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Assessment of gold nanoflowers as contrast agents for photoacoustic imaging

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Background, Motivation and Objective. Photoacoustic (PA) imaging is an emerging method for medical diagnosis. It is based on the photoacoustic effect, in which pulsed electromagnetic waves are absorbed by the tissue, causing thermoelastic expansion, and then emitting acoustic waves. It is a hybrid system of optical excitation and acoustic detection, presenting better molecular contrast than conventional ultrasound (US) due to the different optical absorption properties of the tissues, yet the penetration of the signal is limited (P. Beard, 2011). External contrast agents can be produced to exhibit greater optical absorption in the near infrared window, leading to lower signal attenuation, potentiating PA images at deeper depths. Gold nanoparticles (AuNP) can be synthesized for this purpose, because of the possibility of altering the plasmon surface resonance effect associated with it, changing its size and shape. In previous studies, flower-shaped AuNPs, known as nano flowers, were synthesized with an optical absorption coefficient (μ_a) in a 650 - 1000 nm band (O. A. Santos, 2017). In this study, these flowers-shaped AuNPs were reproduced and adapted for the analysis of behavior as contrast agents for spectroscopy and PA imaging.

Methods. AuNPs were synthesized from a substitution of the PEG-Tiol solvent by a mixture of ethylene glycol (EG) and polyethylene glycol (POLIEG). The synthesis was obtained by mixing 0.9 mL of EG, 0.1 mL of POLIEG, 14 µL of $HAuCl_4$ (25 mM), 15 µL $AgNO_3$ (10 mM), 150 µL of ascorbic acid ($C_6H_8O_6$ - 100mM) and an addition of polyvinylpyrrolidone to stabilize the sample. In one sample, half of the EG was replaced by H_2O. Spectroscopic measurements were carried out through a spectrophotometer and a PA imaging system, irradiated by a pulsed Nd: YAG laser connected to an OPO Rainbow system with wavelength λ range 680 - 950 nm, coupled to an optical fiber and a pulse/receiver ultrasonic transducer (OLYMPUS) to acquire the signal through an oscilloscope (KEYSIGHT), the signals were processed using the peak-to-peak method (J. Laufer, 2005) and the curves obtained of optical absorption coefficient were compared to the ones from the spectrophotometer. PA images were obtained with the production of styrene-ethylene / butylene-styrene (SEBS) polymer phantoms containing a cylindrical inclusion with AuNPs. The images were acquired through a US Ultrasonix device while the samples were irradiated by the laser. The collected data were analyzed considering the number of laser pulses and sample concentrations, those were processed in MATLAB R2016a environment.

Results. AuNP synthesis resulted in nanoparticles with shapes similar to flowers (Figure 1) with an absorption band between 650-1000 nm and size ranging from 90 to 150 nm. The sample with substitution of EG for H_2O showed higher absorption. PA spectroscopy data were obtained for both samples, in which the obtained curve was consistent with the spectrophotometer results. Pulse incidence analysis showed stability of AuNP, and concentration variation showed a proportional change PA spectrum. PA images of the phantoms showed the AuNP response signal, due to the different optical absorption properties, characteristic of the material in different wavelengths (Figure 2).

Discussion and Conclusions. The AuNPs obtained resulted in higher absorption within the near infrared window, allowing higher signals at greater depths in tissue. The substitution of EG by H_2O resulted in higher signal intensity due to the change in the viscosity of the material; lower viscosity allows greater displacement of the material and greater thermoelastic expansion, enhancing the signal. Spectroscopy analyzes indicated that the PA system can be used to evaluate the absorption spectrum since the PA signal amplitude is associated, in its equation, with μ_a. Regarding the pulse incidence, stability of the modified AuNPs was verified, because the nanoparticles supported the thermoelastic expansions and maintained their shape, so that their properties did not change after being submitted to large amounts, approximately 3000, of laser pulses. The study of the concentration variation resulted in a decrease in the signal with a decrease in the sample concentration, as expected because it was directly proportional to the PA signal. The signal intensity in the PA images showed adequate results compared to the ones obtained by the PA spectroscopy, in which the absorption is lower for higher λ. The synthesized AuNPs were shown to be good contrast agents for the spectroscopy and PA imaging methods, and could be applied in future studies as contrast agents in *in vivo* studies.

Figures and Tables (Optional).

Figure 1 – TEM image of the synthesizes AuNP. The white bar represents 100 nm.

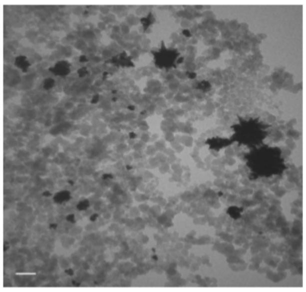
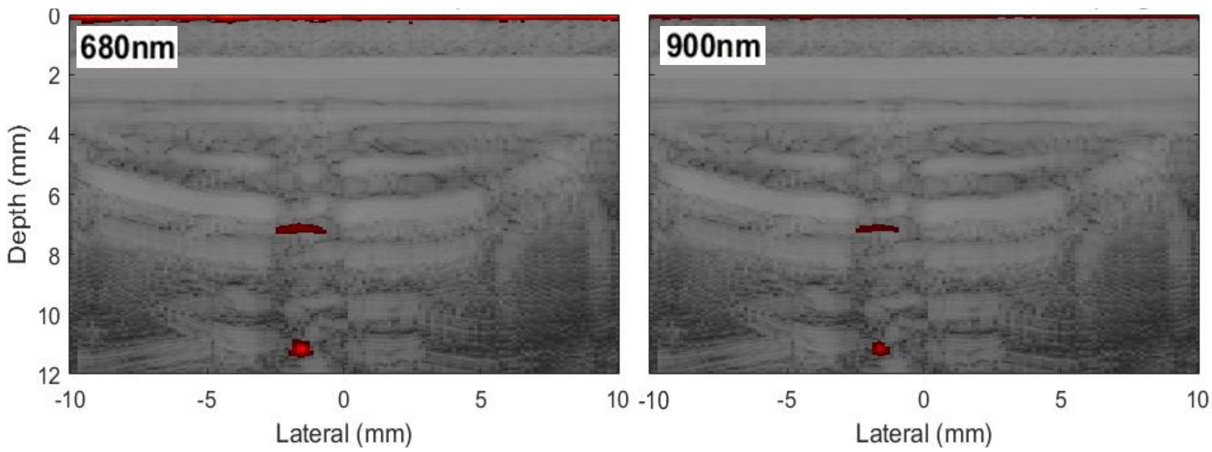


Figure 2 – PA images ("hot" colormap) were overlaid onto ultrasound B-Mode (gray scale) images.



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Keywords. photoacoustics; photoacoustic imaging; gold nanoparticles; contrast agents; spectroscopy; nanoflowers.