Review Article

The use of Scanning Electron Microscopy SEM for Medical Application: A Mini Review

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ABSTRACT

An invaluable method for assessing the surface morphology of a wide range of materials and samples, including those used in medical applications, is scanning electron microscopy (SEM). Scanning Electron Microscopy (SEM) has long been an indispensable tool in materials science and nanotechnology, providing unparalleled insights into the microstructure and surface morphology of various materials. Recent advancements have extended the utility of SEM beyond traditional fields, including its promising applications in medicine and biomedical research. By leveraging the high-resolution imaging capabilities of SEM, researchers can delve deeper into the intricate structures of biological specimens, complexities of cellular architecture, tissue organization, and disease pathology. SEM provides more information on biocompatibility, surface interactions, and structural integrity of medical implants and devices, paving the way for enhanced diagnostic and therapeutic strategies. SEM has long been used to characterize the surface topography of cells and tissues. SEM has been utilized in Cell Surface Imaging, Drug delivery system, Tissue Microstructure, gastrointestinal, and cardiology to advance understanding of disease early stages. SEM can produce high-resolution pictures of inanimate and biological particles, allowing for a thorough examination of a range of medical applications.

Introduction

Scanning Electron Microscopy (SEM) is a powerful imaging technique widely used in various fields, including medicine and dentistry [1]. Scanning Electron Microscopy (SEM) has revolutionized the field of medical research by providing unparalleled insights into the intricate structures and functions of biological systems at the micro- and nano-scale. With its ability to produce high-resolution images and detailed surface topography, SEM has become an indispensable tool for investigating a wide range of medical applications. It involves the use of a focused beam of high-energy electrons to generate signals at the surface of solid specimens, providing detailed, magnified

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images of the sample's surface, and its physical features. SEM is based on the principle of scanning a sample with electron beams, and the resulting images reveal information about the sample's composition, topography, and other properties [2]. In the medical field, SEM has been employed to study a wide range of biological samples, including tissues, cells, and microorganisms, allowing for the visualization and characterization of surface structures with high resolution [3]. This article aims to explore the use of SEM for medical applications, highlighting its potential in advancing research and diagnostics in the field of medicine.

Medical Applications

Cell Surface Imaging

Scanning Electron Microscopy (SEM) is a potent instrument for high-resolution surface imaging of cells. SEM scans a sample's surface using a concentrated electron beam that interacts with the sample's atoms to produce secondary electrons. After that, these secondary electrons are gathered and utilized to create a surface image [4]. Compared to light microscopy, SEM can observe cells at resolutions of up to 10 nano-meters, which is far higher and the resolution can vary depending on the specific SEM setup and sample preparation techniques. This makes it possible for SEM to see minute details of the cell surface, like the configuration of cilia, microvilli, and other surface features [5]. Cells need to be properly cleaned before they can be imaged using SEM. Typically, this entails a number of actions, such as:

i. *Fixation*: To maintain their structural integrity, cells are fixed using a chemical like formaldehyde or glutaraldehyde.

ii. *Dehydration*: To prevent water from interfering with the electron beam, cells are dehydrated [6].

iii. *Coating*: A thin layer of a conductive metal, such palladium or gold, is applied to the cells. In addition to keeping the cells from charging, this coating increases their visibility to the electron beam.

There are numerous uses for SEM in cell medical application. Among the most popular applications are:

i. *Examining a cell's morphology*: SEM can be used to examine a cell's size, shape, and arrangement of surface features.

ii. *Examining cell-cell interactions*: SEM is a useful tool for studying the interactions between cells, including those mediated by cell adhesion molecules [7].

iii. *Analyzing how medications or poisons affect cells*: SEM can be used to look at how drugs or poisons affect a cell's surface.

iv. *Analyzing cell development*: SEM can be used to examine how cells develop from embryonic to mature stages.

Tissue Microstructure

High-resolution images of cell and tissue surfaces are obtained by scanning electron microscopy (SEM), a valuable technique for researching tissue microstructure. To characterize the surface topography of cells and tissues, SEM has been extensively employed in the biomedical sciences. It permits in-depth examination of biological materials' microstructural characteristics and cellular architecture [8]. Using SEM, it is possible to examine both living and inanimate particles at high resolution and magnification for the purpose of diagnosing sepsis due to catheter use. Furthermore, the application of SEM has been employed to get valuable insights into the microstructure of plant, animal, and microbial tissues. SEM is an invaluable tool for study and measurement because of its capacity to provide high-resolution, three-dimensional images, particularly for analyzing tissue microstructure [9]. Medical applications of SEM include the following:

i. *Cellular Morphology*: SEM allows for the visualization of surface morphology of cells with high resolution, providing detailed information about cell size, shape, and surface characteristics. Imaging tissue samples at magnifications ranging from hundreds to thousands of times provides visualization of cellular structures such as cell membranes, organelles, and cytoskeletal elements.

ii. *Ultrastructural Analysis*: SEM provides detailed images of tissue ultrastructure, revealing subcellular features at nano-meter-scale resolution. This includes the visualization of cellular components such as mitochondria, endoplasmic reticulum, and microvilli, as well as extracellular matrix components like collagen fibres and elastin fibres.

iii. *Pathological Studies*: SEM is widely used in pathological studies to examine tissue samples from diseased or pathological conditions. By analyzing tissue morphology at the micro- and nano-scale, SEM identifies abnormalities such as cellular degeneration, necrosis, apoptosis, and pathological deposits.

iv. *Regenerative Medicine*: In regenerative medicine and tissue engineering, SEM is used to characterize engineered tissues and assess their structural integrity and functionality [10].

Biomedical Implants and Devices

When designing and evaluating biological implants and devices, scanning electron microscopy, or SEM, is an indispensable tool. For researchers and engineers working on medical device projects, it offers elemental maps and high-resolution photographs, making it a vital tool [11]. The topography, surface morphology, and surface roughness of medical device materials can all be examined using SEM. Furthermore, a number of biological research domains have utilized SEM, such as tissue engineering, bone grafting, orthodontics, and the analysis of bone microstructure. Because the method may offer precise insights at the nano-scale, it has proven very helpful in the development and examination of medical devices, including implantable glucose monitors, which necessitate precise micro- and nano-scale processes [12].

Pathogen Studies

The study of pathogens has been transformed by scanning electron microscopy, which offers unmatched insights into the microscopic world of these infectious agents. SEM is a vital tool for studying pathogen biology, creating diagnostic instruments, and battling infectious diseases because of its capacity to reveal complex surface characteristics, three-dimensional architecture, and host-pathogen interactions [13]. It is positioned to become even more important as research moves forward to protect human health and understand the intricacies of the microbial world. Its detection of viruses linked to diseases in humans, animals, or plants has been greatly aided [14]. Furthermore, SEM has been utilized for the ultra-rapid microscopy imaging of SARS-CoV-2, showcasing its capabilities in infectious illness detection and microbiological research. In the discipline of microbiology, scanning electron microscopy (SEM) has shown to be a crucial technique in the timely detection of viruses in patient samples as well as in identifying the agents that cause infectious diseases. In the biomedical sciences, it has also been applied to the characterization of cell and tissue surface topography [15].

Drug Delivery System

One useful technique for characterizing and assessing drug delivery systems is scanning electron microscopy (SEM). High-resolution photos from SEM make it possible to see medication transporters and how they interact with bodily fluids up close. SEM provides high-resolution images of biological samples, allowing researchers to visualize structures at the nano-meter scale. Medication transporters and their interactions with bodily fluids can be observed with unprecedented detail, revealing surface morphology, structural features, and spatial relationships. Likewise, SEM is sensitive to surface characteristics, making it ideal for studying interactions between medication transporters and bodily fluids. By scanning the sample surface with a focused electron beam, SEM detects variations in surface composition, topography, and morphology, providing insights into molecular interactions and surface chemistry [16]. Drug carrier production and release mechanisms *in vitro* and *in vivo* have been studied using SEM, which has shed light on the ultra-structural placement of drug carriers in bodily compartments. Furthermore, it has been utilized to evaluate some recipients utilized in the preparation of drug delivery systems as well as polymeric implantable delivery systems. A growing number of pharmacological systems, including solid lipid nanoparticles, various vesicles, nano-fibres, nanoparticles, and nano-emulsions, have been characterized using SEM. The elemental composition of the systems can also be ascertained using analytical electron microscopic techniques like energy-dispersive X-ray spectroscopy or electron energy-loss spectroscopy. SEM is a useful tool in drug delivery system research because it offers crucial insights into the surface properties and microstructural features of drug carriers and their interactions with bodily fluids [16].

Dental Research

Scanning electron microscopy (SEM) is a powerful tool in dental research, providing insights into the intricate structures of dental tissues and materials at the micro and nano-scale. Its primary applications include detailed examination of tooth structures, revealing ultrastructural features essential for understanding the biomechanical properties of these tissues, and understanding the etiology of dental diseases like caries and periodontal conditions. SEM also aids in the investigation of dental materials used in restorative dentistry, assessing their structural integrity, wear resistance, and biocompatibility, contributing to the development of more durable and biologically compatible dental materials [17]. In dental implants, SEM helps study the interface between implant materials and surrounding tissues, ensuring optimal design and surface characteristics for improved integration and long-term success. It also plays a crucial role in the investigation of dental biomaterials at the nano-scale, allowing researchers to analyze the morphology and distribution of nanoparticles, providing insights into their interactions with oral tissues and bacteria [17]. SEM is also integral to the study of dental pathologies, as it visualizes microbial biofilms on tooth surfaces at high magnification, aiding in understanding plaque formation mechanisms and developing targeted therapies to prevent and treat common dental issues. As technology advances, SEM continues to be at the forefront of transformative research, driving innovations in diagnostics, treatment modalities, and the development of advanced dental materials for oral health and overall well-being [18, 19].

Cancer Research

As a crucial tool in cancer research, providing insights at both cellular and subcellular levels, it allows for the examination of cancerous tissues and cells, providing high-resolution images that help identify structural abnormalities and specific markers. SEM also helps study the interactions between cancer cells and surrounding tissues, revealing critical information about cancer progression [20, 21]. This knowledge is crucial for developing targeted therapies to disrupt these processes and prevent cancer spread. SEM also contributes to the study of cancer biomarkers, aiding in the identification and characterization of potential diagnostic markers. It is further used in the development and assessment of nano-medicines for cancer treatment, ensuring their size, shape, and surface properties meet desired specifications. SEM's integration with advanced techniques like energy-dispersive X-ray spectroscopy (EDS) further expands its applications in cancer research [22, 23].

Conclusion

SEM is a powerful tool in medical research and diagnostics, offering high-resolution imaging capabilities for detailed examination of biological specimens at the micro and nano-scale. Its three-dimensional images provide a comprehensive view of cellular structures, enabling researchers to unravel intricate details. SEM has been instrumental in pathology, enhancing our understanding of disease processes at a subcellular level, and in medical implants and devices, assessing biocompatibility and potential complications. It also aids in pharmaceutical research, characterizing drug delivery systems and studying drug-cell interactions, leading to more effective therapeutic interventions. However, SEM has limitations, such as sample preparation challenges, potential artifacts, and the cost and technical expertise required. Despite these challenges, SEM remains a powerful tool in medical research and diagnostics, offering unprecedented insights into the microstructural aspects of biological samples.

Conflict of Interest

The authors report no conflict of interest for the current study**.**

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