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Magnetic nanoparticles in cancer diagnosis and treatment: a review

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ABSTRACT

Diagnosis and treatment of lung cancer have been characterized with a variety of challenges. However, with the advancement in magnetic nanoparticle (MNP) technology, many challenges in the diagnosis and treatment of lung cancer are on the decline. The MNPs have led to many break-through in cancer therapy. This paper seeks to establish the role of MNPs in diagnosis and treatment of lung cancer. It proposes that the existing challenges in the diagnosis and treatment of lung cancer can be addressed through application of MNPs in the process.

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Introduction

In spite of the extreme efforts in the last 50 years, it has only been feasible to slightly, but not considerably, lower the mortality of cancer (Anari et al. 2015). According to the estimates by the US National Cancer Institute, nanomedicine will verify to be trailblazing in the future prevention, diagnostic research, and treatment of cancer (Tiwari 2012).

Lung cancers result from complex, genetic, and epigenetic alterations characterized by stepwise malignant progression of cancer cells in associated with the accumulation genetic changes. Non-small cell lung cancer (NSCLC) accounts for around 85% of all lung cancers. Lung carcinoma (particularly, NSCLC) is the most important reason of cancer-related deaths in the United States and the second widespread cancer in both men and women and is by far the leading reason of cancer death worldwide (Munaweera et al. 2015, Tabatabaei Mirakabad et al. 2016).

Nanotechnology is probable to play a key role in cancer diagnosis by allowing the visualization of the cancer cell at an early step. Magnetic nanoparticles (MNPs) are a most important group of nano-materials with the potential to revolutionize current clinical therapeutic and diagnostic techniques. Apply of nanoparticles based on magnetic in medical uses is a new and highly interdisciplinary field offering great potential in therapeutic and diagnostic testing, *in vitro*, and *in vivo* (Ebrahimi 2016a, Tartaj et al. 2006). First medical applications used iron powder or magnetite directly in treatment methods. Recently, MNPs have become a very noticeable tool in cancer therapy. The nanoparticles including of nickel, cobalt, and

iron can be guided by a magnetic field owing to their ferromagnetism. In biomedicine, mainly, iron oxide nanoparticles are being used (Figure 1).

Currently, there are nanoparticles that are being applied successfully in the diagnosis of cancer and have allowed the health care practitioners to image the specific areas in the body where cancer resides. For instance, the use of magnetic particles together with the MRI scans has greatly helped in increasing the image contrast (Ebrahimi et al. 2016b). The contrast leads to the detection of various small cancer metastases that would otherwise be undetectable (Abdeen and Praseetha 2013). Also, the nanoparticles are used in the physical process of destroying the tumor tissues through the MNP hyperthermia have determined that nanoparticles have multiple applications in the diagnosis and treatment of different types of cancer (Colombo et al. 2012) (Figure 2).

The technology uses the magnetic field to oscillate the iron oxide MNPs that creates heat (Abdeen and Praseetha 2013). The heat works in the form of kinetic energy to significantly reduce the size of the tumor or cancer tissue. Future research will have to focus on the pharmacokinetics of the MNPs to ensure that the particles can remain in the patient's body for longer periods compared to the current period. Also, future research will focus on how the body can react positively to the MNPs (Fallahzadeh et al. 2010). One of the most pursued areas of investigates in the development of cancer treatment strategies is delivery of anticancer drugs by blend with functionalized superparamagnetic iron oxide nanoparticles (SPIONs) to their targeted site. SPION induced

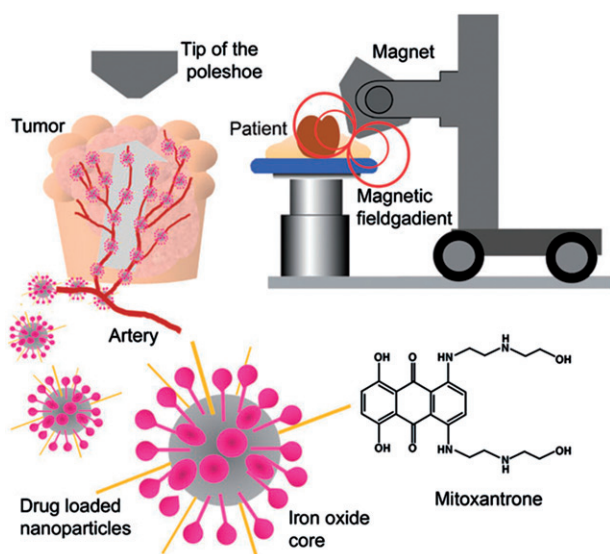


Figure 1. The role of magnetic drug targeting. Nanoparticles-based magnetic iron oxide are functionalized with a chemotherapeutic agent and injected directly into the arterial supply of the tumor (Dürr et al. 2013, Namiki et al. 2009)

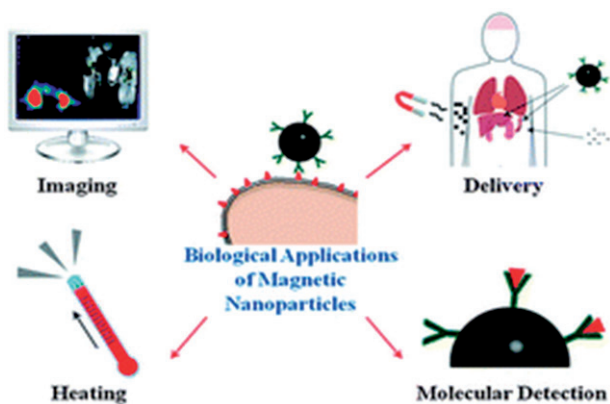


Figure 2. Multiple applications of nanoparticles in the diagnosis and treatment of different types of cancer (Colombo et al. 2012)

hyperthermia has also been used for localized killing of cancer cells. Despite their feasible biomedical apply, modification in gene expression profiles, interruption in iron homeostasis, oxidative stress, and changed cellular responses are some SPION-related toxicological aspects which necessitate owing deliberation (Anderson and Shive 2012, Mahmoudi et al. 2011, Soppimath et al. 2001).

Drug delivery

SPIONs have paying attention in the past decades because of their probable uses in tumor therapy, imaging, and drug delivery (McCarthy and Weissleder 2008, Petters et al. 2014, Salloum et al. 2009). MNPs appear to be extremely suitable for drug delivery. In fact, they can be prepared in diverse sizes and can be functionalized (surface-coated) in order to carry various molecules. Several issues need to be considered when using MNPs as carriers counting colloidal stability and biocompatibility (Faraji et al. 2010, Furlani 2010, Tartaj et al. 2003). The valuable use of MNPs for biomedical applications like targeted drug delivery depends on different factors associated to the size and magnetism of the biocompatible nanoparticles (Akbarzadeh et al. 2012a, Sun et al. 2008) (Figure 3).

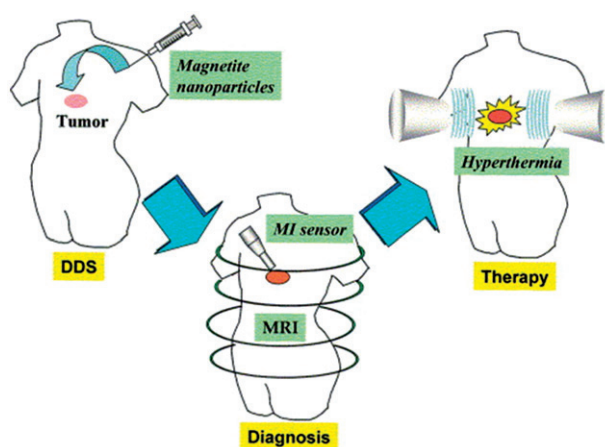


Figure 3. Scheme of the treatment strategy using magnetic nanoparticles (MNPs). Functionalized MNPs accumulate in the tumor tissues by the drug delivery system (DDS) (Sun et al. 2008)

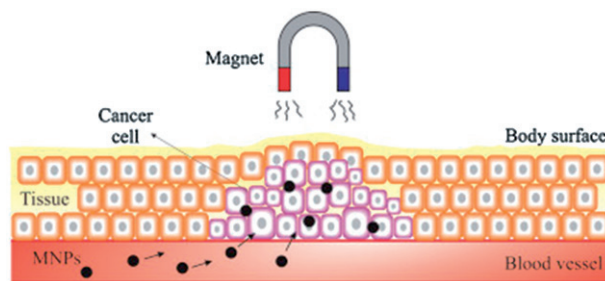


Figure 4. Scheme image of a magnetic drug delivery system

Nanoparticle based drug delivery systems may solve the insurmountable obstacle of treating neurological diseases: delivery across the blood–brain barrier (Nasrabadi et al. 2016, Kreuter 2001). But issues of possible embolization with MNPs aggregate in capillaries and the essential for large distances between the pathological site and external magnetic field still in present as a problem (Schroeder et al. 1998).

The most important problem on chemotherapy treatment is the non-specificity of the drugs, damaging both sick and healthy cells. To solve this problem, as you can see in Figure 4, MNPs can be used to deliver the therapeutic agents to the desired target area, maintaining the particles at the exact location during the drug release, when combined with an exterior magnetic field.

Furthermore, a controlled drug delivery based on MNPs should be able to uphold drug levels inside the necessary concentration range for treatment, avoiding the over dosage and decreasing side effects (Lima-Tenório et al. 2015).

Direct injection of MNP into the tumor

Although most commercially available products using nanoparticles are found as contrast agents, recently milestones have been reached regarding anticancer therapy (Akbarzadeh et al. 2012b). Nowadays, the delivery of MNPs is based on a direct intra-tumoral injection, which restrictions the clinical application of this method (Gobbo et al. 2015). More development of tumor targeting by the SPIONs needs a particular surface coating, which can provide the specificity of these

nanoparticles delivery to the tumor cells *in vivo* (Gupta and Gupta 2005, Maier-Hauff et al. 2011).

Methods and materials

This study applies a review of literature as a method of understanding the application of MNPs in the diagnosis and treatment of lung cancer. It focuses on recent scholarly works in the areas of nanotechnology, MNPs, and lung cancer. Currently, these areas have attracted much scholarly interest, and there are many research works that focus on the areas. Sukumar et al. (2013) identifies that 23% of cancer-related deaths result from lung cancer. They attribute the situation to lack of early diagnosis with about 50% of the cases identified in stage 4, which reduces chances of survival. In the United States, about 85% of the lung cancers are categorized as non-small cell (Hadjipanayis et al. 2010, Kimura et al. 2009, Sukumar et al. 2013). Since it is difficult to access the deeper parts of the lung to conduct conventional therapy, the treatment of lung cancer becomes more complicated (Munaweera et al. 2015). However, development in the area of nanotechnology is changing the situation. Nanotechnology has found application in the fields of biomedicine because it can control the delivery of drugs, provide great contrast in the magnetic resonance imaging (Akbarzadeh et al. 2012b) hyperthermia, and promote tissues and cell targeting. All these applications are useful in cancer therapy (Asin et al. 2012a, Daraee et al. 2015). The utility of the nanoparticles derives from their optical and magnetic properties. The optical and magnetic properties are due to the quantum confinement and large surface area effects that are present at the nanoscale (Asin et al. 2012a, Ding et al. 2013, Kong et al. 2012).

Magnetic hyperthermia, which involves the use of superparamagnetic materials to make heat through application of an exterior alternating magnetic fields (AMF), is a non-invasive method for lung tumor remove. The comparatively inert nature of the magnetic substances in the absence of magnetic field and their efficacy in the attendance of AMF make this procedure very appropriate for achieving an on-demand answer (Sadhukha et al. 2013).

Obaidat et al. (2015) have noted that magnetic particle hyperthermia is useful as a local therapy for the removal of tumors from the body. The therapy uses the MNPs to heat the tumor cells and initiate a non-reversible damage to the tumor cells, as well as, the surrounding tissue (Gorjikhah et al. 2016, Obaidat et al. 2015). When MNPs reach the tumor, a magnet oscillates the nanoparticles to heat up the tumor to about 42 °C to 46 °C (Asin et al. 2012b, Obaidat et al. 2015). The temperature is slightly above the normal body temperature of 37 °C, but it is sufficient to damage the cells and prevent the damaging effects of the cancer cells. However, if it is difficult to reach the tumor, the treatment may not be plausible or effective (Asin et al. 2012b, Cervadoro et al. 2013, Gorjikhah et al. 2016, Landi 2013, Obaidat et al. 2015). Confirm that the challenge is mostly due to the low heat conversion rate. Many metals have magnetic properties, but, the Iron oxide nanoparticles are that preferred particles in cancer therapy (Rivas et al. 2012). The iron oxide is proven to be nontoxic and biocompatible. Such properties are important

because they ensure that the patient is comfortable during the therapy. Furthermore, the iron oxide nanoparticles work great with the magnetic force to heat the target area in cancer therapy (Disch et al. 2012). The nanoparticles are given a special coating particularly the aminosilane before the particles are transmitted to the tumor (Rivas et al. 2012). The coating ensures that the nanoparticles move target tissue rather than spreading out to other parts of the body to cause other complications during the hyperthermia. Nanotechnology is an expanding niche that is revolutionizing cancer management and treatment (Babu et al. 2013). Precisely, the nanoscale drug delivery systems are promising in “successful formulation and enhancement of the therapeutic efficacy of many anticancer agents” (Babu et al. 2013, Jiang et al. 2013). Also, the nanoparticles have superior biocompatibility that ensures the protection of the nucleic acid from degradation and delivering the therapeutic genes to the cancer cells. This makes the nanoparticles ideal system for delivery (Akbarzadeh et al. 2012b). However, still, there are several challenges with the various nanoparticle-based therapies. Only a few of the therapies have indicated clinical success. It is difficult identifying the ideal drug delivery system for the various types of novel drugs with diverse physiological features and varying levels of therapeutic activities (Gudoshnikov et al. 2012, Gudoshnikov et al. 2013).

Results and discussion

Cancer has always presented many difficulties during treatment. In most cases, the challenges are prompted by the late diagnosis of the tumor cells. The traditional methods of detecting cancer often detect cancer when it is already at the point where it is very difficult to treat the cancer especially when the traditional methods of treatment such as chemotherapy and surgery are used. The MNPs technology helps in detecting the tumor early and enables adequate treatment (Akbarzadeh et al. 2012b). The technology is commonly used to increase the contrast in the MRI scans (Baviskar et al. 2012, Hadjipanayis et al. 2010) and to specifically target the affected area by monitoring the tumor cells through surface engineering. It facilitates noninvasive targeting and monitoring the tumors in real time to detect small metastases that would otherwise be undetectable.

Other than the imaging purposes, the MNPs are used in MNP hypothermia therapy (Askari et al. 2015). The magnetic particles are targeted to a tissue, and the magnetic energy absorption of the nanoparticles ensures a localized heating of the targeted cell leading to the death of the cell (Rivas et al. 2012). As such, the increase in temperature of the nanoparticle can be used in killing the cancer cells. Iron oxide nanoparticles are biocompatible and nontoxic implying that they are very suitable for hyperthermia (Disch et al. 2012). There are several works that aim at optimizing the design of nanoparticles and provide the appropriate properties that would allow maximization of the heat generated (Rivas et al. 2012). Also, there is the need for an improved heating power rate. Higher rates of heating can ensure that the patient is given low doses of MNPs and a short time of stay of the nanoparticles in the body (Chung et al. 2016, Rivas et al. 2012).

Table 1. Table of specific absorption rate (SAR) values and parameters of nanoparticles

References	Material	Diameter (nm)	F (kHz)	H (kA m ⁻¹)	f × H (10 ⁹ Hz A m ⁻¹)	f × H ² (10 ¹² A ² m ⁻² s ⁻¹)	SAR _{MNP} (10 ³ W kg ⁻¹)	ILP (10 ⁻¹² W m ² s A ⁻² kg ⁻¹)
Jiang et al. (2013)	Fe ₃ O ₄	9	500	37.3	18.7	695.6	152	219
This work	Fe ₃ O ₄	5	523	10	5.2	52.3	20	382
Jiang et al. (2013)	Fe ₃ O ₄	15	500	37.3	18.7	695.6	333	479
Jiang et al. (2013)	Fe ₃ O ₄	12	500	37.3	18.7	695.6	349	502
Cervadoro et al. (2013)	Fe ₃ O ₄	8	100	23.9	2.4	57.1	52.8	924
Cervadoro et al. (2013)	Fe ₃ O ₄	8	100	9.6	1.0	9.2	17.2	1866
Akbarzadeh et al. (2012a)	Fe ₃ O ₄	12.5	600	3.2	1.9	6.1	21.98	3577
Akbarzadeh et al. (2012b)	Fe ₃ O ₄	15.7	600	3.2	1.9	6.1	28.32	4609

However, there are concerns about the possibility of the direct nanoparticles reaching the damaged tissue (Rivas et al. 2012). While the external magnetic field can ensure that the nanoparticles flow to the target cells, the organic and inorganic molecules in the body can bind on the nanoparticles' surface and trap them from reaching the target area (Gudoshnikov et al. 2012). But, recently an approach that could solve the problem was approved. The approach involves introducing iron oxide nanoparticles that are coated with aminosilane in treating solid brain tumors through hyperthermia therapy (Thakor and Gambhir 2013). The main challenge to the application of nanoparticles in the treatment of lung cancer lies in the low rate of energy conversion in the study, Cervadoro et al. (2013) has identified that the heat absorption rate depends on various factors (Cervadoro et al. 2013). The factors include the nanoparticle characteristics like surface properties, size, and shape, and the functional conditions of the AMF such as the frequency and strength (Obaidat et al. 2015). The study suggests that the MNPs' heating efficiency can be enhanced through proper design of the shape, surface, and composition selection. From the study, the table below represents the list of the specific absorption rate (SAR) values and different nanoparticle parameters (Obaidat et al. 2015) (Table 1).

Conclusion

Lung cancer is a form of cancer that requires early detection and effective treatment as a way of preventing the dangers of the disease. Because of the many challenges posted by the traditional methods of detecting and treating lung cancer, nanoparticles present the opportunity for ensuring the early detection and effective treatment. While there are significant barriers to the effective use of nanoparticles in the diagnosis and treatment of lung cancer, progress is being made, and the use of nanotechnology will be the best strategy for diagnosing and treating lung cancer.

Disclosure statement

The authors report no declaration of interest. The authors alone are responsible for the content and writing of the paper.

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