SCIENCEFORECAST
Connecting Research to Drive Scientific Innovation

Review Article
Published: 14 May, 2018

SF Journal of Nanochemistry and Nanotechnology

Functionalization of Magnetic Nanoparticles for Drug Delivery

Abu-Dief AM* and Abdel-Mawgoud AAH

Chemistry Department, Faculty of Science, Sohag University-82524, Egypt

Abstract

Magnetic nanoparticles (MNPs) possess unique magnetic properties and the ability to function at the cellular and molecular level of biological interactions making them an attractive platform as carriers for drug delivery. Recent advances in nanotechnology have improved the ability to specifically tailor the features and properties of MNPs for these biomedical applications. To better address specific clinical needs, MNPs with higher magnetic moments, non-fouling surfaces, and increased functionalities are now being developed for applications in the detection, diagnosis, and treatment of malignant tumors, cardiovascular disease, and neurological disease. Through the incorporation of highly specific targeting agents and other functional ligands, such as fluorophores and permeation enhancers, the applicability and efficacy of these MNPs have greatly increased. This review provides a background on applications of MNPs as carriers for drug delivery and an overview of the recent developments in this area of research.

Keywords: Magnetic nanoparticles; Nanotechnology; Drug delivery

Introduction

Nanoparticles are key focus of research for a wide outspread novel applications, not only because of their fabulous properties, but also due to nano size compared with their bulk counterparts. Among nano materials magnetic nanoparticles are of keen interest to researchers owing to their praise worthy magnetic properties [1-7]. Magnetic nanoparticles (MNPs) are a major class of nanoscale materials with the potential to revolutionize current clinical diagnostic and therapeutic techniques. Due to their unique physical properties and ability to function at the cellular and molecular level of biological interactions, MNPs are being actively investigated as the next generation of magnetic resonance imaging (MRI) contrast agents [8] and as carriers for targeted drug delivery [9]. Although early research in the field can be dated back several decades, the recent surge of interest in nanotechnology has significantly expanded the breadth and depth of MNP research. With a wide range of applications in the detection, diagnosis, and treatment of illnesses, such as cancer [10], cardiovascular disease [11], and neurological disease [12], MNPs may soon play a significant role in meeting the healthcare needs of tomorrow. Numerous forms of MNP with various chemical compositions have been proposed and evaluated for biomedical applications to exploit anoscale magnetic phenomena, such as enhanced magnetic moments and superparamagnetism. Like other nanomaterial-based systems, advances in nanotechnology now allow for precise engineering of the critical features of these fine particles. Composition, size, morphology and surface chemistry can now be tailored by various processes to not only improve magnetic properties but also affect the behavior of nanoparticles *in vivo* [13,14]. In its simplest form, a biomedical MNP platform is comprised of an inorganic nanoparticle core and a biocompatible surface coating that provides stabilization under physiological conditions. Additionally, the application of suitable surface chemistry allows for the integration of functional ligands [15]. This modular design enables MNPs to perform multiple functions simultaneously, such as in multimodal imaging [16], drug delivery and real-time monitoring, as well as combined therapeutic approaches.

As therapeutic tools, MNPs have been evaluated extensively for targeted delivery of pharmaceuticals through magnetic drug targeting (MDT) [17,18] and by active targeting through the attachment of high affinity ligands [19–21]. In the spirit of Ehrlich's "Magic Bullet" [22], MNPs have the potential to overcome limitations associated with systemic distribution of conventional chemotherapies. With the ability to utilize magnetic attraction and/or specific targeting of disease biomarkers, MNPs offer an attractive means of remotely directing therapeutic agents specifically to a disease site, while simultaneously reducing dosage and the deleterious side effects associated with

OPEN ACCESS

Correspondence:
Ahmed M Abu-Dief, Chemistry Department, Faculty of Science, Sohag University-82524, Egypt.
E-mail: *ahmed_benzoic@yahho.com*

Received Date: *07 Apr 2018*
Accepted Date: *10 May 2018*
Published Date: *14 May 2018*

Citation: *Abu-Dief AM, Abdel-Mawgoud AAH. Functionalization of Magnetic Nanoparticles for Drug Delivery. SF J Nanochem Nanotechnol. 2018; 1(1): 1005.*

ISSN 2643-8135

Copyright *© 2018 Abu-Dief AM. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.*

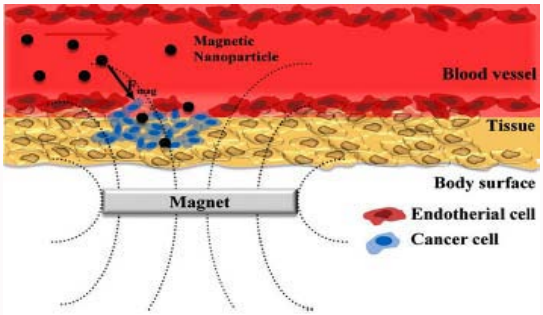

Figure 1: Schematic representation of Magnetic drug delivery system under the influence of external magnetic field. F_{mag} is direction of external magnetic field is targeted.

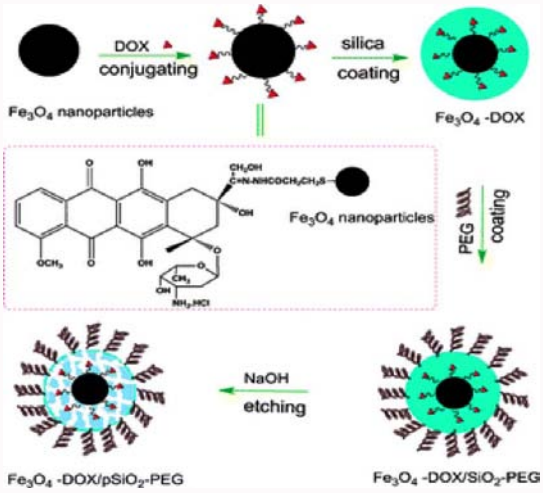

Figure 2: Synthetic Scheme for the development of Doxorubicin loaded magnetic drug delivery system.

nonspecific uptake of cytotoxic drugs by healthy tissue. Also referred to as magnetic targeted carriers (MTC), colloidal iron oxide particles in early clinical trials have demonstrated some degree of success with the technique and shown satisfactory toleration by patients [23,24]. Although not yet capable of reaching levels of safety and efficacy for regulatory approval, pre-clinical studies indicated that some of the short comings of MDT technology, such as poor penetration depth and diffusion of the released drug from the disease site, can be overcome by improvements in MTC design [25,26]. Furthermore, the use of MNP as carriers in multifunctional nanoplatforms as a means of real-time monitoring of drug delivery is an area of intense interest [27,28]. A significant challenge associated with the application of these MNP systems is their behavior *in vivo*. The efficacy of many of these systems is often compromised due to recognition and clearance by the reticuloendothelial system (RES) prior to reaching target tissue, as well as by an inability of to overcome biological barriers, such as the vascular endothelium or the blood brain barrier. The fate of these MNP upon intravenous administration is highly dependent on their size, morphology, charge, and surface chemistry. These physicochemical properties of nanoparticles directly affect their subsequent pharmacokinetics and bio distribution [29]. To increase the effectiveness of MNPs, several techniques, including reducing size and grafting nonfouling polymers, have been employed to improve their "stealthiness" and increase their blood circulation time to maximize the likelihood of reaching targeted tissues [30,31].

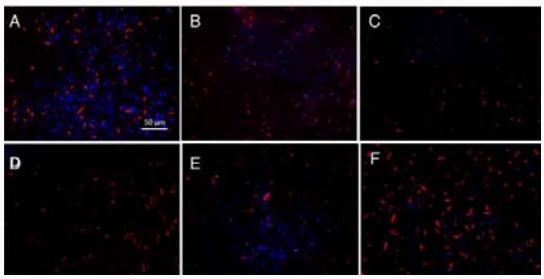

Figure 3:

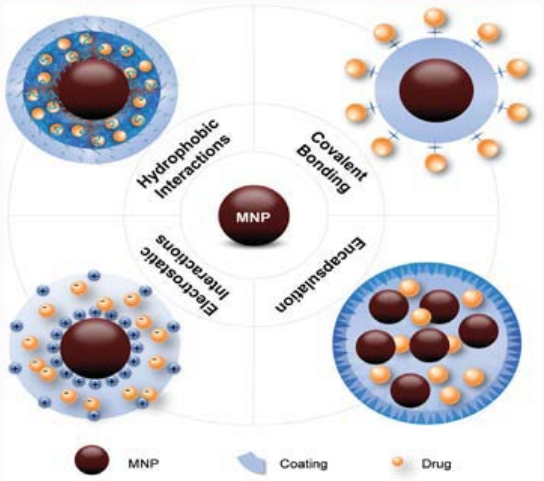

Figure 4:

Literature Survey on Utilizing of Magnetic Nanoparticles as Carrier for Drug Delivery

Here we show spot lines about preparation and functionalization of magnetic nanoparticles for drug delivery.

Mody [2014] et al. [32]

Studied tumor hypoxia, or low oxygen concentration, which is a result of disordered vasculature that lead to distinctive hypoxic microenvironments not found in normal tissues. Many traditional anti-cancer agents are not able to penetrate into these hypoxic zones, whereas, conventional cancer therapies that work by blocking cell division are not effective to treat tumors within hypoxic zones. Under these circumstances the use of magnetic nanoparticles as a drug delivering agent system under the influence of external magnetic field has received much attention, based on their simplicity, ease of preparation, and ability to tailor their properties for specific biological applications. Hence in this review article we have reviewed current magnetic drug delivery systems, along with their application and clinical status in the field of magnetic drug delivery (Figure 1 and 2).

Tietze [2015] et al. [33]

Studied nanoparticles have belonged to various fields of biomedical research for quite some time. A promising site-directed application in the field of nanomedicine is drug targeting using magnetic nanoparticles which are directed at the target tissue by means of an external magnetic field. Materials most commonly used for magnetic drug delivery contain metal or metal oxide nanoparticles, such as superparamagnetic iron oxide nanoparticles (SPIONs). SPIONs consist of an iron oxide core, often coated with organic

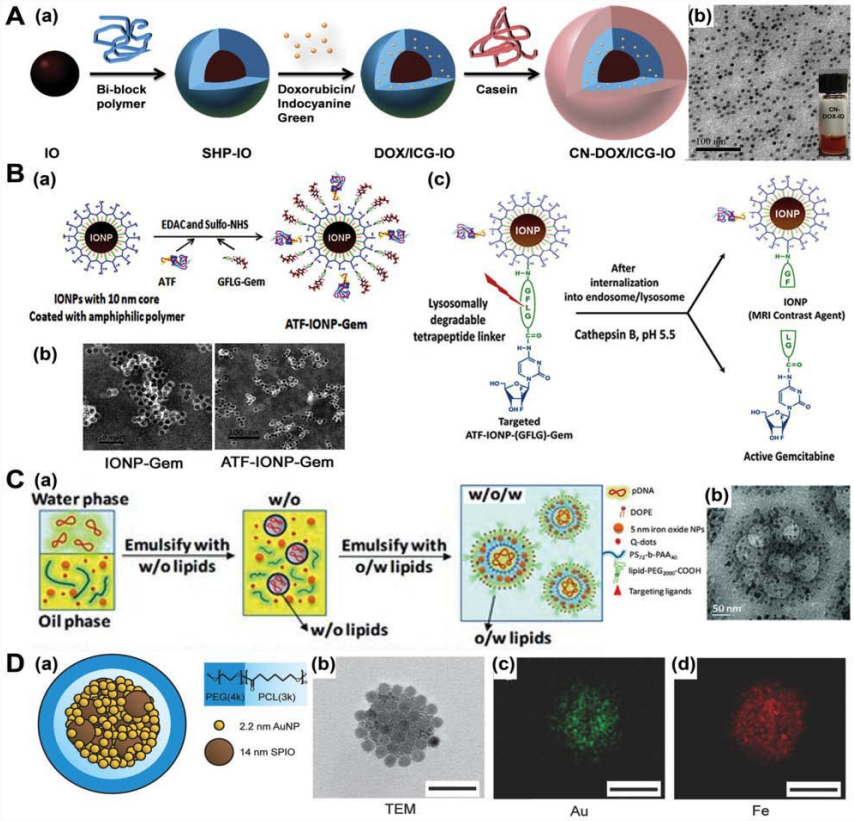

Figure 5:

materials such as fatty acids, polysaccharides or polymers to improve colloidal stability and to prevent separation into particles and carrier medium. In general, magnetite and maghemite particles are those most commonly used in medicine and are, as a rule, well-tolerated. The magnetic properties of SPIONs allow the remote control of their accumulation by means of an external magnetic field. Con- jugation of SPIONs with drugs, in combination with an external magnetic field to target the nanoparticles (so-called "magnetic drug targeting", MDT), has additionally emerged as a promising strategy of drug delivery. Magnetic nanoparticle-based drug delivery is a sophisticated overall concept and a multitude of magnetic delivery vehicles have been developed. Targeting mechanism–exploiting, tumor-specific attributes are becoming more and more sophisticated. The same is true for controlled-release strate- gies for the diseased site. As it is nearly impossible to record every magnetic nanoparticle system developed so far, this review summarizes interesting approaches which have recently emerged in the field of targeted drug delivery for cancer therapy based on magnetic nanoparticles.

Niemirowicz [2016] et al. [34]

Niemirowicz et al. designed to assess the antifungal/anti-biofilm and hemolytic properties of two polyene antibiotics, amphotericin B (AMF) and nystatin (NYS), attached to the surface of magnetic nanoparticles (MNP) against clinical isolates of Candida species and human red blood cells, respectively. The developed nanosystems, MNP@AMF and MNP@NYS, displayed stronger fungicidal activity than unbound AMF or NYS. Synergistic activity was observed with a combination of polyenes and MNPs against all tested Candida strains. Nanosystems were more potent than unbound agents when tested against Candida strains in the presence of pus, and as agents able to prevent Candida biofilm formation. The observed inactivation of catalase Cat1 in Candida cells upon treatment with the nanosystems suggests that disruption of the oxidation–reduction balance is a mechanism leading to inhibition of Candida growth. The significant decrease of polyenes lytic activity against host cells after their attachment to MNPs surface indicates improvement in their biocompatibility (Figure 3).

Magnetic nanoparticles enhance antifungal properties of polyene antibiotics due to induction of oxidative stress and membrane disruption. Percentage of dead cells (red stained by propidium iodide) after treatment with polyene-coated MNPs (C, F) compared to antibiotics in free form (B, E). Confocal images (magnification 40×) of propidium iodide uptake of Candida glabrata blastospores (red color indicates dead cells; blue color indicates live cells). Control sample (A). Treatment with: AMF (B), AMF coated magnetic nanoparticles (C), magnetic nanoparticles (D), NYS (E) and NYS coated magnetic nanoparticles (F). (G) Kinetics of R6G efflux by C. glabrata strains after treatment with AMF, NYS, magnetic nanoparticles, MNP@AMF and MNP@NYS. Immobilization of polyene antibiotics on the MNP surface increases and accelerates rhodamine release.

Huang [2016] et al. [35]

Emerged magnetic nanoparticles (MNPs) as a promising theranostic tool in biomedical applications, including diagnostic imaging, drug delivery and novel therapeutics. Significant preclinical and clinical research has explored their functionalization, targeted delivery, controllable drug release and image-guided capabilities. To further develop MNPs for theranostic applications and clinical translation in the future, we attempt to provide an overview of the recent advances in the development and application of MNPs for drug delivery, specifically focusing on the topics concerning the

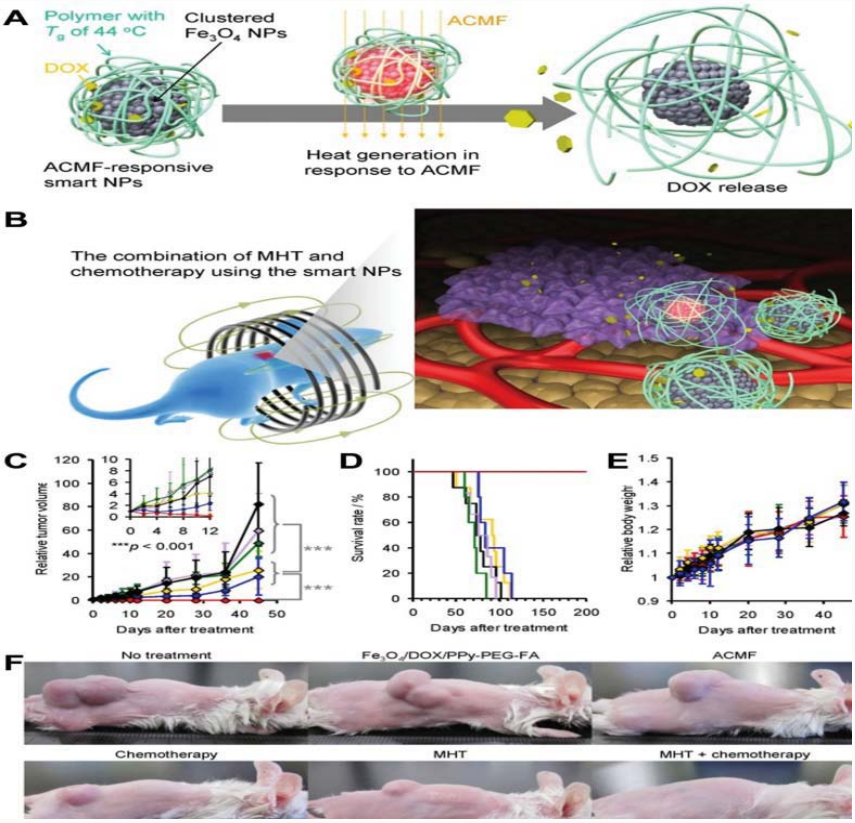

Figure 6:

importance of biomarker targeting for personalized therapy and the unique magnetic and contrast-enhancing properties of theranostic MNPs that enable image-guided delivery. The common strategies and considerations to produce theranostic MNPs and incorporate payload drugs into MNP carriers are described. The notable examples are presented to demonstrate the advantages of MNPs in specifi c targeting and delivering under image guidance. Furthermore, current understanding of delivery mechanisms and challenges to achieve efficient therapeutic efficacy or diagnostic capability using MNP-based nanomedicine is discussed (Figure 4).

Illustration of the methods used for loading drugs into MNP nanocarriers, including loading through hydrophobic interactions, electrostatic interactions, covalent bonding and direct encapsulation (Figure 5).

MNP carriers developed with different drug loading methods

A) Loading through hydrophobic interactions. a) Illustration of drug (Dox) loaded into the hydrophobic layer of a bi-block polymer and wrapped with milk casein protein (CN-DOX-IO); b) Typical TEM images for obtained CN-DOX-IO. B) Loading through covalent bonding. a) Diagram of the conjugation of ATF peptides and GFLG-Gem conjugates to IONPs; b) Typical TEM images for non-targeted IONP-Gem and targeted ATF-IONP-Gem with negative staining; c) Schematic diagram of gemcitabine release from ATF-IONP-Gem by enzyme cleavage. C) Loading through electrostatic interactions. a) Schematic illustration for preparing lipo-polymersome (LPP) nanocarriers with three compartment structures: 1) a cationic lipids/pDNA core, 2) an IO nanoparticles–polymer composite interlayer, and 3) a relatively neutral lipids shell; b) Typical TEM images of as-prepared LLP nanocarriers D) Loading by direct encapsulation. a) Schematic of gold- and IONP-loaded polymeric micelles (GSMs). Gold and IONP are self-assembled into the hydrophobic core of micelles, stabilized with the amphiphilic di-block co-polymer PEG-b-PCL; b) TEM image of a single GSM. (all scale bars = 100nm); c–d) Energy dispersive X-ray spectroscopy analysis on GSM with Au and Fe signals, respectively (Figure 6).

Combination chemotherapy and hyperthermia with MNP carriers

A) Illustration of MNP carriers that produce heat in response to AMF and sequentially release Dox. B) Illustration of cancer treatment with the combination of magnetic hyperthermia and chemotherapy using the smart NPs. Change of C) tumor volume, D) survival rate, and E) body weight: non-treated mice (black), mice treated with chemotherapy (yellow), mice exposed to AMF (green), mice injected with Fe_3O_4 /Dox/PPy-PEG-FA NPs intratumorally (purple), mice treated with magnetic hyperthermia (blue), and mice treated with the combination of magnetic hyperthermia and chemotherapy (red). F) Photographs of non-treated mice, mice treated with chemotherapy, mice exposed to AMF, mice injected with Fe_3O_4/Dox/PPy-PEG-FA NPs intratumorally, mice treated with magnetic hyperthermia, and mice treated with the combination of magnetic hyperthermia and chemotherapy 45 days after treatment.

Patitsa [2017] et al. [36]

Studied therapeutic targeting of tumor cells with drug nanocarriers relies upon successful interaction with membranes and efficient cell internalization. A further consideration is that engineered nanomaterials should not damage healthy tissues upon contact. A critical factor in this process is the external coating of drug delivery

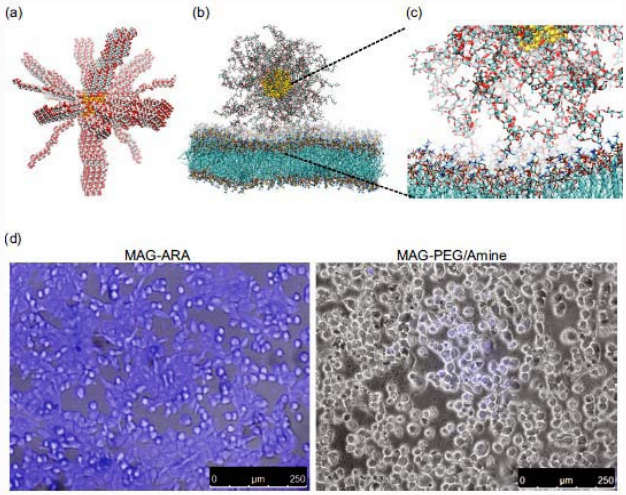

Figure 7:

nanodevices. Using *in silico*, *in vitro* and *in vivo* studies, we show for the first time that magnetic nanoparticles coated with polyarabic acid have superior imaging, therapeutic, and biocompatibility properties. We demonstrate that polyarabic acid coating allows for efficient penetration of cell membranes and internalization into breast cancer cells. Polyarabic acid also allows reversible loading of the chemotherapeutic drug Doxorubicin, which upon release suppresses tumor growth *in vivo* in a mouse model of breast cancer. Furthermore, these nanomaterials provide *in vivo* contrasting properties, which directly compare with commercial gadolinium-based contrasting agents. Finally, we report excellent biocompatibility, as these nanomaterial cause minimal, if any cytotoxicity *in vitro* and *in vivo*. We thus propose that magnetic nanodevices coated with polyarabic acid offer a new avenue for theranostics efforts as efficient drug carriers, while providing excellent contrasting properties due to their ferrous magnetic core, which can help the future design of nanomaterials for cancer imaging and therapy (Figure 7).

Membrane interaction and internalization of MAG-ARA

(a) Initial configuration of the MAR-ARA NP in vacuum. Fe is shown in yellow, oxygen in red, carbon in cyan in van der Waals representation. (b) Final configuration of the MAR-ARA NP in contact with a DPPC bilayer. Fe is shown in yellow, oxygen in red, carbon in cyan in van der Waals representation. (c) Example of L-arabinose and D-galactose hydrogen bonds as they interact with the phosphate group of DPPC. Hydrogen atoms have been omitted for clarity. Oxygen is shown in red, carbon in cyan in licorice representation. (d) Superposition of a confocal fluorescence image (blue) and a bright filed image from MDA-MB-231 breast cancer cells incubated with MAG-ARA and control (MAG-PEG/Amine) NPs.

Hamdipoor [2018] et al. [37]

Studied magnetic drug targeting which is a promising technique that can deliver drugs to the diseased region, while keeping the drug away from healthy parts of body. Introducing a human in the control loop of a targeted drug delivery system and using inherent bilateralism of a haptic device at the same time can considerably improve the performance of targeted drug delivery systems. In this paper, we suggest a novel intelligent haptic guidance scheme for steering a number of magnetic nanoparticles (MNPs) using forbidden region virtual fixtures and a haptic rendering scheme with multi particles. Forbidden region virtual fixtures are general classes of guidance

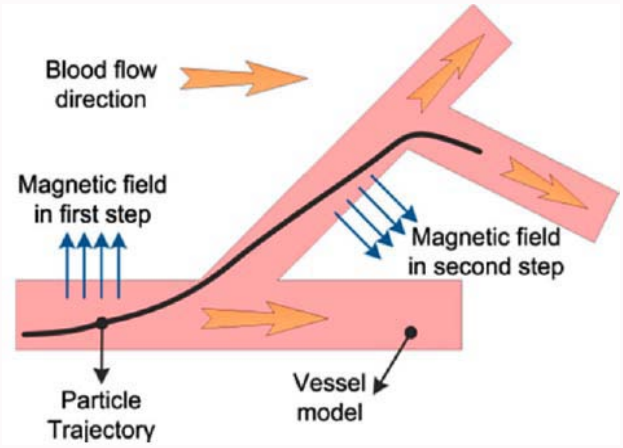

Figure 8:

modes implemented in software, which help a human-machine collaborative system accomplish a specific task by constraining a movement into limited regions. To examine the effectiveness of our proposed scheme, we implemented a magnetic guided drug delivery system in a virtual environment using a physics-based model of targeted drug delivery including a multi-branch blood vessel and realistic blood dynamics. They performed user studies with different guidance modes: unguided, semi virtual fixture and full virtual fixture modes. We found out that the efficiency of targeting was significantly improved using the forbidden region virtual fixture and the proposed haptic rendering of MNPs. They can expect that using intelligent haptic feedback in real targeted drug delivery systems can improve the targeting efficiency of MNPs in multi-branch vessels.

Conclusion

The development of MNPs has been greatly accelerated in the past decade by advances in nanotechnology, molecular cell biology, and small-animal imaging instrumentation. MNPs of various formulations have been developed to diagnose and treat diseases for which conventional therapy has shown limited efficacy. In particular, the use of MNPs as drug carriers has drawn enormous attention, as it holds great potential of providing new opportunities for early cancer detection and targeted therapies. This technology will not only minimize invasive procedures, but also reduce side effects to healthy tissues, which are two primary concerns in conventional cancer therapies. Improvements to MNP technology, such as enhanced magnetic properties, non-biofouling surface coatings, and the integration of multifunctional ligands, continue to be evaluated in an effort to bring these nanostructures from the bench-top to the clinic. A critical component of this translation is the continued investigation into the relationships between the physicochemical properties of these nanostructures and their behavior *in vivo*, which is currently poorly understood. By incorporating advances in nanoscale engineering, molecular imaging, and novel therapeutics, MNP platforms have the potential to enable physicians to diagnose and treat diseases, such as cancer and cardiovascular disease, with greater effectiveness than ever before.

References

1. MAA El-Remaily, AM Abu-Dief. $CuFe_2O_4$ nanoparticles: an efficient heterogeneous magnetically separable catalyst for synthesis of some novel propynyl-1H-imidazoles derivatives. Tetrahedron. 2015; 71: 2579-2584.
2. M Abu-Dief, IF Nassar and WH Elsayed. Magnetic $NiFe_2O_4$ nanoparticles:

efficient, heterogeneous and reusable catalyst for synthesis of acetylferrocene chalcones and their anti-tumour activity Appl. Organometal. Chem. 2016; 30: 917–923.

3. Ahmed M Abu-Dief and Samar K Hamdan. Functionalization of Magnetic Nano Particles: Synthesis, Characterization and Their Application in Water Purification. Amer. J. Nano sciences. 2016; 2: 26-40.

4. Ahmed M Abu-Dief, Abdelbaky, SM Mohammed, David Martínez-Blanco, Zakariae Amghouz, Santigo García-Granda. Effect of chromium substitution on the structural and magnetic properties of nanocrystalline zinc ferrite. Materials Chemistry and Physics. 2016; 174: 164-171.

5. MAA El-Remaily, A M. Abu-Dief and RM El-Khatib. A robust synthesis and haracterization of super paramagnetic $CoFe_2O_4$ nanoparticles as an efficient and reusable catalyst for green synthesis of some heterocyclic rings. Appl. Organometal. Chem. 2016; 30: 1022–1029.

6. Adel A Marzouk, Ahmed M Abu-Dief and Antar A Abdelhamid. Hydrothermal preparation and characterization of $ZnFe_2O_4$ magnetic nanoparticles as an efficient heterogeneous catalyst for the synthesis of multi substituted imidazoles and study of their anti-inflammatory activity. Appl Organometal Chem. 2018; 32: e3794.

7. Ahmed M Abu-Dief and Shimaa Mahdy Abdel-Fatah. Development and Functionalization of Magnetic Nanoparticles as Powerful and Green Catalysts for Organic Synthesis. Beni-Suef University Journal of Basic and Applied Sciences. 2018; 7: 55-67.

8. C Corot, P Robert, JM Idee, M Port. Recent advances in iron oxide nanocrystal technology for medical imaging. Advanced Drug Delivery Reviews. 2006; 58: 1471–1504.

9. J Dobson. Magnetic nanoparticles for drug delivery. Drug Development Research. 2006; 67: 55–60.

10. M Ferrari. Cancer nanotechnology: opportunities and challenges. Nature Reviews. Cancer. 2005; 5: 161–171.

11. SA Wickline, AM Neubauer, PM Winter, SD Caruthers, GM Lanza. Molecular imaging and therapy of atherosclerosis with targeted nanoparticles. Journal of Magnetic Resonance Imaging. 2007; 25: 667–680.

12. C Corot, KG Petry, R Trivedi, A Saleh, C Jonkmanns, JF Le Bas, et al. Macrophage imaging in central nervous system and in carotid atherosclerotic plaque using ultra small superparamagnetic iron oxide inmagnetic resonance imaging. Investigative Radiology. 2004; 39: 619–625.

13. P Tartaj, MD Morales, S Veintemillas-Verdaguer, T Gonzalez-Carreno, CJ Serna. The preparation of magnetic nanoparticles for applications in biomedicine,Journal of Physics. D, Applied Physics. 2003; 36: R182–R197.

14. AK Gupta, M Gupta. Synthesis and surface engineering of iron oxide nanoparticles for biomedical applications. Biomaterials. 2005; 26: 3995–4021.

15. SE McNeil. Nanotechnology for the biologist. Journal of Leukocyte Biology. 2005; 78: 585–594.

16. L Frullano, TJ Meade. Multimodal MRI contrast agents. Journal of Biological Inorganic Chemistry. 2007; 12: 939–949.

17. Senyei, K Widder, G Czerlinski. Magnetic guidance of drug-carrying microspheres. Journal Of Applied Physics. 1978; 49: 3578–3583.

18. T Neuberger, B Schopf, H Hofmann, M Hofmann, B von Rechenberg. Superparamagnetic nanoparticles for biomedical applications: possibilities and limitations of a new drug delivery system. Journal of Magnetism and Magnetic Materials. 2005; 293: 483–496.

19. VP Torchilin. Multifunctional nanocarriers. Advanced Drug Delivery Reviews. 2006; 58: 1532–1555.

20. Y Zhang, N Kohler, MQ Zhang. Surface modification of superparamagnetic magnetite nanoparticles and their intracellular uptake. Biomaterials. 2002; 23: 1553–1561.

21. O Veiseh, C Sun, J Gunn, N Kohler, P Gabikian, D Lee, et al. Optical and MRI multifunctional nanoprobe for targeting gliomas. Nano Letters. 2005; 5: 1003–1008.

22. F Winau, O Westphal, R Winau. Paul Ehrlich — in search of the magic bullet. Microbes and Infection. 2004; 6: 786–789.

23. AS Lubbe, C Bergemann, H Riess, F Schriever, P Reichardt, K Possinger, et al. Clinical experiences with magnetic drug targeting: a phase I study with 4′-epidoxorubicin in 14 patients with advanced solid tumors. Cancer Research. 1996; 56: 4686–4693.

24. AS Lubbe, C Alexiou, C Bergemann. Clinical applications of magnetic drug targeting. Journal of Surgical Research. 2001; 95: 200–206.

25. AS Lubbe, C Bergemann, J Brock, DG McClure. Physiological aspects in magnetic drug-targeting. Journal of Magnetism and Magnetic Materials. 1999; 194: 149–155.

26. JM Gallo, U Hafeli. Preclinical experiences with magnetic drug targeting: tolerance and efficacy and clinical experiences with magnetic drug targeting: a phase I study with 4¢-epidoxorubicin in 14 patients with advanced solid tumors. Cancer Research. 1997; 57: 3063–3064.

27. N Kohler, C Sun, J Wang, MQ Zhang. Methotrexate-modified superparamagnetic nanoparticles and their intracellular uptake into human cancer cells. Langmuir. 2005; 21: 8858–8864.

28. N Kohler, C Sun, A Fichtenholtz, J Gunn, C Fang, MQ Zhang. Methotrexate-immobilized poly (ethylene glycol) magnetic nanoparticles for MR imaging and drug delivery. Small. 2006; 2: 785–792.

29. C Chouly, D Pouliquen, I Lucet, JJ Jeune, P Jallet. Development of superparamagnetic nanoparticles for MRI: effect of particle size, charge and surface nature on biodistribution. Journal of Microencapsulation. 1996; 13: 245–255.

30. R Gref, M Luck, P Quellec, M Marchand, E Dellacherie, S Harnisch, et al. 'Stealth' corona-core nanoparticles surface modified by polyethylene glycol (PEG): influences of the corona (PEG chain length and surface density) and of the core composition on phagocytic uptake and plasma protein adsorption. Colloids and Surfaces. B, Biointerfaces. 2000; 18: 301–313.

31. SM Moghimi, AC Hunter, JC Murray. Long-circulating and target-specific nanoparticles: theory to practice. Pharmacological Reviews. 2001; 53: 283–318.

32. Vicky V Mody, Arthur Cox, Samit Shah, Ajay Singh, Wesley Bevins, Harish Parihar. Magnetic nanoparticle drug delivery systems for targeting tumor. Appl Nanosci. 2014; 4: 385–392.

33. Rainer Tietze, Jan Zaloga, Harald Unterweger, Stefan Lyer, Ralf P Friedrich, Christina Janko. Magnetic nanoparticle-based drug delivery for cancer therapy. Biochemical and Biophysical Research Communications. 2015; 468: 463–470.

34. Katarzyna Niemirowicz, Bonita Durnaś, Grażyna Tokajuk, Katarzyna Głuszek, Agnieszka Z Wilczewska, Iwona Misztalewska, et al. Magnetic nanoparticles as a drug delivery system that enhance fungicidal activity of polyene antibiotics. Nanomedicine: Nanotechnology, Biology, and Medicine. 2016; 12: 2395–2404.

35. Jing Huang, Yuancheng Li, Anamaria Orza, Qiong Lu, Peng Guo, Liya Wang, et al. Magnetic Nanoparticle Facilitated Drug Delivery for Cancer Therapy with Targeted and Image-Guided Approaches. Adv. Funct. Mater. 2016; 26: 3818–3836.

36. Maria Patitsa, Konstantina Karathanou, Zoi Kanaki, Lamprini Tzioga, Natassa Pippa, Constantinos Demetzos, et al. Magnetic nanoparticles coated with polyarabic acid demonstrate enhanced drug delivery and imaging properties for cancer theranostic applications. Scientific Reports. 2017; 7: 775.

37. Vahid Hamdipoor, Muhammad Raheel Afzal, Tuan-Anh Le and Jungwon Yoon. Haptic-Based Manipulation Scheme of Magnetic Nanoparticles in a Multi-Branch Blood Vessel for Targeted Drug Delivery. Micromachines. 2018; 9: 14.