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Role of Bionanotechnology in Surgery Field: Advances, Application, and Future Directions

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ABSTRACT

This literature review provides a comprehensive analysis of the role of bionanotechnology in surgery field. Bionanotechnology is a new nanotechnology subdiscipline, draws influence from biological processes. Bionanotechnology, which combines nanotechnology and biology, could revolutionise healthcare and medicine. This literature review critically examines the existing literature to provide comprehensive insight into the role and potential of bionanotechnology in surgery and anaesthesiology by presenting an up-to-date overview and summarizing current advances in its application in both fields.

KEYWORDS: Bionanotechnology, biotechnology, nanotechnology, surgery, anaesthesiology

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I. INTRODUCTION

Nanotechnology has emerged as a transformative tool for manipulating matter at the nano-scale, leading to advancements in various fields such as biotechnology, medicine, pharmaceuticals, agriculture, food, cosmetics, environmental protection, electronics, information technology, construction, military, energy industry, space industry, and consumer products, among others.[1]

Nanomaterial synthesis has increased fast in the previous 30–40 years. This special issue addresses many medical applications for nano- and biotechnology-derived materials. Materials at the nanoscale scale have great medical promise. The ability to accurately modify and customise their physicochemical properties at the biomolecular scale opens several doors. These include early biomarker identification, precise cell and tissue targeting, enhanced drug delivery systems, illness staging and evaluation, and degenerative disease treatment. The chance to cure severe diseases and discover their causes is important.[2]

'Nano' comes from a Greek prefix meaning 'dwarf' or tiny. It represents one thousand millionths of a metre (10^{-9} m). Nanoscience and nanotechnology must be distinguished. Nanoscience studies structures and molecules from 1 to 100 nm. When comparing, remember that human hair is 60,000 nm thick and the Deoxyribonucleic Acid (DNA) double helix is 1 nm (Figure 1). Nanotechnology uses this knowledge to generate practical applications, including diverse technologies.[3]

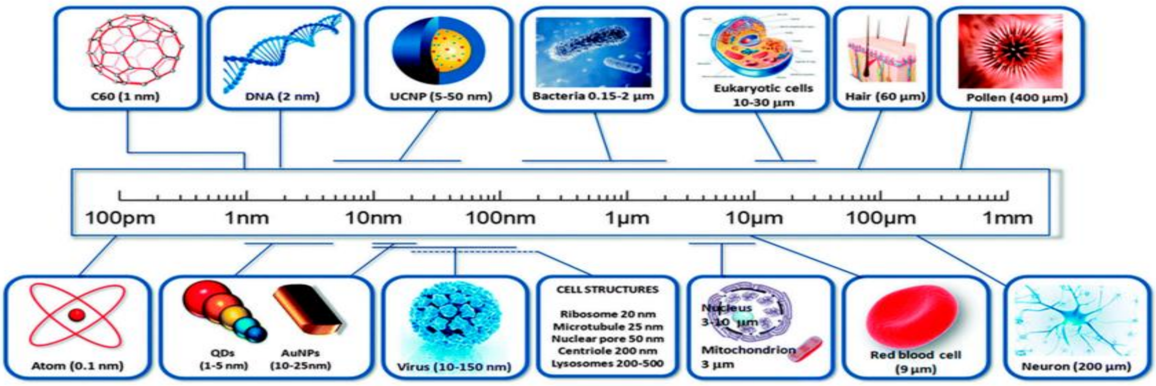

Figure 1. A comparison of sizes of nanomaterial.[3]

There are many definitions of "biotechnology." Biotechnology converts cell and molecular biology into commercial applications. The American Chemical Society defines biotechnology as the use of biological organisms, systems, or processes by businesses to study life and improve drugs, crops, and animals.[1]

Bionanotechnology, a new nanotechnology subdiscipline, draws influence from biological processes. Nanotechnology draws influence from biology for research and manufacture. Nanotechnology uses biological components, including carbohydrates, lipids, proteins, and nucleic acids, with their intrinsic biological activity and specificity, to build nanoscale technology. Bionanotechnology is a subclass of nanotechnology that uses biology as inspiration or a goal, according to some literature.[1]

Nanoparticles are being used to transport drugs, heat, light, and other substances to specific biological populations, including cancer cells. Since many biological molecules are nanoscale, molecular engineering and manipulation have many medical applications, especially in nanomedicine. Nanotechnology is used to develop surgical instruments, suture materials, imaging modalities, targeted medicine delivery systems, visualisation methods, and wound healing methods. Burn scar treatment is a key nanotechnology use.[4]

The first modern anaesthetic was invented by American dentist William T.G. Morton. Morton demonstrated medical anaesthesia with diethyl ether inhalation in 1846. Surgery reached a major milestone with this breakthrough. Thus, this incredible breakthrough has saved many lives worldwide. Clinical anaesthesia has increasingly embraced precision medicine. Precision medicine aims to improve healthcare by customising treatment for each patient's unique requirements and characteristics. Thus, precision anaesthesia has replaced conventional goals in anaesthetic research and development. Precision anaesthesia tailors anaesthesia to each patient. This requires precise anaesthetic delivery to the intended spot. Sometimes many anaesthetics must be given. However, traditional pharmacological formulations may not meet these criteria.[5]

Nanocarriers distribute anaesthetics, creating anaesthetic nanomedicines. This method provides precision and specificity. Nanocarrier technology can modify anaesthetic size, charge, composition, and surface properties. This modification procedure creates nanomedicines with unique properties. Nanomedicine is becoming more popular because it is stable and biocompatible, has a higher chance of working as a therapy, has few side effects, stays in the body for a long time, does not harm healthy tissue, and can use targeted therapy methods to make treatment more precise.[5]

Bionanotechnology, which combines nanotechnology and biology, could revolutionise healthcare and medicine. Nanotechnology emerged as a scientific area because scientists found that nanoscale particles produce unique materials, products, and devices. According to the fundamental rules of physics and chemistry, changes in the size, shape, and arrangement of atoms in a state of matter affect their properties. Nanoscale manipulation techniques have opened up many possibilities, affecting precision, medicine delivery, and medical intervention outcomes.[1,5,6]

This literature review aims to present a current overview of the application of bionanotechnology in the fields of surgery and anaesthesiology, as well as to summarize recent advances in the application of this technology in both fields. This literature review aims to provide comprehensive insight into the role and potential of bionanotechnology in surgery and anaesthesiology by presenting an up-to-date overview and summarizing current advances in its application in both fields.

II. ADVANCES IN BIONANOTECHNOLOGY FOR SURGERY

A. Nanomaterials in Surgical Instruments

1. Nanoscale Coatings for Enhanced Durability and Biocompatibility

All dimensions in zero-dimensional nanomaterials are nanoscale. Nanoparticles are the main zero-dimensional nanomaterials. One-dimensional nanomaterials possess two dimensions at the nanoscale and one dimension at the macroscale. This looks like a needle. Nanotubes, nanorods, thin films, platelets, and surface coatings are one-dimensional. Two-dimensional nanomaterials have one nanoscale and two macroscale dimensions. Two-dimensional nanomaterials are flat plates. Two-dimensional nanomaterials include nanowires, nanofibers, nanotubes, nanofilms, nanolayers, and nanocoatings. Nanocoating, a trend in nanotechnology for corrosion prevention and control, has either the coating thickness or second-phase particles disseminated into the matrix in the nanosized range. Compared to conventional coating, this technology is expanding rapidly in steel substrate corrosion protection and wear resistance. In recent years, conventional, organic, and inorganic coatings have grown in popularity for metal corrosion protection. Despite advances in coating technology, metal protection from harsh environments remains a challenge.[7,8]

Unlike bigger materials, nanomaterials can reduce bacterial multiplication, surface colonisation, and biofilm formation. Nanocoatings kill bacteria by releasing reactive oxygen species or ions, while modified nano-topographies make bacteria-unfriendly surfaces that cause biomechanical damage. Nanocoating is made of silver, copper, gold, zinc, titanium, and aluminium nanoparticles. Nanocoating uses non-metallic substances such as graphene, carbon nanotubes, silica, and chitosan. Black silicon and nano-protrusions change nano-topography. Two or more nanoparticles generate nanocomposites with unique chemical or physical characteristics. This integrates antibacterial action, biocompatibility, strength, and durability. Its wide use in medical engineering has sparked worries regarding its toxicity and risks. Current antimicrobial nanocoating safety regulations are inadequate. Many issues remain regarding risk analysis and occupational exposure limits, especially for coating-based therapies. Bacterial nanomaterial resistance could affect antibiotic resistance, which is concerning. Nanocoating has promising future applications.[9]

2. Nanorobotics for Precise Surgical Manipulations

The term "medical micro/nanorobots" encompasses all structures ranging from nanometers to micrometers in size (300 nm−300μm) that have the ability to convert power sources into kinetic energy. There are primarily three categories of powered micro- and nanorobots that are discussed. Biohybrid technologies combine artificial nanostructures with mobile microorganisms to serve as the power source for the micro/nanorobot. Chemically propelled micro/nanorobots employ asymmetric catalytic engines to specifically transform chemical fuels into movement. Physical means propel nanorobots by utilizing external energy inputs, such as magnetic, ultrasonic, or light fields, to generate translational motion. The nanorobots' engine geometry and material designs determine this motion.[10]

Robotic systems have greatly improved humans' perception, interaction, control, and environmental manipulation. The convergence of various technologies has revolutionised medicine, enabling robotic technologies to improve healthcare. Industrial robots, designed to automate dangerous, large-scale manufacturing procedures, have revolutionised medicine. Medical robots are designed to work in various environments and treat and prevent diseases. Medical robots, unlike ordinary robots, use microscopic components and clever materials to execute complex procedures and interact with the body. Medical robotics has grown exponentially because of advances in motors, control theory, materials, medical imaging, and surgeon and patient acceptability. Robotic surgical systems like the da Vinci system translate the surgeon's manual hand movements into precise and smaller instrument movements inside the patient. Despite the growing use of robotic systems for minimally invasive surgery, major technological problems remain. Current medical robotic systems' mechanical components are big and rigid, making it difficult to access and treat large anatomical regions. Compact and flexible robots a few micrometres or smaller will allow unlimited exploration of the human body, innovative cellular treatments, and more accurate and effective localised diagnostics and therapy. Utilising miniature robotic surgeons has the potential to decrease the need for invasive surgical operations, thereby mitigating patient discomfort and shortening postoperative recovery duration.[10,11]

B. Nanomedicine in Preoperative Planning

1. Nanoparticle-Based Imaging for Diagnostic Precision

The advancement of biotechnology, nanomedicine, and revolutionary medicines often relies heavily on the incorporation of medical imaging into regular clinical procedures. In recent years, there has been a significant focus on the creation of nanometer-sized materials for biological purposes. Their applications have gained significance in the fields of medicine, namely targeted medicines and diagnostics. Contemporary substances such as nanowires, quantum dots, carbon nanotubes, nanoparticles, and nanomaterials are currently receiving significant attention. This is because the size of the particles affects their unique mechanical, chemical, electrical, optical, magnetic, electro-optical, and magneto-optical properties, which differ from their properties in larger quantities.[12]

Imaging is crucial in the identification of diseases, forecasting their outcomes, and tracking the effectiveness of treatments. The imaging techniques commonly employed in regular medical practice include ultrasound, radiography, Computed Tomography (CT) scans, Positron Emission Tomography (PET) scans, Single Photon Emission Computed Tomography (SPECT) scans, and MRI scans, as well as various combinations of these techniques such as SPECT/CT, PET/CT, and PET/MRI. Over the past 20 years, nanoparticles have garnered significant attention as imaging probes. Certain nanoparticles have inherent magnetic or optical properties that allow for direct imaging, whereas others require indirect imaging methods such as labelling with radiotracers or dyes.[13]

Several carbon-based nanoparticle platforms, such as Carbon Nanotubes (CNTs), dots, and graphene oxides, have been developed for medical purposes. Carbon nanoparticles have been used in the clinic to find sentinel lymph nodes that need to be removed during surgery for different types of cancer, including thyroid, breast, and stomach cancer. When carbon nanoparticles were administered in the vicinity of the main tumour location 6–12 hours prior to surgery in patients with gastric cancer, the laparoscopic examination revealed a sensitivity, specificity, and accuracy of 90%, 100%, and 98.9%, respectively, in detecting lymph nodes that exhibited positive staining. Comparable findings were observed in other types of malignancies, where the utilisation of preoperative carbon nanoparticle sentinel lymph node mapping augmented the identification of metastatic lymph nodes and reduced the need for needless surgical procedures.[14]

2. Targeted Drug Delivery Systems

The advancement of nanotechnology has opened up new possibilities and approaches for the diagnosis and treatment of various significant illnesses. Nanomaterials are extensively used in medication delivery systems due to their distinctive physicochemical and biological characteristics. Nano-drug delivery systems have the ability to enhance the effectiveness of drugs by improving their stability, targeted delivery, and controlled release. This is achieved through their unique characteristics of size, shape, and material, which improve the pharmacokinetic and pharmacodynamic properties of the encapsulated drugs.[15]

The physiological impact of a medication on a patient is contingent upon the pharmacological characteristics of the medication. These effects occur as a result of the interactions between the drug and the receptors located at the place where the drug acts. The effectiveness of this interaction between the medicine and its target has been compromised unless the drug is delivered to its intended location with a concentration and speed that results in the least amount of negative effects and the most therapeutic benefits. Targeted drug delivery refers to the precise administration of therapeutic agents to specified tissues while minimizing exposure to the rest of the body. Hence, it selectively administers the medication solely to specific regions of the body. This provides enhanced therapy effectiveness and minimises adverse effects. It distinguishes itself from the traditional method of drug administration by being released in a specific dosage form, whereas the conventional method relies on the medication being absorbed through the body's semipermeable barrier.[16]

An ideal drug-targeting complex should possess the following characteristics: it should be non-toxic, non-immunogenic, biochemically inert, biodegradable, biocompatible, and physicochemically stable both in vivo and in vitro. Additionally, it is important for the drug to exhibit a consistent and manageable pattern of release, be relatively uncomplicated, reproducible, and cost-efficient in its manufacturing, be easily removed from the body, and have minimum drug leakage during transportation.[16,17]

C. Nanomaterials for Wound Dressing

1. Nanoparticles in Wound Dressing

Wound healing is a crucial biological process that helps maintain the structure of tissues after the development of a sudden or long-lasting wound (ulcer) that causes damage to the tissues. Chronic wounds, which are long-lasting and persistent, can be caused by causes such as obesity, microbial infection, aging, or other variables. These wounds can disturb the integrity of the tissue and lead to serious illness and a decrease in quality of life. Developing effective wound healing solutions is difficult due to the need for complex treatment approaches as well as the higher costs incurred by doctors and researchers. Conversely, the World Health Organization (WHO) has recognized wound management as a significant global public health issue.[18]

Inorganic and organic nanoparticles, as well as nanocomposites, categorize the constituents of nanomaterials. These constituents can be further classified as porous materials, colloids, copolymers, and gels. Applications of nanoparticles and nanocomposites in scaffolds and coatings involve the use of hydrogels, nanofibers, and films (Figure 3).[19]

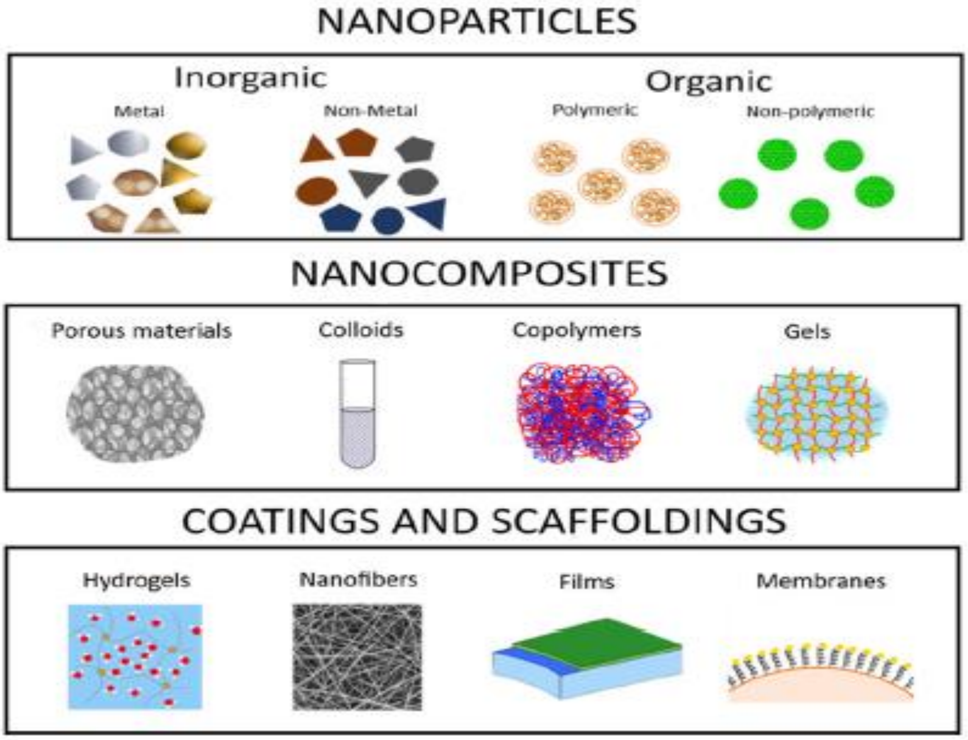

Figure 3. Nanomaterials with potential use for wound treatment.[19]

In wound healing research, researchers have proposed novel treatment methods to develop therapies that target certain stages or the entire process. Nanotherapeutic, stem cell, bioprinting, extracellular matrix, platelet-rich plasma, cold atmospheric plasma, and micro-Ribonucleic Acid (RNA)-based wound healing therapies have been developed recently. These methods promote cell function, collagen formation, angiogenesis, cytokine levels, growth factors, and antibacterial effects. Researchers have used metal, ceramic, synthetic polymeric, natural polymeric, self-assembled, and composite nanoparticles to heal acute or chronic wounds. These nanoparticles, which imitate the wound extracellular matrix, have improved wound care and healing. Metal nanoparticles are selected for their low toxicity and bacteriostatic/bactericidal characteristics. Ceramic nanofibers are used in wound repair with synthetic or natural polymers due to their bioactivity and biodegradability. Additionally, biocompatible, self-assembled nanoparticles can closely mimic the natural extracellular matrix and improve intercellular communication.[18]

2. Nanocomposite in Wound Dressing

In order to expedite the process of wound healing, it is imperative to develop appropriate wound dressings. An optimal wound dressing should maintain a moist environment, facilitate the exchange of gases and nutrients, absorb exudate, avoid sticking to the wound, and provide protection against bacterial infection and allergic reactions. Therefore, a wound dressing should possess the qualities of biocompatibility, biodegradability, swellability, elasticity, and antimicrobial properties. In order to facilitate cell growth, proliferation, migration, and angiogenesis, a dressing should possess permeability. Prudent and precise attention is necessary to produce a suitable wound dressing incorporating all of these components.[20]

A study found the Poly Glycerol Sebacate (PGS)/Gel nanocomposite promising for wound dressing. Chitosan is a linear polysaccharide that is produced naturally. It is made from chitin, one of the most abundant natural polymers. Chitin and chitosan, used in biomedicine, come from crustacean exoskeletons such as crabs, shrimps, lobsters, molluscs, insects, and fungi. Chitosan and its derivatives are cationic polymers with intrinsic antibacterial properties that improve wound healing by activating fibroblasts and osteoblasts and enhancing inflammatory cell activity. Since chitosan is the second-most prevalent biopolymer after cellulose, researchers have focused on its versatility. Chitosan is a clever material for wound dressing due to its biocompatibility, antibacterial, antifungal, and non-toxicity. PGS is a robust polyester made by polycondensing glycerol and sebacic acid. This biocompatible, stretchable polyester is biodegradable. The metabolism gets rid of the byproducts of this substance's breakdown. This polymer lacks water-attracting characteristics and breakdown speed and cannot be spun into fibres to form a nanofibrous structure. Therefore, mix it with hydrophilic polymers. Gelatin, commonly known as gel, is a hydrophilic polymer that occurs naturally and may be formed from collagen, the main protein in the Extracellular Matrix (ECM). Gel's biocompatibility, non-immunogenicity, and biodegradability make it perfect for cell attachment, growth, and proliferation.[20–23]

3. Nanocoating in Wound Dressing

Flat, 2D metal-based biomaterials have a nanometer-scale third dimension. This structure allows substrate molecules to reach surface active areas with low energy barriers, resulting in high biocatalytic activity. Wound healing and tissue engineering research have increased recently. Nanocoatings/films, 2D transition metal dihalides (TMDs), and 2D metal organic frameworks (MOFs) are prized for their mechanical properties, making them ideal for wound healing. 2D metal-based biomaterials can penetrate biofilms and fight bacterial infections in wound care. Due to their antibacterial properties, low medication resistance, and biocompatibility, 2D metal-based biomaterials may treat wound bacterial infections. Effective wound dressing speeds healing. Traditional wound dressings like gauze cannot prevent wound infection. This problem can be solved using metal nanocoating. A study coated cotton gauze on both sides with nanosilver through in situ deposition.[24]

4. Nanoscaffold in Wound Dressing

Metal 3D biomaterial nanoscaffolds have been extensively investigated. Composite 3D biomaterials have one or more low-dimensional structural components. Unlike other metal-based biomaterials, 3D biomaterials contain metal or metal compounds and non-metallic components. Their biocompatibility and functionality improve with complexity. Bioactive glass (BG), mesoporous nanoparticles (MNs), and MOFs are now important parts of 3D biomaterials made from metal. These compounds release metal ions and increase biocompatibility, aiding wound healing. Previous studies have shown that metal elements regulate wound repair, and these materials have been widely used in wound healing studies. 3D metal-based biomaterials also accelerate angiogenesis and wound re-epithelialization. BG stimulates wound blood vessel growth, making it appropriate for wound dressings or tissue engineering scaffolds for continuous wound care.[24]

D. Nanoscale Biomaterials for Tissue Engineering

1. Nanostructured Scaffolds for Regenerative Medicine

Manufacturing, materials, biomedical, and tissue engineering are advancing faster due to 3D printing. In regenerative medicine and tissue engineering, 3D-printing allows the fabrication of spatial geometric configurations with desired internal structure designs for metals, inorganic materials, ceramics, and polymers. Modern 3D printing can create complicated structures that aid tissue infiltration, integration, and regeneration, thanks to technical advances. Biomedical uses include fracture healing, segmental bone defect correction, mouth reconstruction, skin injury repair, cardiovascular disease treatment, and spinal fusion using 3D printing.[25]

Researchers develop nanobiomaterials and nanocomposite scaffolds to mimic natural biology more efficiently and regenerate tissue and organs. Nanoscale material reduction improves surface roughness and the surface area-to-volume ratio. Surface reactivity and physiochemical qualities, including mechanical, electrical, optical, catalytic, and magnetic, can increase. Nanobiomaterials have unique properties that make them attractive for biomedical applications, particularly tissue and organ regeneration.[26]

Few products have been approved to promote 3D tissue growth. The materials must have the same qualities as the native ECM to guide and control cell behaviour and help them grow like the original cells. Three-dimensional polymer biomaterial scaffolds let cells and blood vessels grow and develop. The biomaterials used support 3D cell proliferation, are stable, biodegrade well, and can be derived from natural or synthetic sources, such as collagen, fibrinogen, and hyaluronic acid. Different polymers have different properties. Thus, it is essential to understand the properties of all polymers to choose the best one for the desired purpose or therapeutic need. Polymers like Poly Lactide-co-Glycolide (PLG) produce inflammation when implanted, making them ideal for cancer immunotherapy to increase vascularization. These polymer scaffolds help chondrocytes grow, which makes them perfect for repairing cartilage (for example, matrix-induced autologous chondrocyte implants). Scaffolds are widely employed in regenerative medicine, although manufacturing, stimulation of inflammatory and immune reactions, and breakdown of the materials remain technological hurdles.[27]

2. Integration of Nanoparticles in Artificial Organs

Nanoparticles have the capacity to hinder infection, reduce inflammation, and, overall, enhance the initial development of tissue required to extend the lifespan of implants.[28] According to studies, nanotechnology-based encapsulation systems like nanogland have helped animal models engraft pancreatic islets. These encapsulation mechanisms protect transplanted cells from immunological attack and promote cell survival and vascularization. The latest Nanogland uses Polylactic Acid (PLA)/Polycaprolactone (PCL) biocompatible and bioinert polymers. It compartmentalises insulin-producing pancreatic islets, or islet-like cells. The Nanogland is designed to keep cells close and imitate living conditions. It comprises cells in a growth factor-rich matrix and has customised microchannels on its surface to speed up blood vessel creation in transplanted tissue. Permanent transplant survival and viability are essential.[29]

III. APPLICATIONS OF BIONANOTECHNOLOGY IN ANAESTHESIOLOGY

A. Nanoscale Drug Delivery for Anesthesia

1. Controlled Release of Anesthetic Agents

Nanomedicine uses encapsulated nanoparticles with disease-targeted medicines and surface changes that interact with biological systems. Recently developed medical nanocarriers include nanoparticles, nanoliposomes, liposomes, micelles, solid lipid particles, surfactant vesicles, and others. Many medications' slow-release effects are beneficial. Nanotechnology can improve cancer treatment efficacy, accuracy, and safety. Nanotechnology is also important in drug delivery system therapy, imaging, and immunotherapy because of its particle-size features. Clinical care uses nanotechnology extensively. Nanomedicine is also used in numerous subfields to improve accuracy and personalised care.[30]

Anaesthesia multimodal regimens often use Local Anaesthesia (LA) is a safe analgesic. However, its short duration (less than 24 hours) and potential toxicity (heart and central nervous system damage) limit its use and increase the need to mitigate side effects and relieve pain. Disposable catheters with pumps extend LA; however, catheter dislodgement, infection, and trauma during surgery are still possible. Catheter installation takes time and considerable labour. LA extended-release formulations overcome these drawbacks. They can safely administer a single injection without general anaesthesia, utilising minimally invasive procedures and specialised tools to reduce systemic toxicity. Additionally, a protracted nociceptive block is possible. One discovery related to regulated anaesthetic release.[31]

2. Targeted Delivery to Specific Sites

Nanotechnology allows precise and targeted conveyance to specific areas, improving existing pharmaceutical delivery techniques. Despite these benefits, precise medicine delivery to a specific location is still difficult. Cell receptor-targeted ligands on particles have been added to improve medicine delivery. This is a major improvement in precise pharmaceutical delivery, but the drug carrier must overcome many biological barriers to reach the target. To discharge their cargo and be removed, nanoparticles must pass through the cell membrane and intracellular compartment networks. Lipid-based nanoparticles (LBNPs) are biocompatible and considered "nanosafe" carriers; hence, scientists have concentrated on them recently. Most LBNPs are vesicle-like spherical structures with a lipid bilayer enclosing an aqueous interior. The largest group of lipid-based nanoparticles is liposomes. They are primarily phospholipids and can have one or more vesicles. Liposomes are efficient medication transporters because their composition resembles cell membranes. Biocompatibility and biodegradability improve pharmaceutical stability and biodistribution. Nanoparticle forms, sizes, surface charges, surface changes, and manufacturing procedures affect stability in vivo and in vitro. These properties can be changed during nanoparticle synthesis.[32]

B. Nanosensors for Real-Time Monitoring

1. Nanoparticle-Based Monitoring of Physiological Parameters

The global nanosensor market has grown rapidly in recent decades. Medical diagnostics and other technologies use nanosensors, demonstrating their particular applicability. Colorimetric nanosensor systems' performance depends on the nanomaterial's surface features. This problem may be solved using electromagnetic and chemical nanosensors. Nanosensors detect electromagnetic waves, including quantum phenomena, and molecular nanosensors encode biological communication systems. Mechanical energy from nanosensor vibrations and biological molecules can power molecular nanosensors. Scientists have developed wearable sensors that can detect diabetes by the smell of acetone in the breath. Melanoma odour is also detected by these sensors. These cutting-edge devices use gas sensors and a patternreorganising component to detect more odours than human nostrils. The nanoworld has several unique events compared to the macroscale. Nanosensors are essential for many daily operations, making them useful in many fields to meet demand. Nanosensors detect virus and disease propagation in public settings. In-body networks can monitor blood, illness, and breath in real time. These technologies can be simply connected to health and environmental monitoring wearables.[33]

2. Smart Nanodevices for Closed-Loop Anesthesia Control

In conventional feedback control, creating a Closed-Loop Anaesthetic Delivery (CLAD) system is difficult. A precise brain anaesthetic model is used by a computer-controlled infusion pump to provide an anaesthetic medication to a patient. A unique electroencephalogram pattern determines the control signal, which measures the brain's response to the anaesthetic. An instantly calculated control signal is utilised to provide an error signal that shows the difference between the measured Electroencephalography (EEG) signature value and the required anaesthetic level. The error signal is quickly analysed and used to regulate infusion pump drug delivery with a specific control mechanism. CLAD systems allow continuous and precise anaesthetic modulation with less medication than anesthesiologists.[34]

By combining micro/nanotechnology, chemistry, biology, and engineering, drug delivery devices have improved the diagnosis and treatment of tumours, cardiovascular disease, and infections. Devices that autonomously modify the release profile have been proposed since conventional drug delivery systems (DDSs) such as capsules, tablets, and liposomes without controlled-release features cannot meet the need for on-demand release in therapy. Multiple diseases have been treated with sustained, controlled, and delayed release delivery methods. However, the building block's qualities affect these delivery systems' predetermined release rates. Stimuli-responsive materials have dramatically improved drug delivery systems (DDSs), enabling "smart" DDSs. Intelligent drug delivery systems (DDSs) release medications as needed in open-loop or closed-loop mode. In an open-loop system, heat, light, and ultrasound control medication release without self-feedback. Open-loop controlled devices are better than DDSs but require external stimulation. This may hinder long-term disease therapy and patient autonomy.[35]

C. Nanotechnology in Pain Management

1. Nanoparticle-Based Analgesics

Nanomedicine is growing, but pain physiology and chronic pain have prevented its use in pain management. Future pain remedies will benefit greatly from nanotechnology. Novel nanomaterials release medications stimulus-sensitively to target specific tissues, cell types, and organelles. As nanodevices, they can pinpoint the chemical cause of discomfort. With lower analgesic dosages and longer pain relief, nanoparticle drug carriers work better. The administration of nanoparticle gene therapy improves long-term chronic pain treatment. Clinical trials have shown that viral and non-viral vectors work in gene therapy. Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) is used to modify gene expression to reduce discomfort without eliminating sensitization. Proactive pain management involves removing proinflammatory reactive oxygen species and free nucleic acids. Scavengers target nociceptors and sensitization chemicals, not only pain.[36]

2. Neuromodulation through Nanoscale Devices

Neuromodulation manipulates neuronal activity by applying electrical, optical, chemical, auditory, or magnetic stimuli to neural tissue. It provides powerful tools for understanding brain function and altering malfunctioning neural networks to improve disease progression. Neuromodulation has enabled many scientific results on brain circuit function. Neuromodulation methods that improve, correct, and replace motor, sensory, and cognitive capacities have led to additional neuropsychiatric treatment options and prostheses. Neuromodulation's goal is high spatiotemporal resolution and minimally invasive activation of specific cell types and neuronal circuits in deep brain regions. This goal has not been achieved with current neuromodulation methods. Modern neuromodulation technologies have taken 60 years to develop. Deep brain stimulation (DBS), optogenetics, and chemogenetics are among these technologies. Electrical stimulation is used in deep brain stimulation (DBS), sacral nerve stimulation, and spinal cord stimulation. Nanotechnology has improved neuromodulation procedures. The flexible nanoscience toolkit can improve neuromodulation from bulky devices to smaller ones with soft mechanics, densely packed components, and sustained performance. These nanoscale tools can target specific locations and integrate with neural tissue due to their high spatial resolution. Nanomaterials have useful physical and chemical features that differ from those of larger materials. Nanomaterials could improve neuromodulation technologies on a larger scale.[37]

IV. INTEGRATION CHALLENGES AND SOLUTIONS

A. Biocompatibility and Safety Concerns

1. Addressing Potential Nanotoxicity

With these nanotechnology advances, the question of whether nanomaterials are dangerous has arisen. Nanomaterials' interactions with tissue, cells, and milieus can reveal harmful effects that chemically identical but larger biological equivalents cannot mimic. Nanotoxicology studies how nanoparticles injure humans and the environment. Nanotoxicology studies man-made nanoparticles' side effects. This joint field includes toxicology, biology, chemistry, physics, material science, geology, exposure assessment, pharmacokinetics, and medicine. The painful experiences of people with carcinogenic compounds like nicotine and asbestos, formerly thought harmless, have

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aroused worries about nanoparticles. Many nanoparticles are fibrogenic and dangerous due to their elongated, fibrous shape, like asbestos. Nanomaterial toxicity depends on exposure length, dose, aggregation and concentration, particle size and shape, surface area, and charge.[38]

To ensure a sustainable future, nanomaterials must be designed and produced with size, shape, and surface dangers in mind. Green nanotechnology uses "green chemistry" to create and optimise products and processes to reduce nanoparticle dangers to humans and the environment. Selecting environmentally friendly chemicals, avoiding hazardous nanomaterials, and changing their physical and chemical properties to control their environmental behaviour and make them non-toxic are steps in developing more environmentally friendly nanomaterials and nanomanufacturing methods. To generate safe and efficient nanoscale materials, nanoscience and technology can use green chemistry concepts. 1) Developing nanoparticles with improved safety; 2) ensuring manufacturing safety; 3) minimizing environmental footprint; 4) improving nanomaterial efficacy; 5) increasing energy efficiency; 6) preventing waste.[39]

2. Long-term Implications of Nanomaterials

Insoluble and stable nanoparticles like titanium dioxide, gold, silver, and polymers can enter the body and cause safety hazards. Once in the environment, nanoparticles may interact with metabolic networks and cells. Because natural ecosystems are complex, sufficient measures must be taken when studying these nanoparticles' effects on terrestrial and aquatic ecosystems and establishing their environmental relevance. Nanomaterial trash is disposed of like regular waste without special treatment. Neutralise these nanowastes before disposal because they may be toxic or chemically reactive. To avoid long-term effects, governments should develop strong nanowaste management plans and recycle these materials.[40]

B. Ethical and Regulatory Considerations

1. Patient Consent and Information

Nanomedical technology is constantly evolving; thus, the legal, social, and ethical implications of its therapeutic uses must be considered while considering hazards. Safe and effective nanomedical technology requires extensive research. However, clinical researchers face specific nanomedical research obstacles. Because nanomedical device and technology research is still new and developing, it may become harder to get real informed consent from people who want to take part in the proposed nanomedical device and nano-chemical therapeutic trials. Nanomedical device-based testing may be difficult for medical practitioners to understand because nanotechnology's effects on the body are unknown. Communication with research participants must be careful to ensure they understand the hazards, but how to do so is unknown.[41]

2. Regulatory Frameworks for Nanomedicine in Surgery

Nanotechnology in medicine is predicted to revolutionise healthcare. The original hype has not been met, but most in the field attribute this to nanomedicine's infancy and lack of clinical regulation, which is limiting its translation. Nanomedicine's impact on the pharmaceutical industry is exciting, but regulatory guidance is needed to give manufacturers, policymakers, healthcare providers, and the public legal certainty. Many nanomedicines' interactions with biological systems are yet unknown, making it difficult to analyse, detect, or make inferences regarding their physicochemical and toxicological features. However, without uniform regulatory advice, little will change. In this process, "one size" does not fit all because nanoparticle properties depend on nanoparticle type, surface properties, administration route, and morphology, which can vary, slowing down the regulatory process. A major difficulty for nanomedicine regulation is that regulatory agencies like the Food and Drug Administration (FDA) employ safety data from bulk compounds, which have different pharmacological and pharmacokinetic properties. This means safety and efficacy data will not reflect what will happen when nanomedicine is used in clinical settings after marketing authorization. This makes nanomedicine safety and efficacy regulations difficult because a non-nano version may pass while nanomedicine may not. Nanomedicine regulation by the European Medicines Agency (EMA) follows General Medicinal Product (GMP) laws. It also develops multidisciplinary nanomedicine evaluation competence using risk-benefit analysis. It also defined nanomedicine and released nanomedicine-specific guidelines on its guidance portal. The EMA created the European Nanomedicines Expert Group in 2009 to fulfil stakeholder demand for nanomedicine reviews. Established academics and regulatory science specialists from the Expert Group met with the FDA and other regulatory specialists.[42]

V. FUTURE DIRECTIONS IN BIONANOTECHNOLOGY FOR SURGERY AND ANAESTHESIOLOGY

A. Nanomedicine in Personalized Surgery

1. Customized Nanotherapies for Individual Patients

Nanomedicine, which uses nanotechnology in biomedicine, is a promising method for drug delivery and diagnosis. The success of monofunctional nanomedicines has led scientists to develop "nanotheranostics," nanomedicines combining imaging and therapeutic capabilities. Nanotheranostics can simultaneously diagnose and treat diseases non-invasively and see pharmaceuticals being released and dispersed in real time, making them promising. This predicts and verifies therapeutic efficacy. Nanotheranostics have many advantages for improving cancer and other severe disease treatment outcomes. Next, nanotheranostics will enable genuine personalised medicine, where each patient's unique characteristics are considered. Nanotheranostics would speed disease diagnosis, therapy,

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and efficacy evaluation in clinical settings. This would identify patients who are more likely to respond well to therapy and have a good outcome. Nanotheranostics is appealing because it involves creating customised therapeutic procedures that maximise benefits and safety.[43]

2. Precision Surgery Using Molecular-Level Information

Molecular imaging is essential for precision surgery. This technology is used for early identification, treatment planning, implementation, and accurate evaluation. In minimally invasive surgery, especially robotic surgery, molecular imaging solutions are needed. These devices use Artificial Intelligence (AI), computer-aided visualisation, new molecular imaging, and surgical navigation hardware. Equipment that improves surgical processes has increased due to less-invasive robotic surgery. Precision surgery may benefit from molecular imaging. The robotic platform appears well-suited for image-guided surgery integration. Most technologies have a long road ahead of them. However, the research and engineering communities and the rapid advancement of AI are working to develop precise surgical solutions that seamlessly integrate preoperative, intraoperative, and postoperative imaging to improve patient outcomes. This process requires nuclear medicine for computer-assisted diagnosis, planning, robotic guidance, detection, and verification throughout the surgical pathway.[44]

B. Nanotechnology and Minimally Invasive Procedures

1. Nanorobotics for Microsurgery

Recent advances in micro/nanorobots have shown considerable promise for addressing these limitations and for using these tiny devices for precision surgery. Untethered nanorobotic instruments like nanodrillers, microgrippers, and microbullets enable less invasive surgery. High-precision minimally invasive surgery benefits from micro/nanorobots' dimensions matching those of the small biological entities they treat. Moving micro/nanorobots with nanoscale surgical components can directly penetrate or extract biological tissues for precise surgery using various energy sources. Tiny robots can navigate the body's tiniest capillaries and undertake cellular procedures, unlike giant robots. Tetherless microgrippers are a step towards autonomous microsurgery robots. These mobile microgrippers can grab tissues and cells from hard-to-reach areas. Traditional microgrippers are tethered and controlled by mechanical or electrical signals from control systems via wires or tubes, limiting their miniaturisation and manoeuvrability. Untethered microgrippers grip by opening or shutting, like huge tethered ones. Multiple environmental conditions can autonomously activate a set of responsive microgrippers used as minimally invasive microsurgical tools.[11]

2. Nanoparticle-Assisted Endoscopic Interventions

Traditional endoscopes limit treatment administration and monitoring precision. Nanotechnology and light-triggered therapy have advanced in the past decade. These advances may help diagnose tough lesions and treat gastrointestinal cancers more precisely. Nanotechnology-based theranostics combines diagnostic and targeted treatment in one step. Nanotechnology advances such as nanopowder, nanostents, nanogels, and nanoparticles are examined. Endoscopic ultrasound and experimental endoscopic procedures improve diagnoses and treatments, according to the review. A "smart" multifunctional endoscope for localised colorectal cancer, a near-infrared laser endoscope for gastrointestinal stromal tumours, an endocapsule for obscure gastrointestinal bleeds, and an ultrasound-mediated targeted drug delivery proof-of-concept therapeutic capsule are examples. Translational and clinical trials will be used to integrate new technologies into clinical practice, resulting in more individualised and interdisciplinary diagnosis and treatment. This will improve procedure speed, precision, cost-effectiveness, and reduce recurring procedures.[45]

C. Nanoscale Innovations in Anesthesia Management

1. Development of Next-Generation Anesthetics

Recently, nano-modifications of general anaesthetics have shown promise for the future. General anaesthetic nanomedicines have advanced in practical use in recent investigations. Propofol and etomidate are the main ingredients in these nanomedicines, which use biodegradable synthetic polymers or natural biomacromolecules such as Polyethylene Glycols (PEG), PLA, Polyglycolic Acid (PGA), alginate, starch, amino acids, liquid crystal materials, micelles, and others. General anaesthetic nanomedicines have not acquired FDA approval like local ones, leaving abundant chances for further study, analysis, and market applicability.[5]

2. Advanced Monitoring and Control Systems

Anaesthesiologists can now troubleshoot monitors, properly document case data, and perform therapeutic operations in the operating room. Today, anaesthetists require AI and machine learning to manage information overload. Medical AI has grown rapidly in the past decade. It could change anaesthesia, clinic perioperative care, and imaging analysis. AI allows anaesthetists and doctors to work with computer scientists on computation, predictive analysis, and automation. From smartphones to homes, companies, and cars, artificial intelligence is everywhere. Anaesthetic problems have decreased due to technological advances and automation for the anaesthetist. AI can improve anaesthetists' working conditions and patient safety. Anesthesia Information and Management Systems (AIMS) includes decision-help and target-controlled infusion systems. In addition, sophisticated anaesthesia machine design, closed-loop anaesthesia delivery, and point-of-care ultrasound-guided therapies are excellent examples. Advanced nanotechnology and AI can monitor the human body at the molecular level. Colloidal suspension with millions of active analgesics implanted on the patient's mucosa can cause local anaesthesia in the following days, and nanorobots can route these molecules deep into the tissue, even in the bone or dental canal. To treat pain after surgery, anaesthetists may use a number of different molecular targets.

These include sodium channel blockers (Nav 1.3, Nav 1.7, and Nav 1.8), potassium channel openers, N-type calcium channels (Cav 2.2), P2X4 and P2X7 receptor antagonists in microglia, vanilloid receptor-1 antagonists, and cannabinoid-2 receptor agonists. Nanocarriers inside halothane can improve its pulmonary and cardiovascular anaesthetic properties and prevent liver exposure. Anaesthesia agents like Propofol can benefit from nanomedicine.[46]

VI. CONCLUSION

This extensive literature review examines nanotechnology's growing use in surgery and anaesthesia. Nanotechnology can improve biological system management, illness diagnosis, monitoring, and therapy, reducing patient stress, scarring, and post-operative problems. This literature review also examines the ethical and safety ramifications of nanotechnology in surgical procedures. The literature review covers nanoscale surgical technologies' advancements, applications, and future prospects, emphasising nanotechnology's potential to revolutionise surgical practice and enhance patient outcomes.

The rising use of nanotechnology in numerous surgical disciplines shows the impact of bionanotechnology on surgery's future. Nanotechnology can affect biological system management, disease diagnosis, monitoring, and treatment. This can lessen patient stress, scarring, and post-surgery issues. The growing use of nanotechnology in orthopaedic, neuro, plastic, surgical cancer, cardiac, vascular, ophthalmic, and thoracic surgery shows its versatility and ability to improve patient outcomes. The development of nanorobots for cell surgery and nanotechnology's potential to change anaesthesia, drug delivery, and surgical processes demonstrate its vital role in shaping surgery's future. New nanoscale devices may reduce surgical invasiveness as nanotechnology advances. This may increase surgical precision and patient care. Nanotechnology in surgery has the potential to transform surgical processes and improve patient outcomes.

This literature review emphasises the need for additional research and collaboration to fully use the capabilities of nanotechnology in surgical practice. Moreover, we emphasise the necessity of strong cooperation among the medical, scientific, and technical sectors to guarantee the secure and efficient implementation of nanotechnology in surgical procedures. This study concludes by highlighting the imperative for continuous research and collaboration to fully harness the promise of bionanotechnology in influencing the future of surgery.

REFERENCES

I. Lee Y, Moon J. Introduction to bionanotechnology. Introduction to Bionanotechnology. Seoul: Springer; 2020. 1–234 p.

II. Contera S, De La Serna J, Tetley T. Biotechnology, nanotechnology and medicine. Emerg Top Life Sci. 2021;4(6):551–4.

III. Bayda S, Adeel M, Tuccinardi T, Cordani M, Rizzolio F. The history of nanoscience and nanotechnology: From chemical-physical applications to nanomedicine. Molecules. 2020;25(1):1–15.

IV. Deng Y, Zhou C, Fu L, Huang X, Liu Z, Zhao J, et al. A mini-review on the emerging role of nanotechnology in revolutionizing orthopedic surgery: challenges and the road ahead. Front Bioeng Biotechnol. 2023;11(May):1–12.

V. Zhang S, Wang Y, Zhang S, Huang C, Ding Q, Xia J, et al. Emerging Anesthetic Nanomedicines: Current State and Challenges. Int J Nanomedicine. 2023;18(July):3913–35.

VI. Malik S, Muhammad K, Waheed Y. Emerging Applications of Nanotechnology in Healthcare and Medicine. Molecules. 2023;28(18):6624.

VII. Verme D, Goyal M, Suleria H. Nanotechnology and Nanomaterial Applications in Food, Health, and Biomedical Sciences. Apple Academic Press; 2020. 173 p.

VIII. Bao W, Deng Z, Zhang S, Ji Z, Zhang H. Next-generation composite coating system: Nanocoating. Front Mater. 2019;6(April):1–6.

IX. Butler J, Handy R, Upton M, Besinis A. Review of Antimicrobial Nanocoatings in Medicine and Dentistry: Mechanisms of Action, Biocompatibility Performance, Safety, and Benefits Compared to Antibiotics. ACS Nano. 2023;17(8):7064–92.

X. Soto F, Chrostowski R. Frontiers of medical micro/nanorobotics: In vivo applications and commercialization perspectives toward clinical uses. Front Bioeng Biotechnol. 2018;6(NOV):1–12.

XI. Li J, Berta E, Gao W, Wang J. Micro/Nanorobots for Biomedicine: Delivery, Surgery, Sensing, and Detoxification Jinxing. Physiol Behav. 2017;176(5):139–48.

XII. Ryvolova M, Chomoucka J, Drbohlavova J, Kopel P, Babula P, Hynek D, et al. Modern micro and nanoparticle-based imaging techniques. Sensors (Switzerland). 2012;12(11):14792–820.

XIII. Pallares R, Mottaghy F, Schulz V, Kiessling F, Lammers T. Nanoparticle Diagnostics and Theranostics in the Clinic. J Nucl Med. 2022;63(12):1802–8.

XIV. Ehlerding E, Grodzinski P, Cai W, Liu C. Big Potential from Small Agents: Nanoparticles for Imaging-Based Companion Diagnostics. ACS Nano. 2018;12(3):2106–21.

XV. Cheng X, Xie Q, Sun Y. Advances in nanomaterial-based targeted drug delivery systems. Front Bioeng Biotechnol. 2023;11(April):1–27.

XVI. Prabahar K, Alanazi Z, Qushawy M. Targeted drug delivery system: Advantages, carriers and strategies. Indian J Pharm Educ Res. 2021;55(2):346–53.

XVII. Tewabe A, Abate A, Tamrie M, Seyfu A, Siraj E. Targeted drug delivery — from magic bullet to nanomedicine: Principles, challenges, and future perspectives. J Multidiscip Healthc. 2021;14:1711–24.

XVIII. Dam P, Celik M, Ustun M, Saha S, Saha C, Kacar E, et al. Wound healing strategies based on nanoparticles incorporated in hydrogel wound patches. RSC Adv. 2023;13(31):21345–64.

XIX. Krishnan P, Banas D, Durai R, Kabanov D, Hosnedlova B, Kepinska M, et al. Silver nanomaterials for wound dressing applications. Pharmaceutics. 2020;12(9):1–27.

XX. Naseri M, Hedayatnazari A, Tayebi L. PGS/Gelatin Nanocomposite Electrospun Wound Dressing. J Compos Sci. 2023;7(6).

XXI. Biswal A, Swain S. Chitosan: A Smart Biomaterial. In: Swain S, Biswal A, editors. Chitosan Nanocomposites: Bionanomechanical Applications. Singapore: Springer; 2023. p. 1–25.

XXII. Bagheri M, Validi M, Gholipour A, Makvandi P, Sharifi E. Chitosan nanofiber biocomposites for potential wound healing applications: Antioxidant activity with synergic antibacterial effect. Bioeng Transl Med. 2022;7(1):1–15.

XXIII. Pang Q, Jiang Z, Wu K, Hou R, Zhu Y. Nanomaterials-Based Wound Dressing for Advanced Management of Infected Wound. Antibiotics. 2023;12(2).

XXIV. Wang H, Xu Z, Li Q, Wu J. Application of metal-based biomaterials in wound repair. Eng Regen. 2021;2(September):137–53.

XXV. Liu X, Gaihre B, Park S, Li L, Dashtdar B, Astudillo Potes M, et al. 3D-printed scaffolds with 2D hetero-nanostructures and immunomodulatory cytokines provide pro-healing microenvironment for enhanced bone regeneration. Bioact Mater [Internet]. 2023;27(April):216–30. Available from: https://doi.org/10.1016/j.bioactmat.2023.03.021

XXVI. O'Brien C, Hann S, Holmes B, Zhang L. Nanotechnology: A Toolkit for Cell Behavior. In: Zhang L, Fisher J, Leong K, editors. 3D Bioprinting and Nanotechnology in Tissue Engineering and Regenerative Medicine. Second Edi. Elsevier; 2022. p. 3–23.

XXVII. Altyar A, El-Sayed A, Abdeen A, Piscopo M, Mousa S, Najda A, et al. Future regenerative medicine developments and their therapeutic applications. Biomed Pharmacother. 2023;158.

XXVIII. Teoh G, Klanrit P, Kasimatis M, Seifalian A. Role of nanotechnology in development of artificial organs. Minerva Med. 2015;106(1):17–33.

XXIX. Tasciotti E, Cabrera F, Evangelopoulos M, Martinez J, Thekkedath U, Kloc M, et al. The emerging role of nanotechnology in cell and organ transplantation. Transplantation. 2016;100(8):1629–38.

XXX. Gu S, Luo Q, Wen C, Zhang Y, Liu L, Liu L, et al. Application of Advanced Technologies—Nanotechnology, Genomics Technology, and 3D Printing Technology—In Precision Anesthesia: A Comprehensive Narrative Review. Pharmaceutics. 2023;15(9).

XXXI. He Y, Qin L, Huang Y, Ma C. Advances of Nano-Structured Extended-Release Local Anesthetics. Nanoscale Res Lett. 2020;15(1).

XXXII. Waheed S, Li Z, Zhang F, Chiarini A, Armato U, Wu J. Engineering nano-drug biointerface to overcome biological barriers toward precision drug delivery. J Nanobiotechnology [Internet]. 2022;20(1):1–25. Available from: https://doi.org/10.1186/s12951-022-01605-4

XXXIII. Javaid M, Haleem A, Singh R, Rab S, Suman R. Exploring the potential of nanosensors: A brief overview. Sensors Int. 2021;2(July).

XXXIV. Liberman M, Ching S, Chemali J, Brown E. A Closed-Loop Anesthetic Delivery System for Real-Time Control of Burst Suppression. J Neural Eng. 2014;10(4):1–27.

XXXV. Wang Y, Li Z, Hu Q. Emerging self-regulated micro/nano drug delivery devices: A step forward towards intelligent diagnosis and therapy. Nano Today [Internet]. 2021;38:101127. Available from: https://doi.org/10.1016/j.nantod.2021.101127

XXXVI. Bhansali D, Teng S, Lee C, Schmidt B, Bunnett N, Leong K. Nanotechnology for pain management: Current and future therapeutic interventions. Nano Today [Internet]. 2021;39:101223. Available from: https://doi.org/10.1016/j.nantod.2021.101223

XXXVII. Yang X, McGlynn E, Das R, Paşca S, Cui B, Heidari H. Nanotechnology Enables Novel Modalities for Neuromodulation. Adv Mater. 2021;33(52).

XXXVIII. Akçan R, Aydogan H, Yildirim M, Taştekin B, Sağlam N. Nanotoxicity: A challenge for future medicine. Turkish J Med Sci. 2020;50(4):1180–96.

XXXIX. Mohanta D, Ahmaruzzaman M. Addressing Nanotoxicity: Green Nanotechnology for a Sustainable Future. In: Hussain C, editor. The ELSI Handbook of Nanotechnology: Risk, Safety, ELSI and Commercialization. Scrivener Publishing LLC; 2020. p. 103–12.

XL. Gupta R, Xie H. Nanoparticles in daily life: Applications, toxicity and regulations. J Environ Pathol Toxicol Oncol. 2018;37(3):209–30.

XLI. Wasti S, Lee I, Kim S, Lee J, Kim H. Ethical and legal challenges in nanomedical innovations: a scoping review. Front Genet. 2023;14(May):1–11.

XLII. Foulkes R, Man E, Thind J, Yeung S, Joy A, Hoskins C. The regulation of nanomaterials and nanomedicines for clinical application: Current and future perspectives. Biomater Sci.

2020;8(17):4653–64.

XLIII. Mura S, Couvreur P. Nanotheranostics for personalized medicine. Adv Drug Deliv Rev [Internet]. 2012;64(13):1394–416. Available from: http://dx.doi.org/10.1016/j.addr.2012.06.006

XLIV. Wendler T, Leeuwen F, Navab N. How molecular imaging will enable robotic precision surgery The role of artificial intelligence , augmented reality , and navigation. Eur J Nucl Med Mol Imaging. 2021;48:4201–24.

XLV. Nassani N, Alsheikh M, Carroll B, Nguyen D, Carroll R. Theranostic Gastrointestinal Endoscopy: Bringing Healing Light to the Lumen. Clin Transl Gastroenterol. 2020;11(3):e00119.

XLVI. Naaz S, Asghar A. Artificial intelligence, nano-technology and genomic medicine: The future of anaesthesia. Vol. 38, Journal of Anaesthesiology Clinical Pharmacology. 2022. p. 11–7.