Extended Applications of Laser for Photothermal Treatment

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Advances in nanobiotechnology have resulted in newer and improved diagnostic and treatment methods, including ultrasensitive molecular imaging, delivery of chemotherapeutic drugs, and photothermal treatment (PTT). We discuss characteristics and action mechanisms of PTT. Although the safety of nanoparticles has not yet been fully defined, in the future, PTT using nanotechnology may play an important role in treatment of malignant tumor.

Key words

Photothermal treatment; Nanoparticle

Received June 1, 2014
Revised June 19, 2014
Accepted June 20, 2014

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INTRODUCTION

Over the past 50 years, although there have been advancements in the management of malignant tumors, the survival rates has shown little improvement and some diseases is still incurable.¹ The cause of unsatisfied improvement in survival may be the limitations of surgical resection due to several vital structures adjacent to tumors, the high failure rate and toxicity of radiation therapy for advanced tumors, poor cell specificity and high toxicity of chemotherapy, and the limited supportive role of chemotherapy in concurrent chemoradiation therapy. Therefore, to overcome the limitation of conventional treatments, the previous studies suggested various alternative treatments, including gene therapy, immunotherapy, and hyperthermia.²⁻⁴ Among them, since hyperthermia treatment shows synergistic effect with radiation therapy and chemotherapy, hyperthermia treatment, elevating tissue temperature to more than 40°C, has been used as an adjuvant therapy with chemotherapy and radiotherapy. However, tissue temperature greater than 40°C occurs cellular injury or death through protein denaturation and affects both healthy and cancerous tissues. Therefore, the limitation of conventional hyperthermia may be difficulty of target-specific treatment for malignant tumors.

Recently, photothermal treatment (PTT) using nanoparticles has gained attention as an alternative to hyperthermia treatment through the use of lasers for thermal treatment due to advancements in nanotechnology. The treatment strategy of PTT is similar to photodynamic treatment in terms of the use of light. In photodynamic treatment (PDT), photosensitizer, which absorbs light with specific wavelength, produces reactive singlet oxygen from tissue oxygen and then the reactive oxygen kills tumor cells and cause destruction of tumor

vasculature.⁵ On the other hand, three key components of PTT are nanoparticle, light with specific wavelength, and heat. The heat generated by surface plasmon resonance of nanoparticle is used to kill tumor cells.

NANOPARTICLES

Nanotechnology represents the convergence of multiple scientific fields including chemistry, physics, engineering, molecular biology, and various scientific fields. The advancement of nanotechnology has made nanoparticles to be used to biological field by using various physical properties, including electronic, optical, magnetic, and catalytic characteristics. Especially, the production of nanoparticle with tunable and adequate size and the surface chemical characteristics of nanoparticle, which can be combined various active materials, facilitate extensive application of nanotechnology to biomedical field.⁶ The representative applications of nanoparticle are drug/gene delivery,⁷⁻⁹ diagnosis of cancer cells,¹⁰⁻¹³ cancer therapy such as PTT.¹⁴⁻¹⁵

Nanoparticles can be classified according to composition (gold, carbon, iron oxide, liposomal, dielectric materials), shapes (sphere, rod, star, shell, cage, wire, tube) (Fig. 1).¹⁶ Among the various nanoparticles currently available, plasmonic gold nanoparticles may be a promising particle because of simple fabrication, multifunctional nature, facile surface chemistry, and relative biocompatibility with low toxicity.¹⁶⁻²⁰

SURFACE PLASMON RESONANCE (SPR)

Metal nanoparticles such as gold nanoparticle and gold nanoshells exhibit unique optical properties that are useful for ultrasensitive detection and photothermal treatment. When the nanoparticles are irradiated by light

Fig. 1. Nanoshells (A) and nanorods (B). The optical properties of nanoparticle can be modulated according to its' shape, size, and composition.

Fig. 2. The nude mouse injected cancer cells subcutaneously. (A) Before photothermal treatment. (B) After photothermal treatment, it shows a partial-destroyed tumor mass.

with specific wavelength, the conduction band electrons on the surface of gold nanoparticles oscillate coherently and create a phenomenon known as the SPR. Light energy irradiated on nanoparticles is converted into heat by this phenomenon. Especially, according to the size, shape, composition of nanoparticles, the wavelength of light, in which the particles scatter and absorb light energy, is altered. Therefore, changing the size and shape of gold nanoparticles can alter those peak frequency and they are tunable over the near-infrared region (NIR) of light that has more effective penetration through tissue than the other region of light.

PHOTOTHERMAL TREATMENT (PTT)

The light absorption by gold nanoparticles can be applied to a generation of heat to kill cancer cells. In addition, the manufacturing of nanoparticle can make the tunable gold nanoparticles to have peak absorption on the near-infrared region of light, where tissue penetration of human tissue by light is maximal. Although the heating temperature around nanoparticles by plasmonic PTT can be increased to 70-80°C, cellular injury or death results from protein denaturation at temperature greater than 40°C. Furthermore, since cancerous tissues are more labile to heating than healthy tissues, the effective temperature for PTT effect to kill cancer cells may be from 40 to 50°C. The target temperature of effective PTT was evaluated in the previous study and we suggested it may be about 45°C.²¹ In addition, the cancer cells around nanoparticle-laden macrophages selectively exhibited bubble formation within cytoplasm and cell rupture by irradiating with NIR laser.

In the PTT contrasting with the conventional hyperemia or PDT, which has the limitation of cancer-specificity, the specificity for cancer cells may be achieved by using antibody-conjugated nanoparticles with specificity for surface antigens of cancer or macrophage with

phagocytized nanoparticles (Fig. 2).

However, because it is difficult to predict the toxicity of nanoparticles in vivo, PTT using nanoparticles should be performed with a lower concentration of nanoparticles and a lower laser power for a shorter time to prevent injury to the healthy tissue.

CONCLUSIONS

The advancement of nanotechnology has promoted the clinical application of various types of nanoparticles for diagnosis or treatment of malignant tumor. Even if the toxicity of nanoparticles is an important limitation for clinical application, the various methods increasing specificity for the tumor should enable more selective PTT for cancer cells with reduction of uncontrollable nanotoxicity. If more biocompatible nanomaterials are developed in the future, PTT may be a promising alternative treatment for the malignant tumor.

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