DOI: https://doi.org/10.47275/2332-4864-130
Volume 10 Issue 1
Review Article

Scholit Publishers

Journal of Clinical & Anatomic Pathology

Nanomedicine in Clinical Anatomy and Pathology: A New Diagnostic Frontier

Keerthi Chandana Amudala[1*], Nandini Ahuja[2], Maansi Madadi[3*] and Vaishnavi Sutaram[4]

[1]Sri Venkateshwara Medical College, Tirupati, India
[2]Alte University, Tbilisi, Georgia
[3]Mallareddy Medical College for Women, Hyderabad, India
[4]Mahaveer Institute of Medical Sciences, Vikarabad, India

Abstract

Nanomedicine is rapidly transforming the clinical landscape by enabling precise diagnostic and therapeutic interventions at the molecular level. However, its integration into the domains of clinical anatomy and pathology remains underexplored, despite growing evidence of its potential to revolutionize structural and functional diagnostics. This review addresses this gap by providing a focused synthesis of nanomedicine applications across anatomical and pathological contexts, with emphasis on translational relevance. The review begins with foundational concepts in nanomedicine, including the physicochemical properties of nanoparticles and their interaction with biological systems. In clinical anatomy, it explores nanoparticle-enabled targeted drug delivery, regenerative scaffolds, and advanced imaging modalities enhanced by contrast-generating nanomaterials. Applications in neurological anatomy are discussed in detail, highlighting breakthroughs in overcoming the blood-brain barrier (BBB) to treat neurological disorders like Alzheimer's and Parkinson's disease. The pathology-focused sections examine nanosensors for early disease detection, nanotechnology in histopathology, and nano-polymerase chain reaction (nano-PCR) techniques for molecular diagnostics. The utility of nanomedicine in oncology is addressed through cancer nanodiagnostics and liquid biopsy platforms, while infectious disease diagnostics benefit from nanoparticle-based biosensors and nanovaccine carriers. A dedicated section also covers the integration of artificial intelligence (AI) with nanotechnology for improved diagnostic accuracy and personalized medicine. Future advancements in smart nano-devices, nanosurgical tools, and AI-driven nanoparticle design hold promise for precision diagnostics and individualized therapy. Overcoming current translation barriers will require interdisciplinary collaboration and standardization to fully integrate nanomedicine into routine clinical practice.

Keywords: Artificial intelligence, Clinical anatomy, Clinical pathology, Drug delivery, Imaging nanoparticles, Nanodiagnostics, Nanomedicine, Theranostics

Introduction

Understanding nanomedicine

Nanomedicine encompasses a wide range of applications, including drug delivery, imaging, and diagnostics, all at the nanoscale [1-3]. The unique properties of nanomaterials (Figure 1), such as their high surface area-to-volume ratio and ability to interact with biological systems at the molecular level, make them ideal candidates for medical applications [4]. Recent advancements in nanotechnology have led to the development of novel diagnostic tools and therapeutic agents that can target specific diseases more effectively than traditional methods [5-7].

One of the critical areas of research in nanomedicine is the interaction between nanoparticles and biological systems, particularly the liver. He et al. [8] emphasizes the importance of understanding nanoparticle-liver interactions, noting that the physicochemical properties of nanoparticles can significantly influence their delivery efficiency. The review discusses strategies to enhance delivery by modulating liver Kupffer cells, which play a crucial role in the immune response and can affect the safety and effectiveness of nanomedicines. While liver accumulation poses challenges, it also opens avenues for targeted therapies for hepatic diseases. In the realm of cancer therapy, Wu et al. [9] provides a comprehensive overview of biopolymer-based nanomedicine. They discuss the advantages and limitations of various biopolymers in nano anticancer drug delivery systems, highlighting the need for further research to overcome existing impediments. This comparative analysis aids in understanding the current development status and potential solutions in the field.

The application of nanomedicine extends to neurodegenerative disorders and addiction, as explored by Giménez et al. [10]. Their review focuses on innovative brain stimulation techniques and the role of magnetoelectric nanoparticles in modulating dopaminergic alterations. This underscores the potential of nanomedicine in addressing complex neurological conditions by targeting specific neurotransmitter systems. Pharmacokinetics is

Correspondence to: Keerthi Chandana Amudala and Maansi Madadi, Sri Venkateshwara Medical College, Tirupati, India and Mallareddy Medical College for Women, Hyderabad, India.

Citation: Amudala KC, Ahuja N, Madadi M, Sutaram V (2025) Nanomedicine in Clinical Anatomy and Pathology: A New Diagnostic Frontier. J Clin Anat Pathol, 10(1): 130. DOI: https://doi.org/10.47275/2332-4864-130

Received: February 14, 2025; **Accepted:** June 16, 2025; **Published:** June 20, 2025

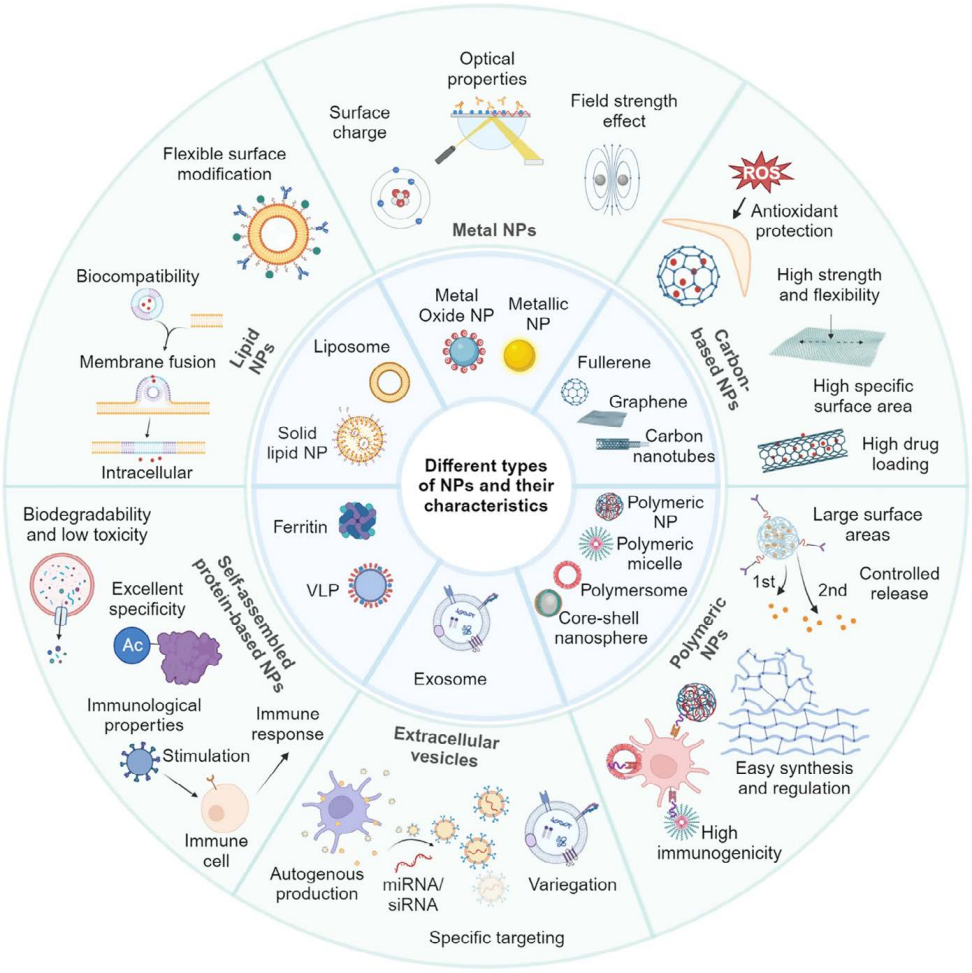


Figure 1: Six common nanomaterials and their characteristics [4].

another critical aspect of nanomedicine, particularly concerning anticancer drug delivery systems. Meng et al. [11] highlight advanced bioanalytical techniques that have emerged over the past five years, emphasizing the complexity of pharmacokinetic studies involving nanocarriers. The review outlines the necessity of analyzing both the released and encapsulated drugs, as well as the nanomaterials themselves, to fully understand their behavior in biological systems.

In the context of autoimmune diseases, Lambuk et al. [12] discussed the role of nanomedicine in targeting TNFR2 for rheumatoid arthritis treatment. They highlight the limitations of current therapies and the promise of nanocarriers that offer controlled drug release and active targeting capabilities, positioning nanomedicine as a viable therapeutic approach for this condition. Moreover, Mohapatra et al. [13] explore the potential of inorganic nanoparticles in inducing ferroptosis, a form of regulated cell death distinct from apoptosis. Their review suggests that combining ferroptosis-inducing nanoparticles with conventional therapies could enhance treatment efficacy for cancers resistant to standard approaches. Finally, the understanding of protein-nanoparticle interactions is crucial for advancing nanomedicine. Su et al. [14] introduce PROTCROWN, a curated database of protein corona data that aims to enhance research in this area. This resource is expected to facilitate deeper insights into the interactions between nanoparticles and biological systems, which are pivotal for optimizing nanomedicine applications.

Nanomedicine has shown significant promise in various medical applications, particularly in oncology, renal management, and drug delivery systems. For instance, prodrug-based cancer nanomedicines have emerged as a solution to the challenges of effective drug delivery to tumor sites. These nanomedicines are designed to be activated by specific stimuli, allowing for targeted therapy with reduced side effects and improved drug load efficiency [15]. Furthermore, polymeric nanomedicines are being developed to enhance drug delivery through active targeting and combinatorial approaches, which could revolutionize cancer treatment [16]. In renal management, nanomedicines are being designed as theragnostic agents that can both diagnose and treat kidney diseases. Recent studies have highlighted the importance of understanding the interactions between nanomaterials and kidney structures to optimize their design for improved renal clearance and reduced toxicity [17]. This dual functionality of nanomedicines exemplifies their potential to transform patient care.

Despite the advancements in nanomedicine, several challenges hinder its clinical translation [18-20]. One major obstacle is the formation of a biomolecular corona around nanoparticles, which can mask targeting moieties and alter their biological identity. This phenomenon complicates the interactions between nanomedicines and cellular receptors, ultimately affecting their efficacy [21, 22]. Additionally, the complexity of biological

systems and the variability in patient responses pose significant hurdles in the development of effective nanomedicines [23-25]. Another challenge is the limited understanding of nano-bio interactions, which are crucial for enhancing the efficacy of nanomedicine. The pharmacokinetics of nanoparticles, influenced by their size, shape, and surface properties, play a vital role in their distribution and therapeutic outcomes [26, 27]. A deeper understanding of these interactions is essential for optimizing nanomedicine design and improving clinical outcomes.

Nanomedicine, the application of nanotechnology in medicine, is revolutionizing the fields of clinical anatomy and pathology by providing innovative diagnostic and therapeutic solutions [28-30]. This article explores the integration of nanomedicine into clinical practices, highlighting its potential to enhance diagnostic accuracy, improve treatment outcomes, and transform patient care.

Nanomedicine in Clinical Anatomy

Nanomedicine, a convergence of nanotechnology and medical science, has begun reshaping the landscape of clinical anatomy [31]. Traditionally, clinical anatomy emphasizes structural-functional relationships to guide diagnosis and treatment. With nanomedicine, anatomical insights are now being augmented by nanoscale tools that enhance visualization, precision, and targeted intervention [32, 33]. This evolution marks a paradigm shift, not just in treatment strategies but in how anatomical structures are studied, visualized, and manipulated at a subcellular level.

The integration of nanotechnology into clinical anatomy is particularly promising in areas such as targeted drug delivery, regenerative medicine, and advanced imaging techniques [34-36]. These applications not only enhance the effectiveness of treatments but also minimize side effects and improve patient outcomes. In clinical anatomy, nanomedicine enhances visualization techniques and improves the understanding of anatomical structures. For instance, the use of engineered extracellular vesicles has shown promise in enhancing imaging diagnostics and targeted therapies [37]. These vesicles can be modified to carry imaging agents, allowing for more precise localization of anatomical features and pathologies. Moreover, advancements in imaging technologies, such as 3D echocardiography, have been complemented by nanomedicine. A novel 3D rendering tool that integrates transparency features has been shown to improve the delineation of cardiac anatomy and pathology, enhancing the visualization of structures and aiding in clinical decision-making [38].

Targeted drug delivery

Nanocarriers-such as liposomes, dendrimers, and polymeric nanoparticles-can be engineered to recognize specific anatomical targets via ligand-receptor interactions [39-41]. This precision allows therapeutic agents to accumulate diseased tissues while sparing healthy structures, minimizing systemic toxicity [42, 43]. For example, tumor vasculature or inflamed endothelium can be selectively targeted in oncology or vascular diseases, guided by detailed anatomical mapping at the nano-bio interface [44]. Nanomedicine enables the development of drug delivery systems that can target specific tissues or cells, thereby increase the efficacy of treatments while reduce side effects. This is achieved through the use of nanocarriers such as liposomes and polymers, which can encapsulate drugs and release them at the desired site of action [45]. The enhanced permeability and retention effect is a phenomenon exploited by nanomedicine to deliver drugs preferentially to tumor tissues, making it particularly effective in cancer therapy [46, 47].

A case study on MM-398 (liposomal irinotecan) is presented, detailing its development and clinical trials. This drug was shown to be more effective than its non-encapsulated counterpart, irinotecan, in treating metastatic pancreatic cancer. The encapsulation helps to reduce toxicity and improve drug delivery to tumor sites [48]. The paper also outlines the results from various phases of clinical trials for MM-398, noting that patients receiving this treatment had better outcomes in terms of tumor response and survival rates compared to those receiving standard treatments.

Nanoparticle albumin-stabilized paclitaxel [49], this specific formulation was evaluated in ten clinical trials. The results indicated a clinical benefit in using nanoparticle albumin-stabilized paclitaxel for treating breast cancer. Notably, it showed reduced toxicity compared to traditional first-line treatments, suggesting a safer alternative for patients. In addition to nanoparticle albumin-stabilized paclitaxel, one clinical trial assessed paclitaxel-incorporating polymeric micelles. However, the paper does not provide detailed results for this specific trial, focusing more on the outcomes of the nanoparticle albumin-stabilized paclitaxel [49].

Regenerative medicine

Nanotechnology is also revitalizing anatomical restoration through regenerative medicine [50]. Nanofibers and nanoscaffolds are designed to mimic extracellular matrix components, guiding cellular behavior and tissue regeneration [51, 52]. This is particularly valuable in reconstructive anatomy, orthopedics, and maxillofacial surgery, where anatomical precision is vital for restoring form and function. The integration of stem cells with nanomaterials further enhances anatomical fidelity during tissue repair. Nanotechnology plays a crucial role in regenerative medicine by facilitating the repair and regeneration of damaged tissues [53, 54]. This is achieved through the use of nanomaterials that can interact with stem cells and biomaterials to promote tissue growth and repair [55]. The combination of stem cells with nanomaterials allows for the regeneration of tissues such as bone, muscle, and nerve, offering potential solutions for conditions that currently have limited treatment options [55].

Nanoparticles are utilized to improve the mechanical, electrical, and biological properties of scaffolds, which are crucial for tissue engineering. These enhancements facilitate better cell attachment and tissue regeneration [56]. Nanofibrous materials mimic the native extracellular matrix, promoting cell adhesion and serving as scaffolds for various tissues, including skin, bone, and the nervous system [57]. Nanoparticles are also employed for DNA transfection, gene delivery, and stem-cell therapy, which are essential for tissue regeneration and repair [56]. Nanotechnology has significantly advanced bone regeneration by developing nanostructured scaffolds that mimic the natural bone environment. These scaffolds enhance osteogenic differentiation and integration of implants, leading to improved bone healing (Figure 2) [58]. Examples include graphene oxide–collagen nanocomposites and polylactic acid–carbon nanotube composites, which promote osteogenesis and angiogenesis, crucial for bone repair [59]. Additionally, strontium nanoparticles have been used to deliver osteoinductive cues, enhancing bone augmentation in spinal fusion models [60].

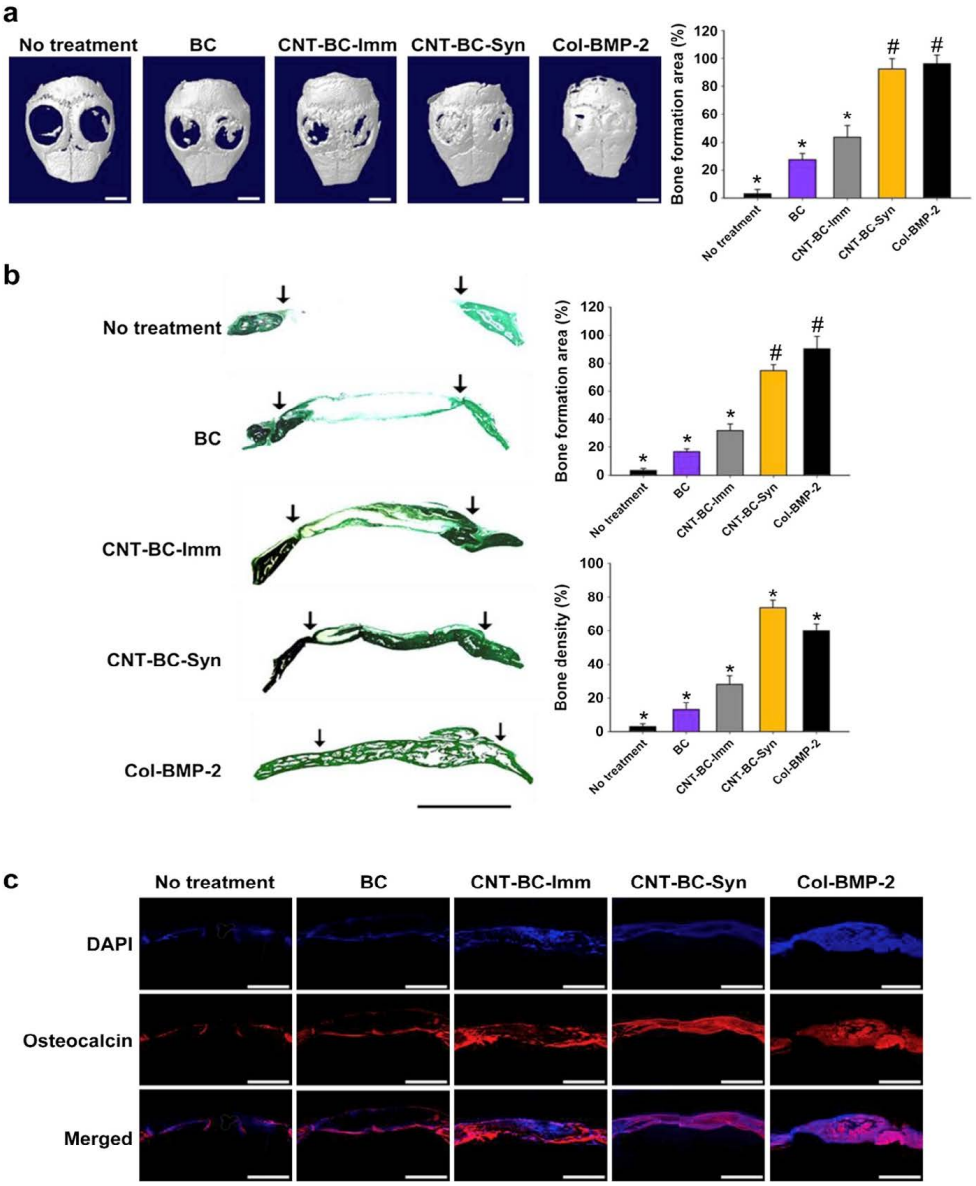


Figure 2: To evaluate bone healing efficacy, various scaffolds were implanted into mouse calvaria defects and monitored for 8 weeks. Collagen scaffolds embedded with BMP-2 (Col-BMP-2) were used as positive control. **(a)** Bone regeneration was assessed via micro-CT, with quantification of newly formed bone area within the defect sites. **(b)** Goldner's trichrome staining was performed on defect sections to visualize bone formation, followed by quantification of both the bone formation area and new bone density. Arrows denote the margins of the defect. **(c)** Immunohistochemical analysis was conducted on defect sites. DAPI staining (blue) identified scaffold osteoconductivity, while osteocalcin staining (red) indicated osteoinductive capacity. Scale bars represent 2 mm. p* < 0.05 vs all other groups; #p < 0.05 vs untreated, BC, or CNT-BC groups [58].

Advanced imaging techniques

One of the most profound contributions of nanomedicine to clinical anatomy lies in imaging. Nanoparticles, quantum dots, and magnetic nanostructures offer enhanced contrast in modalities like magnetic resonance imaging (MRI), computed tomography (CT), and positron emission tomography (PET) [61-63]. These agents facilitate high-resolution imaging of anatomical details, enabling earlier detection of pathologies such as tumors, vascular anomalies, or microstructural degenerations. This nanoscale resolution bridges the gap between gross anatomy and histopathology, offering clinicians a more integrated view of disease progression [64]. Nanomedicine enhances imaging techniques by providing high-resolution, targeted imaging capabilities. Nanoparticles can be used as contrast agents in imaging modalities such as MRI and CT scans, allowing for the precise visualization of anatomical structures and disease states [65, 66]. Molecular imaging facilitated by nanotechnology enables early detection of diseases and real-time monitoring of treatment efficacy, which is crucial for personalized medicine [66].

Superparamagnetic iron oxide nanoparticles (SPIONs) are widely used as contrast agents in MRI, enhancing the imaging of tumors and other pathologies by improving contrast and resolution [67, 68]. Gold nanoparticles have also been explored for their potential to enhance MRI contrast, offering a non-toxic alternative with high biocompatibility [67]. Gold nanoparticles are utilized in CT imaging due to their high atomic number, which provides superior contrast compared to traditional iodine-based agents. This allows for better visualization of vascular structures and tumors

[68, 69]. Nanoparticles can be engineered to target specific tissues, improving the specificity of CT imaging and reducing the required dose of contrast agents [67]. Nanoparticles can also enhance ultrasound imaging by serving as contrast agents that improve the visualization of blood flow and tissue structures. This is particularly useful in cardiovascular imaging and tumor detection [68, 69]. The development of gas-filled nanoparticles has been shown to improve the echogenicity of ultrasound images, providing clearer and more detailed images [70].

Multimodal imaging combines different imaging techniques to provide comprehensive diagnostic information. Nanoparticles are key to this approach, as they can be designed to function across multiple imaging modalities, such as MRI, CT, and PET [71, 72]. This approach is particularly beneficial in cancer diagnostics, where detailed information from different imaging techniques can be integrated to improve diagnosis and treatment planning [73]. Nanoparticles are used in optical imaging to enhance fluorescence and bioluminescence signals, allowing for the detailed visualization of cellular and molecular processes in real-time [71, 74]. Quantum dots and other fluorescent nanoparticles have been employed to track the biodistribution and targeting of drugs in preclinical studies, providing insights into the mechanisms of action of nanomedicine-based therapies [75].

While nanomedicine offers significant advancements in imaging techniques, challenges remain in translating these technologies into clinical practice. Issues such as the long-term safety of nanoparticles, regulatory hurdles, and the high cost of development need to be addressed to fully realize the potential of nanomedicine in imaging. Additionally, there is a need for standardized guidelines and further research to ensure the safe and effective integration of these technologies into routine clinical use [67, 73].

Theranostics

The concept of theranostics, which combines therapy and diagnostics, is a unique application of nanomedicine. This approach allows for simultaneous diagnosis and treatment, improving the efficiency of medical interventions and enabling personalized treatment plans [46]. Multifunctional nanomedicines can deliver therapeutic agents while providing diagnostic information, facilitating immediate responses to treatment and improving patient management [46].

Magnetic nanoparticles are used for both imaging and therapy, particularly in cancer treatment. They can be functionalized to target specific cancer cells, allowing for precise imaging through MRI and targeted drug delivery, thereby reducing systemic toxicity and improving therapeutic outcomes [76, 77]. Quantum dots and semiconductor-based theranostics are employed for their unique optical properties, which make them suitable for imaging and photothermal therapy. They can be used to track drug distribution and release in real-time, enhancing the ability to monitor treatment efficacy [78, 79]. Gold and silver nanoparticles are utilized in photothermal therapy and photodynamic therapy due to their ability to convert light into heat, selectively ablating cancer cells while minimizing damage to surrounding healthy tissue. This approach is particularly effective in treating tumors at the cellular and microenvironment levels [80].

Liposomes and micelles are used for the co-delivery of therapeutic and diagnostic agents. They can encapsulate drugs and imaging agents, providing a controlled release and targeted delivery to cancer cells, which enhances the efficacy of the treatment while reducing side effects [78, 81]. Polymeric nanoparticles and dendrimers offer a versatile platform for theranostics, allowing for the conjugation of multiple therapeutic and diagnostic agents. They are designed to improve solubility, bioavailability, and cellular uptake, making them effective in treating various cancers [79, 82].

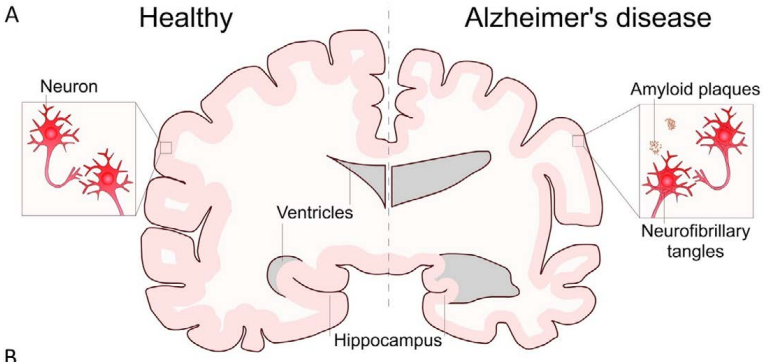
Nanotheranostics have shown promise in the detection and treatment of colorectal cancer, particularly in targeting metastatic sites such as the liver and peritoneum. Various nanomaterials, including carbon nanotubes and silica nanoparticles, are being explored for their potential to improve colorectal cancer outcomes [83]. Despite the promising advancements, challenges such as biocompatibility, potential toxicity, and regulatory hurdles remain. Continued research and development are necessary to overcome these barriers and achieve widespread clinical adoption of nanotheranostic technologies [81, 84].

While nanomedicine theranostics offers significant potential in revolutionizing cancer treatment, it is important to consider the challenges associated with its clinical translation. Issues such as nanoparticle toxicity, unintended accumulation in organs, and the need for rigorous testing and design improvements must be addressed. Additionally, ethical considerations and regulatory hurdles pose obstacles to the widespread clinical adoption of these technologies. However, with ongoing research and collaboration across scientific disciplines, the full potential of nanomedicine theranostics can be unlocked, offering highly individualized treatments that combine therapeutic and diagnostic capabilities [84, 85].

Applications in neurological anatomy

The central nervous system (CNS), protected by the BBB, poses a formidable anatomical challenge for drug delivery. Nanomedicine has developed BBB-penetrating nanocarriers capable of delivering drugs, genetic material, or imaging probes directly to neural tissues [86-88]. These advances are transforming anatomical understanding of CNS pathologies such as glioblastoma, Alzheimer's (Figure 3) [89], and Parkinson's (Figure 4) [89], making nanomedicine a tool not just of therapy, but of anatomical exploration. Nanomedicine plays a crucial role in neural repair by facilitating drug delivery across the BBB, a significant challenge in treating neurodegenerative diseases [90-92]. Nanocarrier systems, such as lipid and polymeric nanoparticles, are designed to transport drugs, genes, or therapeutic molecules to the brain, promoting neural regeneration [93]. These systems not only protect therapeutic agents from degradation but also enable controlled release, enhancing the efficacy of treatments for neural disorders [93].

Nanoparticles are engineered to penetrate the BBB, a significant obstacle in treating CNS disorders. These particles can deliver therapeutic agents directly to the brain, enhancing treatment efficacy [94, 95]. Ultrasound-mediated drug delivery using micro- and nanobubbles is a promising technique to transiently open the BBB, allowing for precise drug delivery to targeted brain regions [96]. Nanomedicine has been applied to treat neurodegenerative diseases such as Alzheimer's and Parkinson's by using nanoparticles to deliver drugs that can inhibit harmful protein

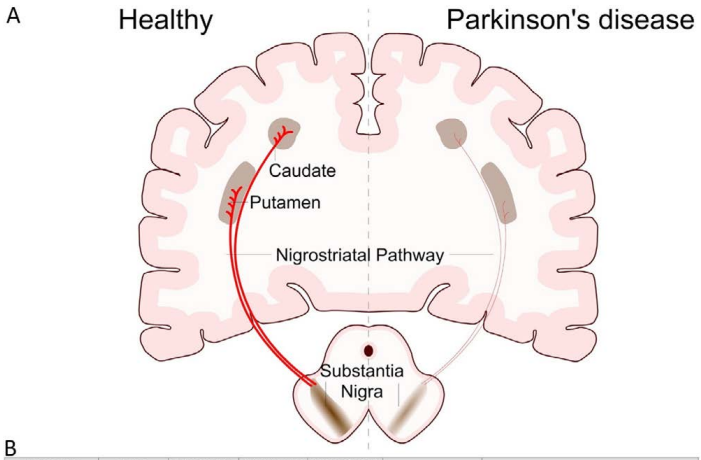


B

Nanoparticle material	Target ligand	Therapeutic agent	Particle size (nm)	Zeta potential (mV)	Model	Remarks
PLA	B6 peptide (transferrin substitute); PEG	NAPVSIPQ (NAP) (neuroprotective peptide)	118.3 ± 7.8	-22.65 ± 0.85	Mice injected with aggregated $A\beta_{1-40}$ peptide	Enhanced drug uptake/accumulation in the brain; Ameliorated learning impairments, cholinergic disruption and loss of hippocampal neurons.
PBCA	Polysorbate 80	NGF	250 ± 30	-	Rats with an acute scopolamine-induced amnesia	Reversed scopolamine-induced amnesia and improved recognition and memory.
PLGA	Trimethylated chitosan	Coenzyme-Q10	150	20	APP/PS1 transgenic mice	Improved uptake to brain regions, namely to cortex, paracoele, third ventricle and choroid plexus epithelium; Reversed behavior performance.
BCA	Polysorbate 80	Amyloid affinity drug ^{125}I-clioquinol	50 ± 5	-	APP/PS1 transgenic mice model; Mice injected with aggregated Aβ42 peptide	High specificity for Aβ plaques both *in vitro* and *in vivo*; Higher brain retention and uptake of nanoparticles in AD mouse models; Promising delivery vehicle *in vivo* for SPECT (^{123}I) or PET (^{124}I) amyloid imaging agent.

BCA, n-butyl-2-cyanoacrylate; NGF, Nerve growth factor; PBCA, Poly(n-butyl cyanoacrylate); PEG, Poly(ethylene glycol); PET, photon emission tomography; PLA, Poly(lactic acid); PLGA, poly(lactic-co-glycolic acid); SPECT, single photon emission computerized tomography.

Figure 3: Pathological features of Alzheimer's disease and nanoparticle-based therapeutic strategies in preclinical models. **(A)** Alzheimer's disease is primarily characterized by two pathological hallmarks: extracellular deposition of amyloid-beta plaques and intracellular accumulation of neurofibrillary tangles within neurons. These abnormalities lead to widespread neurodegeneration, marked by pronounced atrophy of the cerebral cortex and hippocampus, along with ventricular enlargement. **(B)** Various nanoparticle-based therapeutic strategies have been evaluated in preclinical animal models of AD, particularly via intravenous administration. These studies have explored the ability of different nanoparticle formulations to cross the BBB, target pathological lesions, and deliver therapeutic agents. Outcomes from these investigations generally demonstrate improved cognitive function, reduced plaque burden, and neuroprotection, underscoring the potential of nanoparticle systems in AD treatment development [89].



B

Nanoparticle material	Target ligand	Therapeutic agent	Particle size (nm)	Zeta potential (mV)	Model	Remarks
PLGA	-	Dopamine	119.70 ± 2.69	-2.660 ± 0.036	6-hydroxydopamine--injected rats	Increased dopamine levels and reduced dopamine-D2 receptor supersensibility; Prevented dopamine-associated toxicity.
PAMAM	Lactoferrin; PEG	hGDNF gene	196 ± 10.1	29.35 ± 3.27	6-hydroxydopamine--injected rats	Improved locomotor activity, reduced dopaminergic neuronal loss and enhanced monoamine neurotransmitter .
			196 ± 10.1	29.35 ± 3.27	Rotenone-injected rats	
PLGA	Lactoferrin; PEG	Urocortin	~90	~-24	6-hydroxydopamine--injected rats	Improved apomorphine-induced rotation test results; Higher tyrosine hydroxylase imunoreactivity and dopamine content in the lesioned striatum.
PBCA	Polysorbate 80	NGF	250 ± 30	-	MPTP injected mice	Reduced basic symptoms of Parkinsonism: oligokinesia, rigidity and tremor.

hGDNF, Human glial cell line-derived neurotrophic factor; MPTP, 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine; NGF, Nerve growth factor; PAMAM, Poly(amidoamine); PBCA, Poly(n-butyl cyanoacrylate); PEG, Poly(ethylene glycol); PLGA- poly(lactic-co-glycolic acid).

Figure 4: Pathological features of Parkinson's disease and nanoparticle-based interventions in preclinical models. **(A)** Parkinson's disease is defined by the progressive and selective degeneration of dopaminergic neurons within the substantia nigra, leading to a marked depletion of dopamine in the striatum. This neurodegenerative process disrupts the integrity of the nigrostriatal pathway, which is central to motor control. **(B)** Preclinical studies employing systemically administered nanoparticle-based delivery systems have investigated a range of therapeutic strategies aimed at neuroprotection, dopamine restoration, and modulation of neuroinflammation. These approaches have shown promise in enhancing drug delivery across the BBB, improving motor function, and mitigating neurodegenerative progression in animal models of Parkinson's disease [89].

accumulation and regulate cellular processes [97, 98]. Liposomes, nanoscale vesicles, are being explored for delivering drugs like Levodopa directly to the substantia nigra region in Parkinson's disease, minimizing side effects and improving drug efficacy [99].

Nanoparticles are used to support neuroprotection and neuroregeneration by delivering neuroprotective agents and facilitating neuronal repair. This includes the use of biosynthesized nanoparticles with antioxidant properties and enzyme-like activities [98, 99]. Gelatin-based hydrogels, modified with chemical moieties, have shown potential in enhancing neural process outgrowth and neuron viability, contributing to neuroregenerative strategies [99]. Nanoparticles, such as quantum dots and metallic nanoparticles, are utilized for imaging studies due to their sensitivity and selectivity, aiding in the diagnosis and monitoring of neurological diseases [94]. Carbon nanotubes are explored for their potential in neuroprosthetic devices and as regenerative matrices for neuronal tissue, offering new avenues for interfacing with the CNS [100].

Despite the promising applications, challenges such as safety concerns, targeting specificity, and production scalability remain. Ongoing research focuses on addressing these issues to enhance the clinical translation of nanomedicine [94, 97]. The integration of diagnostics with therapeutics through nanobiotechnology is expected to facilitate the development of personalized medicine, tailoring treatments to individual patient needs [101]. While nanomedicine offers significant potential in neurological applications, it is essential to consider the broader implications and challenges associated with its use. Safety concerns, particularly regarding the long-term effects of nanoparticles in the human body, remain a critical area of research. Additionally, the regulatory landscape governing the clinical implementation of nanomedicine is still evolving, necessitating comprehensive studies to ensure the safe and effective use of these technologies in medical practice [102, 103]. As research progresses, the integration of nanotechnology into neurology holds the promise of revolutionizing the treatment and management of neurological disorders.

In summary, nanomedicine offers numerous advantages in clinical anatomy (Table 1), it also presents challenges that need to be addressed. The translation of nanomedicine from research to clinical practice is hindered by issues such as nanotoxicology, regulatory hurdles, and the need for multidisciplinary collaboration [104, 105]. Additionally, the long-term effects of nanomaterials in the human body are not yet fully understood, necessitating further research to ensure their safety and efficacy [46]. Despite these challenges, the potential of nanomedicine to transform clinical anatomy and improve healthcare outcomes remains significant.

Table 1: Nanomedicine applications in clinical anatomy.

Anatomical focus	Nanotech platform	Mechanism of action	Clinical benefit	Key example
Cardiovascular anatomy	SPIONs, gold nanoparticles	Enhanced imaging (MRI/CT), plaque detection	Early diagnosis of atherosclerosis	SPION-based MRI for coronary artery visualization
Neuroanatomy (CNS)	BBB-penetrating liposomes, lipid nanoparticles	Trans-BBB drug delivery	Treats Alzheimer's, glioblastoma	Levodopa-loaded liposomes for Parkinson's
Musculoskeletal anatomy	Nanofibers, collagen nanoparticles	Extra cellular matrix mimicry for regeneration	Orthopedic and maxillofacial reconstruction	Graphene oxide–collagen scaffolds
Oncologic anatomy	Tumor-penetrating nanocarriers	EPR effect, active targeting	Selective tumor drug delivery	MM-398 liposomal irinotecan in pancreatic cancer
Renal anatomy	Theranostic nanoparticles	Imaging + therapy, renal clearance design	Improved renal diagnostics and nephrotoxicity monitoring	Kidney-targeted gold nanoparticles

Nanomedicine in Pathology

Nanomedicine is redefining the scope and precision of clinical pathology by enabling diagnosis and monitoring at the molecular and cellular levels [106, 107]. Traditionally, pathology has relied on morphological assessment of tissues and cells. However, the integration of nanoscale technologies introduces tools that can detect disease markers far earlier and with greater specificity [108, 109]. This innovation not only enhances diagnostic accuracy but also enables real-time monitoring and personalized therapeutic strategies grounded in molecular pathology (Table 2). The integration of nanomedicine into pathology is particularly transformative. Traditional histopathological methods rely heavily on stained tissue specimens, which can be time-consuming and subjective [110-112]. However, emerging technologies such as virtual staining and machine learning are beginning to disrupt this workflow. For example, virtual staining technologies can provide high-throughput analysis of digital pathology images, allowing for more efficient and accurate diagnoses [113].

Table 2: Nanomedicine tools in clinical pathology.

Tool type	Nanomaterial	Diagnostic target	Mode of detection	Application area	Sensitivity/Specificity
Nanosensor (Wearable)	Graphene, Carbon nanotube-based patches	Inflammatory markers (e.g., CRP)	Sweat analysis (real-time)	Cardiovascular, infection	~92% correlation with blood tests
Optical biosensor	Quantum dots	Viral RNA (e.g., SARS-CoV-2)	FRET fluorescence	Infectious disease	99% detection in 15 min
NanoPCR	Gold nanoparticles-assisted PCR	Oncogenes, miRNA (e.g., BRCA1, miR-21)	Amplification + fluorescence	Oncology, genetic screening	Up to 100x sensitivity vs RT-PCR
Liquid biopsy platforms	Magnetic nanoparticles	CTCs, ctDNA	Magnetic capture + qPCR	Solid tumors	95% specificity in early stages
Histopathology enhancer	Iron oxide/quantum dot conjugates	Protein biomarkers (e.g., HER2)	IHC/Multiplexed imaging	Breast, colon, prostate CA	Single-cell resolution

Nanosensors and early disease detection

One of the pivotal contributions of nanomedicine to pathology is the development of nanosensors capable of detecting trace biomarker-proteins, nucleic acids, or metabolites-indicative of early-stage disease [114-116]. These sensors, often functionalized with antibodies or aptamers,

allow ultra-sensitive detection of cancer markers, infectious agents, or metabolic imbalances in blood, urine, or tissue samples [117, 118]. The implication is a shift from symptomatic diagnosis to proactive, preclinical screening, fundamentally altering the pathological workflow. Nanosensors are revolutionizing pathology by enabling early detection of diseases through high-sensitivity biomarker identification. In cancer diagnostics, gold nanoparticle-based sensors detect prostate-specific antigen at concentrations as low as 0.1 ng/ml, facilitating early-stage prostate cancer diagnosis [119]. Carbon nanotube sensors achieve similar precision for breast cancer by identifying RNA biomarkers like BRCA1 with 95% specificity [119]. For cardiovascular diseases, graphene-based nanosensors detect troponin and B-type natriuretic peptide at picomolar levels, providing critical alerts for myocardial infarction risks [119].

In infectious disease management, quantum dot nanosensors demonstrate rapid detection of viral RNA, including SARS-CoV-2 and influenza strains, within 15 min through fluorescence resonance energy transfer mechanisms. This approach achieves 99% accuracy in distinguishing viral subtypes, as validated in clinical trials. Magnetic relaxation nanosensors further enhance bacterial detection sensitivity, identifying *Escherichia coli* at 10 CFU/ml through targeted nanoparticle clustering [120]. Point-of-care nanosensor platforms now integrate multiplexed detection capabilities, simultaneously analyzing up to 12 biomarkers in blood samples using microfluidic cartridges. Portable devices leveraging surface-enhanced Raman spectroscopy provide laboratory-grade accuracy in field settings, validated through World Health Organization endorsed trials for tuberculosis detection. Current developments in wearable nanosensors enable continuous monitoring of inflammatory markers like C-reactive protein through sweat analysis, with clinical studies demonstrating 92% correlation to serum tests [121].

Nanotechnology in histopathology

In histopathological analysis, nanoparticles have been used to enhance staining and labeling, improving the contrast and resolution of microscopic examination [122]. Gold nanoparticles, quantum dots, and iron oxide particles can be conjugated to antibodies or other ligands for multiplexed detection of disease markers in tissue sections [123]. These innovations enable pathologists to identify multiple targets simultaneously, reducing diagnostic ambiguity and facilitating precise disease classification, especially in heterogeneous tumors. Nanotechnology is transforming histopathology through advanced imaging, targeted drug delivery, and biomarker discovery. Nanoparticles like gold and liposomal doxorubicin enhance diagnostic precision by leveraging the enhanced permeability and retention effect for tumor accumulation, while active targeting strategies improve specificity through surface ligand modifications [124, 125]. Quantum dots enable high-resolution imaging of cellular structures, outperforming traditional immunohistochemistry by detecting low-abundance biomarkers with 95% specificity [125]. These innovations address limitations in conventional histopathology, such as delayed detection and insufficient differentiation between benign and malignant tissues.

Nanocantilevers and nanoshells provide real-time biomarker detection at molecular levels. Antibody-coated nanocantilevers deflect upon binding to cancer-specific proteins, enabling rapid identification of tumor-derived biomarkers like prostate-specific antigen and BRCA1. Near-infrared-absorbing nanoshells conjugated with tumor-targeting peptides (e.g., guanylyl cyclase C ligands) allow simultaneous MRI contrast enhancement and thermal ablation of colorectal cancer cells, achieving 85% tumor regression in preclinical models. These systems integrate with portable devices for point-of-care diagnostics, reducing reliance on centralized laboratory infrastructure [126]. Machine learning-driven histopathological biomarkers predict nanomedicine efficacy by analyzing tumor microenvironment features. A biomarker score combining blood vessel density and tumor-associated macrophage distribution correlates strongly ($R^2 = 0.86$) with liposomal doxorubicin accumulation in tumors, validated across 10 patient-derived xenograft models. This approach identifies patients likely to benefit from nanotherapies, with an area under curve of 0.91 for stratifying high- versus low-accumulation subgroups. Such biomarkers enable personalized treatment plans while utilizing existing biopsy protocols, avoiding additional invasive procedures [127].

Advanced imaging modalities like enhanced dark-field microscopy and pH-sensitive nanoprobes resolve subcellular nanoparticle distributions. Dark-field techniques detect crystalline nanoparticles at 100 nm resolution within H&E-stained sections, while pH-activatable nanoparticles fluoresce selectively in acidic tumor microenvironments, improving detection sensitivity by 15-fold compared to conventional dyes [65, 128]. Quantum dot-based immunohistochemistry maps low-abundance receptors (e.g., HER2) with single-cell resolution, guiding therapeutic decisions in breast cancer cases where standard methods yield equivocal results [124, 128].

Toxicologic evaluations ensure nanomedicine safety through multimodal microscopy. Immunofluorescence and confocal imaging track nanoparticle interactions with lymphatic endothelium and subcellular structures, revealing organ-specific accumulation patterns [128]. Studies comparing polymeric nanoparticles and carbon nanotubes show differential toxicity profiles: polyethylene glycol-coated nanoparticles exhibit 90% reduced hepatic clearance compared to unmodified variants, while functionalized nanotubes demonstrate minimized pulmonary inflammation [128, 129]. These findings inform regulatory guidelines for nanomaterial use in clinical histopathology.

Molecular pathology and nano-PCR

Nanomedicine also extends into molecular pathology, particularly through enhancements in PCR based technologies [130]. Nanoparticles can improve thermal conductivity in PCR reactions or serve as carriers for primers and probes, increasing amplification efficiency and specificity [131]. This nanoparticle-assisted PCR allows faster and more accurate detection of mutations, translocations, and epigenetic changes-critical in fields like oncology, infectious disease, and genetic diagnostics [132-134].

Nanomedicine is advancing molecular pathology through innovations in nano-PCR, enabling rapid and precise nucleic acid detection. Plasmonic heating via magneto-plasmonic nanoparticles (Au-Fe_3O_4 core-shell structures) reduces SARS-CoV-2 RNA detection time to 17 min with 100% clinical accuracy in nasopharyngeal and sputum samples. This platform integrates reverse transcription, thermocycling, and fluorescence detection, achieving a limit of detection of 3.2 copies/μl and strong correlation (Pearson r = 0.87) with conventional RT-qPCR. The method's specificity avoids cross-reactivity with SARS-CoV and MERS-CoV, validated across 150 clinical samples [135]. Multiplexed pathogen detection leverages quantum dot-labeled primers for simultaneous identification of 12 viral strains in a single reaction. Cadmium selenide quantum dots

tuned to distinct emission wavelengths enable spectral separation, achieving 99.8% concordance with sequencing results in respiratory virus panels [65]. Gold nanoparticle probes functionalized with thiolated oligonucleotides enhance hybridization efficiency by 40% compared to conventional TaqMan probes, reducing false negatives in low-abundance targets. These systems are being adapted for portable devices using microfluidic chips and smartphone-based fluorescence readers [65].

Targeted nano-PCR systems utilize pH-responsive polymeric nanoparticles for in situ tumor RNA quantification. Poly(lactic-co-glycolic acid) nanoparticles loaded with PCR components release primers and enzymes selectively in acidic tumor microenvironments (pH 6.5 - 6.8), enabling intraoperative detection of breast cancer metastasis with 95% sensitivity. Similarly, lipid nanoparticles conjugated with EGFR-targeting antibodies deliver CRISPR-Cas12a components to circulating tumor DNA, achieving single-molecule detection through collateral cleavage of fluorescent reporters-a method validated in pancreatic cancer liquid biopsies [65]. MicroRNA profiling benefits from dendrimer-entrapped gold nanoparticles, which enhance miR-21 and miR-155 detection sensitivity by 100-fold in formalin-fixed tissues. These nanoparticles prevent PCR inhibition from fixatives while enabling multiplexed analysis of 8 miRNAs per reaction, critical for stratifying lymphoma subtypes [136]. Hybrid graphene oxide–silver nanoparticles further improve specificity by quenching background fluorescence, achieving a dynamic range of 10^{-18} to 10^{-6} M for Alzheimer's-related tau mRNA in cerebrospinal fluid [137].

Challenges remain in standardizing nano-PCR protocols and minimizing nanoparticle batch variability. Recent studies address these issues through machine learning-optimized nanoparticle synthesis ($R^2 = 0.94$ for size uniformity prediction) and lyophilized reagent formulations stable at 25°C for 6 months. Upcoming clinical trials focus on Food and Drug Administration (FDA)-approved IONs (Ferumoxytol) repurposed for tuberculosis RNA detection, showing preliminary 92% sensitivity in sputum samples [135]. These advances position nano-PCR as a transformative tool for precision molecular diagnostics (Table 3).

Cancer pathology and nanodiagnostics

In oncology, nanodiagnostics are making strides in both tissue and liquid biopsy applications. Circulating tumor cells and extracellular vesicles can be isolated using magnetic or surface-modified nanoparticles, offering a non-invasive snapshot of tumor pathology [138, 139]. Additionally, nanoprobes are being developed to identify cancer-specific enzymes or pH changes within tissues, enabling functional diagnostics beyond what conventional histology or cytology can offer [140]. Nanomedicine has revolutionized cancer treatment through enhanced drug delivery systems that address low solubility, poor stability, and short half-lives of traditional agents [141, 142]. Nanoparticles such as mesoporous silica and magnetic carriers enable precise targeting of immune cells and tumor microenvironments, improving the efficacy of immunotherapies. For example, Liu et al. developed magnetic nanoparticles that destroy 98% of lung cancer stem cells under alternating magnetic fields, while Chen et al. [143] engineered silica nanoparticles to deliver antigens to immune organs for activation. These advancements mitigate systemic toxicity and enhance therapeutic precision [143].

Nanotechnology enables early detection through advanced imaging techniques. SPIONs and near-infrared quantum dots improve MRI and optical imaging sensitivity, particularly for lung and colorectal cancers. SPIONs functionalized with EGFR-targeting agents allow noninvasive detection of non-small cell lung cancer metastases, while NIR-II quantum dots (900 - 1700 nm) provide deeper tissue penetration for high-resolution imaging of liver and pancreatic tumors [144, 145]. These tools facilitate earlier diagnosis and real-time monitoring of tumor progression.

Nanocarriers such as liposomes and polymeric micelles address drug resistance in cancer stem cells. For instance, Yin et al. [145] designed nanoparticles co-delivering doxorubicin and enzymes to target breast cancer stem cells, reducing relapse risks. Similarly, albumin-bound paclitaxel (e.g., Abraxane) and PEGylated formulations improve drug bioavailability and tumor accumulation, overcoming limitations of conventional chemotherapy [143, 146]. These innovations enhance therapeutic outcomes by selectively eliminating resistant cell populations. Recent advancements focus on multi-stage targeting, integrating tissue-, cell-, and organelle-specific delivery. Surface modifications with tumor-penetrating peptides like iRGD enhance nanoparticle accumulation and penetration in metastatic breast cancer models. Wang et al. demonstrated iRGD-functionalized nanoparticles for co-delivering photosensitizers and hypoxia-activated prodrugs, achieving synergistic therapy with minimal off-target effects. Such strategies dynamically adapt to tumor biology, improving therapeutic indices [147].

Nanomedicine has transitioned to clinical use, with FDA-approved formulations like Doxil (liposomal doxorubicin) for Kaposi's sarcoma and ovarian cancer. Emerging theranostic platforms combine imaging and therapy, such as dendritic nanoparticles for PET imaging and drug delivery

Table 3: Approved and pipeline nanomedicines.

Product name	Carrier type	Drug cargo	Target disease	Regulatory status	Mechanism of delivery
Doxil	PEGylated liposome	Doxorubicin	Kaposi's, ovarian cancer	FDA-approved	Passive targeting via EPR
Abraxane	Albumin-bound nanoparticles	Paclitaxel	Breast, lung, pancreatic CA	FDA-approved	Solvent-free delivery, increased tumor uptake
Onivyde (MM-398)	Liposomal carrier	Irinotecan	Metastatic pancreatic CA	FDA-approved	Liposomal encapsulation, reduced toxicity
Ferumoxytol	IONs	MRI contrast	Iron deficiency + off-label MRI	Approved	T2 MRI enhancement
BNT162b2	Lipid nanoparticles	mRNA (spike protein)	COVID-19	FDA-approved	Endosomal escape and translation
NBTXR3	Hafnium oxide nanoparticles	Radiation enhancer	Soft tissue sarcoma	Phase III	Physical radiosensitizer
CRLX101	Cyclodextrin-polymer nanoparticles	Camptothecin	Solid tumors	Phase II	Controlled drug release, tumor accumulation

[145, 148]. These systems enable personalized medicine by tailoring treatments based on real-time diagnostic data, significantly improving patient outcomes.

Infectious disease and pathogen detection

Nanomedicine is particularly impactful in the rapid detection of pathogens. Pathology labs can now use nanoparticle-based lateral flow assays, biosensors, or nanoplasmonic devices to identify bacterial, viral, or fungal infections within minutes (Figure 5) [4]. During recent pandemics, such tools have enabled rapid point-of-care diagnostics with laboratory-level sensitivity, reinforcing the central role of pathology in epidemic surveillance and response. Nanocarriers such as lipid-based nanoparticles and polymeric micelles enhance antibiotic efficacy against intracellular pathogens like *Mycobacterium tuberculosis* by improving drug solubility and macrophage-specific delivery [149]. Ligand-anchored chitosan nanoparticles demonstrate sustained drug release, increasing local drug concentrations and reducing systemic toxicity in tuberculosis treatment [149]. Additionally, antibody-functionalized magnetic nanoparticles target *Staphylococcus aureus* biofilms, achieving a 2.5-fold binding improvement and doubling therapeutic efficacy in murine models [150]. These strategies address low bioavailability and drug resistance in infections like HIV and malaria [150].

Virus-inspired nanoparticles and bacterial outer membrane vesicles enable targeted delivery and intrinsic antimicrobial activity. For example, gold nanoparticles coated with *E. coli* outer membrane vesicles activate dendritic cells and induce robust Th1/Th17 immune responses, enhancing vaccine efficacy. Erythrocyte membrane-coated nanoparticles ("nanotoxoids") trap bacterial toxins like staphylococcal α-hemolysin, providing protection against methicillin-resistant *S. aureus* (MRSA) infections. These bio-inspired systems improve biocompatibility and reduce off-target effects [151]. These bio-inspired systems improve biocompatibility and reduce off-target effects.

Nanotechnology enables ultrasensitive biosensors for early pathogen identification. Functionalized nanoparticles, such as antibody-labeled quantum dots, detect *S. aureus* in infected tissues via fluorescence imaging. Magnetic nanoparticles coupled with anti-protein A antibodies allow precise localization of bacterial infections in cutaneous models, improving diagnostic accuracy. Similarly, cyclic peptide-conjugated nanoparticles enhance bacterial targeting in lungs, enabling real-time monitoring of infection progression [150]. Nanocarriers optimize antigen delivery and immune activation. Lipid nanoparticles encapsulate mRNA vaccines, as seen in COVID-19 applications, while outer membrane vesicles-based platforms promote cross-protection against diverse bacterial strains [151]. For tuberculosis, chitosan nanovaccines enhance macrophage uptake and antigen presentation, eliciting durable immune memory [149]. These platforms address challenges like poor immunogenicity in subunit vaccines.

Nanoparticles co-deliver antibiotics with resistance-modulating agents. For instance, vancomycin-loaded nanoparticles functionalized with *S. aureus*-targeting peptides reduce required doses by tenfold while maintaining efficacy [150]. Enzyme-loaded nanoparticles degrade bacterial biofilms, restoring antibiotic susceptibility in chronic infections [151]. Such approaches mitigate resistance in pathogens like *Pseudomonas aeruginosa* and *M. tuberculosis* [150]. Preclinical advances include outer membrane vesicle-based nanotoxoids for MRSA and malaria-targeted nanocarriers that accumulate in parasite-infected erythrocytes [150, 151]. Challenges remain in scalability and long-term safety, but innovations in biomimetic design and multifunctional systems show promise for global infectious disease management [4].

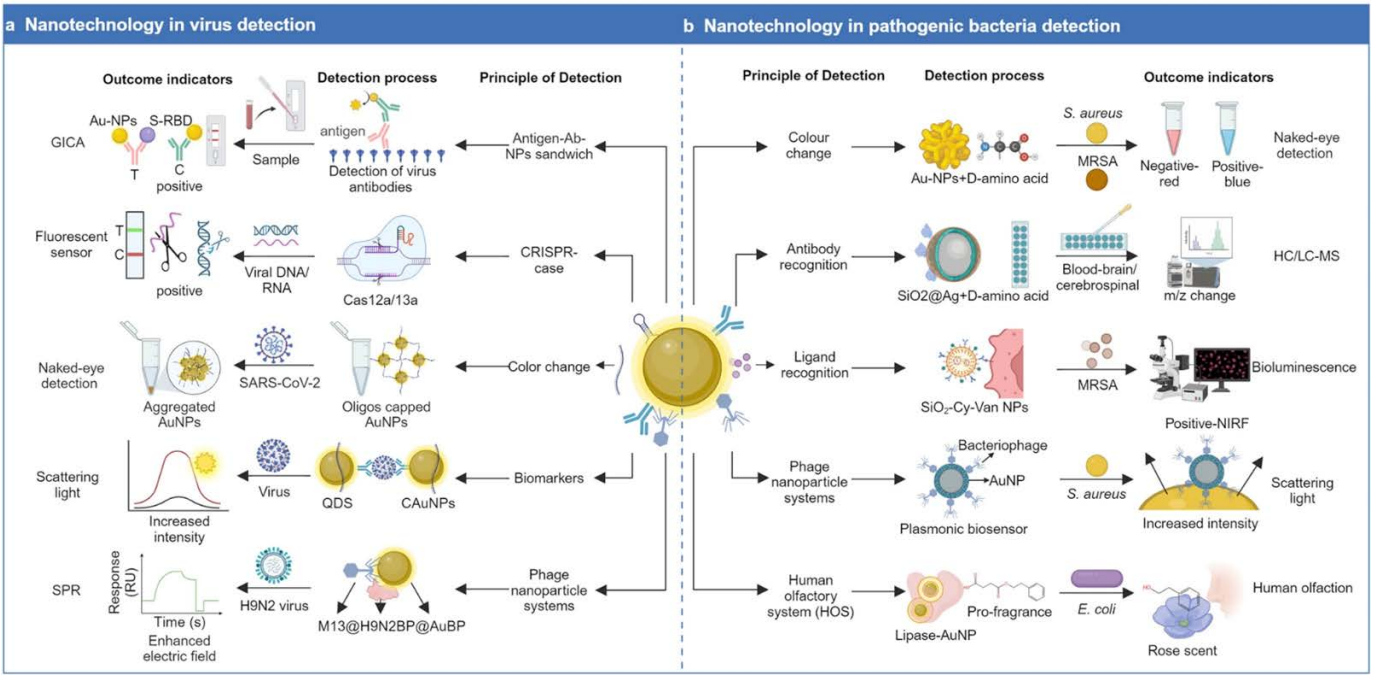


Figure 5: Nanomedicine in virus and pathogenic bacteria detection. Schematic representation of detection principle, process and outcome indicators [4].

Integration with Digital and AI

AI-driven image analysis enhances nanomedicine applications by improving resolution and sensitivity in detecting nanoscale pathological changes (Table 4). For instance, AI algorithms process whole slide images to identify subtle tumor characteristics, while nanoparticles like quantum dots provide high-contrast imaging for early cancer detection [152]. Generative AI models, such as PathChat, integrate vision-language capabilities to generate diagnostic reports from histology images, streamlining workflows in anatomic pathology [152, 153]. This synergy between AI and nanoscale imaging agents enables precise identification of biomarkers in complex tissues, such as liver or pancreatic tumors [154].

Machine learning optimizes nanoparticle formulations for targeted drug delivery by predicting biodistribution and efficacy. For example, AI models analyze patient-specific data to design nanocarriers that selectively accumulate in tumor microenvironments, reducing off-target effects [155, 156]. Integrated systems combine real-time imaging with AI-guided nanorobots to adjust drug release dynamically, as seen in preclinical models of colorectal cancer [155]. These approaches improve therapeutic precision while minimizing systemic toxicity, particularly in drug-resistant cancers. Generative AI creates virtual H&E stains from label-free tissue samples, reducing reliance on physical staining protocols. This technique, validated in renal and digestive tract pathology, preserves tissue integrity and accelerates diagnostic workflows [153, 157]. Synthetic histology images generated by AI also address data scarcity for training algorithms, enhancing model robustness in detecting rare pathologies like early-stage gliomas [152, 153].

AI automates slide quality assessment, flagging artifacts such as staining errors or tissue floaters in whole slide images. This integration reduces manual review time and ensures consistency in high-volume labs, particularly for metastatic cancer screening [152, 157]. AI tools like Path-BigBird extract tumor characteristics from pathology reports in real time, enabling rapid triage of urgent cases [153]. AI combines genomic, proteomic, and nanomaterial data to tailor therapies. For example, AI models predict nanoparticle-drug interactions based on patient-specific biomarkers, optimizing regimens for pancreatic cancer [156]. Federated learning frameworks enable collaborative model training across institutions while preserving data privacy, critical for rare disease research [152, 153]. Generative AI produces synthetic histology datasets for pathology training, simulating rare conditions like amyloidosis or granulomatous inflammation [153, 157]. Virtual microscopy platforms integrated with AI feedback mechanisms enhance trainee diagnostic accuracy, particularly in subspecialties like hematopathology [152, 153].

Furthermore, the development of semi-supervised learning models, such as the Anatomy-Pathology Disentanglement Network, demonstrates the potential of AI in pathology. This model can perform pathology segmentation with limited annotations, significantly improving diagnostic accuracy and efficiency [158]. The combination of AI and nanomedicine is paving the way for more precise and personalized diagnostic approaches. FDA-cleared AI tools, such as those for prostate cancer grading, now integrate with digital pathology platforms, while nanotheranostics like gold nanoparticle-based sensors undergo trials for real-time monitoring [156]. Ethical challenges include mitigating algorithmic bias in underrepresented populations and ensuring transparency in AI-generated diagnoses [152, 153].

Challenges and Future Directions

Despite the promising advancements, several challenges remain in the clinical translation of nanomedicine (Table 5). Issues such as regulatory hurdles, standardization, and the need for increased investment in research and development are critical for the successful integration of nanomedicine into clinical practice [159]. The European Technology Platform on Nanomedicine emphasizes the importance of creating a unified knowledge hub that links academia, industry, and healthcare providers to address these challenges [159]. The development of frameworks such as DELIVER aims to streamline the clinical translation of nanomedicines by addressing design, manufacturing, and regulatory considerations [160]. By fostering collaboration between disciplines such as chemistry, biology, and engineering, researchers can create more effective and safer nanomedicines.

Moreover, the potential of nanomedicine in addressing complex diseases, such as triple-negative breast cancer, is significant. Recent studies highlight the importance of molecular profiling in triple-negative breast cancer, which can be enhanced through nanomedicine approaches that target specific genetic expressions [161]. The future of nanomedicine in pathology and clinical anatomy lies in its ability to provide tailored solutions that improve patient outcomes.

Table 4: AI and digital integration with nanomedicine.

Tech platform	Nanomedicine role	AI function	Clinical benefit
PathChat + quantum dots	Image-guided diagnostics	Vision-language report generation	Faster histological interpretation
Virtual H&E with nanocontrast	Label-free nano-enhanced tissue imaging	Synthetic staining via GANs	Preserves tissue, faster processing
AI-formulated nanodrugs	Predictive nanoparticle design	Predicts formulation for patient-specific needs	Tailored nanotherapies
AI–nano PCR combo	Diagnostic aid in infection and oncology	Detects signal threshold, adjusts cycles	Improved LOD, avoids false negatives
Federated AI for histopathology	Shared model training on pathology + nano data	Preserves patient privacy across institutions	Better rare disease modeling

Table 5: Translational barriers in nanomedicine.

Barrier category	Specific challenge	Impact	Proposed solutions
Biological interaction	Protein corona masking targeting ligands	Alters biodistribution, reduces efficacy	Pre-coating strategies, corona-resistant design
Toxicity and clearance	Reticuloendothelial system uptake	Liver/spleen accumulation, potential damage	PEGylation, size optimization
Manufacturing scalability	Batch-to-batch nanoparticle inconsistency	Poor reproducibility	AI-driven nanoparticle synthesis
Regulatory framework	Lack of nano-specific clinical endpoints	Trial approval delays	Unified EU/US regulatory pathways
Patient heterogeneity	Variable immune/nanoparticle interactions	Poor clinical translatability	Genomic + proteomic patient stratification

As nanomedicine penetrates deeper into clinical anatomy, it raises ethical and pedagogical challenges. The complexity of nanoscale anatomy requires updated curricula for medical education, incorporating nanotechnology principles alongside classical anatomical knowledge. Additionally, ethical issues around nanomaterial toxicity, patient consent, and long-term biocompatibility must be rigorously addressed before full clinical integration.

Conclusion

Nanomedicine represents a new frontier in clinical anatomy and pathology, offering innovative diagnostic and therapeutic solutions that can significantly enhance patient care. As research continues to evolve, the integration of nanotechnology into clinical practice will likely lead to more accurate diagnoses, improved treatment strategies, and ultimately, better patient outcomes. The ongoing collaboration between researchers, clinicians, and industry stakeholders will be essential in overcoming existing challenges and realizing the full potential of nanomedicine in healthcare.

The integration of nanomedicine into clinical anatomy represents a fundamental shift from passive observation to active, nano-enabled manipulation of human structures. Future directions include smart nanodevices capable of real-time anatomical feedback, nanosurgical tools for microinvasive procedures, and personalized anatomical mapping for precision medicine. As anatomical science continues to evolve, nanomedicine will be central not only to understanding structure and function but to actively shaping clinical outcomes at the most fundamental level.

Acknowledgements

None.

Conflict of Interest

None.

References

1. Haleem A, Javaid M, Singh RP, Rab S, Suman R (2023) Applications of nanotechnology in medical field: a brief review. Glob Health J 7: 70–77. https://doi.org/10.1016/j.glohj.2023.02.008
2. Rommasi F, Esfandiari N (2021) Liposomal nanomedicine: applications for drug delivery in cancer therapy. Nanoscale Res Lett 16: 1-20. https://doi.org/10.1186/s11671-021-03553-8
3. Malik S, Muhammad K, Waheed Y (2023) Emerging applications of nanotechnology in healthcare and medicine. Molecules 28: 6624. https://doi.org/10.3390/molecules28186624
4. Huang Y, Guo X, Wu Y, Chen X, Feng L, et al. (2024) Nanotechnology's frontier in combatting infectious and inflammatory diseases: prevention and treatment. Signal Transduct Target Ther 9: 34. https://doi.org/10.1038/s41392-024-01745-z
5. Germain M, Caputo F, Metcalfe S, Tosi G, Spring K, et al. (2020) Delivering the power of nanomedicine to patients today. J Control Release 326: 164–171. https://doi.org/10.1016/j.jconrel.2020.07.007
6. Dessale M, Mengistu G, Mengist HM (2022) Nanotechnology: a promising approach for cancer diagnosis, therapeutics and theragnosis. Int J Nanomedicine 17: 3735- 3749. https://doi.org/10.2147/ijn.s378074
7. Woźniak M, Płoska A, Siekierzycka A, Dobrucki LW, Kalinowski L, et al. (2022) Molecular imaging and nanotechnology—emerging tools in diagnostics and therapy. Int J Mol Sci 23: 2658. https://doi.org/10.3390/ijms23052658
8. He Y, Wang Y, Wang L, Jiang W, Wilhelm S (2024) Understanding nanoparticle-liver interactions in nanomedicine. Expert Opin Drug Deliv 21: 829–843. https://doi.org/10.1080/17425247.2024.2375400
9. Wu X, Xin Y, Zhang H, Quan L, Ao Q (2024) Biopolymer-based nanomedicine for cancer therapy: opportunities and challenges. Int J Nanomedicine 2024: 7415–7471. https://doi.org/10.2147/ijn.s460047
10. Giménez S, Millan A, Mora-Morell A, Ayuso N, Gastaldo-Jordán I, et al. (2024) Advances in brain stimulation, nanomedicine and the use of magnetoelectric nanoparticles: dopaminergic alterations and their role in neurodegeneration and drug addiction. Molecules 29: 3580. https://doi.org/10.3390/molecules29153580
11. Meng X, Yao J, Gu J (2025) Advanced bioanalytical techniques for pharmacokinetic studies of nanocarrier drug delivery systems. J Pharm Anal 15: 101070. https://doi.org/10.1016/j.jpha.2024.101070
12. Lambuk F, Nordin NA, Mussa A, Lambuk L, Ahmad S, et al. (2024) Towards understanding the role of nanomedicine in targeting TNFR2 in rheumatoid arthritis. Immunology 173: 622–633. https://doi.org/10.1111/imm.13855
13. Mohapatra A, Mohanty A, Park IK (2024) Inorganic nanomedicine—mediated ferroptosis: a synergistic approach to combined cancer therapies and immunotherapy. Cancers 16: 3210. https://doi.org/10.3390/cancers16183210
14. Su Y, Fu X, Wei L, Zhang Z, Zou Q, et al. (2025) PROTCROWN: a manually curated resource of protein corona data for unlocking the potential of protein–nanoparticle interactions. Nano Lett 25: 1739–1744. https://doi.org/10.1021/acs.nanolett.4c05955
15. Xie A, Hanif S, Ouyang J, Tang Z, Kong N, et al. (2020) Stimuli-responsive prodrug-based cancer nanomedicine. EBioMedicine 56: 1-12. https://doi.org/10.1016/j.ebiom.2020.102821
16. Fletcher NL, Kempe K, Thurecht KJ (2020) Next-generation polymeric nanomedicines for oncology: Perspectives and future directions. Macromol Rapid Commun 41: 2000319. https://doi.org/10.1002/marc.202000319
17. Jiang D, Rosenkrans ZT, Ni D, Lin J, Huang P, et al. (2020) Nanomedicines for renal management: from imaging to treatment. Acc Chem Res 53: 1869–1880. https://doi.org/10.1021/acs.accounts.0c00323
18. Zhang P, Xiao Y, Sun X, Lin X, Koo S, et al. (2023) Cancer nanomedicine toward clinical translation: obstacles, opportunities, and future prospects. Med 4: 147–167. https://doi.org/10.1016/j.medj.2022.12.001
19. Zheng C, Li M, Ding J (2021) Challenges and opportunities of nanomedicines in clinical translation. Bio Integr 2: 57-60. https://doi.org/10.15212/bioi-2021-0016

20. Agrahari V, Agrahari V (2018) Facilitating the translation of nanomedicines to a clinical product: Challenges and opportunities. Drug Discov Today 23: 974–991. https://doi.org/10.1016/j.drudis.2018.01.047

21. Aliyandi A, Zuhorn IS, Salvati A (2020) Disentangling biomolecular corona interactions with cell receptors and implications for targeting of nanomedicines. Front Bioeng Biotechnol 8: 1-14. https://doi.org/10.3389/fbioe.2020.599454

22. Chen Z, Chen X, Huang J, Wang J, Wang Z, et al. (2022) Harnessing protein corona for biomimetic nanomedicine design. Biomimetics 7: 126. https://doi.org/10.3390/biomimetics7030126

23. Shi J, Kantoff PW, Wooster R, Farokhzad OC. (2017) Cancer nanomedicine: progress, challenges and opportunities. Nat Rev Cancer 17: 20–37. https://doi.org/10.1038/nrc.2016.108

24. Hare JI, Lammers T, Ashford MB, Puri S, Storm G, et al. (2017) Challenges and strategies in anti-cancer nanomedicine development: an industry perspective. Adv Drug Deliv Rev 108: 25–38. https://doi.org/10.1016/j.addr.2016.04.025

25. Wu LP, Wang D, Li Z. (2020) Grand challenges in nanomedicine. Mater Sci Eng C 106: 110302. https://doi.org/10.1016/j.msec.2019.110302

26. Liu Y, Wang J, Xiong Q, Hornburg D, Tao W, et al. (2020) Nano–bio interactions in cancer: from therapeutics delivery to early detection. Acc Chem Res 54: 291–301. https://doi.org/10.1021/acs.accounts.0c00413

27. Meng X, Zhu G, Yang YG, Sun T (2024) Targeted delivery strategies: the interactions and applications of nanoparticles in liver diseases. Biomed Pharmacother 175: 116702. https://doi.org/10.1016/j.biopha.2024.116702

28. Wu G, Hui X, Hu L, Bai Y, Rahaman A, et al. (2022) Recent advancement of bioinspired nanomaterials and their applications: a review. Front Bioeng Biotechnol 10: 1-12. https://doi.org/10.3389/fbioe.2022.952523

29. Ibrahim HK (2024) From nanotech to AI: the cutting-edge technologies shaping the future of medicine. Afr J Adv Pure Appl Sci 3: 410–427.

30. Bodunde OP, Ikumapayi OM, Akinlabi ET, Oladapo BI, Adeoye AO, et al. (2021) A futuristic insight into a "nano-doctor": a clinical review on medical diagnosis and devices using nanotechnology. Mater Today Proc 44: 1144–1153. https://doi.org/10.1016/j.matpr.2020.11.232

31. Bhaskar P, Tripathi R, Singh S, Chattopadhaya A, Verma A, et al. (2024) Navigating the nanoscale frontier: an in-depth introduction to the world of nanomedicine. In Gautam V, Kumar R, Manandhar KD, Kamble SC (eds) Nanomedicine. Nanotechnology in the Life Sciences. Springer, Cham, pp 531–559.

32. Farajollahi A, Baharvand M (2024) Advancements in photoacoustic imaging for cancer diagnosis and treatment. Int J Pharm 665: 124736 https://doi.org/10.1016/j.ijpharm.2024.124736

33. Aktas D, Ortlek BE, Civas M, Baradari E, Kilic AB, et al. (2024) Odor-based molecular communications: State-of-the-art, vision, challenges, and frontier directions. IEEE Communications Surveys & Tutorials.

34. Malehmir S, Esmaili MA, Khaksary Mahabady M, Sobhani-Nasab A, Atapour A, et al. (2023) A review: hemocompatibility of magnetic nanoparticles and their regenerative medicine, cancer therapy, drug delivery, and bioimaging applications. Front Chem 11: 1-14. https://doi.org/10.3389/fchem.2023.1249134

35. El-Tanani M, Satyam SM, Rabbani SA, El-Tanani Y, Aljabali AA, et al. (2025) Revolutionizing drug delivery: the impact of advanced materials science and technology on precision medicine. Pharmaceutics 17: 375. https://doi.org/10.3390/pharmaceutics17030375

36. Akhtar ZB, Gupta AD (2024) Advancements within molecular engineering for regenerative medicine and biomedical applications: an investigation analysis towards a computing retrospective. J Electron Electromed Eng Med Inform 6: 54–72. https://doi.org/10.35882/jeeemi.v6i1.351

37. Wu P, Zhang B, Ocansey DKW, Xu W, Qian H (2021) Extracellular vesicles: a bright star of nanomedicine. Biomaterials 269: 120467. https://doi.org/10.1016/j.biomaterials.2020.120467

38. Karagodin I, Addetia K, Singh A, Dow A, Rivera L, et al. (2020) Improved delineation of cardiac pathology using a novel three-dimensional echocardiographic tissue transparency tool. J Am Soc Echocardiogr 33: 1316–1323. https://doi.org/10.1016/j.echo.2020.08.005

39. Sabir F, Qindeel M, Zeeshan M, Ul Ain Q, Rahdar A, et al. (2021) Onco-receptors targeting in lung cancer via application of surface-modified and hybrid nanoparticles: a cross-disciplinary review. Processes 9: 621. https://doi.org/10.3390/pr9040621

40. Mishra AK, Pandey M, Dewangan HK, Sl N, Sahoo PK (2022) A comprehensive review on liver targeting: emphasis on nanotechnology-based molecular targets and receptors mediated approaches. Curr Drug Targets 23: 1381–1405. https://doi.org/10.2174/1389450123666220906091432

41. Martins C, Sarmento B (2023) Multi-ligand functionalized blood-to-tumor sequential targeting strategies in the field of glioblastoma nanomedicine. Wiley Interdiscip Rev Nanomed Nanobiotechnol 15: e1893. https://doi.org/10.1002/wnan.1893

42. Manzari MT, Shamay Y, Kiguchi H, Rosen N, Scaltriti M, et al. (2021) Targeted drug delivery strategies for precision medicines. Nat Rev Mater 6: 351–370. https://doi.org/10.1038/s41578-020-00269-6

43. Mitchell MJ, Billingsley MM, Haley RM, Wechsler ME, Peppas NA, et al. (2021) Engineering precision nanoparticles for drug delivery. Nat Rev Drug Discov 20: 101–124. https://doi.org/10.1038/s41573-020-0090-8

44. Sanchez-Cano C, Alvarez-Puebla RA, Abendroth JM, Beck T, Blick R, et al. (2021) X-ray-based techniques to study the nano–bio interface. ACS Nano 15: 3754–3807. https://doi.org/10.1021/acsnano.0c09563

45. Abaszadeh F, Ashoub MH, Khajouie G, Amiri M (2023) Nanotechnology development in surgical applications: recent trends and developments. Eur J Med Res 28: 1-33. https://doi.org/10.1186/s40001-023-01429-4

46. Rehan F, Zhang M, Fang J, Greish K (2024) Therapeutic applications of nanomedicine: recent developments and future perspectives. Molecules 29: 2073. https://doi.org/10.3390/molecules29092073

47. Mali S (2013) Nanomedicine–next generation technology revolutionizing medical practice. J Maxillofac Oral Surg 12: 1-2. https://doi.org/10.1007/s12663-012-0400-8

48. Tran S, DeGiovanni PJ, Piel B, Rai P (2017) Cancer nanomedicine: a review of recent success in drug delivery. Clin Transl Med 6: 1-21. https://doi.org/10.1186/s40169-017-0175-0

49. Moreira R, Granja A, Pinheiro M, Reis S (2021) Nanomedicine interventions in clinical trials for the treatment of metastatic breast cancer. Appl Sci 11: 1624 https://doi.org/10.3390/app11041624

50. Kubinová Š, Syková E (2010) Nanotechnologies in regenerative medicine. Minim Invasive Ther Allied Technol 19: 144-156. https://doi.org/10.3109/13645706.2010.481398

51. Ahmadian E, Eftekhari A, Janas D, Vahedi P (2023) Nanofiber scaffolds based on extracellular matrix for articular cartilage engineering: a perspective. Nanotheranostics 7: 61-69. https://doi.org/10.7150/ntno.78611

52. Zhou J, Nie Y, Jin C, Zhang JX (2022) Engineering biomimetic extracellular matrix with silica nanofibers: from 1D material to 3D network. ACS Biomater Sci Eng 8: 2258–2280. https://doi.org/10.1021/acsbiomaterials.1c01525

53. Mijanović O, Pylaev T, Nikitkina A, Artyukhova M, Branković A, et al. (2021) Tissue engineering meets nanotechnology: molecular mechanism modulations in cornea regeneration. Micromachines 12: 1336. https://doi.org/10.3390/mi12111336

54. Moniri Javadhesari S, Koohi M, Jabraili M (2022) Nanomaterials: applications in regeneration of damaged tissues. Adv Ceram Prog 8: 1–14. https://doi.org/10.30501/acp.2022.356039.1100

55. Saha M (2009) Nanomedicine: promising tiny machine for the healthcare in future-a review. Oman Med J 24: 242-247. https://doi.org/10.5001/omj.2009.50

56. Aziz R (2021) Applications of nanomaterials in tissue engineering and regenerative medicine. In Pal K (ed) Bio-manufactured Nanomaterials. Springer, pp 187–202.

57. Alzate-Correa D, Lawrence WR, Salazar-Puerta A, Higuita-Castro N, Gallego-Perez D (2022) Nanotechnology-driven cell-based therapies in regenerative medicine. AAPS J 24: 43. https://doi.org/10.1208/s12248-022-00692-3

58. Park S, Park J, Jo I, Cho SP, Sung D, Ryu S, et al. (2015) *In situ* hybridization of carbon nanotubes with bacterial cellulose for three-dimensional hybrid bioscaffolds. Biomaterials 58: 93–102. https://doi.org/10.1016/j.biomaterials.2015.04.027

59. Mazaheri M, Eslahi N, Ordikhani F, Tamjid E, Simchi A (2015) Nanomedicine applications in orthopedic medicine: state of the art. Int J Nanomedicine 2015: 6039–6054. https://doi.org/10.2147/IJN.S73737

60. Minardi S (2022) Editorial: nano-biomaterials for the delivery of therapeutic and biological cues for regenerative medicine. Front Bioeng Biotechnol 9: 1-2. https://doi.org/10.3389/fbioe.2021.832487

61. Thirugnanasambandan T (2021) Nanoparticles for biomedical imaging advancements. In Nanoparticles in Analytical and Medical Devices. Elsevier, pp 127–154.

62. Bruno F, Granata V, Cobianchi Bellisari F, Sgalambro F, Tommasino E, Palumbo P, et al. (2022) Advanced magnetic resonance imaging (MRI) techniques: technical principles and applications in nanomedicine. Cancers 14: 1626. https://doi.org/10.3390/cancers14071626

63. Molkenova A, Atabaev TS, Hong SW, Mao C, Han DW, Kim KS (2022) Designing inorganic nanoparticles into computed tomography and magnetic resonance (CT/MR) imaging-guidable photomedicines. Mater Today Nano 18: 100187. https://doi.org/10.1016/j.mtnano.2022.100187

64. Alvarez MM, Aizenberg J, Analoui M, Andrews AM, Bisker G, Boyden ES, et al. (2017) Emerging trends in micro- and nanoscale technologies in medicine: From basic discoveries to translation. ACS Nano 11: 5195–5214. https://doi.org/10.1021/acsnano.7b01493

65. Pelaz B, Alexiou C, Alvarez-Puebla RA, Alves F, Andrews AM, et al. (2017) Diverse applications of nanomedicine. ACS Nano 11: 2313-2381. https://doi.org/10.1021/acsnano.6b06040

66. Mishra M, Kumar P, Rajawat JS, Malik R, Sharma G, et al. (2018) Nanotechnology: revolutionizing the science of drug delivery. Curr Pharm Des 24: 5086-5107. https://doi.org/10.2174/1381612825666190206222415

67. Bai S, Kang Y, Li S, Ma S, Sasayama T (2025) Editorial: research on nanomaterials in tumor diagnosis and therapy. Front Bioeng Biotechnol 12: 1-2. https://doi.org/10.3389/fbioe.2024.1545581

68. Patel DK, Kesharwani R, Kumar V (2021) Nanoparticles: an emerging platform for medical imaging. In Nanoparticles in Analytical and Medical Devices. Elsevier, pp 113-126.

69. Butt A, Bach H (2025) Nanomedicine and clinical diagnostics part I: applications in conventional imaging (MRI, X-ray/CT, and ultrasound). Nanomedicine 20: 167-182. https://doi.org/10.1080/17435889.2024.2439776

70. Han X, Xu K, Taratula O, Farsad K (2019) Applications of nanoparticles in biomedical imaging. Nanoscale 11: 799-819. https://doi.org/10.1039/c8nr07769j

71. Butt A, Bach H (2025) Advancements in nanotechnology for diagnostics: a literature review, part II: advanced techniques in nuclear and optical imaging. Nanomedicine 20: 183–206. https://doi.org/10.1080/17435889.2024.2439778

72. Li X, Zhang XN, Li XD, Chang J (2016) Multimodality imaging in nanomedicine and nanotheranostics. Cancer Biol Med 13: 339–348. https://doi.org/10.20892/j.issn.2095-3941.2016.0055

73. Liu CH, Grodzinski P (2021) Nanotechnology for cancer imaging: advances, challenges, and clinical opportunities. Radiol Imaging Cancer 3: 1-14. https://doi.org/10.1148/rycan.2021200052

74. Malatesta M (2022) Molecular imaging in nanomedical research 2.0. Int J Mol Sci 23: 13011. https://doi.org/10.3390/ijms232113011

75. Man F, Lammers T, de Rosales RTM (2018) Imaging nanomedicine-based drug delivery: a review of clinical studies. Mol Imaging Biol 20: 683–695. https://doi.org/10.1007/s11307-018-1255-2

76. Parveen S, Abira R, Paikray S, Sahoo L, Tripathy NS, et al. (2024) Recent advancement of nanotheranostics in cancer applications. Curr Drug Deliv 22: 1073-1091. https://doi.org/10.2174/0115672018307617240514092110

77. Tiwari R, Tiwari G, Parashar P (2023) Theranostics applications of functionalized magnetic nanoparticles. In Jain K, Jain NK (eds) Multifunctional and Targeted Theranostic Nanomedicines. Springer Nature, Singapore, pp 361–382.

78. Sharma I, Bhattacharjee S (2021) Nanotheranostics and biocompatibility. In Nanobiotechnology: Microbes and Plant Assisted Synthesis of Nanoparticles, Mechanisms and Applications. Elsevier, pp 51–60.

79. Sharma R, Mody N, Vyas SP (2017) Bioinspired nanotheranostics for cancer management. In Biopolymer-Based Composites. Woodhead Publishing, pp 269–288.

80. Shoaib A, Javed S, Tabish M, Khan ME, Zaki M, et al. (2024) Applications of nanomedicine-integrated phototherapeutic agents in cancer theranostics: a comprehensive review of the current state of research. Nanotechnol Rev 13: 20240023. https://doi.org/10.1515/ntrev-2024-0023

81. Ahmad MZ, Pathak K, Ahmad J, Aslam M, Bagre A, et al. (2023) Functionalized targeted theranostic nanomedicines. In Jain K, Jain NK (eds) Multifunctional and Targeted Theranostic Nanomedicines: Formulation, Design and Applications. Springer Nature, Singapore, 1–26.

82. Muthu MS, Leong DT, Mei L, Feng SS (2014) Nanotheranostics- application and further development of nanomedicine strategies for advanced theranostics. Theranostics 4: 660-677. https://doi.org/10.7150/thno.8698

83. Kasi PB, Mallela VR, Ambrozkiewicz F, Trailin A, Liska V, et al. (2023) Theranostics nanomedicine applications for colorectal cancer and metastasis: recent advances. Int J Mol Sci 24: 7922. https://doi.org/10.3390/ijms24097922

84. Tian M, Dong B, Li W, Wang L, Yu H (2024) Applications of novel microscale and nanoscale materials for theranostics: from design to clinical translation. Pharmaceutics 16: 1339. https://doi.org/10.3390/pharmaceutics16101339

85. Kim EM, Jeong HJ (2017) Current status and future direction of nanomedicine: focus on advanced biological and medical applications. Nucl Med Mol Imaging 51: 106–117. https://doi.org/10.1007/s13139-016-0435-8

86. Beygi M, Oroojalian F, Azizi-Arani S, Hosseini SS, Mokhtarzadeh A, et al. (2024) Multifunctional nanotheranostics for overcoming the blood–brain barrier. Adv Funct Mater 34: 2310881. https://doi.org/10.1002/adfm.202310881

87. Liu Q, Chen Z, Guiseppi-Elie A, Meng F, Luo L (2025) Recent progress on nanotechnologies for enhancing blood-brain barrier permeability. Smart Mol 3: e20240052. https://doi.org/10.1002/smo.20240052

88. Toader C, Dumitru AV, Eva L, Serban M, Covache-Busuioc RA, et al. (2024) Nanoparticle strategies for treating CNS disorders: a comprehensive review of drug delivery and theranostic applications. Int J Mol Sci 25: 13302. https://doi.org/10.3390/ijms252413302

89. Saraiva C, Praça C, Ferreira R, Santos T, Ferreira L, et al. (2016) Nanoparticle-mediated brain drug delivery: overcoming blood–brain barrier to treat neurodegenerative diseases. J Control Release 235: 34–47. https://doi.org/10.1016/j.jconrel.2016.05.044

90. Akhtar A, Andleeb A, Waris TS, Bazzar M, Moradi AR, et al. (2021) Neurodegenerative diseases and effective drug delivery: a review of challenges and novel therapeutics. J Control Release 330: 1152–1167. https://doi.org/10.1016/j.jconrel.2020.11.021

91. Neganova ME, Aleksandrova YR, Sukocheva OA, Klochkov SG (2022) Benefits and limitations of nanomedicine treatment of brain cancers and age-dependent neurodegenerative disorders. Semin Cancer Biol 86: 805–833. https://doi.org/10.1016/j.semcancer.2022.06.011

92. Wu D, Chen Q, Chen X, Han F, Chen Z, et al. (2023) The blood–brain barrier: structure, regulation and drug delivery. Signal Transduct Target Ther 8: 1-27. https://doi.org/10.1038/s41392-023-01481-w

93. Kecel-Gunduz S, Bicak B, Ozel AE (2020) Drug delivery nanosystems for neural regenerative medicine. In Neural Regenerative Nanomedicine. Academic Press, pp 89–122.

94. Rhaman MM, Islam MR, Akash S, Mim M, Noor Alam M, et al. (2022) Exploring the role of nanomedicines for the therapeutic approach of central nervous system dysfunction: at a glance. Front Cell Dev Biol 10: 1-29. https://doi.org/10.3389/fcell.2022.989471

95. Kumar N, Kumar R (2013) Nanotechnology and nanomaterials in the treatment of life-threatening diseases. William Andrew.

96. Patel PB, Latt S, Ravi K, Razavi M (2024) Clinical applications of micro/nanobubble technology in neurological diseases. Biomimetics 9: 645. https://doi.org/10.3390/biomimetics9100645

97. Sisubalan N, Shalini R, Ramya S, Sivamaruthi BS, Chaiyasut C (2023) Recent advances in nanomaterials for neural applications: opportunities and challenges. Nanomedicine 18: 1979–1994. https://doi.org/10.2217/nnm-2023-0261

98. Islam A, Mehwish S, Riaz F, Khan AU (2025) Applications and safety of biosynthesized nanoparticles in neurological disorders. In Expanding Nanobiotechnology: Applications and Commercialization. CRC Press, pp 212–227.

99. Krsek A, Jagodic A, Baticic L (2024) Nanomedicine in neuroprotection, neuroregeneration, and blood–brain barrier modulation: a narrative review. Medicina 60: 1384. https://doi.org/10.3390/medicina60091384

100. Nunes A, Al-Jamal K, Nakajima T, Hariz M, Kostarelos K (2012) Application of carbon nanotubes in neurology: clinical perspectives and toxicological risks. Arch Toxicol 86: 1009–1020. https://doi.org/10.1007/s00204-012-0860-0

101. Jain KK (2008) Nanomedicine: application of nanobiotechnology in medical practice. Med Princ Pract 17: 89–101. https://doi.org/10.1159/000112961

102. Souto EB, Blanco-Llamero C, Krambeck K, Kiran NS, Yashaswini C, et al. (2024) Regulatory insights into nanomedicine and gene vaccine innovation: safety assessment, challenges, and regulatory perspectives. Acta Biomater 180: 1-17. https://doi.org/10.1016/j.actbio.2024.04.010

103. Abdel-Monaem N (2025) Regulations and ethics of nanomedicine and public acceptance. In Nanocarriers in Neurodegenerative Disorders. Boca Raton. CRC Press, pp 84–93.

104. Đorđević S, Gonzalez MM, Conejos-Sánchez I, Carreira B, Pozzi S, et al. (2022) Current hurdles to the translation of nanomedicines from bench to the clinic. Drug Deliv Transl Res 12: 500–525. https://doi.org/10.1007/s13346-021-01024-2

105. Ahmad A, Imran M, Sharma N (2022) Precision nanotoxicology in drug development: current trends and challenges in safety and toxicity implications of customized multifunctional nanocarriers for drug-delivery applications. Pharmaceutics 14: 2463. https://doi.org/10.3390/pharmaceutics14112463

106. Conte R, Foggia R, Valentino A, Di Salle A, Kandsi F, Calarco A (2024) Nanotechnology advancements transforming molecular diagnostics: applications in precision healthcare. Int J Nano Dimens 15: 1-8. https://doi.org/10.57647/j.ijnd.2024.1503.18

107. Sv S, Augustine D, Hosmani J, Pagnoni F, Reda R, et al. (2024) Nanoparticle-based biomolecules in cancer diagnosis, therapy, drug delivery and prognosis. Front Dent Med 5: 1-15. https://doi.org/10.3389/fdmed.2024.1482166

108. Welch EC, Powell JM, Clevinger TB, Fairman AE, Shukla A (2021) Advances in biosensors and diagnostic technologies using nanostructures and nanomaterials. Adv Funct Mater 31: 2104126. https://doi.org/10.1002/adfm.202104126

109. Barbosa AI, Rebelo R, Reis RL, Bhattacharya M, Correlo VM (2021) Current nanotechnology advances in diagnostic biosensors. Med Devices Sens 4: e10156. https://doi.org/10.1002/mds3.10156

110. Mezei T, Kolcsár M, Joó A, Gurzu S (2024) Image analysis in histopathology and cytopathology: from early days to current perspectives. J Imaging 10: 252. https://doi.org/10.3390/jimaging10100252

111. Malatesta M (2024) Histochemistry for molecular imaging in nanomedicine. Int J Mol Sci 25: 8041. https://doi.org/10.3390/ijms25158041

112. Tian M, He X, Jin C, He X, Wu S, et al. (2021) Transpathology: molecular imaging-based pathology. Eur J Nucl Med Mol Imaging 48: 2338–2350. https://doi.org/10.1007/s00259-021-05234-1

113. Dean W (2020) Emerging advances to transform histopathology using virtual staining. BME Front 2020: 1-11. https://doi.org/10.34133/2020%2F9647163

114. Ahmad A, Imran M, Ahsan H (2023) Biomarkers as biomedical bioindicators: approaches and techniques for the detection, analysis, and validation of novel biomarkers of diseases. Pharmaceutics 15: 1630. https://doi.org/10.3390/pharmaceutics15061630

115. Das S, Dey MK, Devireddy R, Gartia MR (2023) Biomarkers in cancer detection, diagnosis, and prognosis. Sensors 24: 37. https://doi.org/10.3390/s24010037

116. Wang J, Zhang H, Wan W, Yang H, Zhao J (2024) Advances in nanotechnological approaches for the detection of early markers associated with severe cardiac ailments. Nanomedicine 19: 1487–1506. https://doi.org/10.1080/17435889.2024.2364581

117. Chen L, Yang G, Qu F (2024) Aptamer-based sensors for fluid biopsies of protein disease markers. Talanta 276: 126246. https://doi.org/10.1016/j.talanta.2024.126246

118. Umapathy VR, Natarajan PM, Swamikannu B, Moses J, Jones S, et al. (2022) Emerging biosensors for oral cancer detection and diagnosis—a review unravelling their role in past and present advancements in the field of early diagnosis. Biosensors 12: 498. https://doi.org/10.3390/bios12070498

119. Panda AK (2012) Nanotechnology in vaccine development. Proc Natl Acad Sci India B Biol Sci 82: 13–27. https://doi.org/10.1007/s40011-012-0073-6

120. Arndt N, Tran HD, Zhang R, Xu ZP, Ta HT (2020) Different approaches to develop nanosensors for diagnosis of diseases. Adv Sci 7: 2001476. https://doi.org/10.1002/advs.202001476

121. Noah NM, Ndangili PM (2019) Current trends of nanobiosensors for point-of-care diagnostics. J Anal Methods Chem 2019: 2179718. https://doi.org/10.1155/2019/2179718

122. Arms L, Smith DW, Flynn J, Palmer W, Martin A, et al. (2018) Advantages and limitations of current techniques for analyzing the biodistribution of nanoparticles. Front Pharmacol 9: 1-17. https://doi.org/10.3389/fphar.2018.00802

123. Jarockyte G, Karabanovas V, Rotomskis R, Mobasheri A (2020) Multiplexed nanobiosensors: current trends in early diagnostics. Sensors 20: 6890. https://doi.org/10.3390/s20236890

124. Zeghoud S, Chandran D, Amor IB, Hemmami H, Mohankumar P, et al. (2023) Nanotechnology and nanomaterials in the treatment and diagnosis of cancer: correspondence. Ann Med Surg 85: 2258–2260. https://doi.org/10.1097/MS9.0000000000000677

125. Umapathy VR, Natarajan PM, Swamikannu B (2023) Review of the role of nanotechnology in overcoming the challenges faced in oral cancer diagnosis and treatment. Molecules 28: 5395. https://doi.org/10.3390/molecules28145395

126. Laroui H, Rakhya P, Xiao B, Viennois E, Merlin D (2013) Nanotechnology in diagnostics and therapeutics for gastrointestinal disorders. Dig Liver Dis 45: 995–1002. https://doi.org/10.1016/j.dld.2013.03.019

127. May JN, Moss JI, Mueller F, Golombek SK, Biancacci I, et al. (2024) Histopathological biomarkers for predicting the tumour accumulation of nanomedicines. Nat Biomed Eng 8: 1366–1378. https://doi.org/10.1038/s41551-024-01197-4

128. Hubbs AF, Sargent LM, Porter DW, Sager TM, Chen BT, et al. (2013) Nanotechnology: toxicologic pathology. Toxicol Pathol 41: 395–409. https://doi.org/10.1177/0192623312467403

129. Poulios C, Karagkiozaki V, Kapoukranidou D, Chakim Z, Zarampoukas T, et al. (2023) Bringing pathology to nanomedicine: a comparison of *in vivo* toxicity of polymeric nanoparticle carriers with and without chitosan coating. Virchows Arch 483: 775–786. https://doi.org/10.1007/s00428-023-03581-y

130. Yang Z, Shen B, Yue L, Miao Y, Hu Y, Ouyang R (2022) Application of nanomaterials to enhance polymerase chain reaction. Molecules 27: 8854. https://doi.org/10.3390/molecules27248854

131. Zhao X, Peng H, Hu J, Wang L, Zhang F (2024) Nanotechnology-enabled PCR with tunable energy dynamics. JACS Au 4: 3370–3382. https://doi.org/10.1021/jacsau.4c00570

132. Vo DK, Trinh KTL (2025) Polymerase chain reaction chips for biomarker discovery and validation in drug development. Micromachines 16: 243. https://doi.org/10.3390/mi16030243

133. Liu Q, Jin X, Cheng J, Zhou H, Zhang Y, et al. (2023) Advances in the application of molecular diagnostic techniques for the detection of infectious disease pathogens. Mol Med Rep 27: 104.

134. Qin T, Wang J, Cui SJ (2021) Development of a nanoparticle-assisted PCR assay to distinguish canine coronaviruses I and II. J Vet Diagn Invest 33: 104–107. https://doi.org/10.1177/1040638720974114

135. Cheong J, Yu H, Lee CY, Lee JU, Choi HJ, et al. (2020) Fast detection of SARS-CoV-2 RNA via the integration of plasmonic thermocycling and fluorescence detection in a portable device. Nat Biomed Eng 4: 1159–1167. https://doi.org/10.1038/s41551-020-00654-0

136. Telkoparan-Akillilar P, Chichiarelli S, Tucci P, Saso L (2025) Integration of microRNAs with nanomedicine: tumor targeting and therapeutic approaches. Front Cell Dev Biol 13: 1-14. https://doi.org/10.3389/fcell.2025.1569101

137. Hu L, Tao Y, Jiang Y, Qin F (2023) Recent progress of nanomedicine in the treatment of Alzheimer's disease. Front Cell Dev Biol 11: 1-16. https://doi.org/10.3389/fcell.2023.1228679

138. Di Bella MA, Taverna S (2024) Extracellular vesicles: Diagnostic and therapeutic applications in cancer. Biology 13: 716. https://doi.org/10.3390/biology13090716

139.

140. Das U, Banik S, Nadumane SS, Chakrabarti S, Gopal D, et al. (2023) Isolation, detection and analysis of circulating tumour cells: a nanotechnological bioscope. Pharmaceutics 15: 280 . https://doi.org/10.3390/pharmaceutics15010280

141. Sadeghi M, Sadeghi S, Naghib SM, Garshasbi HR (2023) A comprehensive review on electrochemical nano biosensors for precise detection of blood-based oncomarkers in breast cancer. Biosensors 13: 481. https://doi.org/10.3390/bios13040481

142. Wang C, Zhang S (2023) Advantages of nanomedicine in cancer therapy: a review. ACS Appl Nano Mater 6: 22594–22610. https://doi.org/10.1021/acsanm.3c04487

143. Xu M, Han X, Xiong H, Gao Y, Xu B, et al. (2023) Cancer nanomedicine: emerging strategies and therapeutic potentials. Molecules 28: 5145. https://doi.org/10.3390/molecules28135145

144. Chen C, Yuan P, Zhang Z (2024) Nanomedicine-based cancer immunotherapy: a bibliometric analysis of research progress and prospects. Front Immunol 15: 1-15. https://doi.org/10.3389/fimmu.2024.1446532

145. Jin C, Wang K, Oppong-Gyebi A, Hu J (2020) Application of nanotechnology in cancer diagnosis and therapy—a mini-review. Int J Med Sci 17: 2964-2973. https://doi.org/10.7150/ijms.49801

146. Yin W, Pan F, Zhu J, Xu J, Gonzalez-Rivas D, et al. (2021) Nanotechnology and nanomedicine: a promising avenue for lung cancer diagnosis and therapy. Engineering 7: 1577–1585. https://doi.org/10.1016/j.eng.2020.04.017

147. Fan D, Cao Y, Cao M, Wang Y, Cao Y, et al. (2023) Nanomedicine in cancer therapy. Signal Transduct Target Ther 8: 1-34. https://doi.org/10.1038/s41392-023-01536-y

148. Alrushaid N, Khan FA, Al-Suhaimi EA, Elaissari A (2023) Nanotechnology in cancer diagnosis and treatment. Pharmaceutics 15: 1025. https://doi.org/10.3390/pharmaceutics15031025

149. Rao L, Yuan Y, Shen X, Yu G, Chen X (2024) Designing nanotheranostics with machine learning. Nature Nanotechnology 19: 1769-1781. https://doi.org/10.1038/s41565-024-01753-8

150. Marepally S, Sahu T, Tyagi RK (2022) Editorial: nanomedicine in infectious diseases: Drug delivery and vaccines. Front Pharmacol 13: 1-3. https://doi.org/10.3389/fphar.2022.928572

151. Kirtane AR, Verma M, Karandikar P, Furin J, Langer R, et al. (2021) Nanotechnology approaches for global infectious diseases. Nat Nanotechnol 16: 369–384. https://doi.org/10.1038/s41565-021-00866-8

152. Yang G, Chen S, Zhang J (2019) Bioinspired and biomimetic nanotherapies for the treatment of infectious diseases. Front Pharmacol 10: 1-17. https://doi.org/10.3389/fphar.2019.00751

153. Lu MY, Chen B, Williamson DF, Chen RJ, Zhao M, et al. (2024) A multimodal generative AI copilot for human pathology. Nature 634: 466–473. https://doi.org/10.1038/s41586-024-07618-3

154. Brodsky V, Ullah E, Bychkov A, Song AH, Walk EE, et al. (2025) Generative artificial intelligence in anatomic pathology. Arch Pathol Lab Med 149: 298–318. https://doi.org/10.5858/arpa.2024-0215-RA

155. Lee ST, Kuboki T, Kidoaki S, Aida Y, Arima Y, et al. (2024) A plasmonic metasurface reveals differential motility of breast cancer cell lines at initial phase of adhesion. Colloids Surf B Biointerfaces 238: 113876. https://doi.org/10.1016/j.colsurfb.2024.113876

156. Ori MO, Ekpan FM, Samuel HS, Egwuatu OP (2024) Integration of artificial intelligence in nanomedicine. Eurasian J Sci Technol 4: 88–104. https://doi.org/10.48309/EJST.2024.422419.1105

157. Su Y, Guo C, Chen Q, Guo H, Wang J, et al. (2022) Construction of bionanoparticles based on Angelica polysaccharides for the treatment of stroke. Nanomedicine 44: 102570. https://doi.org/10.1016/j.nano.2022.102570

158. Zarella MD, McClintock DS, Batra H, Gullapalli RR, Valante M, et al. (2023) Artificial intelligence and digital pathology: clinical promise and deployment considerations. J Med Imaging 10: 051802. https://doi.org/10.1117/1.JMI.10.5.051802

159. Jiang H, Chartsias A, Zhang X, Papanastasiou G, Semple S, et al. (2020) Semi-supervised pathology segmentation with disentangled representations. In Domain Adaptation and Representation Transfer, and Distributed and Collaborative Learning: Proceedings of DART 2020 and DCL 2020, MICCAI Workshops. Springer, pp 62–72.

160. Soll RF, Ovelman C, McGuire W (2020) The future of Cochrane neonatal. Early Hum Dev 150:105191. https://doi.org/10.1016/j.earlhumdev.2020.105191

161. Joyce P, Allen CJ, Alonso MJ, Ashford M, Bradbury MS, et al. (2024) A translational framework to DELIVER nanomedicines to the clinic. Nat Nanotechnol 19: 1597–1611. https://doi.org/10.1038/s41565-024-01754-7

162. Borri F, Granaglia A (2021) Pathology of triple negative breast cancer. Semin Cancer Biol 72: 136–145. https://doi.org/10.1016/j.semcancer.2020.06.005