

Review Article

A Review of Optical Ultrasound Imaging Modalities for Intravascular Imaging

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ABSTRACT

Recent advances in medical imaging include integrating photoacoustic and optoacoustic techniques with conventional imaging modalities. The developments in the latter have led to the use of optics combined with the conventional ultrasound technique for imaging intravascular tissues and applied to different areas of the human body. Conventional ultrasound is a skin contact-based method used for imaging. It does not expose patients to harmful radiation compared to other techniques such as Computerised Tomography (CT) and Magnetic Resonance Imaging (MRI) scans. On the other hand, optical Ultrasound (OpUS) provides a new way of viewing internal organs of the human body by using skin and an eye-safe laser range. OpUS is mostly used for binary measurements since they do not require to be resolved at a much higher resolution but can be used to check

for intravascular imaging. Various signal processing techniques and reconstruction methodologies exist for Photo-Acoustic Imaging, and their applicability in bioimaging is explored in this paper.

Keywords: Imaging, intravascular, optoacoustic, photoacoustic, reconstruction, ultrasound

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INTRODUCTION

Although ultrasound (US) has been used over decades as real-time imaging technology, using high-frequency sound waves generated by a piezoelectric transducer, it has its shortcomings (Wissmeyer et al., 2018). The shortcomings of the US are not limited to image variability introduced due to body-probe movements, low image spectra and the inability to be used for burnt victims or children. Nevertheless, it is possible to view the internal anatomical structure of human beings and see the movements of internal organs and blood flow using the US by reconstructing the amplitude and time of flight of the reflected acoustic waves into an image that can be displayed, stored, or analysed. Apart from the shortcomings of the US that arise from the movement in the contact of the surfaces, there is also limited signal quality due to the attenuation of the sound waves by air (Omidi et al., 2018). However, this is overcome by using a coupling medium (gel) between the probe and the contact skin. It is not the same as Laser Ultrasound (LUS), as it employs a different signal acquisition mechanism, which uses the light of two or more powered lasers that are transmitted in the air as they measure the acoustic vibrations.

As a result, LUS is applied as a technology that provides a non-contact mechanism and thus can be applied in situations where skin contact must be avoided, such as burn victims or children. We can apply LUS to expose human tissues using acoustic detectors and sources by having adequate resources and applying necessary optical designs and interferometry. The penetration and standoff distance from the target surface depends upon the imaging application and can be incorporated into the design (Berlet et al., 2014). Another optical imaging technology is Photoacoustic Computed Tomography (PACT) which is mainly a soft tissue imaging modality that uses optical contrast mechanism in combination with the conventional ultrasound detection mechanism (Chao et al., 2013). Photoacoustic Imaging (PA) imaging has been employed for the different optical spectra wavelengths ranging from X-Ray to Infrared, with Infrared (IR) having the least bandwidth and the least penetration (Hafizah et al., 2010).

The setup of the basic photoacoustic imaging system is almost the same. It consists of a transducer that transmits the laser pulses and, in turn, acquires the ultrasonic signals that have been reflected. These signals are used to reconstruct an image that will reflect the photoacoustic signals. For this kind of setup, there exist 2 kinds of OpUs interferometry and refractometry (Canagasabey et al., 2011). Interferometry can be realised using Michelson Interferometry (MI), Mach-Zehnder Interferometry (MZI), doppler or the resonator method. MI and MZI use a 2-beam technique in which a laser beam goes through 2 independent paths, one that is the US excited. The other path is used as a reference path, and the change that happens to the path taken by light is caused by the pressure received and instantiates a corresponding change in the beam intensity at the interferometer output. In contrast, in the doppler method, a doppler shift of the received US waves is measured and used to

reconstruct the signal. The resonator method is similar to the 2-beam technique, but the difference is that it uses an optical resonator to detect the US waves (Zhang et al., 2021).

RELATED WORKS

There have been many approaches and advances in the fields of photoacoustic and optoacoustic imaging necessitated by the need to have 1) more volumetric approaches, 2) non-contact methods, and 3) remote scanning of images using the different photoacoustic and optoacoustic imaging techniques (Demian et al., 2014). US methods have produced more volumetric images of human tissues than other imaging modalities like MRI and CT. However, their geometry makes it difficult to use the US for a wider range of applications in terms of where they can be used on a human body. There has been slow progress in research using or adopting LUS as a novel technique for imaging due to its complexity and high cost involved in setting up the equipment required. In published and known research, LUS has been used in non-destructive testing and demonstrated tissue-mimicking phantoms.

Recently there has been progress in the use of LUS for *in vivo* human imaging by a team from MIT led by Zhang et al. (2019). Zhang et al. (2019) used 1,550 nanometres of two pulsed lasers of equal wavelength that turned the sound waves as they were reflected from a distance. They used one of the lasers from their setup for motion indication caused by sound waves, combining it with a mechanical laser scanning system, thus making it easy to generate images without any contact with the human subject. They did *ex vivo* tests using a gelatine-based phantom on pig tissue and four human subjects and compared their images with those from the standard ultrasound technique. In their evaluation, they noted that the images they obtained could not match the conventional US but noted that there is room to improve the image quality. Zhao et al. (2019) published a review article on optical ultrasound generation and detection for intravascular imaging. They reviewed recent developments in optical sound transmitters, detectors and all other optical ultrasound imaging systems applied to intravascular imaging. In their review, they highlighted the importance of having an all-optical based ultrasound imaging system and noted that it could be a breakthrough in imaging technologies. Of importance in their work is that they pointed out the need to have better performing all-optical imaging techniques where a varying pulse laser can be used since the generated ultrasound frequencies depend on the excitation light's pulse width.

The team also noted that various tissues exhibit individual optical absorption spectra; thus, using variegated wavelengths could be useful for profiling several tissue structures. Thompson et al. (2020) designed a laser-induced synthetic aperture ultrasound imaging system and took images using a breast-mimicking phantom. Comparing their results with those obtained using conventional ultrasound, they concluded that the difference between the images they took to those of the mimicking phantom was the contrast due

to the difference in the spectral absorption properties of the tissues under investigation. Finally, DiMarzio and Murray (2003) reviewed the different medical imaging techniques that combine light and ultrasound. Their research highlighted the importance of combining light and ultrasound as applied to spectroscopy and the ability to measure blood volume and blood oxygen, even though this might not yield good results since most biological tissues are highly scattering and their respective spatial resolution is not satisfactory.

In contrast, the use of US provided a better resolution, although not so satisfactory on soft tissues; they highlighted and concluded by recommending the need to combine the two techniques to be explored for different imaging tissues. Research by Halani et al. (2018) did not focus on laser ultrasound but used infra-red-based US imaging to diagnose and manage cutaneous diseases. The goal of combining the two modalities suggested a novel approach to diagnosing and managing skin lesions in a non-invasive manner (Halani et al., 2018). Their work focused on infrared compared to the LUS since there was no need for skin penetration; hence, they used infrared. However, the infrared-based method would offer low spatial resolution and might not produce better results if used for intravascular imaging. Colchester et al. (2019) focused on all-optical ultrasound imaging, where they used light to scan and synthesise an imaging aperture. They designed a handheld probe that provided video-rate imaging, and it was demonstrated *in vivo* on human tissue. It was accomplished using a single optic fibre US detector paired with discrete fibre optic US sources, as images were captured.

Zhang et al. (2019) characterised the sources of US signals as applied to biological tissues for imaging applications. In their work, they used a laser source of 800 to 2000 nm to generate LUS at the surface of the biological tissue. Their observation was that the LUS's energy in biological tissue was between 0.5 and 3 MHz, which led to increased acoustic energy as the optical absorption coefficient increased. The different wavelengths from 800 nm to 2000 nm were used to generate different images. They concluded that LUS has greater potential to be used as an effective imaging modality. Thompson et al. (2020) also concluded that the optical inhomogeneity nature of the biological tissues reduces the signal amplitude that happens because of reduced absorption and increased optical scattering. However, clinical iterations of LUS will require multipoint optical transmission and detection to amplify the acoustic source amplitudes and reduce the data acquisition time.

In their work on reconstruction methodologies, Burgholzer et al. (2008) described laser ultrasonics as having high absorption and penetration of the samples. They conducted this study to determine the contrast by varying acoustic impedance. Other research outputs were directed toward using fibre optics instead of the generated laser. As presented by Colchester et al. (2019), they worked on an optical fibre that produced pulsed excitation light in combination with a photo-acoustically excited coating for the generation of the US beam; using the Fabry-Perot setup, and they investigated the capabilities of imaging intraluminal

carotid arteries. Colchester et al. (2019) used the conventional signal processing technique involving depth-dependent filtering of the acquired image data followed by a fourth-order high pass Butterworth filter. Nuster et al. (2013) worked on a hybrid photoacoustic, and US imaging with optical US detection and images were acquired using the inverse Radon transform. They used phantoms to simultaneously get PA and US images by focusing the detectors onto a selected plane (Nuster et al., 2013).

REVIEW METHODOLOGY

The search protocol used to obtain research information about optical ultrasound technologies is using “optical” AND ‘ultrasound’ AND ‘imaging’ yielding a total of 58 360 results with 37 603 publications done in the last 10 years. The search criteria show that the area of optical ultrasound is a very novel area considering that an estimated 64 per cent of the research has been done in the last 10 years from 1990. Narrowing the search to ‘reconstruction’ AND ‘algorithms’ yielded 44 results of publications in the last 10 years, including books, documents, journals, conference articles and theses. Of the 44 results, only 20 were reviewed and considered significant to this review. In the reviewed articles, we looked at the optical imaging techniques, application domain, signal processing and reconstruction methodologies and finally, the challenges and research opportunities addressed by the published research.

SIGNAL PROCESSING AND RECONSTRUCTION METHODS

For the conventional US, there exist many reconstruction and visualisation techniques. 2D and 3D methods have been used in the past, with 3D methods including mechanical scanning, 2D array, positional tracking based free hand and untracked based free hand being preferred. For example, the most used 3D reconstruction methods are pixel-based, volume-based, and function-based method are the most used 3D reconstruction methods. Several signal processing and reconstruction methodologies exist for PA imaging. This chapter explores the signal processing techniques and the corresponding reconstruction methods used in this paper’s work. The Synthetic Aperture Focusing Technique (SAFT) is the most commonly used method for reconstruction since it is a low-cost and less complex technique (Trots et al., 2011; Kim et al., 2020). In this method, an image is simultaneously acquired from signal lines one frame at a time. The SAFT reduces the data bandwidth and system complexity by using low-rate sampling with signals transmitted to a computational backend computer that can sequentially perform beam forming as it reconstructs each signal to have B-mode images. The SAFT method is a Fourier domain reconstruction method that requires interpolation for spatial discretization (Trots et al., 2011). It is not possible to use the SAFT algorithm for signal processing but rather for optimal performance, to locate the

photoacoustic signals in the sample, time domain delay and sum-focused beam foaming techniques are mostly used. When time delay is used, backpropagation can usually be used for reconstruction, but this causes the introduction of artefacts due to a limited number of view angles. Ultrasound Brightness (US-B) mode images are taken from beamforming, and this technique is used to provide high spatial resolution and better image quality. Other signal processing techniques used with the SAFT algorithm include envelope detection and log compression; both can be used at the backend before reconstruction. In the US-B mode, the image processing steps are reversed to recover the US-post beam foamed Radio frequency (RF) data. The US post-beam foamed RF data is recovered using log compression and convolving the acoustic impulse response and the frequency information using B-mode images as the input. As reviewed in this chapter, several other reconstruction methods have been proposed and used in research. Recent advances in medical imaging research have shown machine learning and artificial intelligence being used for image reconstruction. One such method is using a deep learning algorithm as a reconstruction method, as proposed by Kim et al. (2020) and Peyton et al. (2018). Kim et al. (2020) worked on deep convolutional neural networks to overcome the issue of limited bandwidth and detection views, leading to severe structural loss and low image contrast. The advantage of using deep learning techniques is that they can be used for real-time clinical applications and can be trained. There is evidence from Kim et al. (2020) that if trained, deep learning techniques provide better reconstruction than conventional reconstruction methods, including delay and sum, minimum variance, delay multiply and sum and the iterative methods with compressed sensing. These mentioned methods are computationally complex to be applied for real-time image processing.

Kruizing et al. (2013) proposed a PA image reconstruction method that uses information from US and PA images to simulate the full PA pressure field. The algorithm developed focused on image completion and boundary suppression for the reconstruction. Their approach was similar to the iterative time reversal method that uses the K-wave but different in that the image completion method estimates the spectral proportion of each independent image data. Vu et al. (2018) proposed an image reconstruction algorithm for PA that uses MATLAB/CUDA-without-C++ code (MCC), MATLAB/C++/CUDA code (MCCC) and MATLAB-without-GPU code (MWGC) techniques to compare processing time and image quality using a cross-platform based on MATLAB and CUDA. The approach significantly reduces the reconstruction time by 5 times using the focal time-based backpropagation. Similarly, Nuster et al. (2013) used a method of integrating detectors for image reconstruction. However, they used A-waves are focused on a detecting area that has a size which is greater than the phantom size.

Zhang et al. (2014) proposed a joint variation and Lp-norm-based image reconstruction algorithm where the reconstructed image is updated by computing the sum of the image

variation values and the Lp-nom value. The iterations are used for an operator splitting framework using the Bazilai-Borwein step size selection method. The setup effectively reduced the image scanning time and improved the quality of the PA image.

APPLICATION DOMAIN

A review from previous research showed that PA imaging could be applied for both deep penetration and lower penetration. The applications picked from the review mainly include brain imaging, tissue and vascular imaging and dermatology. The international society of optics and photonics through the work being done by Huang et al. (2013) on a new Ultrasound Computed Tomography (USCT) and PACT reconstruction mechanisms for transcranial brain imaging. This collaboration's main goal is to develop a better image reconstruction algorithm that produces better image quality to compensate for the noise introduced by the vibrations from acoustic aberrations. PA imaging has also been used to detect neurological disorders like stroke, tumour, and Alzheimer's. It was validated by Chen et al. (2021) using the Fabry Perot Interferometry (FPI) mesoscope for cerebrovascular mouse brain imaging using a photothermally tuneable FPI ultrasound sensor.

Another application for PA imaging is tissue and vascular imaging. For this application, novel applications involved using catheters embedded with LUS probes for tissue imaging. For example, a team at UCL developed an imaging probe that visualises tissues (Zhao et al., 2019). The transmission and detection of the US in their design are done using optical fibres, mainly designed for visualisations during clinical applications. Similarly, for tissue imaging, Little et al. (2020) evaluated the use of optical US for real-time visualisations of the coronary vasculature. Their method was intravascular and validated the application of optical imaging for vascular tissues. Little et al. (2020) also applied US imaging for intracoronary imaging, where pulsed OpUS transducers generate the US using the interferometry method to generate images. High-resolution images of less than 60 μm axial and imaging depths of greater than 2 cm were realised using fibre optic transducers with a pressure of 21.5 MPa and bandwidth of 39.8 MHz.

The third most applied domain of PA is dermatology, where PA is used to image the skin and its properties. To validate the applicability of optical US imaging for dermatology, Csány et al. (2021) designed a device based on the optical US for imaging various skin pathogens. Their setup included a handheld device that combines optics and US to record images of various types of skin lesions. IR-based photoacoustic techniques have also been used for preclinical research to image the skin and skin lesions. Duric et al. (2013) used a waveform-based method to reconstruct breast images. As a follow-up to their recommendation in Huang et al. (2013), they are currently working on a new USCT and PACT reconstruction mechanism for transcranial brain injury.

CHALLENGES AND RESEARCH OPPORTUNITIES

The conventional US uses a probe placed on the subject's surface whose biological tissues are under examination. It is not always desirable for children and burns victims because of the pressure required to maintain acoustic distance between the probe and the tissues. The probe consists of a transducer array and is pressed against the skin using a coupling gel to transmit the waves into the tissue. Apart from the pain added to the burn victims due to contact, contact-based US also cause image variability due to contact and movements introduced by both the subject and the physician. The conventional US has a low degree of reproducibility since the user has to define the image orientation and field of view by manually adjusting the transducer placements resulting in acquiring patients' images at different times, making it difficult to compare the images taken. Light ultrasound can be used to tackle the problems of using the conventional US. Another alternative would be to use photoacoustic imaging, but with this method, the light is attenuated by the biological tissue; hence, the laser's penetration is needed for intravascular imaging. One would also note that from the work done so far, there is a need for high accuracy in research. Huang et al. (2013) presented the necessity to compensate for time structures by proposing a hybrid imaging system that makes use of PACT and USCT PA imaging has proved to be able to produce high-quality images with better contrast and high spatial resolution. However, for the materials used, in comparison with other techniques, optical US detection techniques have higher sensitivity over a wider bandwidth. It is easier to miniaturize optical transducers and expand the field of application. For high accuracy, Huang et al. (2013) proposed the necessity for compensating time structures by proposing a hybrid system that uses PACT and USCT. Another challenge of PA imaging, as highlighted by Chen et al. (2019), is that most clinical US systems do not have an interface for synchronising channel data from optoacoustic images. Manwar et al. (2020) noted that optical US detection methods are relatively slow, complex and costly to set up. Continuous-wave lasers in such setups make the system more sensitive to temperature changes and vibrations (Manwar et al., 2020). For the evaluation of the refractometry and the interferometry method, research shows that the phase-sensitive refractometry method has a higher bandwidth than the corresponding MZI and doppler counterparts.

Among other benefits, LUS can help remote imaging without contact with the body surface. Body surfaces can add harmful toxins to patients' skin, which is not always feasible for burnt patients and infants. By using LUS, physicians can image different positions since light can penetrate all directions. In addition, LUS has greater bandwidth and thus can be used to image tissues of different optical spectra. Without contact, there is no damage to the skin since light is used, and a safe range of Laser is used and has no radiation effects.

CONCLUSION AND DISCUSSION

Most research in Photoacoustic Imaging (PAI) has been done using laser and fibre optic cables because of their higher bandwidths and applicability for intravascular imaging. 2 different methods have been reviewed in this paper the Interferometry method and the Refractometry method for the setup of the optical design. In addition, different signal processing techniques and reconstruction methodologies have been reviewed, with the SAFT being the most commonly used reconstruction method. Various application domains for PA have been identified, and it can be concluded that brain imaging, vascular and tissue imaging and dermatology are the main application areas for PAI. Several challenges and opportunities have been presented by different authors in previous research and should be used to perfect research in PAI. The ability to use both PACT and USCT present novel techniques for optical bioimaging using the conventional hardware permitting multimodal imaging that produces high quality images. Optical Coherence Tomography (OCT) has been used as an alternative to LUS but uses ballistic photons for detection.

In contrast, PAI has deeper penetration since it uses diffused photons to provide greater resolution at the end. Therefore, it can be concluded that optical ultrasound has a greater potential in clinical imaging. However, the future use of the technique depends on the changes in data acquisition, laser techniques and the transducer technology based on the application domain.

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