



SCANNING ELECTRON MICROSCOPY

Scanning electron microscopy (SEM) may be utilized for various assessments and analyses including tissue or material characterization after device treatment or implantation *in vivo*, device integrity and failure analysis, cellular morphology, and elemental analysis.

CBSET offers a state-of-the-art Hitachi S-3400N-II fully automated, variable-pressure scanning electron microscope with digital imaging. The SEM capability provided by CBSET is one of few that is compliant with Good Laboratory Practice (GLP) regulations. SEM specimen preparation equipment includes two Quorum E3100 critical-point dryers, and a palladium-gold sputter coater for preparation of tissues and medical devices applying secondary electron (SE) imaging under high vacuum. Beyond conventional SEM, CBSET offers imaging for uncoated and/or “wet”, vacuum-sensitive specimens in their natural state through the use of variable pressure (VP-SEM) imaging, along with the optional use of a Deben cooling stage. Also available is back-scattered electron (BSE-SEM) imaging and energy dispersive X-ray spectroscopy (EDS/EDX) to identify and quantify the elemental constituents of samples.

Variable Pressure SEM: Conventional SEM, while excellent in showing morphological and topographic details, requires the coating of non-conductive samples, preventing nondestructive evaluation of specimens. In VP-SEM mode, the Hitachi SEM is capable of imaging almost any uncoated, untreated, wet or dry sample via the environmental secondary electron detector (ESED). The ability to image without chemical processing and sputter coating is a great advantage for natural-state evaluation of the morphology and topography of non-conductive biomaterials or medical devices and their integration into host tissue.

Deben Cooling Stage: The Hitachi SEM is interfaced with a Peltier-driven cooling stage for VP-SEM applications. For specimens that may be sensitive, subject to beam damage, or may otherwise lose water (i.e., sublime) at ambient temperatures, the stage can be cooled to sub-zero temperatures. Water evaporation may be slowed or, depending on chamber pressure, stopped altogether by cooling a wet specimen for SEM imaging.

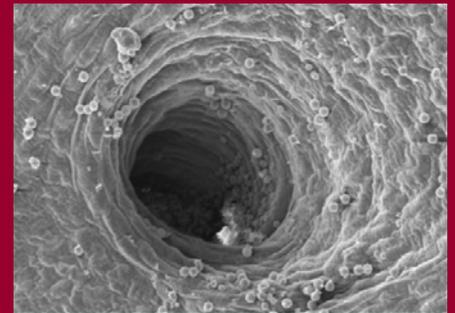
Back-Scattered Electron SEM: The back-scattered electron (BSE) detector in the SEM picks up the electrons reflected from the specimen. BSE-SEM imaging allows heavier elements to be distinguished from lighter elements within a sample by signal intensity. BSE-SEM images are particularly helpful for identifying compositional transitions and material differences within a sample.

Energy Dispersive X-ray Spectroscopy (EDS/EDX): Often used in conjunction with ESED and BSE-SEM imaging, EDS/EDX is a useful technique for evaluating a wide range of materials by identifying, mapping, and quantitatively and/or qualitatively analyzing the elemental constituents of a sample. Typical applications include identification of the chemistry and phases in an unknown material, characterization of internal defects and impurities, and elemental distribution over samples including coatings and polymers.

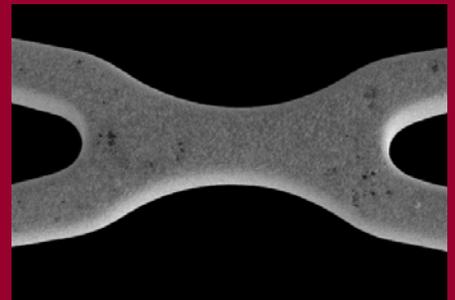
Hitachi S-3400N-II SEM specifications:

- Resolution — 3.0nm High Vacuum Mode @ 30kV 4.0nm (low vacuum 6 Pa pressure).
- Detectors — SE, ESED, and BSE
- Chamber — Accommodates up to 130 mm-inch diameter specimens for imaging.
- Stage — Fully eucentric, 5 axis computer controlled motorized stage for automated montage imaging at various magnifications and regions of the sample.
- Compliant with Good Laboratory Practice (GLP) regulations

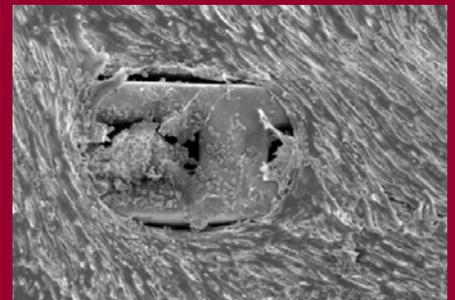
CBSET has fully trained and certified personnel to process, image, and analyze and report data obtained from studies utilizing SEM.



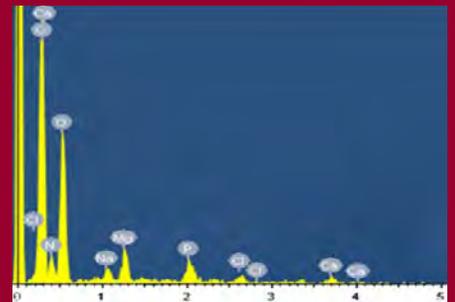
Arteriole from swine heart, SE imaging, high vacuum



Metallic stent hinge, SE imaging, high vacuum



Stent implanted swine artery, SE imaging, high vacuum



EDS spectra from implanted tissue sample

ABOUT CBSET

CBSET is an AAALAC accredited, not-for-profit, pre-clinical research organization dedicated to research, education, and the advancement of early-stage biomedical technologies. Our mission is to assist in methodologies uniquely suited for novel and innovative treatments for complex diseases. We offer a full range of GLP and non-GLP services, ranging from early product evaluation through lead optimization and pre-clinical safety, to physician assessment and training courses. We specialize in the development and application of techniques in the fields of cardiology, electrophysiology, orthopedics, wound healing, regenerative medicine, endoscopy/laparoscopy, drug and device delivery and safety, cellular therapy, and diagnostic imaging. Our world-renowned regulatory and scientific expertise helps transform early-stage concepts into novel therapies.

CBSET EXPERTISE

Our professionally trained staff and consultants provide expertise for all phases of biomedical discovery and development research including regulatory consulting, veterinary medicine, surgery and minimally invasive surgery, imaging, pharmacokinetics and drug metabolism, drug and device safety, pharmacology, lead optimization, and specialized histopathology and pathology. These individuals provide the basis for successful scientific collaborations, rapid concept advancements, unparalleled consultation services, and expert dissemination of information and findings to regulatory and scientific bodies.

CBSET offers a full range of GLP and non-GLP services, from early product evaluation through lead optimization and pre-clinical safety, to physician assessment and training courses. Our expertise includes:

- Stents/balloons
- Novel catheters/wires
- Robotic-assisted surgery
- Vessel sealing/closure devices
- Heart valve replacement/repair
- Cardiopulmonary bypass
- Beating heart technology
- Electrophysiology devices
- Tissue ablation devices
- Endovascular/NOTES surgery
- Laparoscopic surgery
- Orthopedic devices
- Novel surgical instruments
- Wound healing devices
- GLP training and regulatory consulting

CBSET FACILITIES

CBSET offers an unparalleled, GLP-compliant, 30,000 square foot state-of-the-art facility within minutes of Cambridge, Boston, and Logan International Airport. Our facility includes vivariums, catheterization/imaging labs, and full surgical suites containing the latest equipment for fluoroscopy, echocardiography (TEE/TTE), electrophysiology, IVUS, optical coherence tomography (OCT), endoscopy/laparoscopy, orthopedic surgery, and surgical video recording. CBSET offers dedicated labs for GLP-compliant SEM, specialty histopathology/pathology, metabolism and pharmacokinetics



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