

Application of Nanotechnology in Organ Transplantation

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Abstract. Organ transplantation can serve as a blessing for end-stage organ patients, and issues such as organ shortage and transplantation risks also make research on organ transplantation very important. Nanotechnology involves the development of materials called nanoparticles, which are defined as having a one-dimensional range of at least 1 to 100 nm. This paper introduces the application of nanotechnology in overcoming the drawbacks of traditional medicine, and its nanoscale size has also contributed to organ transplantation. The combination of Magnetic resonance imaging (MRI) and Magnetic hyperthermia (MHT), nanoparticles can better capture transplant medical images, and nanotechnology plays an important role in monitoring treatment responses and designing organ transplantation methods. CRISPR/CAS9 system and Entrancer™ can reduce the role in rejection reactions. Normothermic Machine Perfusion (NMP), protein corona, and curcumin can reduce their effects on ischemia-reperfusion injury. The development of nanomedicine can provide a platform for significant progress in transplant vitality. In future research, nanoparticles can also be applied in 3D bioprinting and artificial intelligence (AI) to better assist in transplant therapy.

Keywords: Nanotechnology, drug delivery system, medication.

1. Introduction

Organ transplantation can be a blessing for end-stage organ patients. For thousands of patients with advanced organ failure, transplantation is a treatment option that extends their lives. However, organ transplantation poses many challenges in today's treatment. Every patient who receives a transplant needs to have unique organ needs, which means that a successful transplant requires the donor's organ to perfectly match the organ in the recipient's body, thus avoiding strong rejection reactions. This has also led to a shortage of organ donations. Moreover, after transplantation, patients still need regular examinations and long-term medication to ensure that the transplanted organ does not cause damage to the body. This is a traditional method of organ transplantation [1]. In addition to organ shortages, there are also difficulties in accurately observing transplant outcomes, leading to transplant failure, immune rejection of transplanted organs and internal organs, and damage to the human body caused by ischemia-reperfusion, all of which limit the application of transplant techniques.

Fortunately, the combination of nanotechnology and transplantation methods is changing traditional transplantation methods, making transplantation safer and more reliable. As a new type of technology, nanotechnology can be used in the medical field due to the different types, sizes, shapes, and surface properties of nanoparticles. Nanoparticles are similar in size to cellular components with only 1-100 nm, can enter live cells through cells [2], and play an important role in organ transplantation. For example, it is a big success for imaging technologies such as MRI and MHT to be used in transplantation. The nano system weakens the rejection reaction caused by transplantation; The combination of nanotechnology and machine perfusion, as well as the application of nano-loaded curcumin, have reduced the damage of ischemia-reperfusion to the body.

Nanoparticles (NPs) have great potential, but more research is needed to ensure that their characteristics match different diseases and are combined with clinical transplant treatment methods, which is particularly important. Although this new method can overcome some defects caused by the body or technology, the nanoparticles themselves also have problems. Because immature technology may also lead to more serious impacts on the body. Therefore, in this article, The different

applications of NPs will be reviewed in experimental and clinical transplantation, summarize current research results, and make some expectations for future research directions.

2. Research Progress

2.1. Nanoparticles in medical imaging in organ transplantation

Nanoparticles have played a significant role in medical imaging, and the following will illustrate their role through several different application examples.

NPs are often used as imaging probes in the medical field due to their unique physical and chemical properties and lack of toxicity. Due to the high surface volume ratio of nanoparticles, their functionality in surface modification is also strong. NPs are amplifiers that can be used for in vivo imaging due to their high modification ability [3]. NPs are divided into many different types, each of which contributes differently to medical imaging. Gold NPs are used for contrast-enhanced computer tomography, iron oxide NPs are optimized for localization through rotational relaxation, and quantum dots are used for near-infrared (NIR) fluorescence imaging. NPs can even be used for dual imaging, such as in experiments to observe the transplant specificity of mouse pancreatic islet cells, which can be observed using Poly(D, L-lactide-co-glycolic) acid (PLGA) and iron oxide NPs under the effects of fluorescence and MRI [4].

MRI is a sensitive and non-invasive method to be used for medical imaging to observe transplant reactions. In molecular and cellular imaging, MRI studies rely on imaging comparisons of superparamagnetic or ultra-small superparamagnetic iron oxide nanoparticles due to their high sensitivity. For example, by utilizing the phagocytic ability of bone marrow cells, MHT allogeneic transplant rejection reactions can be monitored through iron oxide nanoparticles that are sensitive to bone marrow. By wrapping a 5-10 nm iron tetraoxide nanoparticle with a layer of hydrophilic material on its surface, it can be injected into the body and accumulate in liver tumors, altering the spin of the water proton thereby achieving enhanced contrast and helping MRI to diagnose liver tumors at an early stage. Recently, positron emission tomography has attempted to use radioactive and right-handed cross-linked nanoparticles. In addition, MRI probes can also be used to detect the effectiveness of immune cells in the human body using magnetic probes. However, due to the large number and complexity of cells in organs, the nanoparticles used also need further processing. Therefore, different nanoparticles will be used for more personalized clinical care to provide diagnostic and prognostic information and to quantify the therapeutic effect of transplant patients [5].

MHT is a heat therapeutic method based on nanotechnology, which dissipates energy through magnetic colloid-induced hysteresis. A key advantage of MHT is that it can provide specific treatment for therapeutic heat deposition in tumor patients. MHT can deposit magnetic nanoparticles (MNPs) in a targeted manner into tumors by carrying MNPs and alternating magnetic fields (AMFs), thereby exposing the area to the AMF. Figure 1 is a schematic diagram of guiding magnetic hyperthermia combined with TACE treatment for liver cancer. Describing the relationship between MNP distribution and liver lobes, tumors, and blood vessels through high contrast and spatial resolution imaging modes, followed by chemical embolization after arterial perfusion of MNPS. This makes it possible to develop specific treatment plans and implement MHP treatment for patients. MNPs can also provide additional imaging functions, which can timely initiate prospective treatment plans and benefit MNPs, enabling better treatment of patients' diseases [6].

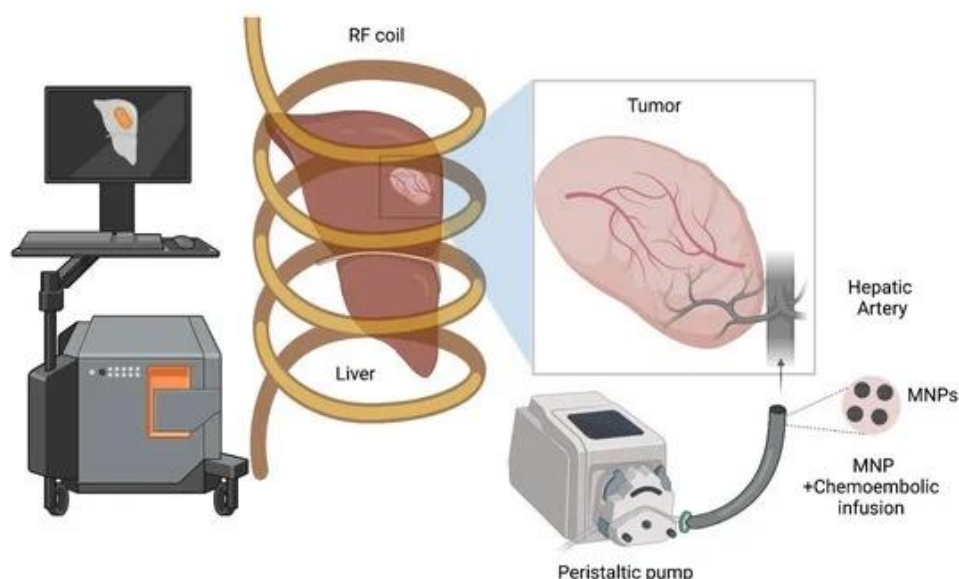


Fig. 1 Magnetic hyperthermia therapy (MHT) combined with TACE in hepatocellular carcinoma (HCC) [6]

2.2. Nanoparticles in Reducing Rejection Reactions

In organ transplantation, rejection is an important issue that affects graft survival and patient recovery. Nanoparticles, as a novel therapeutic strategy, can be used to reduce rejection in organ transplantation. First, nanoparticles can be used for drug delivery. By encapsulating immunosuppressive drugs in nanoparticles, the drugs can be precisely delivered to the graft area, thus reducing the amount of systemic immunosuppressive drugs and reducing side effects. In addition, nanoparticles can be used in gene therapy to modulate gene expression by delivering specific genes into the graft cells, thereby altering the immunogenicity of the graft and reducing the risk of rejection. Second, nanoparticles can be used to improve the biocompatibility of grafts. By modifying the nanocoatings on the surface of the grafts, the adhesion and activation of immune cells can be reduced, thereby reducing the occurrence of inflammatory reactions and rejection. In addition, some nanomaterials can mimic the surface properties of natural cells and interact with them to promote cell adhesion and growth, further improving graft survival. Finally, nanoparticles can also be used for diagnostic imaging. By encapsulating the imaging agent in nanoparticles, the resolution and contrast of imaging can be improved, helping doctors to more accurately monitor the status of the graft and the occurrence of rejection.

The CRISPR/CAS9 system is a novel gene editing tool that utilizes the guidance of a single RNA to effectively eliminate the pathogenic gene Cas9 ribozyme. Nanoparticles can effectively provide the required plasmid for the system, allowing mRNA/gRNA and nuclear proteins in the plasmid to edit genes in cancer cells. This method can apply CRISPR/CAS9 at the genomic level to disrupt CD40. As a result, the human body can not only establish long-term tolerance after transplantation but also avoid the side effects of immunosuppressants and reduce rejection reactions [7].

RNA interference (RNAi) is a method that silences the expression of target genes after transcription, and it has a wide range of applications, which can be applied to all molecules and genes. Research has shown that siRNA technology is a highly effective ophthalmic treatment method. However, the application of vectors plays an important role in the successful transfer of genes. Nonantiviral drugs are widely studied due to their low toxicity, lack of immunogenicity, and high transfection efficiency. Entranster™ is an in vivo transfection reagent serving as a novel carrier for siRNA delivery nanoparticles. It has been studied in various mouse models and the results have shown no side effects. In the future, carriers will become a great in vivo corneal gene therapy method for the face [8].

2.3. Nanoparticles in reducing ischemia-reperfusion injury

Organ preservation is an important step before transplantation. Ischemia-reperfusion injury (IRI) is a serious disease that occurs in organs during transplantation, which may occur in tissues such as the brain, heart, liver, and kidney [9]. At present, the main purpose of research is to continue to function after organs are detached from the body, reducing the damage caused by ischemia-reperfusion.

Normothermic Machine Perfusion (NMP) is currently a method for preserving the kidneys that are about to be applied in clinical practice. NMP-perfused kidneys have less damage to endothelial cells, and the local damage caused by cold ischemia can also be improved. The metabolic function of subsequent organs can be restored, resulting in a perfect outcome for organ transplantation. In animal experiments conducted by scientists, NMP has achieved good results, and it will soon be applied in clinical experiments to prove its superiority.

The addition of nanotechnology also adds bricks and tiles to this technology. Machine infusion provides a transmission channel for nano therapy, and machine infusion can also provide more targeted transplantation for nano therapy. A coating called protein corona is produced due to the binding of NPs with proteins in the organism during treatment. This coating hinders the role of nanoparticles in transplantation, and endothelial cells may die as a result. Combining mechanical infusion with nanoparticles in the treatment of grafts can effectively prevent the aggregation of NPs in the macrophage system and the production of protein corona phenomena, leading to damage to the body [10].

Curcumin, as a natural active ingredient extracted from plants, can protect against IRI damage. However, curcumin has poor water solubility, making it difficult for the human body to absorb and unable to achieve its corresponding therapeutic effects. Therefore, drug encapsulation using NPs is used to improve its water solubility. The number of cell apoptosis effects between unpackaged curcumin and NPs encapsulated curcumin is compared through flow cytometry analysis. As shown in Figure 2, these results indicate that Cur-NPs can protect HK2 cells, enhance the efficacy of curcumin, and alleviate cell apoptosis [11].

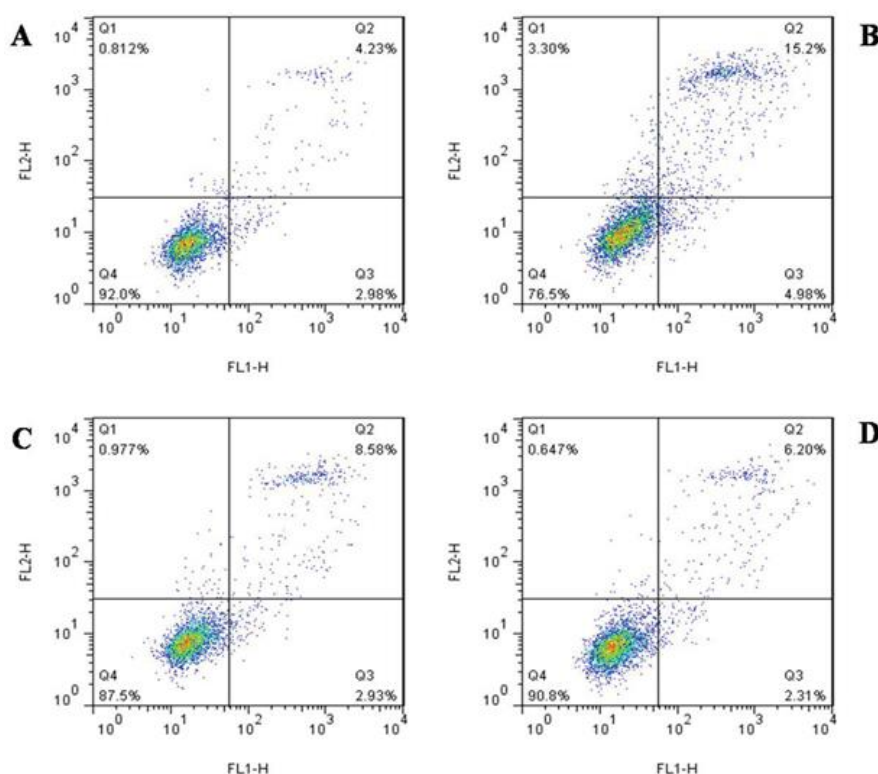


Fig. 2 Flow cytometry detects cell apoptosis: (A) Normal control group, (B) IRI group, (C) IRI+Cur group, and (D) IRI+Cur-NPs group [11].

3. Conclusion

Nanotechnology is a new type of technology that can be applied in many medical fields due to its application in medical imaging, rejection reactions, and injury treatment caused by ischemia-reperfusion. Especially in transplant medicine, NPs can be used as a drug system or loading material to overcome the obstacles faced by patients - the need to maintain the survival ability of the transplant through medication or regular examinations to increase the donor's organ supply and enable the recipient to achieve better postoperative efficacy.

A precise 3D model consisting of bioink (material containing active cells), printer, and substrate with anatomic specification, same as that of the patient body, was printed. It can be used in medical imaging. Besides, "smart" nanoparticles can monitor organ transplantation in real-time, providing data that can be used by AI algorithms to prevent injury. These nanoparticles can be designed to respond to specific changes in the local environment.

Although nanotechnology is widely used in medical transplantation, it still has some limitations and shortcomings. The new NPs may carry the risk of electrostatic or binding interactions, leading to the generation of reactive oxygen species and ultimately cell death due to the misuse of NPs. The human body may also be unable to metabolize excess nanoparticles and cause damage to the body.

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