Quantification of Tumor Gold Nanorod Uptake Using Photoacoustic Multispectral Unmixing Technique

Yanjie Wang[1], Muhannad N Fadhel[1], Eno Hysi[1], Maurice Pasternak[2], and Michael C. Kolios[1]
[1]*Physics Department, Ryerson University, Toronto, Canada,*
[2]*Biological Sciences Department, Sunnybrook Research Institute, Toronto, Canada*

Background, Motivation and Objective

Gold nanorods (GNRs) can be used as contrast agents for tumor photoacoustic (PA) imaging and as drug carriers for cancer treatment. Through active targeting strategy, the GNRs can be delivered into a specific region of interest to improve the sensitivity of tumour detection, and potentially reduce non-specific drug delivery. However, the quantification of GNR uptake remains challenging as it relies on tissue extraction and complex inductively coupled plasma (ICP)-based measurements of gold atom concentration. The goal of this work is to develop a method which can quantify the GNRs in-vivo. The method uses multispectral PA imaging and an unmixing algorithm to estimate GNR concentration in tissue.

Statement of Contribution/Methods

In this study, GNRs and a perfluorohexane (PFH) liquid were encapsulated in the core of a poly(lactic-co-glycolic acid) (PLGA) nanoparticle (NP) (mean size ≈ 300 nm) as a phase-change contrast agent. A Herceptin antibody was conjugated to the PLGA NP surface for targeting the HER2 receptor. Human breast cancer cells BT474 (HER2 positive) were inoculated in the flanks in BALB/c B17 SCID mice four weeks prior to imaging. The PLGA-GNRs were labeled with DiD fluorescence dye and were injected into the mice through the tail vein. Photoacoustic imaging (2D/3D) was performed at 720, 750, and 850 nm with a 21MHz transducer using the VevoLAZR2100 (FUJIFILM Visualsonics, Canada). The wavelengths were chosen to quantify the concentrations of oxy-, deoxy-hemoglobin and GNRs in the tumor through linear spectral unmixing. The GNR distribution maps were compared with PA images, and tissue fluorescence images.

Results, Discussion and Conclusion

The PA images and the accompanying power spectra are shown in Fig. 1A and 1C. The signal intensities are 49 and 55 dB for pre-injection and 3h post-injection, respectively. The GNR distribution maps and GNR average concentration are shown in Fig. 1B and 1D. The GNR concentration is 15 times higher 3h post-injection. The fluorescence images of tumor tissue also show a significant uptake of PLGA-GNR-DiD at 3h post-injection (Fig. 1E1a&1b) compared with the control group (Fig. 1E2a&2b). This work demonstrates the potential of a PA multispectral unmixing technique for quantification of GNR tumor uptake. In the future, the approach will be directly compared with the gold standard of ICP to assess the accuracy of GNR quantification.

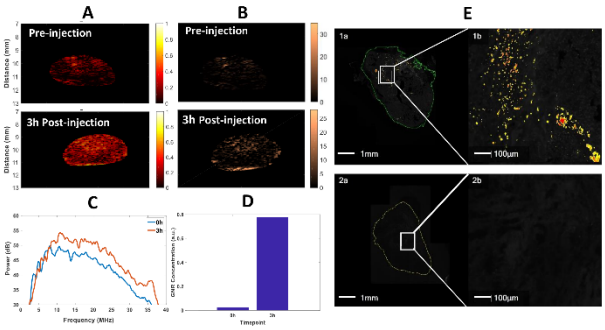

Fig. 1 (A) Tumor photoacoustic images and (B) GNR distribution maps were acquired at pre-injection and 3h post-injection of PLGA-GNR particle. (C) Average PA power spectra and (D) GNR concentration calculated from a 2D frame of tumor image at two time points. (E) Fluorescence images of tumor tissues. (E1a) and (E1b) are images of tumor tissue collected after 3h post-injection. (E2a) and (E2b) are images of a tumor tissue without any particle injection. The yellow and orange dots are the location of the PLGA-GNR-DiD particles.