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REVIEW ARTICLE

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Telepathology: frozen section diagnosis at a distance

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Abstract Telepathology may be used to provide a frozen section service to hospitals without a department or institute of pathology. We have developed a telepathology system using the commercially available Integrated Services Digital Network (ISDN). The main software and hardware elements of our system are: Apple Macintosh workstations, a program for simultaneous transfer of image, voice and data, and a data bank for storage of patients' data and microscopic images. A picture instrument manager (PIM) makes remote control of microscopes or other instruments possible. The system connects the Department of Pathology of the University of Basel with the Regional Hospital of Samedan, 250 km away, and the Regional Hospital of Burgdorf, 100 km away. During a period of 20 months, frozen sections with the hospitals in Samedan and Burgdorf were performed in 53 patients. Between 54 and 58 s were required for the transfer of a diagnostic 8-bit grey level image containing 341±26.1 (standard error) kbytes (n = 13) or a diagnostic 24-bit colour image containing 165±16.9 kbytes (n = 40). Frozen section diagnosis was completed in 20–40 min. True-positive diagnoses of malignant tumours were achieved in 85.7% of cases (sensitivity = 0.857). No false-positive diagnosis was made. In 3 of the 53 cases telepathological diagnosis was not possible for technical reasons.

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Introduction

The need for telepathology

Telepathology is a field of telemedicine that serves two main purposes. It allows for direct consultations between experts and permits immediate diagnostic services to be provided at a distance. We developed a telepathology system in our department in order to determine whether telepathology, using the Integrated Services Digital Network (ISDN) offered by the Post, Telegraph and Telecommunication services of many countries, can help to provide a frozen section service to a hospital without a pathology department.

What is necessary?

Our system had to meet five basic requirements: (1) use of an already existing communication network (ISDN) with a capacity to transfer microscopy images within a maximum of 60 s; (2) use of a system which is easy to handle and to integrate into daily work (user-friendliness); (3) use of a data bank with the capacity to store all images together with the necessary disease- and patient-related information; (4) use of hardware and software modules which are inexpensive and can also be used for other purposes; and (5) use of a system that is accessible at all times and connects as many partners as necessary.

The ISDN communication network was chosen because of its reliability, since it operates like the normal telephone network. In contrast to the normal telephone network, however, ISDN is only accessible to defined user groups. ISDN consists of three main channels: A-channel (analogue telephone channel with a transfer frequency of 4 kHz), B-channel [digital channel for data or voice with a transfer rate of 64 kilobit/second (kbit/s)],

Table 1 Software and hardware key elements

Subarea	Software	Company
Software elements		
Image grabbing	RasterOps	RasterOps Corp. Lindon, Utah, USA
Image processing	Image	W. Rasband, National Institute of Health, Bethesda, Maryland, USA
Image analysis	VIDEOPLAN VIDAS	Kontron Bildanalyse GmbH, Eching, Germany
Conversion of 24-bit images in 8-bit images	ICP (image conversion program)	Authors of this paper
Management of peripheral instruments for capturing images	PIM (picture instrument manager)	Authors of this paper
Communication with other computers also integrated in the local area network (LAN)	AppleTalk	Apple Computer Inc., Cupertino, California, USA
Communication with other workstations, either directly via the public ISDN or via an ISDN switchboard	LeoTalk	Hermstedt GmbH, Mannheim, Germany
Electronic mail	TimbuktuPro	Farallon Computing Inc., Berkeley, California, USA
Voice recording	TimbuktuPro	Farallon Computing
Voice communication	TimbuktuPro	Farallon Computing
Administration (related data bank)	OMNIS 7	Blyth Software Inc., San Mateo, California, USA
Hardware elements		
Workstation	Apple Macintosh (IIci, IIfx)	Apple
Frame grabbers	Screen machine	Screen machine, ProficomP, Karlsruhe, Germany
ISDN-compatible communication tool	LeoTalk	Hermstedt
Network	ISDN	Swiss Post Telegraph and Telecommunication (PTT)
Projection		
macroscopical images	Visualiser	Canon Corporation, Zürich, Switzerland
microscopical images	1CCD video camera (Sony 151C)	Sony AG, Schlieren, Switzerland
Robot microscope		Olympus Optical GmbH (Europa), Hamburg, Germany C.Zeiss, Optical Instruments Oberkochen, Germany
Printer	Apple	Apple
Optical disk	Sony optical disk	Sony
External hard disk	Roi hard disk	R.Obler, Industrie-Elektronik, Martinsried, Germany

and D-channel (digital channel for out-of-band signaling with a transfer rate of 16 or 64 kbit/s). Since coupling two or three B-channels increases the transfer rate considerably, we use two B-channels, which results in a transfer rate of 128 kbit/s.

Installation of a telepathological service for frozen section diagnosis using ISDN is only meaningful if the distance between the pathology department and the hospital is more than 25 km (about 16 miles). The calculation of this minimal distance is based on a comparison of the time needed for the transport of a tissue specimen from the hospital to the department by ambulance or taxi and the time needed for transmitting a frozen section diagnosis via our telepathology system.

User-friendliness

The term "user-friendly" has become a catch-word for software design today, especially in the world of microcomputers [4]. Our system can be considered user-friendly because it is based on: (1) a menu-driven interface in which the user need not remember abstruse commands; (2) logical flow within the menu system; (3) grouping elements by functionality; (4) understandable error messages and easy recovery from error; (5) help messages available on request; and (6) a certain de facto standard of menu operation and keyboard use [4]. This basic equipment allows easy integration into routine diagnostic work in a pathology laboratory.

Data bank

Each document stored in the data bank can be identified by using a standardized designation. The identification code (e.g. SAM.PASS.921217.0943.Mic03) is composed of abbreviations of the following eight positions: (1) the hospital to be served (SAM: Samedan); (2) the hospital unit (PA: pathology); (3) source of image (SS: frozen section); (4) year of consultation (92: 1992); (5) case number during the current year (e.g. 1217); (6) time at start of consultation (0943: 0943 a.m.); (7) image type (Mic: microscopical); and (8) image number (03).

Devices and modules

Hardware and software modules. The system described consists of small and tested hardware and software modules, specified in Table 1. The software is selected from separate off-the-shelf modules and compiled in a program. Only two of the software elements used were programmed by our group: the image conversion program (ICP) and the picture instrument manager (PIM). The PIM constitutes a platform for using many different peripheral instruments for capturing images, independent of their function (from microscopes, frame grabbers, image analysis systems). It means that the instruments can be exchanged according to the specific requirements, independent of their manufacturer, and that the system can be updated and adapted continuously. The modularity of a telepathology system must also be taken into consideration when choosing the instrument for data transfer (images, voice, text). We strived for the greatest possible compatibility by working with various image formats and by integrating the workstations into local area networks (Fig. 1).

Operation modes. A telepathology system should offer two operational modes: an emergency mode and a mail box mode. The emergency mode is actually used for frozen section diagnosis. The mail box is suitable for general consultations or for building up or accessing a teaching case collection [16].

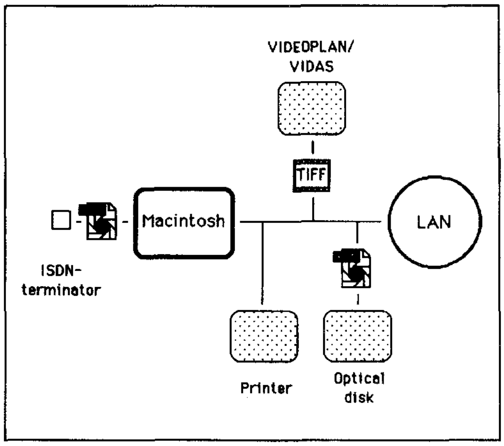

Fig. 1 Interface between the telepathology network and the local area network (*LAN*) at the Department of Pathology of the University of Basel. *VIDEOPLAN/VIDAS* Digital image analysis system (KONTRON, Bildanalyse, GmbH, Eching near Munich, Germany), *TIFF* image format, *PICT* image format (see text)

Generation of images. Images can be generated either by "grabbing" or by "zooming". Grabbing means the conversion of images obtained by a video camera placed over the macro viewer or the microscope into digitized images. Zooming means the presentation of digitized images on the monitor. The fields of view can be grabbed with various contents of information on the image (8 bits or 24 bits). For zooming three "electronic objectives", each with a special resolution of pixels, are available.

Presentation of grabbed images in the video eye. The grabbed image can be stored in a data bank or can be transfered into the video eye. This transfer can be carried out by two different modes: (1) the "scale mode", and (2) the "non-scale mode". These two modes were explained in more detail in an earlier paper [13]. The advantage of the scale mode lies in the fact that all the information on the grabbed image is presented in the video eye on the monitor. If the size of the video eye, which is actually generated by the selected electronic objective, is smaller than the size of the grabbing field of the computer, then the whole grabbed image is linearly reduced until the whole image can be presented in the video eye by using the scale mode. In the non-scale mode, however, a segment is cut out of the whole grabbed image with the size of the video eye. The size of the grabbed image remains constant and is not reduced as in the scale mode. The advantage of this procedure is that the microscopical image generated during the grabbing process is presented in the video eye in its original resolution. The disadvantage is that parts of the grabbed image may be lost.

When should the scale mode be used? The answer depends on the diagnostic decision to be made by the pathologist. When he has to decide whether a tumour is malignant or benign, then the tumour infiltration into the surrounding tissues will be an essential criterion. Accordingly, he works with a relatively low optical magnification and uses the scale mode.

The non-scale mode should be selected to assess small tissue or cytological components in the image (e.g. chromatin texture). In this situation a high magnification is used (Fig. 2). It will be satisfactory if the above-mentioned key elements of the image are present in the video eye on the monitor. Therefore, the original resolution of the grabbed image should be retained and this is guaranteed by the non-scale mode. Loss of parts of the whole grabbed image can be accepted. To date, no techniques or procedures similar or comparable with these two grabbing modes have been published.

Accessibility

A telepathological service for frozen section diagnosis should be as accessible as the conventional services in pathology. This means that the system can be used anytime, independently of technical and instrumental prerequisites. This condition is fulfilled by the ISDN, which is freely available to every user, in contrast to broad band networks which represent point-to-point connections and not a real network. Additionally, the telepathological service in the pathology department should be totally integrated into daily work.

How is it done?

The main steps are as follows: (1) request for a frozen section using a standardized protocol; (2) generation of the patient data; (3) assessment of macroscopical images from the specimen; (4) sampling of tissue; (5) preparation of frozen sections; (6) selection of microscopic fields; (7) assessment of microscopical images; and (8) reporting diagnosis.

Generation of patient data

When a frozen section is requested, a text file containing the administrative and clinical data of the patient is generated. This information, together with macroscopical images, is transferred to the pathology department (Basel). In the hospital (Samedan), the grabbed macroscopical and microscopical images are stored in case-related folders. In the pathology department patient-, case- (or job-), examination- (or task-), and image-related data are stored together with all the images (macroscopical, microscopical and clinical) in a data bank [13]. The structure of our data bank is analogous to the one used by the administrative computer system PATHOSYS [11], which has been in use for 10 years.

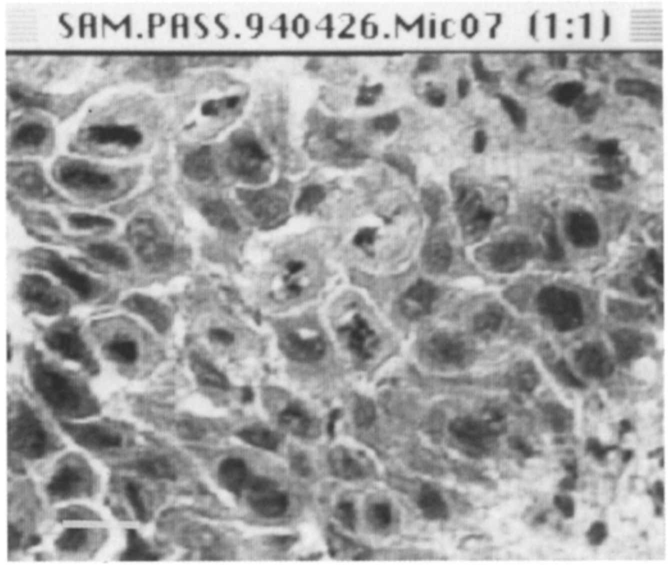

Fig. 2 Histological image from a squamous carcinoma of the larynx. Mitoses and nucleoli are quite visible (magnification: 1:600, *bar* 20 μm). (The original image is a colour image)

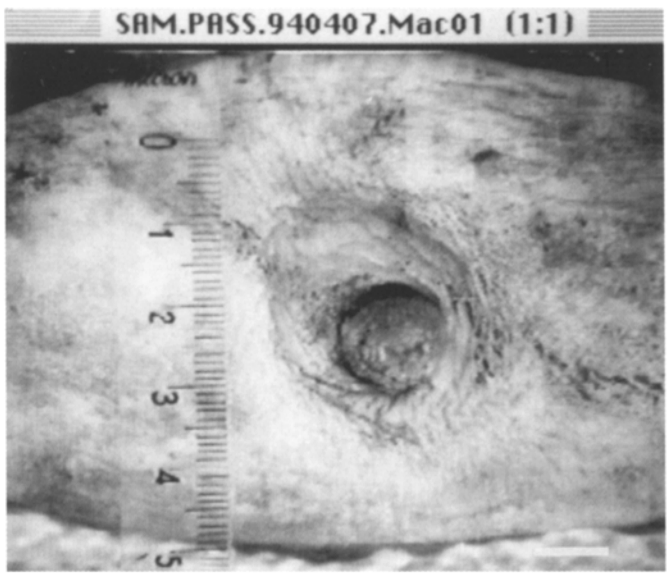

Fig. 3 Macroscopical image of an invasive ductal breast carcinoma, pT4, pN0. (The original image is a colour image)

Tissue sampling and selection of histological fields

Tissue sampling from surgical specimens for frozen section diagnosis is performed at the hospital by a physician or a specially trained technician, supervised by the pathologist via the telepathological system. Figure 3 shows an image of a resection specimen on which the pathologist has to decide from where appropriate tissue samples for histological examination should be taken. Using the voice-channel and a pointer visible on the monitor screen of the system, the pathologist indicates the area to be examined. This procedure led to an acceptable sampling error probability of 0.13.

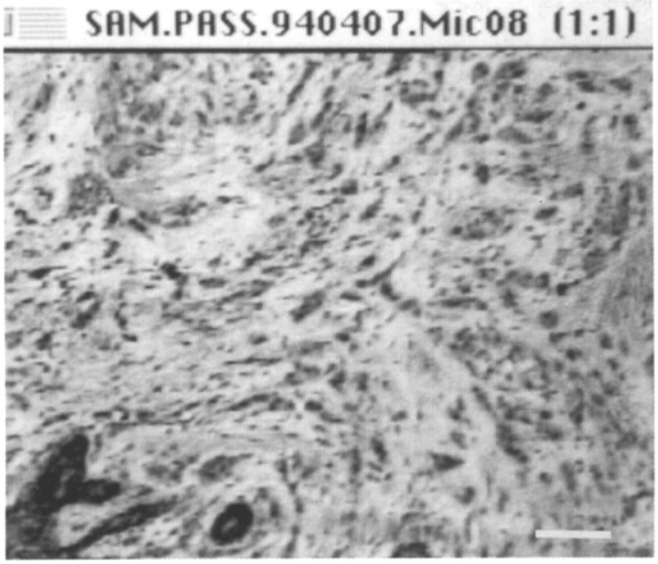

Fig. 4 Histological image from an invasive lobular breast carcinoma. The infiltration of the carcinoma in the surrounding soft tissue environment can clearly be observed (magnification: 1:100, *bar* 100 μm). (The original image is a colour image)

Preparation of frozen sections

The frozen sections are prepared at a laboratory in the hospital (Samedan).

Presentation of optical information by the optical equipment

The optical equipment for assessing frozen sections in the hospital consists of an organ macrospecimen Visualiser (Table 1) and a system for projecting histological or cytological images from a microscope into the video eye of the computer screen. The Visualiser may also record other "documents" than organ specimens.

The histological examination is usually started with the 2.5 or 10.0 objective (25- or 100-fold magnification). However, if requested by the pathologist, further microscopical magnifications (Fig. 4) may be preselected by the partner in the hospital. If such a guided preselection is not possible, the microscope objectives are changed by remote control by the pathologist and automatically focused on the objects. The pathologist is then able to select as many microscopical fields as he wants. However, it is clear that every increase in the number of images also increases the total transfer time.

Report of diagnosis

At the end of the frozen section assessment, a preliminary final report containing the frozen section diagnosis is transmitted to the hospital, by phone (voice channel) and simultaneously in a text document. The completed case- (or task)-related folder is transferred from the hospital to the pathology department. When the final diagnosis is available, usually 3 days later, it is written in a text file, coded according to the systematized nomenclature of medicine (SNOMED) [3], and then transmitted to the hospital.

What are our results?

Analysis of all frozen section cases from Samedan examined during the last 20 months revealed that we failed to provide a diagnosis in only 3 cases (5.7% of all cases) because of inadequate histological preparation or for technical reasons (such as the electronic instability of ISDN). Twenty-two cases (44.0%) concerned diseases of the breast, 12.0% diseases of the thyroid, and 10.0% diseases of the ovaries or salivary glands. Nineteen patients (38.0%) had a non-neoplastic disease. Twenty-eight lesions (57.1%) were benign.

The percentage of true-positive, true-negative and false-positive diagnoses made on the basis of frozen sections and the corresponding embedded tissues is given in Table 2. Eighty-five percent of malignant tumours were correctly recognized on frozen sections, and there was no false-positive diagnosis (Table 2). The percentage of true-positive diagnoses of tumorous and non-tumorous lesions was 90.3% for all cases (Table 2) and 93.8% for the 22 breast lesions. This fact is reflected in the value of 0.105 for the parameter "1-specifity" (Table 2) and concerns the descision "tumour or no tumour" [specifity 0.895 (= 17 of 19 cases)].

The time needed for a remote frozen section consultation ranged between 20 and 40 min. On average, one or two macroscopical images and eight (range: 2–14) microscopical images were analysed. Patients who under-

Table 2 Sensitivity and specificity of telepathology for recognizing malignant diseases and tumours. Total number of allocations by frozen section diagnosis for the allocation group "malignant disease" ($n = 49$), and for the allocation group "tumour" ($n = 50$)

Allocation group	Sensitivity (true-positive)		1-specifity (false-positive)	
	Frozen section diagnosis	Embedded block diagnosis	Frozen section diagnosis	Embedded block diagnosis
Malignant disease	0.857	0.874	0	0
Tumour	0.903	0.939	0.105	0

went frozen section diagnosis via telepathology stayed in hospital 3–6 days fewer than patients subjected to the conventional procedure. This is due to the time required by the normal mail service.

An important issue of telepathology concerns the data storage capacity of the system. In our series the administrative data required 11.6 kilobytes per case (kbytes/case), while the images needed 1.7 megabytes per case (range: 0.4–4.8 mbytes/case).

Statistical analysis

For statistical evaluation of our telepathology system the following parameters were calculated or tests were performed: median value and standard error of the parameters "size of the electronic image", and "number of images used per diagnosis"; sensitivity (percentage of true-positive diagnoses on frozen sections versus final diagnosis); specifity (percentage of true-negative diagnoses); and the descriptor "1-specifity", which means the proportion of false-positive decisions [1]. Another test allowing analysis and interpretation of methodological characteristics is the so-called "relative operating characteristic (ROC) curves" [1].

Conclusions

The results obtained with our system show that hospitals which have no pathology department can be provided with a frozen section diagnosis service via ISDN.

Among the many details which have been improved during the last 2 years the most important have been the transfer time, image quality, camera type, technical stability, and efficiency of the system. The total time currently needed for a frozen section diagnosis, starting with macroscopic viewing of the specimen and ending with the transfer of the text file with the diagnosis, is between 20 and 40 min, a time acceptable to surgeons. It can be anticipated that in the near future the maximum time of 40 min can be reduced to 30 minutes by increasing the number of ISDN B-channels available.

The demands made on video screens used in the context of telepathology were extensively analysed by performance studies [5, 17, 19]. Our own experience does not correspond to that of Weinstein et al. [17, 19]. These authors rejected PAL video screens because of their allegedly inherent limitations for viewing histological images with relatively low power. Eide and Nordrum [5] believe that more experience with video microscopy will probably lead to the quality of frozen section diagnosis being similar to that of direct light microscopy. Our experiences with various cameras convinced us that the quality of the images depends entirely on the quality of the camera. The influences of the technical features of a camera on the results are even more crucial than those of the computer screen or the microscope.

The stability of our system is now well established. When we started, the ISDN was interrupted a few times. This happened because when ISDN became available for our project, Swiss Telecom occasionally carried out tests without advance warning.

The statistical sensitivity and specifity of our data concerned both types of decision which occur in frozen section diagnosis: (1) is the lesion malignant or benign; and (2) is it neoplastic or non-neoplastic? For calculation of the proportion of true-positive and true-negative decisions the final diagnosis made on the whole organ or tissue specimen excised should be used as the gold standard.

There are only a few studies related to telepathological consultations [7, 8, 10, 12, 13] or frozen section diagnosis [5, 12, 13]. The results presented in this study are comparable with those presented by Eide and Nordrum [5], who found a sensitivity of 0.730 for recognizing malignant disease in 50 cases, while we had a sensitivity of 0.857 in 49 cases. They used a broad band network and not ISDN.

The suitability of ISDN as a network for telepathology is still under debate [14, 15]. Some authors have discussed it theoretically and pointed out that ISDN could be suitable for telepathological diagnosis [6, 14], but only three papers have been based on practical experience with a "tele-system" either in pathology or radiology [2, 9, 12]. Evaluation of telepathology under laboratory conditions [8, 10, 18, 19] is not comparable with an analysis of telepathology in daily practice. In the latter situation, stress and the latent danger of making an error are always present and may have a considerable influence on the results. This was one of the reasons why, right from the beginning, we have integrated the telepathology system into our daily diagnostic work schedule.

With increasing use of telepathology in the future, problems concerning legal aspects must also be taken into consideration. These include not only data protection and data security, but also an exact documentation of the images relevant to the final diagnosis. This documentation problem can be solved by routinely, integrating all the images used for diagnosis into the data bank – independent of their quality.

From our own results and the few reports in the literature we conclude that telepathology using ISDN can be considered a valuable new diagnostic tool. The success of telepathology will essentially depend on the extent to which it can be integrated into daily practice and used without special technical knowledge.

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