Breast Cancer RESEARCH

VIEWPOINT

Nanomedicine: making controllable magnetic drug delivery possible for the treatment of breast cancer

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Abstract

A recent study published in *Nano Letters* documents the synthesis and performance of porous silica nanocapsules filled with magnetic nanoparticles as a controllable magnetic drug delivery vector. Under a remotely applied radiofrequency magnetic field, these nanocapsules demonstrate on-off switchable release of the internally loaded drug payload. Both *in vitro* and *in vivo* studies using MT2 mouse breast cancer cell models demonstrate that the magnetic targeting of these nanocapsules allows for deep tumor penetration and subsequent on-demand release of the drug cargo, significantly reducing tumor cell viability.

The rapid development of nanomedicine offers innovative approaches to improving current cancer diagnostic and therapeutic technologies [1,2]. Among the numerous challenges faced by the field of oncology, more efficiently controlled drug release and drug penetration into solid tumors are now thought possible by the use of magnetic nanoparticles [3-6]. A recent study by Kong and colleagues [7] documents the successful creation of a drug delivery system using nanocapsules that provide on-demand drug release by external magnetic stimuli. This technology provides the ability to remotely and repeatedly release an anticancer drug while in the 'on' state, but safely contain the drug within the delivery vehicle in the 'off' state.

Porous silica magnetic nanocapsules (SiMNCs; 100 to 150 nm in diameter) are synthesized with iron oxide (Fe_3O_4) nanoparticles and anticancer drug molecules, such as camptothecin and doxorubicin, intentionally trapped within their hollow interiors. By remotely applying an external switchable on-off radiofrequency (RF) field, controlled release of the anticancer drugs is achieved. The authors propose that localized heating of the iron oxide nanoparticles occurs in a manner similar to the phenomenon observed in RF-induced magnetic hyperthermia of cancer cells [8]. This increase in temperature likely causes accelerated diffusion and subsequent release of the drugs. The proposed mechanism is visually confirmed by the controlled release of a fluorophore (9,10-bis(phenylethynyl)anthracene) from the SiMNCs upon RF magnetic field exposure, suggesting that various molecular cargos can be potentially loaded into and delivered by the SiMNCs.

Due to the nanoscale confinement of the magnetic nanoparticles within their interior, the SiMNCs exhibit enhanced magnetic properties when compared to iron oxide nanoparticles. This enhanced magnetization is exploited to facilitate tumor penetration as deep as approximately ten cell thicknesses (approximately 50 μm) within MT2 mouse breast cancer cell colonies in a gradient magnetic field (approximately 1,200 Oe) for 2 hours. Upon on-off RF field exposure, a significant decrease in tumor cell viability is observed, suggesting successful drug release into the tumor site. Similarly, *in vivo* studies revealed that the SiMNCs can accumulate at a breast tumor site after being intravenously administered into tumor-bearing mice. With a magnet placed in contact with the skin above the tumor site for 2 hours, the average number of SiMNCs trapped in a tumor was 200 times more than for the control.

The advantages of this drug delivery technology are highly promising for cancer therapy. First, the system provides a highly efficient means to safely deliver anticancer drugs to deep tumor sites via magnetic targeting. As noted by the authors, the majority of the administered nanocapsules reach the target site with minimal amounts accumulated in the liver and spleen. Secondly, the silica shell and drug payload of the SiMNCs can be modified to allow for customizable drug administration. The exterior of the porous silica shell can be covalently functionalized with various biomolecules for targeting purposes. In addition to anticancer drugs and fluorophores, other

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molecular cargos, such as microRNAs, peptides, and hormones, can be potentially loaded into and released from the SiMNC particles. Lastly, the magnetic nanoparticles within the SiMNCs are superparamagnetic and can therefore be visualized by T_2-weighted MRI. This capability should be further explored in order to assess SiMNCs as effective 'theranostic' agents.

One drawback in the system design is the inability to target tumors that have not yet been located or those that are not superficially accessible. Currently, the location of the tumor must be known so that an external magnetic field can be applied to the target area to allow for nanocapsule accumulation. The MRI capability of the iron oxide nanoparticles and the possibility of attaching targeting groups to the SiMNC exterior may remedy this limitation. The SiMNCs may not efficiently target a deep-tissue tumor since the applied magnetic field strength decreases with distance, and this could lead to drug accumulation in the region between the external magnet and the tumor. Surgically implanting a magnet closer to the tumor site, as demonstrated in similar studies [9], is a possible way to circumvent this problem.

Several issues must be addressed before clinical implementation. It is important to determine whether the release of the drug payload is a result of localized heating of the magnetic nanoparticles or an increase in the ambient temperature of the SiMNC surroundings. As the authors suggest, a quantitative analysis of the heat generation and conduction within the nanocapsules is necessary to better understand the drug release mechanism. Furthermore, it must also be confirmed that the cell death observed after RF treatment is due only to drug release and not to magnetic hyperthermia produced by the magnetic nanoparticles. As all other nanoparticles, the biodistribution, biodegradation, and *in vivo* efficiency of the SiMNCs under more strenuous physiological conditions, such as blood flow, must also be evaluated before use in human patients can be realized.

Abbreviations

MRI, magnetic resonance imaging; RF, radiofrequency; SiMNC, silica magnetic nanocapsule.

Competing interests

The authors declare that they have no competing interests.

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