

DICOM

Impact on Whole Slide Imaging in Pathology

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Background & Disclosures

- Owner, PixelMed Publishing, LLC
- Radiologist
- Independent Consultant GE, Carestream, Curemetrix, MDDX, Pathcore
- Editor of DICOM Standard (NEMA contract)
- Formerly co-chair DICOM Standards Committee
- Formerly co-chair IHE Radiology Technical Committee

Interoperability

"the ability of two or more systems or components to **exchange** information and to **use** the information that has been exchanged"

IEEE Standard Computer Dictionary: A Compilation of IEEE Standard Computer Glossaries. 1990

JOHN PALFREY AND URS GASSER

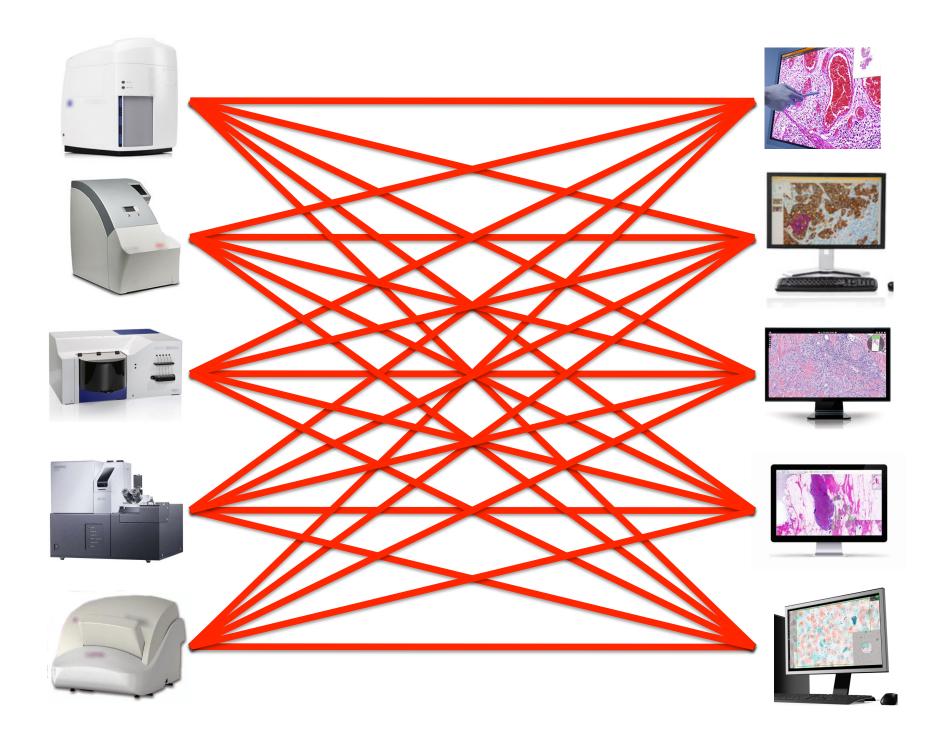
Interop

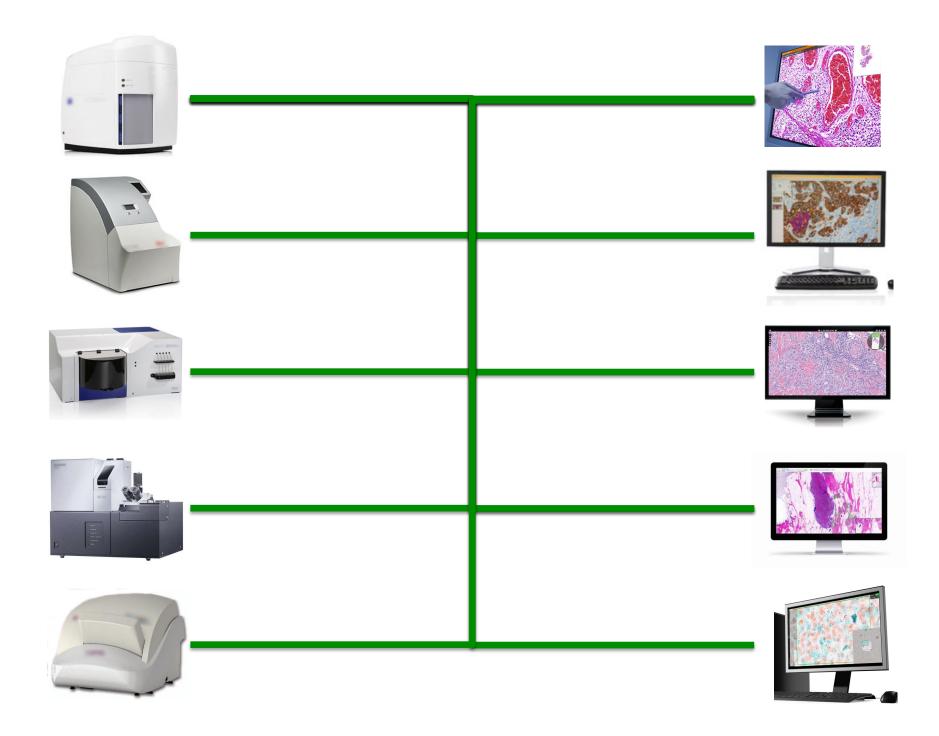
The PROMISE and PERILS of

HIGHLY INTERCONNECTED
SYSTEMS



- layers: technology, data, human, institutional
- consumer empowerment
- privacy, security
- competition, homogeneity, innovation
- efficiencies, complexity
- by design
- over time
- architectures





Photoelectronic radiology department

M. Paul Capp, Sol Nudelman, Donald Fisher, Theron W. Ovitt, Gerald D. Pond, Meryl M. Frost, Hans Roehrig, Joachim Seeger, Donald Oimette

Department of Radiology, University of Arizona Health Sciences Center, Tucson, Arizona 85724

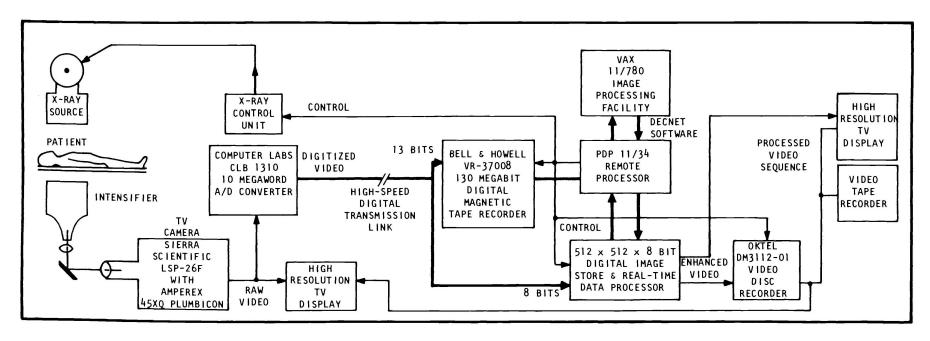


Figure 1. System block diagram of demonstration facility.





Volume 318

1st International Conference and Workshop on

PICTURE ARCHIVING AND COMMUNICATION SYSTEMS (PACS)

FOR MEDICAL APPLICATIONS

Part I

André J. Duerinckx Chairman/Editor





IEEE Catalog No. TH0090-1
IEEE Computer Society Order No.

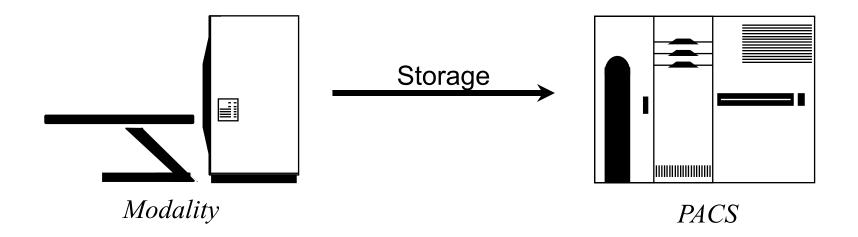
January 18-21, 1982 Newport Beach, California



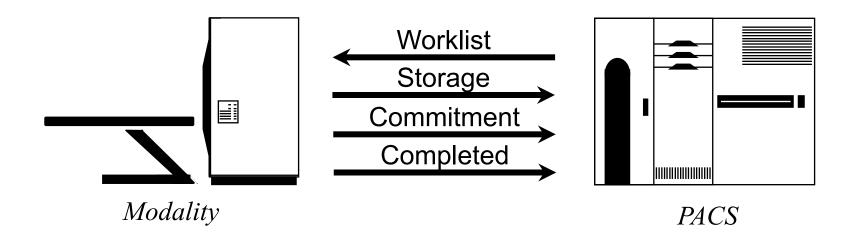
SESSION	9. STANDARDIZATION OF PACS269
318-48	The role of standards in the development of systems for communicating and archiving medical images
318-49	IEEE logical format for external exchange of image data bases
318-50	Characteristics of a protocol for exchanging digital image information
318-51	Landsat computer-compatible tape family
318-52	An American Association of Physicists in Medicine (AAPM) standard magnetic tape format for digital image exchange
318-53	On standards for the storage of images and data
318-54	Proposed standard for variable format picture processing and a codec approach to match diverse imaging devices

32 years ago – radiology PACS and DICOM ubiquitous 15-20 years later!

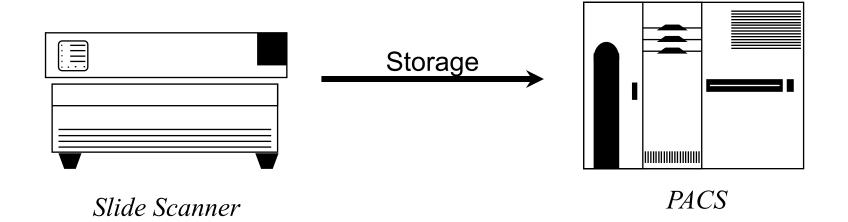
DICOM and Radiology Modality



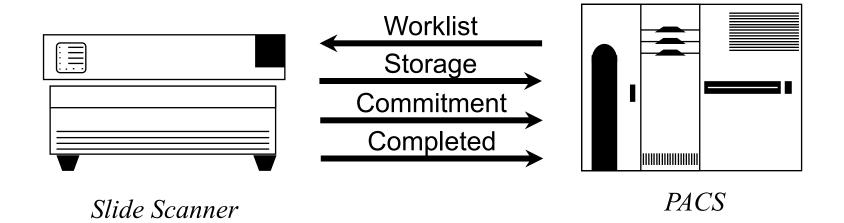
DICOM and Radiology Modality



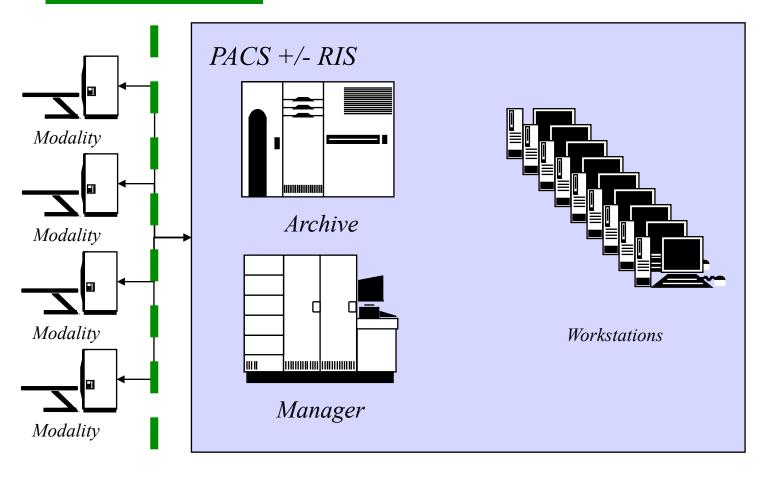
DICOM and Slide Scanner



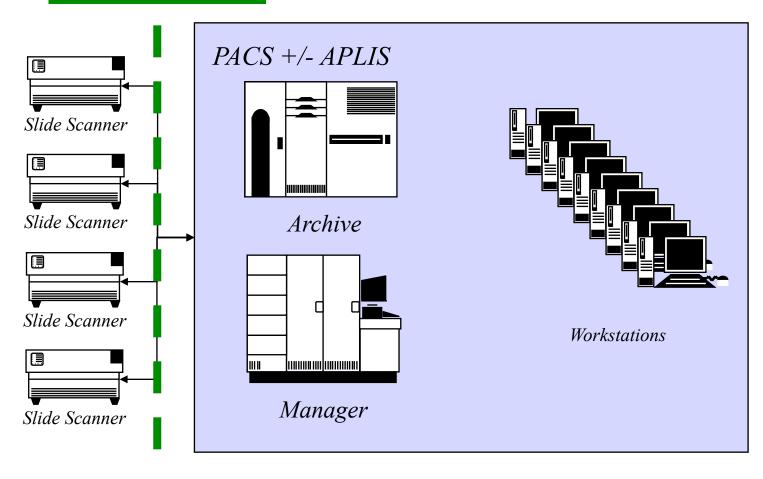
DICOM and Slide Scanner



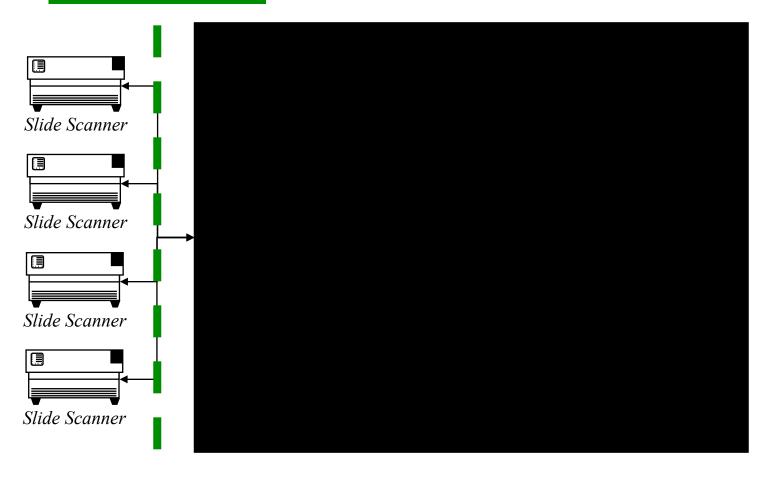
DICOM Modality to PACS



DICOM WSI to PACS



DICOM WSI to Black Box



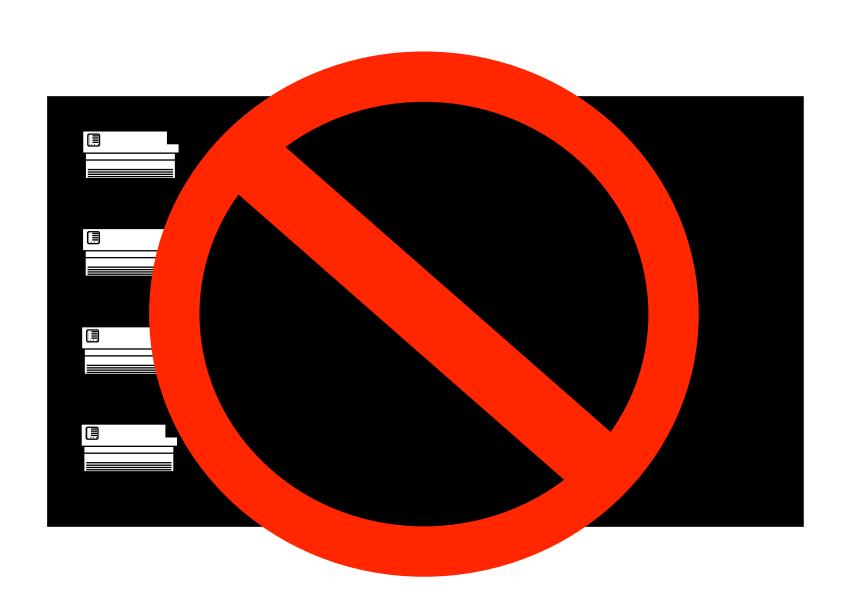
Single Vendor Black Box



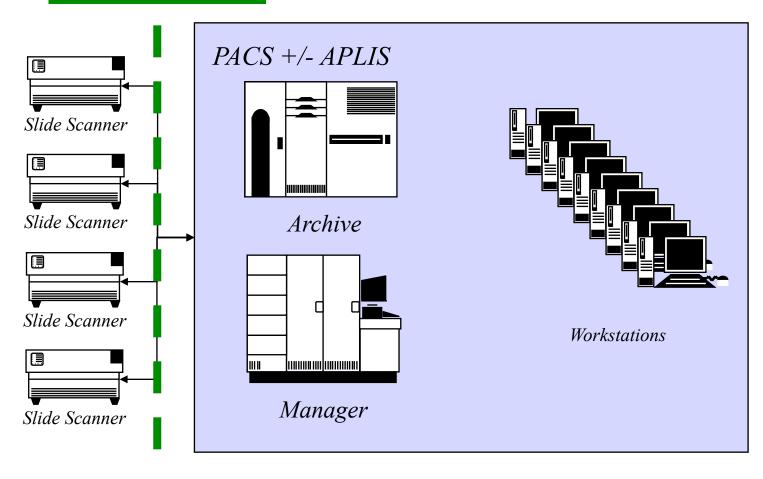
Single Vendor Black Box FDA "entire pixel pathway"



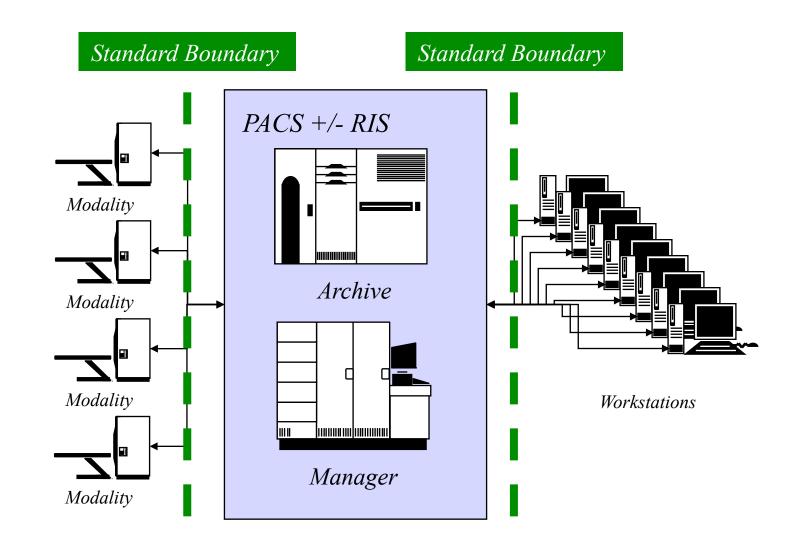
Single Vendor Black Box



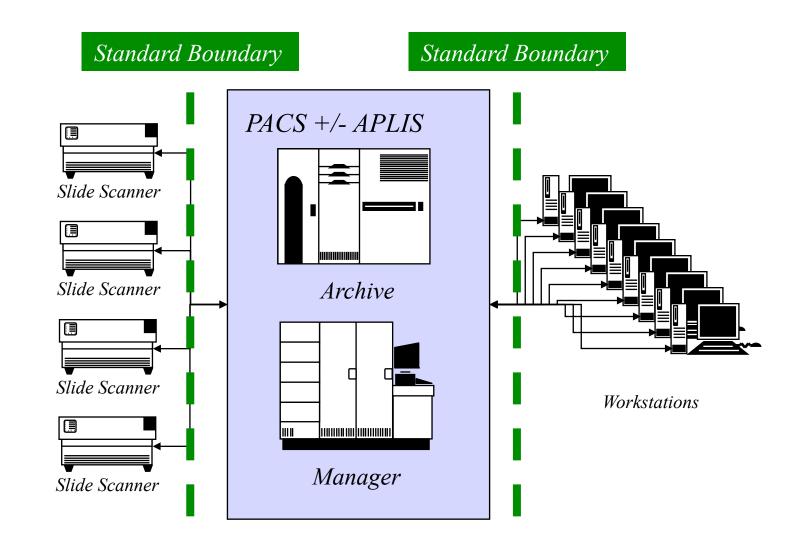
DICOM WSI to PACS



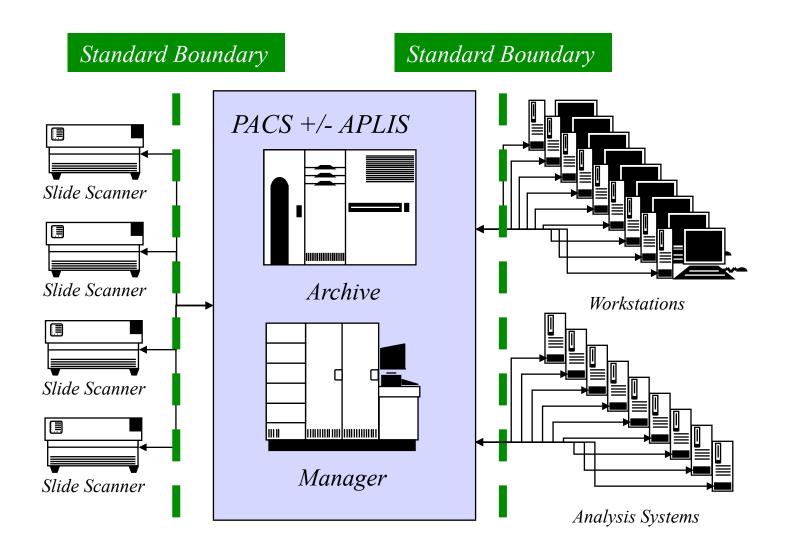
DICOM – Radiology Workstation



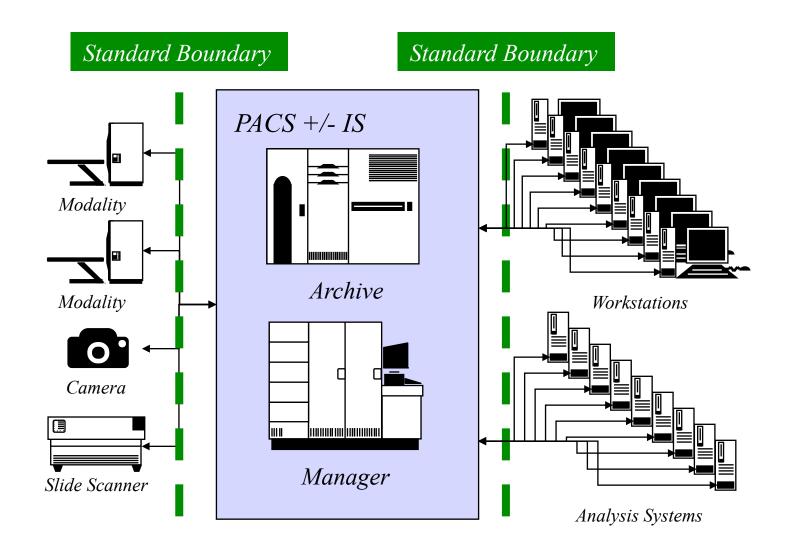
DICOM – Pathology Workstation



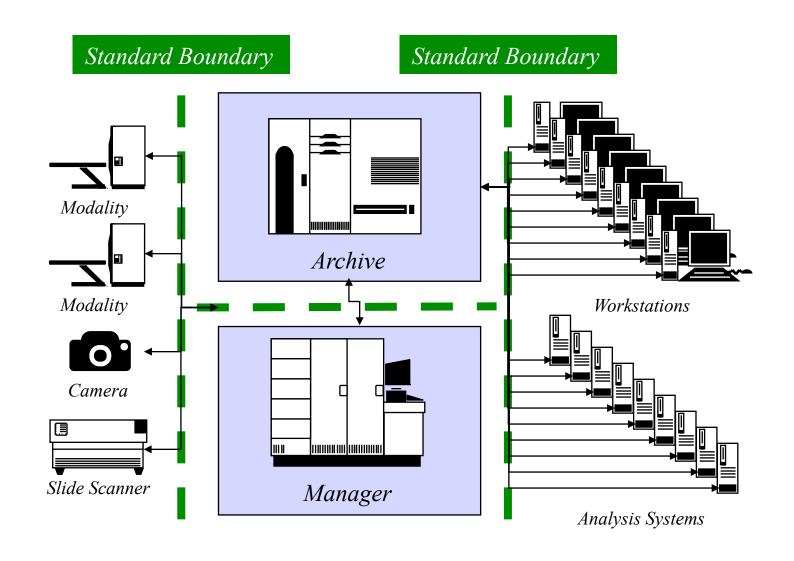
DICOM – Analysis Systems



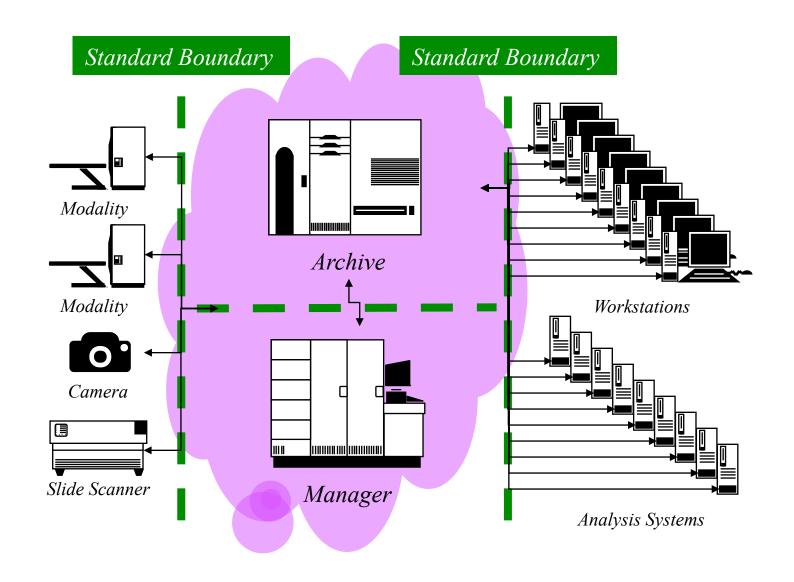
DICOM – Enterprise Imaging



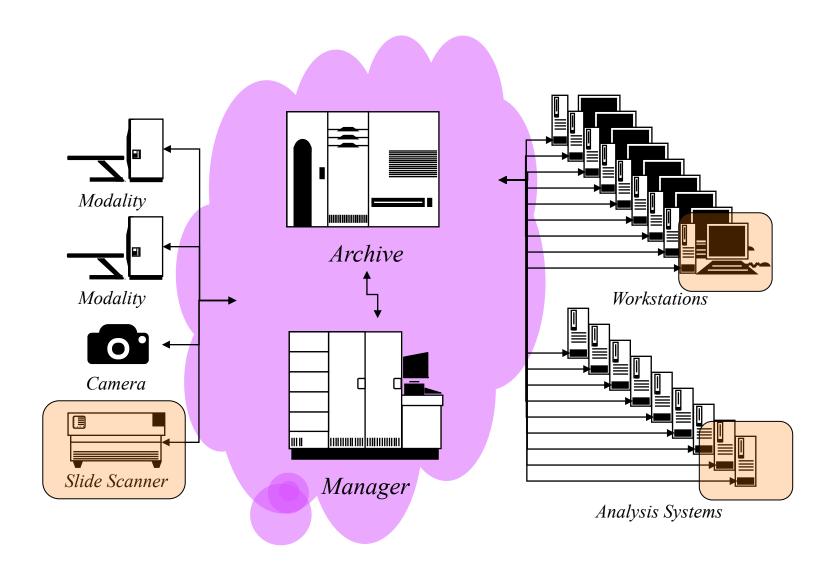
DICOM – Deconstructed PACS



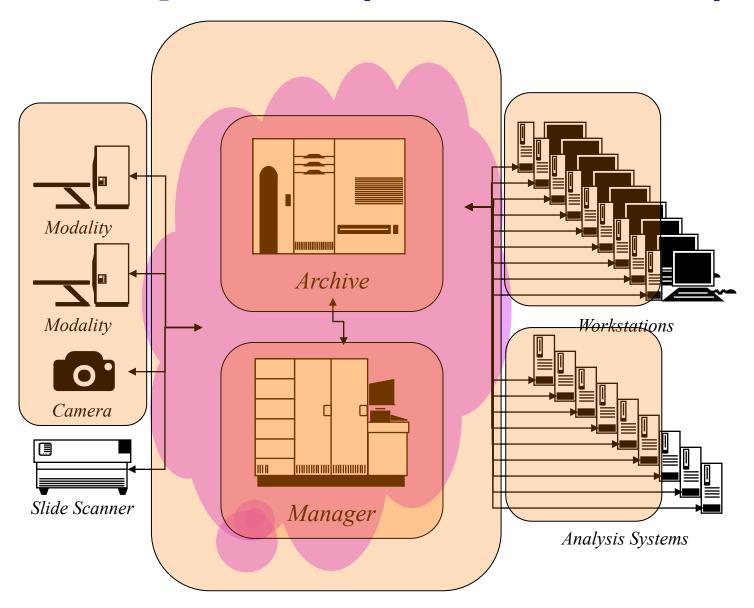
DICOM – Cloud Deconstructed Enterprise Tele* PACS



Pathologist/Department



Enterprise IT (Someone Else)



Single Vendor Black Box Everything is Your Problem



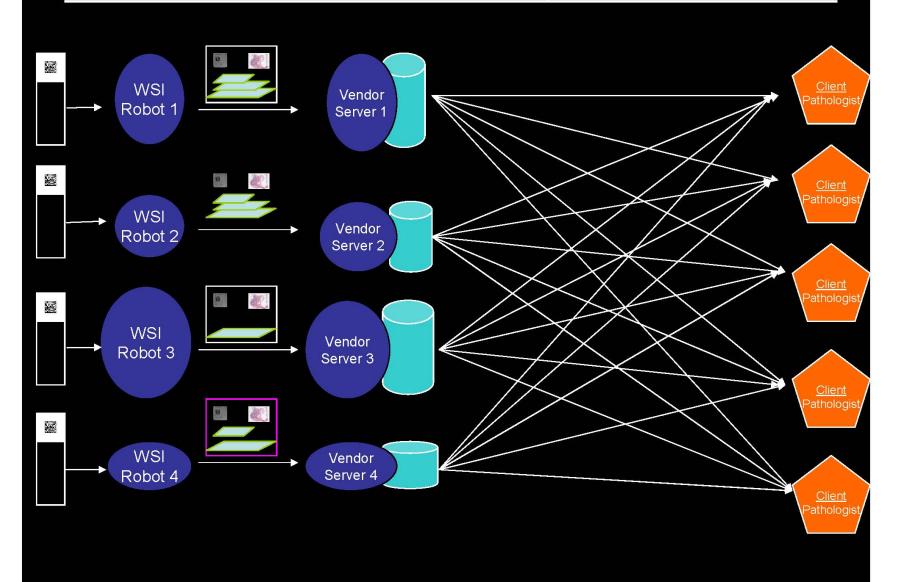
The Integration of Whole Slide Imaging in the Clinical Anatomic Pathology – Limitations of Laboratory Information Systems, Image Capture Systems and Archives

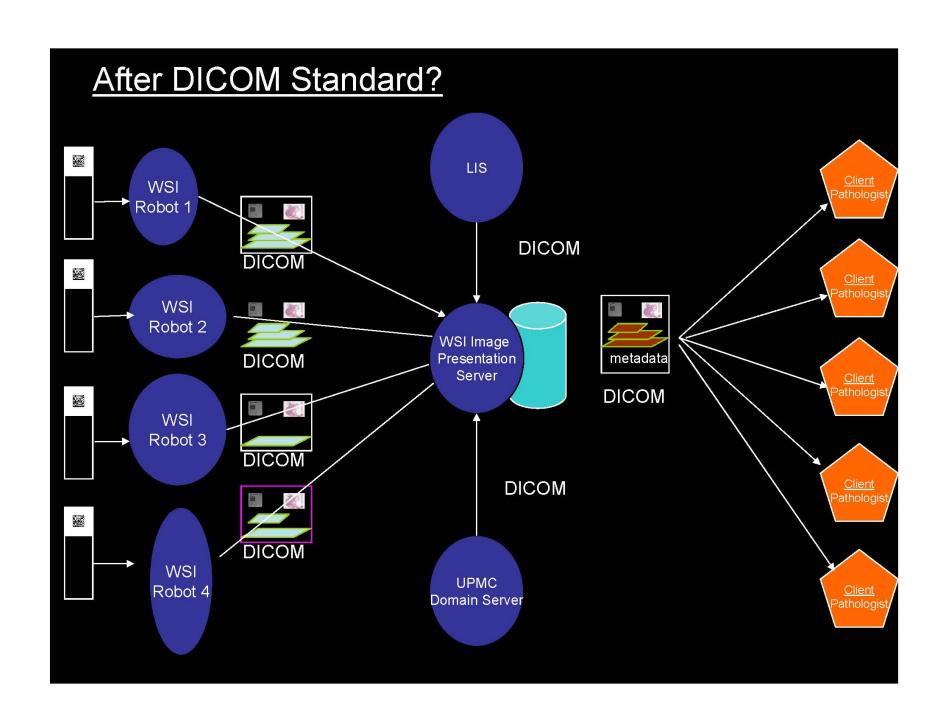
Yukako Yagi, Drazen Jukic, Anil Parwani, Jon Ho, William Gross, Ellen Kokal, Tony Piccoli, Michael Kistler and John Gilbertson

University of Pittsburgh Medical Center (UPMC),
Pittsburgh USA

Budapest 2005

Each vendor has its own formats, servers and clients



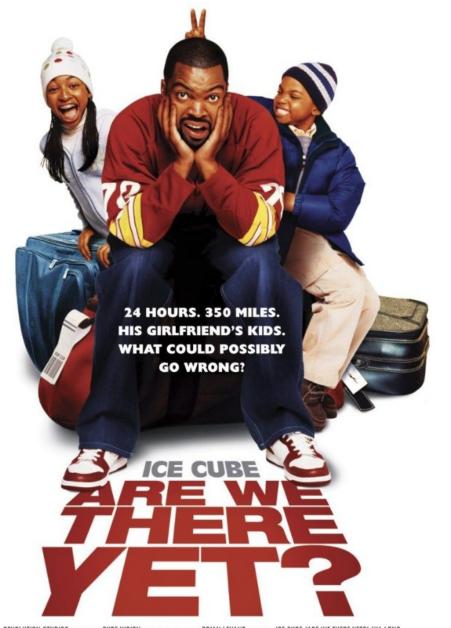


Final thoughts

- 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

DICOM WSI - 2005 to 2017

- 1999 Sup 15 Visible Light Image for Endoscopy, Microscopy, and Photography
- 2005 WG 26 got to work on WSI etc.
- 2006 IHE Anatomic Pathology Domain
- 2008 Sup 122 Specimen Module and Revised Pathology SOP Classes
- 2008 IHE Anatomic Pathology Workflow
- 2010 Sup 145 Whole Slide Microscopic Image IOD and SOP Classes
- ... seven years of silence ...



Are we there yet?

What could possibly go wrong?

REVOLUTION STUDIOS PRESENTS A GUBE VISION PRODUCTION A FILM BY BRIAN LEVANT STARBING: ICE CUBE 'ARE WE THERE YET?' NIA LONG Jay Mohr and tracy morgan ""#David Newman ###Debet odd garner derek dauchy ""#" Steven gary banks & claudia grazioso ***** Steven gary banks & claudia grazioso and J. David Stem & David N. Weigs """#ICE cube matt alvarez dan kolsrud

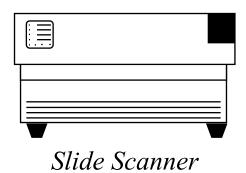
COMING SOON...BY PLANE, BY TRAIN, BY CAR.

What could possibly go wrong?

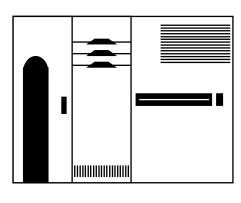
- Tiny, immature market (high risk)
- Inertia (early adopters and vendors)
- Conservative regulator
- Lack of resources
- Lack of customer interest/concern
- Perceived lack of value proposition
- Anticompetitive behavior
- Intellectual property restrictions
- Perceived complexity
- Perceived lack of features
- Perceived or real lack of tools
- Lack of promotion/marketing
- Lack of peers (collective action, chicken and egg)
- Not Invented Here incentive to create competing standards
- Naysayers disillusioned/impatient early adopters
- ...

Collective Action Problem





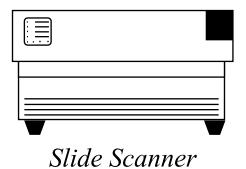




PACS

Collective Action Problem









Workstation

DICOM & DP Value Proposition

- Three fundamental advantages (Soenksen. Digital Pathology - A Bright Future. Pathology Visions 2013)
 - remote access
 - image analysis
 - data management
- Standard format and protocol are essential to all three

Standard Desiderata

- Systems should be able to share image files
- The standards should allow the transmission of information on baseline colors and recommended display parameters
- The images should be useful to the pathologist, not necessarily better or worse than direct examination of a slide under the microscope
- A mechanism to evaluate image quality objectively should be present
- A mechanism to adjust and correct minor errors of tissue processing should be developed
- A public organization should support pathologists in the development of standards

Yagi Y, Gilbertson JR. Digital imaging in pathology: the case for standardization. J Telemed Telecare. 2005 Apr 1;11(3):109–16. doi: 10.1258/1357633053688705

DICOM & Archival Storage

- Using a standard allows for migration
- Files are self-describing embedded metadata greatly facilitates re-indexing and recovery – database can be lost/discarded
- Standard format can be reused by a new local service provider, e.g., change LIS or pathology PACS or EMR ... same files, same place, same format

DICOM & Replacement Cycle

- Devices (scanners, archives, LIS) die
- Actual hardware failure
- End of service contract (hardware, software, OS)
- Vendors die (or lose interest, abandon customers)
- Replace entire infrastructure?
- Migrate entire archive from one format to another?
- Mitigated by best of breed around one standard (DICOM)
- Clean metadata is critical important (garbage in, garbage out ... major lesson from radiology)

DICOM & High Volumes

- Goal is full department, enterprise, region or nation wide clinical use for all clinical cases (total optical microscope replacement)
- DICOM encoded pixel data compressed just like (most) proprietary formats (same schemes, same ratios)
- Metadata size is trivial by comparison with pixel data
- Optimized compact metadata for fast parsing and indexing for viewing (flags for common patterns, re-index on ingestion)
- No reason not to use DICOM format and protocols except for quality of the implementation
- DICOM must be 1st class citizen in scanners produced natively or converted seamlessly in normal production workflow, transmitted without user intervention (no "manual export" one scan at a time)
- APLIS integration to increase productivity (worklists, metadata)

Intellectual Property Problems

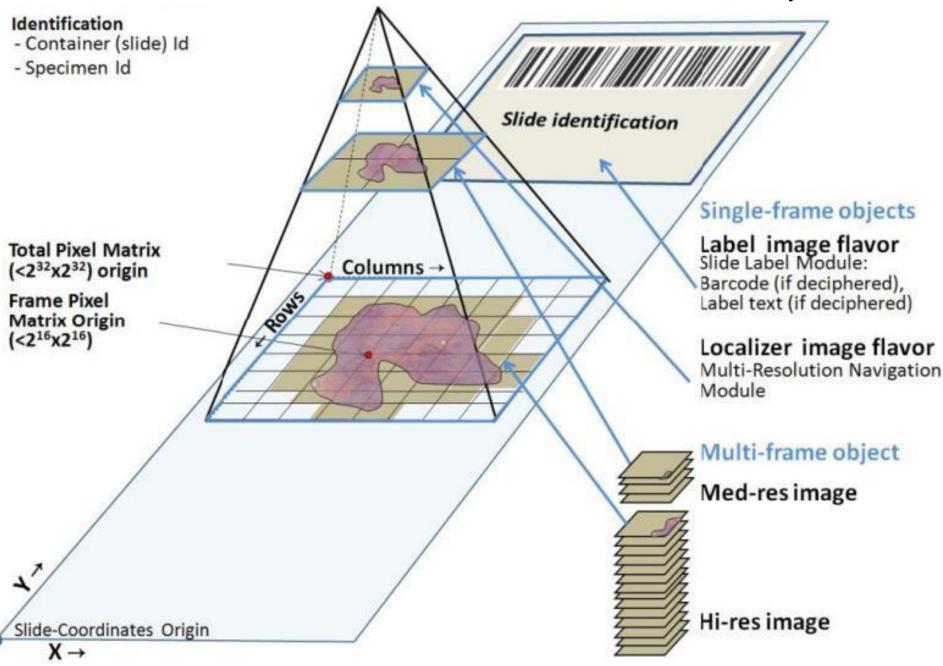
- Vital to have an "open standard" (which DICOM aspires to be)
- Early family of patents related to tiled acquisition
 - Bacus US 6,272,235 "... creating a virtual microscope slide"
 - believed to have expired, questionably relevant
- Patents specific to DICOM by key participant in Sup 145
 - US 8,086,077, US 8,781,261, US 9,305,023, US 20160217155
 - "Method for storing and retrieving large images via DICOM"
 - not initially disclosed (breach of procedures ? à la RAMBUS)
 - ostensibly "defensive", but then Aperio bought by Leica
 - Leica has recently negotiated with DICOM WG 26 participants a NEMA counsel approved royalty-free license to any user
 - Leica reports 3 vendors signed up, 3 in progress
- Significant dampening effect on adoption of DICOM for WSI

Need Reference Implementations

- DICOM in radiology kick-started by professional society funded open source reference implementations (RSNA CTN)
- Others followed many are used in commercial products (e.g., OFFIS dcmtk, Zeilinger dcm4che) esp. analytic applications
- Where are the DICOM WSI open source implementations, e.g., funded by CAP, DPA, API?
- Why does OpenSlide not have DICOM import?
- Reference implementations have limited reusability (languages, platforms), but are always useful for testing and training
- Ideally open license for commercial re-use (BSD not GPL)
- Can leverage mainstream DICOM toolkits rather than build from scratch (parsing, writing, dictionaries, network communications)
- Open toolkits, converters, archives, viewers, analyzers, ...

DICOM WSI - What and How

- File format for:
 - whole slide images (tiled pyramid)
 - single fields slide microscopy
 - gross microscopy
- File contains:
 - compressed pixels (JPEG or JPEG 2000)
 - metadata identifying AND descriptive
- Protocol for sending and receiving, etc.
- Other stuff like workflow, annotation, segmentation, structured reports, ...



DICOM WSI - like TIFF but better

- Similar tile structure
- Same compression schemes (JPEG, J2K*)
- Standard metadata as used by all other specialties (e.g., patient, study, request)
- Has metadata specific for AP processing
- Can be stored in PACS
- Comes with family of services
- Clinical not just consumer/photo features

*JPEG 2000 is not standardized in TIFF but SVS format uses it with a private compression scheme identifier

DICOM versus TIFF

* Unless proprietary tags used (rare), though there is OME-XML ** Palette color only, not RGB *** Also metadata for OCR'd text and barcode

Feature	DICOM	TIFF		
Patient metadata (in file)	Yes	No*		
Specimen/Container/Slide metadata	Yes	No*		
Acquisition process metadata	Yes	No*		
Multiple focal (Z) depths	Yes	Yes (more images in same file*)		
Number of planes different resolution	1 (all tiles same physical size)	Multiple images in same file		
Single frame overview (thumbnail)	Yes (Icon Image Sequence**)	Yes (another image in same file)		
Slide label image	Yes*** (Icon Image Sequence**)	Yes (another image in same file		
Can be archived in ordinary PACS	Yes	No		
Can be archived in VNA	Yes	Maybe, but separated from metadata		

Table 6. Compression Methods and File Formats

Device	Default Compression Method	JPEG2000 Compression Available	Other Optional Compression Methods	Available Uncompressed Format	File Type	File Size ×40
Aperio ScanScope T2	JPEG (libjpeg)	Lossless (1:20). Matrox Imaging algorithm	LZW (lossless)	TIFF	.SVS (modified TIFF 6.0, pyramidal)	1.5 GB
Aperio ScanScope CS	JPEG (libjpeg)	By hardware	LZW (lossless)	TIFF	.SVS (modified TIFF 6.0, pyramidal)	1.5 GB
AI Ariol	JPEG	Yes	No	BMP, JPEG2000, and PNG	JPEG	_
Bacus BLISS	JPEG	No		No	JPEG	
Hamamatsu C9600 NanoZoomer	JPEG	No	No	Under	JPEG development	2 GB
LifeSpan Alias	JPEG o JPEG2000	Yes (Aware Jpeg2000 SDK)	JPEG	TIFF	.TIF	2 GB
Nikon EclipseNet-VSL	JPEG	Yes (max 350 MB)	No	TIFF, BMP	.VSL (JPEG) and :JP2 (JPEG2000)	2 GB (JPEG)
Olympus SIS .slide	CMW (Leadtools Wavelet compressed 1:15)	Yes (with or without loss)	JPEG	TIFF, but not RAW	.VSI (pyramidal, up to 9 resolutions)	1.5 GB
Zeiss Mirax Scan	JPEG	Third party (VMscope)	No	BMP, PNG	.DAT (JPG)	1.5 GB

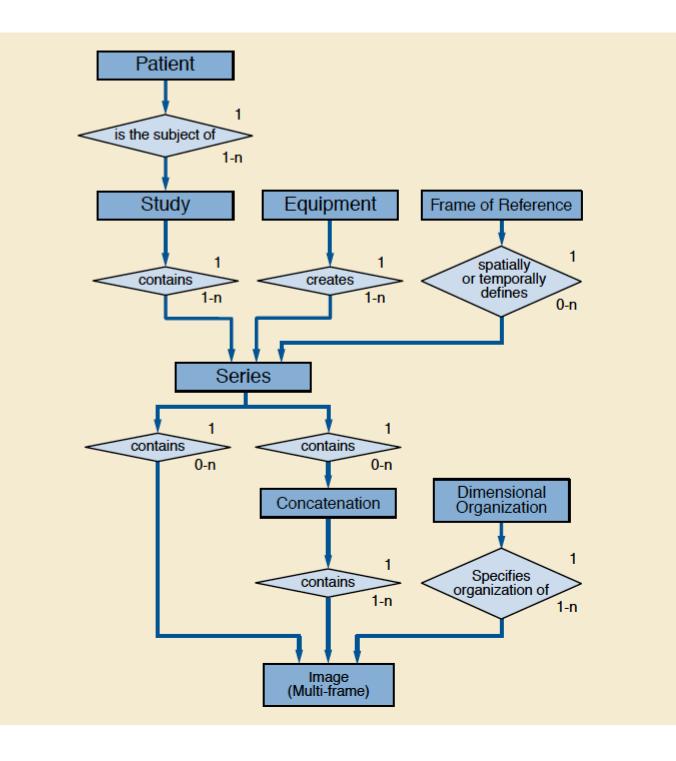
DICOM Compression Schemes

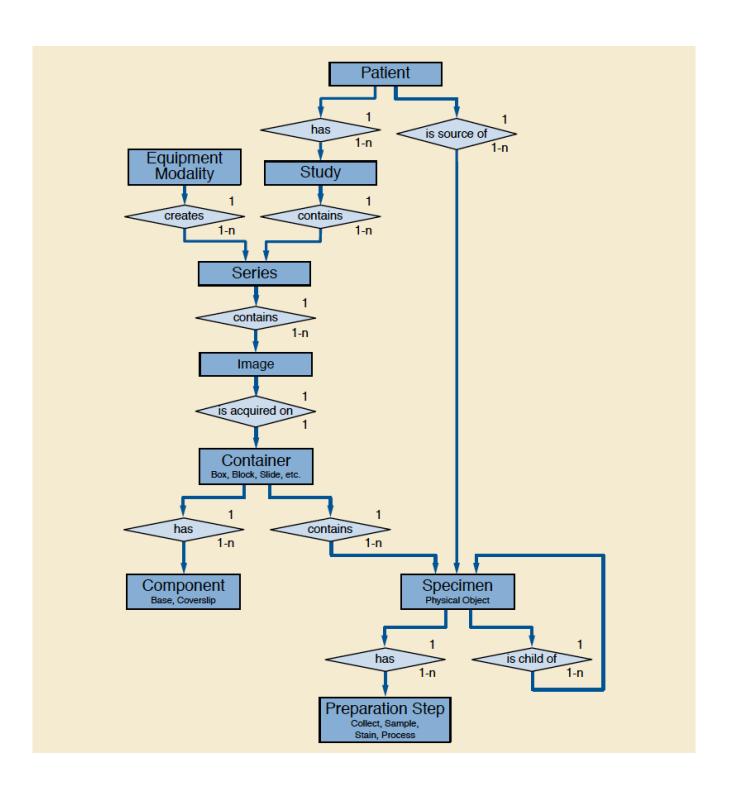
- Called "Transfer Syntax" in DICOM
- For WSI:
 - JPEG baseline (8 bit DCT 8x8 Huffman)
 - JPEG 2000 (reversible, irreversible)
- Is lossless compression ever needed?
 - pretty big, really slow to store, copy, transmit, process
 - special case: may be necessary for images recompressed from proprietary format (e.g., Philips iSyntax)
- DICOM describes but does not dictate amount of lossy compression (image quality)
 - method, ratio can be displayed to user (FDA PACS rqt.)

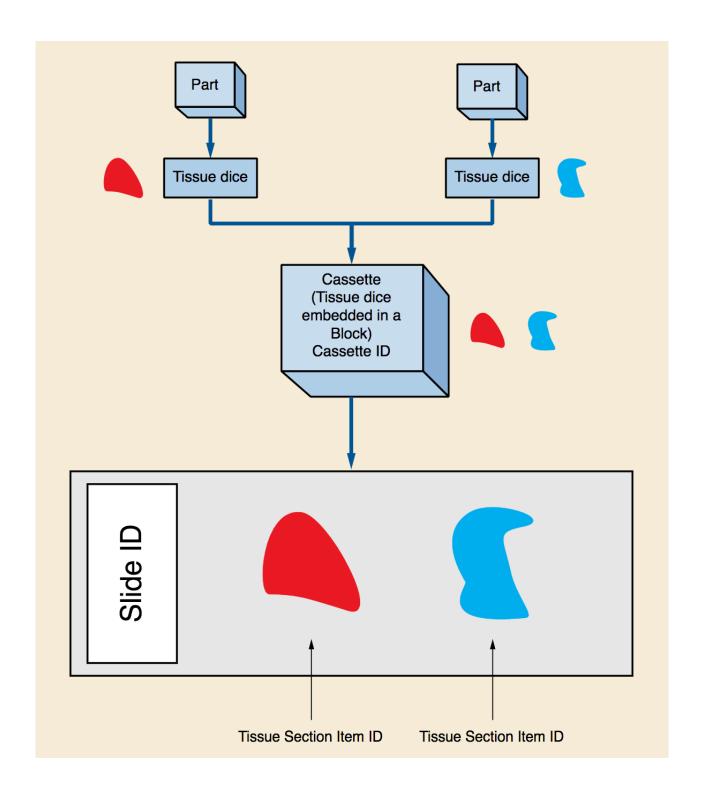


DICOM WSI Identification Model

- To leverage existing PACS (etc.), use conventional Patient/ Study/Series hierarchical model
 - earlier effort to use Specimen instead of (not in addition to) Patient "root" a failure
 - revised specimen identification extend Patient/Study/Series to include specimen-specific concepts (Sup 122 (2008))
- Use cases:
 - One specimen per container
 - Multiple items from same block
 - Items from different parts in same block
 - Items from different parts on same slide
 - Tissue Micro Arrays (TMA)
- "Accession" (Case) in LIS –> DICOM Accession Number
- Distinct from Specimen ID







Coded Specimen Preparation

- Processing type, e.g., (P3-00003, SRT, "Staining")
- Timing, e.g., (111702, DCM, "DateTime of processing")
- Stain, e.g., (G-C350, SRT, "Using substance") = (C-22968, SRT, "hematoxylin stain"), (C-22920, SRT, "spirit soluble eosin stain")
- Can also describe, biopsy, dissection, sampling, etc.
- Use leads to consistency across vendors & sites
- Not buried in proprietary metadata, structured or free text, file name convention, or proprietary APLIS database
- Leverages standard external lexicons, e.g., SNOMED CT

Coded Image Acquisition

- Lens, e.g., (A-0011A, SRT, "High power non-immersion lens")
- Sensor sensitivity, e.g., (R-102C0, SRT, "Full Spectrum")
- Illumination color, e.g., (R-102BF, SRT, "Ultraviolet")
- Illumination method, e.g., (111744, DCM, "Brightfield illumination")
- Illumination type, e.g., (A-00125, SRT, "Tungsten halogen lamp")
- Filters, e.g., (A-010E2, SRT, "Green optical filter")
- Use leads to consistency across vendors & sites
- Not buried in proprietary metadata, structured or free text, or file name convention, or proprietary APLIS database
- Leverages standard external lexicons, e.g., SNOMED CT

Metadata and viewing

- Viewing metadata whilst viewing (single or multiple slides in a case) is key aspect of "multitasking" in pathology reading (*Treanor, Development and Evaluation of a Novel Workstation for Digital Pathology, PV 2012*)
- Where does that metadata for interactive exploration ("annotated slide tray") of the case come from?
- APLIS user interface
- Viewer with query/worklist interface to APLIS HL7
- Image header DICOM

APLIS <-> Scanner Interface (I)

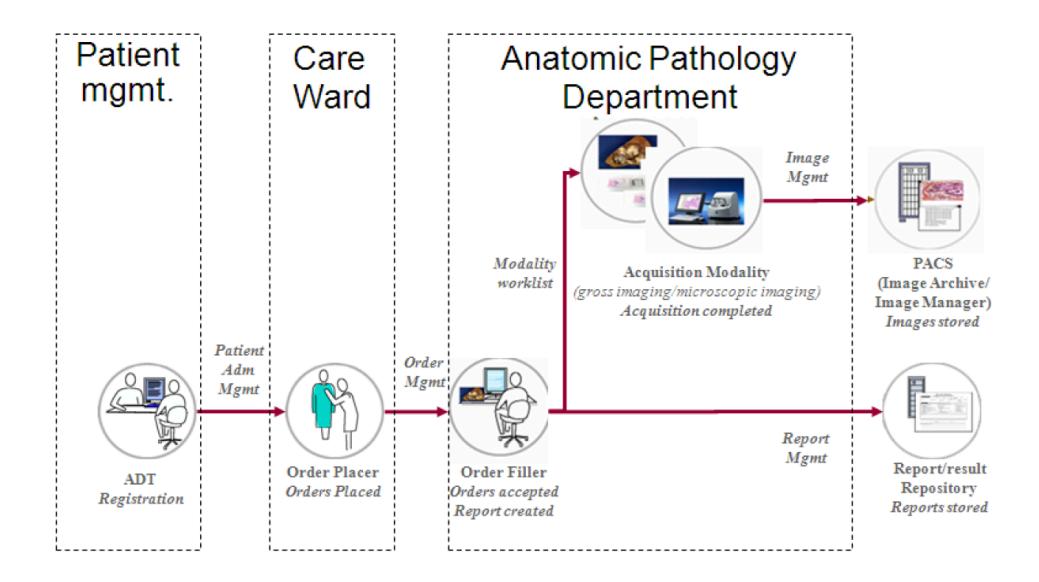
- What is the relationship?
- How does it affect what is in the image file, or not?
- Common denominator slide unique identifier in barcode (automatically scanned and deciphered)
- Slide scanner looks up "stuff" to put in image "header"?
- Identifier/barcode in header used by recipient of image (viewer, archive, analyzer) to look up stuff in APLIS?
- Middleware/proxy between scanner and image archive that takes "thin" header from scanner, looks up stuff in APLIS and copies it into "better" header of image before sending to PACS?
- Can encode lots of metadata within barcode (more than just slide unique identifier)?

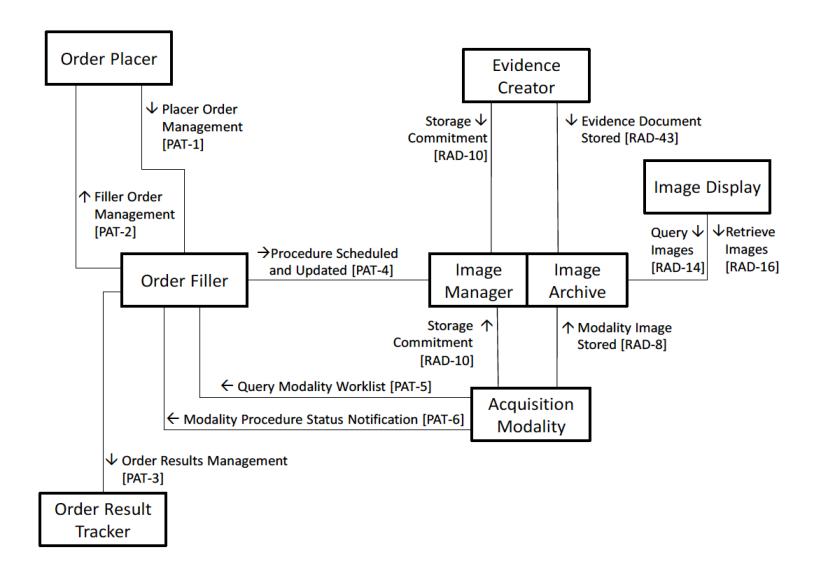
APLIS <-> Scanner Interface (II)

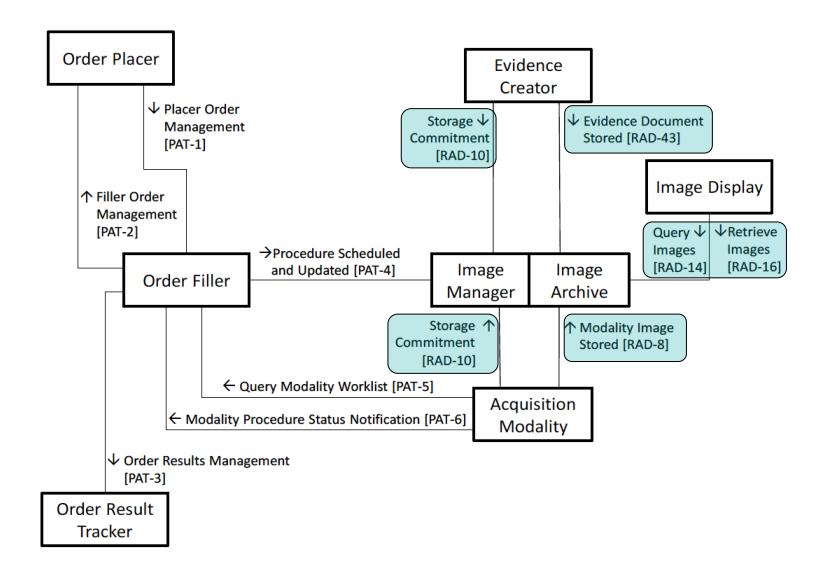
- Key benefit of rich metadata in image header when image is detached from local information systems (e.g., shared beyond department, sent out for or received as referral) – compare with universal use of standard DICOM CDs
- APLIS is closed proprietary silo of mission-critical information; should not be only repository of slide's relevance/context (consider end of life, migration)
- Concerns are reminiscent of early radiology days of "PACS Broker" that interfaced between HL7 RIS world and DICOM image/MWL world and/or "fixed" images from modality
- Now all RIS and all radiology modalities do DICOM MWL, and DICOM image contains rich, reliable, metadata from the beginning
- Another radiology trend RIS being subsumed into EMR/EHR
- Will that happen to APLIS? AP has much more complicated physical handling workflow to track than radiology

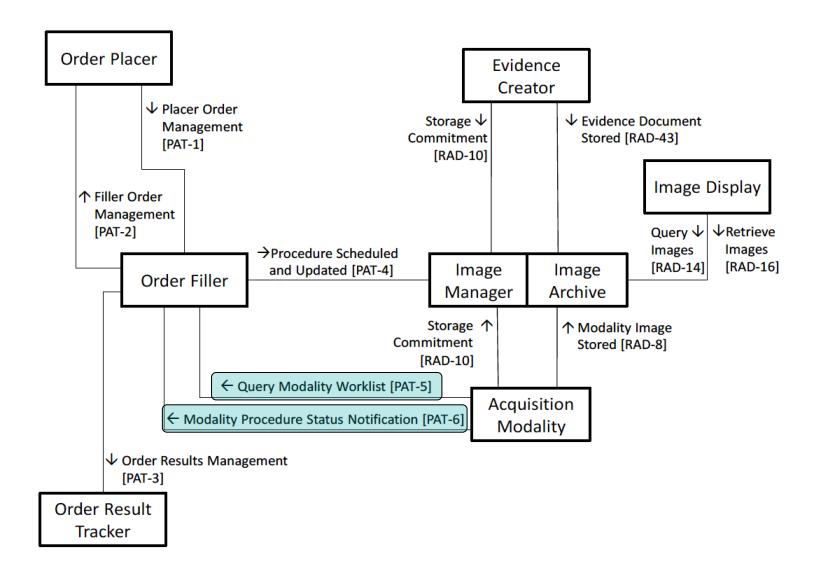
IHE – Anatomic Pathology

- Anatomic Pathology Workflow (APW)
 - ordering, scheduling, acquisition, storage, post-processing
 - attention to specimen identification in various use cases
 - very similar to IHE Radiology Scheduled Workflow (SWF)
 - re-uses Radiology image-related transactions (which are modality and image type neutral +/- various specializations)
 - contemporaneous with but not using DICOM WSI Sup 145, so WSI not (yet) specifically addressed in AP or RAD image transactions
 - have been recent suggestions to not use DICOM MWL but HL7 (v2) to acquisition modality (slide scanner) for scheduling (to be more like lab devices, à la Laboratory Testing Workflow (LTW))







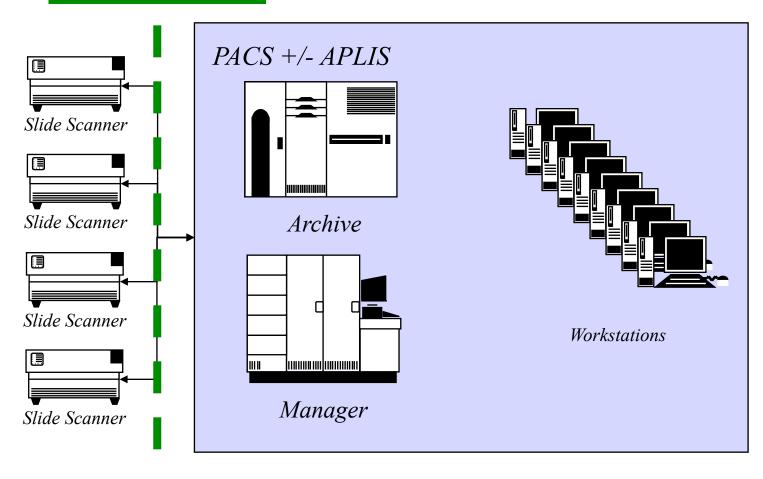


Beyond Store & Regurgitate

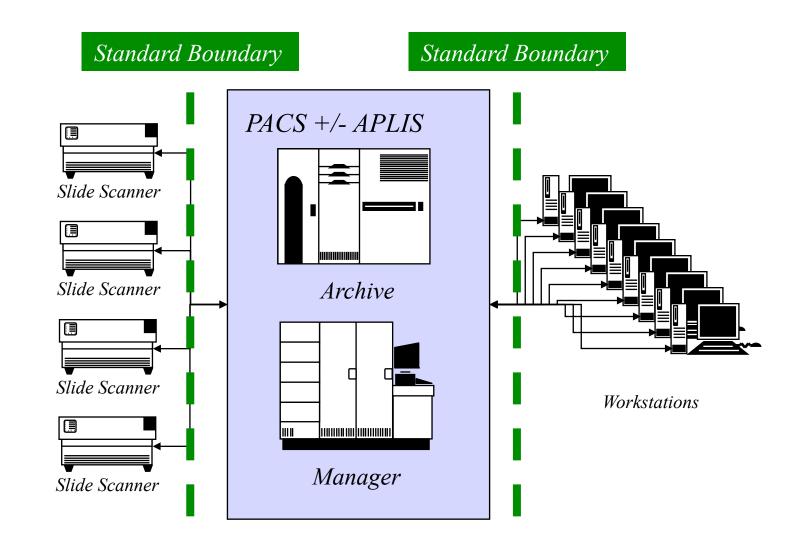


DICOM WSI to PACS

Standard Boundary



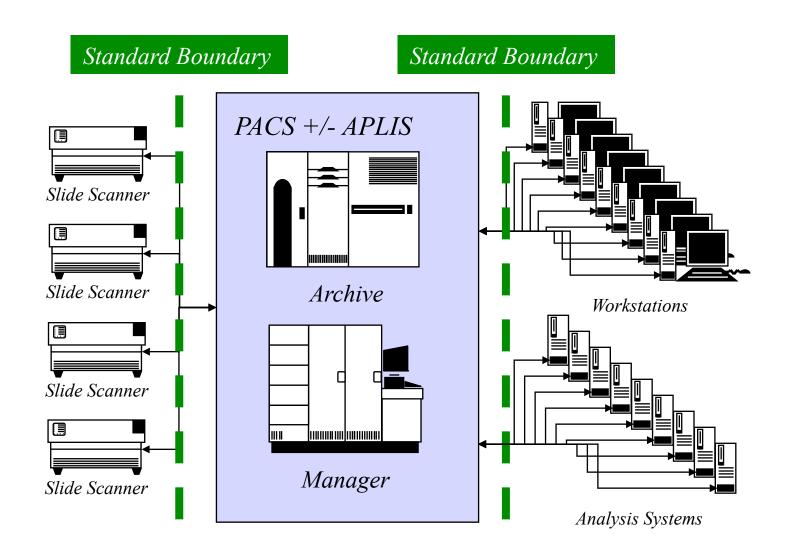
DICOM – Pathology Workstation



DICOM Service Choices

- Traditional radiology PACS ("DIMSE")
 - C-STORE, C-FIND, C-MOVE, +/- C-GET
- "DICOMweb" services: radiology, VL, etc. (HTTP)
 - WADO-URI DICOM PS3.10 file or JPEG
 - STOW-RS, QIDO-RS, WADO-RS
 - DICOM PS3.10 file, XML, JSON
 - retrieve study/series/instance/frames
 - retrieve DICOM, rendered (JPEG, etc.), metadata
- Needed for interactive viewing WSI ("virtual microscopy")
 - C-GET without bulk data (i.e., metadata)
 - C-GET frame level retrieve
 - WADO-RS retrieve frames
 - WADO-RS retrieve metadata

DICOM – Analysis Systems



DICOM and Analysis Systems

- Both inputs and outputs
- Standard scanned image format
- Standard processed result format
- New images
- Annotations contours, segmentations, measurements
- Saved to PACS, viewed normally, or as overlay
- Annotations in radiology regions of interest
- Image fusion in radiology PET on top of CT
- WSI annotations if not selected fields, very large number
- Efficiency of encoding factors (large numbers of pixels, objects)
- Facilitates separate regulatory approval and user validation of acquisition/analysis/display



Test Compliance & Performance

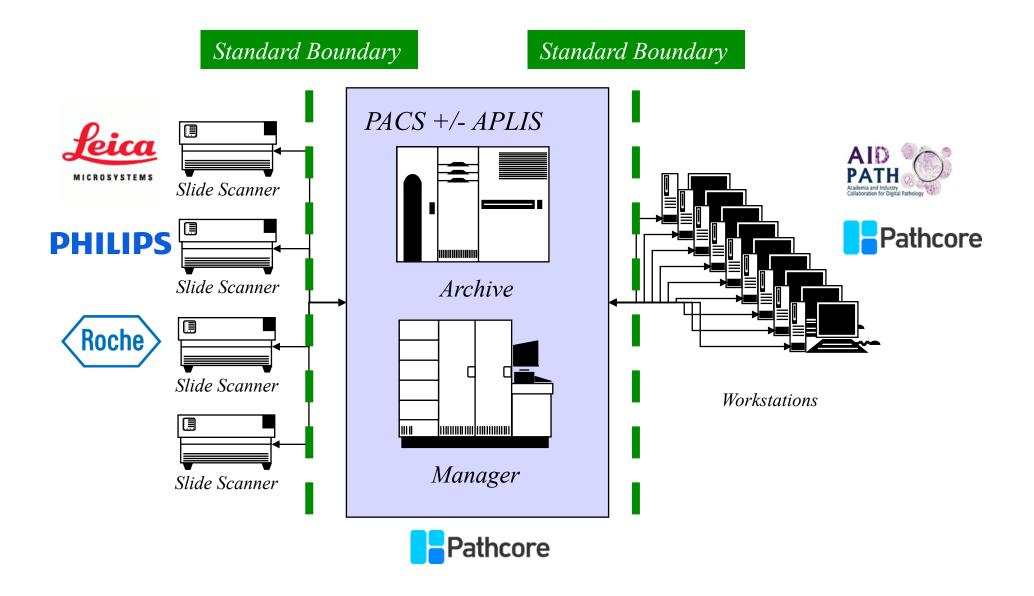
"Доверяйте Но Проверяйте" ("Trust, but verify")

Russian Proverb (Used by Vladimir Lenin, Ronald Reagan)

PV 2017 DICOM Connectathon

- Cooperative effort by DICOM WG 26 and DPA
- Goals: demonstrate feasibility, test implementations, find gaps
- Multiple vendors & implementers
 - slide scanners: 3 Leica, Philips, Roche
 - PACS: 1 Pathcore
 - viewers: 2 Pathcore, AidPath
- Services tested:
 - creating DICOM instances
 - store DICOM images from scanner to PACS with DICOM protocol
 - find images and selectively retrieve tiles on demand for interactive viewing using DICOM protocols
- Not tested (next time):
 - AP LIS integration source of identifying/descriptive metadata

PV 2017 Connectathon



PV 2017 Connectathon Lessons

- which compression schemes (JPEG, or J2K as well?)
- one layer or entire pyramid (viewers expect latter, who makes it?)
- how to recognize which pyramid layer is which (PixelSpacing)
- recognizing a pyramid, in one series, multiple series, multiple per series
- natural order of encoded frames versus their index
- sparseness: entire tile array or selected sub-regions
- tile frame size: same for each resolution layer (e.g., localizer non-square?)
- dimensions described or not?
- localizer with index, or not? in same or separate series?
- concatenations: splitting huge files for transfer, requires reassembly on receipt
- is a label image needed, does it need a barcode? shared between pyramids?
- what optional metadata in image, in query (esp. specimen preparation)?
- specific server services/sequencing for viewing (find vs. metadata retrieve)
- WADO-RS retrieve or retrieve rendered (multipart MIME burden)
- color consistency importance of viewer applying embedded ICC profile

PV 2017 Connectathon Lessons

- Need more Connectathons! Need more testing!
- More specific profiling of requirements
 - WG26 or IHE "profile"?
 - clarify patterns of use for specific use cases
 - make choices where alternatives exist, require optional features
- Just works, or works for the right reasons?
 - importance of validation against formal standard requirements
 - assisted by mechanical tools (dciodvfy) could check more
 - avoid using extensions, options, even if agreed upon
 - check with proxy between devices (as used by IHE)
 - create synthetic objects (good & bad) to stress recipients
- Continuous testing
 - continuous "virtual Connectathon" on Internet

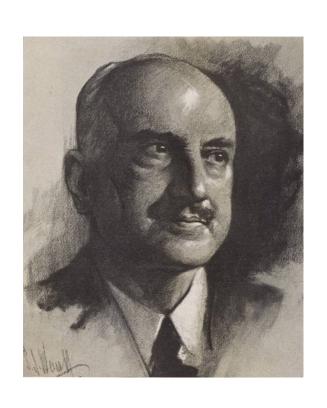
2017: Are We There Yet?

- Don't have (or barely have)
 - commercial implementations of automated high volume
 DICOM transfer of WSI images from scanners
 - commercial DICOM-based viewers
 - commercial DICOM archives with specimen metadata support and frame level retrieval
 - open source DICOM reference implementations and tools
 - support for DICOM in open source format conversion and viewer toolkits
 - general consensus on using IHE APW/DICOM MWL rather than HL7 V2 for providing order/metadata to scanner
 - general consensus on a vendor-neutral architecture

Should you be worried?

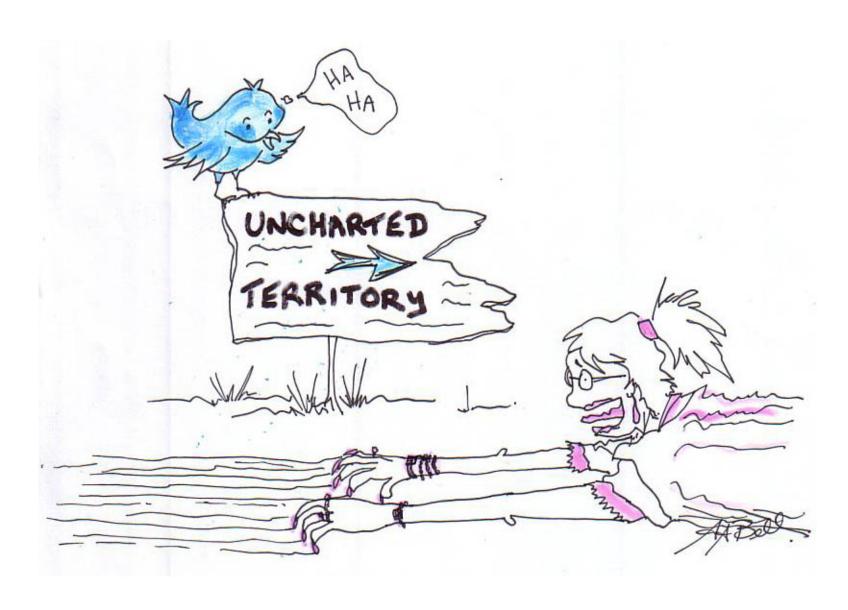
- Every new modality is a challenge to established infrastructure, workflow, standards and systems
- Radiology has its own challenges, incompletely solved fused PET/CT, functional MRI, digital breast tomosynthesis (DBT)
- Challenging data volumes, metadata and especially high efficiency viewer user interface features
- All obstacles are eventually surmounted
- Always a "chicken and egg" problem for the modality and viewer product managers ... someone has to commit first
- Be reassured that anatomical pathology (gross, WSI) is just yet another modality with its own peculiarities, and will be absorbed
- Digital pathology is in its infancy lots of time to repeat every mistake of radiology, cardiology, ophthalmology, ...

Learning from Radiology (etc.)

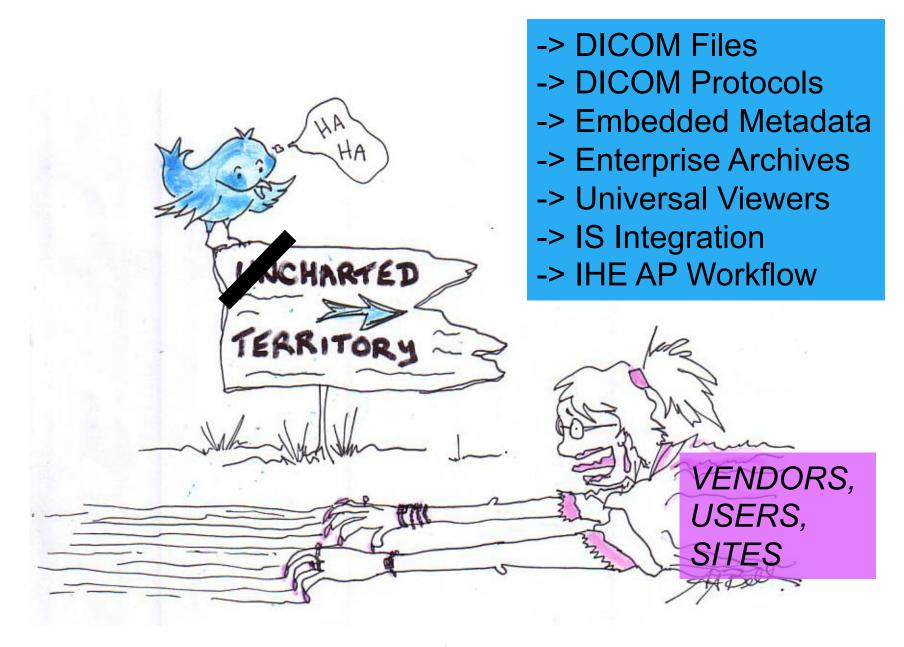


"Progress, far from consisting in change, depends on retentiveness. When change is absolute there remains no being to improve and no direction is set for possible improvement: and when experience is not retained, as among savages, infancy is perpetual. Those who cannot remember the past are condemned to repeat it."

George Santayana. The Life of Reason (1905-1906)



https://supernaturalunderground.blogspot.com/2012/11/super-tweeting-with-royalty.html



Already charted ... just waiting for pathologists to catch up

HOW STANDARDS PROLIFERATE: (SEE: A/C CHARGERS, CHARACTER ENCODINGS, INSTANT MESSAGING, ETC.)

SITUATION: THERE ARE 14 COMPETING STANDARDS.



SITUATION: THERE ARE 15 COMPETING STANDARDS.

https://xkcd.com/927/



https://xncu.com/927/

