Standardization and interoperability in telepathology

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Abstract

The need for greater efficiency and quality in health care including speciality of pathological anatomy, requires new methods and solutions. Digital pathology, including the use of digital slides that can replace the conventional microscope by a computer, can improve the flow of work significantly, increasing productivity while minimizing costs, working with automated image analysis to quantify and improve the quality control. One of the most important challenges that digital pathology or telepathology faces is the limited use of international standards in health informatics and interoperability between systems, although there are already some standards. The number of manufacturers and models of scanners of digital slides is very high and often each manufacturer uses its own file format or compression system, since digital preparations are very complex images that uncompressed can be larger than a 14 GB. In recent years they have developed international standards for telepathology in three major areas: Health Level 7 (HL7) for the exchange of messages and documents, Digital Imaging and Communication in Medicine (DICOM) for storing and sharing images and Systematized Nomenclature of Medicine – Clinical Terms (SNOMED CT) to unify clinical terms. In addition, Integrating Healthcare Enterprise (IHE) has developed technical documentation to optimize the use of the standards mentioned above (HL7, DICOM and SNOMED CT). The pathologist mission is to promote and participate actively in the development of these international standards and promote their use in the systems used in clinical practice

Keywords: *Telemedicine; Telepathology; Pathology.*

Resumen

Normalización e interoperabilid en telepatología

La necesidad de una mayor eficiencia y calidad en la atención en salud, centrándonos en la especialidad de anatomía patológica, requiere buscar nuevos métodos y soluciones. La patología digital, incluyendo el uso de preparaciones digitales que permiten reemplazar el microscopio convencional por una computadora, puede mejorar el flujo de trabajo significativamente, incrementando la productividad a la vez que permite reducir costes, trabajar con análisis de imagen automatizado, cuantificar y mejorar el control de calidad. Uno de los retos más importantes a los que se enfrenta la patología digital o a la telepatología es el escaso uso de normas internacionales de informática de la salud o interoperabilidad entre sistemas, a pesar que ya existen algunas normas. El número de fabricantes y modelos de escáneres de preparaciones digitales es muy elevado y a menudo cada fabricante utiliza su propio formato de fichero o su propio sistema de compresión, ya que las preparaciones digitales son imágenes muy complejas, que sin comprimir pueden tener un tamaño superior a los 14 GB. En los últimos años se han desarrollado normas internacionales para telepatología en los tres ámbitos más importantes: Health Level 7 (HL7) para el intercambio de mensajes y documentos, Digital Imaging and Communication in Medicine (DICOM) para el almacenamiento e intercambio de imágenes y Systematized Nomenclature of Medicine – Clinical Terms (SNOMED CT) para unificar términos clínicos. Además, Integrating Healthcare Enterprise (IHE) ha elaborado documentación técnica para optimizar el uso de los estándares arriba mencionados (HL7, DICOM y SNOMED CT). La misión del patólogo es impulsar y participar activamente en el desarrollo de estas normas internacionales y promover su uso en los sistemas utilizados en la práctica clínica.

Palabras-clave: *Telemedicina; Telepatología; Patología.*

Resumo

Normalização e interoperabilidade em telepatologia

A necessidade de uma maior eficiência e qualidade na atenção à saúde, incluindo a especialidade de Anatomia Patológica, requer a busca de novos métodos e soluções. A patologia digital, incluindo o uso de lâminas digitais que possam substituir o microscópio convencional pelo computador, pode melhorar significativamente o fluxo de trabalho, aumentando a produtividade e, ao mesmo tempo, permitindo reduzir custos, trabalhar com análise de imagem automatizada, quantificar e melhorar o controle de qualidade. Um dos desafios mais importantes enfrentados pela patologia digital ou telepatologia é o uso limitado de normas internacionais em informática em saúde ou interoperabilidade entre sistemas, apesar de já existirem algumas normas. O número de fabricantes e modelos de scanners de lâminas digitais é muito grande e, muitas vezes, cada fabricante usa seu próprio formato de arquivo ou o próprio sistema de compressão, uma vez que as lâminas digitais são imagens muito complexas que, não compactadas, podem ser maiores que 14 GB. Nos últimos anos têm sido desenvolvidos padrões internacionais para telepatologia em três grandes áreas: Health Level 7 (HL7) para a troca de mensagens e documentos; Digital Imaging and Communication in Medicine (DICOM) para armazenar e trocar imagens; e Systematized Nomenclature of Medicine – Clinical Terms (SNOMED CT) para unificar termos clínicos. Além disso, Integrating Healthcare Enterprise (IHE) desenvolveu documentação técnica para aperfeiçoar o uso dos padrões acima (HL7, DICOM e SNOMED CT). A missão do patologista é promover e participar ativamente no desenvolvimento destas normas internacionais e favorecer sua utilização nos sistemas utilizados na prática clínica.

Palavras-chave: *Telemedicina; Telepatologia; Patologia.*

INTRODUCTION

The pathological anatomy is facing a growing challenge of efficiency in the study of tissues and cells and biomedical data management, especially images. Thus, it is necessary to seek new methods and solutions to meet the growing demand of anatomopathological studies, each time with higher prediction and quality.

Since the beginning of this century, the new technologies have evolved to allow full scanning of lamellas (WSI, whole slide scanning) with scanners and robotized microscopes and this has probably been the most revolutionary change that is happening in the medical speciality of pathology, which has led to the concept of digital pathology[1,2], by similarity with the world of radiology.

Not only we can transmit images or photos at a distance (static telepathology) or allow that robotized microscopes can be managed at distance and transmit video signal directly (dynamic telepathology) but a new model of telepathology based on digital slides emerges the advantages of both systems. It also allows to be used in networks of limited bandwidth, as its file structure and advanced scopes only allow to be transmitted, part of the picture or preparation that the user is viewing in a large increase or a low-resolution image when it is examining an overview of the whole preparation[3].

In telepathology but also digital preparations, it is necessary to consider the use of other images, especially images of macroscopic biopsies or surgical specimens, along with medical images, special techniques of microscopic images (immunofluorescence and tissues examined under fluorescent light polarized, for which they do not always have a scanner of preparations).

In digital pathology we work with assumptions that the digital image can improve the flow of work significantly, increasing productivity while minimizing costs, working with automated image analysis to quantify and improve quality control. However, today the efficient use of digital slides systems is still a challenge, especially because the following aspects:

- size of microscopic images;
- scan speed;
- image quality;
- image formats “owners”;
- efficiency in the use of image analysis;
- management of specimen based image;
- lack of experience.

The technological challenges are increasingly conquering and every time we have better scanners of preparations, faster, very well focused and sharp images, in some cases even better than the pictures of a conventional microscope, because the scanners often use optical and objectives of great quality.

There are also techniques of parallelization for the processing and image analysis using parallel computing architectures with distributed memory, with a massive number of parallel processors[4]. In addition, the cloud technology is also considered a good alternative for storing and sharing large images of pathology anatomy by means of secure access[5].

But the main challenge we have advanced relatively little is the use of international standards on health informatics and interoperability between systems, applied to digital pathology or telepathology.

This article aims at describing and analyzing the forms, the standardization and the interoperability in telepathology to optimize clinical practice by pathologists.

METHOD

International standards in telepathology

- **basic levels of standardization:** in the basic hardware specifications, such as spatial resolution (VGA, HDTV), interfaces (USB, firewire), video signal (NTSC, PAL) pixel color depth (8-bit, 24-bit, 32-bit), color model (red-green-blue-alpha in RGBA), etc. there is enough consensus among manufacturers, which allow any image from any scanner can be operated in conventional computers and displayed on conventional monitors;
- **file formats and compression in digital slides:** there is no agreement among manufacturers on what file format to be used in digital slides and with what degree of compression. Although the formats and compression methods most used are: TIFF, JPEG and JPEG2000, there are multiple proprietary formats of image in digital pathology (Mirax of 3DHistech BIF Roche, NDPI Hamamatsu, etc.) that, in practice, prevent an exchange of images among different manufacturers, although in some cases, it is possible to import or export images with formats from other manufacturers.

The Table I shows the list of manufacturers currently available of scanners of digital preparations.

Thus, it is necessary to define high level standards that indicate what is the basic information required in a digital preparation and how we can efficiently transmit digital slides among different systems, even if they are from different manufacturers.

Table 1 - Manufacturers and models of scanners of digital preparations

Manufacturer	Model	Charger capacity	Image format
3DHistech	Pannoramic Confocal	12 preparations. Fluorescence, with focal	Owner. MRXS
	Pannoramic 250 Flash II	250 preparations	
	Pannoramic SCAN	150 preparations	
	Pannoramic MIDI	12 preparations	
	Pannoramic DESK	1 preparation	
Bioview	Encore	100/200 preparations	Owner
	Duet-3	50 preparations	
	Allegro-Plus	8 preparations	
	Accord-Plus	1 preparation	
Claro	Toco 240	240 preparations	Owner. Clear, Zoomify
	Toco	20 preparations	
	Lince	5 preparations	
	Fino	1 preparation	
PerkinElmer	Cri Nuance Vectra	200 p. Fluorescence	Owner. CRi, TIFF
	Cri Nuance EX, FX, TRIO	1 p. Fluorescence, multispectral	
Digipath	PathScope	2 preparations	Open. JPEG, JPG2000, TIFF
General Electric / Omnyx	VL120	120 preparations	Owner. MIG
	VL4	4 preparations	
Hamamatsu	NanoZoomer-XR	320 preparations. Fluorescence	Owner. Ndpi. JPEG
	NanoZoomer 2.0-HT	210 preparations	
	NanoZoomer 2.0-RS	6 preparations	
	NanoZoomer-SQ	1 preparation	
Huron	TissueScope CF	300 preparations. Fluorescence, with focal	Owner. BigTIFF
	TissueScope LE120	120 preparations	
	TissueScope LE	12 preparations	
	TissueScope PE	2 preparations	

Continue…

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Table 1 - Manufacturers and models of scanners of digital preparations

Manufacturer	Model	Charger capacity	Image format
Leica	Aperio AT2	400 preparations	Owner. SVS. SCN. TIFF
	Aperio AT Turbo	400 preparations	
	Aperio CS2	5 preparations	
	Aperio FL	5 p. Fluorescence	
	Aperio CS-O	1 preparation (immersion)	
	Aperio Versa	8 p. Fluorescence	
	Ariol	200 p (SL200). Fluorescence	Owner. Ariol. SCN. TIFF. JPEG
Medite	Precice 600X	480 preparations	Unknown
	Precice 600F	1 p. Fluorescence	
	Precice 500	1 (500A) a 5 (500B) preparations	
	Precice 100	1 preparation	
Menarini	D.Sight 2.0	5 preparations	Open. JPEG2000
	D.Sight F 2.0	5 p. Fluorescence	
Motic	EasyScan Pro	6 preparations	Owner
Olympus	VS120-S6-W	6 preparations	Owner. VSI. JPEG. TIFF
	VS120-L100-W	100 preparations	
Optra Systems	Optra SCAN	10 preparations	Owner. JPEG2000
Philips	IntelliSite Ultra-Fast Scanner (UFS)	480 preparations	Owner. TIFF
Roche / Ventana	iScan HT	360 preparations	Owner. BIF. TIFF
	iScan Coreo	160 preparations	Owner. BIF. TIFF. JPEG2000
Sakura	VisionTek	4 preparations	Owner. Svslide

The practical approaches that have solved better this problem of variety of image formats until the date are:

- viewers that read the main formats from the market (Leica, Hamamatsu, Mirax, etc.) of digital slides.
- manufacturers provide information of exchange, making available libraries in order to create the proprietary formats or at least to export automatically the proprietary files to open formats;
- free Software that can read and transform from a proprietary format (if it is allowed) to another. Highlight the following initiatives:
  - OpenSlide.org, able to read seven formats: Aperio (.svs, .tif), Hamamatsu (.vms, .vmu, .ndpi), Leica (.scn) MIRAX (.mrxs), Philips (.tiff) Sakura (.svslide) Trestle (.tif), Window (.bif, .tif) and TIFF generic frames (.tif) [6];
  - The Open Microscopy Environment (https://www.openmicroscopy.org/). Bio-Formats allow to read until 143 different formats;
- provide manufacturer independent solutions that are able to manage data storage for any type of file, such as “Vendor neutral archive” (VNA), but it does not solve the problem of visualizing the original images correctly.

Fortunately, in digital pathology, it has been done a significant work in developing international standards in three major areas: Health Level 7 (HL7) for the exchange of messages and documents, Digital Imaging and Communication in Medicine (DICOM) to the storage and exchange of images and Systematized Nomenclature of Medicine – Clinical Terms (SNOMED CT) to unify clinical terms.

In addition, today we have an international organization called Integrating Healthcare Enterprise (IHE) that prepares documentation and test bed to optimize the use of the standards mentioned above (HL7, DICOM and SNOMED CT).

HL7

HL7 is a standard that defines the messages between applications, but it is also essential in the pathology image management, then due to these standard messages it is posible to identify and trace correctly the samples

and patients, normalize the structure of pathology reports using the Architecture Clinical Documents (CDA) and report the pathology information system with other information systems[7].

DICOM

In hospitals, for efficient management of images and patient data associated with the same, the great repositories of image are based on a central Picture Archiving and Communication System (PACS), that we connect through DICOM standard of image exchange[8].

The main reasons that DICOM has been chosen for its use in telepathology and digital pathology are, above all, the excellent results obtained in radiology, besides being able to be used today, without any modification of the existing PACS for its use in "smaller images" like the macroscopic pictures. For its use in microscopic images of pathology anatomy, given its big size and complexity (more than 14 GB of information compressing and a size of each image often superior than 64,000 x 64,000 pixels), it was necessary two important changes in the standard DICOM to adapt it to pathology:

- in pathology anatomy, the image is centered in the sample or specimen, not in the patient (unlike radiology). This change was included in the DICOM Supplement 122[9].
- the large images can not be saved directly as the DICOM standard includes a limit on the attributes rows / columns, which can not exceed 2^{16}, that is, 64,000 pixels and this limit has been maintained to ensure compatibility with PACS already installed, so DICOM in the supplement 145, proposed that large images, such as the ones of pathology anatomy, should be divided into series of images (Figure 1)[10].

Until 2015 they have not begun to distribute comercial products of digital pathology that were consistent with the DICOM supplement 145, because the company Aperio, later acquired by Leica, patented the method described in this supplement to store and retrieve images via DICOM (US 20120099769 A1). In 2015 the company Leica Biosystems Imaging authorized the use of the patent, free of charge, for companies involved in DICOM.

Despite having a standardized method of storing and transmitting images and associated data (metadata), it is still necessary to normalize the image format that is going to transmit or exchange and the compression of images. Unlike radiology, the enormous size of pathology anatomy images makes necessary to use efficient compression techniques. Also, it is necessary to create an international standard related to the entries that are made in the images and with the results (data and masks) obtained from automated analysis of microscopic image.

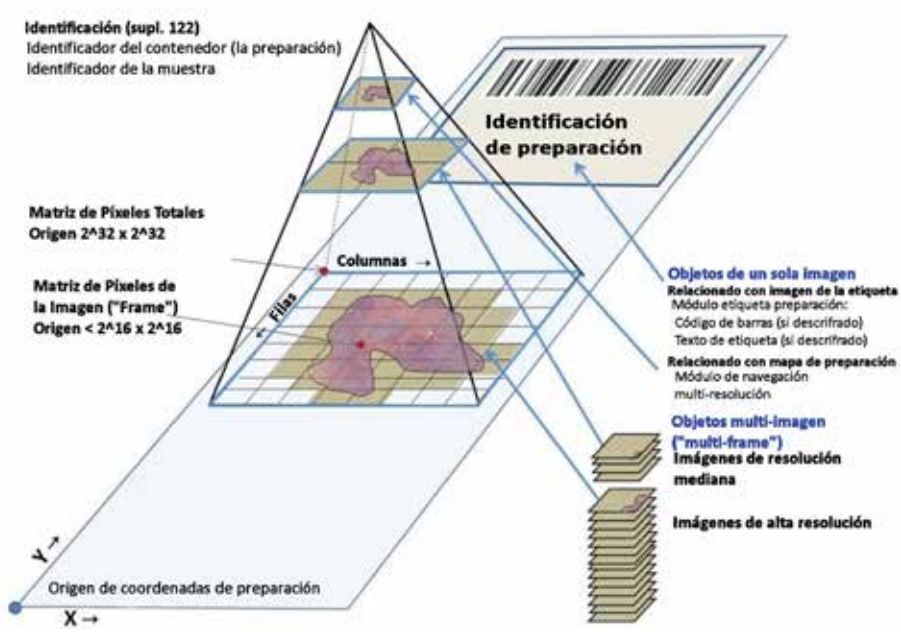

Figure 1 - Representation of a digital preparation according to the DICOM Supplement 145.

IHE

IHE Anatomic Pathology (IHE-AP) is an initiative that helps understand what the best way to use the standards like HL-7 and DICOM is. Since 2010, it has been defined technical profiles of IHE integration for the general circuit in pathology anatomy for the exchange of information with tumor registries and pathological structured reports in pathology anatomy. All these documents are available on IHE website[11].

The April 15, 2010, in the IHE Connectathon held in Bordeaux, the company SATEC presented the proposal of interoperability for implanted telepathology in the Health Service of Castilla-La Mancha (SESCA), Spain. During these tests, it was possible that the telepathology portal of SESCAM (called Serendipity)[12] was able to search, retrieve and properly display images of all ten PACS from different manufacturers at the Connectathon. This was the first "conformace statement" of IHE related to a pathological anatomy solution. Additionally, during the Connectathon, storage tests (storage / commitment) between the telepathology portal and PACS were made and it was also managed to store images of pathological anatomy in the 6 PACS where tests were made, being possible to view them with other manufactures´ viewers.

Recently, they have merged the groups IHE of pathological anatomy and clinical analysis.

SNOMED CT

- there is a group with a special interest in pathology (IPaLM SIG) within SNOMED CT, regulated by the international organization called International Health Terminology Standards Development Organization (IHTSDO). SNOMED CT is the most appropriate terminology to represent concepts used in pathological anatomy for both types of specimens or topographic as well diagnosis. It is also used in structured reports of pathological anatomy of the American College of Pathology and IHE. However, for optimal use of SNOMED CT in pathology, it is necessary to make the following changes in this terminology[13]:
  - it must decide whether anatomopathological diagnoses are coded by morphological findings hierarchy (part of the body structure hierarchy) or are encoded as Clinical Findings. Right now, you need to use mixtures of the two hierarchies to locate all diagnoses used daily.
  - ideally, they should use concepts that were in a single hierarchy if used for the same purpose. It is easy to understand that the term "lupus nephritis" is not the same from the point of view of clinical care from the point of view purely morphological or anatomopathological. For that, it is necessary to complete the corresponding hierarchy. For instance, if it is decided that everything that is in the "final diagnosis" of a pathological anatomy report must be coded with the hierarchy of morphological findings, it will be necessary to add more than 5,000 concepts to this hierarchy of SNOMED CT, then almost dermatopathology or nephropathology diagnoses currently alone are in the hierarchy of clinical findings.

DISCUSSION

The role of the pathologist in the standardization in telepathology today

Pathologists should lead standardization efforts in applied computing to pathology. The best way of doing it is to participate in DICOM WG26, HL7-Anatomic Pathology, IHE-Pathology and SNOMED CT- IPaLM SIG, as they are open groups to the participation of all those who wish to collaborate in the development of these standards. However, the participation of pathologists in these groups is still very small.

As users, pathologists should require companies that distribute products in our countries meet these international standards.

Finally, it is also possible to develop standardization in digital pathology through research and technological innovation. In this sense, between the years 2007-2011 it was developed in Euro-Telepath European project, between short term objectives, the development of international standards as a basis for the creation of telepathology networking. In 2014 they began the european project AIDPATH (http://aidpath.eu/) for the colaboration between companies and the academic world in digital pathology and whose main efforts are focused on the development of processing tools and automated image analysis, to promote the standardization in digital pathology (including standardization of aspects such as the color or the experience of viewing images) and establish the basis for a program of quality assurance in digital pathology.

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