

# TELEPATHOLOGY AT THE ULTRASTRUCTURAL LEVEL

## A Diagnostic Application of Remote Electron Microscopy via Internet

UNIVERSITÄT  
REGENSBURG  
KLINIKUM



Josef A. Schröder, Heiko I. Siegmund, Ferdinand Hofstädter

Department of Pathology, University Hospital, F-J-Strauss-Allee 11, 93053 REGENSBURG, Germany  
email: josef.schroeder@klinik.uni-regensburg.de

The remote operation of microscopes using modern telecommunication links has a great impact on the improvement of telepathology, a technical procedure bridging time and space in rendering pathological diagnoses<sup>1</sup>. The main task of ultrastructural telepathology is to deliver adequate electron microscopy (EM) findings in the shortest amount of time to establish or support pathological diagnoses from a remote location.

EM evidence of specific cell organelles or products (e.g. neurosecretory granules) not visible by LM can be essential in differentiating certain neoplasms or determining the primary site for some metastatic tumors. Other strong indications for ultrastructural pathology are numerous renal, skin, muscle, nervous system, ciliar and storage diseases as well as rapid viral diagnosis (including bioterror scenario, Fig.4; poxvirus). As in light-histopathology, the consultation of experts is essential for complex EM cases, and original specimens need to be examined directly instead of interpreting pre-selected images.

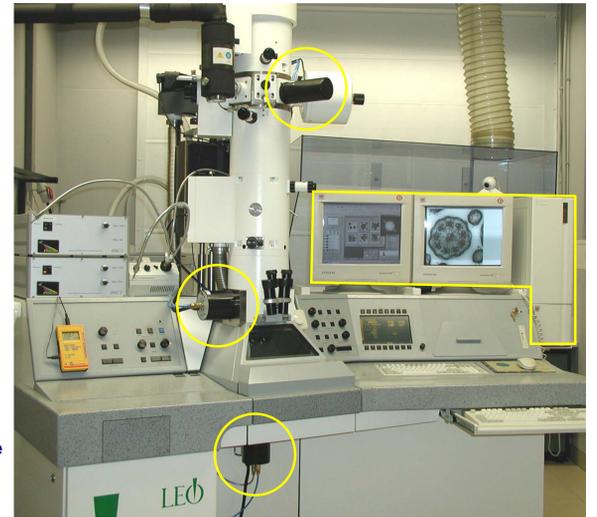
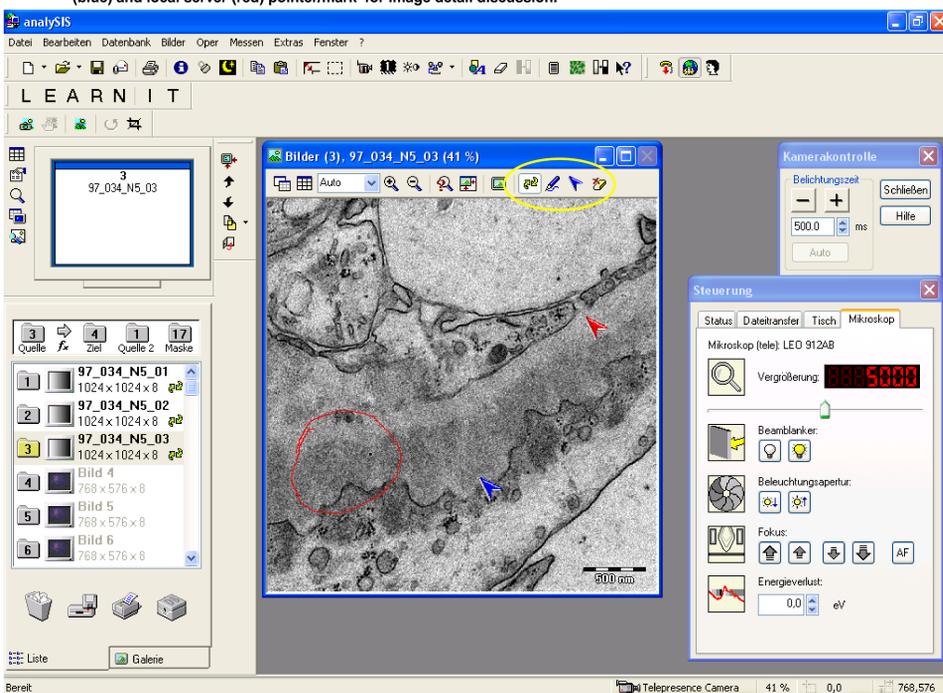


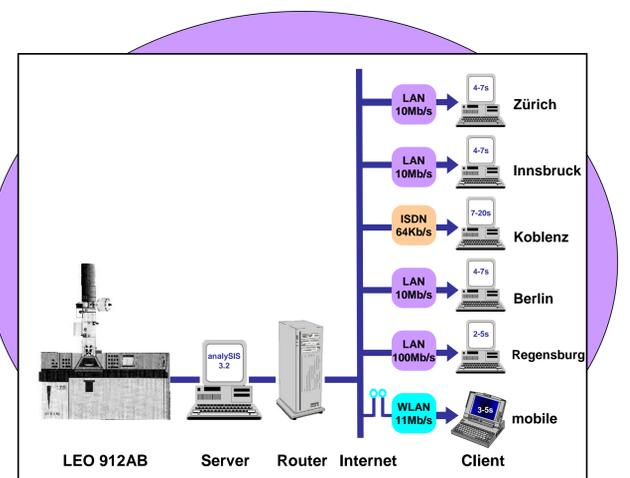
Fig.1 The Internet-connected Remote Controllable LEO912AB TEM equipped with a side- and bottom-mounted CCD slow-scan camera & motorized objective aperture

Fig.2 Screenshot of the "Client Site" Monitor Visible to the Remotely Located Expert. Note the "full resolution" image that can be saved on the local hard drive, the panels for camera and EM control. The magnification, beam blaster, illumination adjustment, control of stage navigation, and coarse- and fine-focus adjustment (autofocus) can be selected by a simple mouse click. Synchronized image: Immunotactoid Glomerulopathy (Orig. mag.: 5,000x, bottom-camera), note the remote client (blue) and local server (red) pointer/mark for image detail discussion.



Recently, the possibility of examining samples live by EM from a remote location has become a reality<sup>2</sup>. This new capability has been established by combining the latest, fully digital and highly automated EMs with digital image acquisition and telepresence microscopy techniques including discussion tools. Based on rapid advances in Internet technology and speed, the concept of direct access to a centralized and unique instrumentation from anywhere will become more common and thus enable high level collaboration in ultrastructural diagnostics, research and teaching, independent of location<sup>3</sup>.

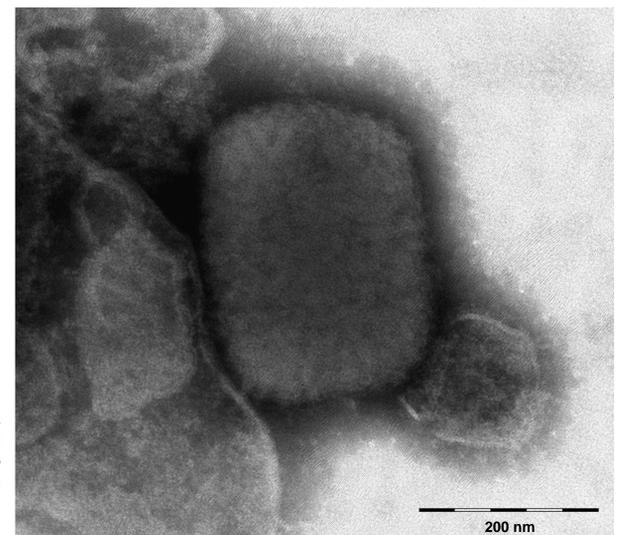
Fig.3 Scheme of the Server-client Architecture of the EM Telepathology System at the University of Regensburg. Note the mean transmission time of full resolution image.



Our experience with a remote EM diagnostic system is based on the LEO 912AB TEM equipped with a side- and bottom-mounted 1024x1024-pixel CCD camera (TRS, Germany) and retrofitted with an automatically adjusted objective aperture for the low- and high-resolution operation mode (Fig.1). The EM located in Regensburg is controlled by the "iTEM" software from the local server and linked via Internet to locations throughout Europe (Fig.3). The standard software "iTEM" (Ver. 5.1, Olympus Soft Imaging Solutions / Muenster, Germany) includes a dedicated TelePresence-Server-Module that handles the communication between the EM and the remote experts. At the "client site" [experts located in Berlin and Koblenz (Germany), Zurich (Switzerland), and Innsbruck (Austria)] standard desktop-PCs or a wireless Internet-connected notebook running the same "iTEM" software expanded with a TelePresence-Client-Add-in are used. Image synchronisation and discussion tools have been implemented in the server and client software enabling an efficient discussion of image details (Fig.2).

Ultrathin sections of selected diseases (skeletal muscle: Minicore disease; skin granuloma: Histiocytosis-X; head tumor: Oncocytoma; and skin tumor: Molluscum contagiosum), inactivated Anthrax samples as well as negative-stained specimens containing adeno-, herpes-, poxvirus, SARS, and rotavirus particles were examined remotely live via Internet. The remote EM control included: stage navigation and search for area of interest at low magnification and resolution, selection of adequate magnification (18-400.000x), focus adjustment, beam brightness and exposure time control, and local image documentation at full resolution.

Fig.4 High-resolution Digital Image of a Poxvirus (potential bio-terrorism agent) Transmitted via Internet to the Remote Expert and Saved on the Local Computer



### References:

1. Kayser, K., Szymas, J., Weinstein, R. (1999) Telepathology. Berlin, Springer.
2. Schroeder, J., Voelkl, E., Hofstaedter, F. (2001) Ultrastruct. Pathol. 25, 301-307.
3. Schroeder, J., Buescher, P. (2003) Business Briefing: Global Healthcare May/2003. World Medical Association, London/UK.