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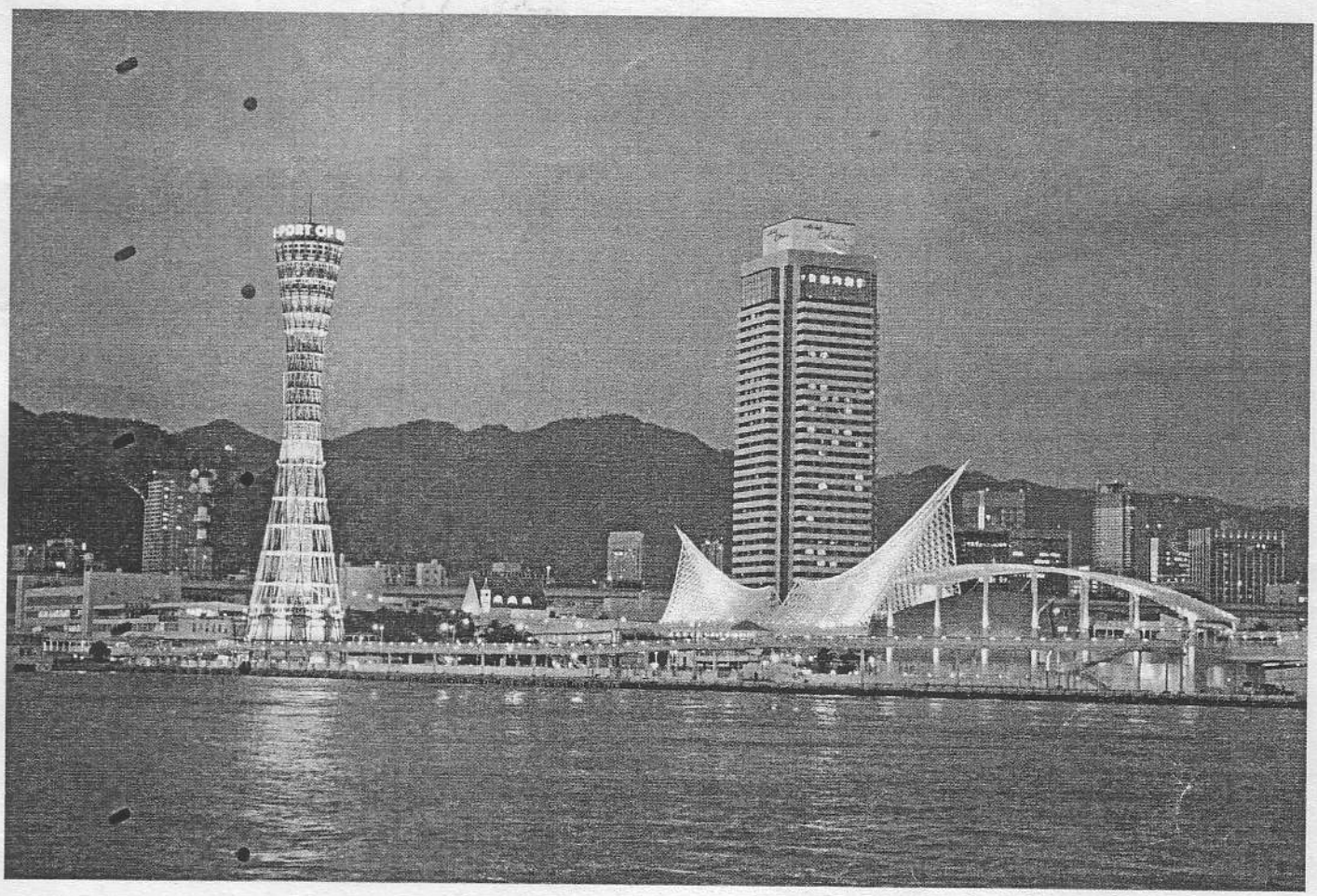

ABSTRACT BOOK

IEEE Ultrasonics, Ferroelectrics, and Frequency Control Society

IEEE

P1-B4 - Acoustic Droplets and Bubbles Applications

Kairaku (posters 1)

Wednesday, October 24, 9:30 AM - 4:00 PM

Chair: **Klazina Kooiman** Erasmus Medical Center

P1-B4-1

Evidence of Laser-Activated Perfluorocarbon Nanodroplet Extravasation In Vivo

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Background, Motivation, and Objective

Laser-activated perfluorocarbon nanodroplets (PFCnDs) are a promising ultrasound photoacoustic (USPA) contrast agent for extravascular imaging. Yet extravasation of PFCnDs has not been demonstrated in a realistic, orthotopic model of cancer. The objective of this work was to provide evidence of extravasation via a PFCnD capable of both USPA imaging and FRET fluorescent emission via histology.

Statement of Contribution/Methods

PFCnDs were made with a perfluorohexane (FluoroMed) core, lipid shell, and near-infrared (NIR) dye (Epolight 3072; Epolin) for optical droplet vaporization. The shell also included a 1:10 ratio of encapsulated Cy3 carboxylic acid (Lumiprobe) and Cy5 PE (Avanti), enabling intact PFCnDs to exhibit FRET. The ratio of PEG2000 PE (Avanti) to Cy5 PE to DSPC (NanoCS) was 8:1:1. PFCnD size distribution was assessed by a NanoSight NS300 (Malvern). Fluorescence emission was recorded by a spectrofluorometer (Fluorolog 3-21; Horiba). USPA images were captured by a Vantage 256 (Verasonics) driving an integrated USPA transducer (LZ400; VisualSonics) coupled to a 10 Hz pulsed Nd:YAG laser (Phocus Mobile; Opotek) outputting 1064 nm light. Six week old athymic female mice (nu/nu; JAX) were inoculated in the right-lower mammary fat pad with $1x10^6$ 4T1 rat breast carcinoma cells in a 1:1 mixture of media and Matrigel Matrix (Corning). Tumors were allowed to grow until they were 5-10 mm in diameter (1 week). After preliminary imaging, mice were injected with 70 µL of $2x10^{10}$ PFCnD/mL solution via jugular vein. Mice were reimaged after 24 hours both *in vivo* and after perfusion prior to tumor resection.

Results/Discussion

PFCnDs had a median size of 240 nm (**Fig. 1A**). These PFCnDs exhibited on-particle FRET *in vitro* (**Fig. 1B**, bottom), with decreased observed fluorescent emission compared to Cy3-Cy5 nanomicelles (**Fig. 1B**, middle) likely due to particle scattering and NIR dye absorption. Imaging shows contrast enhancement at 24 hours compared to pre-injection imaging (**Fig. 1C**) in both PA and differential ultrafast US images (**Fig. 1D**). Contrast persists even after perfusion (**Fig. 1E**). These preliminary results suggest PFCnDs extravasated in an orthotopic primary breast tumor. Ongoing studies will examine histology for FRET signal from intact PFCnDs in the tumor stroma and attempt to localize these in the extravascular space by staining for vascular markers (e.g., VCAM-1).

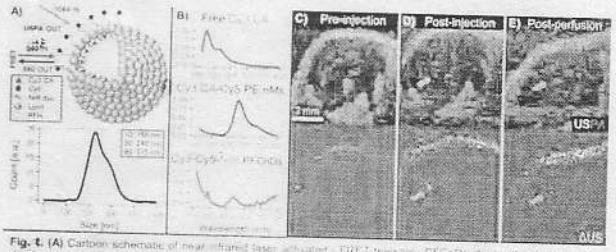

Fig. 1. (A) Cartoon schematic of near-infrared laser-activated FRET-traceable PFCnDs (top) with corresponding droplet size distribution from nanoparticle tracking analysis (bottom). (B) Normalized fluorescence emission [a.u.] after 540 nm excitation for Cy3-CA (top), Cy3-CA:Cy5-PE nanomicelles (middle), and multifunctional PFCnDs (bottom). USPA (top) and differential ultrafast US (bottom) images of the murine breast tumor during pre-injection imaging (C) as well as 24-hour post-injection imaging (D) and post-perfusion imaging (E) showing PFCnDs (arrow).