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# Design of drug delivery systems for physical energy-induced chemical surgery

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## Abstract

Physical energy-induced chemical surgery, a technique that induces antitumor effects by delivering a drug that exerts a therapeutic effect in response to physical energy and irradiating the diseased part with the corresponding physical energy, is a useful method to treat cancers with minimal systemic side effects. Among chemical surgery, photodynamic therapy (PDT) and neutron capture therapy (NCT) require a system that selectively delivers drugs to the diseased site. Although PDT and NCT have a similar concept, drug delivery systems (DDSs) for their purpose need different functions to solve the unique problems derived from the characteristics of respective physical energy. In this review, we will describe recent chemistry-based solutions including ours to overcome these challenges.

**Keywords:** drug delivery system; photodynamic therapy; photochemical internalization; neutron capture therapy; companion diagnostics

## 1. Introduction

Killing cancer cells using physical energy including laser, radiation (X-ray, proton beam, and heavy particle beam), and ultrasound (high intensity focused ultrasound) is a useful technique to offer permanent cure of cancer with minimal invasiveness [1-3]. When treating cancer with the physical energy, distinguishing the diseased part clearly from normal tissues is extremely important to selectively damage the target tumor and avoid untoward effects. However, as one cancer patient does not always have one distinguishable tumor, it is sometimes difficult to accurately find and distinguish the tumor from the normal tissue. Particularly in the case of multiple and diffuse cancers such as bladder cancer [4], detection and treatment of all cancer tissues one by one is technically challenging. One of the solutions to treat such cancers is diagnostic agents that can detect cancers with high sensitivity [5, 6]; and another solution is physical energy-induced chemical surgery, a methodology to deliver a drug that exerts a

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