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Novel optical, optoacoustic, and ultrasound approaches for assessment of nanoparticle-mediated drug delivery in tumors and cancer therapy

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ABSTRACT

We proposed to use interaction of nanoparticles with optical or ultrasound radiation that produces direct thermal or mechanical damage to tumors or enhances delivery of anti-cancer macromolecular drugs and genes in tumors. In our previous works we performed preliminary studies which demonstrated promising results. In this work we used optical, optoacoustic, and ultrasound microscopies *in vivo* in mice with human breast, colon, and prostate tumors and *in vitro* in tumors excised after the treatment. Our results demonstrated that optical, optoacoustic, and ultrasound microscopies provide real-time, continuous monitoring and imaging of nanoparticle kinetics and accumulation in tumors and can be used for assessment of tumor therapy.

1. INTRODUCTION

Poor penetration of anti-cancer drugs and genes in tumors substantially limits efficacy and safety of cancer chemo- and biotherapy. We proposed to use interaction of nanoparticles with optical or ultrasound radiation that produces direct thermal or mechanical damage to tumors or enhances delivery of anti-cancer macromolecular drugs and genes in tumors. Interaction of light or ultrasound with strongly-absorbing or porous nanoparticles may enhance drug and gene delivery or produce damage to tumors without drugs. The nanoparticles can selectively be accumulated in tumor blood vessels using passive delivery based on enhanced permeability and retention (EPR) effect or active delivery using targeting molecules. Our preliminary studies

demonstrated promising results (Larina et al. 2005, Larina et al. 2005, Chumakova et al. 2006, Chumakova et al. 2008, Figueiredo and Esenliev 2012).

2. RESULTS

In this work we used optical, optoacoustic, and ultrasound microscopies *in vivo* in mice with human breast, colon, and prostate tumors and *in vitro* in tumors excised after the treatment. Strongly-absorbing carbon nanoparticles and biodegradable polymer poly (lactic-*co*-glycolic acid) (PLGA) air-filled nanoparticles (150 – 200 nm) were used for optical and ultrasound therapy, respectively. Using a high-resolution ultrasound imaging system (resolution up to 30 microns) Vevo developed by VisualSonics we studied kinetics of the nanoparticles injected in the tail vein of mice bearing human tumors. We invented, developed, and built a novel, optoacoustic system for monitoring kinetics of carbon nanoparticles in the tumors *in vivo* and assessment of the nanoparticle-mediated tumor thermotherapy. After the *in vivo* experiments, distribution of nanoparticles in tumors was studied using an advanced optical microscopy system developed for this project.

3. CONCLUSIONS

Our results demonstrated that optical, optoacoustic, and ultrasound microscopies provide real-time, continuous monitoring and imaging of nanoparticle kinetics and accumulation in tumors and can be used for assessment of tumor therapy.

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