



DICOM Whole Slide Imaging

***Acquire, Archive, View, Annotate,
Download and Transmit***

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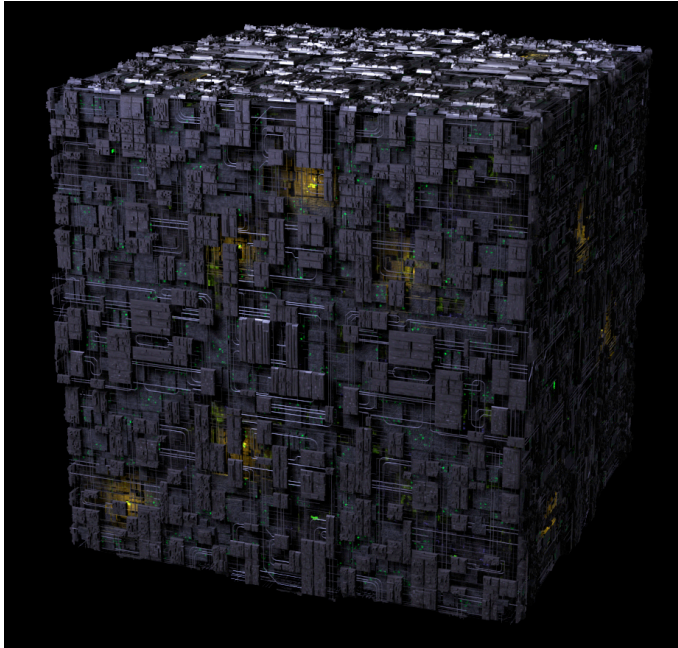
David Clunie, MBBS, FRANZCR (Ret), FSIIM

GE	Consultant-DICOM	Consulting Fees
Carestream	Consultant-DICOM PACS/VNA	Consulting Fees
Curemetrix	Consultant-DICOM CAD	Consulting Fees
MDDX	Consultant-DICOM	Consulting Fees
MITA (NEMA)	Edit DICOM Standard	Consulting Fees

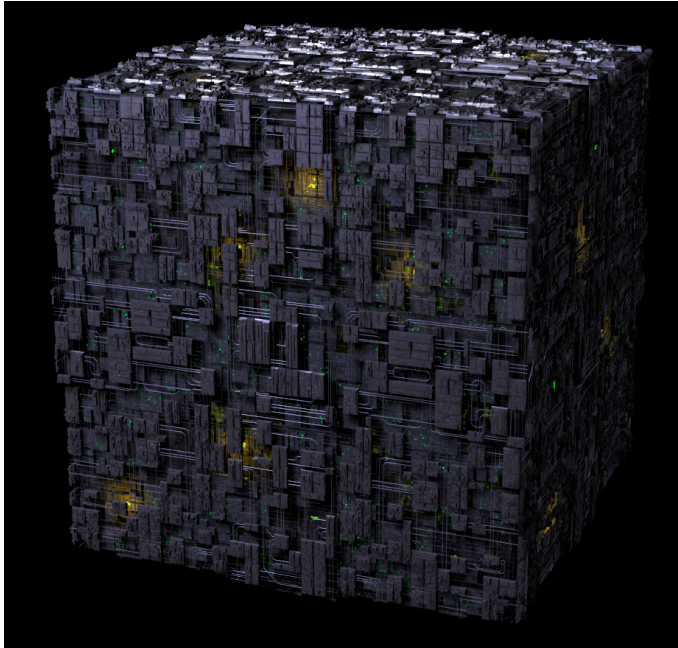
My perspective

- Retired radiologist (neuro)
- Editor of the DICOM Standard
- Evangelist for use of standards and crusader against proprietary formats and exclusive functionality
- No personal stake ... not hampered by practical matters or reality

Will you be assimilated?



Will you be assimilated?



“we will add your biological and technological distinctiveness to our own”

“your culture will adapt to service us”

“resistance is futile”

Why might you want to be?



WSI – Acquire, Archive, View, Annotate, Download, Transmit

- Why such a long title?
- WSI needs more than just a “file format” – needs an entire ecosystem
- PACS – “archive” and “communicate”
- Viewing is “special” for WSI (virtual microscopy) and unlike radiology, etc., (just as “video” was, also special, in different ways)
- Recapitulates EHR Meaningful Use requirements – viewing necessary but insufficient; also: obtain local copies, request to send elsewhere
- Acquisition presupposes reliable identification and metadata provision (recognizing that AP lab specimen processing workflow is complex)
- Annotation addresses the need to provide, store, and distribute analysis results
- Archival implies long term need with later access – clinical, medico-legal, statutory retention, research and sharing for secondary re-use

Why DICOM?

- Enormous experience in radiology and cardiology
- 32 years since ACR-NEMA (1985)
- A consensus of user and industry representatives. later adopted by ISO as ISO 12052
- 80 million CT studies per year in US (CBS News, 2015) – all DICOM
- Huge supporting infra-structure – for both DICOM file format and protocol and services
- All manner of products essentially commoditized: scanners, archives, workstations, viewers, PACS, toolkits for products, testing, analysis, research
- Both commercial and free, closed and open source tools
- Conformance and interoperability testing venues (IHE Connectathons)
- Modality agnostic – e.g., XR, MR, NM also Visible Light, esp. Ophthalmology, Endoscopy
- Application agnostic – human, veterinary, small animal research, non-destructive testing (esp. aerospace and nuclear power), security (esp. baggage scanning)
- Emphasis on reliable, consistent, standard metadata (common data elements, value sets)

Why not DICOM?

- More effort than most trivial file formats – toolkits are generally required
- Complexity is implicit in the use case more than the “format” per se – harder problems require more effort and discipline to be interoperable
- Population of metadata takes effort – is it worth that effort?
- Traditional DICOM network transport protocols are unique, though TCP/IP based – mitigated through more recent use of HTTP (WADO) using XML, JSON metadata
- Pixel data encoding not a perfect match for WSI virtual microscopy – questions of size limits and tile access – multi-frame tiles are a hack (like TIFF), but are workable
- Intellectual property (patent) distractions – now resolved
- Legacy of use of proprietary (albeit mostly TIFF) – why change if downstream users/apps are willing to cope?
- DICOM Conformance is not a panacea – claims of support are limited to query, storage and retrieval, worklists, etc., but NOT visualization (but DICOM does enable viewers)

Status quo for WSI

- Hodgepodge of proprietary file formats
- Some (Big)TIFF-based (good), some not (bad)
- Some with extensions to TIFF (e.g., to signal JPEG 2000 compression)
- Some disclosed publicly, some not
- Usually used with vendor-supplied viewer or proprietary SDK
- Possibly readable by open source or 3rd party
- Limited integration of scanners with Anatomical Laboratory Information Systems (APLIS), if at all, perhaps requiring expensive customization
- Fragile linkage to contextual data (patient, slide, handling, staining) by filename or scanned slide identifier only
- When decoupled from environment (APLIS), lose contextual data

Why care now?

First to market impact

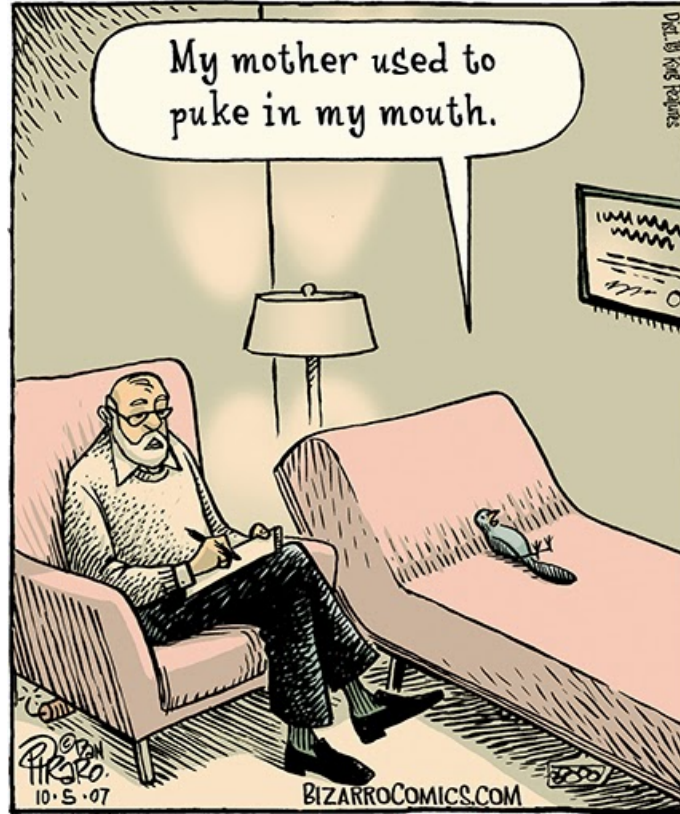
- Lessons from radiology
- First clinically approved systems have huge influence on hospital IT infrastructure choices
- First clinically approved systems are not necessarily those already in widespread research use, and may or may not be standards-based
- Early adopters of research systems often find themselves at dead end
- Second clinically approved systems are often significantly delayed, artificially lowering the pressure for incumbent to “interoperate”, but building large archive of “priors”
- E.g., breast tomosynthesis (DBT) – correct DICOM object was not used by first (US) vendor, rather image pixel data was buried in private fields to get around limitations of legacy PACS but requiring a proprietary viewer – DBT is now mainstream with multiple vendors and well standardized, but huge mess of unreadable garbage in archives, still sent out by some sites – unreadable as priors and cause safety issue
- Lesson – do it right from the start – think beyond the departmental silo – anticipate integration of lots of new players (enterprise archives, cloud distribution, analytic applications) – adoption of the “right” standard helps



DICOM Intent – Storage

- DICOM is primarily an “interchange standard”
- DICOM Sup 145 (2010): IOD/SOP Class for “storage” (transfer) of WSI
- Stated goal: storing, archiving, retrieving, searching, and managing images +/- enabling analysis and storage of results in conventional PACS
- Non-goal: protocol for interactive virtual microscopy viewing BUT “*data organization ... should support ... interactive access patterns*”
- I.e., standard “file format” for store and forward + “accessible”
- Ordinary DICOM (non-WSI-specific) selective frame and meta-data (“header”) retrieval actually permits interactive viewing, but is not specifically designed for it, not supported by most legacy PACS but is by modern archives
- In short – do not expect your ancient PACS to magically be able to do virtual microscopy viewing using DICOM without the addition of a specialized viewer – radiology viewer will show only unorganized tiles

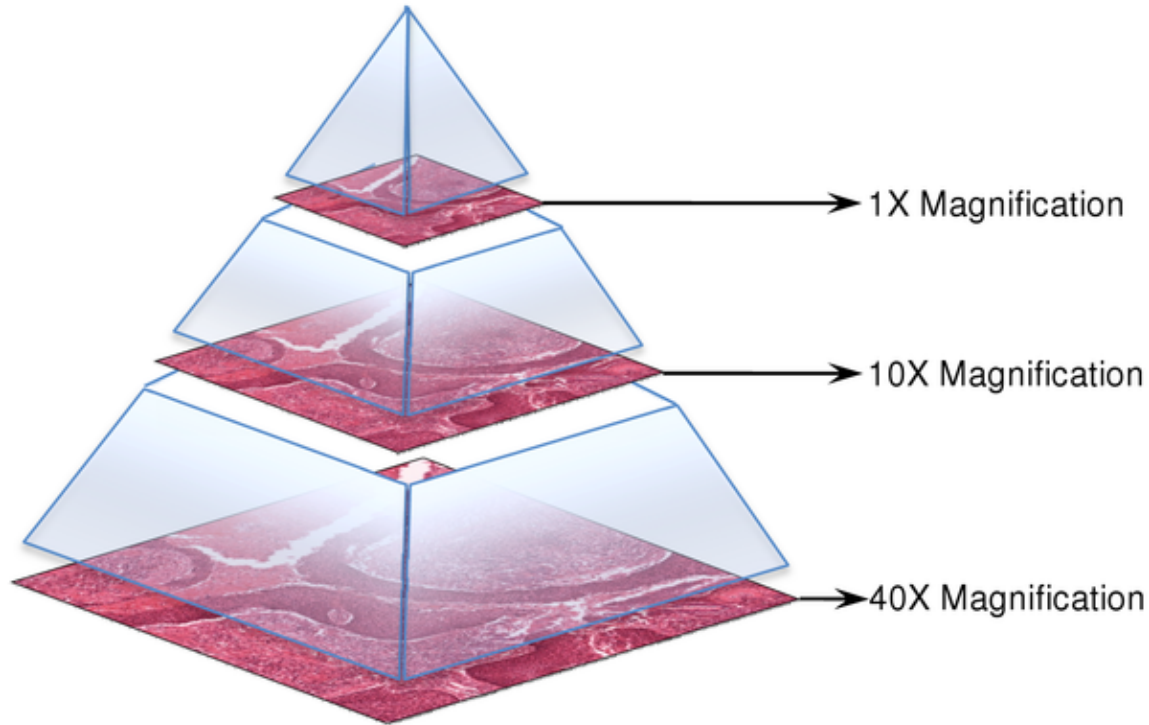
PACS: Store & Regurgitate Only



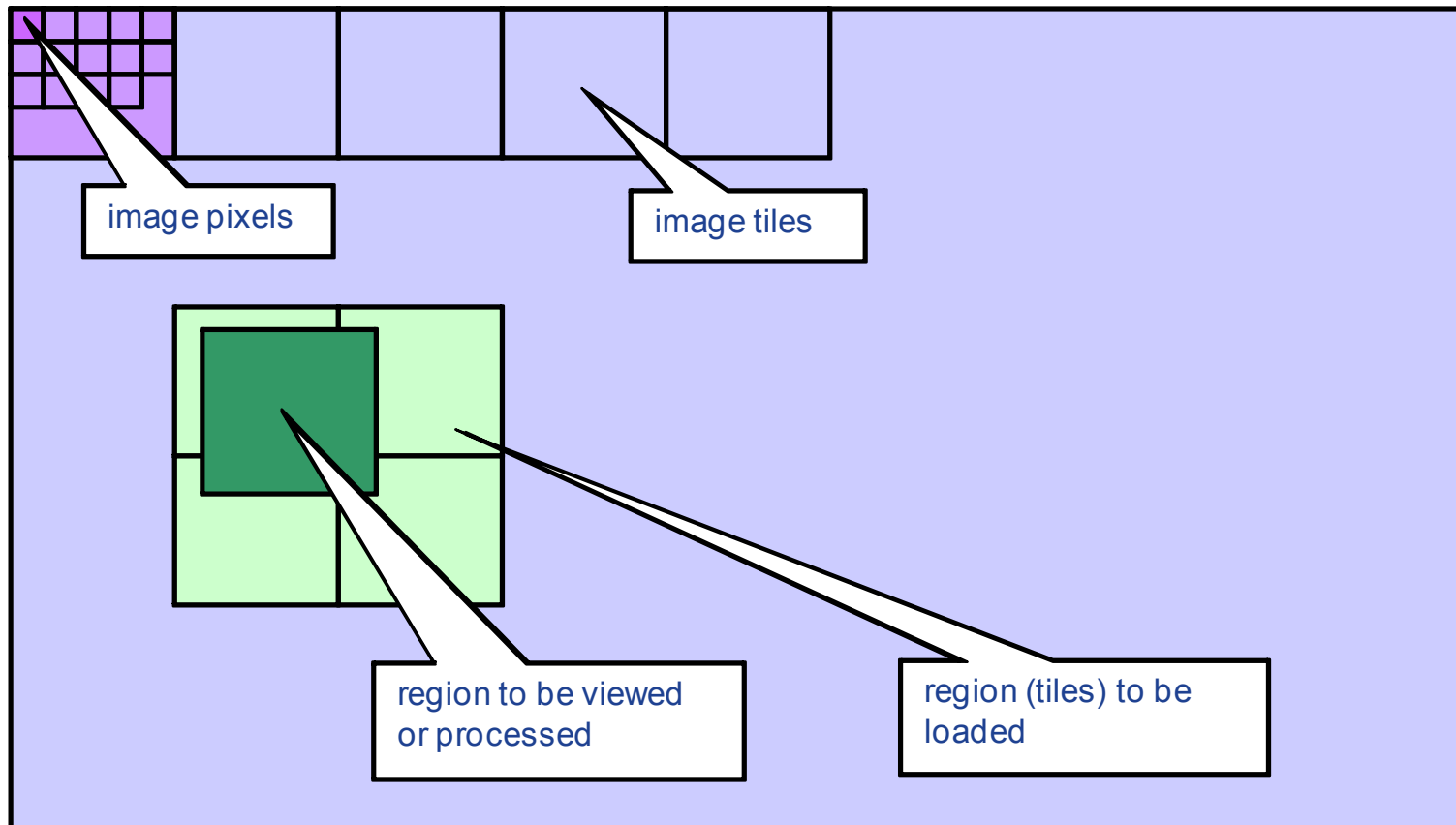
Quest for the Universal Viewer

- Enterprise (CIO/CFO/CSO) level and user experience “holy grail”
- In the beginning, there were PACS
- 1990’s – “filmless, except for mammography”
- Factor out the archive – one enterprise archive, many viewers (VNA)
- Universal viewer – any archive, any modality (one standard interface)
- 2010’s – “universal viewer/one archive, all specialties, except for pathology”
- Result is just a really big (deconstructed) PACS, by any other name
- There is no real reason a “universal” viewer cannot do virtual microscopy as well as everything else and do it well ... one standard format/protocol is key
- Why just one system? TCO, training, support, security, reliability, etc.
- Use of (one) standard still allows for niche add-on viewers, analysis tools, etc.
- Single biggest factor – efficiency (access speed, workflow integration)

An illustration of how digital slides are stored in a pyramid structure.

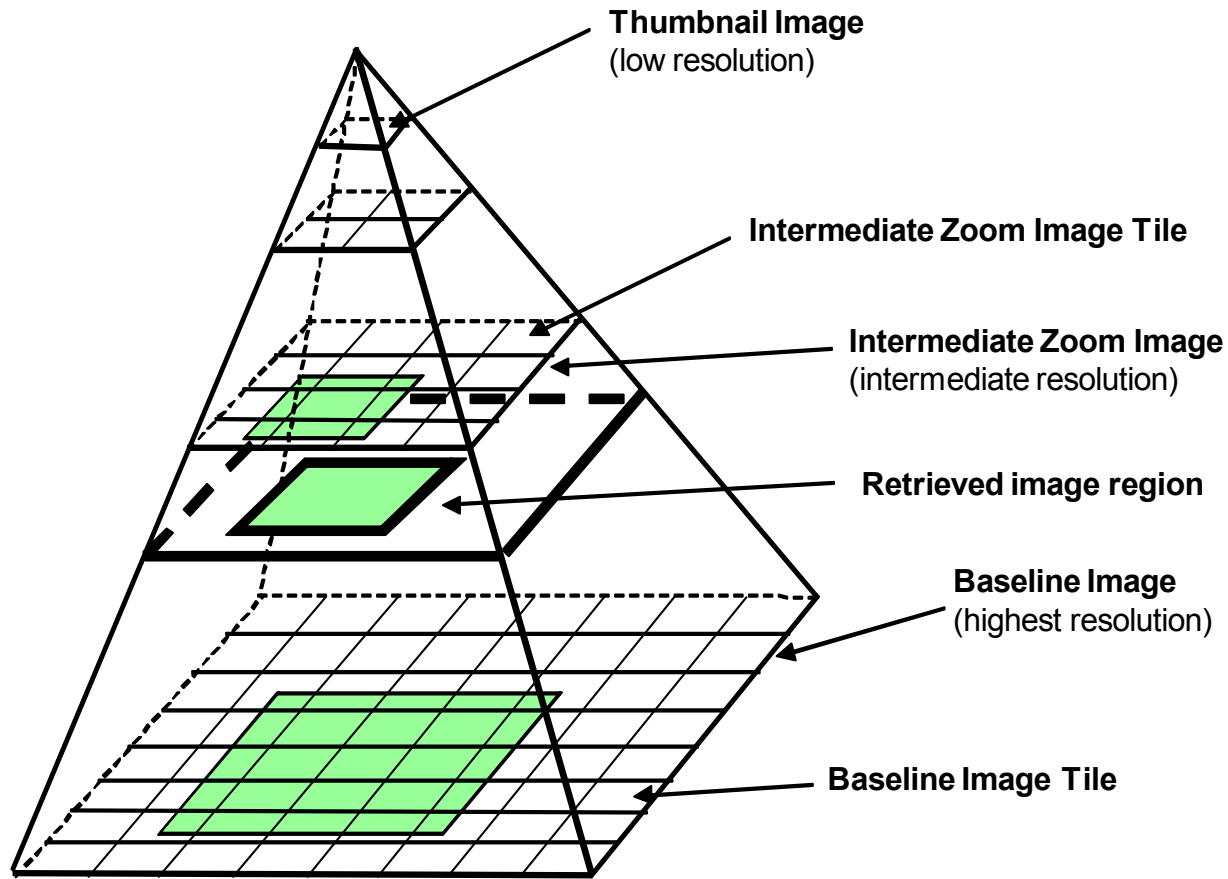


Wang Y, Williamson KE, Kelly PJ, James JA, Hamilton PW (2012) SurfaceSlide: A Multitouch Digital Pathology Platform. *PLOS ONE* 7(1): e30783. <https://doi.org/10.1371/journal.pone.0030783>
<http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0030783>



DICOM WSI: Why tiled pyramids?

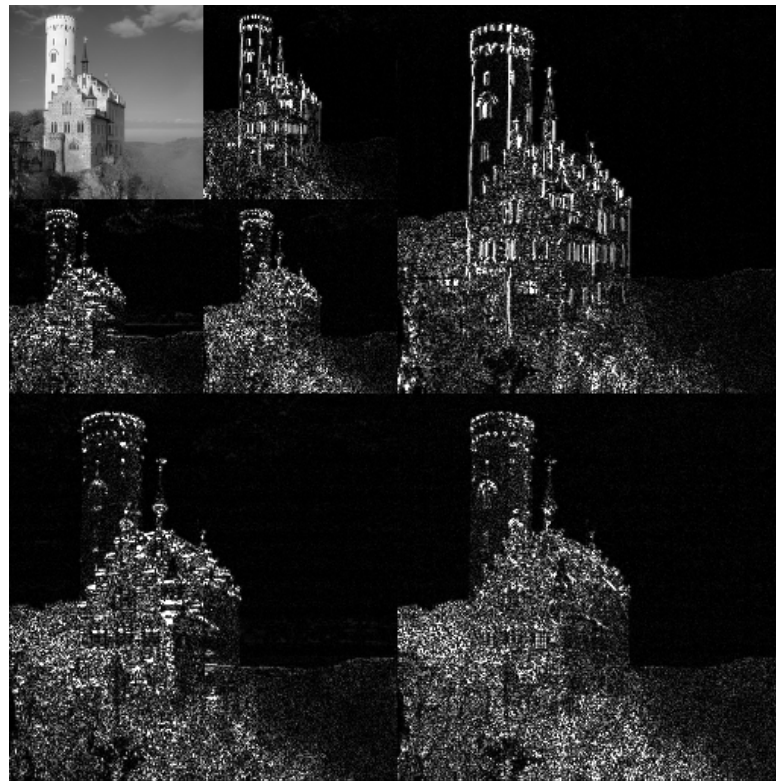
- Tiles are an expedient way of accessing rectangular sub-regions of the highest resolution layer (e.g., compared to stripes or one large image, which might require entire rows to be loaded)
- Since highest resolution layer is so large, lower magnification layers (to facilitate zooming out without resampling) are negligible storage overhead, hence store a multi-resolution “pyramid”
- Each tile can be separately compressed and decompressed (quickly and with little memory consumption)
- Works around DICOM single frame size limitations without having to change fundamentals of DICOM encoding (or change existing DICOM implementations in toolkits and archives)



DICOM WSI: Why not J2K?

- “Multi-resolution decomposition” in wavelet domain
 - i.e., inherently “tiled”, pyramidal (in addition to explicit tiling)
 - DICOM has support for JPIP protocol (to access selected regions) though rarely implemented
- Fundamental limit of 16 bit value for rows and columns 64k x 64k – too small for single frame WSI at 25 microns
 - protagonists rejected proposal to consider adding larger sized row and column attributes (like Aperio’s BigTIFF did to TIFF)
- Concerns about time taken to assemble indexed JPEG 2000 bit stream to enable fast JPIP access

<i>LL</i> level 2	<i>LH</i> level 2	<i>LH</i> level 1
<i>HL</i> level 2	<i>HH</i> level 2	
<i>HL</i> level 1		<i>HH</i> level 1



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Tiles won, so get over it

- Standards are never perfect, neither is this one
- It is sufficient, so better an interoperable standard than proprietary perfection
- Some folks still want to use single large JPEG 2000 image and JPIP in DICOM – workable (apart from max image size) but schism threatens interchange – we only need one format
- Alternative interchange formats were viable until patent issues were resolved, but not any more
- One can still interchange tiled DICOM images, re-index them and serve them up with JPEG 2000 and JPIP for “virtual microscopy” applications (without recompressing if tiles are JPEG 2000 rather than JPEG)

DICOM Size Limits

- These constrain the design choices
 - Rows and Columns of each frame (therefore entire size if one big frame): 65,535 ($2^{16}-1$) (i.e., 16 bit unsigned encoding of value)
 - Number of Frames: 2,147,483,647 ($2^{31}-1$) (i.e., 32 bit signed value)
 - total size of Pixel Data field for all uncompressed frames: 4,294,967,294 ($2^{32}-2$) (i.e., 32 bit unsigned field length, 0xffffffff reserved)
 - maximum size of compressed bit frame in one fragment (not required to be so): $2^{32}-2$ (i.e., 32 bit unsigned field length, required to be even) – compression scheme (e.g., JPEG) may limit total size of one compressed frame (frames compressed separately)
- Net effect
 - one single frame is too big for Rows and Columns Attribute Values
 - uncompressed tiled multi-frame may be too big for Pixel Data Value Length
 - Compressed tiled multi-frame is near unlimited – 140,735,340,806,145 ($(2^{16}-1)*(2^{31}-1)$) total rows and total columns

But wait ... Patents ... Aaargh!

- Early family of patents related to tiled acquisition
 - Bacus US 6,272,235 “Method ... for creating a virtual microscope slide”
 - believed to have expired
- Specific to DICOM encoding by principle participant in Sup 145 development
 - Aperio US 8,086,077, US 8,781,261, US 9,305,023, US 20160217155
 - “Method for storing and retrieving large images via DICOM”
 - ostensibly “defensive” but then Aperio bought by Leica
 - Leica has (finally) negotiated with DICOM WG 26 participants a NEMA counsel approved royalty-free license to any user
- Significant dampening effect on adoption of DICOM WSI
- Arguably not specific to DICOM, but any tiled approach (including TIFF)?
- Some folks want to avoid tiles completely just to be safe

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	JPEG	No	No	Under	JPEG development	2 GB
NanoZoomer	JPEG o JPEG2000	Yes (Aware Jpeg2000 SDK)	JPEG	TIFF	.TIF	2 GB
LifeSpan Alias	JPEG	Yes (max 350 MB)	No	TIFF, BMP	.VSL (JPEG) and :JP2 (JPEG2000)	2 GB (JPEG)
Nikon EclipseNet-VSL	JPEG	Yes (with or without loss)	JPEG	TIFF, but not RAW	.VSI (pyramidal, up to 9 resolutions)	1.5 GB
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
- Relevant to WSI:
 - JPEG baseline (8 bit DCT 8x8 Huffman)
 - JPEG 2000 (reversible, irreversible)
- Is lossless compression ever needed in practice?
 - pretty big and really slow to store, copy, transmit, e.g., 30GB or so uncompressed

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 (just 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 (just another image in same file)
Slide label image	Yes*** (Icon Image Sequence**)	Yes (just another image in same file)
Can be archived in ordinary PACS	Yes	No
Can be archived in VNA	Yes	Maybe, but separated from metadata

DICOM versus TIFF

- DICOM contains metadata, TIFF does not (as implemented by vendors)
- No way to factor out JPEG tables from bit stream like TIFF does, so each frame is a little larger than when encoded with TIFF
- E.g., 200,000 tiles, extra 300 bytes, 60MB
- Navigational metadata overhead (enhanced MF representation, requires ≈ 100 bytes per tile to represent spatial position, since not “implicit”)
- E.g., 200,000 tiles, extra 100 bytes, 20MB
- Not just transfer but parsing/analysis time
- Allows for sparseness, unlike TIFF, but impacts most common use
- CP to flag implicit organization is work in progress

Dual personality – DICOM & TIFF

- For files on interchange media, exchanged via web services
- Discarded during ordinary network transfer, so would need to be reconstructed by recipient, if needed
- Historically was used by some ultrasound carts that had started to use TIFF + private tags before DICOM existed – now dead
- TIFF Image File Directory (IFD) can be buried in spare 128 byte preamble, and rest of TIFF stuff stored in Data Set Trailing Padding, and use TIFF Tile Offsets to point compressed frames in Pixel Data

DICOM Frame Offset Table

- Can store a table of byte offsets to start of frame in the first fragment of “encapsulated” (compressed) Pixel Data
- Can use it combined with (which tile is which) meta-data to navigate directly to relevant frame (tile) without having to parse them all
- No way to retrieve the offset table with any of the metadata retrieval services though, but wouldn’t be useful anyway, because frame retrieval is by frame number not byte offset with the file
- I.e., only useful to systems that have the entire file and serve it up without transforming it or re-indexing it themselves
- C.f. TIFF, for which the only way to encode the tiles is with byte offsets and lengths (no single contiguous stream like DICOM)

Converted stripped images

- Long thin strips (entire width of image) rather than tiles
- E.g., Leica Aperio SVS (BigTIFF) thumbnail
- Could assemble into single DICOM image, but each strip is separately compressed, so would need to be decompressed and recompressed (lossy)
- Also, slide label image is TIFF LZW compressed, not supported in DICOM, but lossless, so can decompress or transcode into another lossless scheme – probably so as not to affect barcode and OCR with lossy compression

Converting TIFF to DICOM

- Physical pixel size
- “Microns per pixel” (MPP)
- There are standard TIFF tags for this: X,YResolution
- Vendors might not use them; instead bury this inside text fields (e.g., SVS: Image Description, MPP =)
- Vendors might not send size for any plane but the highest resolution, and so need to decode the decimation description text to determine for other planes of pyramid (or guess, or resample yourself)
- Needed to populate mandatory Pixel Spacing (0028,0030)

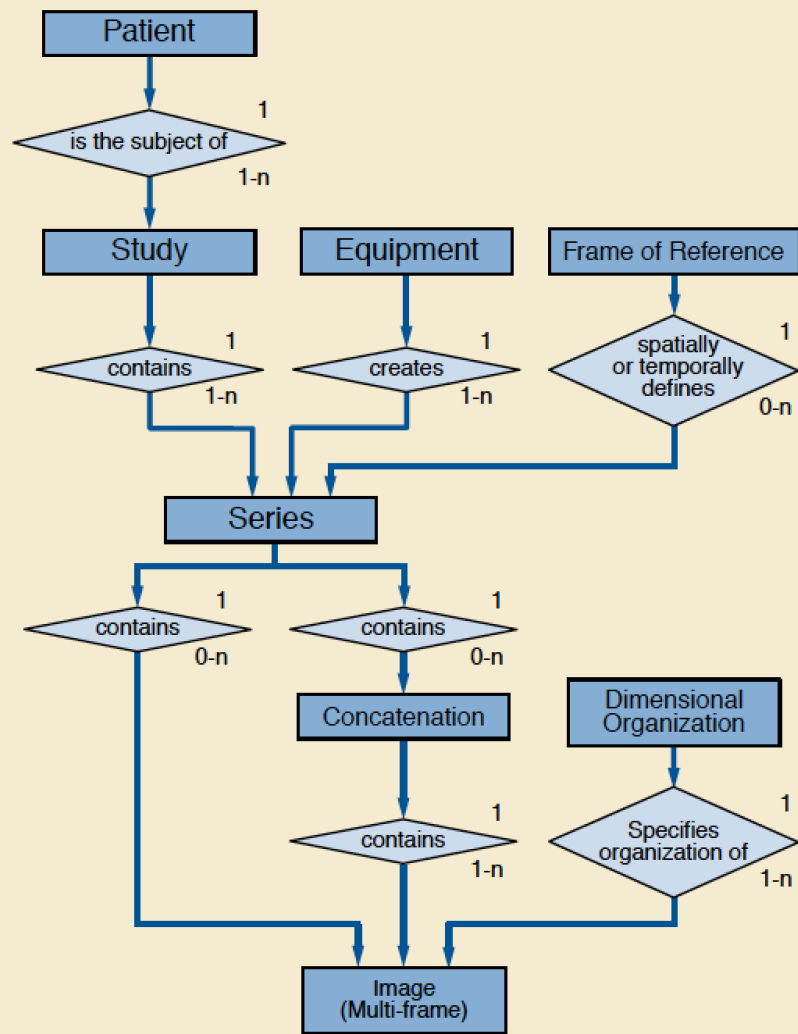


It's the metadata, stupid

<http://medium.com/digital-trends-index/its-the-metadata-stupid-12a4fc121e45#.4zhwdz5y0>

Composite Context

- All of the stuff that is the same across multiple images (files, instances) ... i.e., of the DICOM Composite Information Model:
 - Patient ... same for all instances for patient
 - Study ... same for all instances for procedure
 - Series ... new for each related acquisition or derivation
 - Equipment
 - Multi-Frame Dimensions
 - Frame of Reference ... e.g., if same slide coordinates
- On reading ... relevant to database/browser structure
- On writing ... re-use from input, e.g., for analysis results
- Garbage in, garbage out (GIGO)
 - if invalid on ingestion, if copied and not correct, will be invalid in output

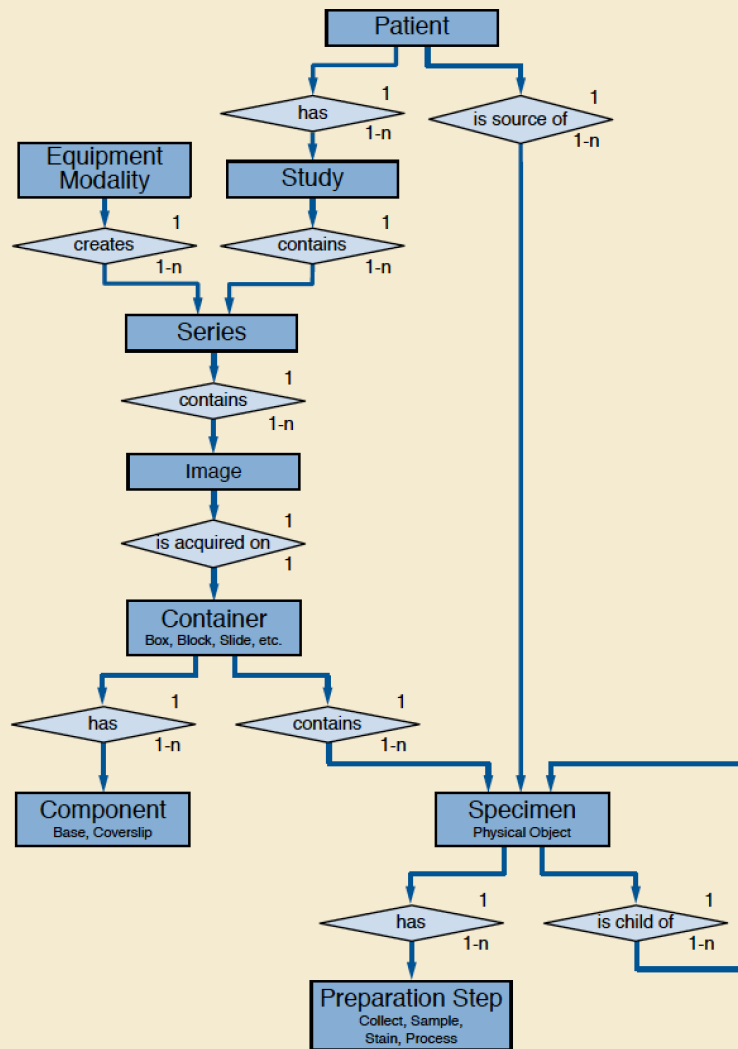


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DICOM WSI Identification Model

- To leverage existing PACS (etc.), must 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) – has number in LIS – relate to DICOM Accession Number
- Distinct from Specimen ID



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Leverage Pan-DICOM Extensions

- E.g., veterinary and small animal (research) patient/
subject descriptions
 - taxon (genus, species), strain
- Cross-enterprise identification
 - Other Patient IDs Sequence

Table A.32.8-1. VL Whole Slide Microscopy Image IOD Modules

IE	Module	Reference	Usage
Patient	Patient	C.7.1.1	M
	Clinical Trial Subject	C.7.1.3	U
Study	General Study	C.7.2.1	M
	Patient Study	C.7.2.2	U
	Clinical Trial Study	C.7.2.3	U
Series	General Series	C.7.3.1	M
	Whole Slide Microscopy Series	C.8.12.3	M
	Clinical Trial Series	C.7.3.2	U
Frame of Reference	Frame of Reference	C.7.4.1	M
Equipment	General Equipment	C.7.5.1	M
	Enhanced General Equipment	C.7.5.2	M
Image	General Image	C.7.6.1	M
	General Reference	C.12.4	U
	Image Pixel	C.7.6.3	M
	Acquisition Context	C.7.6.14	M
	Multi-frame Functional Groups	C.7.6.16	M
	Multi-frame Dimension	C.7.6.17	M
	Specimen	C.7.6.22	M
	Whole Slide Microscopy Image	C.8.12.4	M
	Optical Path	C.8.12.5	M
	Multi-Resolution Navigation	C.8.12.7	C - Required if Image Type (0008,0008) Value 3 is LOCALIZER
	Slide Label	C.8.12.8	C - Required if Image Type (0008,0008) Value 3 is LABEL; may be present otherwise
	SOP Common	C.12.1	M
	Common Instance Reference	C.12.2	M
Frame Extraction	C.12.3	C - Required if the SOP Instance was created in response to a Frame-Level retrieve request	

Table A.32.8-2. VL Whole Slide Microscopy Image Functional Group Macros

Functional Group Macro	Section	Usage
Pixel Measures	C.7.6.16.2.1	M - Shall be used as a Shared Functional Group.
Frame Content	C.7.6.16.2.2	M - Shall not be used as a Shared Functional Group.
Referenced Image	C.7.6.16.2.5	U
Derivation Image	C.7.6.16.2.6	C - Required if the image or frame has been derived from another SOP Instance.
Real World Value Mapping	C.7.6.16.2.11	U
Plane Position (Slide)	C.8.12.6.1	M
Optical Path Identification	C.8.12.6.2	M
Specimen Reference	C.8.12.6.3	U

Table C.8.12.6.1-1. Plane Position (Slide) Macro Attributes

Attribute Name	Tag	Type	Attribute Description
Plane Position (Slide) Sequence	(0048,021A)	1	<p>Describes position of frame in the Total Pixel Matrix and in the Slide Coordinate System Frame of Reference.</p> <p>Only a single Item shall be included in this Sequence.</p>
>Column Position In Total Image Pixel Matrix	(0048,021E)	1	<p>The column position of the top left hand pixel of the frame in the Total Pixel Matrix (see Section C.8.12.4.1.1). The column position of the top left pixel of the Total Pixel Matrix is 1.</p>
>Row Position In Total Image Pixel Matrix	(0048,021F)	1	<p>The row position of the top left hand pixel of the frame in the Total Pixel Matrix (see Section C.8.12.4.1.1). The row position of the top left pixel of the Total Pixel Matrix is 1.</p>
>X Offset in Slide Coordinate System	(0040,072A)	1	<p>The X offset in mm from the Origin of the Slide Coordinate System. See Figure C.8-16.</p>
>Y Offset in Slide Coordinate System	(0040,073A)	1	<p>The Y offset in mm from the Origin of the Slide Coordinate System. See Figure C.8-16.</p>
>Z Offset in Slide Coordinate System	(0040,074A)	1	<p>The Z offset in μm from the Origin of the Slide Coordinate System, nominally the surface of the glass slide substrate. See Figure C.8-17</p> <p>Note</p> <p>Required even if only a single focal plane was acquired.</p>

Table C.8.12.4-1. Whole Slide Microscopy Image Module Attributes

Attribute Name	Tag	Type	Attribute Description
Image Type	(0008,0008)	1	Image identification characteristics. See Section C.8.12.4.1.1 for specialization.
Imaged Volume Width	(0048,0001)	1	Width of total imaged volume (distance in the direction of rows in each frame) in mm. See Section C.8.12.4.1.2
Imaged Volume Height	(0048,0002)	1	Height of total imaged volume (distance in the direction of columns in each frame) in mm. See Section C.8.12.4.1.2
Imaged Volume Depth	(0048,0003)	1	Depth of total imaged volume (distance in the Z direction of focal planes) in μm . See Section C.8.12.4.1.2
Total Pixel Matrix Columns	(0048,0006)	1	Total number of columns in pixel matrix; i.e., width of total imaged volume in pixels. See Section C.8.12.4.1.3
Total Pixel Matrix Rows	(0048,0007)	1	Total number of rows in pixel matrix; i.e., height of total imaged volume in pixels. See Section C.8.12.4.1.3
Total Pixel Matrix Origin Sequence	(0048,0008)	1	Location of pixel 1\1 of the total pixel matrix in the Slide Coordinate System Frame of Reference. Only a single Item shall be included in this Sequence. See Section C.8.12.4.1.4 and Section C.8.12.2.1.1 for further explanation
>X Offset in Slide Coordinate System	(0040,072A)	1	The X offset in millimeters from the Origin of the Slide Coordinate System.
>Y Offset in Slide Coordinate System	(0040,073A)	1	The Y offset in millimeters from the Origin of the Slide Coordinate System.
Image Orientation (Slide)	(0048,0102)	1	The direction cosines of the first row and the first column of the total pixel matrix with respect to the Slide Coordinate System Frame of Reference. See Section C.8.12.4.1.4
Samples Per Pixel	(0028,0002)	1	Number of samples (color planes) per frame in this image. Enumerated Values: 3 1 See Section C.8.12.4.1.5 for further explanation.
Photometric Interpretation	(0028,0004)	1	Specifies the intended interpretation of the pixel data. See Section C.8.12.4.1.5 for Enumerated Values.
Planar Configuration	(0028,0006)	1C	Indicates whether the pixel data are encoded color-by-plane or

Table C.8.12.5-1. Optical Path Module Attributes

Attribute Name	Tag	Type	Attribute Description
Optical Path Sequence	(0048,0105)	1	Describes the optical paths used during the acquisition of this image. One or more Items shall be included in this Sequence. See Section C.8.12.5.1.1
>Optical Path Identifier	(0048,0106)	1	Identifier for the optical path specified in the Sequence Item. The identifier shall be unique for each Item within the Optical Path Sequence.
>Optical Path Description	(0048,0107)	3	Description of the optical path specified in the Sequence Item.
>Illuminator Type Code Sequence	(0048,0100)	3	Type of illuminator. Only a single Item is permitted in this Sequence.
>>Include Table 8.8-1 "Code Sequence Macro Attributes"			Context ID may be defined in the IOD constraints.
>Illumination Wave Length	(0022,0055)	1C	Nominal wavelength of the illuminator in nm. Required if Illumination Color Code Sequence (0048,ee08) is not present. May be present otherwise.
>Illumination Color Code Sequence	(0048,0108)	1C	Color of the illuminator. Only a single Item shall be included in this Sequence. Required if Illumination Wave Length (0022,0055) is not present. May be present otherwise.
>>Include Table 8.8-1 "Code Sequence Macro Attributes"			Context ID may be defined in the IOD constraints.
>Illumination Type Code Sequence	(0022,0016)	1	Coded value for illumination method. See Section C.8.12.5.1.2. One or more Items shall be included in this Sequence.
>>Include Table 8.8-1 "Code Sequence Macro Attributes"			Context ID may be defined in the IOD constraints.
>Light Path Filter Type Stack Code Sequence	(0022,0017)	3	Filters used in the light source (excitation) path. One or more Items are permitted in this Sequence. See Section C.8.12.5.1.3.
>>Include Table 8.8-1 "Code Sequence Macro Attributes"			Context ID may be defined in the IOD constraints.
>Light Path Filter Pass-Through Wavelength	(0022,0001)	3	Nominal pass-through wavelength of light path filter(s) in nm
>Light Path Filter Pass Band	(0022,0002)	3	Pass band of light path filter(s) in nm. This Attribute has two Values. The first is the shorter and the second the longer wavelength relative to the peak. The values are for the - 3dB nominal (1/2 of peak) pass through intensity. One of the two Values may be zero length, in which case it is a cutoff filter.
>Image Path Filter Type Stack Code Sequence	(0022,0018)	3	Describes stack of filters used in image (emission) path between the imaging target and the optical sensor. One or more Items are permitted in this Sequence.

A.32.8.3.1 VL Whole Slide Microscopy Image IOD Content Constraints

A.32.8.3.1.1 Optical Path Module

The Code Sequences within the Optical Path Sequence (0048,0105) of the Optical Path Module (see Section C.8.12.5) are constrained as follows:

Baseline CID for Illuminator Type Code Sequence (0048,0100) is CID 8125 “Microscopy Illuminator Type”.

Baseline CID for Illumination Color Code Sequence (0048,0108) is CID 8122 “Microscopy Illuminator and Sensor Color”.

CID 8122 Microscopy Illuminator and Sensor Color

Type: Extensible
Version: 20100824

Table CID 8122. Microscopy Illuminator and Sensor Color

Coding Scheme Designator	Code Value	Code Meaning	SNOMED-CT Concept ID	UMLS Concept Unique ID
SRT	R-102C0	Full Spectrum	414298005	C1532530
SRT	R-102BE	Infrared	414497003	C1532326
SRT	G-A11A	Red	371240000	C1260956
SRT	G-A11E	Green	371246006	C0332583
SRT	G-A12F	Blue	405738005	C1260957
SRT	R-102BF	Ultraviolet	415770004	C1532472

Table CID 8123. Microscopy Illumination Method

Coding Scheme Designator	Code Value	Code Meaning
DCM	111741	Transmission illumination
DCM	111742	Reflection illumination
DCM	111743	Epifluorescence illumination
DCM	111744	Brightfield illumination
DCM	111745	Darkfield illumination
DCM	111746	Oblique illumination
DCM	111747	Phase contrast illumination
DCM	111748	Differential interference contrast
DCM	111749	Total internal reflection fluorescence

DICOM-related WSI Workflow

- Providing the identification
- Reliable source (integrated IS – RIS, (AP)LIS)
- Indexed by automatically scanned barcode
 - just contained identifier(s)
 - identifiers looked up by recipient to get metadata
- Barcode contains everything
 - not just an identifier into an index
 - entire acquisition context
- Worklist (DICOM Modality Worklist query)
 - protocol templates, parameters, codes (CP 1148)

Table TID 8010. Slide Imaging Parameters

	VT	Concept Name	VM	Req Type	Condition	Value Set Constraint
1	CODE	EV (112706, DCM, "Illumination Method")	1-n	U		DCID 8123 "Microscopy Illumination Method"
2	NUMERIC	EV (112707, DCM, "Number of focal planes")	1	UC	XOR Row 3	UNITS = EV ({planes}, UCUM, "planes")
3	CODE	EV (112707, DCM, "Number of focal planes")	1	UC	XOR Row 2	DT (112714, DCM, "Multiple planes")
4	NUMERIC	EV (112708, DCM, "Focal plane Z offset")	1-n	U		UNITS = EV (um, UCUM, "um")
5	CODE	EV (112709, DCM, "Magnification selection")	1	U		DCID 8132 "Magnification Selection"
6	NUMERIC	EV (112710, DCM, "Illumination wavelength")	1-n	U		UNITS = EV (nm, UCUM, "nm")
7	CODE	EV (112711, DCM, "Illumination spectral band")	1-n	U		DCID 8122 "Microscopy Illuminator and Sensor Color"
8	CODE	EV (112712, DCM, "Optical filter type")	1-n	U		DCID 8124 "Microscopy Filter"
9	CODE	EV (112713, DCM, "Tissue selection method")	1	U		DCID 8133 "Tissue Selection"

Table CID 8131. Pathology Imaging Protocols

Coding Scheme Designator	Code Value	Code Meaning
DCM	112700	Peri-operative Photographic Imaging
DCM	112701	Gross Specimen Imaging
DCM	112702	Slide Microscopy
DCM	112703	Whole Slide Imaging
DCM	112704	WSI 20X RGB
DCM	112705	WSI 40X RGB

Table CID 8132. Magnification Selection

Coding Scheme Designator	Code Value	Code Meaning
DCM	112715	5X
DCM	112716	10X
DCM	112717	20X
DCM	112718	40X

Table CID 8133. Tissue Selection

Coding Scheme Designator	Code Value	Code Meaning
DCM	112719	Nominal empty tile suppression
DCM	112720	High threshold empty tile suppression
DCM	112721	No empty tile suppression

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)
- Used by slide scanner to look up “stuff” to put in image “header”?
- Barcode in header used by recipient of image (viewer, 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?
- Lots of metadata encoded in barcode (more than just slide unique identifier)?

APLIS <-> Scanner Interface (II)

- 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
- Key benefit of rich metadata in image header is 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 (e.g., consider end of life, migration)
- Another radiology trend – RIS being subsumed as an EMR/EHR “module”
- Will that happen to APLIS? AP has *much* more complicated physical handling workflow to track than radiology

Standard External Lexicons

- Sources of “codes”
 - SNOMED CT
 - LOINC
 - FMA
 - NCI Thesaurus
- UMLS Metathesaurus
 - cross-mapping between sources – listed in DICOM if known
- Either completely open or free for use in DICOM
 - license agreement with IHTSDO/SNOMED for “DICOM subset”
- DICOM defines its own codes if can’t find them elsewhere
 - PS3.16 Annex D

Coded Image Acquisition Values

- 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

Explicit Image Relationships

- Reduces need for vendor-specific guesswork
 - like “first image in IFD is always the base resolution”
- Relates images for same acquisition at
 - higher/lower resolution
 - different focal depth
 - different spectral band
- Localizer
- Imaged container label

DICOM Itself Machine Readable

- In 2013 converted from Word source to DocBook XML
- Rendered in many forms: PDF, Word, ODT, HTML, chunked HTML
- “Current” release – always same URL, updated five times per year
- Tables (etc.) follow recognizable pattern – e.g., can automatically extract
 - lists of Storage SOP Classes
 - IOD modules
 - IOD functional group macros
 - modules and macro attribute tables
 - element data dictionary and encoding
 - context groups (value sets)
 - protocol, acquisition context, reporting templates
 - DCM code dictionary

Radiology Experience – Images

- Acquisition modality vendors are easy
 - to get on board with saving as standard like DICOM
 - their expertise and added value is not in archival/distribution/analysis/viewing (just a burden to them)
- Archival/distribution vendors are easy
 - standard input means less work for them
 - standard metadata within input image files means one less additional user/system interface
- Analysis/viewer vendors are easy
 - standard input means less work for third party or standalone vendor
 - performance & functionality challenge “myth or reality” – some pressure to merge with archival function (hence “PACS”), but integration of special stuff hard (e.g., 3D, interactive image analytics)
- Myth of the “complete solution”
 - OK for early adopters, regulatory (PMA) trials, small silos, but rapidly becomes untenable
 - need “best of breed” options for scalability, referrals (inbound or outbound), acquisitions & mergers (customer and vendor)
 - vendor “lock in” sucks (competitively, feature improvement, maintenance, fails or loses interest)

Radiology Experience – IS

- Information system integration
- Workflow
- Reporting system (voice) integration
- EMR/EHR integration
- DICOM Modality Worklist
 - identification
 - ordering
 - scheduling
 - protocoling – acquisition context
- For WSI – Acquisition Context Templates (Sup 122)
 - Specimen Preparation, Sampling, Staining, Slide Imaging Parameters

Radiology Lessons Learned

- At first grateful to store at all
- Reliable demographics (MWL)
- More complex use cases:
 - hanging protocols
 - retrieval of relevant priors
- Special purpose analysis
 - DCE-MRI (e.g., of breast) – multiple image types
 - recognizing the appropriate input images
 - storing the appropriate derived images/structured results

IHE – Beyond DICOM (and HL7)

- “Profiles” existing standards for specific use cases
- Combination of “transactions” into sequence of operations
 - e.g., radiology – Scheduled Workflow (SWF)
- More detailed content (payload)
 - creation side (mandatory attributes/values)
 - consumption side (display features)
 - e.g., radiology – Mammography Display (MAMMO)
- Testable and tested (“Connectathons”)
- IHE Anatomic Pathology -> now merged with Lab into single “Pathology and Laboratory Medicine (PaLM)” domain

IHE – Anatomic Pathology

- Anatomic Pathology Workflow (APW)
 - ordering, scheduling, acquisition, storage, post-processing
 - special 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, e.g., MAMMO)
 - contemporaneous with but not using DICOM WSI Sup 145, so WSI not specifically addressed in AP or RAD image transactions
 - were more recent suggestions to eliminate DICOM MWL and use HL7 (v2) to acquisition modality (slide scanner) for scheduling (to be more like lab devices, à la Laboratory Testing Workflow (LTW))
- Anatomic Pathology Reporting to Public Health (ARPH) (TI)
- Anatomic Pathology Structured Reports (APSR) (TI)
 - is an HL7 Clinical Document Architecture (CDA) implementation guide

Patient mgmt.

Care Ward

Anatomic Pathology Department



ADT
Registration

*Patient
Adm
Mgmt*



Order Placer
Orders Placed

*Order
Mgmt*



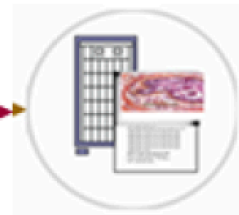
Order Filler
Orders accepted
Report created

*Modality
worklist*



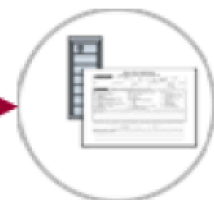
Acquisition Modality
(gross imaging/microscopic imaging)
Acquisition completed

*Image
Mgmt*

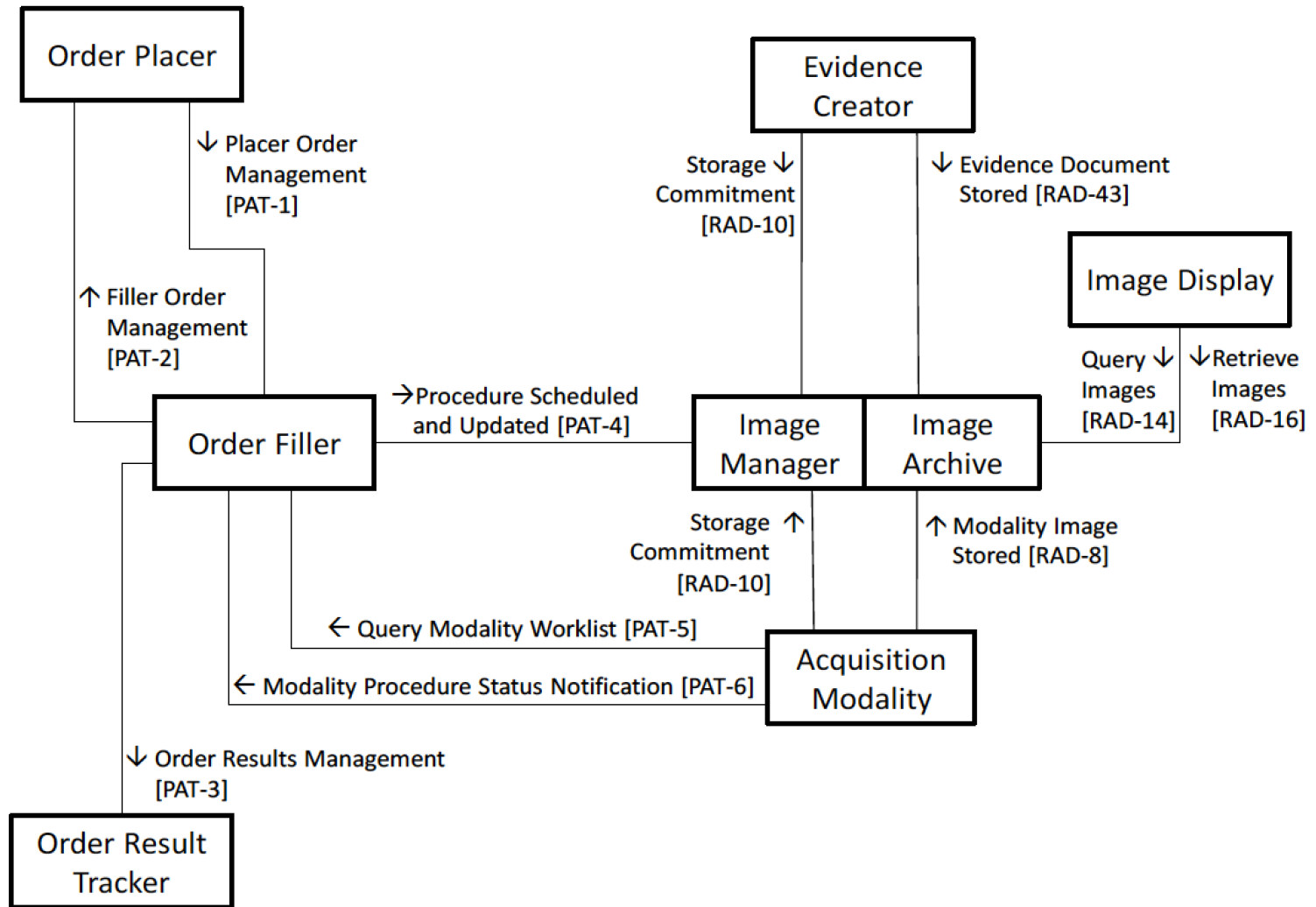


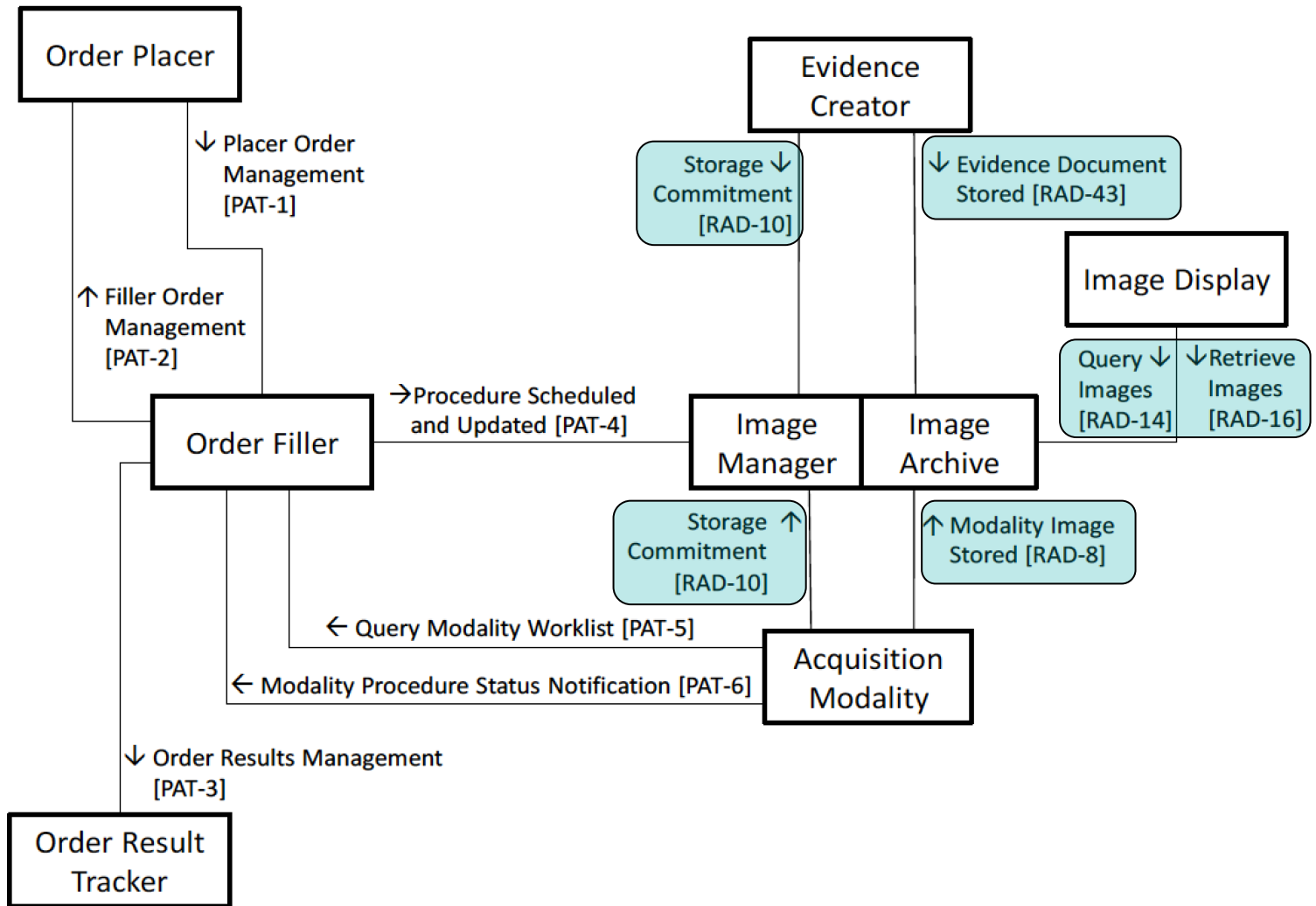
PACS
(Image Archive/
Image Manager)
Images stored

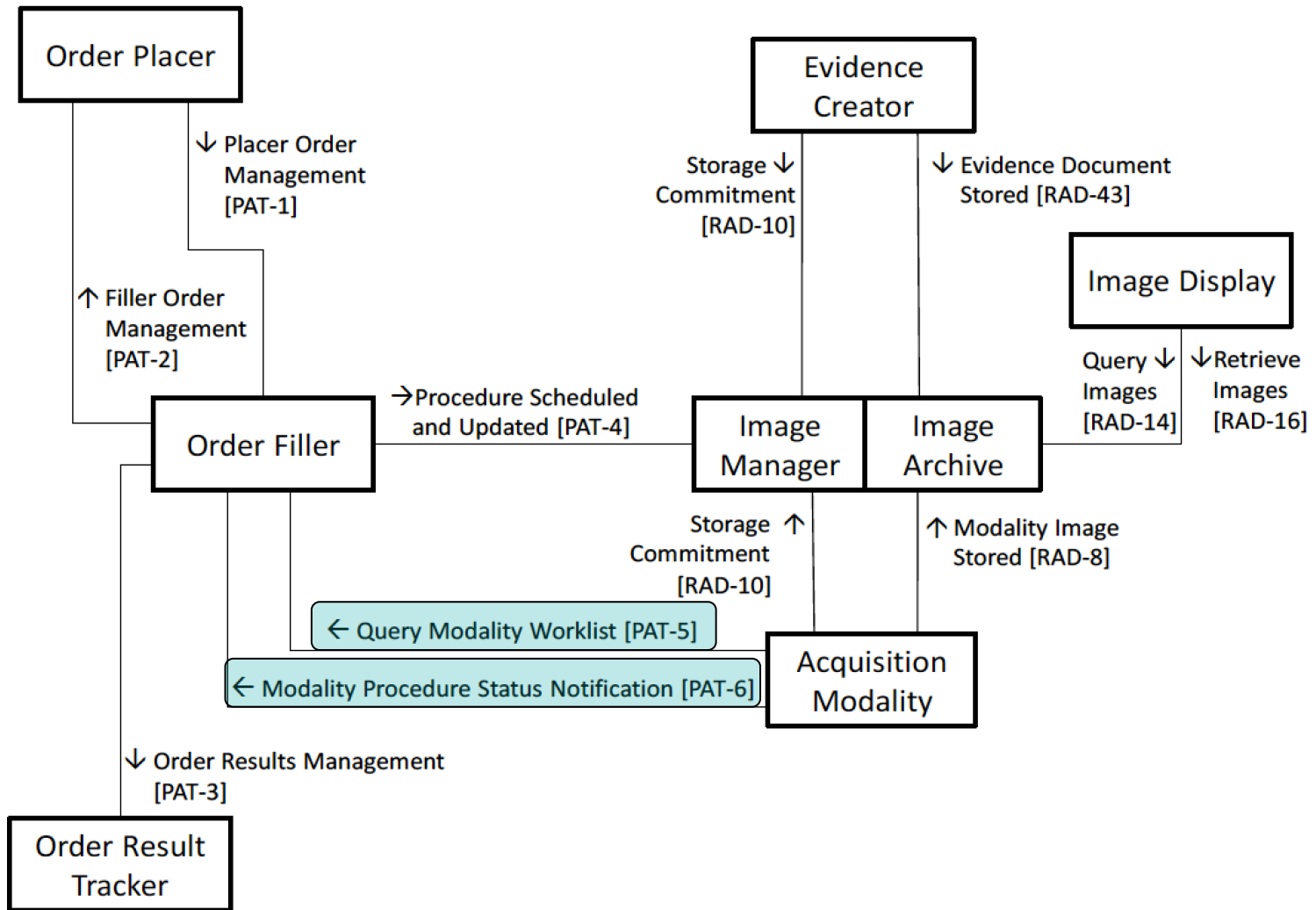
*Report
Mgmt*

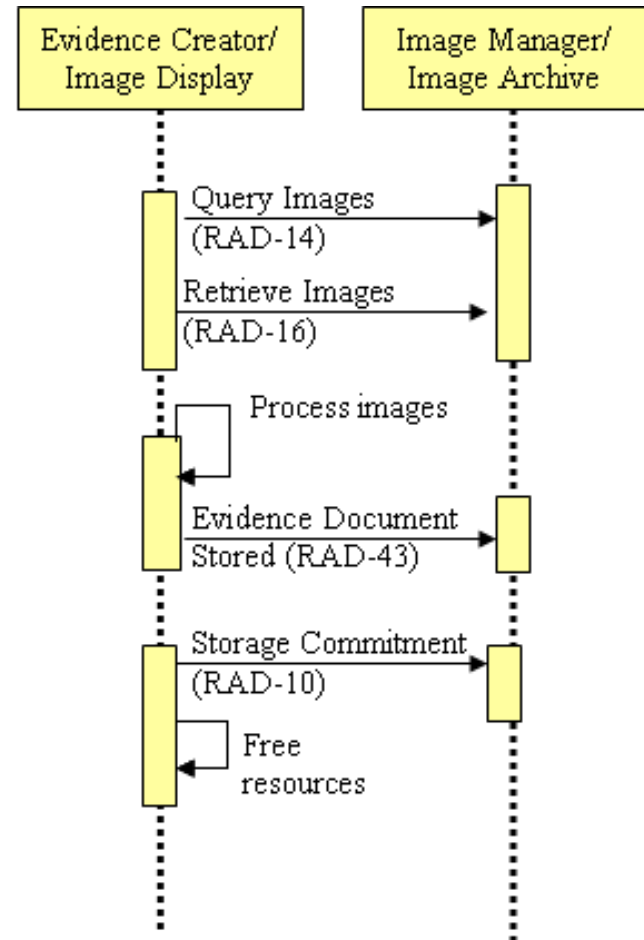
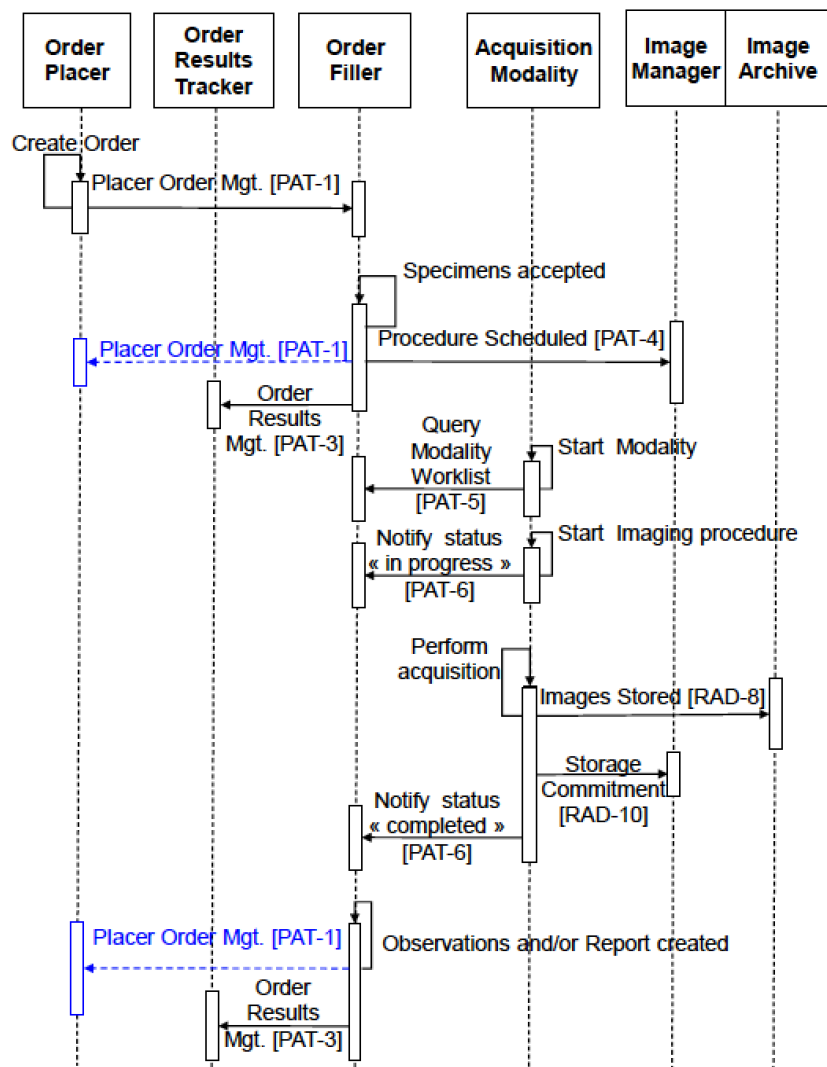


Report/result
Repository
Reports stored









API, REST, Web, XML, JSON

- DICOM is more than just a file format – traditional and new protocols
- API = “Application Programmer Interface”
- Use (misuse?) of term in “Web API” to mean a bunch of URLs (REST) or SOAP operations
- Different from traditional TCP-IP based “protocols” like FTP, HTTP, SMTP or DICOM PS3.8 “message service element” (DIMSE)
- DICOM has been adding “Web services” since 2000 – Web Access to DICOM Objects (WADO), most recently family of RESTful services that parallel traditional DICOM services for query (QIDO-RS), retrieval (WADO-RS), store (STOW-RS)
- More API-like services for Application Hosting (plugin interface) – SOAP-based web services to access hosted data from hosted application – never popular and can probably ignore these; may be revisited with RESTful approach
- XML and JSON representations of DICOM metadata separate from “bulk data”

Web (WADO), XML, JSON

- Web Access to DICOM Objects (WADO) (2000)
- WADO-RS – REST not SOAP (-WS is being “retired”)
- JPIP – access to DICOM JPEG 2000 regions
- Separate metadata from bulk data (pixels)
- Encode as XML – added with Application Hosting API
- Encode as JSON – added with WADO-RS
- Bottom line – can use URL request and Media Type to retrieve (≈ C-GET)
 - e.g., image/jpeg for selected multi-frame tile(s)
 - e.g., application/json+dicom or application/xml+dicom metadata
- Also query (QIDO-RS ≈ C-FIND) and send (STOW-RS ≈ C-STORE)





**Suppose information doesn't want to be free?
Suppose what information really wants is to be meted out
in tiny, controlled doses at an outrageously high price?**



Serial number:



100001

Need for Security

- Hot topic – you will be hacked and you will be fined if you haven't done your risk analysis, planning, remediation, etc.
- Regardless of real risk to WSI (impact of denial of service, privacy impact)
- A nominally physically or logically isolated network is not sufficient
- Bar is set higher for digital than analog/physical (box of slides lost in transit)
- Security policy and multi-layered protection needs to be in place
- Yet another reason why you need to leverage enterprise IT support (aka., control, responsibility) and use of appropriate common enterprise wide standards
- Security is not all bad – convenience of single sign on (SSO)
- Lesson from radiology – scanners do get hacked and may be the weakest link due to sluggish application of upgrades to a turnkey product

Security status quo in WSI

- Proprietary, black box, turnkey acquisition and distribution products
- Files floating around aimlessly and wantonly
- Plain text (unencrypted) data in transit (network) and at rest (on disk)
- Maybe HTTP or DICOM over TLS (SSL) (HTTPS) or VPN?
- Local caches in server and viewer not flushed immediately after use
- Single factor sign on (just password, not something you know/have/are)
- No stratified or role-based access control (any patient not just yours, etc.)
- No risk analysis/mitigation, no plan, no penetration testing
- Do need to consider impact of encryption/decryption on performance since WSI large but beefy hardware is cheap (compared to DHSS fines)

DICOM Security Opportunities

- Secure in transit – network over TLS for both traditional DIMSE and Web protocols
- Secure in transit – interchange media (DVD, Memory sticks, external hard drives) – Secure DICOM Files are defined (using standard IETF CMS) but rarely used
- Secure at rest – in local or cloud archive or viewer server – Secure DICOM Files theoretically – in practice usually whole disk encryption at operating system level, etc.
- Authentication – usual measures for Web protocols (large variety, even OAuth2), theoretically have User Identity Extended Negotiation, including Kerberos and SAML – at device/application level by TLS Client Certificates (IHE ATNA)
- Access control – largely beyond the scope of the standard (server policy based on reliably authenticated identity, which can be communicated *vide supra*)
- Audit trail – IHE ATNA and related profiles for events in DICOM PS3.15
- Standards are all very well, but no use if not implemented in tools, products, sites

Standards and Performance

- Is it necessary to separate the “archive” server from the “viewer server”?
- Short term cache vs. long term (operational or medico-legal) archive
- Can access tiles directly from DICOM PS3.10 multi-frame disk in archival format
- They are just bytes on disk in one big file (per resolution layer) – can memory map, scatter/gather, cache, etc., if appropriately indexed *in advance of need*
- No DICOM requirement for any particular internal architecture
- Frame retrieval protocols (DIMSE or REST) can be served up from whatever internal source, format, database, etc., is effective, using intermediate index or transformed copy
- As long as entire DICOM multi-frame image can be externalized (reconstructed) if required
- Challenge for third party integration, e.g., different vendor of archive server and “universal” viewer client communicating entirely using standard protocols
- Long radiology history of tiered (hierarchical) access – fast vs. slow hard disk backed by slower optical media or tape – nowadays solid state disks (SSD) and offsite (cloud) – service level agreement (SLA) for different ages, categories, use cases

Analysis Results and Queries

- What
 - locations, ROIs, measurements/features on ROIs, scores
 - vast numbers of automatically generated vs. human on few fields
 - spatial queries (regional overlap)
- Systems
 - Cell Centered Database (CCDB)
 - Pathology Analytic Imaging Standards (PAIS)
- Distinction between:
 - operational format – indexed in queryable database
 - interchange format – serialized for bulk transport – DICOM

DICOM for Analysis Results

- Beyond single attribute (ER +ve/-ve) in HL7 OBX with LOINC code
 - Segmentation – which pixels (label map), in DICOM SEG image
 - Coordinates – outlined ROIs, in DICOM SR (good) or PS (weak)
 - Measurements and scores – in DICOM SR
 - Human (“synoptic”) report – in DICOM SR or HL7 CDA
-
- DICOM Segmentation Image (SEG)
 - DICOM Structured Report (SR)
 - DICOM Presentation State (PS)

Research, Clinical Trials

- Clinical (standard of care) images reused
- De-identification, pseudonymization
- “Burned in” identification – slide label
- DICOM PS3.15 specifies requirements per-attribute

Why reinvent OME-TIFF?

- Open Microscopy Environment
- Data model and XML metadata

- Real question is, why reinvent DICOM?
- OME is a dead end in any enterprise already committed to a single format for all modalities
- Just another silo, even if it is “open”
- Need to make sure everything in OME data model can be encoded in DICOM (i.e., no meta-data gaps, reuse the domain expertise)

HOW STANDARDS PROLIFERATE:

(SEE: A/C CHARGERS, CHARACTER ENCODINGS, INSTANT MESSAGING, ETC)

SITUATION:
THERE ARE
14 COMPETING
STANDARDS.

14?! RIDICULOUS!
WE NEED TO DEVELOP
ONE UNIVERSAL STANDARD
THAT COVERS EVERYONE'S
USE CASES.



SOON:

SITUATION:
THERE ARE
15 COMPETING
STANDARDS.

<https://xkcd.com/927/>

Why not OpenSlide?

- Instead of single format, have universal reader
- Reads many (all?) proprietary formats
- Not scalable
- Non-trivial testing (and regression testing) burden
- Vendors change their formats

- OpenSlide cannot read DICOM yet ☹️
- OpenSlide can only read, not write (i.e., cannot convert to DICOM)

DICOM WSI – Software Tools

- For store, query and regurgitate – nothing special needed
- Ordinary toolkits for creation, parsing, transfer, protocols, servers
- Many free open source toolkits in many languages, e.g.:
 - C++ – dcm4che
 - Java – dcm4che
 - Python – pydicom
- What would be useful on top of these toolkits that is special for WSI:
 - an API for the “tile” abstraction mapped to the “multi-frame” concept
 - which tile (frame) – spatial location on the slide and zoom level
 - find the right slide (image) – additional query keys in the server

DICOM WSI – Software Tools

- Free open source
- Conversion
 - Orthanc WSI Dicomizer – uses OpenSlide if not ordinary TIFF
 - other direction: Orthanc DicomToTiff
- Server/viewer
 - Orthanc WSI viewer plugin
 - REST API used by viewer is not standard (not WADO-RS, QIDO-RS)
- <http://book.orthanc-server.com/plugins/wsi.html>
- <http://www.orthanc-server.com/static.php?page=wsi>
- <http://wsi.orthanc-server.com/demo/>

DICOM WSI – Software Tools

- Free, not open source
- FFEI DICOM image viewer
 - Uses patched OpenSlide
 - Windows executable only
- https://s3-eu-west-1.amazonaws.com/uk-co-ffe-sierra/Downloads/SierraConverter_Setup_x86.exe
- https://s3-eu-west-1.amazonaws.com/uk-co-ffe-sierra/Downloads/SierraConverter_Setup_x64.exe
- Old – 2014 – users guide and OpenSlide patch links dead

DICOM WSI – Software Tools

- Free open source
- Validation that encoding complies with the DICOM standard
 - `dicom3tools dciodvy`
 - `dicom3tools dcentvfy`
- <http://www.dclunie.com/dicom3tools.html>
- <http://www.dclunie.com/dicom3tools/dciodvfy.html>
- Template-driven source as well as macOS and Windows executable

DICOM WSI – Software Tools

- Free, not open source
- JVSdicom Compressor
- JPEG 2000 conversion (not Sup 145 but legal)
 - JPEG 2000 file
 - DICOM with JPIP URL reference for Pixel Data
- http://jvsmicroscope.uta.fi/?q=jvsdicom_compressor/
- Old (2008) but mentioned for completeness and for comparison
- JVSview – JPEG2000 virtual slide viewer

DICOM WSI – Software Tools

- Analysis tools and toolkit support – basic DICOM, if at all, not WSI specifically
- MATLAB
 - native TIFF
 - native DICOM (including multi-frame)
 - Fordanic: OpenSlide (if DICOM were to be added)
- ImageJ
 - native DICOM
 - LargeTIFF
 - NDPI Tools
 - OME Bio-Formats
 - LOCI browser
- Batool N. *A Review of Online Digital Pathology Resources*. 2016.
 - does not even mention DICOM

DICOM WSI – Sample Images

- Early efforts – not necessarily perfect
 - official NEMA site
 - <ftp://medical.nema.org/medical/dicom/DataSets/WG26>
 - currently only Hamamatsu
- Third party sites – conversion output
 - <http://wsi.orthanc-server.com/demo/>
- Notably, no DICOM image sites are listed on DPA's site:
 - <https://digitalpathologyassociation.org/whole-slide-imaging-repository>

DICOM WSI Summary

- Normal DICOM Composite Context (Patient/Study/Series)
- Augmented by Specimen Identification
- Normal (enhanced multi-frame) image pixel data description and encoding (including standard compression schemes)
- Recapitulates widely used TIFF pattern of tiling in a standard format
- Supplemented with slide coordinates and tile location within a “volume” of tiles
- Anatomical pathology and whole slide acquisition context, including description of sensor, illumination, lenses, filters, etc.
- Usual ICC Profiles for color consistency
- Standard protocols and services for storage, query, retrieval and frame access
- DICOM is the one true format for multi-modality enterprise-wide imaging ...

