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A COMPREHENSIVE REVIEW ON DESIGN OF NANOROBOTIC SWIMMING CAPSULE A MINIMALLY INVASIVE TREATMENT

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Abstract:

Cancer remains one of the leading causes of mortality worldwide, with conventional diagnostic and therapeutic strategies often limited by systemic toxicity, low specificity, and invasive procedures. In response to these challenges, recent advances in nanotechnology and biomedical engineering have led to the emergence of swimming capsule Nano robot a transformative innovation in the field of precision oncology. These miniature, capsule-shaped devices are engineered to autonomously or remotely navigate through biological fluids, including blood vessels and the gastrointestinal tract, offering targeted delivery of therapeutic agents and real-time diagnostic capabilities at the cellular or molecular level. Swimming capsule Nano robots are typically composed of biocompatible and biodegradable materials and are powered by various propulsion mechanisms such as magnetic fields, acoustic waves, enzymatic reactions, or chemical fuels. Their structural design allows for the encapsulation of imaging agents, drugs, biosensors, or gene-editing molecules, enabling them to perform multiplexed tasks such as early tumour detection, localized drug release, and monitoring of treatment response all with minimal invasion and maximal precision. This review provides a comprehensive overview of the design principles, propulsion technologies, and navigation strategies employed in swimming capsule Nano robots. It further highlights recent preclinical studies demonstrating their effectiveness in diagnosing and treating various types of cancer, such as colorectal, pancreatic, and breast cancers. Additionally, the review discusses the key advantages of these Nano robots, including reduced systemic toxicity, improved bioavailability, enhanced tumour penetration, and the ability to bypass biological barriers. Despite their promise, several challenges remain, including immune clearance, long-term safety, real-time control, and scalability for clinical use. The review concludes with future perspectives on integrating artificial intelligence, real-time imaging systems, and smart biosensors to enhance the functionality and clinical applicability of swimming capsule Nano robots in oncology. By merging the fields of robotics, Nano medicine, and oncology, swimming capsule Nano robots represent a significant step toward personalized, precise, and minimally invasive cancer care, potentially revolutionizing the way we detect and treat malignancies in the near future.

Keywords: *Swimming capsule Nano robot/Nanobot, precision oncology, diagnosis, targeted therapy, minimally invasive, real-time imaging, tumour targeting, drug delivery, theranostics, magnetic navigation.*

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INTRODUCTION:

The nanorobotics swimming capsule is a revolutionary development in Nano -medicine that combines biomedical engineering, robotics, and nanotechnology to provide minimally invasive therapy, targeted medication delivery, and diagnostics. With the help of sophisticated propulsion motors, these Nano- or microscale robots may swim through biological fluids and reach specific areas inside the human body. The size of the nanobots is usually between 100 nm to 1 µm. The swimming capsule Nano robot's outer shell is composed of hydrogels, silicon, and polymers like PEG and PLGA. In targeted cancer therapy, nanorobotics swimming capsules are a new and extremely accurate technique. To navigate through body fluids and tissues, these tiny robots are designed to follow chemical gradients or magnetic fields.

They can deliver chemotherapeutic medications directly to the cancer cells once they reach the tumour site, they can lessen the negative effects on healthy tissue. Some are externally fuelled by catalytic processes (such as the breakdown of hydrogen peroxide) Using ligands or antibodies, their surfaces can be functionalized to enable particular recognition and binding to cancer cell receptors[1].

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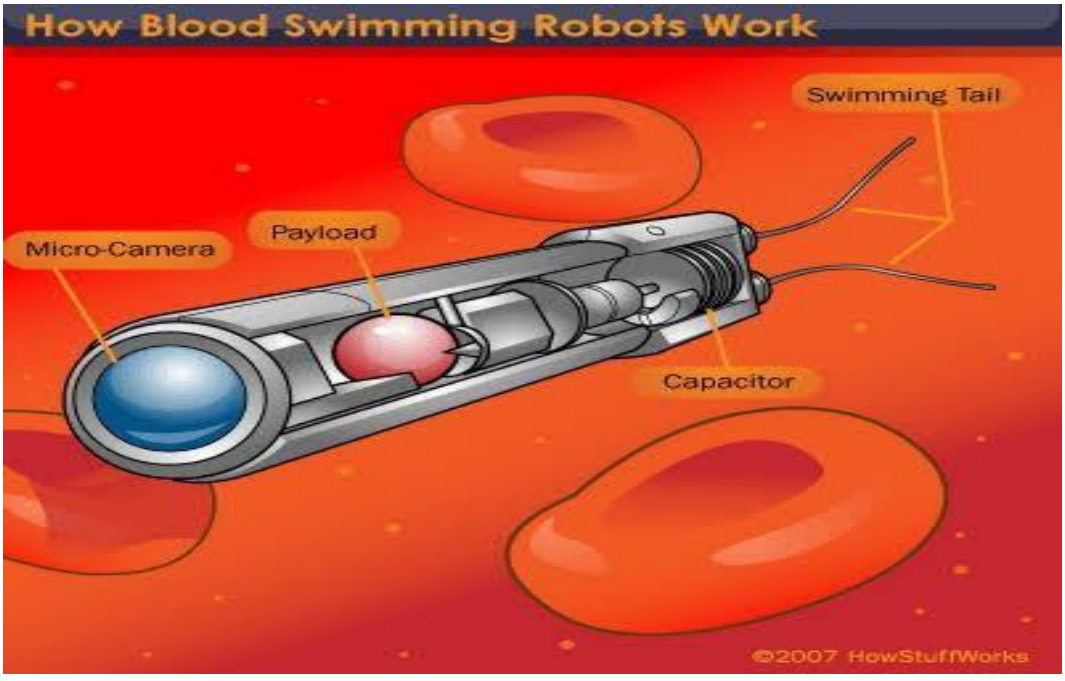
S .No	CAPSULE TYPE	SIZE RANGE	DRUG LOAD (APPROX)
1.	Micro\Nano capsule	1-10µm (lab scale)	1-10µg(micrograms)
2.	Smart pill capsule	~11×26mm(clinical)	1-100mg(milligram)
3.	Theranostic capsule	~1-5mm(experimental)	10µg-10mg

Table 1 .types of capsule , its size and drug upload



SWIMMING CAPSULE

AIMS AND OBJECTIVES:

AIM:

To develop and implement nanorobotics swimming capsules as a cutting-edge precision oncology tool for early diagnosis, targeted drug delivery, and minimally invasive treatment of cancer, thereby improving therapeutic efficacy and reducing side effects.

OBJECTIVES:

The objectives of this study are to develop a biocompatible swimming capsule Nano robot with precise navigation, enable real-time tumour detection and monitoring, incorporate targeted drug delivery triggered by tumour-specific signals, ensure safety, biodegradability, and minimal side effects, utilize advanced control systems for accurate operation, and test and validate its performance in preclinical and clinical settings.

WORKING MECHANISM OF NANOBOTS:

For effective swimming, nanorobotic swimming capsules need external actuation or non- reciprocal propulsion techniques since they function in a low Reynolds number regime that is dominated by viscous forces[3]. In biological contexts, nanorobotic capsules can be safely and precisely remotely actuated and guided by magnetic fields, allowing for deep tissue navigation[4]. Systemic toxicity is decreased and therapeutic accuracy is improved by stimulus-responsive systems, such as pH- or enzyme-triggered drug release[5]. Targeted surface functionalization and active propulsion enhance tumour growth and extracellular matrix penetration. In order to enable real-time tracking while navigating, it can be designed to be compatible with clinical imaging modalities like MRI. Materials that are both biocompatible and biodegradable are necessary to reduce immunological responses and guarantee safe breakdown. Adaptive therapeutic interventions and accurate targeting are made possible by closed-loop control systems that integrate sensors and AI-based feedback[6].

ADVANTAGES OF SWIMMING CAPSULE NANOBOT

- The speed and resilience of the bots are their main advantages.
- Nano robotic drug delivery system employees more bioavailability
- Less post-treatment care is required because it is a minimally invasive technique.
- A speedy conclusion to sickness
- It reduces surgical errors.
- The ability of Nano robots to eradicate illnesses that develop in the body without our knowledge is one of their many uses[7].

DISADVANTAGES OF SWIMMING CAPSULE NANOBOT

- The body may generate clusters when several Nano robots are implanted to treat various illnesses.
- The price of installation is rather high.
- The Nano robot must have high accuracy to prevent dangerous situations.
- The robot has an intricate design.
- The danger of cancer.
- Communication with organic systems might be challenging[8].

APPLICATIONS

1. **MEDICAL APPLICATIONS:**
   - ✓Targeted drug delivery
   - ✓Minimally invasive surgery
   - ✓Disease diagnosis
   - ✓Cell repair & regeneration
   - ✓Cancer treatment
   - ✓Blood clot removal
2. **BIOLOGICAL & GENETIC APPLICATIONS:**
   - ✓Gene therapy
   - ✓Immune system support
3. **MILITARY & DEFENSE:**
   - ✓ Surveillance
   - ✓ Biological Threat Detection
   - ✓ Nanorobotics can identify and neutralize biological and chemical warfare agents
4. **MINIMALLY INVASIVE SURGERY**
5. **IMAGING AND BIOPSY**[9]

IDEAL CHARACTERISTICS OF SWIMMING CAPSULE NANOROBOT

a. Mobility in biological fluid
b. Controlled drug release
c. Biodegradability or Retrievability
d. Real time navigating
e. Miniaturized size
f. Stability in biological conditions
g. Bio compatability[10]

ADVERSE DRUG REACTION OF SWIMMING CAPSULE NANOBOT

- ✓ Immune activation/Inflammation
- ✓ Allergic/hypersensitivity reaction
- ✓ Material toxicity (metal ion release, degradation products)
- ✓ Pre mature drug release
- ✓ Long-term accumulation in organs
- ✓ Endothelial damage/haemolysis
- ✓ Vascular blockage[11-18]

PRE- CLINICAL VALIDATION OF NANOROBOTIC SWIMMING CAPSULE IN CANCER THERAPHY

1. LUNG METASTATICS:

a. In vivo efficacy in a lung metastasis model:

Female C57BL/6 mice were given an intravenous injection of 1 × 105 B16-F10-Luc2 cells (ATCC CRL-6475-LUC2) into their tail vein in order to create an experimental lung metastasis model. On days 1, 3, 5, and 7 following tumor cell injection, the mice were treated intratracheally with free DOX, NP(DOX), and algae-NP(DOX)-robot. As controls, mice that received no therapy were

employed. On days 12, 16, 20, 24, and 28 following tumor cell injection, the mice received 200 µl of d-luciferin (5 mg ml^{-1}; Syd Labs) intraperitoneally in Dulbecco's Phosphate-Buffered Saline (DPBS, Gibco) to track tumor growth. A PerkinElmer Xenogen IVIS 200 system was used to detect bioluminescence signals. Throughout the investigation, each mouse's body weight and survival were also tracked. Either death or moribundity upon observation was considered the survival endpoint.

b. In vivo safety evaluation:

Every other day, four intratracheal injections of free DOX, NP(DOX), and algae-NP(DOX)- robot were administered to healthy female C57BL/6 mice. Mice in the control group were not given any medication. 24 hours following the final treatment, blood samples were taken via submandibular puncture into Microvette 100 EDTA K3E tubes (Sarstedt) in order to count the quantity of blood cells. Without the use of any anticoagulants, blood samples were drawn, let to stand at room temperature for 30 minutes, and then centrifuged for 10 minutes at 3000 g to obtain serum for a comprehensive chemical analysis of the blood. The blood cell quantification and blood chemistry analyses were performed at the UCSD Animal Care Program Diagnostic Services Laboratory. The kidneys, liver, spleen, heart, and lungs were removed and preserved in Fisher Chemical's phosphate-buffered 10% formalin for histological examination. Hematoxylin and eosin staining and sectioning were then performed. The Moores carried out these histology methods.Tissue Technology Shared Resource at the Cancer Center[19].

2. ACUTE BACTERIAL PNEUMONIA:

a. In vivo survival study:

A combination of xylazine and ketamine was used to induce anesthesia in male CD-1 mice. They received 5 × 106 CFU of P. aeruginosa from an intratracheal inoculation, followed by intratracheal administration of TAP buffer, NP-Cip, 5 × 106 algae-NP(Cip)-robots, or 5 × 106 static algae-NP(Cip) at a comparable Cip dosage (500 ng). Thirty minutes after bacterial inoculation, animals received separate intravenous injections of a clinical dose (1.64 mg) and a comparable Cip quantity (500 ng) to compare with the IV therapy. Every mouse's survival was tracked every day.

b. In vivo safety studies:

Following intratracheal delivery of TAP buffer or a 5 × 106 algae-NP(Cip)-robot for sample collection, mice were put to sleep at 24, 72, and 168 hours. Serum and whole blood samples were taken for the complete metabolic panel and blood cell counts. The Diagnostic Services Laboratory of the UC San Diego Animal Care Program conducted the laboratory tests. Major organs underwent H&E staining for histological examination. The lungs were cleaned five times with 1 ml of 0.5% (v/v) fetal bovine serum (Gibco) and 2 mM EDTA in PBS using a 23-gauge needle to obtain bronchoalveolar lavage fluid (BALF), which was then put into PTFE tubing (Cole Parmer) that was inserted into the trachea to measure the cytokine levels. For cytokine analysis, the supernatant was extracted from the BALF by centrifuging it at 700 g for five minutes. In triplicate, the cytokine levels in BALF were assessed using the multiplexed sandwich enzyme-linked immunosorbent assay (ELISA) kit (BioLegend). Histology slices of lung tissue were evaluated by the Tissue Technology Shared Resources at the UC San Diego Moores Cancer Center. Blinding was used for all histological evaluations to prevent observer bias.

c. In vitro cytokine production:

The J774A. A 6-well plate containing 1 × 106 macrophage cells was grown in DMEM. After that, they were incubated for 24 hours with either 100 ng ml^{-1} flagellin obtained from Salmonella Typhimurium bacteria (InvivoGen), 5 × 10^6 algae-NP-robots, 5 × 10^6 static algae-NP, or 5 × 10^6 algae-NP-robots that had been cryotreated. BioLegend ELISA kits were used to measure the levels of cytokines[20].

3. PHOTO DYNAMIC THERAPY OF TUMORST:

a. In vivo PDT tumor treatment:

Six-week-old female Balb/c mice with 4T1 tumors were randomly assigned to one of five groups (n = 5): PBS + NIR, C + NIR, CurNPs + NIR, CurNPs-C, and CurNPs-C + NIR. The concentration of Cur was 10 µg mL^{-1}, and the concentration of C was 109 cfu per mL. On days 1, 3, 5, and 7, 4T1 tumor-bearing mice were given an intravenous (i.v.) injection of CurNPs, C, or CurNPs-C when the tumor volume reached approximately 100 mm^3.. The tumors of the PBS + NIR, C + NIR, CurNPs + NIR, and CurNPs-C + NIR groups were then sequentially exposed to a 660 nm laser irradiation (0.1 W cm^{-2}) for 30 minutes at 1 hour or 12 hours following intravenous injection. Every other day, body weight and tumor volume (V = (ab2)/2, where a and b represent the tumor's length and width, respectively) were assessed in order to examine the PDT-based anticancer effect. 4T1 tumor- bearing mice were put to sleep 15 days after their tumors were treated, and their tumors, major organs, and serum were collected. To examine the PDT-mediated anti-tumor effect of CurNPs-C, pictures were taken, and the tumor weight of four T1 tumor-bearing mice from each group was calculated. Following slicing, TdT-mediated dUTP nick-end labeling and H&E staining. (TUNEL) assay of the tumor, the tumor-inhibiting impact of CurNPs-C was investigated by monitoring necrosis or apoptosis of the cells. HIF-1α staining was used to determine the impact of the C photosynthesis in vivo on tumor hypoxia.

Histological analysis of the primary organs of 4T1 tumor-bearing mice was carried out 15 days following tumor treatment in order to investigate biosafety. Tissue slices stained with H&E were examined under a microscope. Utilizing a liver or renal function activity assay kit, liver indicators (ALT/AST) and serum renal indicators (UREA/CREA-S) were assessed in order to determine the hepatorenal toxicity of CurNPs-C. The biodegradability of CurNPs-C was investigated by injecting the drug intravenously (i.v.) into 4T1 tumor-bearing mice, and one hour after the injection, the tumor was sequentially exposed to irradiation with a 660 nm laser (0.1 W cm^{-2}) for 30 minutes. Tumor tissue coating was used to count the amount of C colonies in tumors that we removed from 4T1 tumor-bearing mice on days 1, 3, 7, 15, and 18[21]

TREATMENT

1. LUNG METASTATICS:

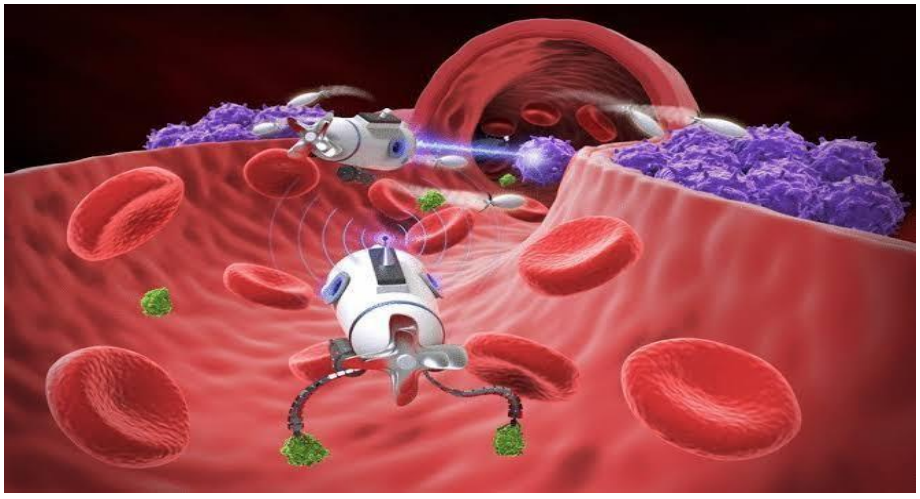
Nanorobotic swimming capsules are micro/nanoscale devices designed to actively travel through the circulation to reach lung metastases under the guidance of magnetic or acoustic fields. Targeting ligands (such as antibodies or peptides) that identify tumor-specific markers on circulating tumor cells (CTCs) or metastatic lesions in lung tissue can be functionalized into these capsules for the treatment of lung metastases. These can be loaded with: For direct cytotoxic activity, chemotherapy medications such as doxorubicin, paclitaxel, and cisplatin are used. photosensitizers for photodynamic therapy, such as indocyanine green and chlorin e6, and miRNA and siRNA for metastasis-promoting gene silencing. They attain high local drug concentration, lessen systemic adverse effects, and may aid in the removal of CTCs prior to their seeding of new tumors by actively navigating to the lungs. This presents a potential strategy for the prevention and treatment of metastases[19]

2. ACUTE BACTERIAL PNEUMONIA:

Nanorobotic swimming capsules are actively propelled micro/nano devices that can travel through the bloodstream or respiratory system and deliver targeted medicine directly to affected lung tissue. These devices are frequently directed by magnetic or ultrasonic signals. When bacterial pneumonia is acute, these capsules may be loaded to deliver antibiotics directly to the site of infection, such as vancomycin, levofloxacin, and azithromycin. Targeting ligands (peptides, antibodies) that attach to receptors on inflammatory lung tissue or bacterial surface markers functionalize them, equipping them to break down bacterial biofilms and enhance antibiotic penetration by using biofilm- disrupting chemicals (such as DNase and dispersin B)[20].

3. PHOTO DYNAMIC THERAPY OF TUMORST:

Nanorobotic swimming capsules are tiny, actively moving machines that can travel through the body and reach tumor areas. They are frequently controlled by magnetic or ultrasonic forces.When used in photodynamic therapy, these capsules contain a photosensitizer (such as Chlorin E6, Indocyanine Green, Methylene Blue, or Rose Bengal) that is dormant until a particular wavelength of light activates it.When the nanorobot arrives at the tumor, external light—typically near-infrared—is applied, stimulating the photosensitizer and producing reactive oxygen species (ROS), which kill cancer cells only.When paired with magnetic navigation, this technique could improve the treatment of deep-seated or difficult-to-reach tumors by avoiding damage to healthy tissue and combining accurate tumor targeting with localized therapy[21].



PHOTODYNAMIC THERAPY

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