Ultrasound Molecular Imaging: On the Move

Reports of new agents and systems for ultrasound molecular imaging are rapidly increasing. Stabilized gas bubbles (~1 micron in diameter) are frequently used as ultrasound contrast agents, typically remaining within blood vessels and targeting receptors on the vessel wall (*1–6*). Photoacoustic technologies show potential to broaden the targets for molecular imaging with acoustic waves, but are not yet widely available (*7*). Integration of molecular microbubble imaging into preclinical scientific studies has been advanced recently by the platform agent for preclinical imaging commercially available from Targeson, LLC (Charlottesville, VA). Targeson has also recently announced the completion of a licensing arrangement with SibTech, Inc. (Newington, CT), facilitating a new line of preclinical microbubble products targeted to VEGFR-2.

Commercial ultrasound systems also continue to develop sensitive modes for contrast imaging, with quantitative 3-dimensional acquisition on the horizon (*8*). Although specialized molecular imaging tools do not yet exist on commercially available clinical systems, quantitative ultrasound molecular imaging is now supported by the preclinical Vevo 770 system from Visualsonics (Toronto, Ontario).

The development of ultrasound molecular imaging is also now reflected at major meetings. The joint meeting of the Academy of Molecular Imaging (AMI) and Society for Molecular Imaging (SMI) will feature oral and poster sessions on ultrasound molecular imaging this year, as will the Institute of Electrical and Electronics Engineers Ultrasonics Symposium, and the American Institute of Ultrasound in Medicine.

Topics to be included at the AMI/SMI meeting will include new technology that would allow images of bound targets to be acquired with ultrasound prior to wash-out of the circulating agent. One such report, "Towards real-time ultrasound molecular imaging," from the Ferrara laboratory at the University of California, Davis, uses changes in the echoes of ultrasound contrast agents when bound, as well as the controlled destruction of ultrasound contrast agents, to facilitate the real-time differentiation of circulating and bound agents.

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A second imaging mode, also proposed for fast ultrasound molecular imaging by combining high and low frequency ultrasound pulses, will be reported in "Radial Modulation Imaging of Microbubbles at High Frequency" by Emmanuel Cherin, representing the laboratory of Stuart Foster, at the University of Toronto (Ontario, Canada). Specific microbubble targets, including integrins and selectins, will be reported by Kwon-Ha Yoon and Muzaffer Celebi, respectively.

Two examples of research in the new areas of targeted photoacoustic and thermoacoustic imaging include those of Kang Kim, "Cardiovascular Inflammation Detection by Cell Targeted Photoacoustic Imaging using Gold Nanorods and Sibaprasad Bhattacharyya, "NIR-Dye Labeled Herceptin as Thermoacoustic Computed Tomography (TCT) Probe for Breast Cancer Imaging."

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REFERENCES

1. Ferrara K, Pollard R, Borden M. Ultrasound microbubble contrast agents: fundamentals and application to gene and drug delivery. *Annu Rev Biomed Eng.* 2007;9: 415–447.
2. Bloch SH, Dayton PA, Ferrara KW. Targeted imaging using ultrasound contrast agents. Progess and opportunities for clinical and research applications. *IEEE Eng Med Biol Mag.* 2004;23:18–29.
3. Lindner JR. Microbubbles in medical imaging: current applications and future directions. *Nat Rev Drug Discov.* 2004;3:527–532.
4. Kaufmann BA, Lindner JR. Molecular imaging with targeted contrast ultrasound. *Curr Opin Biotechnol.* 2007;18:11–16.
5. Klibanov AL.Ligand-carrying gas-filled microbubbles: ultrasound contrast agents for targeted molecular imaging. *Bioconjug Chem.* 2005;16:9–17.
6. Klibanov AL.Microbubble contrast agents: targeted ultrasound imaging and ultrasound-assisted drug-delivery applications. *Invest Radiol.* 2006;41:354–362.
7. Li L, Roger JZ, Gina L, George S, Lihong VW. SPIE. 2007;12020504
8. Bhan A, Kapetanakis S, Rana BS, Ho E, Wilson K, Monaghan MJ. Real Time 3D Myocardial Perfusion—Is it Feasible? *12th European Symposium on Contrast Imaging*, 2007.