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## ARTICLE

### **Development of Present and Future of Telepathology in Hungary**

Sándor VÁRI,<sup>1</sup> Mária CSERNEKY,<sup>2</sup> Anna KÁDÁR,<sup>3</sup> Béla SZENDE<sup>2</sup>

<sup>1</sup>Varimed Ltd, <sup>2</sup>1<sup>st</sup> Department of Pathology and Experimental Cancer Research, Semmelweis University and <sup>3</sup>International Academy of Pathology, Hungarian Division, Budapest, Hungary

Pathologists in Hungary evaluate several hundred thousand histological specimens yearly, and a second opinion is requested in 5-10 percent of cases. Application of multimedia systems (i.e. telepathology) is convenient and efficient to establish a correct diagnosis in such cases. The first telepathology connection in Hungary has been established between the 1<sup>st</sup> Department of Pathology and Experimental Cancer Research, Semmelweis University and the Department of Pathology, Central Hospital of the Ministry of the Interior. Further development occurred in the course of various projects, supported by the EU (Interpath, Retransplant, BePro): new stations were established in three university institutes

Key words: telepathology, consultations, diagnosis, database

### Introduction

The level of prevention and early diagnosis of diseases is an indicator of health care in a country. The establishment and operation of a well-organized medical record system is needed to continuously follow up also patients at various levels of health care.<sup>1-5</sup> The same system should also provide current data on morbidity and mortality, furnish databases for various medical specialties, and also be available for consulting specialists on a national and international level. A part of such a system is telepathology, which had been introduced a few decades ago in some countries of Europe and in the United States. The first two telepathology stations in Hungary were established in 1995.<sup>1</sup> These stations (1<sup>st</sup> Department of Pathology and Experimental Cancer Research, Semmelweis University, and the Department of Pathology, Central Hospital of the

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and six county hospitals. Electronic fixation of the images and their transmission by telephone line (ISDN) is easily available and an important feature of the multimedia system applied in telepathology. The system used by us is suited to evaluate frozen or paraffin-embedded histologic sections, as well as immunohistochemical and cytologic specimens, if necessary supplemented with transmission of macroscopic pictures. Our experience with bilateral consultations has proven the importance of telepathology. The telepathology system established in Hungary is now ready to join the telepathology network of the EU. (Pathology Oncology Research Vol 11, No 3, 174–177)

Ministry of the Interior) were connected by telephone line. However, the technical level of these stations was far from perfect and the establishment of a contemporary informatics infrastructure of telepathology was urgently needed.

## Telepathology in Hungary, supported by the European Union

Hungarian pathologists first joined the Research Program FP-4 of the European Union, which included the Interactive Histopathology Consultation Network (Interpath – PL-96112). This project supported the establishment of two up-to-date complete telepathology sender and receiver stations, one at the 1<sup>st</sup> Department of Pathology and Experimental Cancer Research, and the other at the Department of Transplantation and Surgery, both at Semmelweis University in Budapest. The aim was to test the new equipment and to enable these two Departments to expedite the evaluation of intraoperative frozen sections which were made at the surgical department and diagnosed at the distant department of pathology.

This project was highly successful and made possible the second step, i.e. to join the Regional and International

*Correspondence:* Dr. Béla SZENDE, 1<sup>st</sup> Department of Pathology and Experimental Cancer Research, Semmelweis University, Üllői út 26., Budapest, H-1085, Hungary. Tel./fax: 36-1-266-0451, e-mail: bszende@korb1.sote.hu or mari@korb1.sote.hu



**Figure 1.** Number of consultations between November 1, 2001 and June 16, 2002 according to Departments. 1: Department of Pathology, Central Hospital of Ministry of the Interior, Budapest; 2: Flór Ferenc Hospital, Kistarcsa; 3: Markhot Ferenc Hospital, Eger; 4: Markusovszky Hospital, Szombathely; 5: County Hospital, Kecskemét; 6: 1<sup>st</sup> Department of Pathology, Semmelweis University, Budapest; 7: 2<sup>nd</sup> Department of Pathology, Semmelweis University, Budapest; 8: Szt György Hospital, Székefehérvár; 9: Department of Pathology, Szeged University, Szeged

Integrated Telemedicine Network for Medical Assistance in end-stage diseases and organ transplantation (Retransplant – HC-IN4028). Retransplant extended the telepathology network to three more departments of pathology in the country, and also supported the diagnostic work of departments of radiology i.e. performed teleradiology. Encouraged by the success of this program, a nationwide teleconsultation system has been established within the BePro (Best Practice in Pathology and Oncology) project of the European Union.

### Structure and function of BePro in Hungary

### General considerations

Yearly 600 to 700 thousand of histopathological diagnoses are made in Hungary, and in 5 to 10 percent of the cases a second opinion is requested. The geographical distribution of hospitals in the country and the decreasing number of skilled pathologists urges the construction of a telepathology network covering the whole country. Priority should be given to 6 county hospitals (Budapest, Eger, Kecskemét, Kistarcsa, Székesfehérvár, Szombathely) and

*Table 1.* Statistical data of consultations (November 1, 2001–June 16, 2002)

Cases (total)	161
Image numbers (total)	786
Duration of consultations (minutes/case, mean)	13.18
Participating pathologists (department/case)	3
Average age of patients	52
– female	53
– male	49

two universities (1<sup>st</sup> and 2<sup>nd</sup> Department of Pathology, Semmelweis University, Department of Pathology, University of Szeged), as well as to small municipal hospitals which need continuous diagnostic help from the county hospitals and university departments, respectively (*Figure 1*).

Furthermore, telepathology consultations between Hungarian pathologists and European experts are desirable in difficult diagnostic problems, primarily with tumors, where prognostic and therapeutic considerations are particularly critical.

### Number and structure of the telepathology stations

Three university departments and five county hospital departments of pathology were included in the project. Bilateral consultations were performed between the various stations, utilizing the possibilities provided by both ISDN telephone lines and the internet. The software used for the consultations was the telepathology software (TPS) produced by Samba Technologies (France).

All clinical data of the patients were stored and sent in so-called eForm (HTML/XML). The images, sent to the consultant pathologist in peer to peer system, were put in DICOM (Digital Imaging and Communications in Medicine) form and stored also at the consultants' stations. The images, digitized with SonyDCX390P camera in a resolution of 700x600 DPI, are attachments from eForm. The eForms and the static images became part of the protocols of the consulting department.

All participants and the organizer department (1<sup>st</sup> Department of Pathology and Experimental Cancer Research, Semmelweis University, Budapest) registered the consultations in order to document and evaluate their performance in support of the pathologists' diagnostic service.



*Figure 2.* Number and organ type of consulted cases. 1: brain, 2: intestine, 3: skin, 4: bone, 5: bone marrow, 6: breast, 7: stomach, 8: nerve, 9: soft tissue, 10: liver, 11: uterus, 12: parathyroid gland, 13: adrenal gland, 14: mesentery, 15: salivary gland, 16: lymph node, 17: ovary, 18: thyroid gland, 19: pancreas, 20: retroperitoneum, 21: oral cavity, 22: lung, 23: kidney



*Figure 3.* Location and number of tumors where the second opinion modified the initial microscopic diagnosis

# *Function of the BePro project between November 2001 and June 2002*

In the above period online consultation was performed in 161 cases by transmission of 786 images. These cases were of real diagnostic problem, and there was a need for a second opinion. The time for case input and creating digital images took 8-10 minutes. The average real consultation time was 13.18 minutes (*Table 1*). Pathologic changes, first of all tumors, were consulted in the case of the following organs and tissues: brain, intestines, skin, bone, bone marrow,

breast, stomach, peripheral nerve, soft tissue, liver, uterus, parathyroid glands, thyroid gland, adrenal gland, mesentery, salivary glands, lymph nodes, ovary, pancreas, retroperitoneal tissues, organs of oral cavity, lungs, kidney. The type of organ or tissue and the number of consulted cases are indicated in *Figure 2*. The most frequently consulted tumors were those of the skin, breast and the thyroid gland.

Discrepancies between the diagnoses of the sender and the consultant department were found in altogether 14 cases, comprising tumors of the lung, breast, skin and soft tissues. The number of these cases is shown in *Figure 3*.

A database has been created from the stored material and has been available for all participants (*http://www.varimed.hu*). The following case illustrates the work of the consultants.

### Case report

A 46-year-old man was admitted to a hospital because of an irregular mediastinal roentgenographic shadow, detected on routine screening. Bronchoscopy revealed a partly ulcerated and necrotic mass protruding into the lumen of



*Figure 4.* Image archivation by DICOM, data transmission through XML data-structures. (a) Histological image of the biopsy. Note squamous epithelium on the surface and tumor tissue in the deeper layers (HE, x150). (b) The tumor cells possess abundant granular cytoplasm (HE, x600). (c) The tumor cells show S100 positivity (immunoperoxidase, x300). (d) The tumor cells are negative for cytokeratin; epithelial cells show positivity (cytokeratin immunoperoxidase, x600).

PATHOLOGY ONCOLOGY RESEARCH

the left inferior main bronchus. A biopsy was taken and was diagnosed as "Necrosis due to foreign body", however, the clinician requested a second opinion. Consultation was asked from one of the university departments via telepathology.

The image of an HE-stained histologic slide showed squamous metaplasia on the mucosal surface. In the deeper parts, tumor tissue was observed (*Figure 4a*), which at higher magnification showed round, dense nuclei and abundant eosinophilic granular cytoplasm (*Figure 4b*). The diagnosis of a granular cell tumor was suggested. Subsequent immunoperoxidase reactions proved to be positive for S100 (*Figure 4c*) and negative for cytokeratin (*Figure 4d*), confirming the diagnosis. After complete excision of the tumor the patient was discharged and remains symptomless.

### Main results of the BePro project

The telepathology network established in the course of this project provides the basis for the application of telepathology, integrated to a sophisticated informatics system.

New standards such as Digital Imaging and Communications in Medicine (DICOM), CEN TC251, etc., created by the European health care telematics providers were implemented in the network. The use of extended applied language (extensible Mark-up Language, XML) made possible filling up, actualization, and harmonization of oncopathological databases, thus professional practice information as well as distribution of the results on the Internet and regulation of data handling.

The XML developmental environment enabled the participating pathologists to actively contribute to Web-based electronic protocols in their everyday practice.

The system proved suitable for the transmission of across and microscopic images, including paraffin-embedded or frozen sections stained for routine histology or with special stains, as well as cytological smears.

The telepathology system provided an opportunity to discuss difficult cases, and this consultation led to improved diagnosis in several cases.

Hungarian law on human rights (LXIII/1992 and XLVII/1997) ensures legal basis for confidential data protection in the course of nationwide telepathology consultations.

### Discussion

Cancer morbidity and mortality in Hungary is one of the highest in Europe.<sup>7</sup> The leading causes of death are tumors of the lung and breast. Therefore, prevention, screening and early diagnosis is of particularly high priority with these neoplasms.

The efforts of pathologists, clinicians and professionals in informatics to establish a reliable telemedicine system in Hungary are reflected in the aims and achievements of BePro. This program is based on the best results of European experts. It is reasonable to expect that more extended use of telepathology may shorten the duration of hospitalization and decrease the time of anesthesia if frozen sections are used. The hospitals without pathologists would benefit from telepathology. Last but not least, establishing databases of histological images can be of benefit for postgradual training.

New technical tools which enable us to perform online communication and consultation should be introduced in the future. Improvement of the quality of transferred images is constantly required. A further requirement comprises the establishment of facilities for teleconferences. The emerging method of virtual microscopy<sup>8</sup> may contribute in the future to telepathology, first of all to archivation of images.

Extension of the telemedicine network, including telepathology would cover the entire country, as it has been the aim of all European programs. The expected results could significantly improve early diagnosis and possibly decrease cancer mortality in Hungary. Pathologists, clinicians and experts in informatics are prepared to contribute to such an extension of telemedicine.

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