# Telepathology: a great opportunity for improving cancer diagnostics in Sub-Saharan African countries

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**Abstract**
According to the World Health Organization (WHO), deaths from non-communicable diseases (NCDs) are increasing globally, with the largest increase being on the African continent. Projections have indicated that deaths from NCDs will exceed all combined communicable, maternal, perinatal and nutritional diseases as the most common causes of death by 2030 in Africa. Hence, the importance of a functional and improved approach to Pathology in the diagnosis of cancer cannot be debated. How can we deliver a better and more acceptable quality of healthcare within the limits of current resources? WaidX telemedicine platform application to Virtual Telepathology tries to give valid answers to this urgent requirement.

**Keywords**
Telepathology, Digital Pathology, WaidX, Telemedicine, Developing Countries, Virtual Microscopy, Virtual Slide.

## 1. Introduction

Africa is a continent of opportunities for growth, undergoing a rapid economic transformation, which, however, will result in an increase of noncommunicable diseases (NCDs). Estimates in 2015 suggested that the annual number of new cases over the next 5 years will grow to above 1 million. Predicted deaths from NCDs over the next 10 years will also increase globally by 17%, the greatest increase being in Africa (27% or 28 million

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deaths) [1,2,3]. Data updated to 2020 confirms the accuracy of these estimates [4].

The ability to provide early diagnosis, treatments, and follow-up care has a large impact on care efficacy and patient survival. The importance of pathology in correct diagnostics and further adequate cancer treatments cannot be emphasized enough. There are currently still a high number of African countries in which pathology services are struggling with a limited number of available pathologists, inadequate infrastructure and with severely restricted budgets from the governments, although in recent years several developing countries are facing the challenge of introducing modern approaches to oncology. At the same time, pathology unarguably remains the backbone of the success of the cancer care.

The challenges facing pathology diagnostics, training and oncology research in Africa, are multiple and daunting. They include the lack of or inadequate infrastructure and personnel, both pathologists and technical personnel; limited opportunities for professional education or training; 'brain drain' following many years of mismanagement of the health-care services; a lack of or insufficient funding for basic laboratory materials such as reagents.

While we acknowledge these challenges, custodians of African pathology and clinical oncology are asking new and pragmatic questions, for example: how can we deliver a better and more acceptable quality of services within the limits of current resources? The 'game plan' must address the following, immediately and in a sustained way:

- define ways for updating the knowledge base of practicing pathologists, addressing the enhancement of training for pathologists and technical staff;
- explore the need for continuous capacity building and quality improvement;
- develop new models based on modern digital health technologies.

## 2. Telepathology in developing countries

Telemedicine consists in many services and applications such as VoIP and web conferencing, teleconsulting, remote tumor board, medical records software, digital imaging, e-learning and several others. The World Wide Web (WWW) and the Information & Communications Technology (ICT) play a pivotal role in telemedicine diffusion.

Telepathology is the practice of pathology at a distance. It uses ICT to facilitate the transfer of image-rich pathology data between distant locations for the purposes of diagnosis, education, and research [5,6]. Performance of Telepathology requires that a pathologist selects the video images for analysis and the rendering of diagnoses[7].

Despite the term "Telepathology" was defined more than 30 years ago, Telepathology practice largely remains a privilege of high-income countries. Digital Divide, the economic and social inequality of peoples in their access, use or knowledge of ICT, plays a determining role in curbing the spread of Telepathology, such as the lack of solutions tailored for the developing countries needs.

The divide is hugely remarkable between developing and developed countries in terms of technological gap, social engagement, information poverty, and Internet access diffusion.

However, other "divides" exist: Sub-Saharan African Countries suffer a dramatic shortage of medical pathologists, in the range of 1 to 10 pathologists per 10 million people.

During the last two decades, Pathology has benefited from the rapid progress of image scanning technology. Progress in improving this technology has led to the creation of slide scanners that are capable of producing digital images of a complete histological cut, that can be exploited by image viewers in a manner comparable to the conventional microscope, with considerable comfort for pathologists compared to viewing on a traditional microscope. When the slide is digitally scanned in its entirety in high resolution (Whole-Slide Imaging), the resulting digital image is called "virtual slide".

Although the capture of photos of microscopic views opened the road to "static Telepathology" based on store-and-forward model, Telepathology based on virtual slides sharing offers a much more effective means to view an entirely digitized slide, allowing the remote browsing of the slide by running image management software on a standard web browser [8].

File size of the virtual slides usually ranges from a few hundred Megabytes to several Gigabytes, which routinely address storage and image management challenges in daily clinical practice.

Virtual slides are used in pathology for educational purposes, diagnostics (clinical-pathological meetings, consultations, reviews, panels, and increasingly for remote diagnostics), research and archiving. Digitisation of slides provides several advantages, but the diffusion of Digital Pathology in developing countries opens new challenging issues to be faced including costs for virtual slide scanning, accessibility limitations imposed by local Internet Service Providers (ISPs), management of huge sized files, security for sensitive data.

## 3. The Mwanza cancer project and WaidX

"Associazione Vittorio Tison ONLUS" is an Italian no-profit organization devoted to develop the Clinical Oncology facility of the Bugando Medical Centre (BMC) in Mwanza, one of the main cities of Tanzania, according to a long-term capacity building program that took into account all the main aspects of the oncology discipline[9]. Amazing achievements were growing in a scenario characterized by the resource poverty and a strong digital divide issue, with a dramatic impact on the efficacy of the effort put by project managers and volunteers coming from Italy.

This scenario stimulated out team in undertaking the design of an intercontinental telematic platform oriented to oncology and its related branches, able to interconnect BMC Oncology and Pathology Departments with the Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori (IRST IRCCS) – Italy, to allow for:

- conference calling and remote tumor boards between the institutes' teams;
- second opinion, e-learning and quality control;
- sharing of clinical data on the IRST medical records software;
- remote control of medical equipment;
- carry out GCP clinical trials through data collection, monitoring and evaluation;
- activate a Telepathology

facility for simultaneous counselling sharing microscopy images.

After a long development phase and an accurate fine tuning of the platform, we launched the novel telemedicine platform performing a complete demo of the system during the AORTIC East African Regional Meeting hosted at BMC (25-26 June 2015).

From this pioneeristic experience, the WaidX – World Aid Exchange project was founded, with the aim of consolidating and prosecute the development of the original telemedicine platform through the implementation of new applications, giving valid answer at the different requests we were rapidly collecting.

WaidX consists in a global telematics platform devoted to the remotization of healthcare process, resulting in a critical enhancement of the transmission performance between facilities sited in developed and developing countries, using low cost and poor quality connections, overcoming the accessibility problems induced by local ISPs, introducing many benefits like an high level of service continuity, privacy for sensitive data, a strong integration of concurrent IT applications on a converged global network, all this oriented to promoting the development of Digital Health applications based on cost-effective resources. WaidX core is based on an Italian Computer-Telephony Integration (CTI) technology, appropriately customized for the telemedicine purposes.

## 4. APOF NGO

The Mwanza oncology project led by Tison Association started in 1999 with the establishment of the anatomic pathology laboratory at BMC, with sponsoring the training of a pathologist, a medical oncologist and four oncology nurses. Soon after that, the Oncology Department was started and BMC became a specialized hospital in north-west Tanzania. The hospital has 850-bed capacity for a catchment population of 20 million, equivalent to one-third of the population of Tanzania. The histopathology laboratory, whose staff currently includes different pathologists, has the capacity to perform more than 10,000 histological analyses and about 3,000 cytological diagnosis per year.

This prodromic arm of the Mwanza project gave birth to Associazione Patologi Oltre Frontiera NGO – APOF (Pathologists Beyond Borders NGO). The main aim given to the newborn NGO was to promote the growth of Pathological Anatomy in developing countries, implementing projects for preventive medicine and cancer diagnostics.

The following APOF projects focus on the diffusion of histological and cytological diagnostics, through the training of technical and medical personnel, the direct engagement in the reporting of biopsy and surgical cases, the support to cancer prevention programs, the construction or upgrading of laboratories, the introduction of digital technologies, in order to achieve the full autonomy of the patronized facilities in a long-term perspective. Furthermore, the supported facilities are offered the possibility of accessing the global Telepathology network based on WaidX, continuing the capacity building process.

During its first decade of activity, APOF took up the challenge of new technologies introducing static Telepathology contributions to support the remote diagnostic. This experience has reached its peak thanks to the first "Zambia

project", designed with the objective of inspecting the potential of Telepathology for assisting surgical and cytologic pathology in developing countries[10]. The results demonstrate a high correlation between Telepathology and traditional microscopy and indicate that the project may be repeated similarly in other developing countries. Nevertheless, different factors restrain the spread of this model: high costs for satellite connections, limitation in transmission speed and quality combined with the asynchronous workflow for remote pathologists. It was clear that static Telepathology couldn't address all the open questions concerning the establishment of a diagnostics routine in such very poor contexts.

The large number of pending issues indicates the need of a more adequate and modern approach to deal with Telepathology requirements, so we decided to support APOF projects with the design of WaidX applications devoted to virtual dynamic Telepathology.

## 5. Telepathology in the Horn of Africa

The commitment of WaidX in favour of APOF takes shape on the "Horn of Africa" Project, towards the ambitious goal of creating a network of Pathology laboratories among different countries of the Greater Horn of Africa.

Since 2010 APOF patronized a project in the Hospital of Balbala, Republic of Djibouti, aimed to the institution and the development of the first Pathology Department of the country. At present this department is fully operative, with complete equipment, four well-trained technicians and two full time medical pathologists. Subsequently the second pathology department in Djibouti was created at the Djiboutian Military Hospital, equipped with the Digital Pathology facility since its inception.

In 2015 APOF received a request from the Hargeisa Group Hospital (HGH) of Hargeisa, Somaliland, concerning the institution of a Pathology Department. So, we started a project aimed to create a network of Pathology labs through the "Hub & Spoke" model, where the more equipped laboratories of Djibouti should act as hub of competencies for the Pathology lab of Hargeisa with no available pathologists at that time. To optimize the use of ICT resources, the virtual slide files should be stored in the production sites and made available for viewing and by browsing by remote pathologists.

In order to reach this goal, several hot points were identified:

- The technicians should be fully trained on the preparation not only of the biopsies but even of the surgical specimens.
- The slides should have an optimal preparation quality.
- The pathologists need to be trained for making diagnosis on remote virtual slides.
- A slide scanning system with a proper tropicalization and a powerful Telepathology platform is needed.

Since WaidX platform was ready to comply all Telepathology requirements enabling a good level access of remote pathologists to the virtual slides stored locally in their respective production sites, we ventured with the development of a Digital Pathology solution based on manual whole-slide scanning, adequate for the needs of a remote lab with a limited number of slides to be managed (few thousands per year) and no local pathologists. This goal has been firstly

reached through a system integration task, adopting the Microvisioneer software suite in association with the Olympus CX33 Microscope coupled with a Basler CCD camera, running on a basic HP workstation with an EIZO high resolution monitor. This set allows the whole slide image scanning through a manual process, performed by local lab technicians after a 3-hours training course. Once the virtual slides are saved on the workstation, the local operator can share them into the Telepathology collector with a simple drag & drop action, and remote pathologists can immediately access them through the telematic connections handled by WaidX.

We connected to WaidX the two Internet access lines previously serving the Hospital network, both provided by Djibouti Telecom: a WiMAX bridge with a download bandwidth of 3 Mbps and upload of 2.5 Mbps, and an ADSL line with a download bandwidth up to of 8 Mbps and upload of about 0.7 Mbps (tests performed on the national ISP's servers). The upload values were very weak and particularly impacted from a high frequency of transmission defects (packet loss, significant variance in data packet transmission latency), drawing a prohibitive framework in which we had to perform the live tasks of virtual Telepathology with the other concurrent telematics applications. To benefit from all its features, WaidX became as the border gateway for the entire Hospital network. We defined a set of policies concerning LAN-WAN traffic prioritization, link aggregation, UDP encapsulation of traffic on international routes, recovery of transmission defects and a redundant connection topology optimized to confer high availability to the telematics services. The outcome of adopting this design was the achievement of more than 5 Mbps of stable upload effective-bandwidth, allowing us to perform a good level Telepathology activity assuring the Internet service for the common needs of the Hospital network on the same two connections.

This model addresses the main issues involved in the Telepathology process: solidity and affordability of the local equipment, integration of the Telepathology platform in the existing IT infrastructure, accessibility for remote pathologists, efficacy and efficiency of the whole diagnostic process running on poor connections.

The first WaidX-based Digital Pathology facility within the "Horn of Africa" Project was put into operation in early 2018 at Balbala Hospital. The roadmap continued with the installation of the platform at the Djiboutian Military Hospital, and in 2021 in the HGH where an automatic slide scanning system manufactured by West Medica was installed. The laboratory nodes connected subsequently to the pilot installation in Balbala benefit from slightly better internet access, although without the use of WaidX it would not be possible to guarantee a routine telepathology activity.

The platform resulted easy-to-use, all sanitary operators involved in the solution testing find it friendly and effective. The virtual slides remotely viewed are fully compliant with the diagnostic requirements in terms of definition and magnification. The images browsing on the screen is fast and precise enough, professional operators evaluated the effectiveness of this solution equivalent to the use of the microscope and much more comfortable for the user.

We presented the first achievements at World Cancer Congress 2018, held in Malaysia, where we chaired a 90-minute session dedicated to Teleoncology and Telepathology [11,12]. The session was aimed at illustrating the potential of the ECHO e-learning project[13] and of remote oncology diagnostics in association with virtual Telepathology, relatively to developing countries requirements. After the presentations given by the speakers from the involved organizations, we moved to the discussion of a patient case via remote tumor board collecting different teams of medical oncologists and pathologists, spread over 4 continents (Malaysia, New York, Djibouti, Tanzania, Italy and San Marino). The session audience was very impressed by the powerful interaction gained by our telemedicine model, fueling an intense discussion during the final question time.

During 2018 the first database of virtual slides, related to clinical cases managed by the Balbala Pathology Department, has been digitized. In 2019 a quality control study on the whole Digital Pathology and Telepathology process was be carried out through review of diagnoses performed with double check of physical and virtual slides, confirming excellent diagnostic concordance.

This represents the first experience of a model involving exclusively African departments of pathology through Telepathology. The "Hub & Spoke" method is demonstrating its efficacy in allowing the optimization of the local resources and is being extended to other pathology departments of the Greater Horn of Africa.

## 6. Development scenarios

Our commitment to the development of Telepathology in favour of developing countries is an ongoing work in progress. To strengthen our action and broaden the range of our initiatives, in 2024 we founded the Pathoxphere consortium which brings together all the medical, scientific and industrial main partners who collaborate in various capacities on our projects.

One area of particular interest concerns the digitization of cytology. Cytologic examinations may be performed on body fluids or on material that is aspirated from the body. Cytology also involves examinations of preparations that are scraped from specific areas of the body. A common example of cytologic diagnostics is the evaluation of cervical smears. In order for cytologic evaluation to be carried out, in the classical approach the material to be examined is spread onto glass slides and stained. A pathologist then uses a microscope to examine the individual cells in the sample. Currently, PAP smears test represents the 50% of total cytology tests, such a figure is decreasing thanks to the primary screening switching to HPV. On the other side, non-gynaecological cytology is rapidly increasing.

Liquid-based thin layer cytology represents the set of methods that allow the production of monolayer cytological slides on which the cell fields are deposited on the same plane and hopefully clearly distinct from each other. Among the many advantages of this approach, thin layer slides can be digitized effectively unlike classical cytology slides. Hospitex International, a partner of the Pathoxphere consortium, has developed the cytological sample processing system CYTOfast, based on the innovative technology called Custom Density Monolayer – Liquid Based Cytol-

ogy. We can identify several strengths in the CYTOfast solution: the capability of optimal preparation of any cytological sample through this technology; the low cost of the system and sample preparation kit; the extreme simplicity of use of the equipment according to a semi-automatic preparation process, accessible even to less skilled operators; the possibility to store samples at room temperature for at least 60 days thanks to the CYTOfast fixative solution; after the preparation of the monolayer slide, the availability of a portion of the original fixed sample to perform further diagnostic continuation tests. Thanks to the integration of CYTOfast in our Digital Pathology model, we are offering healthcare organizations new diagnostic models that are easily scalable on large numbers of samples and patients, overcoming the typical limitations of conventional cytology diagnostics. Of particular importance is the implementation of screening programs on the population for the early diagnosis of different pathologies, targeted to obtain a high impact on tumor pathologies which represent the top killers for developing countries.

After over 10 years of presence of WaidX applications in Ethiopia, our activity in this country is intensifying thanks to the engagement of new Telepathology and laboratory implementation projects, developed with different Ethiopian healthcare institutions and university. Although the Ethiopian context presents several challenges, the implementation of digital health projects for cancer diagnostics represents a huge opportunity for expanding the access to healthcare for the population.

A development area of particular interest is the implementation of Pathomics algorithms dedicated to computerized diagnostic support in cytology. We are undertaking various initiatives to quickly obtain the first operational prototypes of pre-diagnostic software applicable to our Digital Pathology model.

Given the particular importance of ancillary diagnostics for obtaining a complete and effective laboratory medicine diagnosis, we have opened a research branch dedicated to the application of Telepathology in the related fields of clinical pathology, oncology and microbiology, with the scientific support of the University of Chieti – CAST institute and the Unit of Clinical Pathology and Microbiology in the Department of Medicine Free University of the Mediterranean LUM of Bari, affiliated to the Miulli Regional General Hospital in Acquaviva delle Fonti (Bari), institutions that also act as training centres for students coming from twinned project sites in developing countries. In addition to molecular and biochemical diagnostics, this area of investigation deals with immunophenotypic diagnostics, with particular reference to flow cytometric confirmation of myelogenic/lymphoid leukaemia and lymphoma. As a matter of fact, malignant lymphoproliferative diseases have historically been a widespread problem in sub-Saharan African populations.

## 7. Conclusions

Information and Communication Technologies are triggering stellar improvements in healthcare: the collaboration between remote specialists through Telepathology represents a virtuous capacity building model in order to support developing countries in providing an appropriate level of diagnostics to the whole population. The implemen-

tation of a digital pathology workflow based on WaidX for rapid remote diagnostics is an example of how technological innovation can act as a game changer, if conceived for the specific needs of contexts characterized by resource poverty.

This model is driven by a truly cooperative intent: switching the focus from the simple providing of laboratory equipment to developing countries and of diagnoses coming from abroad, to a vision strongly centred around a pervasive action of capacity building, knowledge transfer and interaction between the available local health specialists adequately supported, enhancing the diffusion of modern healthcare to the disadvantaged populations and averting new forms of scientific colonialism such as the so-called "helicopter science" [14].

Moreover, it shows how the development cooperation can be a challenging ecosystem for the growth of highly innovative solution like WaidX, increasing the diffusion of good health practices and boosting the use of modern technologies in developing countries.

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