

The Digital Microscopy in Organ Transplantation: Ergonomics of the Tele-Pathological Evaluation of Renal, Liver and Pancreatic Grafts

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Abstract—Introduction: The process to build a better safety culture, methods of error analysis, and preventive measures, starts with an understanding of the effects when human factors engineering refer to remote microscopic diagnosis in surgery and specially in organ transplantation for the remote evaluation of the grafts. It has been estimated that even in well-organized transplant systems an average of 8% to 14% of the grafts (G) that arrive at the recipient hospitals may be considered as diseased, injured, damaged or improper for transplantation. Digital microscopy adds information on a microscopic level about the grafts in Organ Transplant (OT), and may lead to a change in their management. Such a method will reduce the possibility that a diseased G, will arrive at the recipient hospital for implantation. **Aim:** Ergonomics of Digital Microscopy (DM) based on virtual slides, on Telemedicine Systems (TS) for Tele-Pathological (TPE) evaluation of the grafts (G) in organ transplantation (OT). **Material and Methods:** By experimental simulation, the ergonomics of DM for microscopic TPE of Renal Graft (RG), Liver Graft (LG) and Pancreatic Graft (PG) tissues is analyzed. In fact, this corresponded to the ergonomics of digital microscopy for TPE in OT by applying Virtual Slide (VS) system for graft tissue image capture, for remote diagnoses of possible microscopic inflammatory and/or neoplastic lesions. Experimentation included: a. Development of an OTE-TS similar Experimental Telemedicine System (Exp.-TS), b. Simulation of the integration of TS with the VS based microscopic TPE of RG, LG and PG applying DM. Simulation of the DM based TPE was performed by 2 specialists on a total of 238 human Renal Graft (RG), 172 Liver Graft (LG) and 108 Pancreatic Graft (PG) tissues digital microscopic images for inflammatory and neoplastic lesions on four electronic spaces of the four used TS. **Results:** Statistical analysis of specialist's answers about the ability to diagnose accurately the diseased RG, LG and PG tissues on the electronic space among four TS (A,B,C,D) showed that DM on TS for TPE in OT is elaborated perfectly on the ES of a Desktop, followed by the ES of the applied Exp.-TS. Tablet and Mobile-Phone ES seem significantly risky for the application of DM in OT ($p < .001$). **Conclusion:** To make the largest reduction in

errors and adverse events referring to the quality of the grafts, it will take application of human factors engineering to procurement, design, audit, and aware ness-raising activities. Consequently, it will take an investment in new training, people, and other changes to management activities for DM in OT. The simulating VS based TPE with DM of RG, LG and PG tissues after retrieval; seem feasible and reliable and dependable on the size of the electronic space of the applied TS, for remote prevention of diseased grafts from being retrieved and/or sent to the recipient hospital and for post-grafting and pre-transplant planning.

Keywords—Organ Transplantation, Tele-Pathology, Digital Microscopy, Virtual Slides.

I. INTRODUCTION

IT is a common knowledge that ignoring the human factors in the design process will more likely lead to a poorly designed human-machine interface which are often the culprits in adverse events. Poorly designed systems may originate from external vendors or from internal developers. Both cases present the opportunity for the risk manager or clinician to implement a human factors process. The process to build a better safety culture, methods of error analysis, and preventive measures, starts with an understanding of the effects when human factors engineering refer to remote microscopic diagnosis in surgery and specially in organ transplantation for the remote evaluation of the grafts during the coordination process in the so called procurement phase of organ transplantation (OT).

An excellent example of the significance of the above-mentioned statement has been presented by Professor P. Friend in 2010 referring to a high percentage (ranging from 8% to 14%) of solid organs (grafts) that arrive at the recipient hospitals and are considered as injured, damaged or improper for transplantation in the UK [1].

Digital microscopy adds information on a microscopic level about the grafts (G) in Organ Transplantation and may lead to a change in their management. Such a method will reduce the possibility that a diseased, injured or damaged G, will arrive at the recipient hospital for implantation [2]. For the application of digital microscopy a systematic and integrated communication method for determining appropriate assessment, intervention, and remote organ evaluation in the sequence of the coordination process and of the procurement phase of OT, is needed. In technological terms, this is realized first by the replacement of the current fax and telephone based communication among coordinators, the coming -to the donor

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hospital-grafting team and the -based in the recipient hospital-transplant team, with telemedicine systems (TS), integrated with the so called Virtual Slide (VS) system [2]-[5].

Viewing slides through the computer monitor with easy access to the multi-functionality of a computer is much more ergonomic than peeping through the ocular of an optical microscope. Experience shows that even pathologists with high affection to conventional microscopy respect the benefits of digital microscopy if they spend enough time on practicing. The computer generated image pyramid format of digital slides allows in-focus navigation through continuously changing magnifications without the need for changing objectives, realigning the focus or the lighting conditions [2]. Digital magnifications beyond that used for scanning could still reveal fine microscopic details hidden at the original magnification. Slides can be tilted arbitrary for proper orientation and preview images of the whole slide are available simultaneously on the monitor where navigation history of high power analysis can also be traced [2]. Thus, a new architecture is proposed in the procurement phase of OT, over telecommunication networks, based on TS integrated with VS systems, for remote recognition of diseases of G on a microscopic level, for saving these data in the electronic medical record of the donor and for sharing digital images among the coming grafting team surgeons and the transplant team that may contribute positively after the retrieval and in the pre-transplant preoperative planning [6]-[9]. The project studies the ergonomics of the application of digital microscopy, as a part of the tele-pathological evaluation (TPE) by specialist pathologists in the transplant team in the recipient hospital just after retrieval in the procurement phase of OT in the donor hospital - as a method to reduce the diseased tissues of renal (RG), liver (LG) and pancreas (PG) grafts, suffering from inflammatory and/or neoplastic diseases that may be sent from the donor hospital to the recipient hospital for OT [2]-[5].

II. MATERIAL AND METHODS

By experimental simulation, we analyzed the value of the electronic space of TS in terms of the ergonomics of DM for TPE of RG, LG and PG which in fact corresponded to the ergonomics of digital microscopy for TPE in OT by applying VS for remote diagnoses of microscopic inflammatory and/or neoplastic lesions. Experimentation included: a. The development of an OTE-TS similar Experimental Telemedicine System (Exp.-TS) for simulating the b. integrated VS based microscopic TPE of RG, LG and PG (Table I) [2], [4]-[6].

Simulation of TPE of RG, LG, PG and UG for microscopic inflammatory and/or neoplastic lesions, by two specialists based on the examination of two sets of digital microscopic images (RG:N1=238 and LG:N2=172, PG:N3=108, digital microscopic images in total, stored in a way that contributed DICOM) [6], [7]. Each set contained both normal and pathologic renal, hepatic and pancreatic tissue images respectively (inflammatory and/or neoplastic graft pathologies) [8]. The first examiner was the standard, and the

diagnoses of the second were compared to those of the first for each digital microscopic image after projection, magnification and scrolling (microscopic virtual benching) on the electronic space of: A: the Desktop, B: the Exp.-TS, C: a Tablet and D: a Mobile phone (Fig. 1). The statistical analysis based on the answers of the second specialist examiner a. matched with the standard ones and b. based on his satisfaction level (ranging from the minimum -3,-2,-1, to the maximum 1,2,3) regarding the size of four suggested electronic spaces including the Exp.-TS. (A=Desktop, B=Exp.-TS, C=Tablet, D=Mobile Phone), for each type of the three examined grafts [9]-[12].

TABLE I
COMPARISON OF MODULES OF OTE-TS AND OF EXP.-TS

MODULES	OTE-TS	Exp.-TS
a. Medical record process	+	+
b. Examinations results.	+	+
c. Capture scanning and imaging.	+	+
d. DICOM and PACS vision.	+	+
e. Real-time teleconference	+	+
f. Chat and whiteboard facilities	+	+
g. Application sharing.	+	+
h. Tele-secretary facilities	+	+
j. Tele-Mentoring facilities	+	+
k. Tele-communication net	ISDN	Internet
i. Virtual Slide integration	-	+

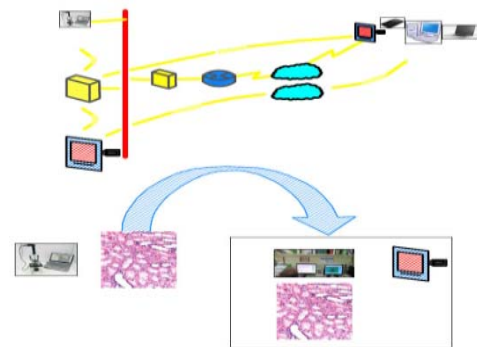


Fig. 1 DM based TPE simulation, between the Grafting Team in the Donor Hospital (DH) and the Transplant Team in the Recipient Hospital (RH) over integrated Exp.-TS and VS: The pathologist locating in the RH accessed the donor's microscopic graft tissue images captured by the VS (green image on the top in left) in the DH standard (yellow box and red/blue box in left behind the red wall). After remote microscopic evaluation of the graft tissue in the internet and notification in the electronic medical record of the donor, indications may be reset (blue arrow)

III. RESULTS

Integrated analysis using SPSS (version 19.0) and applying the Wilcoxon-signed rank test for the comparison among the size of the four suggested TS electronic spaces (A,B,C,D) and the classification of answers of the examiner (ranged for each graft tissue microscopic digital photo: -3,-2,-1,0,1,2,3) showed that the examiner could define the microscopic inflammatory and/or neoplastic lesions on the electronic space of the four used TS, while comparisons of his answers analysis about the

ability to diagnose accurately the diseased RG tissues on the electronic space among four TS (A,B,C,D) resulted as in Table II [9].

Results proved that the electronic space of a mobile-phone (D) has the least ability to drive to the right microscopic remote diagnosis about the inflammatory and neoplastic lesions of tissue RG in comparison to a Desktop (A), to the Exp.-TS (B) and to a Tablet (C). Also, the electronic space of a Tablet (C) has a significantly low ability to drive to an accurate diagnosis in comparison to a Desktop (A) and to the Exp.-TS (B). The electronic space of Exp.-TS (B) has the same possibility to drive to the right diagnosis about inflammatory and neoplastic diseases of the tissue RG tissue, in comparison to the Desktop (A). The results about the liver tissue graft digital image remote examination on the four electronic spaces are in Table III. Thus, the electronic space of the mobile phone (D) has the least ability to drive to the right remote microscopic diagnosis about inflammatory and/or neoplastic lesions of LG tissues in comparison to a Desktop

(A), to the Exp.-TS (B) and to a Tablet (C). Also, the electronic space of a Tablet (C) has a significantly low ability to drive to an accurate diagnosis in comparison to a Desktop (A) and to the Exp.-TS (B). Hence, Exp.-TS has significantly less possibility to drive to the right diagnosis of LG tissue, in comparison to the Desktop (A). With regard to the analysis of PG the results about pancreas tissue graft digital image remote examination on the aforementioned four electronic spaces are in Table IV. Thus, the electronic space of the mobile phone (D) has the least ability to drive to the right remote microscopic diagnosis about inflammatory and/or neoplastic lesions of PG tissues in comparison to a Desktop (A), to the Exp.-TS (B) and to a Tablet (C). Also, the electronic space of a Tablet (C) has a significantly low ability to drive to an accurate diagnosis in comparison to a Desktop (A) and to the Exp.-TS (B). Hence, Exp.-TS has significantly less possibility to drive to the right diagnosis of the PG tissue, in comparison to the Desktop (A).

TABLE II
SIMULATED VS BASED TPE OF RG

	N1	A vs B	A vs C	A vs D	B vs C	B vs D	C vs D	p
A. Inflammatory lesions	98	1	<.001	<.001	<.001	<.001	<.001	p
B. Neoplastic lesions	135	1	<.001	<.001	<.001	<.001	<.001	p

N=Number of digital microscopic photos of graft tissues diagnosed remotely and accurately on the electronic space of the given TS: A=Desktop, B=Exp.-TS, C=Tablet, D=Mobile phone

TABLE III
SIMULATED VS BASED TPE OF LG

	N2	A vs B	A vs C	A vs D	B vs C	B vs D	C vs D	p
A. Inflammatory lesions	82	<.001	<.001	<.001	<.001	<.001	<.001	p
B. Neoplastic lesions	82	.001	<.001	<.001	<.001	<.001	<.001	p

N=Number of digital microscopic photos of graft tissues diagnosed remotely and accurately on the electronic space of the given TS: A=Desktop, B=Exp.-TS, C=Tablet, D=Mobile phone

TABLE IV
SIMULATED VS BASED TPE OF PG

	N3	A vs B	A vs C	A vs D	B vs C	B vs D	C vs D	p
A. Inflammatory lesions	38	<.001	<.001	<.001	<.001	<.001	<.001	p
B. Neoplastic lesions	70	.001	<.001	<.001	<.001	<.001	<.001	p

N=Number of digital microscopic photos of graft tissues diagnosed remotely and accurately on the electronic space of the given TS: A=Desktop, B=Exp.-TS, C=Tablet, D=Mobile phone

A.Human Factors and Digital Microscopy in OT

The role of human factors in the design of medical devices and medical information systems is the topic of a growing number of published articles. The need for user needs analysis in the discovery phase of device design is analyzed by [12], [13] which propose several methods for assessing usability of information technology in healthcare. On the other hand several studies prove the positive impact of human factors engineering on the design of medical devices, providing evidence of better usability, reduced errors, and reduced mental workload in a system designed using structured and well-studied processes [12]. In fact when human factors engineering is not considered in the design of computer systems, the user needs and their existing problems are rarely identified and hence not properly addressed [6], [14], [15]. Unfortunately, when this occurs, many computer systems in

healthcare solve the wrong problem or do not address the error in a usable manner. At best, the computer does nothing to eliminate errors [8], [13], [14]. At worst, it introduces insidious new problems [9]. By simulating DM on TS for remote microscopic evaluation of the quality of the grafts, we found that the design is feasible for the grafting and the implantation team to mutually and remotely evaluate RG, LG and PG tissues after retrieval and decide, whether G are worth being sent to the recipient hospital for implantation [11], [15]-[17]. Additionally it is proven that the electronic space of a Desktop seems to be the best option for remote microscopic visualization while the Exp.-TS seems comparable, however depended on the type of the G. Microscopic visualization on the electronic space of tablets and mobile-phones, have high possibility to mislead pathologists in OT [12], [14], [18]. However, it has to be taken into consideration that the

aforementioned analysis is based on a simulating experimental model. Clinical research protocols of DM in OT are being developed for clinical evaluation.

B. More Training and More Technology May Not Help

Explanations of errors rarely penetrate the true underlying causes. Therefore the solutions have only a limited effect. For example, some usual solutions are to increase training of personnel or to introduce computers and technology. As we will see the condition since 70's, this does not always solve the problem [18]-[20].

C. Training

In studying errors that occur in medicine and in surgery, researchers often believe that the source of the problem is the individual committing the error [9]. However, the fact that even highly trained professionals can make errors points to the need for alternative methods to reduce errors [20]-[22]. Device related user errors often stem from human-machine interaction rather than from the individual exclusively [8], [12]. Machines that are not designed to accommodate the limitations of human performance or the needs of the task at hand are doomed to promote more human-machine interaction errors, no matter how well trained the individual [14]. Human factors studies of error in medicine provide broader insight into the sources of problems, and as a result, provide a broader set of implications that reach beyond the reprimand of the individual [9], [12], [13]. While the training solution may help to control the problem, the source of the problem will continue to persist [16], [17], [23]. There is broad and deep evidence that the relatively new discipline, human factors engineering, can make a big impact on healthcare errors in OT [9], [11], [12]. Better yet, a person could start including human factors engineering into the framework and techniques for error investigation tomorrow. To make the largest reduction in errors and adverse events referring to the quality of the grafts, it will take application of human factors engineering to procurement, design, audit, and awareness-raising activities [20]-[22]. Thus, it will take an investment in new training of coordinators, transplant surgeons, nurses, pathologists, laboratory technicians, biomedical and bioinformatics specialists to transplant management [1], [11], [12], [23].

D. Technology

Ideally, computers should be used for tasks computational in nature, require flawless and extraordinary memory re-call, and perfect vigilance over extended periods. Many in healthcare have identified the role of computers in effectively addressing errors, including medication errors and as reminders for often forgotten clinical interventions increasing safety and reliability in OT [11], [14], [20].

IV. CONCLUSION

The simulating VS based TPE with DM of RG, LG and PG tissues after retrieval, seems feasible and reliable and dependable on the size of the electronic space of the applied TS, for remote prevention of diseased grafts from being

retrieved and/or sent to the recipient hospital and for post-grafting and pre-transplant planning.

REFERENCES

- [1] P. Friend, Organization of organ retrieval-bitter lessons and ambitious plans, Proceedings of lectures in the Hammersmith Hospital of London, 2010 (Available at: <http://vincentbourquin.files.wordpress.com/2010/11/friend-Hammersmith-11-10-10.pdf>, Accessed on 17/07/2012).
- [2] AR Graham, AK Bhattacharyya, KM Scott, F Lian, LL Grasso, LC Richter, et al. Virtual slide tele-pathology for an academic teaching hospital surgical pathology quality assurance program. *Hum Pathol.*, vol.40, pp.1129-36, Jul. 2009).
- [3] C.S. Mammas, G.P. Economou, N. Arkadopoulos, G. Kostopanagioutou, G.J. Mandellos, P. Lymberopoulos, V. Smyrniotis, D. Lymberopoulos, ELMP for TS in the coordination process as a method to optimize quality in organ transplantations, Proceedings of the 16th Congress of the Hellenic Society of Organ Transplantation, Thessaloniki, 2011, pp.24.
- [4] CS Mammas, G. Mandellos, G.-P Economou. and D. Lymberopoulos, "Structuring Expert-Leaded Medical Protocols for Telemedicine Systems", in Proc. 23rd Annual International Conference of the IEEE Engineering in Medicine and Biology, Constantinople, 2001, pp.3529-32.
- [5] E. Karavatselou, GP. Economou, C. Chassomeris, V. Danelli and D. Lymberopoulos, OTE-TS: A new value added telematics service for telemedicine applications, *IEEE Transactions on Information Technology in Biomedicine*, vol. 5(3), pp210-224, Sept. 2001.
- [6] R.H. Morgan. Computer network security for the radiology enterprise Computer network, *Radiology.*, vol.220, pp.303-09, Aug.2001.
- [7] P.N. Furness, WM Bamford, Tele-pathology. *Curr Diag Pathol*, vol.7, pp. 281-291, Dec.2001.
- [8] E. Coiera. *Guide to health informatics*, CRC, 2015.
- [9] S. Martorell, CG Soares, J. Barnett. *Safety, Reliability and Risk Analysis: Theory, Methods and Applications*, CRC, 2014.
- [10] K. Kayser, S. Borkenfeld, J.Görtler, G.Kayser. Image standardization in tissue - based diagnosis. *Diagnostic Pathology*, vol.3, pp.17-25, Apr.2008.
- [11] KY Jen, JL Olson, S. Brodsky, XJ Zhou, T. Nadasdy, ZG Laszik., Reliability of whole slide images as a diagnostic modality for renal allograft biopsies, *Human Pathology*, vol.44(5), pp.888-94, 2013.
- [12] E. Krupinski. Human factors and human-computer considerations in teleradiology and telepathology, *Healthcare*, vol. 2(1), pp.94-114, Feb.2014.
- [13] MY Gabril, GM Yousef. Informatics for practicing anatomical pathologists: marking a new era in pathology practice. *Mod Pathol.*, vol.23, pp.349-358, Jan.2010.
- [14] L. Pantanowitz, K. Dickinson, A. J. Evans, L. A. Hassell, W. H. Henricks, J. K. Lennerz, et al. ATA Clinical Guidelines for Telepathology. *Telemedicine and e-Health*, vol 20(11), pp.1049-70, May 2014.
- [15] G. Kayser, J. Görtler, N. Kluge, T. Wiech, M. Werner, K. Kayser. Standards in virtual microscopy: from tissue processing to image acquisition and visualization. *Diagnostic Pathology*, vol.5 (Suppl 1), pp.10, 2010
- [16] K. Kayser, S. Borkenfeld, T. Goldmann and G. Kayser. Virtual slides in peer reviewed open access medical publication. *Diagnostic Pathology*, vol. 6, pp.124-131, Dec.2011.
- [17] L. Pantanowitz, PN Valenstein, AJ Evans, KJ Kaplan, JD Pfeifer, DC Wilbur et al. Review of the current state of whole slide imaging in pathology. *J Pathol Inform.*, vol.2, pp.36-45, Aug.2011.
- [18] L. Főnyadl ı́, T. Krenács ı́, P. Nagy ı́, A. Zalatnai ı́, J. Csomor ı́, Z. Sapi ı́ et al. Validation of diagnostic accuracy using digital slides in routine histopathology *Diagnostic Pathology*, vol.7, pp.35-41, Mar.2012.
- [19] F. Ghaznavi, A. Evans, A. Madabhushi, M. Feldman. Digital imaging in pathology: Whole-slide imaging and beyond, *Annual Review of Pathology: Mechanisms of Disease*, vol.8: pp.331-59, Nov. 2012.
- [20] G. Romero, L., William C. Andrew L., Eugene T., Jeff M., Anil Parwani, L. Pantanowitz. Digital Pathology Consultations—a New Era in Digital Imaging, Challenges and Practical Applications, *Journal of Digital Imaging*. vol.26 (4), pp. 667-68, Jan.2013.
- [21] S. Kothari, J. H. Phan, T. H. Stokes, M. D. Wang. Pathology imaging informatics for quantitative analysis of whole-slide images. *Journal of*

the American Medical Informatics Association, vol.20 (6),pp.1099-1108,Nov. 2013.

[22] T. C. Allen. Digital pathology and federalism, *Archives of pathology & laboratory medicine*, vol.138 (2): pp.162-165, Feb. 2014.

[23] Eric F. Glassy. Rebooting the pathology journal: learning in the age of digital pathology, *Archives of Pathology & Laboratory Medicine*, vol.138 (6), pp.728-729, Jun.2014.