Ann Ist Super Sanità 2010 | Vol. 46, No. 2: 123-129
DOI: 10.4415/ANN_10_02_04

How do young and senior cytopathologists interact with digital cytology?

Maria Rosaria Giovagnoli[a], Enrico Giarnieri[a], Elisabetta Carico[a] and Daniele Giansanti[b]

[a] *Seconda Facoltà di Medicina e Chirurgia, Università Sapienza, Rome, Italy*
[b] *Dipartimento di Tecnologie e Salute, Istituto Superiore di Sanità, Rome, Italy*

Summary. Today thanks to the technological advances in information technology the scenario of utilization of digital cytology has radically changed. New competitive systems, such as client-server architectures are now available in digital cytology. Their application in telemedicine should be investigated. A new interactive tool designed for the final destination user (the cytopathologist) has been proposed. Taking into account the different expertise of the subjects of the study, the investigation was focused both on the senior cytopathologist and on the younger student pathologist. The methodology was tested on 10 students of a Master in cytopathology and on 3 senior cytopathologists. The study showed that the use of digital cytology applications is effective and feasible for telediagnosis. In particular, the study on younger and senior expert investigators showed that, although they interacted with the novel technology of the virtual slide in a different manner, all of them reached the objective of a "correct diagnosis". This investigation, in consideration of the effectiveness of the digital cytology, also showed other indirect and tangible cost-benefit and quantitative advantages. In particular for the learning methodologies for the students of the Master itself and for the biomedical personnel involved in diagnosis.

Key words: telemedicine, digital cytology, tele-pathology.

Riassunto *(In che modo i citologi giovani e quelli esperti interagiscono con la citologia digitale?)*. Oggi grazie ai progressi tecnologici nelle tecnologie dell'informazione e della comunicazione lo scenario dell'utilizzo della citologia digitale è radicalmente cambiato. Nuovi sistemi competitivi, come ad esempio le architetture client-server sono oggi disponibili in citologia digitale. Il problema dell' analisi di queste nuove tecnologie sta diventando pertanto un aspetto importante in telemedicina. Un nuovo strumento interattivo che si basa sulla figura dell'utente finale cito-patologo è stato proposto per questo scopo. In particolare, tenendo conto delle differenze nella pregressa formazione, la metodologia è stata focalizzata sia sul cito-patologo esperto che su quello giovane in formazione universitaria. La metodologia è stata testata su 10 studenti di un master in citopatologia e 3 esperti in citopatologia. Il lavoro ha dimostrato che l'uso delle applicazioni di citologia digitale è efficace e fattibile per la tele-diagnosi. In particolare, la ricerca ha dimostrato che nonostante i due gruppi interagissero con la tecnologia in modo diverso entrambi hanno raggiunto l'obiettivo della "corretta diagnosi". Questa ricerca in considerazione della provata efficacia della citologia digitale inoltre ha mostrato vantaggi tangibili. In particolare sono stati intravisti dei vantaggi costo-beneficio nell' ambito della formazione (nell'immediato nel master stesso) e per il personale addetto alla diagnosi nel laboratorio biomedico.

Parole chiave: telemedicina, citologia digitale, tele-patologia.

INTRODUCTION

Up to 5-10 years ago digital cytology was principally based on the design and construction of a few identical and expensive platforms with microscope units and software tools for the display and for the point to point tele-control (zooming, moving cutting of pieces of images). Today, thanks to the wonderful development of information technology, the diffusion of new visualization strategies and the availability of low cost or free visualization proprietary tools the scenario has radically changed [1-3]. New competitive systems as client-server architectures are now available. In a typical today's architecture there is an on site server with a scanner or alternatively a remote digital cytology third party server (as the web service such as the Leeds' centre (www.virtual-

Address for correspondence: Maria Rosaria Giovagnoli, Università Sapienza, Seconda Facoltà di Medicina e Chirurgia, Azienda Ospedaliera Sant' Andrea, Via di Grottarossa 1035-1039, 00189 Rome, Italy. E-mail: mariarosaria.giovagnoli@uniroma1.it.

pathology.leeds.ac.uk/index.php) for the creation of the slides and low cost (or free) user-friendly applications proprietary software tools for the navigation on the virtual slide which can be installed in remote clients. This new methodology especially the one based on a third party server is rapidly spreading and is becoming a useful means for:

- the discussion of complex cases;
- the minimization of resource requirements (more hospitals could share the same cytologists);
- e-learning [4-8].

PURPOSE

The investigation of the uses of new technologies is becoming a primary aspect of studies in telemedicine. The task to investigate the new technologies is becoming a core aspect in telemedicine. However very few studies have focused on this in digital cytology and mainly only on single aspects, and more importantly no one on the destination-user of the technology: cytopathologist.

The aim of the study is to:

1. design an environment to investigate the technologies relevant to digital cytology with particular reference to the technologies related to the core element virtual slide, starting from a previous study on technology assessment (TA) in telepathology [9] in which it has also been reported a review of studies in this field. Telecytopathology requires a different methodological approach than telepathology. Cytopathology has the further need of focus functions that complicate the management of the files representing virtual slides. A TA study on digital cytology should therefore take into account these additional aspects in comparison to a TA centered on telepathology [9];
2. investigate by means of the designed questionnaires how young (students) and senior cytopathologists relate with a digital cytology application during routine diagnosis.

MATERIALS AND METHODS

A workgroup that included the authors has designed two electronic questionnaires based on interactive forms. One of these was to investigate the acceptance of the technologies for scanning and navigating the virtual slide; the other to evaluate the acceptance of the digital cytologic diagnosis, both starting from a previous version centered in tele-pathology [9] (see in [9] for more details about the constructions of the forms).

Questionnaire for the acceptance of the digital cytology technology

The first questionnaire has been designed to investigate the software package tool itself. It has been organized into 6 sections. *Table 1* details each section with the correspondent description. The second point concerning the methodology is centred on the figure of the cytopathologist: in spite of the fact that a wide range of objective quantitative methods of evaluations are available, the subjective aspects in the field of evaluation have always been considered the most important ones: it is on the opinion of the destination-users (based on their internal neural mechanisms) that is constructed the diagnosis and not on the basis of an objective tool for the image quality assessment. *Figure 1* details a section (3) of the questionnaire (translated into English).

Table 2 shows in details the content of the section 5 "Requirements of the platform" for the standardization of the personal computer. The conditions of the test have been standardized according to this section.

Table 1 | *Sections of the questionnaire designed to investigate the acceptance of the technology*

Section number	Section title	Description
1	General data	Contains the general data of the package and of the subject involved in the study.
2	Perception of the subjective quality	Contains a number of questions on the subjective perceived quality with a scoring based on 4 levels. This section also contains specific questions of interest for pathology such as chromatin details, degree of recognition of cytotype, degree of recognition of nuclear pile.
3	Navigation system	Contains a number of questions on the navigation with a scoring based on 4 levels. This section contains specific questions on the translation, zooming system and also a free comment.
4	Selection of the details	Contains a number of questions on the selections of the basic details with a scoring based on 4 levels. Also open question are available in this section such as the force and weakness points of the package.
5	Requirements of the platform and connection	This section is for the designers of the test. It contains the minimal requirements of the system according to the producers' datasheets.
6	Final comment	

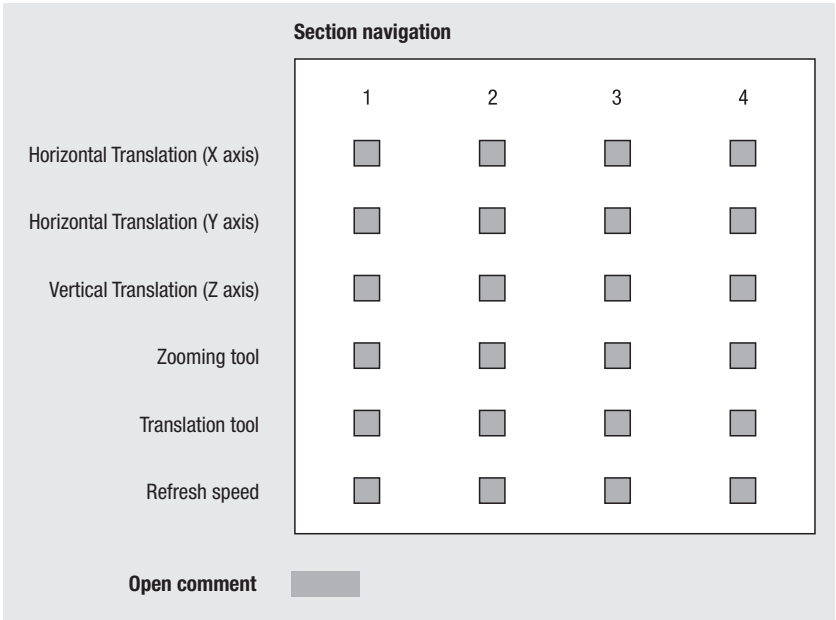

Fig. 1 | *Section 3 (navigation system) of the questionnaire designed to investigate the acceptance of the technology.*

Questionnaire for the acceptance of the digital cytologic diagnosis

The second questionnaire has been designed to investigate the acceptance of the digital cytologic diagnosis. *Table 3* details the sections with the correspondent objective.

For the design of the second section it should be taken into account that in a virtual-slide a region can be univocally detected by means of the following three methods of the software ImageScope or Web Viewer designed by Aperio (Aperio, CA) (www.aperio.com):

a) three types of information: X, Y coordinates with the Zooming factor (Image Scope viewer;
b) snapshot (usually a small size TIF image) (ImageScope Viewer) *(Figure 2)*;
c) an internet link address pointer to the region of the slide (Spectrum Web Viewer) allowing the remote exchange of a selected image *(Figure 3)*.

Table 2 | *Standardized requirements of the personal computer*

Description	Characteristics
Microprocessor	Dual Core Intel(R)Xeon(R) Processor 5160 (4MB L2 cache, 3.00 GHz 1333MHz FSB)
Ram	4GB(1GB*4) quad-channel DDR2-SDRAM memory (667 MHZ, ECC)
Cache	SATA No RAID (HDD*1 or HDD*2) 500GB SATA 3.0Gb/s NCQ HDD (7200 rotation)
Monitor	20inch TFT (1600*1200)
Board video	ATI(R) FireGL V3400 128MB DDR

Selection criteria of virtual slides

Pap-test glasses have been chosen to be converted into virtual slides. The Scanscope XT equipment has been used for the digitalization.

Thin layer Pap-tests were used instead of the traditional ones The advantages of this choice were the small surface that needs to be scanned and thus a shorter time frame for the testing, homogeneity of the sample and the decreased amount of time for inspection by the cyopathologist. Other considered parameters have been the staining and the absence of artifacts or bubbles.

Table 3 | *Sections of the questionnaire for investigating the acceptance of the digital cytology diagnosis*

Section number	Section title	Description
1	General data	Contains the general data of the software and of the subjects involved in the study and a description of the virtual glass.
2	Test ad detection of a region	Contains: An edit box for the total time of investigation: A list of fields with comments and edit boxes for the selection of coordinates X, Y, zoom and a snapshot of the individuated area with the detail of interest or alternatively a link internet address pointer to the region.
3	Diagnosis	It contains edit boxes for the diagnosis according to the Bethesda method. (www.cytopathology.org/NIH/).
4	Final comment	

Test and detection of a region

See instructions

Total time

N	Coordinate or PATH of the virtual slide	Eventual comment
1	X Y Zoom snapshot PATH	
2	X Y Zoom snapshot PATH	
3	X Y Zoom snapshot PATH	
4	X Y Zoom snapshot PATH	
5	X Y Zoom snapshot PATH	
6	X Y Zoom snapshot PATH	
7	X Y Zoom snapshot PATH	
8	X Y Zoom snapshot PATH	
9	X Y Zoom snapshot PATH	
10	X Y Zoom snapshot PATH	
11	X Y Zoom snapshot PATH	
12	X Y Zoom snapshot PATH	
13	X Y Zoom snapshot PATH	
14	X Y Zoom snapshot PATH	
15	X Y Zoom snapshot PATH	

Fig. 2 | *Section 2 (test and detection of a region) of the questionnaire designed to investigate the diagnostic accuracy using the virtual slide.*

Finally, samples with different diagnosis have been chosen (from negative to HSIL), in order to investigate by means of digital cytology different cytotypes and their nuclear and cytoplasmatic characteristics (physiological and not) and microbic flora.

Protocol and subjects

The selection was driven, as explained above, by the need to investigate subjects with a different expertise but who could be potential users of digital cytology.

Two groups were selected for the study:

- group A) 3 senior cytopathologists who had more than a 10 year working experience;
- group B) 10 students who were completing their Master in "diagnostic cytopathology and screening of population" after their Bachelor of Science or Medical Degree.

The defined protocol instruction was : assess the time spent to complete the diagnosis; select cytologic significant fields (optional). Time spent for selection was not calculated.

The protocol has been applied to 6 different scanned cytological glasses (virtual slides) chosen in consideration of the difficulty in the diagnosis. These slides came from 6 glasses with a full detailed diagnosis by standard microscopy, performed by other cytopathologists not involved in this investigation.

Architecture of the tele-cytology application

Different manufacturers were invited in this study. Aperio agreed to participate in this specific investigation. *Figure 4* details the architecture:

1. the scanner and Web server were in Bergamo in the Milestone centre (www.onlinetelepatologia.com/contacts.html);
2. the clients with Web-Viewer for the remote consulting were installed at the Sant'Andrea Hospital in Rome.

RESULTS AND DISCUSSION

Above all the function allowing the extraction of an internet path as a pointer of an analyzed region of the tool Web-Viewer installed in the clients computers at the Sant'Andrea Hospital was found very useful. Comments, in this case, showed the utility of exchanging this path by email or even by a simple chat on the web. Moreover was found that, also with pc arranged by a very basic configuration (sufficient to run the Microsoft Office tools) different from the standardized one shown in Table 2, it was possible to navigate the virtual slide without too many delays.

All the subjects involved in the study reached the objective of a "correct diagnosis". *Figure 4* shows some relevant snapshots from the virtual slides attached to the questionnaires. However younger and senior investigators related themselves

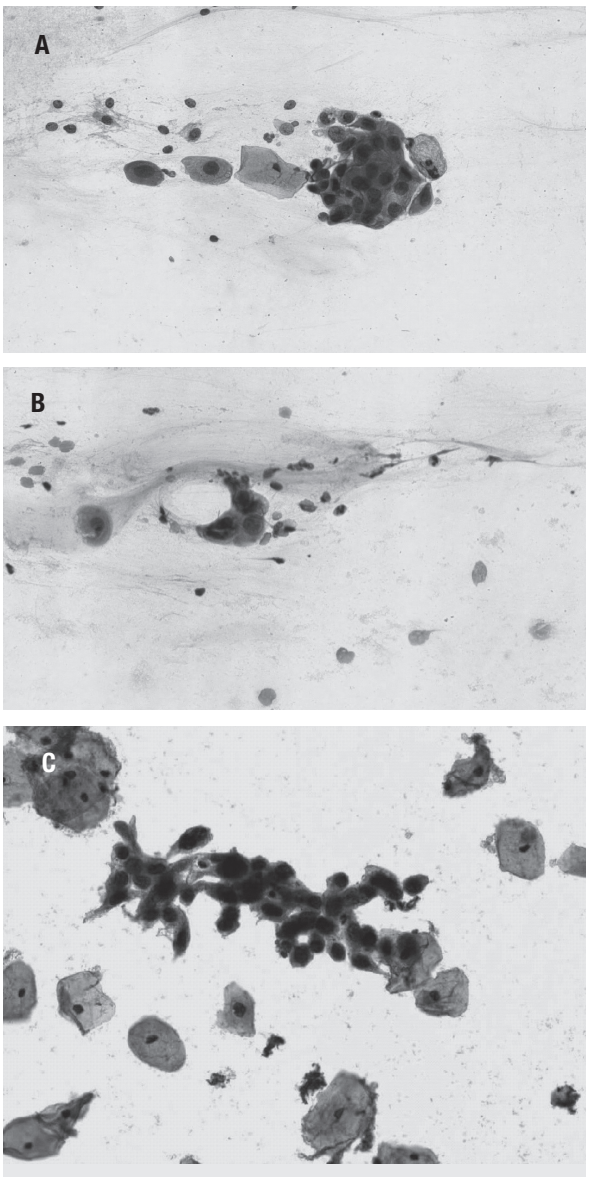

Fig. 3 | *(A-C) Snapshots from the digital cytology investigation attached at the questionnaires for the diagnosis.*

with the digital cytology application in a different manner depending on their previous biological experience/knowledge and informatics background. Even if the younger investigators had more practice with navigation / informatics tools the experts, during comparison reached the target within a very short time *(Table 4)*. *Table 5* details the outcome from the different sections of the questionnaire about the acceptance of the tool.

It has been shown that all the items from *Tables 1 and 3* received a high degree of acceptance. Younger investigators showed a high uniformity of responses in the section 3 on navigation. This intuitively depends on their previous and recent background of informatics courses specifically designed on image navigation [9] so that they had familiarity with similar navigation interfaces. When compared to senior investigators they showed a high variance in section 2 on the subjective perceived quality; this depended from the fact that not every subject has the same expertise thus the perceived quality is different. The experts assigned the lower scores to the questions of section 4 on the selection of details and on a specific question "speed of refresh" of section 3.

This can be explained by the fact that the subjects with higher expertise with traditional microscopy are not used to the latency time due to the "speed of refresh".

Experts showed a high uniformity of responses in the section 4 on selection of details. Section 5 was not submitted to the investigators but compiled by the authors of the study.

Table 4 | *Time of diagnosis using digital cytology*

Group	Mean time	Maximum time	Standard deviation
Students	58 min	78 min	15 min
Experts	22 min	32 min	7 min

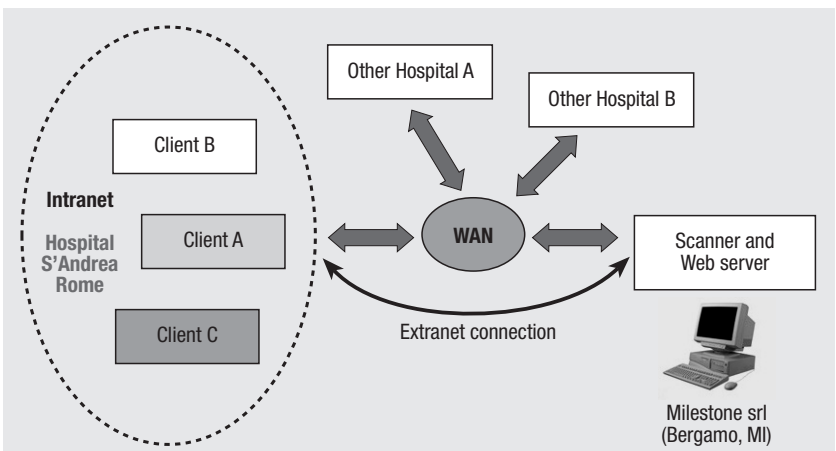

Fig. 4 | *Architecture of the digital cytology application.*

Table 5 | *Acceptance of the technologies of digital cytology*

Group	Section n	Section description	Mean score	Maximum score	Standard deviation
Students	2	Perception of the subjective quality	3.1	4	0.8
Students	3	Navigation system	3.9	4	0.2
Students	4	Selection of the details	3.2	4	0.8
Experts	2	Perception of the subjective quality	3.5	4	0.2
Experts	3	Navigation system	3.1	4	0.4
Experts	4	Selection of the details	2.5	3	0.2

Table 6 | *Significance of the investigation obtained using the Wilkoxon test to investigate the differences in the responses provided by the two groups in the questionnaire designed to investigate the acceptance of the technology*

Section n	Section description	Wilkoxon
2	Perception of the subjective quality	> 95 %
3	Navigation system	> 99 %
4	Selection of the details	> 95 %

Statistical significance

The statistical significance of the two outcomes from the questionnaires has been also investigated using two different methodologies Wilkoxon and Anova.

The first one (Wilkoxon) has been used to investigate the significance of the difference between the two groups (students, experts).

The second one (Anova) has been used to investigate the significance of the data obtained by means of the two tests.

For the investigation two different software tools have been used:

1. Matlab R13 (The Mathworks, USA) for the Anova test (www.mathworks.com);
2. Stata vers 3 (Stata; USA) for the Wilkoxon test (www.stata.com).

The significance obtained by means of the Wilkoxon test used to investigate the difference in the time used for scanning the virtual slide between the two groups was > 99%.

The significance obtained by means of the Wilkoxon test used to investigate the differences in the responses provided by the two groups in the questionnaire designed to investigate the acceptance of the technology was always > 95% as shown in *Table 6*.

Anova showed a significance always > 95% for the investigated data.

CONCLUSIONS

The work conducted at the Sant'Andrea Hospital in Rome showed that the use of digital cytology applications is effective and feasible for tele-diagnosis. The investigation based on the proposed methodology on younger and senior expert investigators showed that, although they interacted with the novel technology for the virtual slide in a different manners, they all reached the target "correct diagnosis". This investigation on the effectiveness of tele-cytopatology also showed other indirect and tangible cost-benefts and quantitative advantages especially for the learning methodologies [4-8] for the students of the Master itself and for the biomedical personnel involved in diagnosis, in details:

1. advantages for the students, who can analyze glasses in the form of a virtual slide at home without needing to go to the hospitals;
2. advantages for the hospital who can minimize resource requirements (more hospitals could share the same cytologists);
3. advantages for the personnel who has the possibility to perform cooperative diagnosis from home or from the hospital desk without needing to go to the microscope laboratory.

Conflict of interest statement

There are no potential conflicts of interest or any financial or personal relationships with other people or organizations that could inappropriately bias conduct and findings of this study.

Submitted on invitation.
Accepted on 5 May 2010.

References

1. Demichelis F, Barbareschi M, Boi S, Clemente C, Dalla Palma P, Eccher C, Forti S. Robotic telepathology for intraoperative remote diagnosis using a still-imaging-based system. *Am J Clin Pathol* 2001;116(11):744-52.
2. Dalla Palma P, Morelli L, Forti S, Barbareschi M, Piscioli F, Galvagni M, Boi S, Demichelis F. Telemetric intraoperative diagnosis among hospitals in Trentino: first evaluations and optimization of the procedure. *Pathologica* 2001;93(1):34-8.

3. Demichelis F, Barbareschi M, Dalla Palma P, Forti S. The virtual case: a new method to completely digitize cytological and histological slides. *Virchows Arch* 2002;441(2):159-64.
4. Giansanti D, Castrichella L, Giovagnoli MR. Telepathology training in a master of cytology degree course. *J Telemed Telecare* 2008;14(7):338-41.
5. Giansanti D, Castrichella L, Giovagnoli MR. E-learning for laurea in biomedical laboratory technicians: presentation of a pilot study. *Conf Proc IEEE Eng Med Biol Soc* 2007;11:3745-7.
6. Giansanti D, Castrichella L, Giovagnoli MR. How do young and senior cytopathologists interact with tele-cytopathology applications? Procedings of the 35th Congress of cytology. Lisboa: Blackwell publishing; 2009. 20 (Suppl. 1) p. 470.
7. Giansanti D, Castrichella L, Giovagnoli MR. New models of e-learning for healthcare professionals: a training course for biomedical laboratory technicians. *J Telemed Telecare* 2007; 13(7):374-6.
8. Giansanti D, Castrichella L, Giovagnoli MR. Tele-pathology requires specific training for the technician of the biomedical laboratory. *Telemed J E Health* 2008;14(8):801-7.
9. Giansanti D, Castrichella L, Giovagnoli MR. The design of a health technology assessment system in telepathology. *Telemed J E Health* 2008;14(6):570-5.