

# Defining the clinical niche for photoacoustic imaging



**Biomedical imaging continues to advance, providing ever more refined methods to diagnose and monitor diseases. Photoacoustic imaging, a hybrid modality that combines optical and acoustic technologies, stands out for its ability to deliver high-resolution images at a greater depth than optical microscopy. However, as with any imaging technology, its success will hinge on identifying specific clinical applications for which it offers clear advantages over established methods.**

The utility of any imaging modality is determined by its ability to effectively address clinical gaps. The history of medical imaging provides numerous examples of this pattern: computed tomography (CT) did not replace X-ray radiography but found its niche in cross-sectional imaging. Ultrasound was not displaced by CT but excelled in real-time guidance and fetal imaging. Similarly, magnetic resonance imaging (MRI) now complements CT in neuroimaging owing to superior tissue contrast and functional imaging capabilities.

Photoacoustic imaging, based on the detection of ultrasound waves generated by pulsed light absorption in tissue, now faces the same challenge of niche identification. This technology provides stronger optical contrast and spatial resolution compared to optical systems that suffer from limited penetration depth. However, as Vasilis Ntziachristos discusses in a *Comment* in this issue, its clinical adoption will depend not only on technical specifications but also on addressing clinical needs that other modalities cannot satisfy.

In cardiovascular medicine, for example, photoacoustic imaging can visualize microvascular structures and measure oxygen saturation with high accuracy, offering insights that conventional ultrasound or MRI cannot easily achieve, as discussed by Sarah Bohndiek, Lihong V. Wang, Chulhong Kim and colleagues in a *Review* in this issue. In metabolic assessment, photoacoustic imaging enables label-free visualization of blood oxygenation, lipid content and blood volume. These features make it valuable for monitoring cardiometabolic health, evaluating nutritional status and assessing responses to physical activity. Unlike modalities reliant on radiotracers or ionizing radiation, photoacoustic imaging could provide a safer option for repeated measurements.

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Another promising niche has emerged through optoacoustic mesoscopy, which operates at frequencies above 10 MHz, unlike macroscopy, which works at frequencies below 10 MHz. This variant can visualize skin microvasculature and other cutaneous features with unprecedented details. The raster-scan optoacoustic mesoscopy (RSOM) system, introduced in 2017<sup>1</sup>, has already been tested in several clinical studies correlating cutaneous vascular patterns with disease progression (see *Comment* by Ntziachristos, and *Review* by Bohndiek, Wang, Kim and colleagues).

Despite its promising features, photoacoustic imaging faces an uphill battle for adoption in applications, for which established imaging methods, such as MRI, CT and ultrasound, are already fully established in clinical workflows. Consider the case of breast cancer imaging; photoacoustic imaging has been used to visualize tumour vasculature and hypoxia in several recent clinical trials. However, X-ray mammography, ultrasound and MRI already provide substantial diagnostic accuracy; therefore, to justify adoption, photoacoustic imaging would need to considerably reduce the number of necessary biopsies or provide unique diagnostic information.

Practical challenges also remain. Standardization across systems and clinical sites is essential to ensure consistent and reliable results. Photoacoustic systems must also be cost-effective, portable and easy to operate in diverse healthcare settings. Integrating this technology with other modalities, such as ultrasound, may enhance diagnostic accuracy and broaden its clinical utility. Advances in data analysis techniques, particularly those that leverage machine learning, could further streamline image interpretation and improve diagnostic performance. Regulatory approval processes require robust evidence of safety, accuracy and clinical utility, necessitating validation through large-scale, multi-centre studies. Moreover, conducting large-scale trials focused on specific diseases will be vital to validate applications of photoacoustic imaging and establish evidence-based niches. Community-led efforts have already led to the foundation of the **International Photoacoustic Standardisation Consortium (IPASC)**, which aims to tackle some of these issues.

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## References

1. Aguirre, J. et al. Precision assessment of label-free psoriasis biomarkers with ultra-broadband optoacoustic mesoscopy. *Nat. Biomed. Eng.* **1**, 0068 (2017).