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# MAGNETIC NANOPARTICLES USING FOR IMAGING AND TREATMENT CANCER

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**Abstract:** Nanotechnology based on the use of submicronic particles of inorganic and/or organic origin has the potential to revolutionalize the cancer therapy; distinguish benign and malignant tumours, if applied magnetic relaxometry, with using superconducting quantum interference device (SQUID) sensors ,which is fast and potentially more specific than mammography because it is designed to detect tumour-targeted iron oxide magnetic nanoparticles and will reducing the false positive rates and effects of therapy is now real. Especially, iron oxide super paramagnetic nanoparticles which are coated with polymers have shown clinical utility in cancer imaging and drug delivery and some formulations are now FDA-approved for use in the clinic. The prospects of magnetic nanoparticles in cancer imaging and treatment are reviewed.

**Keywords:** Submicromic Nanoparticle, Magnetic Relaxometry, SQUID, Mammography.

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## INTRODUCTION

Early detection and treatment of cancer are critical factors for a favorable prognosis. Cancer diagnosis using nanotechnology is an emerging field.Theranostic nanoparticles that simultaneously deliver both imaging and therapeutic agents have gained significant attention for disease management in recent years. Disease management not only includes the highly specific diagnosis and treatment of the diseased cells, but also the monitoring of the drug delivery process and therapeutic efficacy Advances in nanotechnology have permitted new possibilities for theranostics, which are defined as the combination of therapy and imaging within a single platform. Nanotechnology is applied to molecular imaging in the form of imaging probes capable of enhancing the sensitivity of the image and the specificity toward the target tissue. [1-9]

Super paramagnetic iron oxide nanoparticles (SPION) have emerged as an MRI contrast agent for tumour imaging due to their efficacy and safety. Their utility has been proven in clinical applications with a series of marketed SPION-based contrast agents. Extensive research has been performed to study various strategies that could improve SPION by tailoring the surface chemistry and by applying additional therapeutic functionality. Research into the dual-modal contrast uses of SPION has developed because these applications can save time and effort by reducing the number of imaging sessions.[10]

In addition super magnetic iron oxide nanoparticles are at the leading edge of the rapidly developing field of nanotechnology. Magnetic nanoparticles for cancer therapy and diagnosis have been developed on the basis of their unique physico-chemical properties not present in other materials. Their versatility is widely exploited in such diverse techniques as cell and macromolecule separation and purification, immunoassays, targeted drug delivery, controlled material release, electromagnetic hyperthermia, gene therapy, or magnetic resonance imaging.[11]

In this review we concentrate on the physical principles of magnetic drug targeting and biomedical applications of this technique. We examined several databases, Pub Med, ISI Web of Knowledge, and Scopus, for the period 1985-2009, with specific attention to studies that used targeting of magnetic nanoparticles especially in the therapy and diagnostics of tumours. [12]

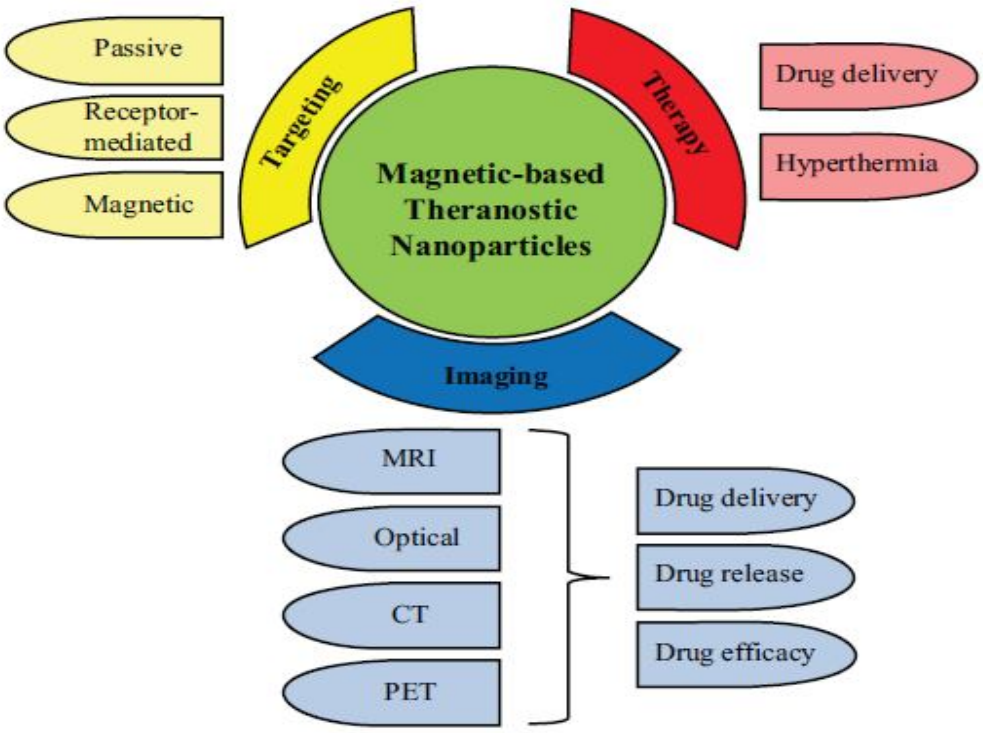


**Fig:1 Mechanism of action of Magnetic –based Thernostic Nanoparticles**

**MAGNETIC PROPRETIES OF NANOPARTICLES [3]**

1) Magnetic particles for bioseparation consist of one or more magnetic cores with a coating matrix of polymers, silica or hydroxylapatite with terminal functionalized groups.

2) The magnetic core generally consists either of magnetite ($Fe_3O_4$) or maghemite (gamma $Fe_2O_3$) with superparamagnetic or ferromagnetic properties.

3) On request, we can produce magnetic cores made with magnetic ferrites, such as cobalt ferrite or manganese ferrite.

**Theory of Magnetic Nanoparticles**

MNPs are composed of ferromagnetic elements such as iron, cobalt, nickel, or their oxides and alloys MNPs made of iron oxide (magnetite Fe3O4 or magnemite Fe2O3)and gadolinium (chelated organic gadolinium complexes) have been widely used as contrast agents in MRI for biological applications due to their ability to dissociate into iron and oxygen inside the body, which can safely be eliminated and utilized in metabolic and oxygen transport systems. When fabricated into nanoparticles of approximately 10 nm in diameter, iron oxide nanoparticles begin to exhibit a superparamagnetic behavior (superparamagnetic iron oxide nanoparticles,

SPIONs) leading to improved dispersive properties in the absence of a magnetic field, and laterguided to accumulate to the site of interest in the presence of a magnetic field, which is of great importance in targeted drug delivery applications .MNPs also possess low cytotoxicity and have been approved by the United States Food and Drug Administration (FDA) for clinical MRI applications.[13-17]

***Preparation of $Fe_3O_4$ Nanoparticles***

$Fe(acac)_3$(2.12 g, 6.0 mol) was dissolved in a mixture of benzyl ether and oleylamine (30ml:30ml) and were stirred by magnetic stirrer. The solution was dehydrated at 120 °C for 1h using Dean-Stark apparatus and under flow of argon. After 1 h, temperature was raised quickly to 270 °C for 2 h under argon. The reaction mixture was cooled down to room temperature and then ethanol (80 ml) was added to the dark brown mixture and precipitated with centrifuge at 5000 rpm. The product was re-dispersed in 30 ml n-hexane and stored at 4 °C.18 Figure 1 Step 1 represents this process. The yield was 1.8 g, i.e. 84.9 %.[18-19]

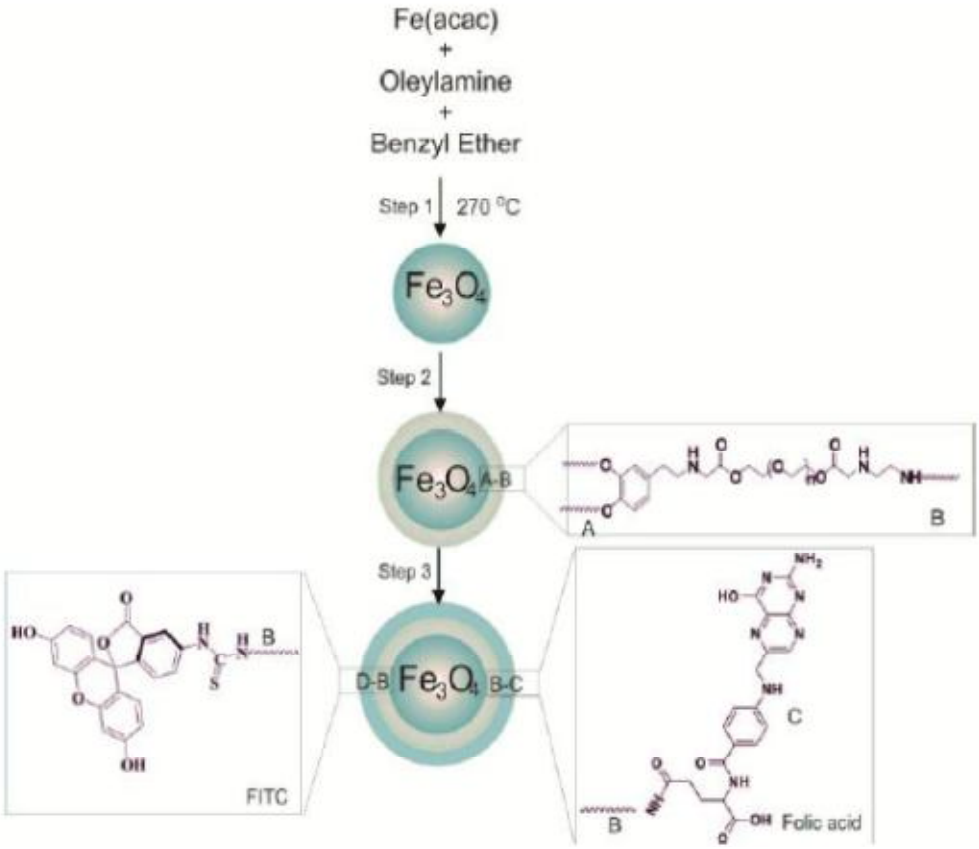


**Fig: 2 Preparation of magnetic nanoparticles**

**PREPARATION OF MAGNETIC NANOPARTICLES/FE3O4 COATED WITH POLYMER :**

In this study, a novel approach to prepare magnetic polymeric nanoparticles with magnetic core and polymeric shell using inverse micro emulsion polymerization process is reported. Poly(ethylene glycol) (PEG)-modified superparamagnetic iron oxide nanoparticles with specific shape and size have been prepared inside the aqueous cores of AOT/n-Hexane reverse micelles and characterized by various physicochemical means such as transmission electron microscopy (TEM), infrared spectroscopy, atomic force microscopy (AFM), vibrating sample magnetometry (VSM), and ultraviolet/visible spectroscopy. The inverse micro emulsion polymerization of a polymerizable derivative of PEG and a cross-linking agent resulted in a stable hydrophilic polymeric shell of the nanoparticles. The results taken together from TEM and AFM studies showed that the particles are spherical in shape with core-shell structure. The average size of the PEG-modified nanoparticles was found to be around 40-50 nm with narrow size distribution. The magnetic measurement studies revealed the superparamagnetic behavior of the nanoparticles with saturation magnetization values between 45-50 electromagnetic units per gram. The cytotoxicity profile of the nanoparticles on human dermal fibroblasts as measured by standard 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay showed that the particles are nontoxic and may be useful for various in vivo and in vitro biomedical applications.[20]

**Magnetic nanoparticles as coated magnetic nanocrystals which can be obtained in different size by using different coated materials** [4]

**A. Magnetic Iron oxide Nanocrystals in non-polar Solvent:**

5nm.10nm, 20nm, 30nm.

**B.Magnetic Iron oxide Nanocrystals in water:**

Coated with Antibodies or Protein G or Enzymes or Streptavidin: 10nm.15nm.20nm, 25nm, 30nm.

Coated with Carboxylic acid & PEG: 10nm.15nm.20nm, 25nm, 30nm.

Coated with Carboxylic acid: 10nm.15nm.20nm, 25nm, 30nm.

Coated with Dextran: 20nm, 50nm, 100nm, 130nm, 250nm.

Coated with Oleic acid: 5nm, 10nm, 20nm.

Coated with PEG: 10nm.15nm.20nm, 25nm,30nm.

Coated with Polydimethylammounium chloride PDDA: 10nm.

Coated with Polyethylenimine PEI: 10nm.15nm.20nm, 25nm, 30nm.

Coated with Silica:250nm,500nm,750nm

**C. Magnetic Iron Oxide Powder**

$Fe_3o_4$ Nanocrystals:5nm

$Fe_3o_4$ Nanocrystals:10nm

$Fe_3o_4$ Nanocrystals:15nm

$Fe_3o_4$ Nanocrystals:20nm

**IMAGING OF CANCERCELLS BY USING MAGNETIC NANOPARTICLES**

A MBTN (magnetic based Theranostic nanoparticles) having ability to specifically target the diseased site and bypass healthy tissues. difficulty for MBTN are met by various challenges such as selecting the appropriate target, methods to incorporate the correct targeting moieties, and strategies to avoid the rapid clearance of the delivery vehicles from the body . The two basic mechanisms of targeting diseases are passive and active targeting. Passive targeting is neither associated with the conjugation of antibodies nor influenced by any external forces. Instead, accumulation of the theranostic vehicle within the tumour site is accomplished by the enhanced permeability and retention (EPR effect) of tumour neovascularisation .[19-21]

Magnetic nanoparticles conjugated to targeting ligands can be used to detect disseminated metastatic cells in presence of magnetic field and monitor disease status during treatment (Alexiou et al., 2006).Superparamagnetic contrast agents have greater magnetic susceptibility than traditional MRI contrast agents (e.g., gadolinium) and some are commercially available (suspensions of polymer-coated ferromagnetic nanoparticles in water) (Alexiou et al., 2006).[1]

Ex[15-22]

- Gadolinium (gadodiamide/Ommiscan) approved for Cranial& Spinal MRI ,
- Gadolinium (gadopentetic acid/Magnevist) approved for MRI of blood vessels and intracranial lesions,
- Gadolinium (gadoversetamide /OptiMARK) approved for Brain,Spine,Liver MRI,
- Gadolinium (gadoteridol /Prohance) approved for MRI of central nervous system.

Unlike their low uptake in metastatic nodes, nanoparticles preferentially accumulate in tumours due to enhanced permeability and retention effects, causing MRI signal loss. Magnetic nanoparticles are being engineered to provide cancer-specific MRI enhancement, for instance, by detecting changes in MRI contrast due to telomerase activity of cancer cells or apoptosis

(cell shrinkage and membrane blebbing) to monitor therapeutic responses in vivo (Cuenca et al., 2006)[1]

**THERAPY OF CANCER BY USING MAGNETIC NANOPARTICLES:**

Magnetic targeting uses a strong, high-gradient external magnetic field to capture and concentrate nanoparticles in target areas, facilitating delivery to tissues with poor accessibility (Alexiou et al., 2006). [1]

Magnetic nanoparticles act as carriers for site-specific drug delivery. Effective delivery of magnetic nanoparticles depends on physical (field strength, gradient, magnetic properties), hydrodynamic (blood flow rate, ferrofluid concentration, infusion route, circulation time), and physiological (tissue depth to target site, reversibility, strength of drug/carrier binding, tumour volume) parameters. A major challenge is providing sufficiently strong magnetic fields to focus particles on small areas whilst counteracting linear blood-flow rates. Magnetic targeting is more feasible with larger particles (~1µm) that can better withstand flow dynamics and in regions of slower blood flow or those amenable to close association with magnets. [1]

A recently novel approach achieved in intra-arterial administration.[23-29]

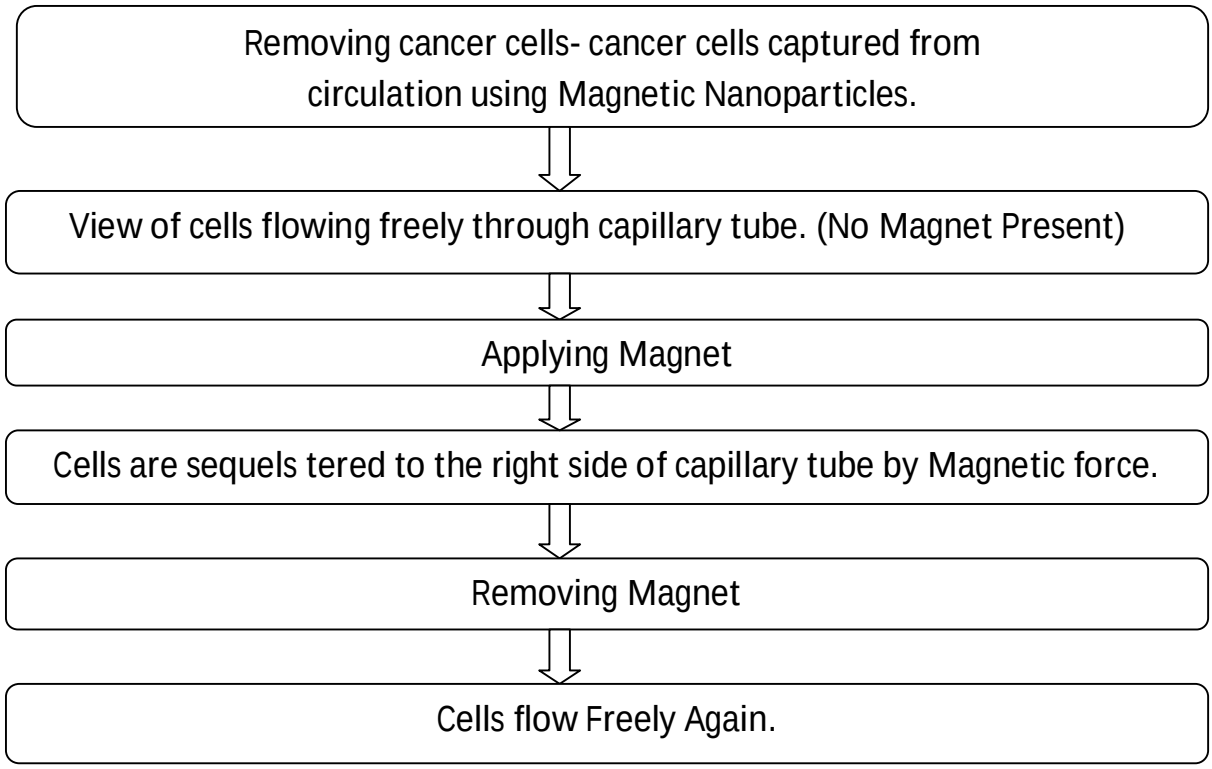


**Fig:3 Flow chart of administration of nanoparticles therapy for imaging and treatment cancer.**

**Conclusion**: Nanotechnology in cancer for imaging and therapy is based on the design and engineering of <100nm particles of inorganic and/or organic origin. Advantages include biocompatibility; selective accumulation in tumours cells, and reduced toxicity .Earlier detection as well as therapy is possible by applied magnetic nanoparticles. Considerable research is underway into the use of nanoparticles as enhancement agents for radiation therapy and photodynamic therapy, where they may be used to deliver treatment agents, produce localized enhancements in radiation dose and selectively target tumours cells for localized damage. Superparamagnetic nanoparticles with polymer coating gives better aqueous stability.& Recently Novel approach found in intra-venous drug delivery. Nanotechnology by using Magnetic Nanoparticles which can be applied in various tumours .

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