A Remote Imaging Revolution:
Telemicroscopy & Telepathology—at 'Net Speeds

Tools are arriving, now, to bring those speeds (and 3-D) to the desktop—inexpensively.

Yes...it's brewing right now. Coming on the wings of the Internet, it will impact microscopists and common citizens alike. It will amplify research, simplify and augment quality control and failure analysis, and enhance medical care. It's real-time, Internet-based telemicroscopy, and it constitutes a remote imaging revolution.

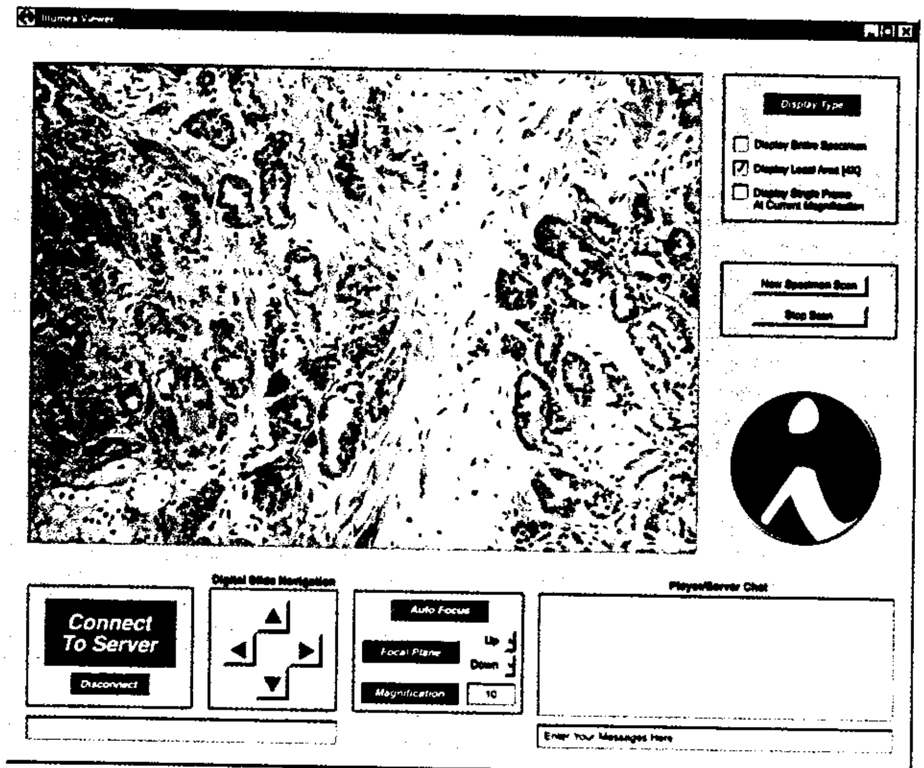
Logical outgrowth of telemedicine

Much of current telemicroscopy arrived in conjunction with the already rapidly-growing field of telemedicine. Offering quality health care to prisons, the military, and rural areas requires considerable time and logistics for transport of either patient or doctor. The advent of digital stethoscopes, otoscopes, dermoscopes, and other remote monitors (cardiac, blood sugar, etc.) now enable the doctor to be in one location and the patient and nurse or nurse practitioner to be at some distance.

East Carolina University's Telemedicine Center, discussed in these pages previously in some detail, is an excellent case in point. According to its director, Dr. David C. Balch, their four call centers—basically specially-fitted mini-teleconferencing centers—have by now proved so successful in covering their 10,000-square-mile rural region that they are adding another four.

And telemicroscopy adds yet another dimension to this extended medical outreach by providing the ability to read pathology slides quickly and efficiently, as well as expanding the availability for consultation with other expert pathologists, such as those at AFIP (the Armed Forces Institute of Pathology at Walter Reed Medical Center, Bethesda, MD).

Pathologists are not the only beneficiaries of telemicroscopy. Thousands of companies that are involved in all sorts of production (plastics, metals, ceramics, and the resulting products) use microscopy for quality control, quality assurance and failure analysis, of course—and many have multiple facilities, both domestically and multinationally. Over the past 20 years, shrinking resources have left these facilities with a few central service labs, limited personnel with advanced analytical capabilities, and more equipment than staff to run it. This situation is a perfect scenario for the introduction of real-time telemicroscopy. Knowledgeable microscopists at one site can check on problems across the globe; researchers and analysts in remote facilities can make better use of microscopes which would otherwise lie dormant.



FiberPix: first commercial telemicroscopy solution to use proprietary streaming technology for real-time image acquisition and navigation.

Some of the greatest winners in this new technology area will be failure-analysis engineers in the semiconductor fab lines. Currently, when a problem arises on the line, they have to walk across a large industrial campus, take 10-15 minutes to don a "bunny suit", then enter a clean room. In many instances, the problem can be solved in a short period of time, but they lose still more time returning to street clothes and their desks. A better approach would be to have a technician who is already in the fab prepare the sample and put it on a microscope, and then have the engineer remotely navigate and analyze the failure.

Sounds great! So where's the problem?

Practicing microscopists are used to well-designed, easy-to-use computer interfaces and fluid movement in their hardware control and image response. In telemicroscopy, the size of the information files creates problems in these areas. Although real-time remote control of the microscope from nearby labs has been well-known for decades, transporting those controls over the Internet often produces hysteresis: a feedback mechanism which makes navigational movements like stage position jerky and unpredictable.

Bandwidth is, of course, another part of this problem. As shown in Table 1 on the next page, there are (in 1999) a number of different telecommunication modes available, but the ones with the type of bandwidth necessary for high-resolution, analytical imaging are still very expensive for the budgets of many, even most microscopists. A 1.5 Mb T1 line, for example, can cost $2,000-$3,000/month.

The video signal from any type of non-digital camera used today in microscopy presents images at a rate of 30 fps. Typically, each of those images would be 640 x 480 pixels, and, if color is important in your application, 24-bit color, totaling about a megabyte of data, trying to travel through the telecommunications system (modem, phone lines, LAN, etc.) at 30 fps.

Looking at image information from *this* perspective makes a number of issues clear:

• *The impossibility of real-time navigation.* Unless something is done to reduce the size of the image file, there will always be an inevitable lag between any controlling signal (move left, focus, change objective) and the response in the image.

One solution is JPEG compression, as available in the widely-used Adobe PhotoShop. The smaller file size *does* speed things up, but JPEG is a one-step compression algorithm, producing only a static snapshot of the specimen. It treats all components of the image similarly and can cause the image to lose fine detail, edge information, color, and sharpness. It may even become pixelated, producing the well-known "jaggies" (step-like edges).

• *The limited resolution available through standard video transport mechanisms.* Standard TV-style NTSC and related video conferencing solutions just don't provide the resolution and clarity for diagnoses and failure analysis. One way telepathologists have solved this problem in many cases is by resorting to "store and forward". These systems lower the spatial resolution of the image while navigating then acquire in high-resolution mode. The last step is still very time-consuming, often taking from tens of seconds to minutes, depending on the size and resolution desired.

Other pathologists have followed more of an image analysis path—viewing a low magnification for context, then moving to higher magnification for detail.

At the higher magnification, they scan in smaller image "tiles", then stitch them together to make a larger, high-resolution image. Several problems are inherent in this approach, ranging from variations in background lighting to loss of information as tiles are aligned for the stitching process. Like the other approaches, tiling is time-consuming.

• *Storage issues.* Part of this issue involves simple space. Even if each of these images were only 1 MB, it would not take much time in a busy lab to completely fill a hard drive. Additional purchases become necessary. The other part of the problem is access. A database and a carefully-structured, searchable archiving system are critical.

True telemicroscopy is limited

Acquiring a digital image, storing it on a server or desktop computer, and e-mailing it to a friend or colleague is fairly routine these days, even though it may be time-consuming. A recent study involving 229 cases using diagnosis by e-mail was conducted between the departments of Pathology at the University of Udine and the City Hospital of Trento (both in Italy). While the clinical findings were positive, the slow speed limited this approach to second-opinion consultation, remote image processing, quality assessment and continuing education.

However, true telemicroscopy (the ability to run a microscope remotely and acquire images) is limited. Few pathologists, QA/QC engineers, and practicing microscopists have access to the elaborate hardware and advanced telecommunications necessary to solve its problems, so the ability to provide true telemicroscopy currently resides in the hands of a few gurus, national labs and major universities. Luckily, most of these groups are willing to share information. Some, like the Telepresence Microscopy Laboratory at Argonne National Laboratories and BEN:LINCS (Bethlehem Education Network: a Local Instructional Network for Culture and Science, via the Lehigh University Electron Microscopy Laboratory), even provide access to elaborate equipment. While many of these sites offer high-resolution images, be prepared to be patient for the inevitable lag between control movement and image response.

Telecommunication mode	Speed (per sec.)	Cost
POTS, analog modem	56.6 Kb max	Monthly phone rate
Multiple modem solution (3 phone lines)	56K x 3 = 168 Kb	"pay when you drink"
ISDN	64K x 2 =128 Kb	$300/month
ASDL	1.5 MB	$500
T1	1.5 Mb	$1500-$3000/month
LAN/Ethernet	100Mb	
LAN/Token Ring	4-16Mb	
ATM (future)	155 Mb	$15K-$40K

Table 1. Various common telecommunication modes and relative costs.

Enter Internet video

Microscopy has *always* demanded unique eye-brain-hand coordination. But many of the existing telemicroscopy systems thwart that coordination, because limited bandwidth cannot provide the real-time navigation. Widespread acceptance of the Internet has changed the dynamics for bandwidth cost, making it cheaper and more accessible to a broader range of customers. For many in this arena, the Internet is really a mixed blessing.

On one hand, the Internet is simply too *variable* to make it a reliable method for transmitting real-time imagery. When images are compressed using conventional video approaches, it is sent out as one, unified stream (streaming video). However, any disruption of that stream disrupts the video images on the receiving end. ISDN and T1 lines are dedicated, so no other data will be sent over that connection: the video signal is always received intact.

However, if the same video stream is sent over the Internet, data may be lost, resulting in fragmented and jerky images. On the other hand, its low cost and easy accessibility make the Internet the ideal communication medium for telemicroscopy. *Is there a middle ground* which will enable the speed of streaming video to work with the Internet to provide economical, accessible real-time imaging?

FiberPix: impressive, low-cost Internet solution

Late this summer, **Illumea Corp.** (Newport Beach, CA) will announce FiberPix, the first commercially-available solution use proprietary streaming technology to fulfill the microscopists' dream: the ability to navigate a slide, remotely, in real time, and generate high-res, 24-bit color images, without irritating lag. *The entire slide will be instantly available at every magnification.*

Working with USC Medical School and a group of key pathologists and microscopists, the engineers behind FiberPix have made life simple and cost-effective. Finally, setting up a real-time telemicroscopy lab will not be cumbersome or overly expensive. Currently, controllers are available for mid-range Nikon and Olympus microscopes using modestly-priced Prior stages. Support will also be available for high-end research systems from other manufacturers.

Since the system is compliant with VideoForWindows, FiberPix accepts video input from analog and digital cameras as well as HDTV and FireWire. Even the host computer, a beefed-up Pentium III, has been specially engineered with an eye to fiscal responsibility, reducing the total system price by about 70% compared to earlier entries in this market.

This simplicity and ease of use extends to telecommunications networks as well. The system does not require expensive ISDN or T1 lines or elaborate satellite connections. It is designed to use standard 56K modems and existing Internet connections (including LANs and WANs) for both the acquiring end and the remote viewer. The proprietary technology also enables an upgrade path which does not require any upgrading software.

The same attention to detail and budget were engineered into the remote viewing site. Anyone with a Pentium II running under Windows 95/98 or NT 4.0 can download a free viewer from the Illumea Web site—*www.illumea.com*. The proprietary streaming technology provides real-time navigation for the remote viewer, even during acquisition. In stark contrast to the tiling approach, the system collects a single, seamless, large format image of the whole slide. For a closer look, electronic zoom instantly magnifies the feature of interest, again, in high-resolution, true color. When you unzoom, the system marks that location for later reference.

Storage was the third challenge of existing telemicroscopy systems. Illumea addresses that problem by providing space by subscription on their secure server. Since each large format occupies a hefty 100 MB, this service is valuable for any lab which does not have a huge mainframe. The images can be available only by password to a select audience or available as part of an annotated image library which can be used for consults or distance learning. And because images and related text are available via streaming video, there is none of the typical wait for an Internet download.

Implications

The results have just started coming in regarding the cost and usage impact of both telemedicine and telepathology, but the results for analyses of all sorts by remote microscopy imaging are very positive.

Telemedicine was the model for telemicroscopy, and its success can provide an indication as to the potential for real-time, Internet telemicroscopy. Newly released data from a study commissioned by the U.S. Military Healthcare system bodes well for both the clinical and business case for telemedicine in Europe. In addition to a cost-benefit analysis, the study evaluated 2000 consecutive air referrals to determine whether telemedicine could have avoided evacuation. The results: "31,000 conventional consultations could be replaced by telemedicine in Europe each year [with a] potential savings [of]$3.7M in travel costs and 25,000 working days." Another study conducted by the U. S. Navy found that 17% of the MEDEVACs could be prevented with telemedicine with a reduction in travel of 155,000 miles per year and a savings of $4,400 per MEDEVAC.

As with any new technique, there are always questions about the impact on accuracy. Again, looking to telepathology as a model for telemicroscopy in general, a number of recently released studies indicate high agreement between live and remote diagnoses. Dr. Mea and associates compared the results for 60 frozen sections, 64 cases of gastrointestinal pathology, and 60 cases of urinary pathology and obtained diagnostic agreement ranging from 90% in urinary cytology to 100% in frozen sections. Dr. Takahashi and colleagues found 97.6% agreement for 82 cases of breast cancer, with a false positive rate of only 1.2%.

Clearly, real-time remote control of a microscope provides incredible opportunities for distance learning. Students, be they in elementary, graduate school, or the work environment, can learn how to run new instrumentation on their own schedules. Libraries of large format, high resolution images available by proprietary streaming technology are an invaluable resource for anyone learning to recognize and diagnosis problems, from Pap smears to electronic circuits to faulty polyurethane foam formation.

Real-time Internet telemicroscopy will also have an impact on the availability of rare resources and equipment. There will be new implications for shared equipment grants and new profit centers for departments and Centers for Excellence. The potential audience for equipment use won't just be local researchers and analysts, it will be a state, federal, and global population.

There are also interesting ramifications for central service labs, which now have too much equipment and not enough educated personnel to run it. More people throughout the company can be trained in specific technologies and can use that equipment remotely. While this tack involves an up-front investment in workshops, there are big dividends in terms of having expensive equipment used more frequently.

Finally, real-time Internet telemicroscopy offers intriguing opportunities when buying a new microscope. Since all forms of microscopy are now capable of computer control, you can "drive it on the Internet before you buy". LEO, a scanning electron microscope manufacturer, has taken this capability a step further by offering remote diagnostics. See *www2.eng.cam.ac.uk/~nhmcl/firstaid.html.*

Not even the tip of the iceberg

With the advent of Illumea's FiberPix, affordable, accessible real-time Internet microscopy has become a reality. As wonderful as the prospects are for this emerging technology, we can only guess at its final impact—and we haven't even begun to talk about the interface of information technology with microscopy.

Bioinformatics, the exciting convergence of medicine, biology, computers, and information theory, suggests that each of us will soon have integrated medical records. These records will contain everything in one master file—from our X-rays, chemical tests, gross and clinical anatomy findings, to diagnoses, treatment, and follow-up. If Dr. Michael Becich of University of Pittsburgh has his way, it will also have the ability to conduct Internet searches for corroboration on difficult cases. This master file will be available to all of the medical personnel involved in our treatment and, equally importantly, to us. If telemedicine predicts the direction of telemicroscopy, does this mean we can look forward to an expansive world of "Micro-informatics"? This is just the beginning. ■

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