Nanodroplets loaded with tetrapyrrolic dyes for photoacoustic tomography

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Photoacoustic tomography (PAT) is an emerging imaging technique. The contrast agents used in PAT transform, through non-radiative decay, absorbed pulsed laser light into an ultrasound wave, called photoacoustic wave (PAW). Hemoglobin can be used as a PAT endogenous contrast agent, but the translation to clinical settings requires the development of better contrast agents that allow a higher resolution and enhanced contrast [1].

Tetrapyrrolic macrocycles have an intense absorption in the phototherapeutic window and can be used in PAT. The complexation of porphyrins derivatives or phthalocyanines with a paramagnetic metal increases the non-radiative decay yield. This allows a rapid transformation of the absorbed light into heat and the subsequent release of a pressure wave that can be detected outside the body.

Nanodroplets are metastable particles composed of a shell (lipid, protein or polymer) and a perfluorocarbon core. The perfluorocarbons used usually have low boiling points facilitating a phase transition and the formation of microbubbles upon small temperature or pressure changes [2]. Nanodroplets have been investigated in ultrasound and PAT, and in this work they were used to carry a tetrapyrrolic contrast agent and increase the photoacoustic contrast upon its activation.

The nanodroplets produced for this study have a perfluoropentane core and an albumin (bovine serum albumin, BSA) shell. New porphyrins and phthalocyanines were synthetized with fluorinated chains to try to increase the solubility in the perfluoropentane. Different paramagnetic metals were used for the complexation reactions to increase the non-radiative decay and photoacoustic signal production (Fig. 1).

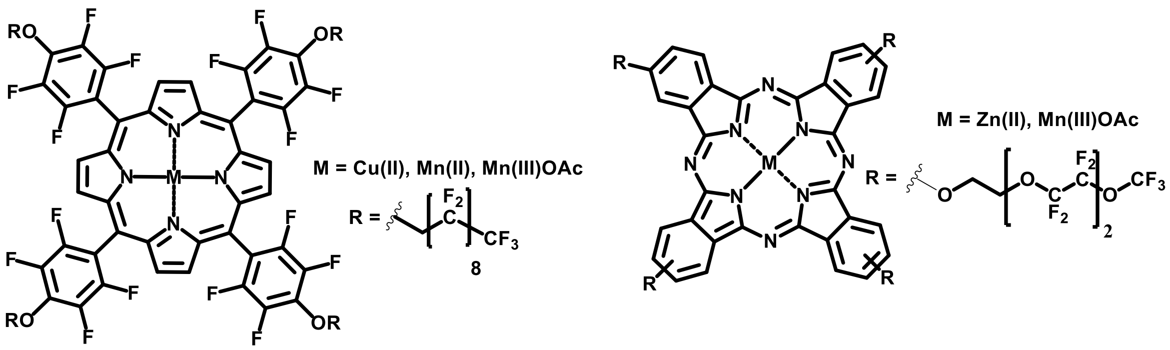

Fig. 1. Schematic representation of the porphyrins (left) and phthalocyanines (right) synthesized.

A diethyl ether stock of each dye is prepared and added to an aqueous BSA solution (2 mg/ml). Perfluoropentane is added to this BSA solution and the final mixture is sonicated to produce dye loaded nanodroplets. To evaluate the vaporization of these structures after pulsed laser light absorption a photoacoustic calorimetry apparatus was used [3].

The photoacoustic signal produced by the nanodroplets was always compared to the respective BSA solution, to evaluate if we were in the presence of a vaporization process. The photoacoustic signal detected after the excitation of the contrast agents is higher in the nanodroplets compared to the BSA solutions, suggesting that the contrast in PAT can be enhanced by using these structures.

The best candidates after the photochemical and photoacoustic characterization are being analyzed with the Vevo LAZR-X Multi-modal Imaging Platform from Fujifilm VisualSonics in animal models. We believe the vaporization of the nanodroplets produced from these dyes will increase the contrast and allow a higher contrast in PAT.

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References

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