PHOTOTHERAPY TECHNIQUES FOR CANCER DIAGNOSIS AND TREATMENT

Saba Goodarzi[1] and Masoud Mozafari[2]

1. *Biomaterials Group, Faculty of Biomedical Engineering, Amirkabir University of Technology*
2. *Bioengineering Research Group, Nanotechnology and Advanced Materials Department, Materials and Energy Research Center (MERC)*

1. INTRODUCTION

Light plays a significant role in our life. It is used in compact disc (CD) players, in which a laser reflecting off a CD converts the returning signal into music. In grocery store checkout lines, laser beams read bar codes for prices. Laser printers record images on paper by using laser beams. Light is the foundation of the technology which allows computers and telephones to be connected to one another over fiber-optic cables. And light is used in medicine, to produce images used in hospitals and in lasers that perform eye surgery and also cancer treatment. Light therapy or phototherapy contains exposure to daylight or to specific wavelengths of light using polychromatic polarized light, lasers, light-emitting diodes, fluorescent lamps and etc.

Phototherapy is a technique of medical treatment in which light is used to treat diseases such as cancers and peripheral infections to normalize the body and relieve the depression.

2. CANCER TREATMENT

Cancer is defined as an uncontrolled growth of cells. The uncontrolled growth of body cells generates lumps or masses of tissue called tumors. There more than 200 types of cancer including skin cancer, lung cancer, prostate cancer, breast cancer, and colon cancer. Cancer is one of the most terrible diseases in the world and every year millions of people are dying because of this disease. Existing cancer therapies generally include surgery, chemotherapies, and radiotherapies. While surgery in many cases is not able to completely remove all cancer cells in the human body, chemotherapy and radiotherapy possess severe toxic side effects for normal tissues and inadequate specificities to cancer cells. Phototherapies induced by light, preferably near-infrared (NIR) light with greater tissue penetration ability, usually comprise phototherapeutic agents with little toxicity in dark, phototherapy could selectively kill cancer cells under light irradiation, without causing much damage to normal tissues in dark.

Photothermal therapy (PTT) and photodynamic therapy (PDT) are the two types of phototherapy used for the treatment of diseases so far. In PTT, a photothermal (PT) agent is employed for the selective local heating for healing abnormal cells or tissues; while, in PDT, the treatment occurs via a series of photochemical reactions activated by photoactivated molecules or materials called photosensitizer (PS) drugs.

a. PHOTTHERMAL THERAPY

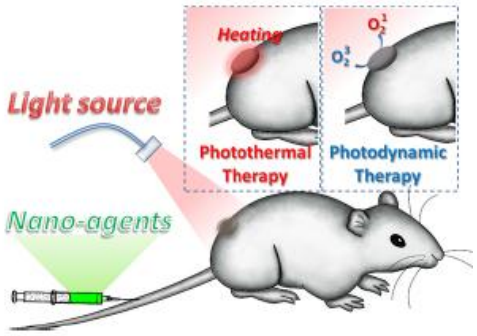
Photothermal therapy (PTT) employs photoabsorbing agents to generate heat from light, leading to thermal ablation of cancer cells and the following cell death. By local heating or hyperthermia, cells undergo irreversible destruction due to the denaturation of proteins and the disruption of the cell membrane. But these thermal treatments damage the healthy tissues as well. More recently, inclusion of laser radiation treatment in thermal cancer therapy resulted in a photothermal method for the selective treatment of cancers, in which a PT agent assistances the selective heating at the local tissue.

For clinical therapy, NIR lasers are selected because of their higher penetration in human tissue resulting in minimal damage. Ideal photothermal agents should display strong absorbance in the NIR region, which is a transparency window for biological tissues, and could efficiently transfer the absorbed NIR optical energy into heat.

b. PHOTODYNAMIC THERAPY

Different from PTT, which relies on photothermal heating to "cook" cancer, photodynamic therapy (PDT) uses singlet oxygen (SO) or reactive oxygen species (ROS) generated from photosensitizer (PS) molecules under light exposure to kill cancer cells. The basic principle underlying PDT of cancers is a sequence of photochemical reactions activated by a photoactivated PS drug. PDT is an externally activable treatment modality for various diseases, and has already been approved for cancer treatment in the clinic. Upon administration of PS molecules, the lesion is then selectively illuminated with light of appropriate wavelength, which, in the presence of oxygen, leads to the generation of cytotoxic oxygen species by PS molecules and consequently to cell death and tissue destruction. A wide range of PS molecules, most of which contain porphyrin structures, have been applied in the PDT.

PS-carrying nanoparticles could increase the water solubility of PS molecules, enhance their tumor accumulation, and thus improve the therapeutic efficacy and specificity of PDT. In addition, nanotechnology provides a platform for the integration of multiple functionalities in a single construct. Various nanomaterials such as liposomes, polymeric nanoparticles, magnetic nanoparticles, quantum dots, carbon-based nanomaterials, mesoporous silica nanoparticles, as well as a number of other functional nanoparticles with interesting chemical and physical properties have been established for the delivery of PDT, showing encouraging results in vitro and in vivo.



Photothermal and photodynamic therapy

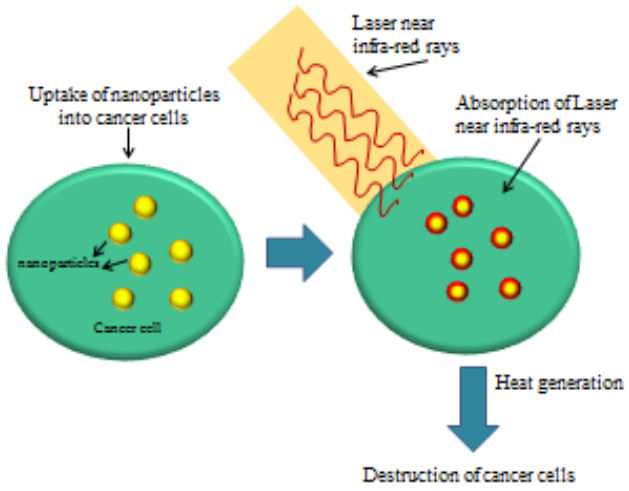
3. BIOIMAGING

Now MRI, CT, SPECT, and PET are noninvasive bioimaging modalities used for disease diagnosis and treatment (e.g., tumor detection) in humans. Molecular imaging is then rational next step in the progress of medical imaging after an atomic imaging (e.g., CT) and functional imaging (e.g., MRI). Molecular imaging has been defined as the in vivo characterization and measurement of biological procedures at the cellular and molecular level, or more generally speaking, as a method for direct or indirect monitoring and recording the temporal and spatial distribution of molecular or cellular routes for biochemical, biological, diagnostic, or therapeutic application. Furthermore, progresses stated in the field of molecular imaging based fluorescent NPs largely focus on NIR fluorescence imaging. Until now, fluorescence in vivo imaging has typically deployed animal models, although there is a clear trend toward using human subjects instead. However, exploiting animal models as test beds in optical imaging is beneficial for developing NPs that could be used for other imaging modalities.

In the field of bio imaging nanoparticles play an important role in diagnosis and treatment of cancer via PDT and PTT. Nanomaterials with desirable shape, size, composition and surface functionalities provide multifunctional platforms for cancer management. Considerable absorption of electromagnetic radiation in the visible to NIR regions coincided with intense scattering of light or ejection of fluorescence photons makes nanomaterials an ideal candidate for non-invasive bioimaging.

Although phototherapy has advantages compared to traditional cancer treatment methods, there are still some challenges that limit clinical use of phototherapy.

One challenge in phototherapy of cancer is the inadequate light penetration depth. For photothermal therapy, NIR absorbing photothermal agents are preferred over those with visible absorption considering the reduced light absorbance and scattering in the NIR window. Regarding photodynamic therapy, the visible light used in traditional PDT is not the perfect light source. Although progress has been made in the development of NIR-induced PDT, great efforts are still needed to improve new generations of PDT agents which can be more efficiently excited by the NIR light.



A schematic of photothermal therapy

4. CONCLUSION AND FUTURE OUTLOOK

Even if NIR light is used in phototherapy, since NIR are not able to penetrate deeper than 1 cm. For some types of cancers, such as skin cancers, oral cancer, esophageal cancer, and even stomach cancers, light can be induced to locally expose the tumors with the help of certain devices (e.g., gastroscopy, endoscopy). For other types of cancers with tumors located deeply inside the body, effective phototherapy would need the suitable design of medical devices (e.g., with optical fibers) that can deliver light into the body. Every therapeutic approach could possess its own advantages and limitations. Although phototherapy has great potential, it is still not rational to expect that phototherapy by itself would win the fight against cancer. It seems that future cancer therapies would very much likely rely on the mixture of a set of diverse treatment approaches, which may include surgery, radiotherapy, chemotherapy, gene therapy, as well as photothermal and photodynamic therapies mentioned in this essay.

Nonetheless, it is believed that phototherapies based on functional nanoagents, due to their unique attractions such as minimal side effects and high efficacies, would play increasingly noteworthy roles in the cancer treatment.

References:

1. Cho, Kwangjae, et al. "Therapeutic nanoparticles for drug delivery in cancer." *Clinical cancer research* 14.5 (2008): 1310-1316.
2. Yao, Jun, Mei Yang, and Yixiang Duan. "Chemistry, biology, and medicine of fluorescent nanomaterials and related systems: New insights into biosensing, bioimaging, genomics, diagnostics, and therapy." *Chemical reviews* 114.12 (2014): 6130-6178.

3. Shibu, Edakkattuparambil Sidharth, et al. "Nanomaterials formulations for photothermal and photodynamic therapy of cancer." *Journal of Photochemistry and Photobiology C: Photochemistry Reviews* 15 (2013): 53-72.
4. Nolsøe, C. P., et al. "Interstitial hyperthermia of colorectal liver metastases with a US-guided Nd-YAG laser with a diffuser tip: a pilot clinical study." *Radiology* 187.2 (1993): 333-337.
5. Shibu, Edakkattuparambil Sidharth, et al. "Nanomaterials formulations for photothermal and photodynamic therapy of cancer." *Journal of Photochemistry and Photobiology C: Photochemistry Reviews* 15 (2013): 53-72.
6. Cheng, Liang, et al. "Functional nanomaterials for phototherapies of cancer." *Chemical reviews* 114.21 (2014): 10869-10939.