# Development of an online slide library

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## ABSTRACT

Digital Cytology consists in the conversion of a glass slide into a digital image. The application of digital cytology in education, conferences, telecytology, publications and cytology websites has shown increased accessibility to cytology, along with the quality and efficiency improvement of the health services.

In this study we intend to develop an Online Slide Library of gynecological cytology available to students for the gynecological cytology

One hundred samples of gynecological cytology were selected and scanned by the whole slide imaging method. The Online Slide Library was created with HyperText Markup Language 5 and the digital images sharing within the Library was conducted using the institution network server.

In education, the Online Slide Library developed allows the easier access to the study of gynecologic cytology as well as the access to rare and/or old samples. Also several students can observe the same case simultaneously with this method of digital cytology.

The results of the present work allow to conclude that the Online Slide Library is a complementary tool for the gynecological cytology study.

**Key-words:** Digital Cytology, Online slide library, Gynecological Cytology, Education

## INTRODUCTION

The impact of technological innovation is becoming more and more visible, particularly on the methods and techniques for diagnosis in several areas of intervention within the health field. In cytopathology, optical microscopes have been continually shaped in order to enhance ergonomic conditions and image quality. In this extent, technological advances allied to the constant challenges of diagnosis prompted the development of microscopes with a capacity of digitizing cytological preparations, which are becoming more and more useful to practitioners[1-6]. In the domain of Anatomical Pathology, the possibility of scanning samples has made fundamental changes in areas such as Histology, Cytology, Immunohistochemistry and Cytogenetics, contributing to an automatization of the diagnosis[1,6].

In the health field, digital cytology can be applied by developing a slide archive, allowing health services to better manage the lab's physical space, have easier access to information and also ensure the quality and integrity of the cytological image in the course of time[7]. On the diagnosis sphere, the reviewing of cases or the request for a second opinion to other health institutions (telecytology) has been more and more executed by practitioners, avoiding not only expenses with the shipment of cytological preparations, but also displacements of pathologists and possible losses of material[1,2,8,9]. Digital cytology allows equally to increase the quality and efficiency of the service, as it simplifies the internal and external quality control in due time. The progresses in the technological field have also allowed performing automated screenings, based on the analysis of images obtained by scanning samples[2]. Furthermore, considering the significant increase in the volume of samples of gynaecological cytology in Anatomical Pathology services as a consequence of the adhesion to the implemented Screening Programmes, the use of digital cytology constitutes itself of extreme importance in the training of technicians and cytotechnicians, ensuring the improvement and innovation of the screening practice through a correct interpretation of premalignant cytological lesions and infections[2,10-12]. In the field of Education, digital images have allowed studying rare and old samples, but on top of that it has enabled distant learning, taking cytology to students anytime and anywhere. Besides these applications, digital images can also be used in conferences, in the continuous assessment of health professionals, in the elaboration of tests for students and professionals' admission, and in websites for instant access[-9,12,13]. Nowadays, illustrations on publications (such as books and scientific journals) are also performed through this innovating method, enabling the creation of documents with high-definition images[1].

Digital cytology consists on performing the screening through a bi or three-dimensional image displayed on a monitor[2]. There are several methods to capture and produce digital images - for instance, the *Whole Slide Imaging* (WSI) technique, which allows the complete scanning of the entire slide through high-resolution scanners[1,2,10,14,15].

Processing the image involves its capture by digitization, followed by storage in a device with high memory capacity, edition (if necessary) and, finally, the observation, presentation or sharing[2,8]. Identically to the screening in a traditional optical microscope, the obtained digital image can be manipulated with the help of an image viewer software, by dragging, magnifying and focusing through the mouse or the keys of the keyboard which move the cursor, allowing a complete and detailed analysis of the sample[1-3]. However, the nature of a cytological sample owns special characteristics, and its digitization constitutes a bigger challenge when compared to other types of samples[1,2,16]. While a histological sample might fit in a single focal plane, as it is represented by a plain histological cut, the nature of a cytological sample (often three-dimensional) requires the use of a microscope with a high-resolution lens, enabling the application of numerous focal points so that the original image is correctly presented[1]. Thus, it is important to choose the most appropriate equipment in order to obtain an image onto which is possible to observe, as sharply as possible, all the cells contained in a cytological preparation. The *z-stack* function, available in some equipment, allows scanning different focal points

of the same slide, focusing the images manually and in different planes. As a result, it is possible to obtain a single image through sequential aggregation of the digitization of the various planes, ultimately allowing the observer to use the focus function in digital form for the correct visualization of the smear, especially in overlapped and three-dimensional groups[1,16,17].

As already mentioned, this method presents multiple advantages, susceptible of application in numerous fields. However, some limitations linked to the scanning, storage and transference of the images have not made possible, until this date, the spreading of this method through the numerous health services and teaching institutions[2].

The aim of this work consists in the scanning of slides of gynaecological cytology samples, in order to develop an Online Slide Library, shared online with the students of the Bachelor Degree in Anatomical Pathology, Cytologycal and Tanatological (APCT).

## METHODS

### Selection of the Cases

One hundred samples of gynaecological cytology were selected from the Slide Archive of the Technical and Scientifical Area of APCT (School of Allied Health Technology of Porto – ESTSP). This archive is constituted by cytological preparations performed upon spare collected samples, kindly provided by Anatomical Pathology labs for academic purposes. The anonymity of all samples was guaranteed before the yielding. The diagnostic categories of the selected samples are identified in **Table 1**.

**Table 1** – Number of cases, by cytopathological diagnosis, selected to the Online Slide Library

| Cytopathological Diagnosis | | | | Number of cases |
|---|---|---|---|---|
| Unsatisfactory | | | | **2** |
| Negative for Intraepithelial Lesion or Malignancy (NILM) | Negative for Intraepithelial Lesion or Malignancy (NILM) | | | **8** |
| | Reactive changes associated with | Radiation | | **3** |
| | | Inflammation | | **3** |
| | | Atrophy | | **4** |
| | Microorganisms | *Trichomonas vaginalis* | | **9** |
| | | Fungi morphologically compatible with *spp Candida* | | **9** |
| | | Imbalance of the flora suggestive of bacterial vaginosis | | **2** |
| | | Bacteria morphologically compatible with *Actinomyces* | | **8** |
| | | Cellular changes compatible with *Herpes simplex* virus | | **4** |
| Atypical/Abnormal Epithelial Cells | Squamous Epithelium | Low Grade Squamous Intraepithelial Lesion (LSIL) | | **10** |
| | | High Grade Squamous Intraepithelial Lesion (HSIL) | | **9** |
| | | Atypical Squamous Cells (ASC) | Of Undetermined Significance (ASC-US) | **7** |
| | | | Cannot Exclude HSIL (ASC-H) | **6** |
| | | Squamous Cell Carcinoma | | **3** |
| | Glandular Epithelium | Adenocarcinoma | Endometrial | **2** |
| | | | Endocervical | **2** |
| | | | No other Specification (NOS) | **5** |
| | | Atypical Glandular Cells (AGC) | | **4** |
| Total Number of Cases | | | | **100** |

The sample selection process was performed based on the quality of the smear and the amount of cytological material. Among the selected cases are liquid-based cytology samples (*Thinprep*®, *Surepath*® and *CellPrep*®) and conventional smears. The clinical information of each case was registered and made available on the Online Slide Library.

### Image Digitization

The scanning of the selected smears was performed in the Institute of Molecular Pathology and Immunology of the University of Porto (IPATIMUP) through the WSI method and using the *NanoZoomer 2.0HT* equipment (Hamamatsu, Japan). All the smears were digitized using the *line scanning* technique, with a 40x magnification. The *z-stack* functionality was used in the digitization of all the conventional smears with nine focal planes in a 1 µm interval, as well as on some liquid-based samples with five focal planes and a 1 µm interval. The obtained images were converted in *NanoZoomer Digital Pathology Image* format (.ndpi).

### Online Slide Library

The Online Slide Library was developed in *HyperText Markup Language* 5 (HTML5). The images representing each one of the integrated cases were obtained through the *Export* function of the *NDP.view* viewing software (Hamamatsu, Japan).

The uploading and access to the images available on this platform were achieved using the ESTSP network server. The access was assured by creating a shortcut file in *ScanScope Image Set* (.sis) format to each case on the *Aperio ImageScope* software (Leica, Germany), to download and display through the ESTSP's wireless network.

### Image Viewing Software

The visualization of the digital Images was performed using the *Aperio ImageScope* software (Leica, Germany), available to download in the Online Slide Library's page. The main control panels and the main navigation tools used to display the digital images are identified in **Fig.1**.

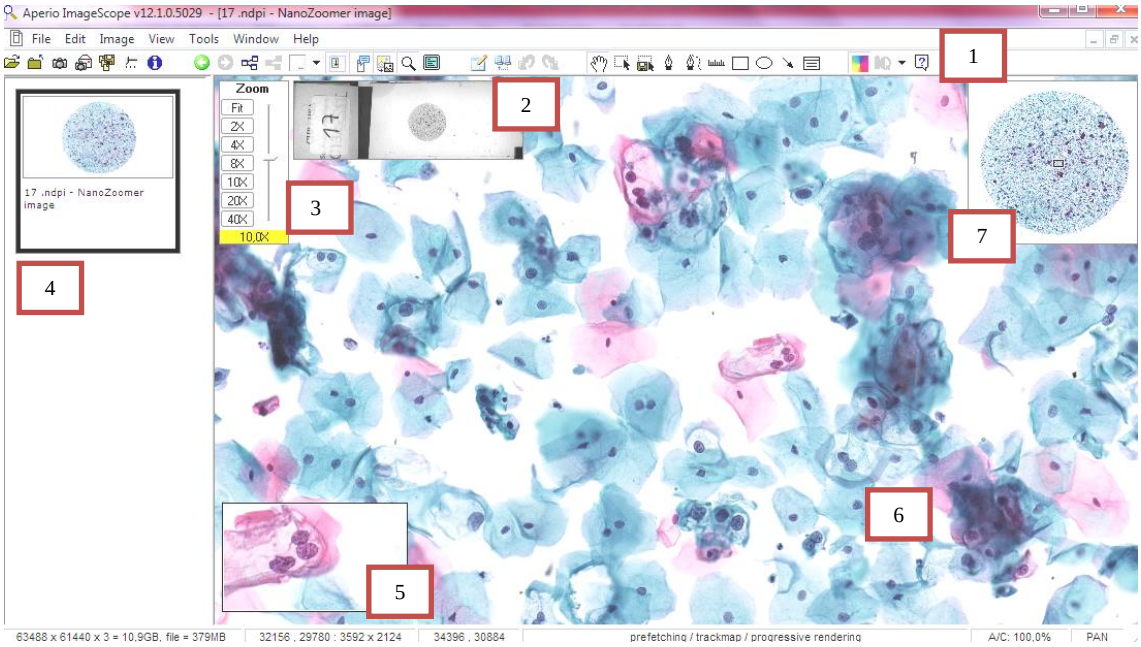


**Fig.1** – Main control panels and navigation tools of the *Aperio ImageScope* software (Leica, Germany). (1) Toolbar, (2) Label Window, (3) Zoom Toolbar, (4) Filmstrip, (5) Magnifier Window, (6) Main Image and (7) Thumbnail Window.

## RESULTS

### Online Slide Library

The Online Slide Library is available online at www.estsp.ipp.pt/sites/laminotecadigital. It consists of different sections in a single web page: “Início” (Home), “Citologia Digital” (Digital Cytology), “Aperio Imagescope” and “Casos” (Cases) (**Fig.2**, **Fig.3**, **Fig.4** and **Fig.5**). In the centre of the section “Home”, there is a link to the section “Cases” (**Fig.2**). On the section “Digital Cytology”, it is possible to observe a brief description of the concept of Digital Cytology, as well as the main employments of the method and its main advantages in Education (**Fig.3**). On the section “Aperio Imagescope” there is a link to download the Image Viewing software, as well as some illustrative images of the program (**Fig.4**). Finally, on the section “Cases”, there is a list of the one hundred cases of Gynaecological Cytology available in the Online Slide Library. This list is organized according to the diagnosis specified in **Table 1.** Each case contains the most relevant clinical information useful to understand the diagnosis, as well as the declared cytopathological diagnosis. This information can be consulted by dragging the cursor across the image which illustrates the case. On the left side of the section “Cases”, it is also possible to find a group of filters, which assure to the student an easier access by choosing the diagnostic categories he wants to observe (**Fig.5)**. The digitizing of each case resulted in digital images with dimensions varying from 297 *megabytes* to 39 *gigabytes*, depending on the cytology type and the use of the *z-stack* function. In total, 125 *gigabytes* of the ESTSP network server were filled.

The amount of focal planes of the digital images obtained through the *z-stack* function varied from nine planes (to the conventional smears) and five planes (to the liquid-based cytology samples). As an example, **Fig.6** shows a sequence of images of the same cellular group from case number 17, in the five different focal planes.

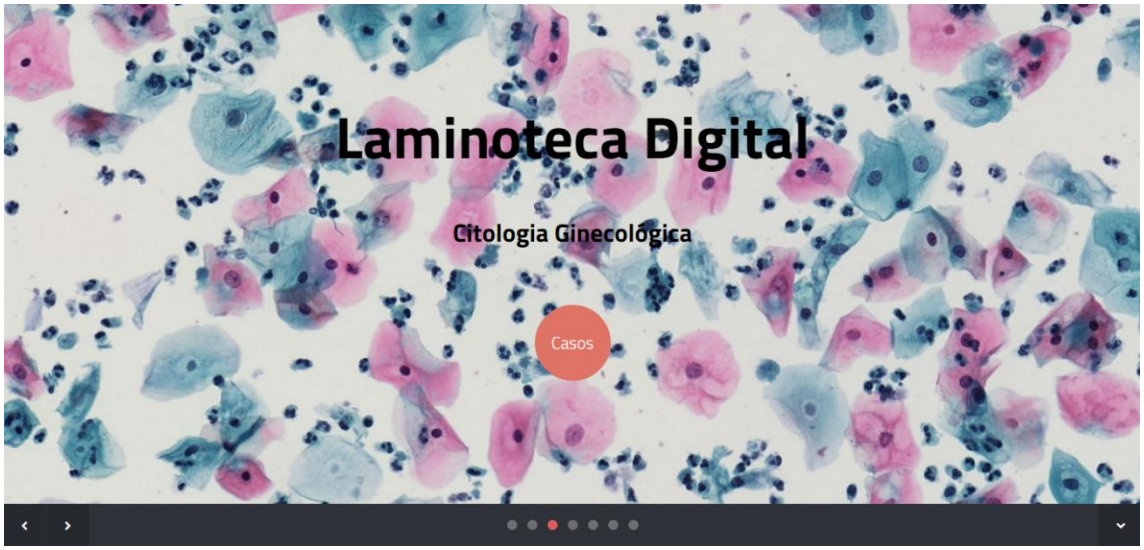


**Fig.2 -** Illustration of the contents in the section “Início” (Home) with introductory images to the Online Slide Library.


**Fig.3 -** Illustration of the contents in the section “Citologia Digital” (Digital Cytology).

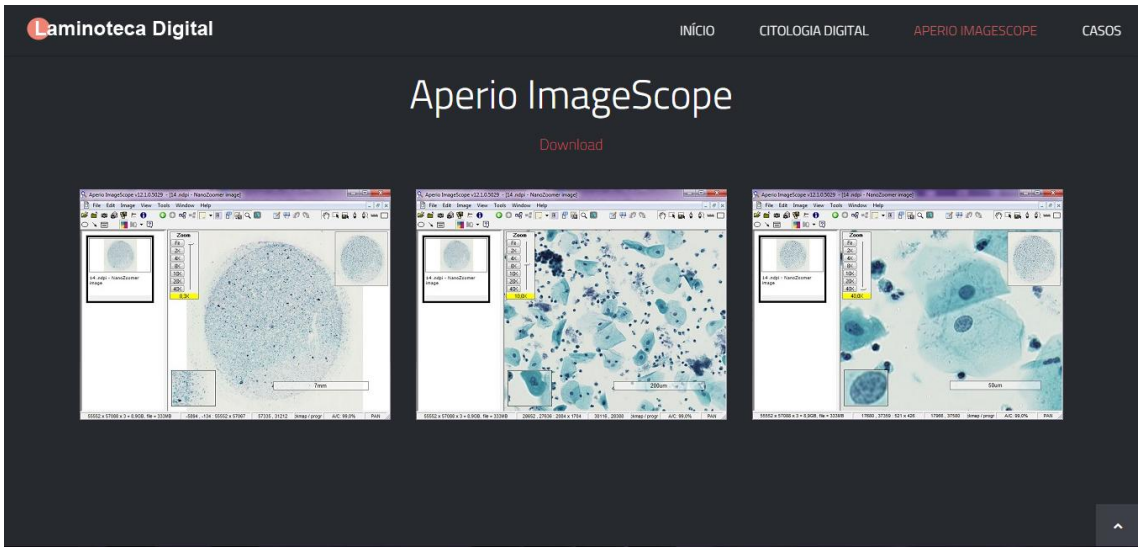


**Fig.4 -** Illustration of the contents in the section “Aperio Imagescope”.

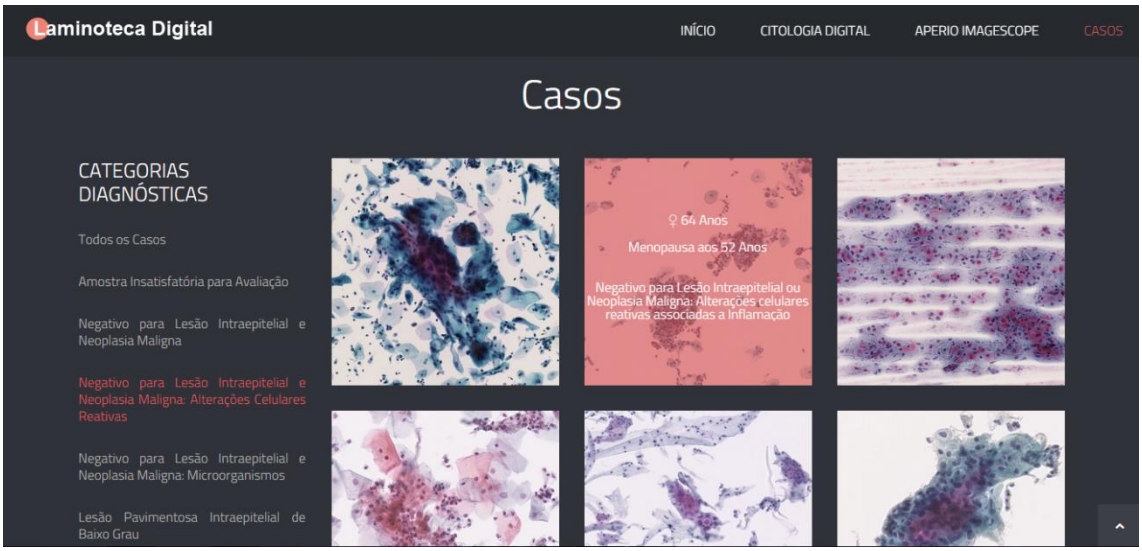


**Fig.5 -** Illustration of the contents in the section “Casos” (Cases). Presentation of the medical information associated with one of the cases of the Online Slide Library.

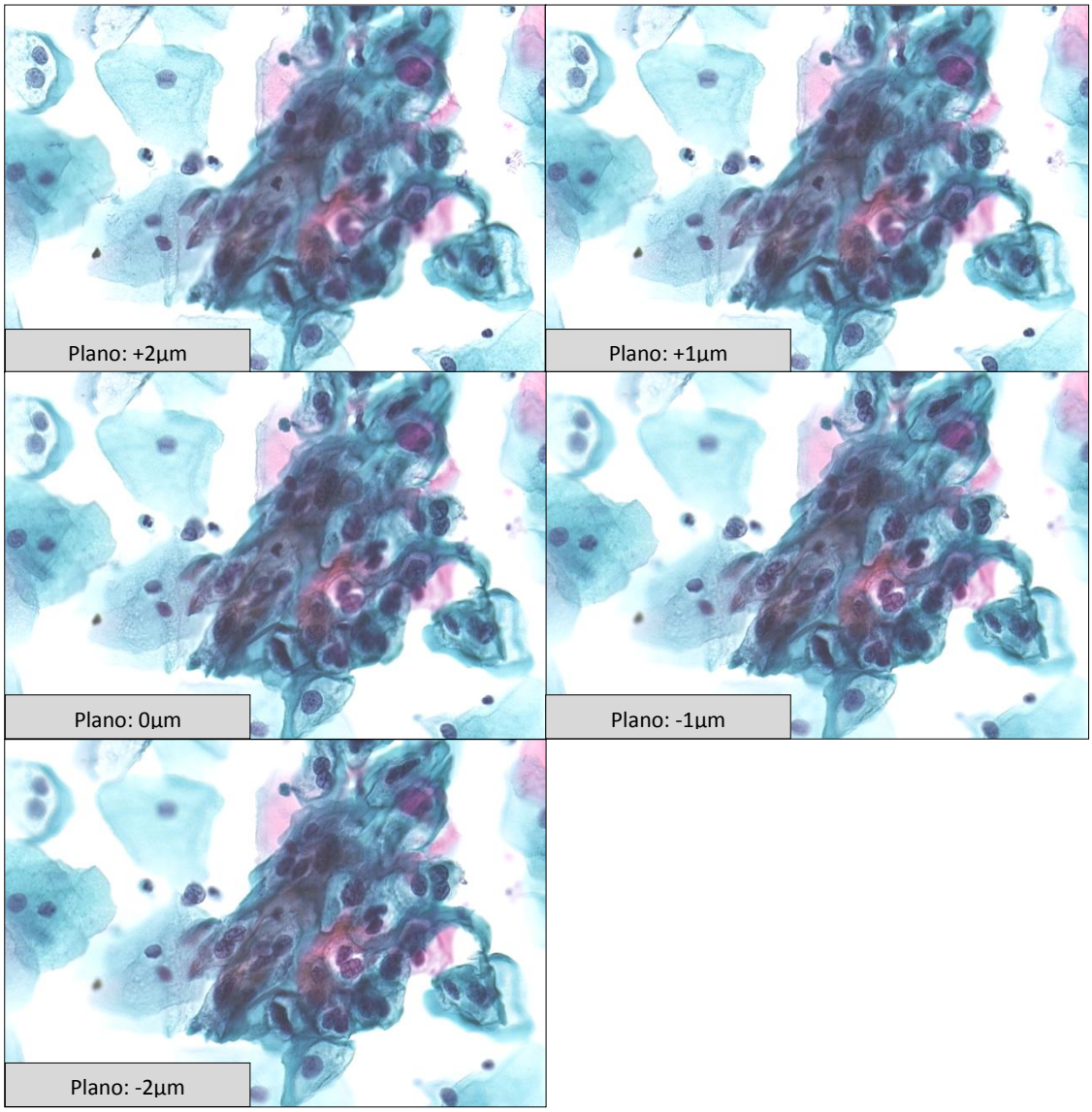


**Fig.6** – Sequence of images of the same cellular group in the five different focal planes, from case number 17. Images magnification: 40x.

## DISCUSSION

Since 1999, when *Art Wetzel* and *John Gilbertson* created the first high resolution digitizing equipment of slides, endowed with great speed and total automatization, the interest in the use of scanners by the WSI technology is getting higher and higher[18].

In the present work, a library of slides of gynaecological cytology was created, in digital form and available online (Online Slide Library) with the purpose of being used for the study of gynaecological cytology by the students of the Bachelor Degree in APCT of ESTSP.

The Online Slide Library was projected as a dynamic, appealing, intuitive, informative and user-friendly webpage, in order to encourage the students to make use of it, in a simple and interactive way.

The inclusion of digital images in the Online Slide Library constituted one of the main technical problems faced during the development of the project, due to the size of the files. To supplant this difficulty, it was

necessary to create a shortcut file to the original file, in a different format and with a much lower dimension, which would allow a fast upload and download of the images.

In order to evaluate the utility of this digital archive as a tool to complement the training in gynaecological cytology, a survey was conducted among the students of the Bachelor Degree in APCT. The results of the survey allowed to observe a great interest in the use of this web-based application, with a medium classification of 4.85 out of 5 in the parameters linked to the "Utility of the Online Slide Library". These results lead to the conclusion that the Online Slide Library is a useful complementary resource in the training in gynaecological cytology.

Despite the numerous applications of digital cytology, the intention of this project was to use this platform for educational purposes. Traditionally, the study of cytology is made upon books, slides and microscopes. However, this innovating method will permit, from now on, that the study is performed without the need of displacement or availability of the aforementioned material, making cytology easily accessible[2,16,19]. Furthermore, the use of an appropriate software allows that a significant number of students may access simultaneously to the same case, contributing to a more interactive and less individual study of cytology, and conducing to an improvement in pedagogic training[1,2,16]. Image digitizing also enables the study of rare cytological samples which are often restrained from observation, since they can easily be broken or lost. Another advantage of this method resides in the fact that even the slides of least recent cases which were digitized at the appropriate time can be indefinitely accessed, without the need of applying a new stain or re-mounting of the original slide[2].

In spite of the aforementioned applications and respective advantages associated, some disadvantages have prevented the method from expanding itself to all the services of Anatomical Pathology. The need for a digitizing equipment and a computer capable of matching its great functioning, as well as high capacity storage devices, lead to considerable expenses to the institutions interested in adhering to this technology. In addition to this, the studies conducted to validate the method are scarce and extremely limited, and there is not a defined pattern for its use (several equipment and software available). Additionally, as a consequence of being a relatively recent method, it also requires the need for a specialized training on the correct use of the equipment by health professionals[20]. On the other hand, the advantages of using the traditional microscope are well-known among practitioners, such as the familiarity with the equipment, ease in moving the slides and absolute control over the focus and zoom functions. For all these reasons, digital cytology is a reality only in some services of Anatomical Pathology.

The aim of this study is not replacing the traditional screening method; it is, instead, to implement a futuristic methodology, addressing the use of new technologies currently widespread among young people, and allowing a more comprehensive and attainable study of gynaecological cytology. Through the developed website and the results of the conducted survey, it is possible to conclude that the Online Slide Library proves to be a very useful complementary tool in the training in gynaecological cytology.

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