Dual-Model Molecular Imaging and Therapeutic Evaluation of Coronary Microvascular Dysfunction using Indocyanine Green-Doped Targeted Microbubbles

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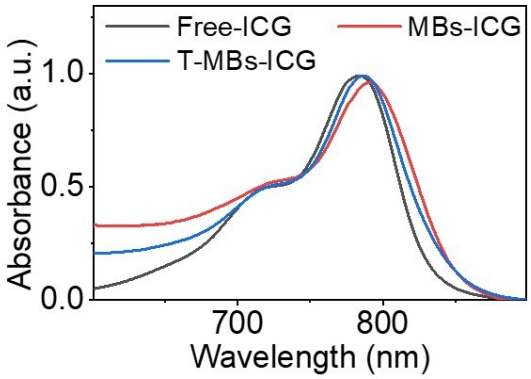


Figure S1. Normalized UV-Vis-NIR absorption spectra of free ICG, MBs-ICG and T-MBs-ICG solutions.

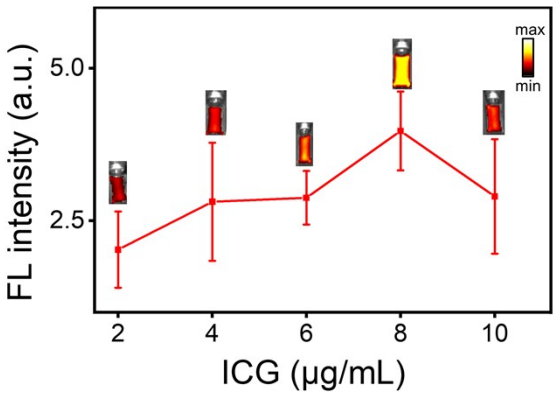


Figure S2. Fluorescence (FL) intensity of T-MBs-ICG with ICG concentration from 2 to 10 μg/mL. The inset is fluorescence images of the corresponding T-MBs-ICG solutions.

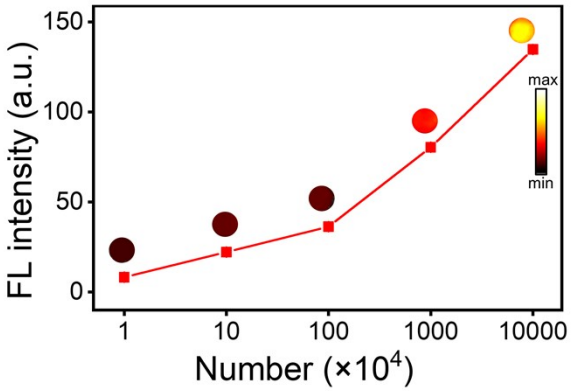
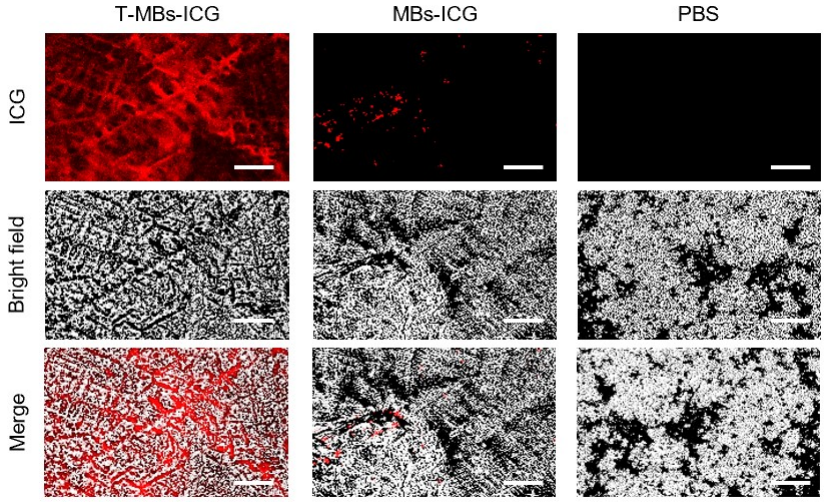


Figure S3. Fluorescence (FL) intensity of the T-MBs-ICG microbubbles (ICG = 8 μg/mL) with different concentration, Inset shows NIR FL images of the T-MBs-ICG microbubbles solution.



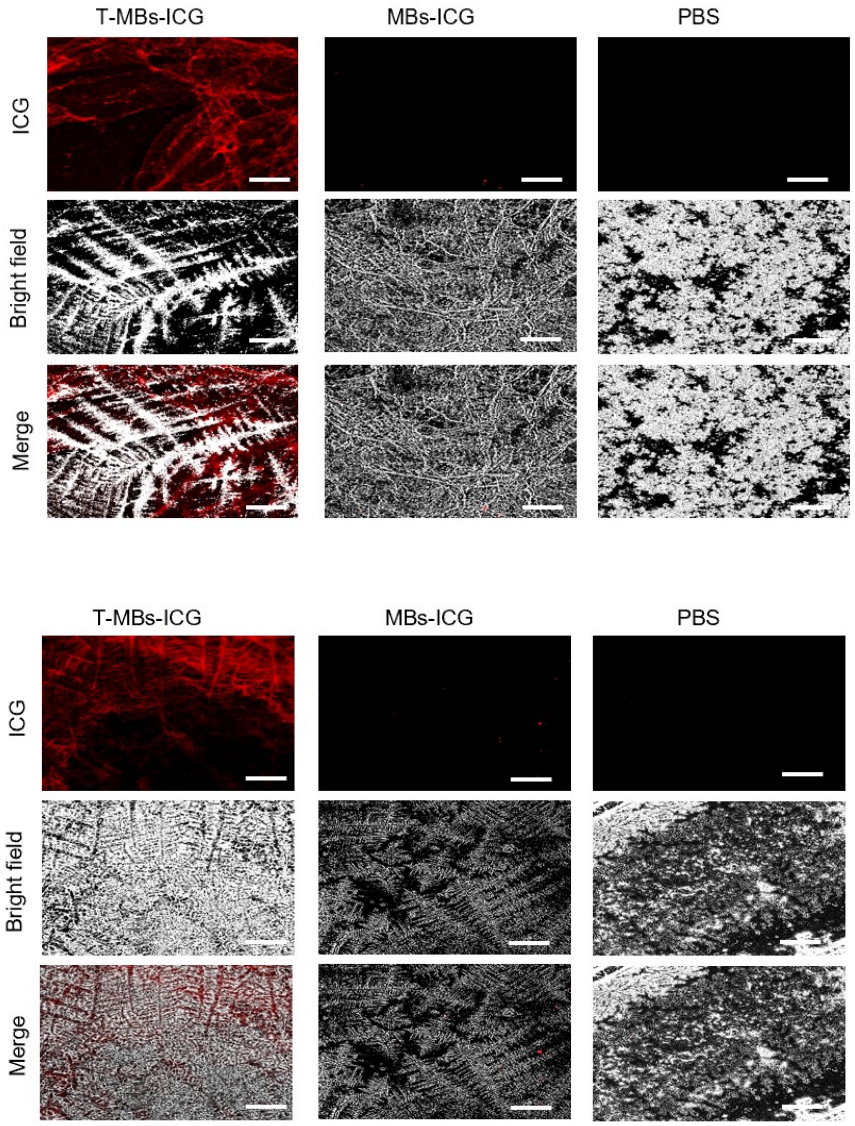


Figure S4. Three repeated fluorescence microscopy images of fibrin clots incubated with T-MBs-ICG, MBs-ICG, and PBS, respectively. Scale bars: 100 μm.

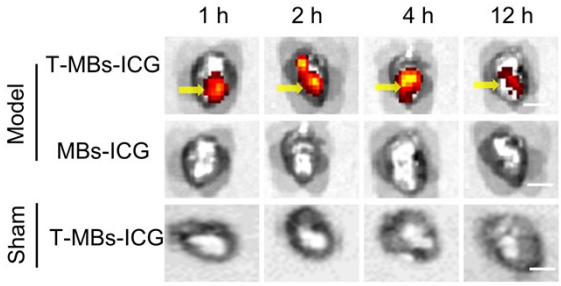


Figure S5. *In vitro* fluorescence images of the isolated heart at 1, 2, 4, and 12 h, The yellow arrows represent the fibrin formation area. Imaging condition: Ex: 745 nm; Em: 840 nm.

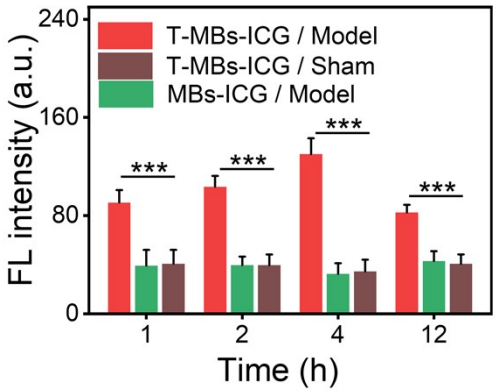


Figure S6. Quantitative analysis of NIR fluorescence imaging of isolated heart tissues at different time points (***$P < 0.001$).

Table S1. Comparison of different imaging modalities for CMD diagnostics.

Modality	Advantages	Disadvantages	References
PET	High-sensitivity, good reproducibility, extensive prognostic data	radiation exposure, expensive	J. Med. Chem., 2022, 65, 497-506
MRI	no radiation exposure, excellent spatial resolution	time consuming, expensive	JACC Cardiovasc. Imaging, 2020, 13, 140-155
CT	validated against invasive measurements	radiation exposure, low sensitivity	J. Clin. Med., 2021, 10, 1848
US	inexpensive, high feasibility, deep tissue resolution	operator-dependent, low contrast	Front. Cardiovasc. Med., 2022, 9, 899099.
FI	high sensitivity, high-contrast, low cost	low tissue resolution	J. Biophotonics, 2022, 15, e202200142
US&FI	high sensitivity, high contrast, deep tissue resolution	lack dual-modal imaging instrument	This work

Note: PET: Positron emission tomograpgy; MRI: Magnetic resonance imaging; CT: Computed tomography; US: Ultrasound Imaging; FI: Fluorescence Imaging.