

"Nanoparticle-Mediated Imaging Strategies for Therapeutic Guidance"

Evangelia Siomou¹, Christiana Christodoulou², Achilleas Gerou-Christov², Anna Nikolaidou², Ioanna Stamatelatou², Evgenia Alamani¹, Efstathios P. Efstathopoulos¹

¹2nd Department of Radiology, Medical Physics Unit, Medical School, National and Kapodistrian University of Athens, 1 Rimini str., Chaidari, 12462, Athens, Greece ²Medical School, National and Kapodistrian University of Athens, Athens, Greece



Background:

- Traditional imaging modalities (CT, MRI, etc.) have been critical in medical diagnostics.
- Limitations in real-time insights and molecular/cellular-level detection prompt a need for integrated solutions.
- Nanoparticles (NPs) offer a dual capability for both imaging and therapy, addressing these limitations.

Aim:

- Evaluate the existing literature on image-guided treatment based on nanoparticles.
- Explore the potential of multimodal nanoparticles in enhancing the precision and effectiveness of imageguided therapy (IGT).
- on synthesizing and characterizing • Focus nanoparticles for image-guided therapy.



2. Materials & Methods

Search Strategy and Article Retrieval

Search Strategy Databases Searched:

- PubMed: 728 articles.
- Scopus: 820 articles.
- Citation searches also conducted.

Keywords Used: "Nanoparticles," "Image-Guided Therapy," "Imaging," "Theranostics," "Drug Delivery."

Initial Results: Total of 1,548 articles retrieved from PubMed and Scopus.

Refinement Filters Applied:

- Publication Date: 2019–2023.
- Study Type: Reviews and original research.
- Language: English.
- Availability: Full-text.
- Focus: Clinical, pre-clinical, and in vivo studies.

Article Selection Process (PRISMA)

- Selection Process: Evaluated studies following PRISMA 2020 Guidelines.
- Final selection: 54 articles based on inclusion criteria. PRISMA Flow Diagram:



Nanoparticles in Imaging Modalities

Imaging Techniques:

- MRI: High spatial resolution, good soft-tissue contrast.
- CT: High spatial resolution, short scan time.
- PET: Extremely high sensitivity, ideal for non-invasive tumor detection.
- Fluorescence Imaging (FI): High spatial resolution, short scan time.
- Ultrasound (US): Real-time imaging via high-frequency sound waves.

Nanoparticles Used in Imaging:

- Liposomal NPs: Encapsulate drugs/imaging agents; improve solubility & targeting.
- Polymeric NPs: Biodegradable, used for controlled drug release.
- Inorganic NPs (SPIONs, Gold, Silica): Enhance MRI contrast, CT imaging, surgical guidance.
- Quantum Dots: Ideal for fluorescence imaging.
- Superparamagnetic Iron Oxide NPs (SPIONs): Enhance MRI contrast; used in hyperthermia therapy.
- Gold NPs: Used in both imaging and therapy.

<u>Multimodal Imaging</u>: Combines multiple techniques for higher diagnostic accuracy and better treatment planning.

Applications of Nanoparticles in Image-Guided Therapy

Nanoparticles in Cancer Therapy

- Drug Delivery: Nanotechnologies enhance targeted drug delivery (e.g., Doxil[®] for cancer treatment).NPs like Liposomes, Polymeric Micelles, and Inorganic NPs improve drug distribution and reduce toxicity. Ultrasound-guided therapy with nanoparticles enhances early detection and precise drug delivery.
- Photothermal Therapy (PTT): Gold & Silver NPs convert NIR light to heat for targeted cell destruction. Allows real-time temperature monitoring and combination therapies (e.g., photothermalchemotherapy).
- Hyperthermia: Magnetic NPs raise tissue temperature via electromagnetic fields, selectively targeting • cancer cells. Combined with the EPR effect, nanoparticles enhance heat delivery to tumors. Used for thermochemotherapy and improved cancer treatment precision.





Nanoparticles in Cardiovascular Diseases Therapy

Nanoparticles in Imaging

Key Non-Invasive Imaging Techniques:

- MRI: Characterizes atherosclerotic plaques, using SPIONs (signal loss in T2-weighted images) and Gdcontaining NPs.
- CT: Monitors atherosclerotic macrophages in coronary arteries using iodinated and gold NPs.
- PET: Detects macrophage-mediated inflammation using 18F, 89Zr, or 65Ga-labelled NPs.
- FI: Images macrophage-rich vascular lesions with upconversion NPs and quantum dots.

Example Nanoparticles in Use:

- 18F-Macroflor: Visualizes atherosclerotic plagues and infarcted myocardial tissue in animal models.
- 89Zr-labelled NPs: Characterize atherosclerosis in animal models.
- 65Ga-labeled NPs: Target atherosclerosis biomarkers with extremely short blood circulation time. •

Nanoparticles in Neurodegenerative Disorders Therapy

Nanoparticle Applications

Challenges in Treating NDDs: Complex pathophysiology, lack of biomarkers, Blood-Brain Barrier (BBB) restrictions.

Nanoparticles for Diagnosis

- SPIONs and Liposomal NPs: Accumulate on amyloid plaques, enhancing MRI for early Alzheimer's diagnosis.
- Gold NPs: Bind to amyloid-β deposits, altering surface plasmon resonance (SPR) signal for spectroscopy detection.

Nanoparticles for Therapy:

- Gold NPs (ApoE3): Disintegrate amyloid plaques via surface plasmon resonance in Alzheimer's.
- Chitosan Nanomicelles: Show neuroprotective effects in Parkinson's disease.
- Solid Lipid NPs (Rosmarinic Acid): Improve behavior and reduce oxidative stress in Huntington's disease. •

Future Prospects:

Addressing challenges in safety, efficacy, and regulation is key to advancing nanoparticle-based therapies for NDDs.

Advantages of Nanoparticles in Medical Imaging, Therapy, and Theranostics

<u>Medical Imaging</u>: Improved Resolution & Contrast, Targeted Imaging, Accessibility, Customizability, **Biological Compatibility**

<u>Therapy</u>: Versatility in Design, Targeted Drug Delivery, Enhanced Drug Stability, Controlled Release, Combination Therapies, Reduced Side Effects

Theranostics: Multifunctionality, Optimized Treatment Response, Personalized Medicine, Real-Time Monitoring, Improved Treatment Planning: Lowers risk of resistance or failure.

Challenges:

Biocompatibility & Toxicity, Biodistribution & Clearance, Imaging Resolution & Sensitivity, Targeting Specificity, Regulatory Hurdles, Long-term Stability & Immunogenicity

4. Conclusions

- The current state of nanoparticle image-guided treatment marks a revolutionary convergence of • nanotechnology and medical imaging.
- Significant progress has been made in using nanoparticles for accurate diagnosis and focused ٠ treatment interventions.
- Nanoparticles have enhanced the precision and efficacy of medical treatments, providing targeted ۲ therapy with improved outcomes.
- The integration of nanoparticles in image-guided therapy is reshaping the future of medical diagnostics ۲ and treatment, offering a more effective, accurate, and patient-centered approach to healthcare.

Smart Nanoparticles

- Respond to stimuli (physical, chemical, biological) to enhance treatment. ٠
- Used in diseases like brain tumors, prostate cancer, and cardiovascular diseases. •
- Real-time modifications improve treatment outcomes. ullet

Green Nanoparticles

- Eco-friendly synthesis: Better biocompatibility and environmental safety. •
- Used in MRI, fluorescence imaging, and photoacoustic imaging. ۲
- Enhance contrast in imaging, offering sustainable treatment options. •

Nanoparticles & AI for Image-Guided Therapy

- Al-assisted nanoparticle synthesis: Predicting optimal designs. ٠
- Real-time decision support: Al-guided precision drug delivery. ٠
- Intraoperative guidance: AI + nanoparticles improve surgical precision and treatment efficacy.

- 1. Mohanty, A., Uthaman, S., & Park, I. (2020). Utilization of Polymer-Lipid hybrid nanoparticles for targeted Anti-Cancer therapy. Molecules, 25(19), 4377. https://doi.org/10.3390/molecules25194377
- 2. Vangijzegem, T., Lecomte, V., Ternad, I., Van Leuven, L., Müller, R. N., Stanicki, D., & Laurent, S. (2023). Superparamagnetic Iron Oxide Nanoparticles (SPION): From fundamentals to State-of-the-Art Innovative Applications for cancer therapy. Pharmaceutics, 15(1), 236. https://doi.org/10.3390/pharmaceutics15010236
- 3. Li, Z., Mu, Y., Peng, C., Lavin, M. F., Shao, H., & Du, Z. (2020). Understanding the mechanisms of silica nanoparticles for nanomedicine. WIREs Nanomedicine and Nanobiotechnology, 13(1). https://doi.org/10.1002/wnan.1658
- 4. Lombardo, D., Киселев, M. A., & Caccamo, M. T. (2019). Smart Nanoparticles for drug delivery application: Development of versatile nanocarrier platforms in biotechnology and nanomedicine. Journal of Nanomaterials, 2019, 1–26. https://doi.org/10.1155/2019/3702518
- Katsuki, S., Matoba, T., Koga, J., Nakano, K., & Egashira, K. (2017). Anti-inflammatory nanomedicine for cardiovascular disease. Frontiers in Cardiovascular Medicine, 4. https://doi.org/10.3389/fcvm.2017.00087
- 6. Ayana, G., Ryu, J. M., & Choe, S. (2022). Ultrasound-Responsive Nanocarriers for breast cancer chemotherapy. Micromachines, 13(9), 1508. https://doi.org/10.3390/mi13091508
- 7. Salimi, M., Mosca, S., Gardner, B., Palombo, F., Matousek, P., & Stone, N. (2022). Nanoparticle-Mediated Photothermal therapy limitation in clinical applications regarding pain management. Nanomaterials, 12(6), 922. <u>https://doi.org/10.3390/nano12060922</u>
- 8. Włodarczyk, A., Gorgoń, S., Radoń, A., & Bajdak-Rusinek, K. (2022). Magnetite nanoparticles in magnetic hyperthermia and Cancer therapies: Challenges and Perspectives. Nanomaterials, 12(11), 1807. <u>https://doi.org/10.3390/nano12111807</u>
- 9. Wu, D., Chen, Q., Chen, X., Han, F., Chen, Z., & Wang, Y. (2023b). The blood–brain barrier: structure, regulation, and drug delivery. Signal Transduction and Targeted Therapy, 8(1). https://doi.org/10.1038/s41392-023-01481-w
- 10.Cano, A., Turowski, P., Ettcheto, M., Duskey, J. T., Tosi, G., Sánchez-López, E., García, M. L., Camins, A., Souto, E. B., Ruiz, A., Marquié, M., & Boada, M. (2021b). Nanomedicine-based technologies and novel biomarkers for the diagnosis and treatment of Alzheimer's disease: from current to future challenges. Journal of Nanobiotechnology, 19(1). <u>https://doi.org/10.1186/s12951-021-00864-x</u>
- 11.Lamptey, R. N. L., Chaulagain, B., Trivedi, R., Gothwal, A., Layek, B., & Singh, J. (2022h). A review of the common neurodegenerative disorders: current therapeutic approaches and the potential role of nanotherapeutics. International Journal of Molecular Sciences, 23(3), 1851. <u>https://doi.org/10.3390/ijms23031851</u>
- 12.Zielińska, A., Costa, B., Ferreira, M. V., Miguéis, D., Louros, J. M. S., Durazzo, A., Lucarini, M., Eder, P., Chaud, M. V., Morsink, M., Willemen, N., Severino, P., Santini, A., & Souto, E. B. (2020c). Nanotoxicology and Nanosafety: Safety-by-Design and Testing at a Glance. International Journal of Environmental Research and Public Health, 17(13), 4657. https://doi.org/10.3390/ijerph17134657
- 13.Sun, L., Li, H., Ye, Y., Yang, L., Islam, R., Tan, S., Tong, R., Miao, Y., & Cai, L. (2023). Smart nanoparticles for cancer therapy. Signal Transduction and Targeted Therapy, 8(1). https://doi.org/10.1038/s41392-023-01642-x
- 14.Vijayaram, S., Razafindralambo, H., Sun, Y., Vasantharaj, S., Ghafarifarsani, H., Hoseinifar, S. H., & Raeeszadeh, M. (2023). Applications of green synthesized metal nanoparticles a review. Biological Trace Element Research. <u>https://doi.org/10.1007/s12011-023-03645-9</u>
- 15.Nuhn, L. (2023). Artificial intelligence assists nanoparticles to enter solid tumours. Nature Nanotechnology, 18(6), 550–551. https://doi.org/10.1038/s41565-023-01382-7