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Research progress of photoacoustic imaging technology in brain diseases

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Highlights

- This review introduces the basic principles and features of photoacoustic imaging technology.
- This review illustrates the application of photoacoustic imaging in the study of brain diseases.

Abstract

Photoacoustic imaging (PAI) technology, characterized by its high resolution, minimal biological impact, and high sensitivity, has become a cornerstone in biomedical research. Its application spans various domains, showing significant promise for disease diagnosis. Currently, the majority of PAI research is conducted using animal models, with human clinical applications still in early development. This paper reviews the fundamental principles of PAI and explores its use in animal brain imaging studies. It addresses the current challenges and limitations of the technology and evaluates the potential for extending these techniques to human cerebral imaging. PAI offers substantial benefits for diagnosing neurological disorders, and its adaptation for human brain studies is crucial for advancing our understanding of neuropathogenesis, improving early disease detection, and monitoring treatment effectiveness. Continued advancements in PAI are expected to not only augment its role in neuroscience research but also establish it as a valuable tool in clinical diagnostics.

Keywords: Brain diseases, photoacoustic imaging, brain imaging, deep learning

Introduction

According to 2019 statistics, brain diseases have emerged as a leading cause of death among Chinese residents, with a notable increase in their contribution to mortality and disability [1]. Stroke is the foremost cause of death and significantly impacts years of life lost. Alzheimer's disease (AD), the most common type of dementia, has escalated from 28th to 8th in disease ranking. First described by German physician Alois Alzheimer in 1906, AD is a degenerative neurological disorder characterized by memory loss, aphasia, dysarthria, impaired visuospatial skills, executive dysfunction, and changes in personality and behavior [2]. The pathogenesis of AD remains largely unclear, and diagnosis primarily depends on neuropsychological evaluations. Epidemiological projections suggest that by 2050, over 131.5 million people globally could be affected by AD. Additionally, cancers of the brain and central nervous system have moved from the 30th to the 23rd position in disease burden. Neurological disorders have also escalated in their rank as causes of disability, moving from 6th to 5th place. Consequently, brain diseases now pose the most significant health threat to the Chinese population, imposing a substantial burden on both individuals and society.

Despite a century of research, our understanding of the brain remains incomplete. Neuroscience posits that the brain is responsible for all conscious human activities, yet the exact mechanisms by which it generates consciousness and behaviors are still largely unknown due to the complex correlations between neuronal activities and these functions. While interventional electrodes allow for the observation of

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Table 1. Comparison of high-resolution optical imaging modalities

Modality	Penetration	Primary contrast
Confocal microscopy	~0.5 mm	Scattering, fluorescence
Two-photo microscopy	~0.5 mm	Fluorescence
Optical coherence tomography	~1 mm	Scattering, polarization
PAI	~3-30 mm, scalable	Absorption

Note: PAI, photoacoustic imaging.

a limited number of neurons, they fall short of fully satisfying scientific curiosity about broader brain functions. Since 2013, several countries including the United States, China, Australia, the European Union, Japan, South Korea, and Canada have launched comprehensive "brain programs" aimed at exploring various aspects of brain function and the links between neural structure damage and disease [3-5].

Advancements in modern brain imaging techniques have significantly improved disease detection capabilities. Current imaging modalities include CT, MRI, Positron Emission Tomography (PET), Optical Imaging, Ultrasound, and Photoacoustic Imaging (PAI). However, these techniques have inherent limitations. For instance, CT, PET, and MRI often suffer from low temporal resolution, which can affect the quality of imaging. Furthermore, the equipment required for CT and MRI is not only bulky and costly but also entails high maintenance expenses and extended durations for scanning [6].

Since the 20th century, significant advancements have been made in PAI, but it was not until the early 21st century that its application in biomedical detection began to flourish. This development was largely driven by the pioneering work of Professor Wang LV's research group at the University of Washington, who explored bio-PAI techniques [7]. This research marked the onset of PAI's rise as a bio-imaging technology based on the photoacoustic effect. Currently, PAI is categorized into three main types: photoacoustic computed tomography (PACT), photoacoustic microscopy (PAM), and photoacoustic endoscopy (PAE). PACT is extensively used in human studies due to its deep tissue penetration capabilities. In contrast, PAM provides higher resolution for biomedical applications but at a reduced penetration depth. PAE, a specialized form of PAM, employs a unique scanning method to miniaturize the system for high-resolution imaging of internal organs [8].

PAI has demonstrated significant utility across various biomedical fields, including oncology, cardiovascular diseases, breast cancer, ophthalmology, and otorhinolaryngology, as well as in vivo measurements of cerebral oxygenation and microcirculation studies [9-14].

Currently, research on PAI primarily involves animal studies and has not yet fully transitioned to human clinical trials. This paper will introduce the principles of PAI technology and the application of deep learning-based PAI algorithms in brain imaging. It will also discuss the development and challenges of PAI in animal brain studies and evaluate the potential for its application in human brain imaging.

Principles of PAI

PAI operates on the principles of the Lambert-Beer Law, a fundamental law of absorption photometry that is applicable across all forms of electromagnetic radiation and to all light-absorbing entities, including gases, solids, and liquids, as well as molecules, atoms, and ions. This law forms the foundation for quantitative spectral analysis, as depicted in equation (1).

$$A_\lambda = -\log_{10} T = kbc \tag{1}$$

Where A_λ is the absorbance at wavelength λ, T is the transmittance, k is the absorption coefficient, b is the thickness of the absorbing layer, and c is the concentration of the light-absorbing substance [15]. As shown in the **Table 1**, PAI exhibits greater sensitivity to light absorption compared to other optical imaging modalities [7].

The principle of the PAI technique is shown in **Figure 1**. When pulsed laser light irradiates target tissue, chromophores within the tissue absorb the energy, leading to a non-radiative transition as described by the Lambert-Beer Law. Specifically, molecular chromophores absorb photon energy, transition from the ground to an excited state, and subsequently release energy as heat. This heat causes the temperature of the target tissue to increase, inducing thermoelastic expansion that generates acoustic waves. These waves propagate as photo-

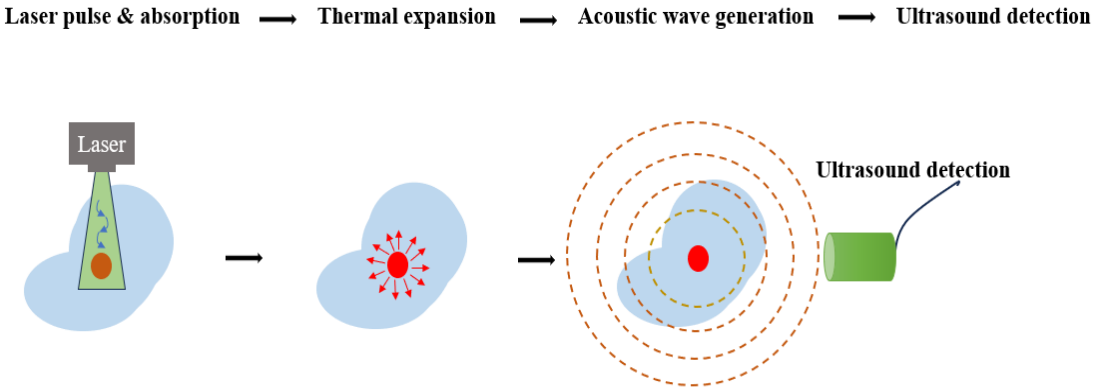

Figure 1. Schematic diagram of photoacoustic imaging.

acoustic signals (PAS) [16-19]. The photoacoustic effect, discovered by Alexander Graham Bell in 1880, occurs when tissues are exposed to nanosecond or picosecond pulsed lasers, producing ultrasound waves [20]. The initial sound pressure of a photoacoustic signal is calculated using the following formula:

$$P_0 = \Gamma \eta_{th} \mu_a F \quad (2)$$

Where P_0 is the initial pressure, Γ is the Grüneisen parameter, η_{th} is the photothermal conversion efficiency, μ_a is the optical absorption coefficient, and F is the luminous flux. This equation illustrates that the photoacoustic signal is directly proportional to the optical absorption coefficient. A small change in the optical absorption coefficient ($\Delta\mu_a$), results in a corresponding change in the initial sound pressure (ΔP_0), maintaining the ratio $\Delta P_0 / P_0 = \Delta\mu_a / \mu_a$ [7]. Here the effect of F on ΔP_0 can be neglected.

Therefore, any fractional change in the optical absorption coefficient directly corresponds to an equivalent fractional change in the photoacoustic signal. Given that the propagation time of acoustic signals in biological tissues is substantially longer than the wavelength of light and experiences minimal attenuation, the PA signals captured by an ultrasound transducer reliably conform to Equation (3).

$$\nabla^2 P(r,t) - \frac{1}{c^2}\frac{\partial}{\partial t^2} = -P_0(r)\frac{\partial \tau(t)}{\partial t} \quad (3)$$

where $P_0(r)=\Gamma(r)A(r)$ represents the initial acoustic pressure source distribution, c represents the speed of sound in the tissue, $\tau(t)$ represents the pulse width of the laser pulse, and $\Gamma(r)$ and $A(r)$ are the spatial distribution functions of the Grüneisen parameter and the optical absorption coefficients of the imaging region. The Grüneisen parameter is dimensionless and relates to the elastic modulus and specific heat capacity of the tissue.

When utilizing short-pulsed lasers with nanosecond or picosecond pulse widths as the excitation source, the duration of each pulse is significantly shorter than the thermal relaxation time of biological tissues. This temporal discrepancy ensures that heat is confined within the illuminated area, meeting the thermal confinement condition. Consequently, the absorbed material experiences an instantaneous temperature rise, leading to the generation of a shockwave with a rapid front velocity that enhances the amplitude of the resulting photoacoustic signal. Therefore, selecting a nanosecond-level pulse width for the excitation light source is critical for achieving higher signal conversion efficiency. Following this, data processing techniques are applied to the PAS to reconstruct the initial pressure distribution within the tissue and to invert the spatial distributions of optical absorption coefficients and thermal expansion characteristics, thereby providing detailed insights into the tissue's structure and function. The ultrasound detector captures the PAS induced by the photoacoustic effect in biological tissues, which underpins the application of PAI in biomedicine. The varying intensities of ultrasound generated by different biological tissues (directly proportional to the absorbed light energy) allow for the differentiation between normal and diseased tissues [8].

Brain imaging based on deep learning

The development of PAI techniques has spurred the advancement of various PAI image reconstruction algorithms. Standard PAI reconstruction methods include Filtered Bach-Projection, Delay-And-Sum beamforming, Fourier Transform-based algorithm, and Time Reversal method. In recent years, the adoption of Deep Learning algorithms in medical image processing has grown extensively. Particularly, Convolu-

tional Neural Network (CNN) have become the favored approach for medical image processing and analysis, including brain imaging research.

PAI reconstruction algorithms based on deep learning can be divided into two categories:

• Learning-based image optimization, where a standard reconstruction algorithm first reconstructs low-quality photoacoustic images containing artifacts from incomplete measurements. These images are then enhanced using a well-trained CNN, which removes artifacts and noise, improving image quality.

• Model-based learning and reconstruction, which incorporates a predictive photoacoustic imaging physical model into the training of CNNs for image reconstruction. The CNN serves as an iterative framework to solve the optimization problem, learning a priori knowledge for solving inverse problems from the measurement data [21]. CNN is widely used in brain imaging, with specific architectures such as U-net, Fully Dense U-net (FD U-net) being particularly popular.

Guan proposed a novel deep learning method called Pixel-Deep Learning, which first employed pixel-level interpolation controlled by the physics of photoacoustic wave propagation, followed by image reconstruction using a CNN [22]. This method was trained using a synthetic vasculature system model dataset and tested on a mouse cerebral vasculature system experiment. The results demonstrated that Pixel-Deep Learning consistently surpassed traditional post-processing reconstruction in terms of mean peak-signal-to-noise ratio and structural similarity index, achieving performance comparable to that of iterative reconstruction methods.

Using a dataset derived from the mouse cerebral microvascular system, DiSpirito et al. evaluated several CNN architectures and selected the FD U-net model for its superior performance in reconstructing undersampled PAM images [23]. This choice avoided the typical trade-off between spatial resolution and imaging speed. The FD U-net demonstrated robust capabilities in reconstructing PAM images using as little as 2% of the original pixel data, effectively reducing imaging time without compromising image quality.

Zhu et al. employed a deep learning model to enhance real-time whole-brain imaging of hemodynamics and oxygenation at microvascular resolution through ultra-fast wide-field photoacoustic microscopy [24]. The FD U-net was particularly effective in upsampling PAM images, addressing the issue of undersampling. Compared to the undersampled images, the upsampled images featured smoother vessel boundaries, reduced undersampling artifacts, and more consistent vessel intensities and contours.

Zhang et al. utilized a 2D-photoacoustic tomography (PAT) numerical model of the human brain, encompassing six tissues: scalp, skull, white matter, gray matter, blood vessels, and cerebrospinal fluid, for optical simulation [25]. The model facilitated the determination of the photoacoustic initial pressure based on the optical properties of the human brain. Subsequently, two different k-wave models were employed for cranial acoustic simulation. The photoacoustic sinusoidal maps with cranial-induced aberrations served as inputs to the U-net, while the cranial-exfoliated photoacoustic sine map acted as the supervised map for training the network. The final experimental results indicated that U-net correction effectively mitigated cranial acoustic aberrations, significantly enhancing the quality of PAT human brain images reconstructed from corrected PAS, which clearly depicted the distribution of cerebral arteries within the skull.

With the advancement of high-performance processors, big data technologies, and the proliferation of open-source databases, the application of deep learning in medical image reconstruction, particularly in PAI, has expanded significantly. Utilizing deep learning algorithms in brain studies enhances the quality of PAI, aligns with contemporary technological trends, and opens up new possibilities for the future development of PAI. However, it is crucial to recognize the limitations of deep learning algorithms, such as the need for extensive training datasets, high computational requirements, susceptibility to overfitting, and the potential loss of high-frequency detail information. These challenges highlight the ongoing need for further development in deep learning-based PAI technology.

Progress in PAI in diagnosis of brain diseases

Progress in PAI for animal brain experiments

Imaging small animals is vital in preclinical research, providing crucial physiological, pathological, and phenotypic insights with clinical relevance [26]. The necessity for animal experiments has prompted researchers to employ mouse models. Currently, many models with

Table 2. Examples of animal brain experimental research from 2008 to 2022

Year	Subject	Modality	Resolution (unit: μm)
2008 [7]	Rats	PAT	Lateral resolution: 60
2015 [29]	Rats	PAT	Lateral resolution: 243
2016 [30]	Rats	3D-wPAT	In-plane spatial resolution: 200
2017 [26]	Rats	SIP-PACT	125
2018 [31]	Rats	PACT	75
2019 [32]	Rats	ORPAM	Lateral resolution: 2.25 axial resolution: 105
2019 [4]	Rats	MSOT	100
2021 [33]	Monkey	p(portable)-ORPAM	Lateral resolution: 15 axial resolution: 120
2022 [34]	Rats	Photoacoustic neuroimaging	Axial resolution: 110

Note: PAT, photoacoustic tomography; wPAT, wearable photoacoustic tomography; SIP, single-impulse; PACT, photoacoustic computed tomography; ORPAM, optical resolution photoacoustic microscope; MSOT, multispectral optoacoustic tomography.

simplified geometries are unable to accurately validate PAI systems. This limitation led Grasso et al. to design and develop a stable model that closely mimics the detailed morphology of a mouse, serving as a realistic tool for PAI [27]. The creation of such mouse simulation models could diminish the need for animals in validation and standardization studies of preclinical PAI systems, thereby facilitating the transition of PAI technology into clinical research.

Several research groups around the world have conducted small animal brain imaging studies using PAI, as documented in **Table 2** [28]. The table summarizes studies from 2008 to 2022, including the year of study, experimental subjects, PAI modes, and specific resolutions achieved. Notably, PAI has significantly advanced in imaging resolution, exemplified by studies on the cerebral cortex and blood vessels of experimental rats using contrast agents at the University of Washington, USA, in 2008.

As indicated in the table, the lateral resolution of the images referenced in the literature is notably lower [32]. This reduction in resolution is attributed to the curvature of the micro-electro-mechanical-system scanner and the mismatch of refractive indices between air, glass, and water in the optical path. However, this configuration also ensures that the laser energy reaching the cerebral cortex is moderated to avoid damaging the animal tissue.

Tang et al. investigated cerebral hemodynamics and brain function in experimental rats using a novel, miniaturized 3D wearable PAT (3D-wPAT) system designed for mobile lab rats [29, 30]. This approach eliminated the potential confounding effects of anesthetics on neuronal excitability, cerebral hemodynamics, vascular reactivity, cerebral metabolism, and other physiological indices. The 3D-wPAT system featured three elevation layers with a fully functional acoustic transducer array, each consisting of 3×64 elements. Functional imaging was performed under hyperoxia conditions using multi-wavelength optical excitation (710 nm and 840 nm). The wPAT images captured from each ultrasound detection layer of the behaving rats demonstrated the capability of 3D-wPAT in imaging the brain of mobile rats. Compared to the state of the technology in 2008, spatial resolution and imaging speed have significantly improved in PAI, with 3D-wPAT requiring only 163 milliseconds to capture images, marking substantial progress in rat brain imaging [7, 29, 30].

In a related approach, Zhang also utilized behaving lab rats as experimental subjects [31]. Using a PACT system equipped with a high-frequency linear array transducer, Zhang mapped the entire brain microvascular network of rats with intact skulls to study hemodynamic activities [31]. The limited field of view of the linear array meant that only vessels perpendicular to the acoustic axis were clearly reconstructed, while vessels deviating from this axis were barely visible. To overcome this limitation, the linear array was mounted on a rotating platform centered on the rat's brain. Without altering the laser illumination, the brain was scanned comprehensively, and the images were processed to produce a full-view image. These full-view images demonstrated that the PACT system with high-frequency linear arrays could achieve high-resolution, deep functional imaging of the entire brain in mobile rats using in vivo photoacoustic computed tomography.

Chen et al. introduced a wearable, robust

optical resolution photoacoustic microscope designed for freely moving rodents [32]. This device features a small, lightweight, and fast optical scanner that provides high spatiotemporal resolution, a large field of view, easy assembly, and adjustable optical focus for in vivo experiments, allowing it to image cerebral cortical activity effectively. Conversely, Qin et al. developed a fast, portable photoacoustic microscope for high-resolution in vivo imaging of the cerebral cortex in rhesus monkeys [33]. By measuring vascular diameter and functional connectivity, they analyzed the structural and functional responses of cerebral vasculature to alternating normoxic and hypoxic conditions.

Penn et al. utilized multispectral optoacoustic tomography (MSOT) to monitor neurovascular changes in a laboratory rat model of repetitive traumatic brain injury [35]. MSOT was employed to track hemoglobin content under oxygenated and deoxygenated conditions during treatment, assessing its efficacy. This study revealed MSOT's potential as a noninvasive method to monitor neurovascular changes in repetitive traumatic brain injury models, suggesting it could significantly enhance the monitoring of such injuries, which is currently costly and invasive for patients with mild conditions.

Salvas employed high-resolution ultrasound and PAI equipment (LRQA Iso9001; France Life Imaging (grant ANR-11-INBS-0006); IBISA; Leducq Foundation (RETP); I-Site Muse) to track neurovascular oxygenation and cardiac function trajectories [36]. This application of PAI in preclinical models highlighted trends in pathophysiological biomarkers that may offer new insights into the physiopathology of cardiac arrest and resuscitation.

Zhang et al. investigated PAI at three levels, i.e. brain tissue slices, isolated whole brains, and whole brains in vivo, using mice with AD pathologies [16]. The study involved APP/PS1 transgenic mice and their non-transgenic wild-type littermates. The PAI system, equipped with a 532 nm laser and a 10 ns pulse width, was used to analyze differences in brain structure and vascular networks. The distribution of photoacoustic signal amplitudes in the cerebral cortex of both mouse types was statistically analyzed. Results indicated that the amplitude distribution of PAS in the wild-type mice's cerebral cortex was narrowly ranged and smaller, whereas it was broader and higher in AD mice. These findings highlight the capacity of PAI to capture the heterogeneity of brain structure in AD, demonstrating its significant potential for monitoring structural changes and vascular characteristics in the brain during the progression of brain diseases. This technology provides deeper insights into brain science studies and the development of brain disease pathology.

The continuous exploration of PAI in animal brain imaging has led to remarkable improvements in both image penetration depth and resolution. Overall, the advances in PAI within this field offer numerous possibilities and opportunities, with the potential for further breakthroughs in bioimaging.

Feasibility study of PAI for diagnosis of human brain diseases

The effectiveness of biological tissue imaging is contingent upon photon penetration depth, resolution, and tissue contrast. While most deep brain functional studies currently rely on functional magnetic resonance imaging, this modality faces several limitations in achieving optimal spatiotemporal resolution and contrast. Specifically, the challenges with functional magnetic resonance imaging include: 1) relatively low spatial resolution; 2) slower temporal resolution; 3) dependency on changes in blood oxygen levels, which can be limiting; 4) susceptibility to interference from head movements.

Photon propagation in soft tissue can be segmented into four distinct regions, each defining the penetration limits for various high-resolution optical imaging modalities such as conventional planar optical microscopy, confocal microscopy, two-photon microscopy, and optical coherence tomography. As depicted in **Figure 2**, these penetration limits are set at 100 μm (aberration limit), 1 mm (diffusion limit, also referred to as the "soft limit"), 10 cm (dissipation limit), and 1 m (absorption limit) [37]. Traditional optical imaging techniques are constrained by the diffraction limit and scattering limit, which have historically impeded high-resolution imaging. However, the introduction of PAI has shown potential to surpass these longstanding barriers, offering new avenues for high-resolution imaging in the diagnosis of human brain diseases.

The penetration limits shown are order-of-magnitude approximations; wavefront-engineered penetrations are theoretical projections; this classification applies to light-scattering dominated media. Traditional optical imaging techniques face significant challenges due to strong optical scattering in tissues, which impedes high-resolution imaging beyond an optical diffusion limit of approximately 1-2 mm depth. While diffuse optical imaging methods can penetrate

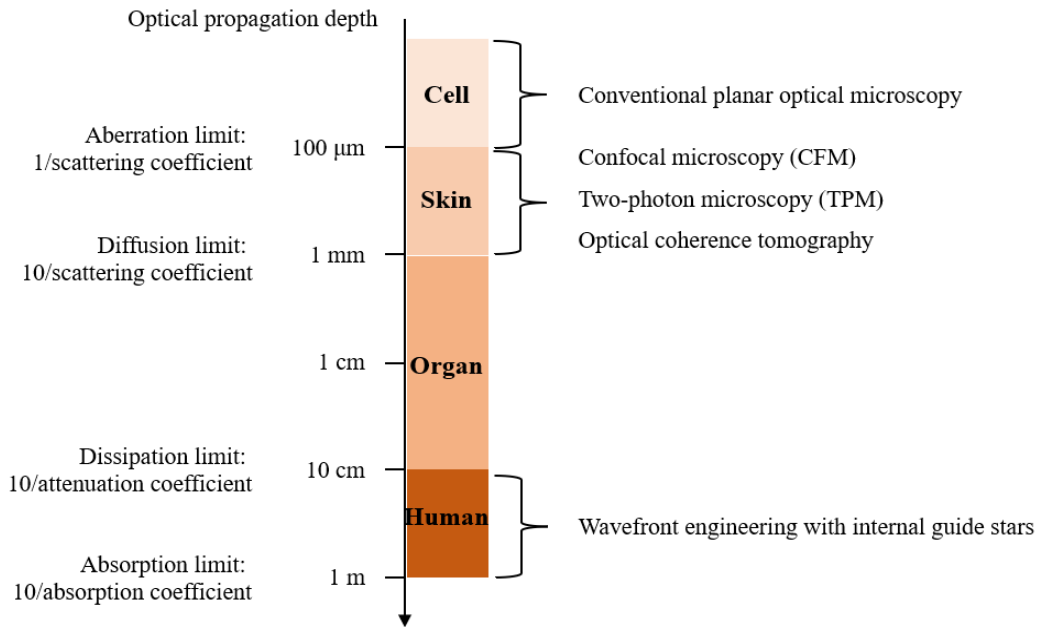

Figure 2. The propagation of photons in soft tissue.

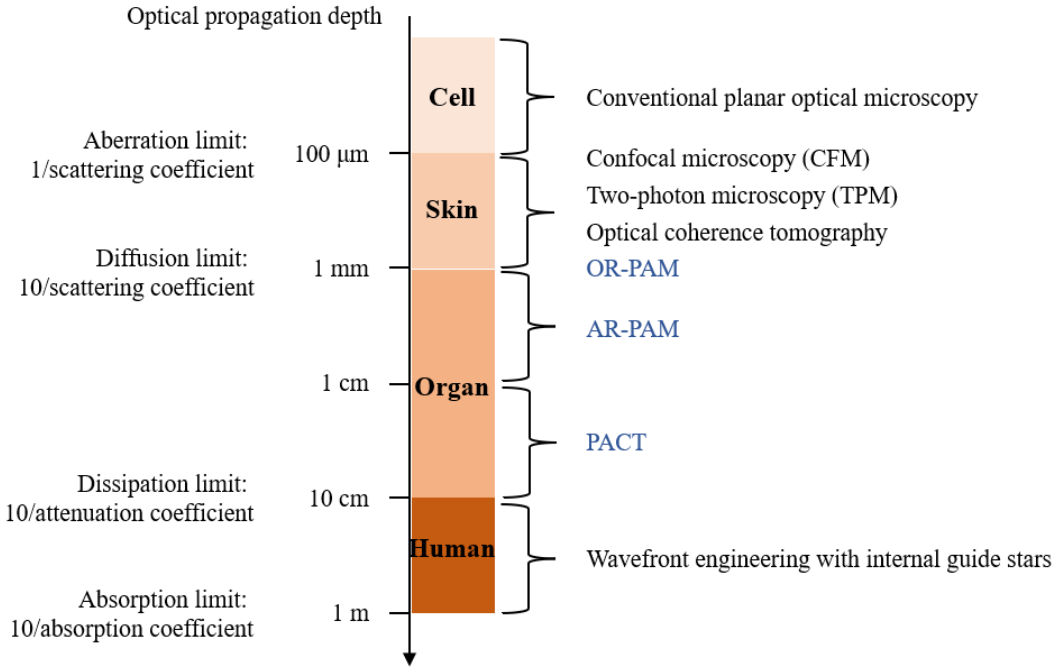

Figure 3. Approximate positions of the three photoacoustic modes in the diagram of the penetration limit relationship. OR-PAM, optical resolution photoacoustic microscope; AR-PAM, acoustic resolution photoacoustic microscopy; PACT, photoacoustic computed tomography.

to depths of several centimeters, their resolution remains low, approximately one-third of the penetration depth [26].

PAI, a hybrid imaging modality, merges the high contrast and spectral recognition capabilities of optical imaging with the deep penetration and high resolution of ultrasound imaging. This modality is poised to surmount the limitations of traditional optical imaging techniques by providing high-resolution images at significant depths.

Compared with conventional medical imaging technologies, PAI offers distinct advantages:

• It achieves selective excitation of specific spectral tissues, capturing both structural and functional imaging features, thus introducing a novel imaging method distinct from traditional techniques.

• By combining the benefits of optical and acoustic imaging, it overcomes the "soft limit" of depth in high-resolution optical imaging, such as laser confocal microscopy, two-photon excitation microscopy, and optical coherence tomography, while simultaneously achieving higher resolution for molecular imaging.

• PAI is a non-invasive, non-ionizing, and damage-free technology [38].

Figure 3 illustrates the approximate positions of three typical PAI modalities (OR-PAM, AR-PAM, and PACT)—in relation to the penetration limit. The spatial resolution of PAT varies with imaging depth, transitioning from the quasi-ballistic state (typically ≤1 mm in tissue) to the diffuse state (typically ≥10 mm in tissue), and reaching up to the dissipation limit (approximately 10 cm in tissue). Reducing the imaging depth in PAT can effectively enhance its spatial resolution, offering a strategic approach to improving image quality.

As early as 2013, Gong provided an overview of biomedical PAI technology, which has since become one of the fastest-growing technologies in the field due to advances in laser and ultrasound detection technologies [39]. In terms of laser technology, to ensure higher signal conversion efficiency, the pulse width of the excitation light source is typically selected at the nanosecond level. By choosing specific wavelengths of light, targeted absorption can be identified based on differences in absorption coefficients. For instance, deoxy-hemoglobin (HbR) is more sensitive at 710 nm, while oxy-hemoglobin (HbO) is more sensitive at 840 nm. Using these wavelengths, Tang et al. conducted three-layer ultrasound detection for brain imaging in behaving rats [29].

In terms of ultrasound detection, the choice of detection method significantly affects imaging quality, depending on the intensity of the generated sound waves. For example, current PACT systems primarily use arrayed ultrasound transducers. These transducers can be categorized into planar, cylindrical, and spherical arrays. Planar array transducers, often integrated with the light source, are low-cost and straightforward to construct, making them prevalent in PACT applications. Conversely, cylindrical, and spherical array transducers, which are typically customized, are more costly and bulky but are necessary for specific imaging requirements, such as small animal imaging and functional imaging of brain structures. Matching the ultrasound transducer's spectrum with the photoacoustic signal's spectrum, utilizing higher central frequencies, and employing wider bandwidths can all enhance imaging quality. Therefore, it is crucial to consider various factors based on actual imaging needs to select the appropriate ultrasound transducers and detection methods for high-quality PAI.

Understanding how our brain functions represents a significant challenge in the field of PAI. Probing the brain is crucial not only for unraveling profound scientific mysteries but also for advancing our understanding and treatment of neurological disorders, such as AD and Parkinson's disease [2]. In summary, PAI offers several feasible capabilities:

• PAI transcends the fundamental depth limitations of current high-resolution optical imaging modalities. It holds significant promise for human brain imaging due to its high spatial resolution, tissue quantification, and deep imaging capabilities [36].

• The relationship between imaging depth and spatial resolution is approximately constant, maintaining proportionality as both dimensions are scaled.

• PAI exhibits high sensitivity to light absorption, enabling precise detection of changes within tissues.

• PAI facilitates functional imaging by exploiting physiologically specific endogenous optical absorption contrasts.

• PAI has the potential for real-time imaging applications, enhancing its utility in dynamic clinical environments.

• PAI is safe for human use, making it a promising tool for clinical applications.

Conclusion

After decades of development, PAI technology has diversified, merging the strengths of pure optical imaging and ultrasonography. It plays a pivotal role in studying various brain tissues, notable for its high resolution, minimal biological damage, and high sensitivity, showcasing its potential for biomedical applications. However, current research on PAI for brain imaging is predominantly confined to small animal models. The intense scattering and attenuation of ultrasonic signals by human cranial bones lead to weakened PAS and expanded bandwidth, consequently impairing imaging depth and spatial resolution. The primary challenges facing PAI in brain imaging include: 1) limited penetration

depth; 2) the trade-off between resolution and depth; 3) dependency on tissue optical properties; 4) interference from cranial bones; 5) hurdles in clinical applications.

In conclusion, PAI offers significant advantages for diagnosing brain diseases. Nevertheless, substantial challenges remain for its widespread clinical application in humans, particularly in understanding the pathogenesis of brain diseases, achieving early diagnosis, and monitoring treatment effectiveness. With ongoing advancements and broader adoption of PAI technology, its potential in brain disease research and other medical fields is promising, positioning it as an important tool for clinical diagnosis.

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