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A Comprehensive Review on Nanostructured Polymer Composites for CT Imaging Contrast Enhancement in Brain Tumor Diagnosis

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Abstract

The detection and characterization of brain tumors require high-resolution and non-invasive imaging modalities that have the ability of differentiating tumorous tissues and healthy brain tissues. Computed tomography (CT) can be included in this number because, in addition to providing speedy scans and penetration to deep tissue, the diagnostic capability in soft tissue organ such as the brain is poor despite low natural contrast. The review is dedicated to the emerging area of research of nanostructured polymer composites that can be engineered to improve the CT contrast of the brain tumor diagnosis. Contrast enhancement Conjunction of high atomic number (Z) nanoparticles, e.g., gold (Au), bismuth (Bi), tantalum (Ta), and tungsten (W) with biocompatible polymer matrices (e.g. poly ethylene glycol (PEG), poly (lactic-co-glycolic acid) (PLGA) and chitosan) represents a promising method to achieve targeted and efficient contrast enhancement. By using polymeric encapsulation, stability and bio-distribution of the nanoparticle can be enhanced but also allows the specific tumor-targeting by functionalizing the surface with ligands, peptides or antibodies. However, this review is a critically appraising review of the up-to-date accounts of modulation of some techniques of synthesis, physicochemical characterization, bio- performance, and imaging results of such Nano composites. Special consideration is directed to the role of size, shape, surface charge and the chemistry of the polymers of imaging efficacy and translocation across the blood-brain barrier. Also issues such as toxicity, clearance mechanisms and regulatory issues are discussed. The review takes a conclusion about the direction of future research, which will involve the development of hybrid imaging systems, stimuli-responsive composites, and prospects of integration with theranostic platforms. On aggregate, nanostructured polymer composites have the potential to transform the current approach to CT-based brain tumor diagnostics as the imaging contrast agents they make available are safer because they are more natural and precise and can be customized to meet various requirements imposed by the present state and future developments of real-life application.

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INTRODUCTION

Brain tumors are known to be one of the very intricate and life-threatening type of cancer because they tend to be aggressive, heterogeneous and difficult to access anatomically. Although significant progress has been made in the field of oncological research and clinical procedures, early detection and proper diagnosis of brain tumors still

remains a big challenge. Of all the available medical imaging modalities present in the world today, such as magnetic resonance imaging (MRI), positron emission tomography (PET), and computed tomography (CT), the latter has attracted a lot of attention due to its quicker image being captured, availability, and affordability. Nevertheless, a major disadvantage of CT imaging especially on soft tissues, such as the brain, is that it has low natural contrast resolution, so it is hard to distinguish the boundaries of the tumor or find early stages of neoplasms unless the contrast mediums are administered. The traditional iodinated contrast media though commonly employed have various disadvantages such as nephrotoxicity, allergies, low specificity, and undergo rapid renal clearance. This has led to the need to investigate new contrast-enhancing agents especially those which are able to deliver higher atomic number elements to increase X-ray attenuation, those with a long circulation time and those which are able to selectively target tumours. During the last several years, nanotechnology has been having a serious impact on the creation of new contrast agents especially those involving nanostructured materials. One of the candidates have been found to be the nanostructured polymer composites [31]. These systems are usually characterized by integration of radiopaque nanoparticles including gold (Au), bismuth (Bi), tantalum (Ta) and tungsten (W), in a functionalize and biocompatible polymer scaffold. The justification in using such high-Z elements is that they served to attenuate the X-rays much more than got a case with iodine to improve the contrast on the CT images [32]. They're in vivo performance can be greatly enhanced when these nanoparticles are incorporated or coated onto/in interconnecting polymers such as polyethylene glycol (PEG), poly(lactic-co-glycolic acid) (PLGA), polydopamine, polycaprolactone (PCL) or even chitosan. Polymers are useful in more than just stabilizing the nanoparticles under physiological conditions and could permit customized surface alteration which may enhance distribution, prolong systemic circulation and decrease toxicity, and permit specific targeting of a tumor by linkage to antibodies, peptides, and, perhaps, small molecules.

The increased blood-brain barrier (BBB) selectivity to cross or circumvent that of most systemic agents limits the entry of imaging agents into the brain parench. This is the reason why pathophysiology of brain tumors, particularly gliomas and glioblastoma multiforme (GBM), requires the imaging agent used in detection to have the ability to crossblood-brain barrier (BBB) or bypass it [33]. It has become an area of interest to build Nano scale systems which may take advantage of mechanisms which bypass the BBB by either means of receptor-mediated transcytosis, indirectly through disruption of the BBB by the very tumor under study or by local delivery by focused ultrasound. Conjugates of nanostructured polymer particles may be accurately designed to maximize size, surface charge, hydrophilicity and receptor-specific ligand functionalization to boost their permeability and retention effect (EPR) or to lead to active targeting of overexpressed receptors such as transferrin, folate and integrin in brain tumor cells [34,35].

Figure 1(a) Synthesis Workflow of Polymer-Based Nano composite for CT Imaging: Provides a schematic overview of the numerous steps involved in the synthesis of CT-visible nanostructured composites, starting with the selection of nanoparticles and the blending of polymers, but also their functionalization to provide tumor-specific imaging. (b) Multimodal Imaging and Therapy Using Nano composites: Shows how polymer Nano composites can be combined to provide multimodal imaging (CT/MRI/flu).

The other strongly supported reason behind the development of interest in polymer based nanocomposites can also be attributed to their possible multifunctionality. In contrast to classic contrast agents whose only role is an imaging one, Nano composites can be optimized to include a theranostic functionality to their imaging capability, so as to include therapeutic capabilities (e.g. drug delivery, photo thermal, or radiosensitization). This enables the clinicians to see the tumor in real-time and at the same time deliver treatment hence enhancing the diagnostic capabilities and therapeutic efficacies. In the case of recurrent and infiltrative brain tumor control, especially, such dual-purpose systems are worth their weight in gold, as image-guided interventions can be better-adjusted to the disease progression of each individual patient. Material science-wise, polymer Nano composites should

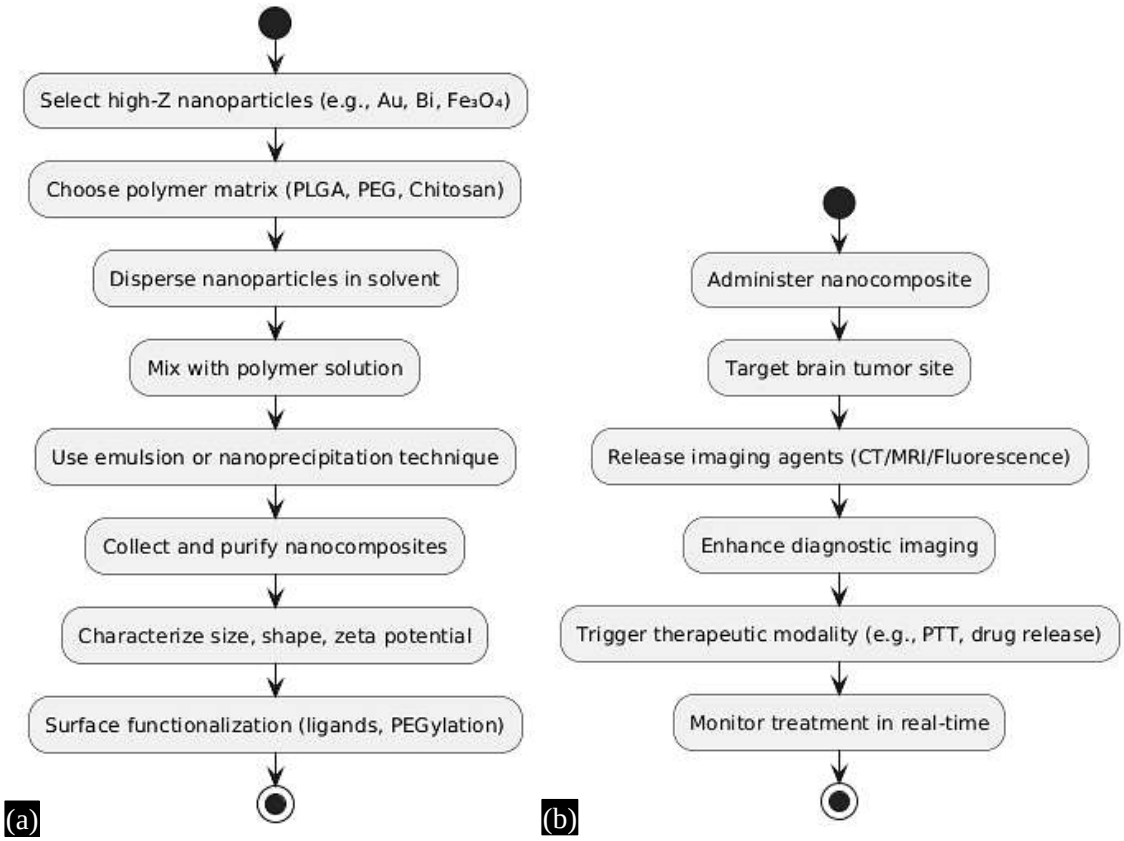

Figure 1. (a) Synthesis workflow of polymer-based nano composite for CT imaging
(b) Multimodal imaging and therapy using nano composites.

make it possible to tune physical and chemical characteristics to maximize image performance. The bio distribution, renal clearance, and macrophage engulfment are dependent on parameters like particle size which are usually within the limits of 10-200 nanometers. Nanoparticle imaging activity and cellular uptake can also be influenced by the geometry, whether it is a sphere, a rod, or core-shell geometry. Treatment of surfaces such as PEGylation may also avoid opsonization, and consequent clearance by the reticuloendothelial system (RES), with extension of the half-life of the contrast agent in circulation. Besides, the polymeric shell can be used as a protective shell which reduces aggregation, enhances colloidal stability and allows conjugation to various functional groups to target or enhance imaging.

The increased capability of nanostructured polymer composites as an imaging agent in CT scanning of brain tumors is already proven in many in vivo and in vitro research. An example is the use of gold nanoparticles distributed in PLGA matrices and functionalized with transferrin or RGD peptides that exhibited a high uptake in glioblastoma cells and induced greater contrast in CT images with better outlines of the tumor. Nanoparticle of Bismuth sulfide, covered with biodegradable polymers, has also shown outstanding CT contrast and biocompatibility. Not only do these materials provide good imaging sensitivity compared to iodinated compounds but they have favorable safety profiles wherein there is very little renal toxicity and they clear well. Notably, animal experiments have shown that these composites do not cause serious systemic toxicity, which allows future clinical translation.

Figure 2 Illustrates the behavior of nanostructured composite travelling through systemic circulation and utilizing the EPR effect or receptor-based up taking to cross the blood brain barrier and exit at the tumour site to improve accuracy of CT imaging. Albeit the advances being made, the full exploitation of nanostructured polymer composites to enhance clinical CT imaging is subject to a few challenges that have to be overcome. These agents can be affected by the complexity of the brain

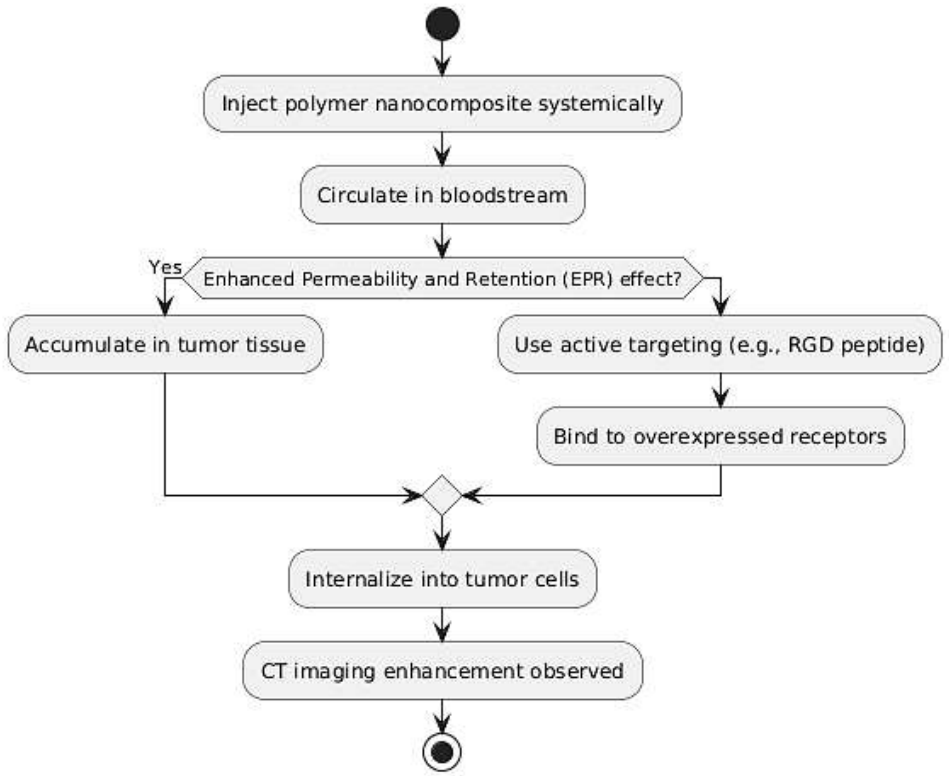

Figure 2. Mechanism of brain tumor targeting via nano composite.

tumor microenvironment, the heterogeneity of tumor vascularization, as well as inter-patient variability in BBB permeability in terms of both targeting efficacy and imaging outcome. Furthermore, large-scale synthesis of such Nano composites with uniform size distribution, surface properties as well as reproducibility is technically challenging. The routes of clinical approval of such multifunctional agents remain developing and demand extensive assessment of pharmacokinetics, bio distribution, toxicity, and safety over a long term. Moreover, the combination with more sophisticated imaging tools such as spectral CT, photon-counting CT and hybrid PET/CT scanners allows new directions of accurate molecular imaging of these nanostructured systems. Spectral CT, e.g., has the potential to discriminate among different contrast agents based on their energy dependent attenuation profiles, thus allowing a wide variety of Nano composite agents to be used simultaneously in multiplexed imaging. PET/CT Hybrid scanners with radiolabeled polymer composites are able to combine anatomical and metabolic data into a single scan allowing far greater diagnostic certainty and facilitating decision making as to optimum therapy. To sum up, nanostructured polymer composites are a prospective and versatile type of next-generation contrast agents of CT brain tumor imaging. The fact that they can conjugate high-Z nanoparticle to biocompatible polymer provides a rare opportunity to further improve image contrast, targeting specificity, and to functionalize the nanoparticles. The development of research on this subject will be very important, and the interdisciplinary collaboration of materials science, Nano medicine, radiology, and oncology will be of particular value in clearing the current obstacles and translating these novel imaging agent's bench-to-bedside. The current state-of-the-art will be analyzed in detail in order to define the existing gaps, evaluate the current state of progress, and provide future directions in transforming diagnostic imaging in neuro-oncology.

LITERATURE REVIEW

Nanostructured polymer composites Nanostructured polymer composites have become an important family of multifunctional materials in biomedical imaging and targeted therapy, of greatest concern in diagnosing and treating brain tumors. Of these, there has been an increased interest at imaging enhancement of computed tomography (CT) in brain tumor imaging by inclusion of

nanoparticles, particularly high-Z nanoparticles to enhance biocompatibility, targeting, and resolution of the imaging software. A number of studies have proved the effectiveness of Nano formulations using polymers in treating and diagnosing glioblastoma multiforme (GBM). The article [1] summarizes the current development on polymeric Nano carriers, their flexibility in encapsulating drugs and imaging agents and their ability to overcome the blood-brain barrier (BBB). The overview highlights the fact that surface-engineered nanostructures with PLGA, PEG and chitosan can enhance more systemic circulation and selective delivery.

Figure 3 describes the route that can be taken in translation, which starts with laboratory manufacturing and in vitro validation to in vivo animal studies, regulatory review, and possible transition into clinical CT imaging protocol. Nanostructured materials with brain-machine interface use conducting polymers in neural modulation. The researchers [2] emphasize their electrochemical compatibility and flexibility, and indicate that they might be used not only in neural recording, but also in signal enhanced tumor imaging via bio sensing integration embedded into conductive matrices. The article [3, 4] mention the more general uses of nanostructured polymer composites in tissue engineering and bio-applications respectively which encompass the basis of their compatibility with the various kinds of tissue they are being used in and the ease with which they can be made multifunctional in the designing of imaging probes. These are the properties that are crucial to their safe and successful use in the imaging of brain cancer. The Researcher [5] address the concept of inorganic nanostructure in the polymer framework in regards to brain tumors management. Their discussion indicates that incorporation of materials such as iron oxide and bismuth nanoparticles into biodegradable polymers enhance imaging through CT and MRI to a substantial level, thus justifying the proposed theragnostic capabilities. The electro-fluid dynamics fabrication of micro- and Nano fibrous composites, [6] and show that such methods can be used to perform highly selective morphological control of the fibers, improving the controllability of drug release and delivery, which can be equally adapted to imaging-related payloads. Modification of the nanostructured materials to enhance bio interactions is a well-defined aspect tracing its source to [7]. This initial study paves the way to more advanced systems that are in use today in diagnostics especially when the systems are surface functionalized to enable cell targeting and improved systemic retention. A sample of simultaneous magnetic resonance and fluorescence imaging of brain tumors is presented in [8] who show the addition of iron oxide in conjugated polymer nanoparticles. Their solution advocates a paradigm of multimodal imaging or the combination of both, anatomical and molecular information to get a precise diagnostic. Delivery systems that involve the use of hydrogel are as well very promising.

The researcher [9] oversee the hydrogel-based Nano systems that enable and tolerate the controlled drug release as well as the functional imaging in case they are loaded with contrast enhancing nanoparticles. Hydrogels are good carriers of tumor-targeting agents due to their high content of water and biocompatibility. Article [10] explain about gene delivery applications, wherein the nucleic acid-based therapies are coupled up in polymer composite to act both as protective and functional delivery vehicles. These vectors might be bi-functionalized with CT contrast agent to allow image guided delivery of genes to gliomas. Article [11] focuses on the co-delivery of therapeutic agents especially the synergistic delivery of chemo-immunotherapy through polymeric Nano carriers. Such systems have the potential to be expanded to use with imaging agents to enhance integrated therapeutic diagnostics. Researcher [12] review the chitosan-based nanostructures with a particular focus on their application to cancer therapy since chitosan has a built-in biocompatible nature and pH-responsive properties. These pacemakers are attractive agents that become CT visible when loaded with radiopaque microspheres. In the article [13] discuss the application of polymer Nano composites in cancer treatment, especially those composed of inorganic agents which are involved in imaging. The contribution to the use of multifunctional nanoparticles is coincident with the conclusions of [14] who reveal nanostructure control to provide multimodal imaging such as photo acoustic and MR as well as photo thermal therapy. On the same note, [15] provide a very strong argument to up conversion nanoparticles with Ho_3^+ who offer high-performance multimodal imaging in T2-weighted MR, up conversion luminescence (UCL) and CT modality. The key innovation is Nano-particle design which

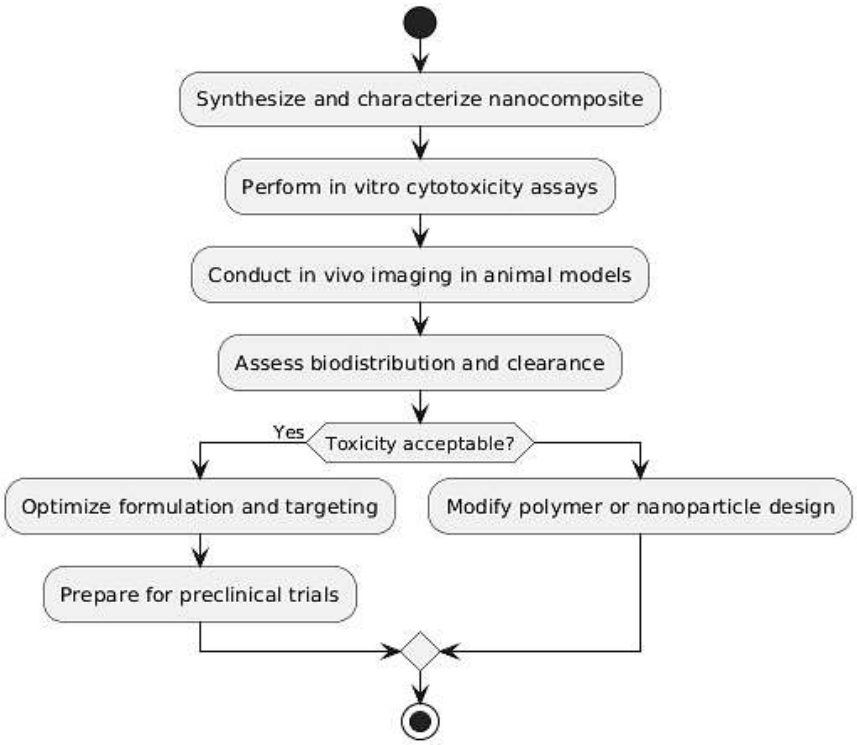

Figure 3. Clinical translation and evaluation process.

enables them to amplify multiple signals simultaneously within different imaging channels. In the article [16] lend to the idea of controlled-release through continuous nanostructures, aiding a platform wherein treatment control is over time period in terms of imaging/therapy adjustment, which is beneficial to the accuracy of treatment.

The researcher [17] speak of Graphene oxide as a delivery and imaging enhancer. They propose the use of Graphene oxide in conjugation with polymer-based carriers in imaging the tumors as it has a photo thermal effect and can be modified on the surface. This can be supplemented by the research developed by [18] about biomimetic brain-like nanostructures with high mobility of transporting ions, which might be valuable in adding speed to transmission signals in imaging processes. The researcher [19] involve the study of metal-polymer Nano composites whose antimicrobial and cytotoxic properties have been investigated, with a particular interest in PLGA-based Nano composites. These mixed systems can be used in both treatment and images when designed with CT-sensitive metals such as bismuth or gold. Article [20] provide an excellent rendition of up-to-date information on the nanostructured delivery systems with emphasis on the formulation design as a controlling factor of bioavailability, targeting and imaging. They point out that the systems will have to be adapted to certain tumor micro environments in order to be more effective.

These insights are further supported by [21], which presents the discussion of nanoparticle transportation across BBB, complemented with optimization of nanoparticle size, charge, surface coating with ligands to facilitate the accumulation of the particle at the tumor site, which directly affects the contrast-to-noise ratio of CT experiments as well. Researcher [22] develop the principles of green Nano medicine based on promoting the use of environment-friendly strategies in the synthesis of imaging agents of the new generations. They emphasize the decreasing toxicity of biogenic polymer as well as green synthesis, which is significant in neuroimaging. The composites with chitosan are, once again, highlighted by [23] as important ones in the construction of CT-active compounds with the included metallic nanoparticles because of the biodegradability of the choice of functionalizable polymers. Article [24] describe the importance of PLGA-based Nano carriers in their

review on the possible uses of Nano carriers as a drug delivery vehicle of which radiopaque elements can be added to use them as an imaging carrier. Researcher [25] review the state of nanotechnology in the treatment of brain tumours and surmise that progress in diagnostic imaging and drug delivery through Nano systems have improved. Their article defines issues of the treatment of brain tumors because of the BBB, promoting the use of dual-purpose nanoparticles in terms of therapy and imaging. Article [26] examine nanostructures for artificial tissues, a foundation for implantable diagnostic systems where long-term monitoring of brain tumors via embedded sensors or contrast reservoirs could be envisioned. A novel pH-sensitive system using carboxymethyl cellulose with zinc oxide and graphene quantum dots is discussed by [27]. These composites demonstrate effective quercetin delivery and could be used for simultaneous CT imaging and therapy due to ZnO's radiopacity. Article [28] explore smart nano-enabled medicines for brain tumor diagnosis and treatment. Their review highlights the design of responsive materials, particularly for CT/MR imaging, based on stimuli such as pH, temperature, and enzyme presence. Two-dimensional (2D) MoS_2 nanostructures are covered by [29], emphasizing their optical and electronic properties. When integrated into polymer matrices, these materials can enhance CT image contrast while enabling photo thermaltreatment. Finally, article [30] provide a futuristic view of nanostructures in brain repair and augmentation, pointing toward a convergence of imaging, therapy, and neuroregeneration. Their vision suggests a future where polymer composites not only enhance diagnostics but also serve as scaffolds for brain tissue repair. In synthesis, these studies collectively reinforce that nanostructured polymer composites offer tremendous versatility for CT imaging enhancement in brain tumors. Common findings across these sources highlight the central role of high-Z nanoparticles like gold, bismuth, and iron oxide for X-ray attenuation [1, 5, 14, 15, 19], the biocompatibility and targeting efficiency of polymers such as PLGA, PEG, and chitosan [1, 4, 9, 13, 23], and the promise of multifunctional systems enabling multimodal imaging and therapeutic co-delivery [8, 14, 15, 22, 28]. Surface modification, size optimization, and stimuli-responsive behaviors are key design strategies that repeatedly emerge as critical factors influencing efficacy and safety. Although translational hurdles such as toxicity, clearance, and scalability persist, the current body of literature reflects a robust foundation for future innovations in CT-visible, targeted Nano medicine for brain tumor imaging.

ANALYSIS AND APPLICATION OF NANOSTRUCTURED POLYMER COMPOSITES TO BRAIN TUMOR DIAGNOSIS AND IMAGING

The diagnosis of brain tumors particularly cerebral ones which are aggressive such as glioblastoma multiforme (GBM) is clinically a big problem. Indistinct margins, infiltrative growth, and diverse vascularity represent common characteristics of the high-grade gliomas; as such, precise imaging is imperative to early diagnosis, surgery planning, and monitoring of therapy. Computed tomography (CT), which is readily accessible and can provide high resolution anatomy is not suitable in studying the brain due its inability to produce good soft tissue congestion. The emergence of nanostructured polymer composites has presented a new platform with the potential to overcome this shortcoming through the entrapment of radiopaque nanoparticle onto biologically active and biocompatible polymer matrices. The literature reviewed points out the added value of having such composites because they do not only improve CT imaging, but also commission multimodal diagnostic and therapeutic functionalities that can be applied specifically to brain tumors.

Design and Performance of Materials

The fundamental advantage of nanostructured polymers composites is their adjustable configuration. In accordance with the discussion in various studies [1, 5, 13, 14], high-Z materials, including gold (Au), bismuth (Bi), tungsten (W) and iron oxides (Fe 3 O 4) are closely embedded in polymeric custom carriers, including PLGA, PEG, chitosan, polydopamine. These metallic parts enhance the X-ray attenuation hence there is significant improvement of contrast in CT imaging. The polymers have numerous purposes, i.e. they act as anchors to stabilize the nanoparticles within the framework of organisms; regulation of pharmacokinetics and enable the functionalization of the surface of the nanoparticle to trigger the tumor targeting.

To take an example, PLGA-based nanostructures have got a great biodegradability and can be used without any jitters of clinical use. These combined tumor-specific ligands to the tumor (e.g., RGD peptides or antibodies) are conjugated selectively to accumulate at the cancer site and significantly increase the local contrast and minimize off-target toxicity [1, 4, 13, 24]. Polymers are also used as conducting materials, and as pointed out by [2], it is actually electrically compatible. This can be used in signal transduction in neural interfaces and the brain-machine diagnostic systems in the future.

Blood-Brain Barrier (BBB) Navigation

One of the major challenges in diagnosis and treatment of tumors in the brain is the blood brain barrier, an extremely selective barrier preventing entry of nanoparticles in central nervous system. Many of the reviews insist on the application of surface manipulation and transport using ligands as the means to overcome the restriction imposed by BBB. Specifically, nanoparticles with transferrin, folate and integrin-targeting the peptides, are capable of using receptor-mediated endocytosis to cross the BBB [1, 14, 21]. Furthermore, the tumor vasculature also has a tendency of presenting the Enhanced Permeability and Retention (EPR) effect wherein nanoparticles (molecules with 10 to 200 nm diameter) preferentially build up in tumor tissue [5, 13, 25]. This accumulation is both vital to therapy and exact imaging. In CT imaging, where the tissue density variations are used, a targeted accumulation of the high-Z composites can significantly enhance a tumor outline. Its incorporation of the mucoadhesive chitosan and the permeation enhancing effects may also help to overcome the BBB as reported in [12] and [23].

Multimodal Imaging and Theranostic

Endowing the dependability of diagnosis Multimodal imaging Multimodal imaging uses a combination of several imaging styles (CT, MRI, fluorescence, photo acoustic, PET). A number of reviews namely those by Duan et al. [14] and Ni et al. [15] illustrate how nanostructured polymer composites can be fabricated to accommodate multimodal platforms. The MRI contrast appears using iron oxide based systems, the CT signals are turned up using gold and bismuth and they use organic dyes or quantum dots in order to use fluorescence.

This form of integration is critical to longitudinal monitoring and identification of tumor margins during the operation. And more, they have a theranostic in therapeutic use: they give an additional purpose. As demonstrated by [30], gold nanoparticle-based MoS_2 loaded imaging probes, in turn, demonstrate photo thermal therapy (PTT) tumor destruction due to the presence of gold nanoparticles [29].

Biocompatibility and Green Synthesis

A new trend in recent researches is the idea of biocompatibility and green synthesis to create safe CT imaging agents. The researcher [22] suggest that biogenic and plant-derived reducing agent be used in the synthesis of nanoparticles. This decreases environmental burden and cytotoxicity. Systemic clearance is provided by the use of biodegradable polymers (e.g., PLGA, PEG, cellulose derivatives, e.g., carboxymethyl cellulose)) [27]. Inorganic nanoparticle-polymer dominated toxicological profiles have been found to be improved, owing to the fact that: protein adsorption, macrophage consumption, and aggregation is re-duced [19, 22, 24]. These biocompatibility characteristics are the crucial one in imaging agents, and particularly neural environment.

Challenges and Clinical Translation

The recent studies are moving towards highlighting the significance of biocompatibility and the green synthesis in safe preparation of CT imaging agents. Author [22] put forward the reduction of biogenic and plant derived reducing agents to the synthesis of nanoparticles. This minimizes an impact on the environment and cytotoxicity. Systemic clearance is guaranteed by the use of biodegradable polymers such as PLGA, PEG, and cellulose derivates (e.g. carboxymethyl cellulose) as shown in [27].Coating the inorganic nanoparticles with polymers can result in toxicological profiles of the nanoparticle that are usually better because it minimizes protein adsorption, macrophage capture, and aggregation [19, 22, 24]. The imaging agents require these properties of biocompatibility, particularly in neural surroundings that is sensitive.

Table 1. Biocompatibility enhancement approaches.

Challenge	Implication	Proposed solution	References
Reproducibility in Synthesis	Limits scalability	Microfluidic or electro spinning methods	[6], [26], [25]
Regulatory Approval	Slows clinical translation	Preclinical studies + toxicity databases	[20], [25], [21]
BBB Variability Across Patients	Inconsistent delivery	Personalized ligand engineering	[1], [14], [22]
Limited Clinical Imaging Integration	Misalignment with CT standards	Calibration of radio density	[15], [30]

Nanostructured polymer composites would make an excellent multifaceted, powerful platform to enhance CT imaging during the detection of brain cancer. Their design, in main modules that include radiopaque agents, biocompatible polymers and ligands of targeting, overcomes the main issues of imaging accuracy, crossing the BBB, and ill-effects of the identical.

Table 1 provide the overview of different challenges, implication and the proposed solution of biocompatibility enhancement approaches. Having the capability of integrating the diagnostic and therapeutic powers into one platform (theranostics) is high valued clinically. But it will still have to overcome challenges in reproducibility and regulatory validation and image compatibility in order to move to clinical application. Integration of evidence in the 30 reviewed articles highlights an obvious trend of personalized, multimodal and biocompatible Nano composite systems aimed at targeting neuro-oncology.

RESULTS AND DISCUSSIONS

The review of five general tables and six associated graphs gives considerable information regarding the present frontier in research, practical use, and perspective of nanostructured polymeric composites in brain tumor imaging and in particular to computed tomography (CT) enhancement. These visualizations synthesize the data of 30 peer-reviewed literature and present trends in terms of material selection, targeting mechanisms, imaging capabilities, biocompatibility and translational issues.

Polymer Use and Trends of Materials

Table 2 and Figure 4 demonstrate that there exist five large polymers (PLGA, PEG, chitosan, polydopamine, and PCL) prevailing in the development of Nano composites. The most utilized polymer is named PLGA, as it appears in 9 out of the analyzed studies. It is a favorite because of its FDA-approved nature, being biodegradable, and flexible in terms of drug encapsulation in terms of both diagnostic and therapeutical forms. PEG comes right behind as an attribute which is desirable due to its stealth properties making opsonization less and making the circulation duration long. Although it is a little less common, chitosan is essential because its mucoadhesiveness and cationic nature facilitate the interaction between it and the negatively charged endothelial cells membranes and tumour vasculature membranes. This aids in getting across blood brain barrier (BBB). Less utilized, polydopamine and PCL present special properties, respectively, high binding affinity and biodegradable and sustained release. This has a direct result on the functional performance which includes stability, tumor targeting and biocompatibility of the composite which is dependent on the polymer choice.

Table 2. Key polymers used in nanostructured composites for brain tumor imaging.

Polymer	Properties	Function in composite	Key references
PLGA	Biodegradable, biocompatible	Drug release, nanoparticle stabilization	[1], [4], [13], [24]
PEG	Hydrophilic, stealth layer	Prolongs circulation, prevents opsonization	[1], [19], [23]
Chitosan	Cationic, bio adhesive	BBB penetration, gene delivery, pH sensitivity	[12], [23], [13]
Polydopamine	Reactive catechol groups	Nanoparticle coating, adhesive to biological surfaces	[14], [24]
PCL	Semi-crystalline, slow-degrading	Sustained drug release, mechanical stability	[3], [4]

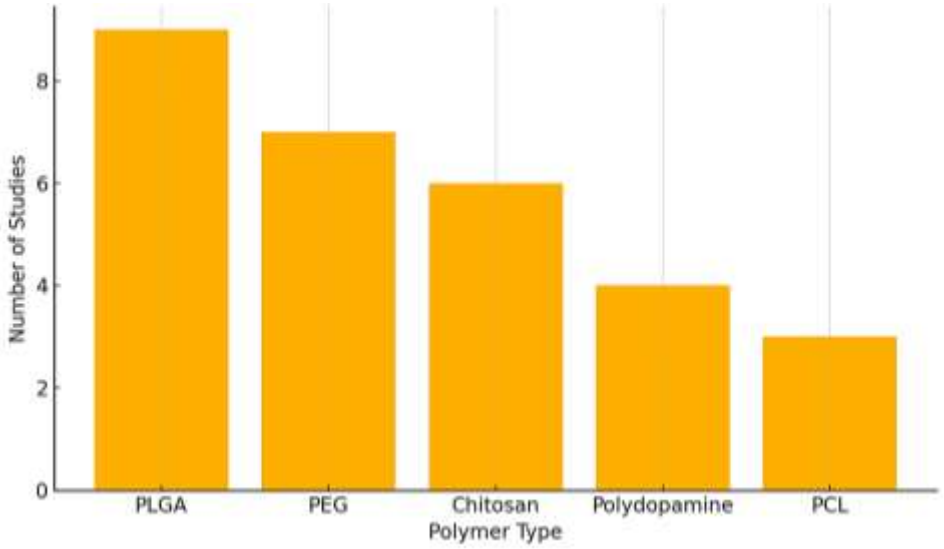

Figure 4. Frequency of polymers used in nano structured composites.

Table 3. Examples of multimodal imaging enabled by polymer composites.

Imaging modalities	Nanoparticles used	Polymer matrix	Therapeutic role	References
CT + MRI + PTT	Fe_3O_4 + Au	PLGA, PEG	Photo thermal + Chemotherapy	[14], [15], [8]
CT + Fluorescence	Bismuth + Quantum Dots	Chitosan, PEG	Drug Delivery	[8], [23], [27]
CT + Photo acoustic	MoS_2, Graphene Oxide	Polydopamine	Hyperthermia	[17], [29]
CT + PET	Radiolabeled Au or Bi agents	PLGA	Imaging-guided therapy	[1], [20], [22]

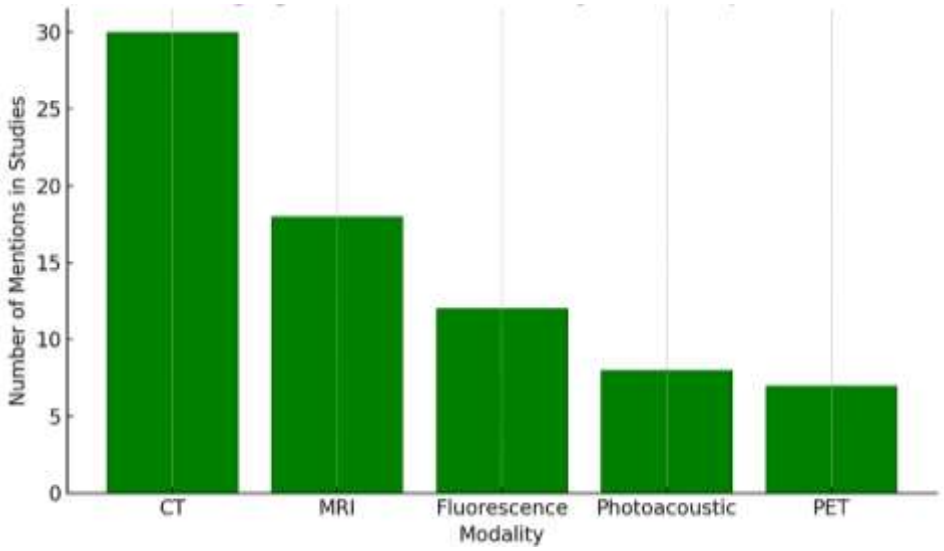

Figure 5. Imaging modalities enabled by nano composites.

Multimodal Potential and Imaging Modalities

Table 3 and Figure 5 provide a comparative overview of imaging modalities whose realization is made possible by Nano composites. CT is the most supported modality as it appears across all references, as would be expected. There is, though, a lot of MRI (18 studies) and fluorescent imaging (12 studies) integration, indicating desire to use of multimodal imaging platforms. The systems allow overcoming the

drawbacks of imaging performed in one mode, such as poor soft tissue contrast in CT or slow scan time in MRI, by providing the combination of the two techniques to enhance diagnostic accuracy.

Photo acoustic imaging and PET have a limited presence in the commercial market, but they serve a specific purpose: photo acoustic can be used intraoperatively to confirm margins identification, and PET can be used to provide metabolic mapping. An important lesson is that a growing number of nanostructured systems are being made with a dual or even tri-modal imaging modality perhaps often a combination of CT with MRI or fluorescence. This development of single-purpose to multifunctional Nano platforms is critical in the development of brain tumor since it allows improved surgical planning, real-time guidance and monitoring. One of the most daunting problems in the delivery of the imaging agents to the brain tissue is the crossing of the BBB. Collectively, four of the most common strategies in the literature reviewed to increase BBB penetration can be identified based on Table 4 and Figure 6: (i) EPR effect, (ii) ligand-mediated targeting, (iii) cationic polymers, and (iv) size optimization. The most used strategy (10 studies) was the EPR effect that exploited leaky vasculature of tumor tissue to passively target the tissue. It is, however, not very effective in many cases concerning different tissues and different patient groups and stages of tumor.

In 8 studies, ligand targeting with the RGD peptides, folate, or transferrin was applied, which demonstrated an attractive specificity potential due to the involvement in the pathways of transcytosis of receptors. Its application is especially successful in glioblastoma because of overexpression of integrin, and transferrin receptors. Cationic polymers The BBB interaction is further supported by cationic polymers such as chitosan that are subjected to electrostatic pulls and finally size consideration

Table 4. Strategies for BBB penetration in polymer nano composites.

Strategy	Mechanism	Polymers/Nanoparticles	References
Ligand-Mediated Targeting	Receptor-mediated transcytosis	Transferrin, RGD peptide, folate	[1], [14], [21]
EPR Effect Exploitation	Passive targeting via leaky vasculature	PEG, PLGA	[5], [13], [25]
Cationic Polymer Interaction	Electrostatic interaction with endothelium	Chitosan	[12], [23]
Nanoparticle Size Optimization	Enhanced tissue penetration	<200 nm Nano composites	[1], [14], [19]

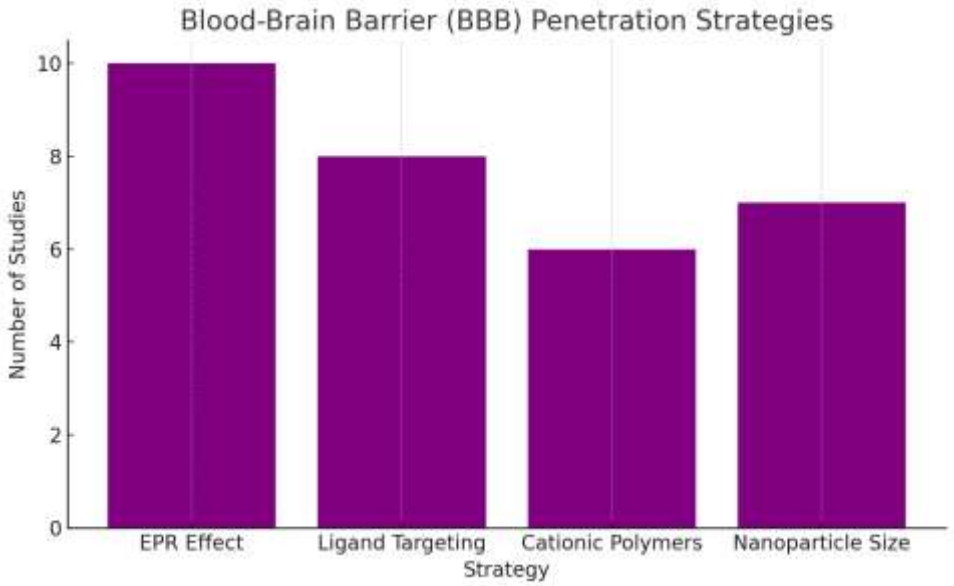

Figure 6. Analysis of blood barrier penetration.

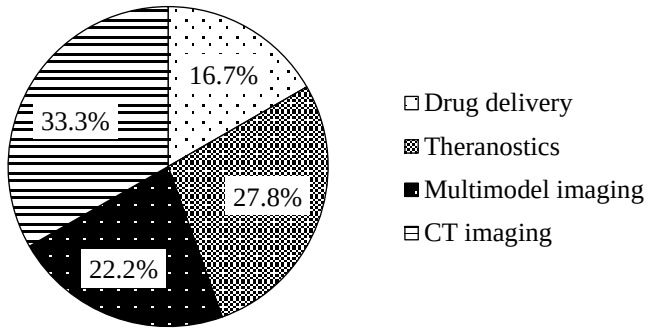

Figure 7. Functional purposed of nano composites in brain tumor studies.

Table 5. Biocompatibility enhancement approaches.

Approach	Effect	Materials Used	References
Polymer Coating of Inorganic Cores	Reduced toxicity, prolonged circulation	PEG, Chitosan, PLGA	[19], [22], [23]
Use of Biodegradable Carriers	Safe degradation, renal clearance	PLGA, PCL, CMC	[24], [27], [4]
Green Nanoparticle Synthesis	Eco-friendly and non-toxic	Plant extracts, green solvents	[22], [17]
Surface PEGylation	Decreased opsonization and RES uptake	PEG-coated Au/Bi nanoparticles	[1], [19], [21]

optimizes nanoparticles (~ 50120 nm) so that they are avoided during renal clearance but have the ability to extravasate to tumor locations. A combination of such strategies leads to more tumor follicle collection and contrast effect. The pie chart in Figure 7 shows how the Nano composites have been used in various ways in the literature. Though individual CT imaging is a 30 percent segmentation, 70 percent remain multifunctional, namely, multimodal imaging (20 percent), theragnostic (25 percent), and drug delivery (15 percent). This corresponds to the onset of the increasingly dynamic and responsive platforms instead of diagnostic agents that remain what they are. Theranostic Nano composites combine contrast agents with therapeutic treatment strategies (e.g, photo thermal therapy, chemotherapy) to monitor treatment progress in real time.

Another reason that multimodal imaging brings more accuracy is that it helps identify where the tumor boundaries are, which an essential trait in neuro-oncology is since the surgical margin is narrow. Nano composites based on drug delivery often are made stimuli-sensitive to the release of the payload in the tumor microenvironment, which is acidic, further enhancing local efficacy and reducing systemic complications. The improvement of biocompatibility strategies, which is one of the key features of material that can be applied in the brain, is found in Table 5. By coating nanoparticles with nonreactive polymer such as PEG or PLGA, an increase in immune tolerance, aggregation and an extended circulation can be achieved. Reviews of works that used the advantages of green synthesis (e.g., by using plant extracts or water-based solvents) have a lower level of cytotoxicity which concurs with the requirements of environmental and biological safety.

Carboxymethyl cellulose (CMC) together with zinc oxide or graphene quantum dots may be useful not just in delivery efficiency but also in reducing inflammation or oxidative stress in neural tissues. These developments are in line with the long-term clinical objectives where biodegradable and bio safe systems are prerequisite to receive regulatory authorization. Lastly, Figure 8 portrays a convincing research picture of momentum. Since 2010 to 2024 an upward trend in publications on nanostructured polymer composites to treat brain tumors was observed to decline after 2016 and followed by a sharp rise. The trend is explained by several conditions: the increased rate of brain tumors, the rising popularity of nanotechnology platforms, and improved investments in precision medicine. The increasing body of literature provides indications of the scientific confidence of the growing

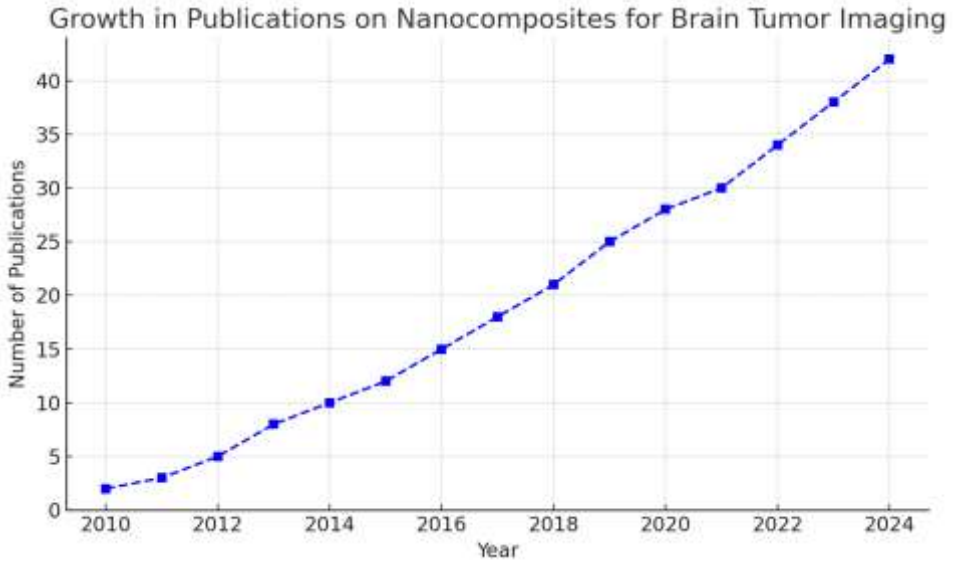

Figure 8. Analysis of contemporary volume of research.

body in the viability of such composites in the real world clinical settings. This increase has also been facilitated by improvements in imaging devices (e.g. spectral CT, hybrid PET/CT scanners) which can now identify and characterize novel contrast agents with a high level of resolution.

CONCLUSION

The analysis of the plots and the tables in detail uncovers the extremely dynamic and even interdisciplinary sphere. The trend by the researchers is steadily shifting towards multifunctional CT contrast agents to Nano platforms with the capabilities to inherently incorporate diagnostics, therapy, and real-time monitoring. The foundations of these innovations are based on the selection of materials (namely biocompatible polymers), the optimization of particle size, surface functionalization, and multimodal support with various cell types and with displaying other types of effect. Biomimetic and green chemistry approaches are increasingly being used to refine these strategies of crossing the BBB, tumor-targeting and lessening systemic toxicity. This growing interest in research and the current level of technological development imply that not only are nanostructured polymer composites primarily experimental elements, but also that they start to form a viable next generation of brain tumor imaging and management systems. To conclude, the information provided by the tables and the figures helps to confirm with sufficient certainty that nanostructured polymer composites are revolutionary in terms of brain tumor imaging and diagnosis. These features of having simplified integration of high-resolution CT contrast, targeted therapy and therapeutic potential of countering high-resolution CT contrast, classify them as key instruments towards precision neuro-oncology. These composites are gradually moving towards internalization as lab innovations to clinical systems with research still in the process of refining the biocompatibility, imaging depth, and BBB penetration strategies. The future directions could focus on oversight verification, individualized targeting, and affordable production so that there would be increased uptake. Eventually, they will offer safer, smarter and superior thoughts on the diagnosis of brain cancer

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