The use of photoacoustic imaging in treatment monitoring of vascular targeting agent (DMXAA) through methemoglobin quantification

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Background, Motivation and Objective

Cancer therapeutic drugs are often targeted to reduce the accumulation to normal tissues. Vascular targeting agents are one those classes taking advantages of the genetic stability of the tumor vascular and the changes in the tumor microenvironment to damage the tumor vessels, cutting nutrition and oxygen supply. After vessel damage, red blood cells escape the vascular system. Agents in the extracellular matrix oxidize hemoglobin into methemoglobin. The goal of this work is to use photoacoustic (PA) imaging to monitor the efficacy of the vascular targeting agent 5,6-Dimethylxanthenone-4-acetic acid (DMXAA) through methemoglobin quantification.

Statement of Contribution/Methods

Six BALB/c type mice were injected subcutaneously into the right hind leg with $5x10^5$ 4T1 cells. One week after, half of the mice were treated with DMXAA and the other half with saline through tail vain injection. All mice were imaged using the VevoLAZR X PA system prior to, 4 hours after and 24 hours after the treatment. The imaging was done at the wavelengths 680, 796 and 910 nm. The wavelengths were selected by minimizing the variation inflation factor of the extinction conflictions of oxy, deoxy and methemoglobin. Variation inflation factor is used to minimize the collinearity of the wavelengths selected for unmixing which will result in more stable solution. Linear spectral unmixing was applied to the PA images to quantify the three chromophores. After, the tumors were extracted and stained with TUNEL to detect DMXAA-induced apoptotic cell damage.

Results/Discussion

The ratio of percent change of methemoglobin for the six mice at 4 and 24 hours post treatment are shown in Fig 1a. For the saline treated mice, an increase in methemoglobin percentage was not detected (M1-M3). The increase in methemoglobin percentage by a factor of two was present for two of the treated mice (M4, M6). Mouse 5 did not show an increase in methemoglobin percentage. This could be due to that fact that the treatment was not as effective for mouse 5. This is supported by the TUNEL staining acquired from the tumors (Fig 1b). DMXAA treated mice demonstrate a larger presence of TUNEL staining for M 4 and 6 relative to mouse 5 and the saline treated mice, indicative of larger cell death in those mice. This study demonstrates the capability of PA modality in monitoring vascular targeting agents e.g. DMXAA through methemoglobin quantification.

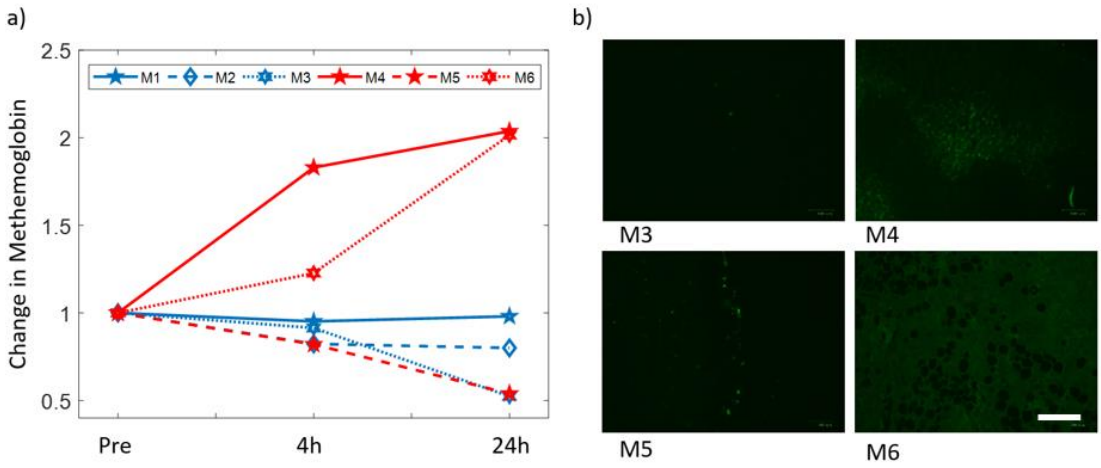

Fig. 1: (a) Ratio of percent change of methmolgobin 4 and 24 hours after treatment. Blud and red lines represent saline and DMXAA treated mice, respectivly. (b) TUNEL staining of four representative mice. Scale bar represent 200 µm.