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Monte Carlo Simulations in Nanoparticle-Enhanced Radiotherapy: Mechanisms, Implications, And Limitations: A Review

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ABSTRACT

Indeed, the problem of cancer is still a prominent one, hence a need for highly accurate treatment technologies remains topical. While radiotherapy is commonly known as one of the treatment methods that help control the development of tumours, the effectiveness of the therapy is constrained by the inability to deliver the desired amount of ionising radiation to the target tumour cells while minimising side effects caused by the exposure of neighbouring healthy cells to radiation. It is against such a background that new advances in nanoparticle-enhanced radiotherapy that promise more local energy delivery and increased radiosensitisation have started gaining more prominence in recent years. In this regard, Monte Carlo methods have become an irreplaceable means for modelling of radiation processes, nanoparticle interactions with ionising radiation, secondary electrons generation, and the dose enhancement factor. The present review is dedicated to the problem of nanoparticle-enhanced radiotherapy and is focused on discussing the major enhancement mechanisms, aspects influencing the dose amplification, approaches in the simulations, and the drawbacks of current models, as well as emerging trends in the field of Monte Carlo methods in radiotherapy.

Keywords: Nanomedicine, Radiotherapy, Monte Carlo Simulations, Nanoparticle-Enhanced Radiotherapy

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Introduction:

The rising global burden of cancer demands continuous advancements in strategies of its treatment worldwide [1]. To improve patient outcomes, various therapeutic approaches are employed either individually or in combination [2]. Among these, radiotherapy is one of the most widely used and effective methods for treating tumour cells [3]. Radiotherapy is a technique which employs ionising radiation, such as photons and electrons, to irradiate the tumour or target volume within the patient to achieve effective cancer control [4]. The treatment process consists of the development of a detailed radiation plan by a multidisciplinary team comprising a radiation oncologist, medical physicist, and radiotherapist. The main goal of this planning is to deliver a sufficient radiation dose to the tumour while simultaneously reducing exposure to the adjacent healthy tissues and critical organs. This balance between tumour control and the protection of normal tissues continues to be one of the key challenges in conventional radiotherapy [5].

The effectiveness of radiotherapy relies heavily on the interactions of ionising radiations at both the atomic and molecular levels in matter. During the process of ionising radiation passing through a biological tissue, the deposition of energy takes place during each individual encounter between the rays and atoms or molecules, resulting in ionisation or excitation effects, as well as secondary electron production that plays a crucial part in the local energy deposition. This energy can cause damage to DNA through the breaking of both strands of DNA directly or indirectly through water radiolysis, leading to the formation of reactive oxygen species (ROS). Physically speaking, the energy distribution at microscopic and nanoscopic levels governs the whole process of radiation response. In spite of the considerable advancements that have been made regarding the delivery of radiation to cancerous cells, there are some limitations associated with the radiotherapy procedures that are based on physical and biological factors. One of the most important aspects of such limitations relates to the fact that energy deposition cannot take place strictly in the tumour region but would be inevitable at other surrounding tissues. Furthermore, certain differences in tissue composition, the energy of radiation, and the nature of the tumour environment may affect energy transfer and interaction probabilities [6-9].

Several methods have been suggested to overcome the aforementioned drawbacks in order to increase radiation doses at the target site and reduce the dose delivered to adjacent organs and healthy tissues. One of these methods is to use nanoparticles with high atomic number (high Z), which act as radiosensitisers for improving efficacy and targeting of the radiation treatment procedure. With the use of high atomic numbers, high-Z nanoparticles would have a greater chance of interacting with the ionizing radiation. This process can be carried out via the photoelectric effect with high absorption coefficients. Irradiation causes the production of various kinds of secondary electrons such as photoelectrons, Auger electrons, Compton electrons and δ-electrons, whose function is energy transfer at microscopic and nanoscopic scales. As far as efficiency of the dose enhancement mechanism is concerned, it largely depends on the characteristics of these particles. The particle size, its shape and the quantity of these particles along with their spatial distribution inside the tumour can determine how effectively radiation dose enhancement occurs. In general, particles with small sizes would be able to emit low-energy secondary electrons which could

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penetrate deep into the surrounding medium while larger particles would confine more energy in themselves. Interaction of radiation with nanoparticles also causes production of certain reactive species via secondary electrons that have impact on the radiation response of the system. Another important factor affecting dose enhancement is energy and nature of the incident radiation. Low-energy radiation would cause localized interactions while high-energy radiation would cause a wider energy deposition in the system [10-17].

A Monte Carlo simulation represents a computer-based stochastic approach that repeatedly samples randomness for modelling radiation propagation among other processes controlled by probabilistic interactions. It is considered one of the best techniques to describe the dynamics of the photon, electron and other charged particles' interaction within various materials. Through the use of particle histories along with simulations of their interaction, such as scattering, attenuation and secondary electron production, it becomes possible to achieve high-quality estimations of space dose deposition. This ability is particularly important for the success of radiotherapy, as its efficiency highly relies on a proper distribution of the absorbed dose in the tumor tissue and surrounding healthy tissues. As it pertains to nanoparticle-mediated radiotherapy, Monte Carlo simulations have been extensively used for evaluating the dependence of local dose enhancement on different factors like the type of nanoparticles, their concentration and size, as well as radiation energy. The method is also applied for thermal energy modelling in the case of nanoparticle-mediated therapies and is important for cancer therapy treatment planning. However, while Monte Carlo simulation produces higher precision when compared with analytical and deterministic approaches, particularly for complicated geometrical, heterogeneous tissue structures and microenvironments, this comes at the cost of computational time. Thanks to these capabilities, the Monte Carlo simulation becomes a useful tool for studying advanced irradiation technologies and nanotherapy [18-21].

This review intends to give a complete description about the application of Monte Carlo simulations in nanoparticle-assisted radiotherapy. Emphasis has been given on the fundamental principles of dose enhancement involving the physical phenomenon behind radiation and nanoparticles interaction and secondary electron generation at micro-scale levels. In addition, the clinical and technical significance of Monte Carlo simulation in the context of treatment planning and optimisation and personalisation in radiotherapy have also been addressed. At the same time, the existing limitations involved in the current models such as complex computational processes, uncertainty in nanoparticle distribution and nanodosimetry issues have been examined [22, 23].

Fundamentals of Nanoparticles-Enhanced Radiotherapy:

Basic Properties of Nanoparticles:

Nanoparticle-enhanced radiotherapy is a process where nanosized substances are administered to the tumour area for modification of radiation reactions. Nanoparticles are nanometer-scale materials, and as such, they have special physical and chemical properties that are not shared by bulk materials because of their high surface-to-volume ratio and dimensional characteristics. In radiotherapy, a significant amount of research has focused on the use of nanoparticles that have relatively high atomic numbers, because they increase the chance of interaction with radiation compared to

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other soft tissues. Consequently, higher energy deposits occur around these nanoparticles, and this can help to increase the effects of radiation inside the cancerous tissue while minimising the total dose. Several factors determine how pronounced this effect will be; therefore, nanoparticles should be understood properly in order to achieve successful results from their use in radiotherapy [24, 25].

Radiation Interaction Mechanisms:

The enhancement effects related to nanoparticles mostly arise from the interactions of radiation with nanoparticles at micro- and nano-levels. In cases involving photons, particularly those with energies in the keV range, use of high-Z nanoparticles significantly boosts photoelectric absorption causing the production of secondary particles like photoelectrons, Auger electrons, and characteristic X-rays. The deposits of energy created by the secondary emissions take place over extremely small ranges around the nanoparticles thus giving rise to dose enhancement that is localized to a large extent. With high photon energies, however, Compton scatter predominates while the enhancement effect declines but secondary electron transport can lead to extra dose delivery. Charged particle therapies too are influenced by the interaction process that is facilitated by inelastic scattering and secondary electron emission [26, 27].

Factors Affecting Dose Enhancement:

The radiosensitizing capability of nanoparticles depends on many factors. Among these factors, the size of nanoparticles seems to be a crucial parameter as it affects the chances of secondary electron escape and secondary electron range. As the size of nanoparticles decreases, the probability of electron release in the medium becomes more; however, large nanoparticles store more energy within them. The geometry of nanoparticles impacts their cross-section interactions and localized electric fields. In addition, the concentration and clustering of nanoparticles at tissue levels contribute to the enhancement effect. Furthermore, it should be mentioned that the localization of nanoparticles at cellular, sub-cellular, or vascular levels impacts the efficiency of energy transfer to radiosensitive regions. Another important parameter is the energy of radiation; for instance, low-energy photons possess greater enhancement capabilities compared to high-energy MeV beams due to the photoelectric process [28-30].

Clinical Significance and Current Challenges:

Nanoparticle-assisted radiotherapy holds promise for increasing the tumour dose while maintaining a similar level of exposure to adjacent healthy tissue. This could lead to an increased tumour control probability with minimal treatment toxicity. Nevertheless, many issues remain to be solved before such a technology could be implemented in clinical practice. They include uncertainties associated with nanoparticle transport and retention, toxicity, non-uniform biodistribution, and the problem of modelling the deposition of energy at the nanoscale with the use of conventional macroscale dosimetry models. In addition, moving from preclinical results to clinical application involves the development of robust treatment planning protocols and validation frameworks. This is why computer simulation techniques,

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especially Monte Carlo simulations, play a crucial role in studying and optimizing nanoradiotherapy techniques [31, 32].

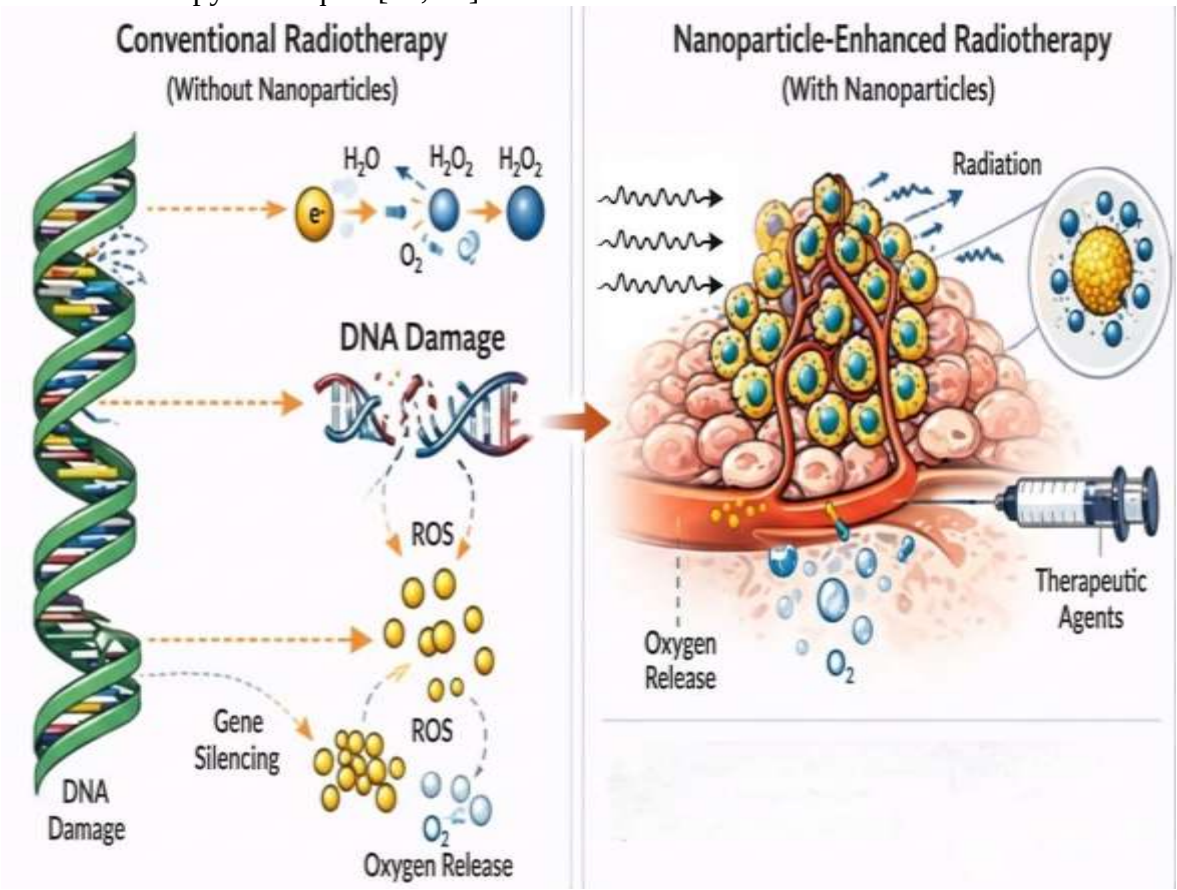


Figure 1. Schematic comparison between the radiotherapy technique without nanoparticls and the radiotherapy technique with nanoparticles, emphasizing the enhancement in the localization of the effect of radiation, ROS production, DNA damage, and tumour cell death

Monte Carlo Simulation Techniques:

Overview of Monte Carlo Methods:

Monte Carlo simulation is a computational technique based on mathematical methods that employs repeated random sampling to model physical processes governed by probability. In radiation physics, it is widely used to simulate the transport of photons, electrons, protons, and other particles through matter by tracking their individual paths and stochastic interactions. During each particle history, events such as scattering, absorption, ionisation, and secondary particle generation are sampled using established interaction cross-sections and probability distributions. By repeating this process for a large number of particles, statistically reliable estimates of absorbed dose, particle fluence, and energy deposition patterns can be obtained. Because of its ability to represent complex radiation transport phenomena with high accuracy, Monte Carlo simulation is considered one of the most reliable tools in medical radiation dosimetry and treatment modelling.

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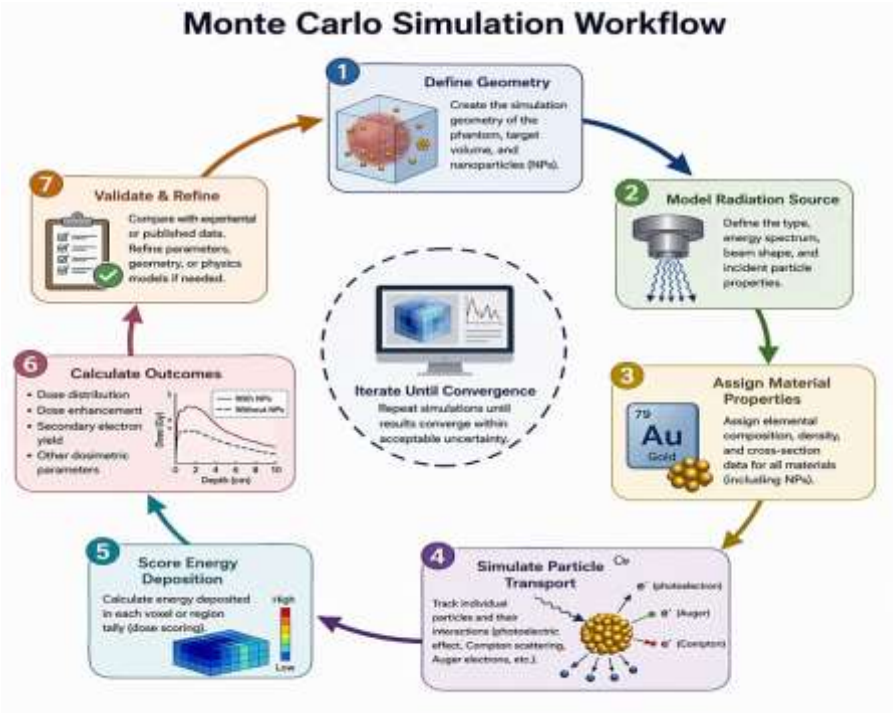


Figure 2. Schematic representation of the Monte Carlo simulation workflow used in radiotherapy studies, including geometry definition, radiation source modelling, material assignment, particle transport, energy deposition scoring, result analysis, and iterative validation.

Major Monte Carlo Codes in Radiotherapy:

Several Monte Carlo codes have been developed for radiotherapy applications, each offering distinct advantages depending on the treatment modality and the scale of interest. Commonly used platforms include EGSnrc, which is highly effective for electron and photon beam dosimetry; MCNP, widely applied to coupled particle transport problems; PENELOP, well-suited for low-energy interaction studies; and GEANT4, which has become highly popular due to its flexibility in geometry construction, material definition, and multi-scale physics modelling. In nanoparticle-enhanced radiotherapy, Geant4 and its extension Geant4-DNA are especially valuable, as they enable detailed particle tracking and the simulation of microscopic and nanoscopic energy deposition in the vicinity of nanoparticles [33, 34].

Applications in Radiotherapy Treatment Modelling:

Monte Carlo techniques are extensively applied in external beam radiotherapy for modelling treatment heads, beam-shaping devices, patient geometries, and absorbed dose distributions. This is due to their ability to simulate complex treatment systems, including linear accelerators, kilovoltage X-ray units, brachytherapy sources, and particle therapy beams. In comparison to simplified analytical algorithms, Monte Carlo methods can more accurately account for tissue heterogeneities, irregular geometries, and interface effects, which are particularly important in the treatment of lung, bone, and head-and-neck tumours. In modern treatment planning, Monte Carlo-

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based dose calculation engines are increasingly integrated to improve the precision of dose calculations and support personalised radiotherapy strategies [35, 36].

Role in Nanoparticle-Enhanced Radiotherapy:

The application of nanoparticles in radiotherapy allows one to employ Monte Carlo simulations as an excellent tool for studying their effect on radiation transport and dosimetry in the vicinity of nanoparticles. The technique is frequently used for determining dose enhancement factors, analyzing the role of nanoparticle sizes and concentrations, and comparing different types of radiation energies and modes of radiation beams. Using Monte Carlo simulations, it is possible to determine the amount of localized energy release near the surface of nanoparticles through photoelectric absorption, Compton scattering, Auger cascades, and secondary electron transport [24, 37].

Advantages and Current Limitations:

One of the key strengths of Monte Carlo simulation methodology is the high level of physical realism and flexibility with which it can accommodate radiation from different sources. It allows for greater precision in modelling complicated geometry, inhomogeneities, tissue heterogeneity, and radiation-tissue interactions compared to other existing techniques. However, in spite of this, such techniques are more computationally demanding, involve extended simulation time and even statistical errors due to insufficient number of particle tracks if not enough data points are considered. This is particularly the case for nanoparticle research where additional complications stem from the uncertainty of the nanoparticles' location, their agglomeration, intracellular distribution and the difficulty of translating physics into biological outcomes [38].

Dose Enhancement Mechanisms:

Fundamental Basis of Dose Enhancement:

Enhancement of dose due to the use of nanoparticles during radiotherapy therapy depends on the increase in the absorption of radiation energy in the tumours that have nanoparticles embedded in them. In the case where nanoparticles are incorporated in the irradiated tissue, they tend to change the probability of interaction between incident radiation and thereby produce secondary radiation particles, leading to more local energy deposition than in cases of tissue alone. Enhancement of dose due to nanoparticle use becomes more significant where the nanoparticles have higher effective atomic numbers, as radiation interaction tends to be higher with increased atomic numbers for low-energy photon beams [38].

Photon-Nanoparticle Interactions:

For photon beams, the major cause of enhancement effects changes greatly according to the beam’s energy. For example, at keV energies, photoelectric interaction becomes an important process and causes local enhancement of doses near nanoparticles. Photoelectric interaction ejects photoelectrons and causes vacancies, which result in Auger and characteristic radiation. Since most of those electrons travel for very short distances, the dose deposition becomes localised near the nanoparticle surface. When

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photons have energies of several MeV, the major interaction type is Compton scattering, and the enhancement factor is usually lower than when dealing with keV energies. However, some local enhancement of energy deposition could still be observed through secondary electrons and altered electron transportation [39, 40].

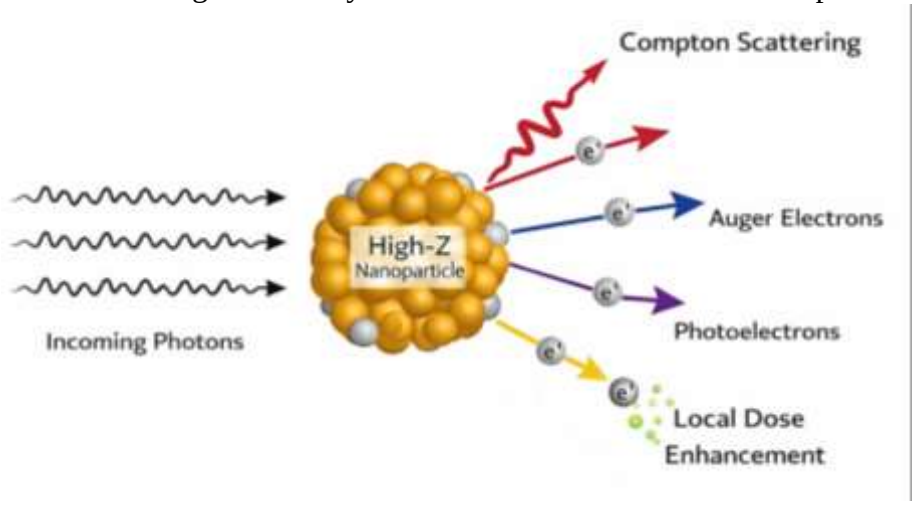


Figure 3. The diagram depicts the primary channels of interaction between the incident photons and the high-Z nanoparticles, highlighting the process of Compton scattering, creation of photoelectrons, emission of Auger electrons, and consequent dose enhancement in the vicinity.

Secondary Electron Production:

Secondary electrons are an integral part of nanoparticle-based radiosensitisation processes. Photoelectrons, Compton electrons, Auger electrons, and δ-electrons belong to the group of secondary electrons. Low-energy electrons are of particular importance since they have high linear energy transfer and a short range of motion. Hence, the amount of emitted electrons, their energy distribution, and escape probabilities depend on various parameters, including the chemistry of nanomaterials, the sizes of nanoparticles, geometries, and embedding media. Therefore, modelling of secondary electron transport should be performed to estimate the effect of nanomaterials on the enhancement of the absorbed dose [41].

Influence of Nanoparticle Parameters:

The extent to which dose enhancement occurs is highly dependent upon the properties of the nanoparticles used. Size affects the possibility of electrons escaping out of the nanoparticle into the surrounding tissue or the possibility that they remain in the nanoparticle and deposit their energy in the surrounding tissue. The former is more probable in smaller nanoparticles, while the latter is more probable in larger nanoparticles. Shape affects the distribution of the local electric fields as well as the geometry of the interactions between the nanoparticles and the radiation. Concentration affects the number of available interaction sites. Localisation inside the tumour, either in the extracellular environment, cytoplasm, or near the nucleus, is another factor [42].

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Indirect and Biological Contributions:

While the physical increase of absorbed dose is the main factor, there are other secondary factors that contribute to improving therapy. For instance, secondary electrons may promote water radiolysis to produce reactive oxygen species (ROS) that will cause further cellular damage. According to some reports, the improvement of therapy is larger than that expected based on macroscopic dose enhancement, and this implies that nanoparticle-induced changes at the nanometer scale could have an impact as well. Thus, for a thorough analysis of radiosensitisation by nanoparticles, both approaches should be considered [43].

Importance for Radiotherapy Optimisation:

It is crucial to comprehend dose enhancement mechanisms in order to select appropriate beam energies, nanoparticle designs, and treatment conditions. It also provides the theoretical foundation for advanced simulation studies and future clinical translation. By controlling the factors that influence local energy deposition, nanoparticle-assisted radiotherapy may improve tumour control while reducing collateral damage to surrounding healthy tissues [44].

Key Factors Affecting Dose Enhancement:

Radiation Energy and Beam Quality:

Among the various physical factors affecting dose enhancement, radiation energy can be considered the most significant. For example, keV photon beams will show better enhancement due to the contribution of photoelectric absorption. As the probability of photoelectric processes increases with the increase in atomic number, nanoparticles can help greatly enhance energy deposition when the source is of low energy. On the other hand, high-energy sources like MeV photons are expected to have their interaction mechanisms mostly governed by Compton scattering. Hence, macroscopic dose enhancement will likely be minimal, but there can still be contributions from the microscopic processes involving secondary electrons [45].

Nanoparticle Size:

Particle size has a strong influence on the generation and escape of secondary electrons. Smaller nanoparticles often permit a larger fraction of low-energy electrons to escape into the surrounding medium, thereby enhancing local dose deposition. Larger particles may absorb more radiation overall, but a considerable portion of the generated electrons can lose energy within the particle before escaping. For this reason, many studies report an optimum size range rather than a simple assumption that larger particles always produce greater enhancement [42, 45, 46].

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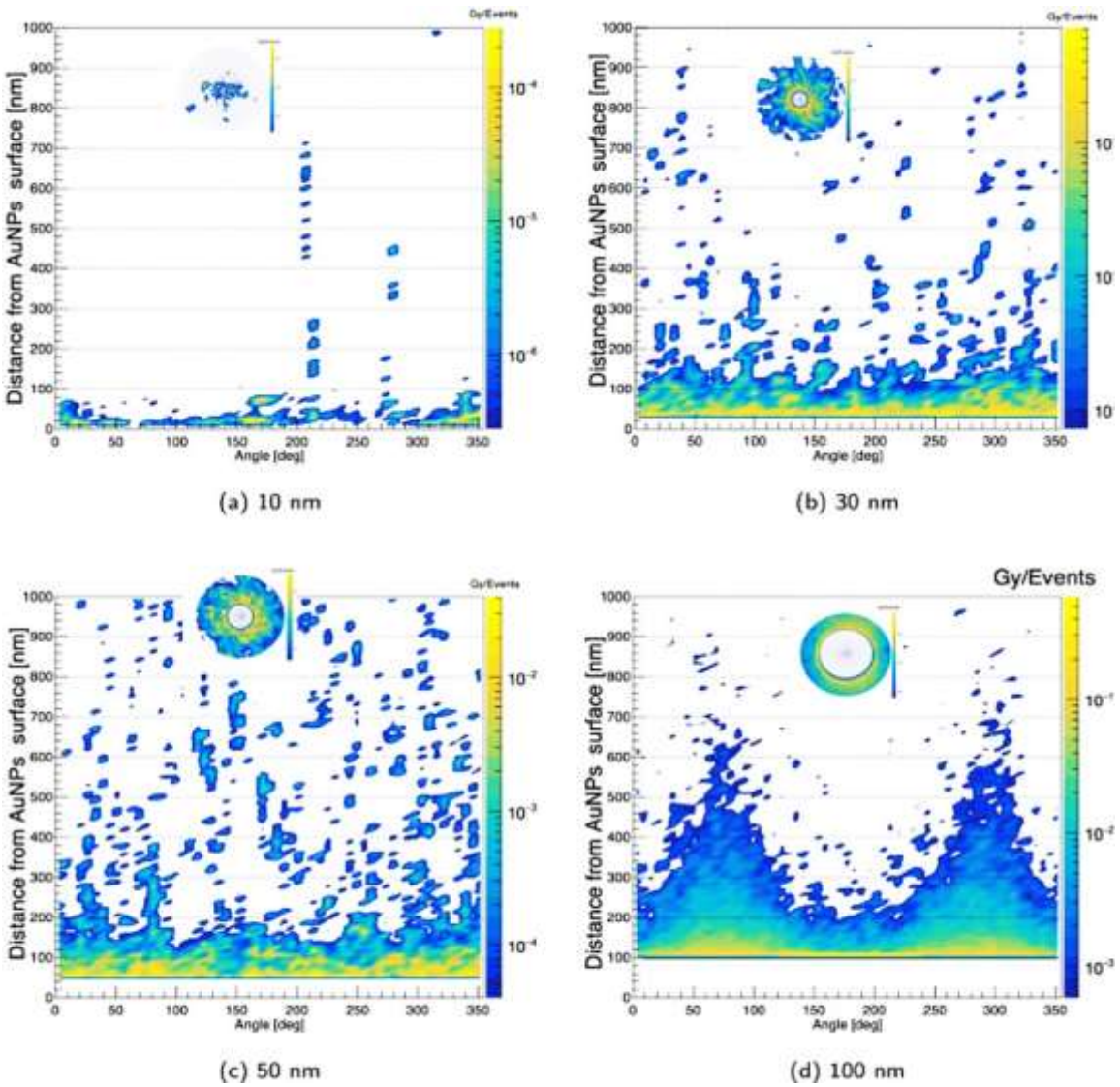


Figure 4. Representative Monte Carlo simulation maps demonstrating the impact of nanoparticle dimensions (10, 30, 50, and 100 nm) on the spatial deposition of energy near high-Z nanoparticles. Dose event variations suggest that local effects are highly sensitive to particle dimensions.

Particle Shape and Surface Morphology:

The shape of nanoparticles is also another critical factor in defining interaction characteristics. The spherical nanoparticle has been the focus of many studies since it is easier to synthesise and analyse. There have been studies on rod-shaped, shell, cage, and even star-shaped nanoparticles, which may possess different surface area and local electric field characteristics. Differences in shape may affect the interaction by influencing the scattering characteristics, secondary electron emission, and energy deposition.

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Concentration and Spatial Distribution:

Another parameter worth considering in this case relates to the density of nanoparticles inside the tumour volume. Greater densities would mean more available binding sites, thus leading to increased deposition of the local dose. At the same time, very high densities will be associated with greater tendency for aggregation and unequal clustering, hence lower efficiency in nanoparticle distribution within the tumour. Spatial localization should also be considered as nanoparticles that lie near radiosensitive cellular sites would exhibit a greater effect.

5.5 Material Composition and Atomic Number:

The elemental composition of the nanoparticles greatly contributes to their interaction cross sections with the incoming radiation. Nanoparticles with elements that have higher atomic numbers will be more suitable when using photon beams, as they possess greater absorption probability. Yet, other features, such as the density, electronic configuration, stability, and compatibility of the nanoparticles, also affect their efficiency. Hence, the choice of nanoparticles should consider their effectiveness in dose enhancement, as well as their use in biomedicine.

Biological and Microenvironmental Conditions:

Although energy depositing in tumour cells for treatment purposes can be analysed through physical aspects, biological aspects in the same tumour may also affect the outcome of the therapy. Some of these include the rate of cellular uptake, localisation of the physical energy in the cell, oxidative state, and the antioxidant levels. This means that the same physical enhancement factor may produce varied results in differing biological circumstances.

Modelling and Simulation Conditions:

The predicted enhancement factor is also subject to the simulation approach used. Aspects such as voxel resolution, scoring volume, transport thresholds, cross-section databases, and geometry description can greatly affect the outcome of a Monte Carlo simulation. Discrepancies observed among various simulations cannot be attributed to physical effects alone, as they could have originated from other considerations, such as the simulation method and scale used.

Limitations of Current Models:

Simplified Geometrical Assumptions:

The majority of current models employ geometrical simplifications, such as those of an isolated nanoparticle having a spherical shape, a homogeneous tissue phantom, or a homogenous tumour region. While these assumptions facilitate computation, they fail to account for the intricate structure of biological systems. In actual practice, the shape of the nanoparticle can be highly irregular, while its distribution can be clumped or heterogeneous. Therefore, idealised models can lead to either underestimation or overestimation of local dose enhancement.

Uncertainty in Nanoparticle Distribution:

One important limitation in many published studies is the assumption that nanoparticles are distributed uniformly throughout the tumour volume. In reality,

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nanoparticle delivery is affected by several factors, including vascular permeability, tissue structure, cellular uptake efficiency, diffusion, and biological clearance processes. Because of this, real tumours often display highly uneven nanoparticle accumulation. Since dose enhancement is strongly influenced by local concentration and spatial location, unrealistic assumptions about nanoparticle distribution can lead to significant errors in predicted treatment outcomes.

Macroscopic Dosimetry vs Nanoscale Effects:
In general, the dosimetry of traditional radiotherapy treatments is mostly dependent on the idea of macroscopic absorbed dose. Nevertheless, nanoparticle-assisted radiotherapy entails localised energy deposition occurring on the microscopical and nanoscale close to the surface of the nanoparticles. In some cases, the localised energy depositing may not be appropriately characterised by the current method of scoring used.

Limitations in Physics Models and Cross-Section Data:
Monte Carlo simulations rely heavily on the accuracy of the data for cross sections and transport processes involved. In the case of low energies, where several phenomena relating to nanoparticles are most significant, errors in electron transport, relaxation processes, Auger processes, and surface interactions may affect the outcome. The various Monte Carlo simulation codes available may use different physics libraries and approximations.

Incomplete Coupling of Physical and Biological Effects:
A significant number of recent theories are concentrated solely on physical effects without taking into account the ensuing chemical/biological reactions. Such elements as secondary electron effect, generation of reactive oxygen species, complexity of the DNA damage process, its repair and other biochemical mechanisms are often underestimated in these models. This means that the predicted physical enhancement cannot be easily extrapolated to biological radiosensitisation.

Computational Cost and Practical Constraints:
Detailed Monte Carlo simulations, particularly at cellular or nanoscopic scales, often require substantial computational resources and long execution times. A large number of particle histories is needed to reduce statistical uncertainty, especially when scoring energy deposition within very small regions. These computational demands can restrict routine clinical implementation as well as large-scale parametric studies.

Lack of Standardisation Across Studies:
Comparison with published studies is often difficult because of variations in beam energy, nanoparticle size, concentration, geometry setup, scoring methods, and the definitions used for enhancement factors. Inconsistent methodologies may lead to conflicting conclusions even when similar systems are being investigated. Greater standardisation is therefore needed to enable reliable benchmarking and support clinical translation.

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Translation to Clinical Practice:

While many studies involving simulations and pre-clinical tests have shown positive results, the actual implementation into clinical settings has yet to occur. The main obstacles that still need to be addressed are reliable nanoparticle delivery, toxicity evaluation, obtaining regulatory approval, confirmation using imaging technology, and incorporation into treatment planning software.

Future Directions:

Advanced Multi-Scale Modelling:

It may be stated with certainty that future developments in this field would hinge on the development of multi-scale modelling tools that consider the connection between macro-level irradiation and processes of energy transfer at micro- and nano-levels. Most models that have been developed till now focus on either of these scales separately, but in order to produce an adequate prediction, all three scales should be considered.

Improved Nanodosimetry and Track-Structure Methods:

Since dose enhancement around nanoparticles happens within very small distances, there is a need for future research to focus more on nanodosimetry and track-structure models. This approach will offer an in-depth analysis of electron transport, energy clustering, and localised damage that cannot be achieved using normal average dose assessments. The development of new scoring procedures could enhance our knowledge of the biological relevance of nanodimensional phenomena.

Integration of Physical, Chemical, and Biological Processes:

The integration of physical radiation transport with the following chemical and biological effects will be one of the main goals for the future. Apart from the first step, which is the absorption of radiation, there are many more steps involved in the process, including the formation of secondary species, oxidative stress, DNA repair, and cell survival. Incorporation of these steps into the models may bring simulation results closer to the observed phenomena.

Optimisation Through Computational Intelligence:

The growing availability of high-performance computing and data-driven methods offers new opportunities for optimisation. Machine learning, surrogate modelling, and hybrid computational strategies may help reduce simulation time while maintaining acceptable accuracy. Such approaches could support rapid parameter screening, treatment planning, and the design of personalised nanoparticle-assisted radiotherapy strategies.

Patient-Specific and Image-Guided Applications:

The application of this technology in clinical practice will likely be aided by the creation of personalised models using imaging techniques, tumour morphology, and predicted biodistribution of nanoparticles. The use of simulation technology combined with imaging-guided verification could improve the accuracy of treatment and help identify those patients who would respond well to nanoparticle-based therapy.

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Standardisation and Experimental Validation:

In order to facilitate rapid clinical adoption, there must be increased uniformity in the simulation approach, data reporting, and definition of enhancement factors. Benchmark tests using similar geometries and radiation parameters would allow for more effective comparisons between groups. On the other hand, increased cooperation between theoretical and experimental approaches is necessary for validation purposes.

7.7 Emerging Physical Frameworks:

As modeling techniques improve, further research might also consider more precise physical models of the interaction between radiation and matter on a microscopic scale, especially in situations where existing assumptions no longer apply. This could lead to an improvement in the predictive power of simulations for radiotherapy using nanoparticles.

Conclusion:

Nanoparticle-enhanced radiotherapy has already been acknowledged as one of the most groundbreaking approaches for increasing the efficiency of radiation therapy treatment. It makes it possible to increase the localized accumulation of energy in tumours while reducing the negative impact on healthy tissues, which helps to achieve better results from therapy. The effectiveness of the treatment will largely depend on several factors, including radiation type, beams' energy, nanoparticles used, and microscopic mechanisms of interaction, for instance, secondary electron generation and transport. Monte Carlo models are rather efficient in exploring the interaction of nanoparticles with radiation and its effect on dose enhancement.

This review article noted the important role played by MC methods in revealing the processes of particle movement and the way they affect the dose distribution within heterogeneous media. Thanks to the high accuracy at the microscopic level and in heterogeneous media, MC techniques can be particularly effective when applied to nanoparticle therapy.

There remain certain difficulties that should be addressed further. In particular, they include uncertainty about the distribution of nanoparticles throughout the body, lack of accurate dosimetry procedures at the nanoscale level, weak connection between physics and biology, and the computational burden.

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