

Theranostics and Image Guided Drug Delivery. Edited by Maya Thanou

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Theranostics and Image Guided Drug Delivery

By providing the possibility of real-time, *in vivo* assessment of drug biodistribution, pharmacokinetics or release and therapeutic outcome, imaging has an increasing role in drug development and drug therapies. Theranostic agents comprise diagnostic and therapeutic properties within the same unit (particle or molecule) and allow direct monitoring of drugs in the body, yielding primer information on drug safety and efficiency. The development of theranostic agents and their application in drug delivery is a fast emerging field and represents an important step towards more personalized medicine. There has been great technological progress both in terms of dedicated equipment and the chemistry of the agents used. Theranostic probes involve primarily nanoparticles, which can most easily combine drug carrier and imaging capabilities.

In this complex and multidisciplinary field, the book "*Theranostics and image guided drug delivery*" offers a comprehensive and well-balanced view on the state-of-the-art methods and agents available today, with emphasis on theranostic approaches that have the promise of clinical translation in a close future.

This book is divided into 9 chapters focusing either on the chemical design of nanoparticles dedicated to various imaging techniques (including MRI, NIR optical imaging, PET, or microwave imaging), on drug release mechanisms (such as ultrasound activation, photothermal control, hyperthermia, etc) or on therapeutic approaches (chemotherapy, PDT, etc). Amongst the different types of particles that start to evolve, are in advanced clinical trials or already approved, liposomes have a major importance, with some commercially available formulations. This preponderance is well reflected in the book, although several other types of nanoparticles are also extensively discussed.

Chapter 1 explores image guided focused ultrasound (FUS) for targeted drug delivery. FUS generates local temperature increase initiating focal drug delivery, increased membrane permeation or enhanced drug diffusivity. Potential applications have been illustrated in hepatocellular carcinoma, prostate cancer, uterine myomas or breast tumors. The chapter presents several examples, with an extensive discussion on doxorubicin-loaded thermosensitive liposomes. The local release of the drug cargo from such liposomes is triggered by FUS-induced hyperthermia. Various liposome systems incorporating Gd³⁺ complexes and allowing for MRI monitoring are compared. Later *Chapter 6* comes back in more detail on liposomes for hyperthermia triggered drug release. Therein, a full description of the chemical design and testing procedures are presented regarding the lipid constituents, the role of cholesterol, ways of tuning *in vivo* stability, drug loading efficiency and drug release, or the influence of tumor environment on liposome stability.

In *Chapter 2*, NIR-absorbing nanocarriers are discussed in the context of photothermal cancer chemotherapy. The bases of these techniques are presented, together with an overview of recent progress in the development of nanocarriers dedicated to photothermal therapy, involving both organic-and inorganic-based functional nanomaterials.

Magnetic nanoparticles (MNPs) for multimodal imaging are covered in *Chapter 3*. An outline of the magnetic-based imaging techniques is presented, with a brief description of magnetic resonance imaging, magnetic particle imaging, magneto-motive ultrasound imaging and magneto-photoacoustic imaging. Finally, the applications and challenges of MNPs in drug delivery, as well as a summary of the different nanoparticles available are addressed.

Photodynamic Therapy (PDT) is an established technique that relies on the use of a photosensitizer which generates reactive oxygen species upon light irradiation. The fundaments of PDT, the photochemical properties of the photosensitizers approved for clinical use, the challenges associated with the drug selectivity, delivery and examples of PDT theranostic agents and their dosimetry are outlined in *Chapter 4*.

Chapter 5 discusses the use of positron emission tomography (PET) as a complementary technique in a multi-modal *in vivo* tracking approach for liposomal nanomedicines. Different labeling strategies with PET isotopes such as ¹⁸F, ⁶⁴Cu and ⁸⁹Zr are compared, and the advantages and limitations of such labeled nanoparticles for clinical translation are discussed.

Chapter 7 deals with targeted delivery using ultrasound activated nano-encapsulated drugs, and with the combination of physical and chemical methodologies to exploit the best features of each leading to better controlled drug delivery. The use of ultrasound mediated methods for local drug release can influence cell permeability. The authors present how permeability is enhanced through mechanical and thermal mechanisms. An important part is dedicated to the discussion of novel chemically modified cyclodextrin-based systems in the context of doxorubicin delivery.

Chapter 8 has a specific focus on the gastrointestinal tract and discusses the possibilities to combine capsule endoscopy with ultrasound mediated drug delivery. After a detailed description of the gastrointestinal system, including its most common diseases, video capsule endoscopy (VCE) is presented in detail. The important technological progress, which results from miniaturisation of electronics, wireless communications and efficient electrical power delivery, brings this technique towards therapeutic applications (therapeutic capsule endoscopy, TCE). This is exemplified by a proof-of-concept theranostic device with the potential to treat conditions such as inflammatory bowel disease and colon cancer.

Lastly, *Chapter 9* deals with microwave imaging (MWI) and the potential of dedicated agents for theranostics use. The bases of this emerging technique as an alternative method based on nonionizing electromagnetic signals, and mainly used for breast imaging, are presented and the main underlying parameters (relative permeability and effective conductivity) are depicted. The potential of MWI on inducing thermal therapy is mentioned. The introduction of tailor made agents which affect the dielectric properties of the medium (tissue) and which enhance microwave dielectric contrast may provide a very useful clinical tool. Microbubbles or carbon nanotubes are examples of such nanoparticle agents.

A major merit of this book is to combine an up-to-date overview of the more "classical" methodologies such as image-guided, hyperthermia-triggered drug release, with an introduction to less advanced and less known techniques like microwave imaging or capsule endoscopy and their potential use in theranostics. This balanced collection of very different approaches makes the book attractive and valuable for a diverse readership interested in theranostics.

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