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### Authors

Kim, Chulhong

Chen, Zhongping

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# Multimodal photoacoustic imaging: systems, applications, and agents

Chulhong Kim<sup>1,2</sup>  · Zhongping Chen<sup>3</sup>

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Many conventional medical imaging modalities, such as magnetic resonance imaging (MRI), X-ray computed tomography (CT), and positron emission tomography (PET), have been routinely used in clinical practices to screen and diagnose diseases as well as to monitor therapies. MRI is superior for imaging soft-tissues while CT is preferable when studying bone structures. PET is exceptional for imaging molecular information and metabolic activities of diseases, but the image resolution is poor compared to that of CT and MR. Thus, multimodal information, such as ones provided by PET–MRI or PET–CT, to provide high-resolution structural images and superior disease sensitivities and specificities within the same image have significant clinical impact for advanced diagnosis and treatment [1]. Ultrasound imaging (USI) is another medical imaging modality routinely used in many settings from physicians' offices to large hospitals for several clinical applications, such as ob/gyn, cardiology, radiology, and interventional procedures. The key attributes of USI are real-time imaging, portability, low cost, and its noninvasive nature. USI can fuse real-time information of ultrasound images with other imaging modalities, such as CT and MRI, to provide complementary information of the underlying anatomy from the field of view. Photoacoustic imaging (PAI, also referred to as optoacoustic imaging) can be a great complementary imaging modality for easy integration with conventional USI [2, 3].

PAI, based on the photoacoustic (PA) effect, has been increasingly investigated for biomedical applications in the last decade. PAI provides molecular contrast of optical absorption while utilizing the deep imaging capabilities of ultrasound imaging. The PA effect is based on the following two sequential steps: optical excitation and ultrasound (US) detection. In the optical excitation phase, a flash of light illuminates biological tissues, and the light is absorbed by imaging targets. The absorbed light is then converted into heat, leading to the expansion and contraction of the object, where acoustic waves (US) are emitted by the targets in the object. In the US detection phase, acoustic waves propagate in the medium and are sensed by conventional US transducers to create images with optical absorption contrast. Due to the natural combination of light and sound, PAI can be easily integrated with conventional USI, inheriting all of the advantages of USI [4, 5]. PAI is inherently a multimodal imaging modality, since it fuses the morphological image of USI with the functional image of PAI. In the literature, a wide variety of multiscale PAI systems have been explored from microscopy to tomography systems [6–8].

This special issue on multimodal photoacoustic imaging introduces significant recent advances in this exciting research field. Review contributions in this issue cover a wide range of vibrant research areas ranging from hardware/software system development to preclinical and clinical imaging applications, contrast agent development, and commercialization.

A detailed introduction of each review contribution is as follows. The first paper entitled “Clinical Photoacoustic Imaging Platforms” by Choi et al. [9] compares various clinical PAI systems based on data acquisition systems and US detectors. The second paper entitled “Development and Clinical Translation of Photoacoustic Mammography” by Shiina et al. [10] introduces a prototype of PA mammography (PAM) to diagnose breast cancers in humans using hemispherical US sensors. The paper covers the clinical translation of PAI, which is one of the many exciting topics in the PAI field. This project is a collaborative effort between Kyoto University and Canon, and is funded

✉ Chulhong Kim  
chulhong@postech.ac.kr; chulhong@postech.edu

Zhongping Chen  
z2chen@uci.edu

<sup>1</sup> Department of Creative IT Engineering, Pohang University of Science and Technology (POSTECH), 77 Cheongam-Ro, Namgu, Pohang, Gyeongbuk 37673, Republic of Korea

<sup>2</sup> Department of Electrical Engineering, Pohang University of Science and Technology (POSTECH), 77 Cheongam-Ro, Namgu, Pohang, Gyeongbuk 37673, Republic of Korea

<sup>3</sup> Department of Biomedical Engineering, The Henry Samueli School of Engineering, University of California, Irvine, Irvine, CA 92697, USA

through the ImPACT Program of the Council for Science, Technology, and Innovation, Cabinet Office, Japan. This collaboration is a good example of an industry-academy relationship with successful outcomes. The third paper entitled “Fast Photoacoustic Imaging Systems Using Pulsed Laser Diodes—A Review” by Upputuri et al. [11] reviews the recent advances of the PAI systems based on the near-infrared pulsed laser diodes, which are reliable, fast, cost-effective, hand-held, and light-weight. On the contrary, typical light sources based on Q-switched Nd:YAG lasers are slow, bulky, heavy, and relatively expensive. The fourth paper entitled “Multimodal Photoacoustic Imaging as a Tool for Sentinel Lymph Node Identification and Biopsy Guidance” by Kim et al. [12] discusses the role of PAI on real-time sentinel lymph node detection and biopsy guidance. The fifth paper entitled “Multimodal Intravascular Photoacoustic and Ultrasound Imaging” by Li et al. [13] addresses the recent advances on the multimodal intravascular PA/US catheters to morphologically and chemically image atherosclerotic plaques in coronary arteries. The sixth paper entitled “Photoacoustic Microscopy: Principles and Biomedical Applications” by Liu et al. [14] introduces the fundamental principles and system configurations of PA microscopy and preclinical/clinical applications of the systems. PA microscopy has become a premier tool in biomedical research, providing structural, physiological, and molecular signals of diseased tissues. The seventh paper entitled “Naphthalocyanines as Contrast Agents for Photoacoustic and Multimodal Imaging” by Chitgupi et al. [15] highlights novel contrast agents and naphthalocyanines nanoformulates for PAI. The naphthalocyanines nanostructures have superior near infrared extinction coefficients, biocompatibility, and multimodal imaging capability compared to PET. The eighth paper entitled “Optically-Triggered Phase-Transition Droplets for Photoacoustic Imaging” by Chen et al. [16] introduces a novel contrast agent for dual modal PA/US theranostics, referred to as optically-triggered phase-transition droplets. Due to optical droplet vaporization, the PA signals can be significantly enhanced. In addition, these agents can be potentially used as therapeutic delivery vehicles as well.

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## Compliance with ethical standards

**Conflict of interest** Dr. Chulhong Kim has a financial interest in OPTICHO, which, however, did not support this work. Dr. Zhongping Chen has a financial interest in OCT Medical Imaging, Inc., which, however, did not support this work.

**Human and animal rights** Not applicable.

**Informed consent** Not applicable.

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