Photoacoustic Contrast Agents for Deep Tissue Imaging

Onseok Lee, Jaeyoung Kim, Chilhwan Oh, and Seunghan Ha

Abstract--- Quaterrylenediimide-cored dendrimers may serve as exogenous contrast agents in the field of photoacoustic imaging (PA) for deep tissue imaging. The purpose of this study is to show the feasibility of the potential of two hydrophilic and photostable Quaterrylenediimide-cored dendrimers dyes for deep tissue PA imaging. These dendrimers exhibit high PA signal intensity and remarkable chemical and photo stability.

Index Terms--- Photoacoustic, Deep tissue imaging, contrast agent, Dye

I. Introduction

Photoacoustic (PA) imaging techniques for deep tissue imaging relies on the PA contrast agents to absorb light energy to generate acoustic propagation wave. Recently, it has become a rapidly growing biomedical imaging modality and attracted great interest of scientists due to its high spatial resolution and the absence of ionizing radiation.[1] In order to image deep tissues, the near infrared (NIR) wavelength light source is typically used in the PA imaging. High performance PA contrast agents should possess strong light absorption ability and efficiently convert the light energy to acoustic propagation wave. One of the most commonly used exogenous contrast agents for PA imaging is indocyanine green (ICG),[2] the only FDA approved NIR dye. However, the relatively poor chemical and photo stability, as well as limited efficiency of converting absorbed light to acoustic propagation wave, limits the application of PA imaging. An NIR dye with high absorption extinction coefficient, low fluorescence quantum yield and high chemical and photo stability will be more desirable for PA deep tissue imaging.

Recently, *P. Shao* [3] reported two hydrophilic NIR dendrimers, QR-G1-COOH and QR-G2-COOH. The dendrimers was based on quaterrylenediimide with four biocompatible dendronized polyamides covalently attached to the bay regions. QR-G1-COOH and QR-G2-COOH possess twelve and thirty-six carboxyl acid groups respectively, which not only increase hydrophilicity but also introduce multiple-functionality. Although these dendrimeric NIR dyes shown remarkable chemical and photo stability, the fluorescence signal was rather weak. However, such weakness for fluorescence imaging may be advantageous for PA imaging, as less fluorescent dyes may be able to convert more absorbed light energy into PA signal.

The purpose of this study is to show the feasibility of quaterrylenediimide-cored dendrimeric dyes for deep tissue PA imaging.

II. Materials And Methods

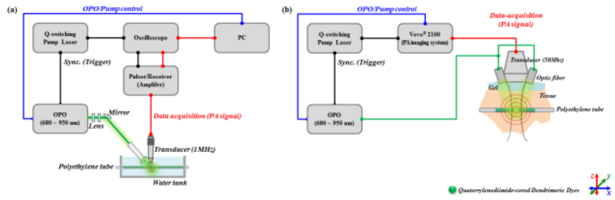

Fig. 1 Experimental setups for acquiring of photoacoustic signals using quaterrylenediimide-cored dendrimeric dyes. (a) PA system for measurement of PA signal intensity using a single element transducer (b) PA system for deep tissue imaging using a linear array transducer.

Figure 1 (a) show the experimental set up for measuring of PA signal intensity.[4] Nd:Yag pulsed Laser (Quantel, Bozeman, MT, USA) pumps an optical parametric oscillator (OPO, Vibrant HE532I, OpoTek, Carlsbad, CA, USA) to generate 5 ns pulses at 10 Hz. Selected range of wavelength was 800 nm (OPO Range : 680 ~ 950 nm). The laser beam of OPO output was directly illuminated into QR-G1-COOH, QR-G2-COOH or ICG in a thin Polyethylene tube (PE10: ID 0.28mm, OD 0.61mm, Becton Dickinson). The laser light at 800 nm was illuminated with two different energy levels (0.8 mJ and 1.2 mJ). The laser light beam size was > 10 mm on the sample, which was large enough to uniformly illuminate the imaging area. A focused single element ultrasonic transducer (1MHz, Olympus, MA, USA) was used to detect the PA signal in water tank experiment (see Figure 1(a)). The PA signal was averaged 10 times at each scanning grid point. The PA signal was then normalized to the measured average pulse energy (J-50MB-YAG Energy MaxTM Sensor, Coherent, Portland, OR). The ultrasonic transducer output was amplified (model 5900PR, Olympus, MA, USA), digitized, and recorded by a digital oscilloscope (WaveSurfer 452, LeCroy Corp., NY, USA) synchronized to the laser. For deep tissue PA imaging (See Figure 1 (b)), the experimental configuration and condition of Nd:Yag pulsed Laser, connected with OPO, was the same as water tank experiment. The laser light was delivered by the optic fiber combined with ultrasound transducer (50MHz, VLZ550, VisualSonics, Toronto, Canada) holder, illuminating top surface of the chicken breast tissue. The same thin polyethylene tube for

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water tank experiment, filled with QR-G1-COOH or QR-G2-COOH, was embedded in the tissue at 5.5mm below the tissue surface.

III. Results and Discussion

The synthesis of QR-G1-COOH and QR-G2-COOH was reported by P. Shao.[3] QR-G1-COOH and QR-G2-COOH was biocompatible and show intense NIR absorption bands centered at 788 nm in DMSO, with remarkable chemical and photostability. Specifically, when exposed to the ambient light for 3 days, the dendrimeric dyes showed almost no change in the absorption whereas ICG sample completely lost NIR absorption.[3] Such spectroscopic properties was favorable in signal quantification and long-term PA imaging.

Under the same conditions of laser illumination, QR-G1-COOH and QR-G2-COOH show higher PA signal intensity than ICG (See Fig. 3). Specifically, QR-G1-COOH, QR-G2-COOH and ICG showed PA intensity of 2.5, 2.5 and 2.0 V respectively at 0.8 mJ of light irradiation (@800 nm), and 6.7, 6.8 and 6.0 V respectively at 1.2 mJ light irradiation (See Fig. 3). As shown in Fig 4, with significant PA signal from QR-G1-COOH and QR-G2-COOH, the dye solution in the tube was clearly identified and imaged at the depth of 5.5 mm of chicken breast tissue. These results indicate that quaterrylenediimide-cored dendrimers have ample potential as noble contrast agent for deep tissue imaging in PA imaging.

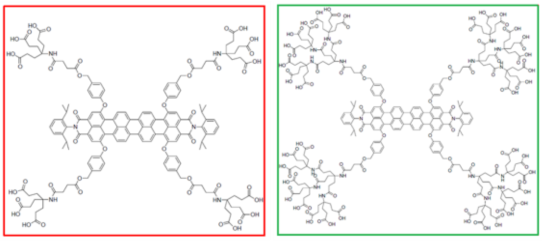

Fig. 2 The chemical structures of Quaterrylenediimide-cored dendrimers.

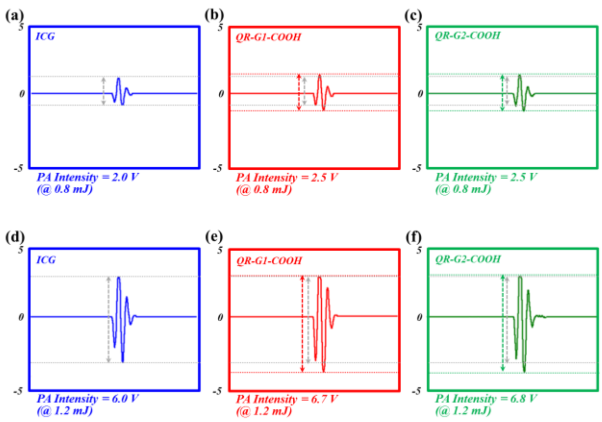

Fig. 3 The comparison of PA signal intensity among ICG ((a), (d), bule color), QR-G1-COOH ((b), (e), red color), and QR-G2-COOH ((c), (f), red color) at the same conditions.

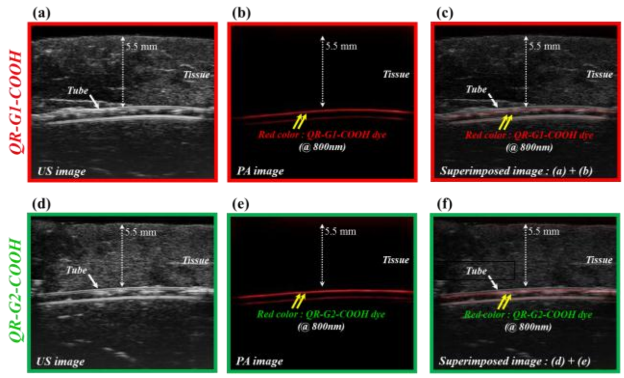

Fig. 4 PA imaging of QR-G1-COOH (top panels, Red color), and QR-G2-COOH (bottom panels, Green color) in a thin Polyethylene tube embedded in chicken breast tissue. Left panels are ultrasound B-scan images for morphological information ((a), (d)), middle panels depict PA images ((b), (e)), and ultrasound B-scan and PA images are overlaid in the right panels ((c), (f)).

IV. Conclusion

NIR QR-G1-COOH and QR-G2-COOH dendrimeric dyes show several favorable spectroscopic properties for PA imaging, including hydrophilicity, biocompatibility, high chemical and photo stability and intense PA signal. These properties, coupled with the prospect of attaching targeting and therapeutic agents to the denrimeric structure, provide promise of the quaterrylenediimide-based dendrimers for PA applications. Further deep tissue imaging studies are in progress.

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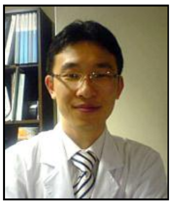

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