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Editorial

Innovations in medical imaging and virtual microscopy

The study of time lines for the diffusion of innovations in medical imaging into medical practice is instructive. Early phases of the innovation cycle include conceptualization, research and development, fabrication and testing of prototype systems, proof-of-concept demonstrations, clinical validation, and early commercialization. In aggregate, these initial aspects of the innovation cycle take years. After the initial commercialization of a medical imaging device, the diffusion of the technology into medical practices is typically slow and may involve significant re-engineering of several generations of devices. The curve representing the usage of an imaging technology may remain relatively flat for a long period of time. On the other hand, a medical imaging technology that will ultimately be successful eventually enters an exponential growth phase in its usage. Various factors can trigger this upswing in activity.

A graph plotting years into an innovation cycle *versus* a performance metric (e.g., numbers of installations, numbers of patients benefiting from procedures, expenditures on systems, etc.) for a successful innovation is often sigmoidal. This is referred to as an "S curve" of innovation. Students of innovation study interrelations of factors that influence the time interval between early proof-of-concept demonstrations of a technology and the upward inflection of its S curve. Venture capitalists may use the upward inflection as a marker of the time when a technology is ripe for investment.

Teleradiology and telepathology provide interesting case studies of medical innovations. Teleradiology began its exponential growth phase recently so that its time from inception to implementation can be measured. The findings raise interesting questions for telepathology. What were the teleradiology success factors and are these factors relevant to the build-out of telepathology? How long did it take to implement teleradiology?

The initial demonstration of teleradiology was in Canada, in 1959. Other demonstration projects followed, but the extent of the use of teleradiology remained very limited for the next quarter of a century [1].

During its long incubation period, although little was happening in the clinical arena, important progress was being made in the development of radiology digital imaging, mass storage for radiology image data, telecommunication network technologies needed to send large digital image files from one place to another, and integrating these technologies into a radiology Picture Archiving and Communications System (i.e., radiology PACS). Often, the early teleradiology demonstration projects served as justifications for ongoing research and development in radiology digital imaging and teleradiology. The early proof-of-concept demonstrations provided an important frame of reference for subsequent research and development activities. Based on these innovations and others, digital radiology eventually evolved into a viable clinical application. Today, the majority of radiology departments in the United States are going "filmless and fully digital." Radiology digital imaging and teleradiology are linked through shared technologies.

How common is the use of teleradiology? Technically, physicians analyzing digital radiology studies stored on a server, whether at video terminals on hospital wards or in their offices, are using a form of teleradiology. This is being implemented at many institutions. With respect to remote diagnostic services, in the United States, the use of teleradiology services is 24/7 at rural hospitals. For nighttime coverage at many urban hospitals, it has increased dramatically in recent years. For example, 22 hospitals in Arizona and neighboring states now receive teleradiology diagnostic services from faculty radiologists at the University of Arizona College of Medicine in Tucson, up to 400 miles away. In the year 2004 alone, 80,000 teleradiology studies were performed on patients obtaining services through the Arizona Telemedicine Program [2]. Additional Arizona hospitals get coverage for radiology services from teleradiologists elsewhere in Arizona as well as from other states and abroad. Thus, teleradiology is now a growth industry in Arizona and elsewhere. The upward inflection of the S curve for the teleradiology innovation occurred

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rather abruptly, nearly 40 years after its first proof-of-concept demonstration.

If telepathology tracks along a similar time line, then telepathology could be approaching the upward inflection on its own S curve of innovation. It remains to be seen if some of the factors that stimulated the growth of the teleradiology industry will come into play for telepathology as well.

The first proof-of-concept telepathology demonstration (initially called "television microscopy") was in 1968, 9 years after the initial teleradiology proof-of-concept demonstration (J. Sanders, personal communication, March, 2005). As was the case for teleradiology, implementation of telepathology has also been slow [3]. On the other hand, many of the innovations in digital imaging, mass storage, and telecommunications developed for teleradiology are applicable to telepathology as well. Will these technologies affect the growth of telepathology? Also, would the migration of digital imaging into pathology laboratories on a large scale, once that becomes technically feasible, catalyze sustained growth of telepathology services as it has with teleradiology?

In the past, pathology slide digital imaging was time consuming and labor intensive [4]. It has been technically challenging to do whole-slide high-resolution digital imaging (i.e., produce "virtual slides") for all surgical pathology cases in production laboratories. This could change with the introduction of the ultrarapid virtual slide processor (DMetrix, Inc., Tucson, Ariz). The array microscope-based ultrarapid virtual slide processor was designed, in collaboration with engineers at a world-class optical sciences center, to enable pathology laboratories to go entirely digital for the first time [5,6].

Until recently, virtual slide digital scanning and processing times were typically 30 minutes or longer. A bottleneck in virtual slide processing, using earlier generations of virtual slide scanners, was the use of single-axis-optical systems for their digital imaging. The invention of the array microscope for use as the imaging engine of a virtual slide processor is, arguably, a major advance in virtual slide technology.

What distinguishes the array microscope from the conventional light microscope is its unusually large field of view (FOV) [5,6]. This is 20 times greater than that of the 20X objective lens of a conventional light microscope and nearly the width of a histopathology glass slide cover slip. With an array microscope, an entire glass slide can be scanned in a single sweep. The array microscope captures thousands of images per second from 80 miniaturized microscopes. Massive parallel processing of data enables the instrument to scan glass slides in less than one minute. It is predicted that the ultrarapid virtual slide processor will achieve virtual slide processing rates 5 to 6 times faster within a few years.

The high virtual slide throughput rate makes the ultrarapid virtual slide processor suitable for use as a pathology digital image input device for a large pathology Picture Archiving and Communications System (pathology PACS). A ripple effect could be the acceleration in the growth of the field of telepathology, as occurred after radiology departments implemented digital imaging.

Is virtual microscopy being used at the present time? Although there is considerable interest in the use of virtual microscopy for diagnostic pathology and telepathology, the principle applications to date have been in education and testing. A number of medical schools have incorporated virtual microscopy into their pathology courses. Pathology textbooks now include virtual slides, either as an enclosed CD-ROM or by providing book purchasers with access to the publisher's web site. "Boxes" of student virtual histopathology slides and histology slides are available on the web. For students, residents, and practicing pathologists, virtual microscopy may be especially well suited for targeted training and proficiency testing in specific areas, such as the training and testing available through the web-based Gleason's grading of prostate cancer tutorial described by Helin *et al* in the current issue of *Human Pathology* [7].

In the United States, virtual slides are already used for major examinations. For example, the American Board of Pathology carefully studied the efficacy of using virtual slides as test materials and, based on its findings, incorporated virtual slides into its certifying examinations. The implementation of virtual microscopy for licensure and certifying examinations strongly encourages pathologists to gain experience with virtual microscopy and to acclimate themselves to viewing histopathology slides on a video monitor. In the foreseeable future, looking at glass slides through a light microscope in a medical school course might seem archaic.

Virtual microscopy is already being used for pathology diagnostic service applications [8]. For example, US LABS (Irvine, Calif) recently established an innovative surgical pathology reference laboratory service. With their web-based service model, hospital pathologists ship paraffin blocks to US LABS in California, where the blocks are sectioned and stained. Virtual slides of the glass slides are processed and posted on the web for immediate viewing by the hospital pathologist. The hospital pathologist is then given the option of reading out the virtual slides from a distance, by telepathology, or having a US LABS pathologist read out the case in California. The virtual slides are stored on a US LABS server but viewed on the referring pathologist's own desktop video monitor. US LABS also provides analytical software so that the hospital pathologist who sent the case can perform quantitative studies of the virtual slides on line and can enter these results, along with self-selected digital images, into a customized pre-formatted surgical pathology report. The US LABS service model enables the hospital pathologist to bill for the professional component of the surgical pathology virtual slide read-outs. This service model may be of particular interest to pathologists without in-house immunohistochemistry or *in situ* hybridization laboratories. The US LABS service model successfully leverages telepathology in order to redistribute pathology expertise.

The comparison of teleradiology and telepathology shows that they have much in common. The possibility remains that teleradiology and telepathology will end up having nearly identical S curves for innovation when adjustments are made for differences in starting dates. And, sometime in the future, both teleradiology and telepathology might be correctly regarded as successful by-products of the digital revolution in health care.

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