17a-D4-9

Enhanced Delivery of AuNPs with Acoustic Cavitation for Photoacoustic Imaging and Photothermal Therapy

Yu-Hsin Wang[1] and Pai-Chi Li [1,2]

[1] Institute of Biomedical Electronics and Bioinformatics, [2] Department of Electrical Engineering
National Taiwan University
E-mail: paichi@ntu.edu.tw

1. Introduction

Among various molecular imaging modalities, ultrasonic imaging and photoacoustic imaging provide unique advantages and also face specific challenges. Ultrasonic molecular imaging, on one hand, is based on mechanical properties of the image object and many unique applications have been developed. With the aid of superior spatial resolution, high frequency ultrasound imaging has also evolved from clinical anatomical imaging to probing of molecular processes on small animals for pre-clinical research. Photoacoustic imaging, on the other hand, combines advantages of both optics and acoustics. Research developments in imaging physics and instrumentation have also found promising biomedical applications. In addition, microbubbles typically used in ultrasonic imaging as the contrast agent present unique mechanical properties and the associated acoustic cavitation has been exploited for therapeutic purposes. Similarly, gold nanoparticles (AuNPs) are found to be an ideal contrast agent for photoacoustic imaging for its bioconjugation capabilities and presumed safety. The efficient light absorption of AuNPs and abilities to tune their optical properties have also led to new photothermal therapy techniques. In the past, we have developed instrumentations that were used for applications of ultrasonic and photoacoustic imaging. New development in combined diagnosis with therapy for both modalities have also been introduced.

2. Research Results

AuNPs incorporated with microbubbles (AuMBs) have been introduced as a photoacoustic and ultrasound dual-modality contrast agent. Applications can be extended to theranosis purpose with its unique characteristics. In this study, an enhanced delivery method of AuNPs is proposed by using microbubbles as a targeted carrier and by inducing acoustic cavitation to improve the permeability. The hypothesis is confirmed with *in vivo* and *in vitro* examinations. First, these AuMBs are modified with anti-VEGFR2 so as to bind to angiogenesis. The targeting efficiency was observed by an ultrasound system and the extended retention was recorded for 30 minutes in a CT-26 tumor bearing mouse. Second, cavitation induced by time-varying acoustic field is also applied to disrupt the microbubbles and induce increased transient cellular permeability (a.k.a., sonoporation). Photoacoustic and phototehrmal experiments were conducted and results were correlated with the cavitation dose. At least 10 times improvement in AuNP delivery and twenty degrees of temperature elevation were achieved. An optical microscope which collects the two photon fluorescence emitted by AuNPs further supports the enhanced delivery. Finally, *in vivo* delivery of AuNPs was demonstrated with t laser-induced thermotherapy that showed hyperthermia (>45℃) with sonoporation. Therefore, controlled release of AuNPs is feasible with acoustic cavitation and the procedure can further improve therapeutic effects of the AuNPs.

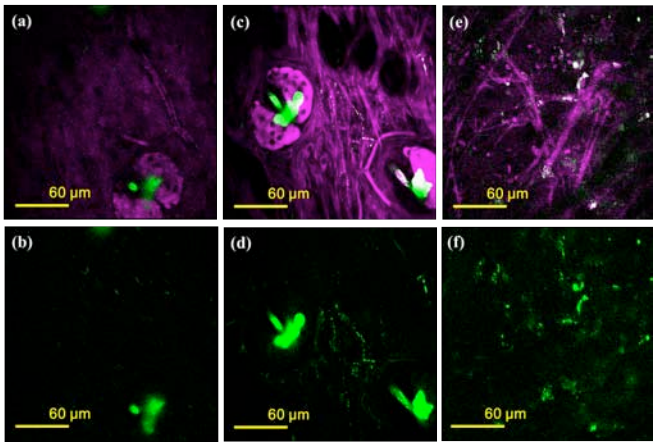

Figure: Nonlinear optical microscopy of mouse ears (magenta: THG, green: 2PF). Panel (a) and (b) are THG-2PF and 2PF-only images without AuMB injection, respectively. After injection and sonoporation, images of a normal mouse's ear are shown in (c) and (d), while panel (e) and (f) are images acquired in the tumor.

Acknowledgements

This study was financially supported by the National Science Council of Taiwan under grant 99-2221-E-002-046-MY3 and National Health Research Institutes of Taiwan under grant NHRI-EX101-10136EI.