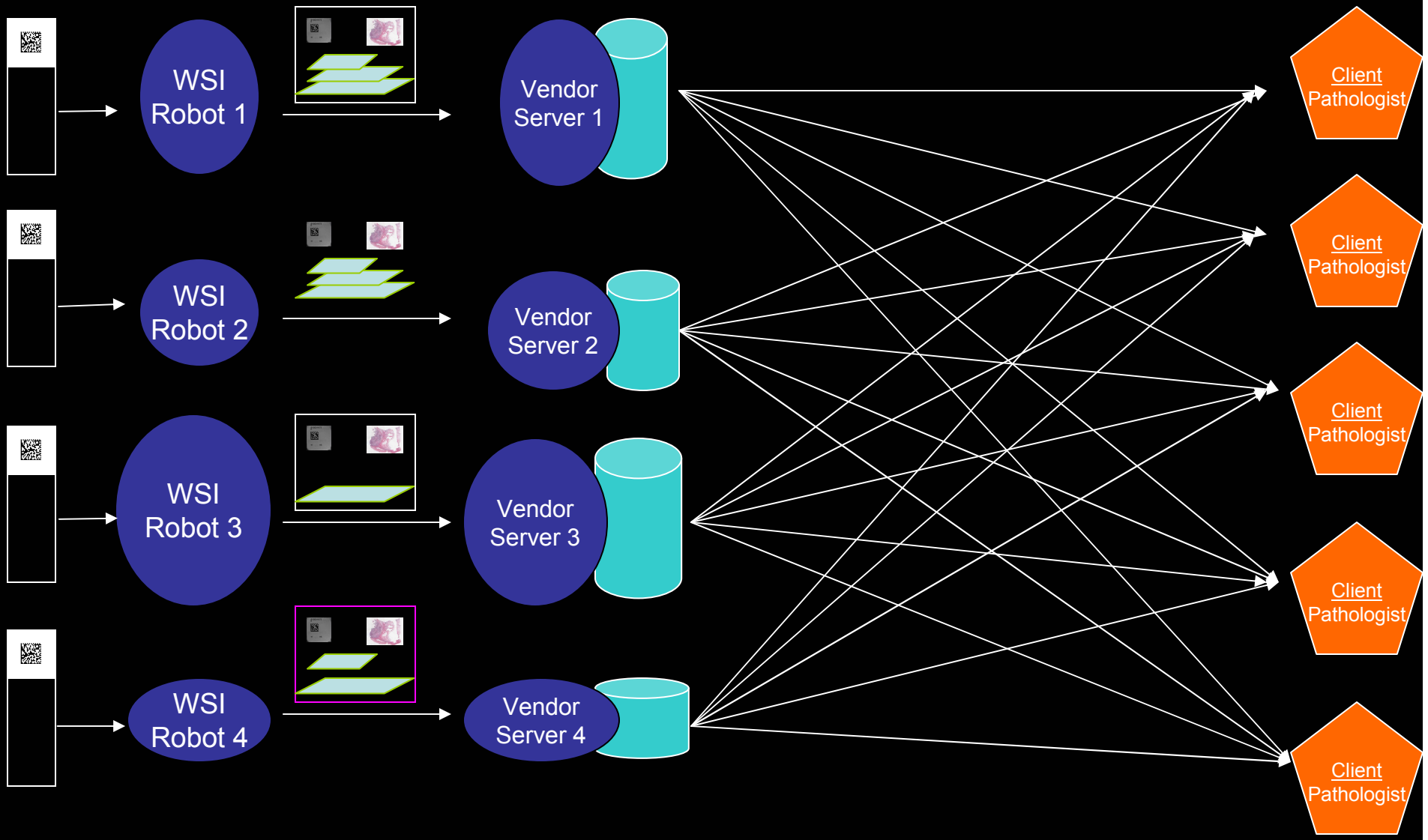


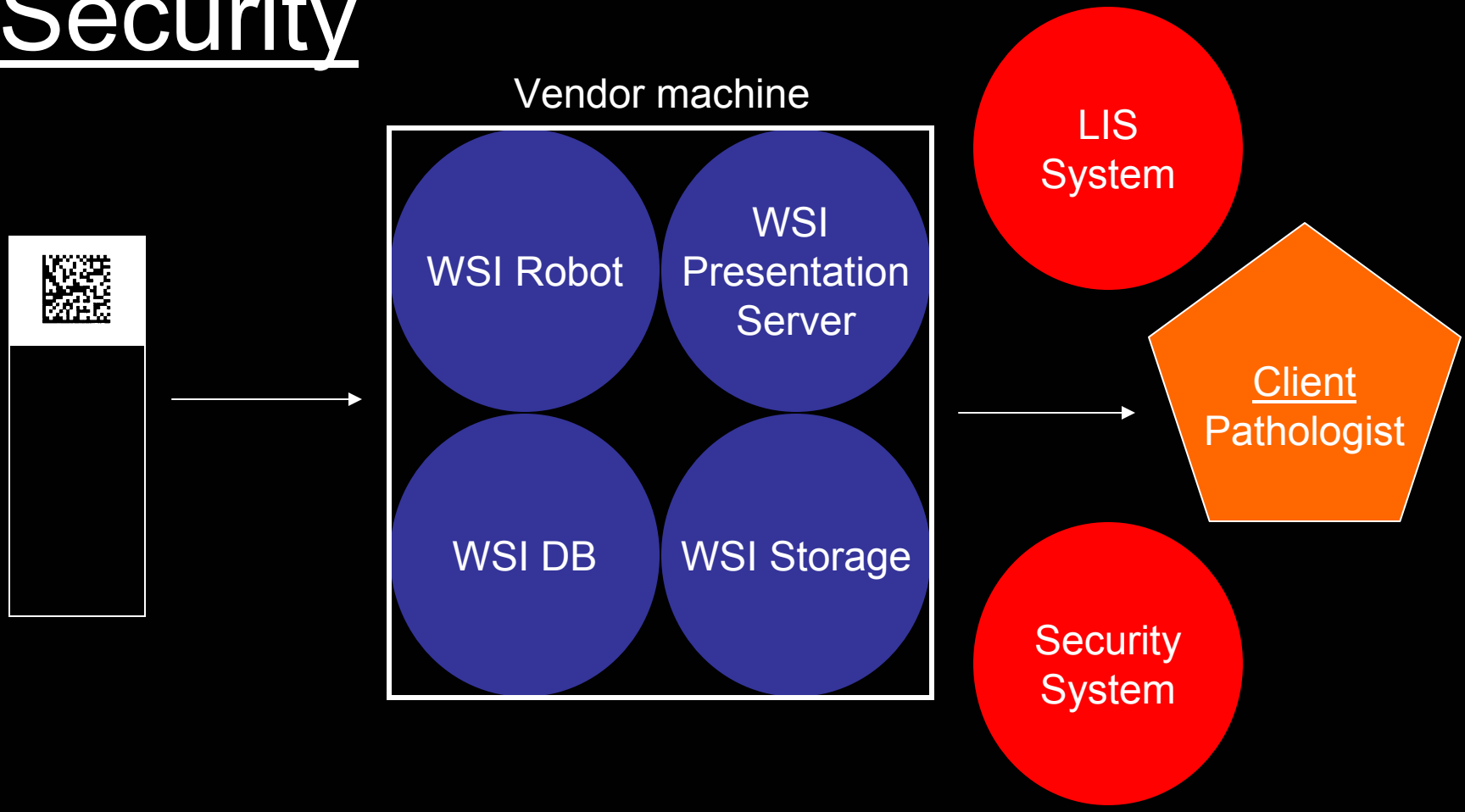
Image Capture



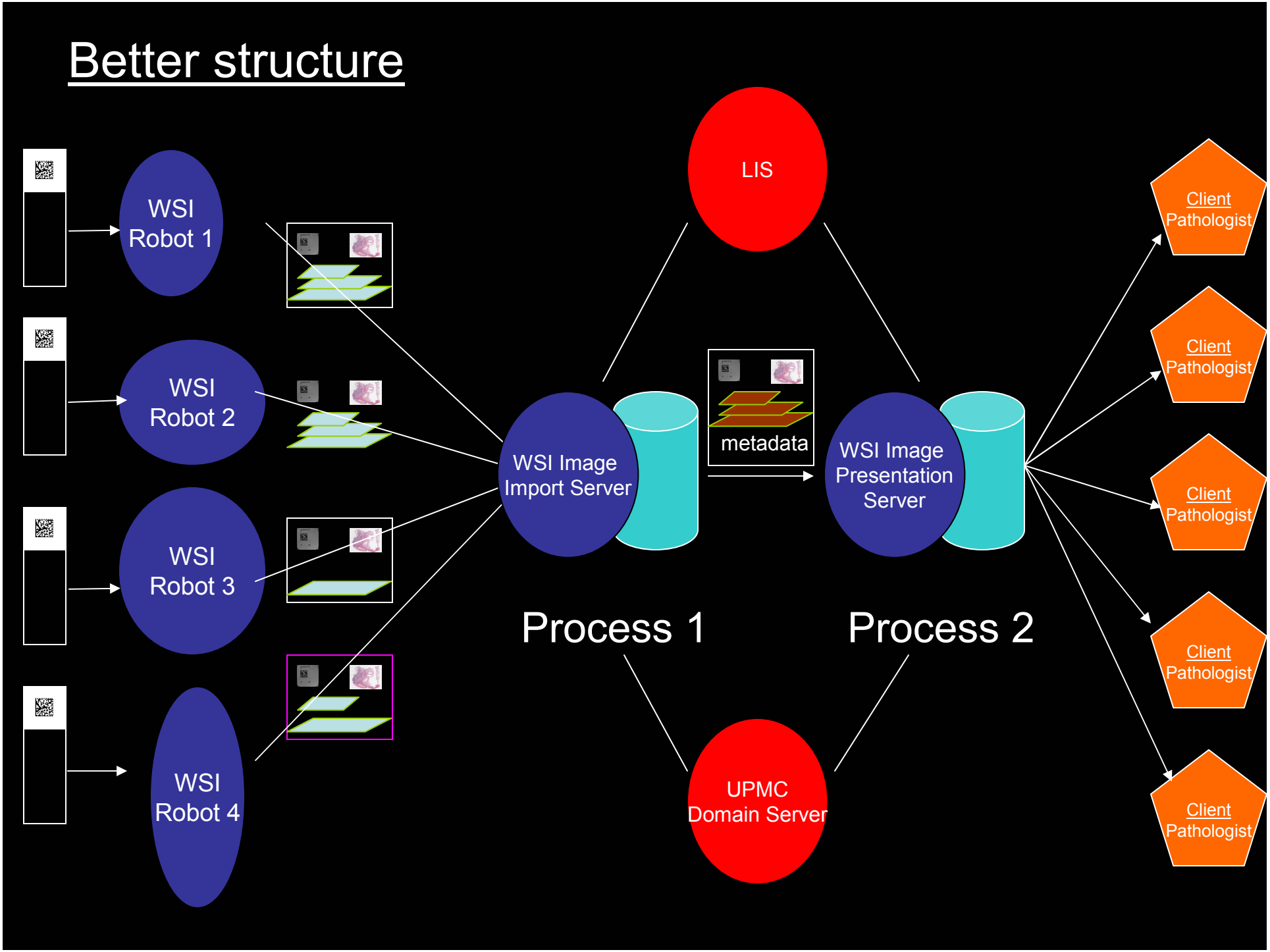
Each vendor has its own formats, servers and clients



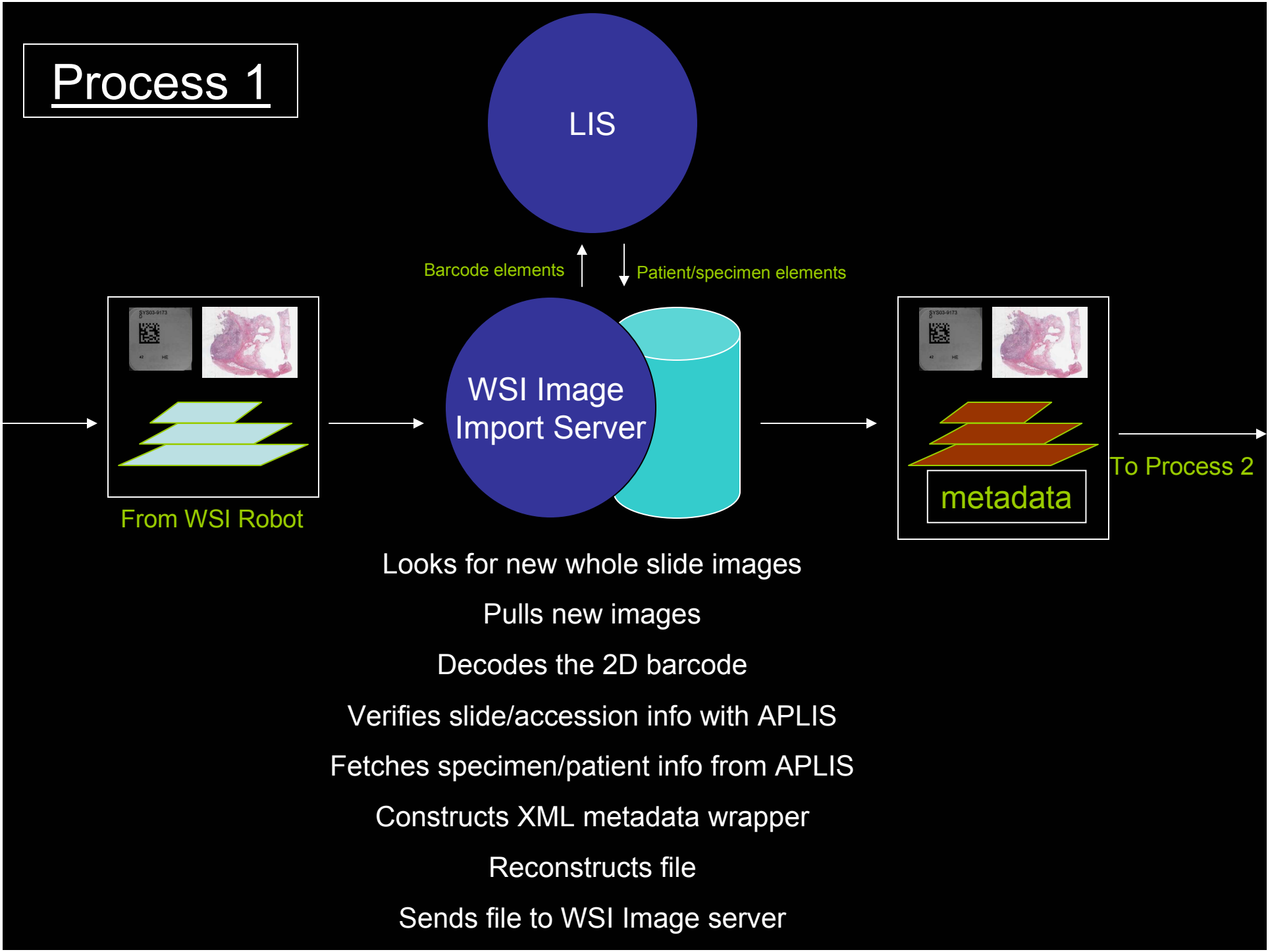
No real integration with LIS or Security



Better structure



Process 1



Looks for new whole slide images

Pulls new images

Decodes the 2D barcode

Verifies slide/accession info with APLIS

Fetches specimen/patient info from APLIS

Constructs XML metadata wrapper

Reconstructs file

Sends file to WSI Image server

Metadata wrapper

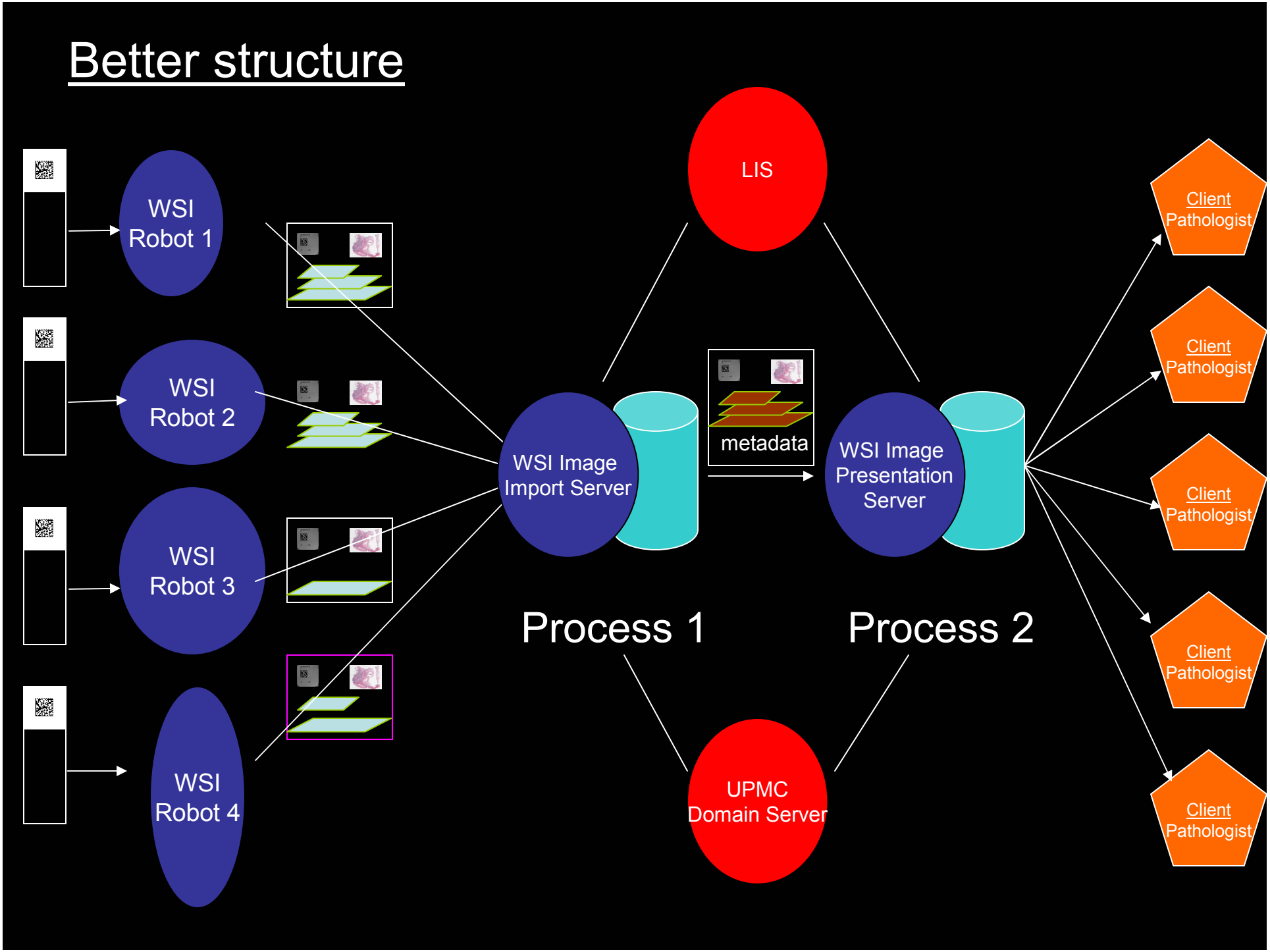
- UID 1.2.840.152371.157.229.222.79.20050706.121311.30.1
- XML
- Patient level (last name, first name, med rec num, sex, birthdate…)
- Accession level (Accession number, date, time, pathologist…)
- Study level (Modality, date, time, manufacturer, IP address…)
- Series level (whole slide image)
  - Part
  - Block
  - Slide number
  - Stain
  - Components and descriptions (thumbnail, label, base image…)
- Image level (describes each component)

Example of metadata wrapper

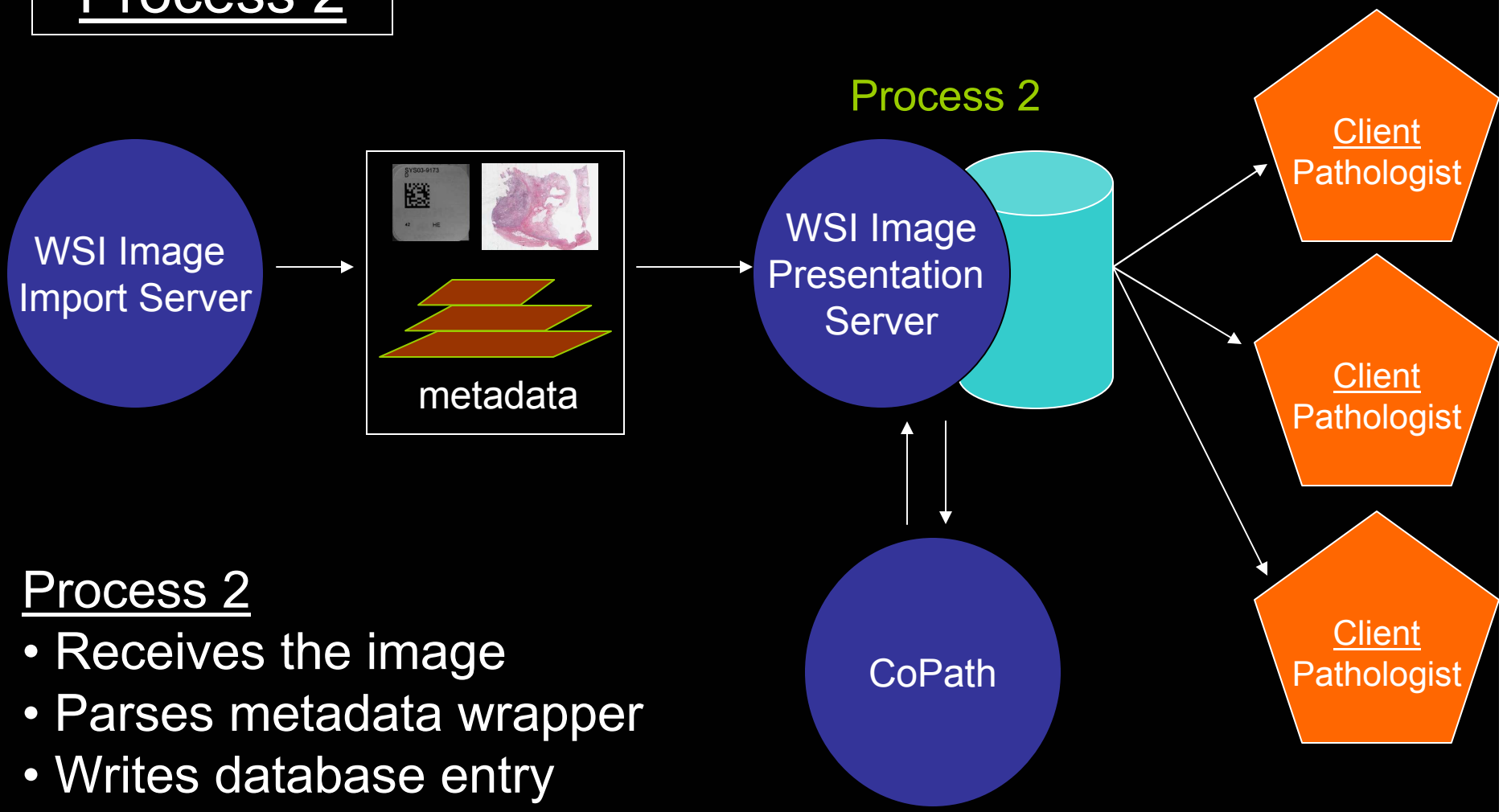
```
<SeriesLevel>
        #A Series is effectively one slide imaged one time.
        #A Series has multiple images usually in a TIFF container
        #Some images are "real" optical images, others are sampled as part of a Pyramid:
    <S.1>
        #Series Identification:
<UID>1.2.840.152371.157.229.221.31.20050322.112447.30.1</UID>
        <PartNumber>1</PartNumber>
        <BlockNumber>A</BlockNumber>
        <SlideNumber>1</SlideNumber>
        <PartDescription>Colon Resection</PartDescription>
    <BlockDescription>Proximal Margin</BlockDescription>
        <SeriesBeginTime>143456</SeriesBeginTime>
        <SeriesEndTime>144056</SeriesEndTime>
        <SeriesFileDescription>WSI-TIFF</SeriesFileDescription>
    <PixelSize>N/A</PixelSize>
        <SeriesComment>NA</SeriesComment>
    <Paths>
      <P.1>C:\Image Quality\Images\Focus Measure\Yukako Images</P.1>
    </Paths>
    <Images>
      <I.1>Thumbnail.jpg</I.1>
        <I.2>SlideLabel.tif</I.2>
        <I.3>BaseImage.jp2</I.3>
        <I.4>Level1Image.jp2</I.4>
        <I.5>Level2Image.jp2</I.5>
        <I.6>ScoutCameraImage.jpg</I.6>
    </Images>
```

```
<DICOMMetaTags>
<x00020002>1.2.840.10008.5.1.4.1.1.7</x00020002>
<x00020003>1.2.840.152371.157.229.221.31.20050322.112447.30</x00020003>
    <x00020010>1.2.840.10008.1.2.4.50</x00020010>
    <x00020016>SimpleDICOMWrap</x00020016>
    <x00080005>ISO_IR 100</x00080005><!-- specific character set -->
    <x00080008>ORIGINAL\\PRIMARY</x00080008><!-- Image type -->
    <x00080016>1.2.840.10008.5.1.4.1.1.7</x00080016><!-- SOP class UID -->
<x00080018>1.2.840.152371.157.229.221.31.20050322.112447.30.1.1</x00080018><!-- SOP instance UID -->
    <x00080020>20050322</x00080020><!-- Study Date -->
    <x00080023>20050322</x00080023><!-- Content Date -->
    <x00080030>112447</x00080030><!-- Study Time -->
    <x00080033>112447</x00080033><!-- Content Time -->
    <x00080050>1234</x00080050><!-- Accession Number -->
    <x00080060>OT</x00080060><!-- Modality -->
    <x00080070>Olympus</x00080070><!-- Manufacturer -->
    <x00080080>UPMC Presbyterian</x00080080><!-- Institution Name -->
    <x00080090>Dr. John Kirkwood</x00080090><!-- Referring Physician's Name -->
    <x00081010>Olympus CC12</x00081010><!-- Station Name -->
    <x00081030>N/A</x00081030><!-- Study Description -->
    <x0008103E>N/A</x0008103E><!-- Series Description -->
    <x00081040>MEDICAL MEDIA</x00081040><!-- Institutional Department Name -->
    <x00081060>Number Two</x00081060><!-- Name of Physician(s) reading study -->
```

Better structure

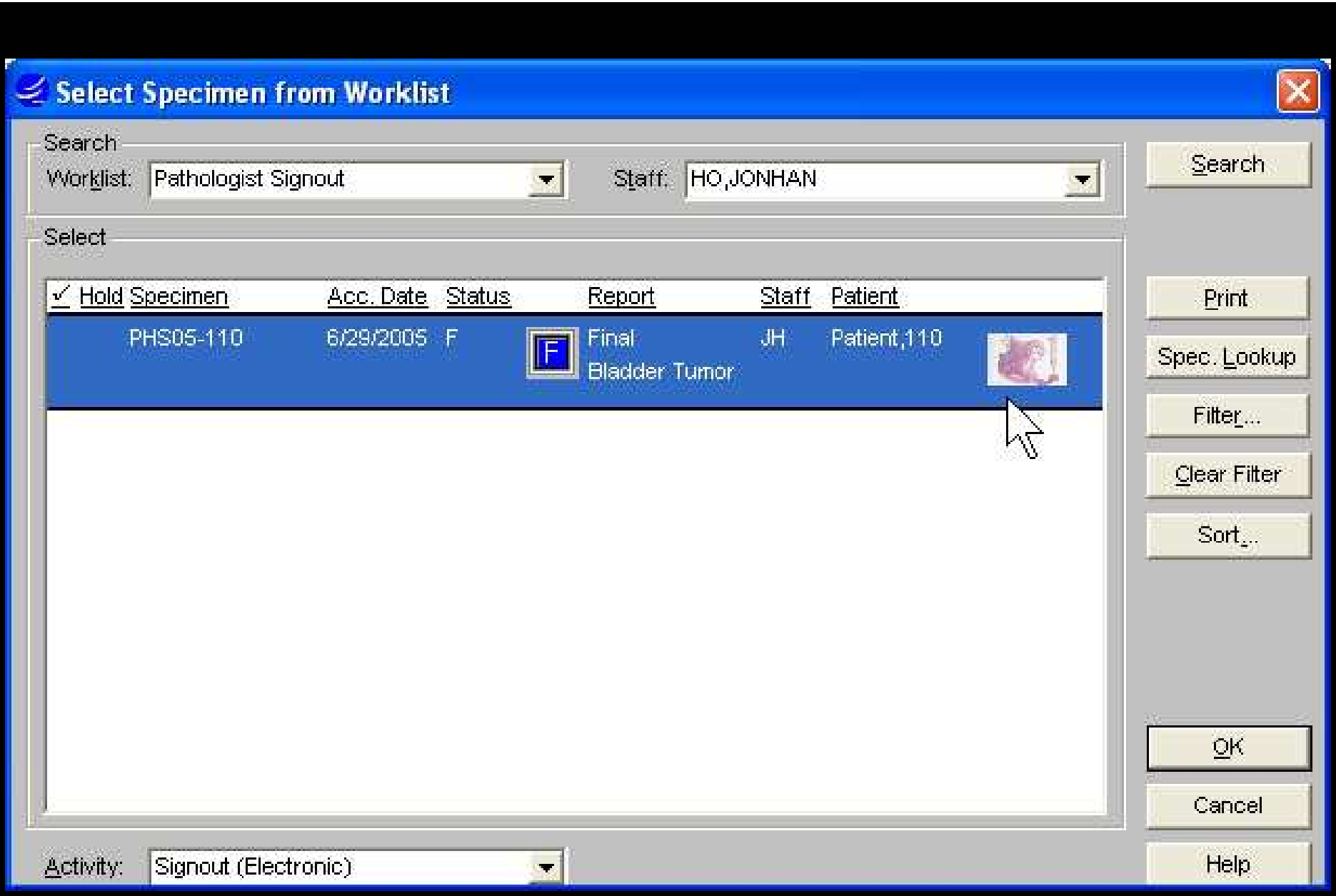


Process 2



Process 2

- Receives the image
- Parses metadata wrapper
- Writes database entry
- Stores the image
- Updates LIS on image status
- Fetches image's context
- Serves the image



System communicates image status to LIS

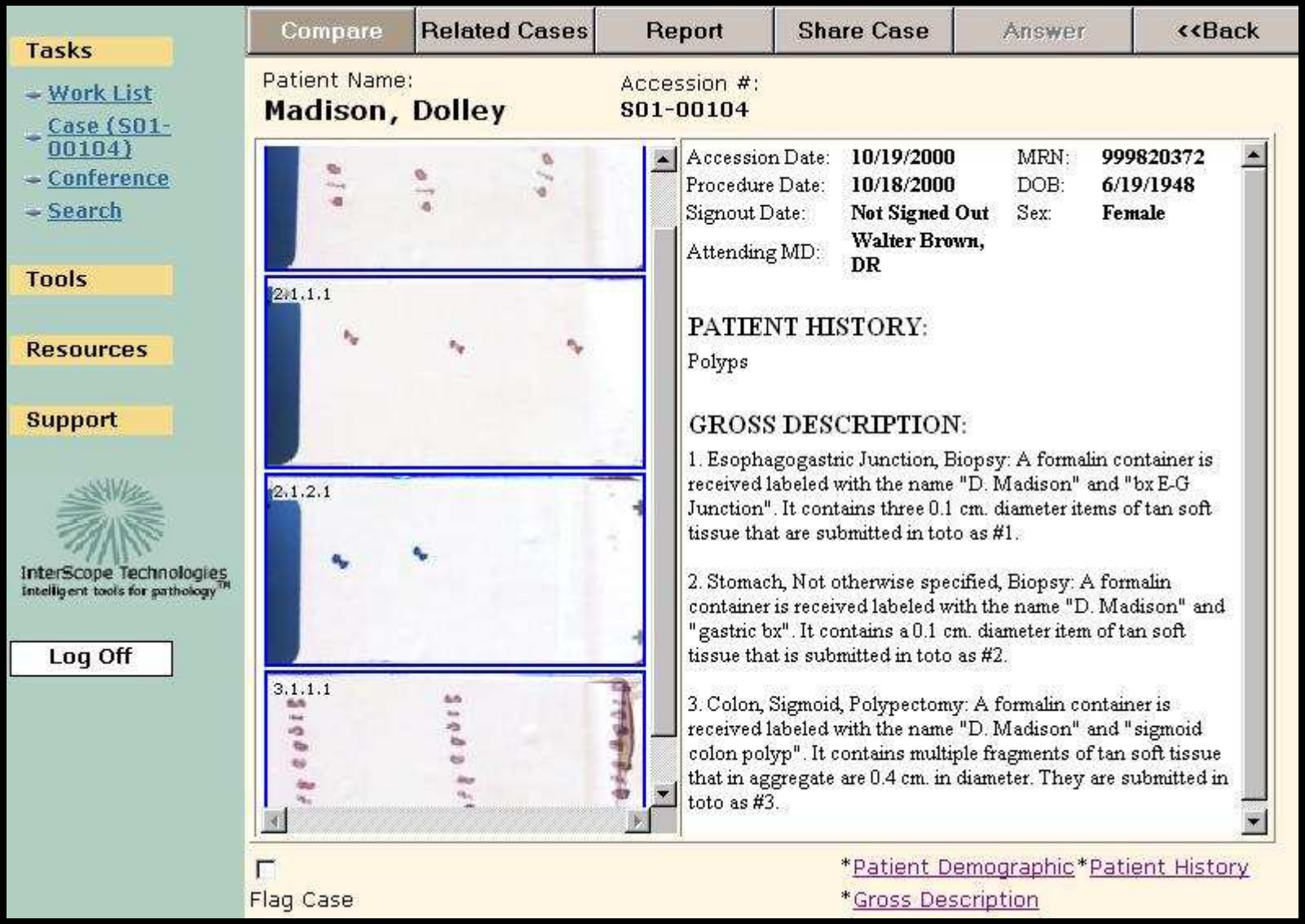
Results & Discussion

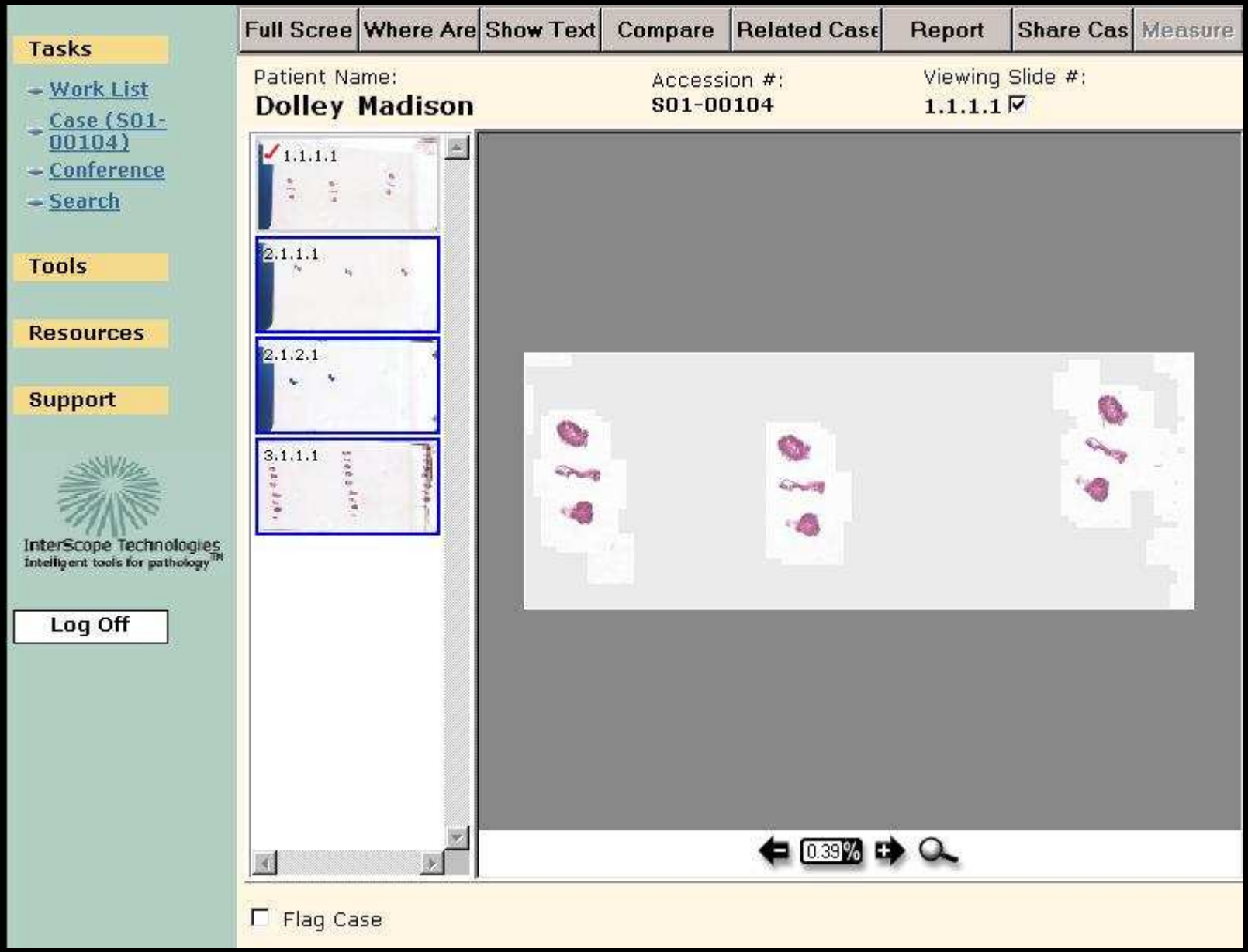
The work revealed a number of structural and procedural issues in the LIS, Imaging System and Archive the hindered the implementation of large scale imaging in pathology. Some of these issues include:

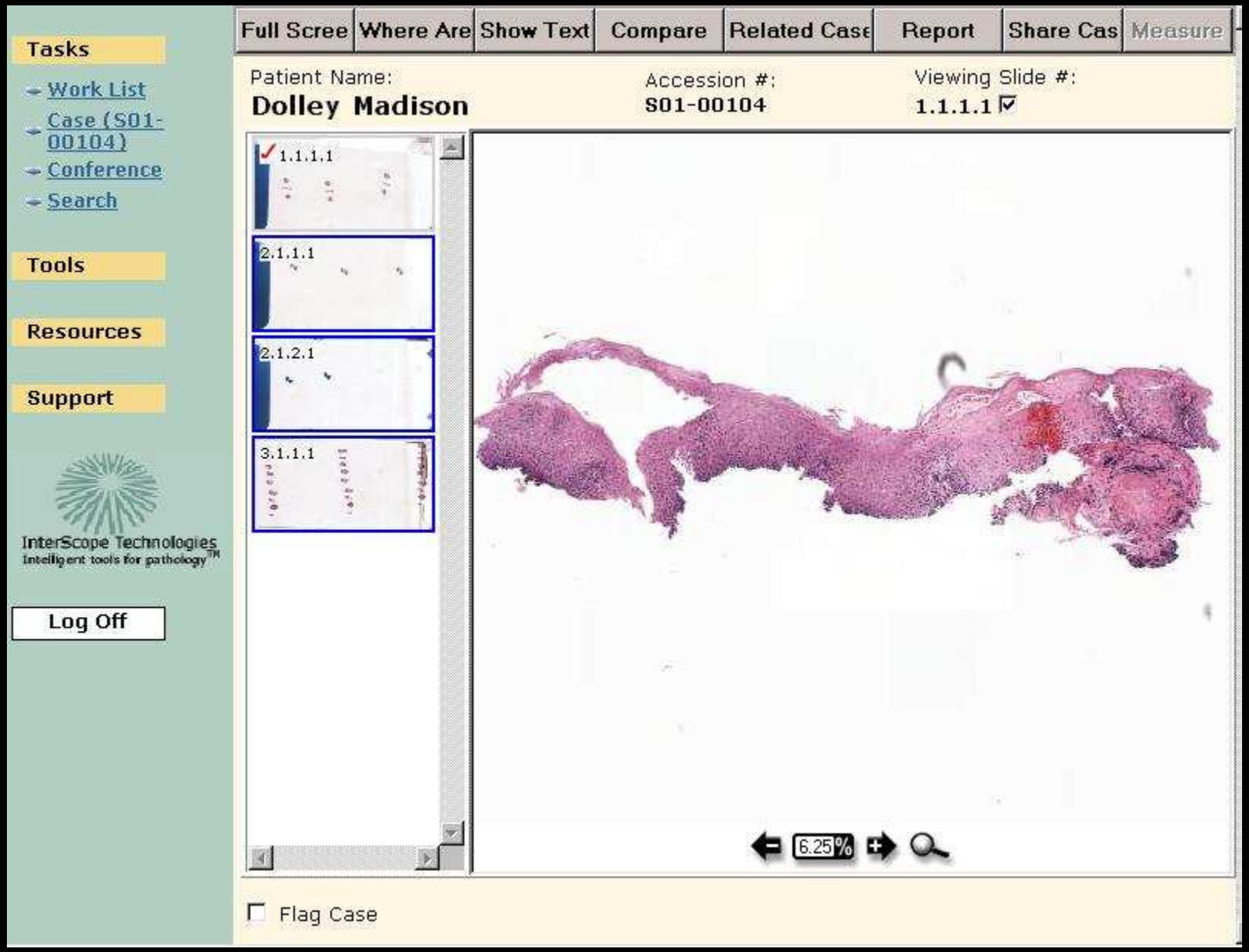
- LIS systems did not support the concept of an whole slide image
- Current pathology imaging systems did not well support the “groups of associated images (i.e. “series”)
- The Enterprise Image Archive had difficulties with the size of the WSI and the proprietary internal structure of some of the WSI image files.

The team implemented a series of work-arounds for these problems and tested them as part of clinical evaluations. On the basis of there results, we are working to develop long term solutions.

Integrated Clinical Application




Tasks
Work List
Case (S01-00104)
Conference
Search
Tools
Resources
Support
InterScope Technologies
Intelligent tools for pathology™
Log Off
Full Scree
Where Are
Show Text
Compare
Related Case
Report
Share Cas
Measure
Patient Name:
Dolley Madison
Accession #:
S01-00104
Viewing Slide #:
1.1.1.1
1.1.1.1
2.1.1.1
2.1.2.1
3.1.1.1
0.39%
Flag Case


Tasks
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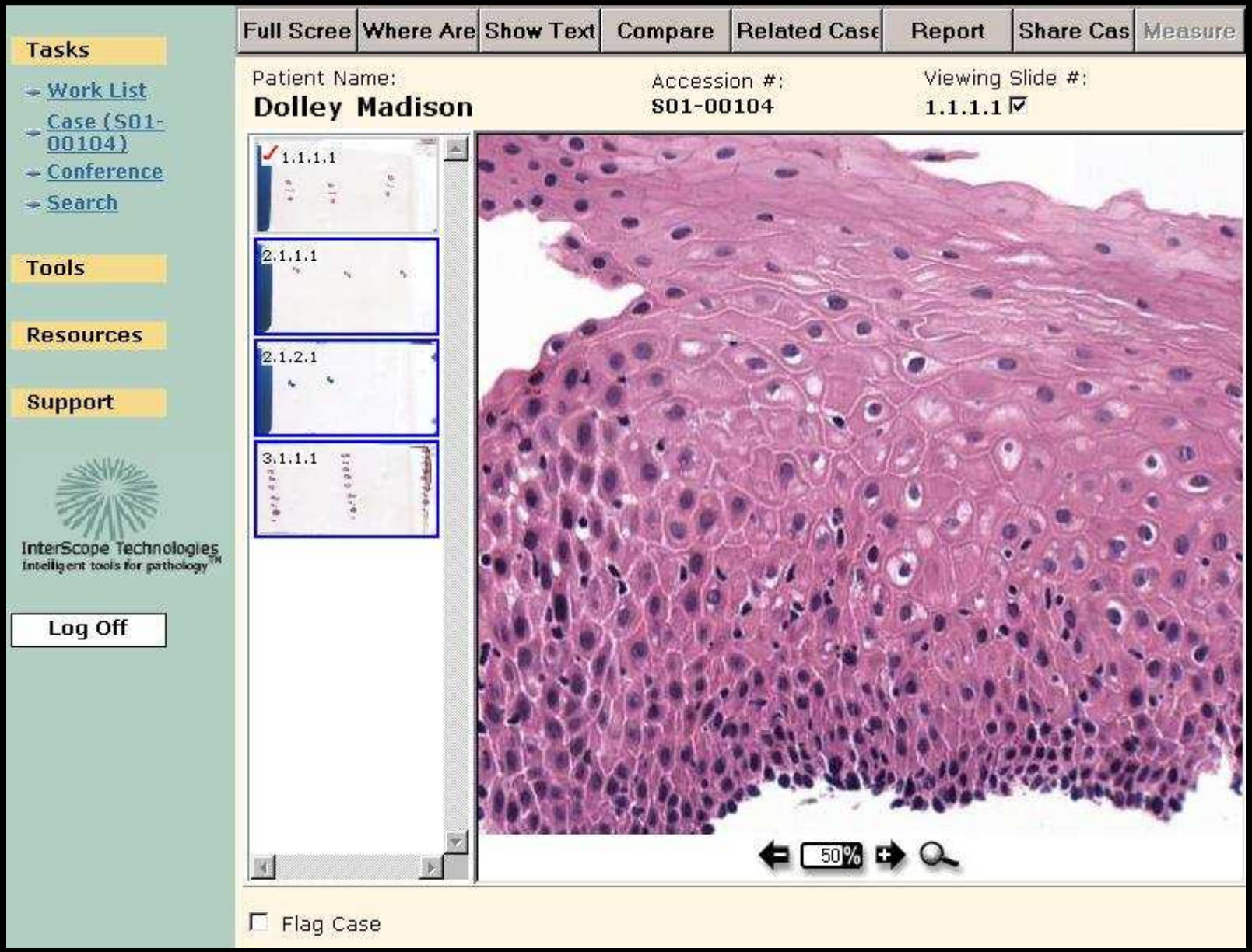
Patient Name:
Dolley Madison
Accession #:
S01-00104
Viewing Slide #:
1.1.1.1
1.1.1.1
2.1.1.1
2.1.2.1
3.1.1.1
6.25%
Flag Case


Tasks
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Case (S01-00104)
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InterScope Technologies
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Log Off
Full Scree
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Show Text
Compare
Related Case
Report
Share Cas
Measure
Patient Name:
Dolley Madison
Accession #:
S01-00104
Viewing Slide #:
1.1.1.1
1.1.1.1
2.1.1.1
2.1.2.1
3.1.1.1
50%
Flag Case

Pathology Report: S01-00112 - Microsoft Internet Explorer

File Edit View Favorites Tools Help | Address http://dfdis7/interslidedemo/DynReport.asp?AccessID=54&NEW=YES | Go

Compare | Related Cases | Report | Share Case | Answer | <<Back

Tasks
- Work List
- Case (S01-00112)
- Conference
- Search

Tools

Resources

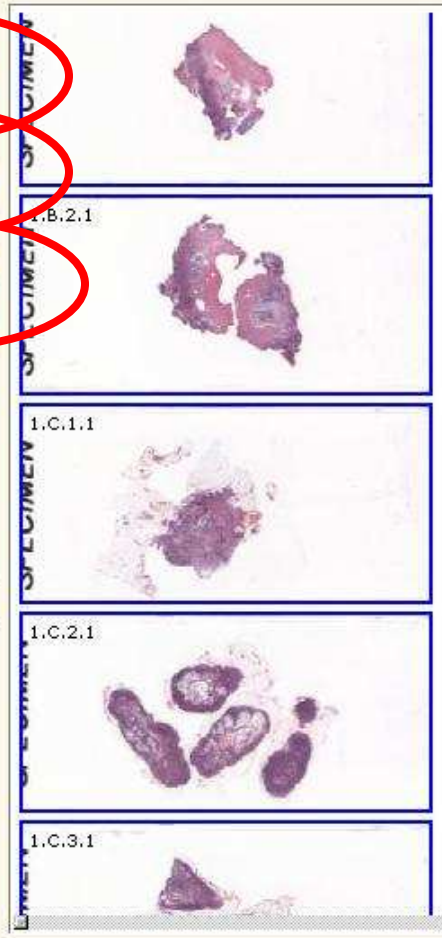
Support

InterScope Technologies

Log Off

Patient Name:
Taft, William Howard

Accession #:
S01-00112



Accession Date:	**10/19/2000**	MRN:	**111222333**
Procedure Date:	**10/24/2000**	DOB:	**7/21/1940**
Signout Date:	**Not Signed Out**	Sex:	**Male**
Attending MD:	**Thomas Dewey, M.D.**		

PATIENT HISTORY:

60 year old man with mass of ascending colon.

GROSS DESCRIPTION:

The specimen is submitted as right hemicolectomy. It consists of an unfixed segment of colon with attached adipose tissue 24 x 4 cm in diameter. The serosal surface is tan gray. The resection margins are stapled. On opening there is a 2.5 x 2.2 x 1.1 cm ulcerated gray coinlike mass at 10 cm from the closest resection margin. On sectioning the mass if firm and gray. It extends into but not through the wall of the colon. The remaining mucosa is unremarkable. On examination of the attached adipose tissue twelve lymph nodes are found. The largest is 1.5 cm in greatest dimension. On sectioning the largest node is firm and gray. The remaining lymph nodes are soft and tan yellow on sectioning. The specimen is submitted as follows; Resection margins A, Tumor B1-B3, Lymph Nodes C1-C4.

HISTO TISSUE SUMMARY:

A H&E X1
B1 H&E X1
B2 H&E X1
C1 H&E X1
C2 H&E X1
C3 H&E X1
C4 H&E X1

☐ Flag Case

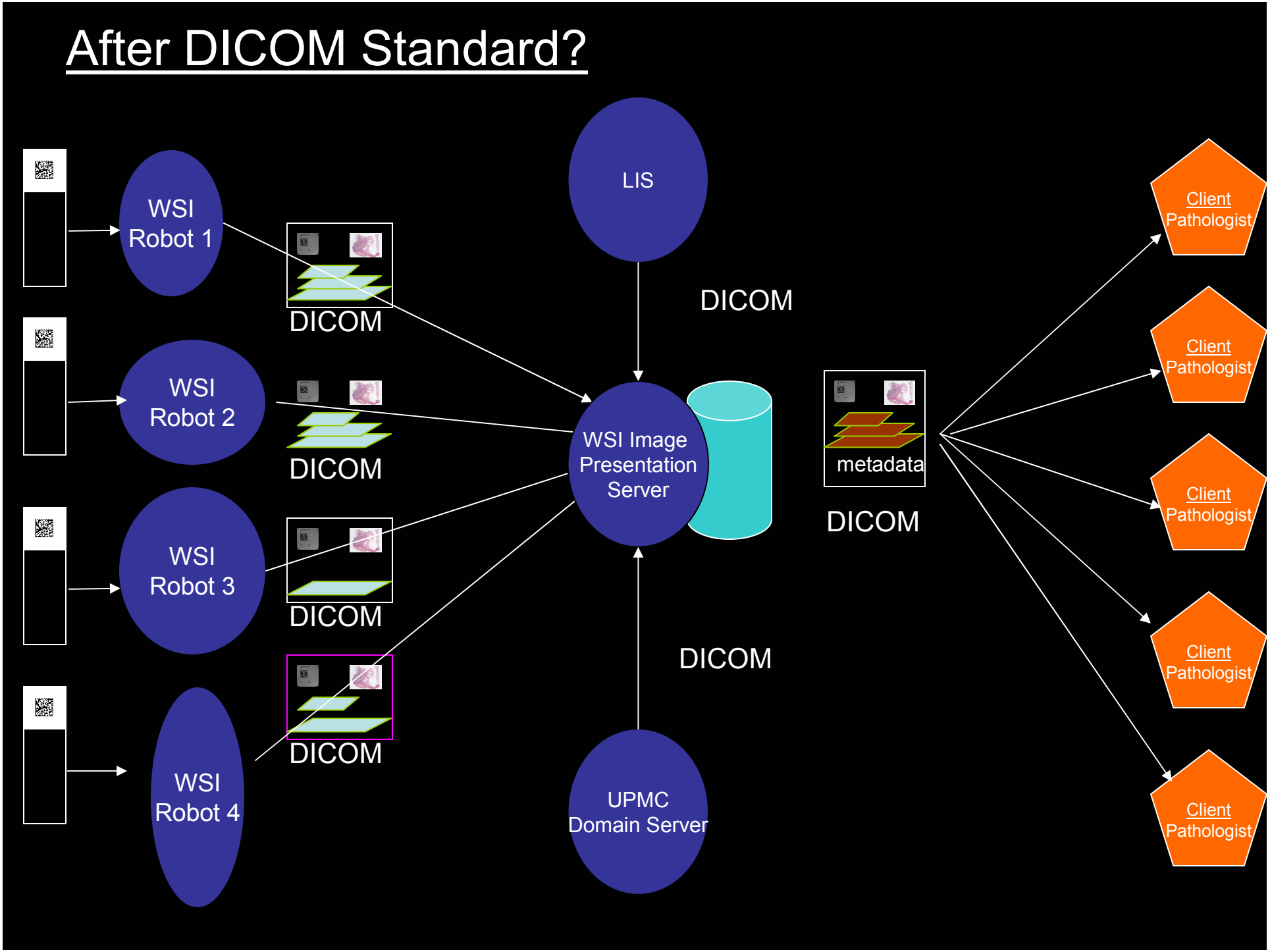
*Patient Demographic *Patient History
*Gross Description

Local intranet

Final thoughts

- The real world
  - Multiple vendors
  - Multiple information systems to interface with
- Difficulties we encountered
  - LIS limitations (Unique slide problem)
  - Lack of standard for modality output format
  - Lack of DICOM standards for whole slide images

After DICOM Standard?



Thank you!