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The Design and Realization of a Dual Mode Photoacoustic and Ultrasound Imaging Camera

Zichao Han
zh7474@rit.edu

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The Design and Realization of a Dual Mode Photoacoustic and Ultrasound Imaging Camera

by

Zichao Han

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Chester F. Carlson Center for Imaging Science College of Science Rochester Institute of Technology

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Signature of the Author

Accepted by

Coordinator, Ph.D. Degree Program

Date
The Ph.D. Degree Dissertation of Zichao Han has been examined and approved by the dissertation committee as satisfactory for the dissertation required for the Ph.D. degree in Imaging Science.

Dr. Navalgund Rao, Dissertation Advisor

Dr. Daniel Phillips, External Chair

Dr. María Helguera, Committee

Dr. Vikram Dogra, Committee

Date
The Design and Realization of a Dual Mode Photoacoustic and Ultrasound Imaging Camera

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Zichao Han

Submitted to the
Chester F. Carlson Center for Imaging Science
in partial fulfillment of the requirements
for the Doctor of Philosophy Degree
at the Rochester Institute of Technology

Abstract

Prostate cancer is currently the second leading cause of cancer death in American men. Diagnosis of the disease is based on persisting elevated prostate-specific antigen (PSA) levels and suspicious lesion felt on digital rectal examination (DRE) prompting transrectal ultrasound (TRUS) imaging guided biopsy. This method, however, has long been criticized for its poor sensitivity in detecting cancerous lesions, leading to the fact that these biopsies generally are not targeted but systematic multi-core in nature that try to sample the entire gland. This thesis presents a new modality that, in combination of ultrasound (US) imaging with multi-wavelength photoacoustic (PA) imaging, improves the physicians ability to locate the suspicious cancerous regions during biopsy.

Here, building further on the innovation of an acoustic lens based focusing technology for fast PA imaging, a novel concept with the use of a polyvinylidene fluoride (PVDF) film that incorporates US imaging into our existing PA imaging probe is presented. The method takes advantage of the lens based PA signal focusing technology, while simultaneously incorporates US imaging modality without interfering with the current PA imaging system design and structure. Simulation and experimental support on tissue equivalent phantoms are provided in detail for the performance validation and quality metrics determination of
the dual mode imaging probe. The thesis also elaborates on the signal-to-noise ratio (SNR) improvement of the US imaging component by driving the film with pulse compression technology based frequency modulated (FM) signals, the use of which in conjunction with acoustic lens based focusing is another contribution to the field. In addition, a custom-designed US simulation software that is developed to explore and evaluate various system design options is discussed. The dual modality transrectal probe for optical absorption based PA contrast imaging and backscattered echo signal focusing based US imaging prototype is intended as a first step. The long term goal is to facilitate locating the cancer region in-vivo with PA imaging, transfer it to co-registered US image, and then use the real time US imaging for needle guidance during biopsy. With biopsy proven evidence from a cohort of internal review board (IRB) approved studies, PA imaging may ultimately prove effective in reducing the number of biopsies. Beyond prostate, applications in thyroid and breast cancer management are also feasible.
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Dedicated to mom and dad, and to all who made him who he is today. As with any journey, who to travel with is always more important than the final destination. Thank you for visiting him in this amazing exploration of his life...
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Chapter 1

Introduction

1.1 Significance of the study

1.1.1 Current state for prostate disease management

According to statistics from the American Cancer Society for the most recent year of 2017, the estimation of the diagnosed population of new prostate cancer cases for the year 2018 is 164,690, and there will be approximately 29,430 deaths rising from prostate cancer in the United States [1]. From 2006 to 2010, the annual incidence of prostate cancer was 152 per 100,000 [2]. Prostate cancer has become the second leading cause of cancer death in American men, just behind lung cancer. About 1 man in 9 will be diagnosed with prostate cancer during his lifetime. The actuality is even worse for men over 65, with a probability of diagnosed cases around astonishing 60% [1].

In contrast with this astounding fact, diagnosis and prognosis of this disease do not meet the requirements at this time. Suspicion of the disease is usually based on an elevated prostate-specific antigen (PSA) test or abnormal digital rectal exam (DRE), followed by transrectal ultrasound (TRUS) guided biopsy of the prostate for definitive diagnosis. The
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sensitivity and specificity of TRUS in detecting prostate cancers is reported to be 41% and 81%, respectively, while the positive predictive value (PPV) and the negative predictive value (NPV) of TRUS are found to be 52.7% and 72%, respectively, with an average accuracy of 67%, far behind expectations [3]. Therefore, current TRUS is not fully capable for prostate cancer detection and localization. However, despite its unreliable results, it has been the only available choice to performing biopsies for years until now. The prostate biopsies under TRUS guidance are now largely systematic with many popular schemes in use [4, 5]. Typically 5 to 12 core samples are taken from various regions of the gland [1]. Due to sampling errors, there is more than a 30% chance of misleading the diagnosis.

This reality has a much wider impact for patients who actually suffer from the disease. Take patients who are found to have low Gleason score on their first biopsy test for example, since there are no definitive guidelines on the prognostic value for when to stop performing biopsies, even if their PSA is rising after several biopsy sessions, they still need to remain a diagnostic dilemma on when to stop it. These patients are put on an active surveillance program where they have to get periodic biopsies, because ultrasound (US) has no prognostic value. These repeated biopsies cause tremendous anxiety to patients and increase the incidence of possible complications, not to mention the added cost burden to the medical system. Upon review of clinical literature, American Urology Association guidelines, updated in 2007 [6], concludes that there is insufficient clinical data to provide definitive guidelines for prostate disease management. Worse yet, there is no adequate imaging modality that could be used to generate such data on which one could build treatment planning guidelines.

For the reason of increasing the sensitivity of TRUS, US based techniques that can be easily integrated to produce co-registered images have been investigated in recent research projects. Notable examples are contrast-enhanced US (CEUS) and real-time elastography (RTE). The sensitivity of CEUS in detecting prostate cancer is 65% to 68%, while the
sensitivity of RTE is only 60.8% [7]. Moreover, the ability of RTE to detect cancer lesions that are less than 10 millimeter (mm) in size is reported to be only 16%. Therefore, it also has limited value in prostate cancer diagnosis [8]. Other imaging modalities including magnetic resonance imaging (MRI), computed tomography (CT), positron emission tomography (PET), and radionuclide scintigraphy (Prostascint) have demonstrated limited use in the detection of prostate cancer, and are primarily reserved for the evaluation and staging of advanced cancer [9]. Furthermore, they are expensive and cannot be easily integrated with TRUS to produce co-registered images to be used during biopsies.

Obviously at this point, the need for a system with new imaging modalities is pressing. The new imaging technique should not only take the responsibility of accurately detecting prostate cancer with high sensitivity, but should also meet imaging requirements of low cost and real time as TRUS does as well. Considering the fact that TRUS will still remain a preferred modality for prostate biopsy, it is highly desirable that any new modality to be integrated with US provides near real-time guidance in the prostate cancer diagnosis and disease management. For these reasons, a device which can integrate an emerging functional imaging modality, namely photoacoustic (PA) imaging with US, is proposed and implemented in this study. The approach is to invent a method to incorporate US imaging into our existing acoustic lens based focusing technology that was primarily developed for PA imaging.

1.1.2 Why photoacoustic imaging

PA imaging is a new imaging modality which has not been largely applied to the clinics yet. However, it has already been promised to become a valuable tool in many clinical areas where there are unmet needs, as evidenced by several review articles written in the past decade [10, 11, 12]. As the name suggests, the PA imaging modality takes the advantages from both the optics and US [13]. It’s known as the PA effect, referring
to the phenomenon where the tissue interacts with a near infra-red (NIR) laser pulse correlating to a 700 to 1000 nanometer (nm) wavelength range in a very short duration of just few nanoseconds (ns). A short time duration US wave, also referred to as PA signal, is generated due to this effect. The combination of the use of light and sound makes this modality seize the benefits of the two [10, 13]. Pure optical imaging system uses light as input source and always suffers from low image resolution. This problem can be solved by PA imaging by converting optical radiation into a much less scattered US wave. The amplitude of the PA signal is proportional to the absorption coefficient of the absorber. Notably hemoglobin in the tissue is the dominant absorber in the NIR range. The tissue and its major constituents, i.e., water, oxy and de-oxy hemoglobin in blood, lipid, fat, melanin, collagen, etc., have widely varying absorption spectra in the NIR region [11] that not only provide abundant contrast features, but also open the door for PA imaging based spectroscopy, non-invasive tissue characterization and functional imaging. With PA imaging, one can depict optical absorption property of the tissue constituents up to a few centimeters (cm) deep with sub-mm resolution. The team has previously developed a prototype PA imaging probe with lens based focusing for ex-vivo studies [13], in which a biopsy example of human prostate specimens was examined for PA imaging at wavelengths of 760 nm and 850 nm. Cancerous regions were found to be more hypoxic than benign ones, where the differentiation of the two prostate tissue with hight specificity of 96.2% and good sensitivity of 81.3%, with PPV of 92.9% and NPV of 89.3% was demonstrated.

1.1.3 Why co-registering ultrasound image

It is worth noting that using PA imaging device the malignant tissue produces strong signals which could clearly display the corresponding abnormal areas [14]. However, since the main constituent of blood is hemoglobin, and it composes the foremost absorber of the tissue within the corresponding NIR range, the demonstrated area of the malignant
tissue is always isolated from that of the benign ones. Typically, the excised prostate
gland is inked using different colors prior to slicing in pathology, which is later used to
generate PA signals that are recorded by the system during rasterization. These recorded
signals from the ink serve as a guided boundary outline on our PA images for every imaged
specimen, which are then used to help select region of interest on the PA images using
marked digital histopathology slides as ground truth. Therefore, it is also expected that
PA image will also be dominated by the isolated regions in the in-vivo setting, where
hemoglobin concentration is high with little signal from other parts of the tissue [13]. The
PA imaging, simply put, is able to provide useful evidence in recognizing the suspicious
lesion, but without efficient signals from the background, physicians always need to face
the dilemma on how to precisely localize the cancerous regions which, without doubt, is one
of the most crucial steps in the disease diagnosis and prognosis. For this reason, the need
for an imaging device that is able to depict echoes from the soft tissue background as well
as other anatomical structures is highly necessary and desirable at this point. Summing up
all these factors, we believe that there is a very urgent need to further improve our existing
acoustic lens based PA imaging device to a more clinically practical imaging device with
synergistic dual modalities of PA and US.

US imaging modality is based on the backscattered US signals through tissue reflec-
tion, which is capable of depicting the background information of the tissue organ itself.
The signal can be correspondingly served as the localization clues, with which the physi-
cians will have a familiar framework along with diagnostic and prognostic information
coming from PA images superimposed for informed decision and targeted biopsy. The
dual modality imaging probe may predict growth of the cancer, detect any new changes
in the prostate cancer in response to medicines, or even detect cancer recurrence. On top
of all of these potential advantages of producing much more acceptable quality images
for disease management, both PA and US are safe due to their non-ionizing radiation
properties, which on the other hand, greatly enhance its clinical feasibility in the future. Its low cost feature from a business point of view is also a huge plus over other imaging modalities like MRI or CT.

1.1.4 Comparison with MRI guided TRUS biopsy

Multiparametric prostate MRI is emerging as a possible modality that can detect clinically relevant cancer [15, 16]. Even though accuracy parameters are not clear yet, it holds promise for urologists to progress from blind, systematic biopsies to biopsies in which MRI information is mapped and tracked on TRUS for guidance. However, the MRI guided prostate biopsy has some obvious shortcomings compared to the technology we proposed to develop. First, it is expensive, making routine diagnostics prohibitive. Second, MRI image fusion requires prior MRI session and an expensive hardware and/or software system. Artemis device [17] with fiducaries markers to track and map MRI data onto TRUS in real time. This can be cumbersome, prone to registration inaccuracies and not to mention the expense and inconvenience to physicians and patients. In comparison, with our probe PA and US images will be inherently co-registered, one will be able to switch from one to the other without disturbing probe location, and even though PA image frame rate will be typically 10 times lower than its US counterpart, information transfer from PA to US will be fast and cost effective such that ultimately its use in a primary care physician’s office may become a reality.

1.1.5 Goals and impacts of the study

In summary, considering the current situation of prostate cancer detection, we believe the need for a new pragmatic imaging system which is able to address the clinical challenges mentioned above in prostate disease diagnosis and management is urgent. Such a system
should incorporate two synergistic modalities of PA and US into one single probe. The scoop of the research includes taking the idea from proof of concept to a working prototype of a dual mode transrectal probe ready to be used in a canine model, or more specifically, to explore a novel approach to integrate the US imaging modality to the existing PA imaging probe for ex-vivo experiments. The dual mode imaging probe will, first of all, significantly improve the ability of clinicians to diagnose the disease. Second, it will enable systematic clinical studies to validate its impact on prostate disease management. On the scientific side, it will also help accelerate investigations related to the possible joint role of PA and US biomarkers. These markers may be endogenous, such as oxy and deoxy hemoglobin, water, lipid, and US signal analysis based tissue textural features extracted from region-of-interest (ROI) defined by co-registered PA image or exogenous, such as targeted molecular contrast agents.

The dual modality transrectal probe, however, is only intended as a first step. The long-term goal of a bigger project is to facilitate locating the cancer region in-vivo with PA imaging, transfer it to co-registered US image, and then use the real time US imaging for needle guidance during biopsy. The final goal of the big project is to develop an imaging modality that can clearly differentiate cancerous from benign prostate tissue in patients with positive PSA results. The significance of the study is obvious: on one hand, it will greatly reduce the burden of both clinicians and patients on diagnosing the prostate cancer disease by helping identify patients who do not need further treatment, as well as in reducing false negative results due to poor cancer targeting of TRUS biopsy needles; also from a scientific perspective, the possible joint role of acoustic lens based dual mode PA and US imaging modalities is an order of magnitude less expensive than the competitors. As a result, the investigations will fill the research gap in the area by eliminating major R&D investment necessary for dedicated software and hardware for PA image reconstruction. The use of frequency modulated (FM) signals to the US component
to deliver adequate energy for deep tissue imaging is also a contribution to the field, which will eliminate the need for expensive US sources. The target community and the market are primarily spanned by radiology departments at numerous hospitals and imaging centers that perform diagnostic procedures for breast, prostate, thyroid, and skin. A secondary market of primary care physicians may also develop later on. The commercialization plan would involve an exit strategy to be executed after developing the technology to a certain point with the help of key players and partners.

To the best of our knowledge, no such lens based focusing imaging devices have ever been developed and fabricated. Traditional TRUS probe employs a convex array with a hardwired scheme where US is transmitted and/or received over a narrow beam, which then scans over a 150 to 200 degree arc to produce a sector B-scan image. Our probe design, however, is based on PA signal and acoustic lens system. For PA tomography (PAT) based imaging, the signal has to be received from all of the tissue absorbers and by all of the sensor elements. Use of linear array for dual mode has been demonstrated by Xu et al. [10], but it is not real-time and the geometry is not suitable for prostate. Oraevsky et al. [18], in a preliminary attempt, has shown that convex arrays are ill-suited for PAT, resulting in arc shaped noise artifacts, poor effective aperture resulting in poor image contrast. By using our own technology instead of PAT, we maintain the advantages of simplicity, cost effectiveness, ease in design and fabrication, and flexibility of imaging in three orthogonal planes with one probe.

### 1.2 Project innovation

In this section, the feasibility and capability of an acoustic lens based focusing technology for PA imaging is discussed, followed by the introduction of methodology to the synergy for a dual mode imaging camera between existing laser excited PA waves and echo based
US waves. The idea of lens based PA imaging has already been theoretically and experimentally proved by the previous research team [13]. Based on the existing results, incorporation of US imaging modality becomes the main focus of the study.

1.2.1 Concept of lens based photoacoustic imaging

In collaboration with the University of Rochester Medical Center (URMC) and the Institutes of Optics at the University of Rochester, the previous interdisciplinary team combined the acoustic lens based focusing idea with PA imaging methodology, and has successfully designed, developed, and fabricated the first generation of PA imaging prototype camera for ex-vivo experiments. The technology simultaneously focuses PA signal originating from a large volume, typically the size of the prostate gland. Focused B-scan, i.e., coronal and sagittal plane images, can be created in near real time in about 1 second (s) and three-dimensional (3D) volumetric data and C-scans, i.e., transverse plane images, can be produced in less than 1 minute (min). Consequently, our lens based PA system is faster with no errors in the reconstructed image due to spatial and temporal sampling of the signal, especially when compared with the alternate technology, PAT, in which a large amount of PA signal data from multiple US sensors has to be digitized, stored, and processed off line, with time consuming and expensive dedicated hardware and software to tomographically reconstruct the image. The proposed dual mode device is also inexpensive to design and implement, near real-time, and portable.

Fig. 1.1 illustrates the concept behind our lens based focusing approach.

The singlet element acoustic lens is with focal length $f$ and diameter $d$, and is held by a cylindrical probe filled with water in the experiment (not shown in the figure). The PA imaging system is designed in a $4f$ configuration to produce PA images of magnification of $-1$. The 3D object or tissue organ to be imaged is placed in contact with the probe using US coupling gel, at a distance $2f$ to the left of the lens on the object plane. Similar
CHAPTER 1. INTRODUCTION

Figure 1.1: Introduction to an acoustic lens based PA imaging camera. From left to right: the incident laser beam, tissue volume containing multiple NIR absorbers, acoustic lens and transducer array. The PA signal will be generated by the NIR absorbers in the tissue, then focused by the acoustic lens and collected by the transducer array at the image plane.

to other optical imaging systems, an appropriately designed converging lens focuses the waves accurately to the image plane. Based on the thin lens equation [19]:

\[
\frac{1}{f} = \frac{1}{d_0} + \frac{1}{d_i},
\]

where \(d_0\) and \(d_i\) denote the object and image distance, respectively, and \(f\) is the focal length of the system, the image plane where US sensor array locates should be at the same \(2f\) distance to the right of the lens [20]. When the tissue is exposed to a short pulse of NIR laser, point absorbers expand and relax, generating a short pulse of US waves via PA effect as has been discussed earlier in the chapter. The generated US waves, which is also referred to as PA waves, are brought to focus by the acoustic lens at the image plane onto the transducer. The acoustic lens simultaneously focuses all points in the focal
plane with a resolution of 0.7 mm. Furthermore, the depth of field of the lens is such that absorbers within approximately 1 cm zone around the focal plane also maintain a resolution within 60% of the best value, as will be discussed in detail later in Sect. 3.3.4. The object plane here corresponds to a coronal plane in the tissue, unlike sagittal or transverse planes imaged by a conventional US imaging system. Image plane is defined by time delay measured with respect to $t = 0$ when the laser illuminates the tissue. A good resolution in PA imaging results from the fact that the US can be focused easily and the speed of propagation does not deviate much, so that the wave arrival time can provide information about the depth. Photoacoustically generated US waves and typical echo-based US waves are similar from a detector standpoint, as all that is needed to capture the signals is an US transducer.

Images of these coronal planes are referred to as C-scan images. Considering different ways in which the images will be presented in the subsequent simulations and experiments, they will be explained in details in Sect. 5.2.1. Specifically, C-scans, which are the key consideration of data presentation in the study, represent laser absorption by different regions of the tissue that are intersected by that plane, much like CT scan images. The photoacoustically generated US waves travel with finite speed around 1500 meter/second (m/s) in the soft tissue. Therefore, a pragmatic way to capture focused signal from a predetermined coronal plane is to time gate it when it is detected in the image plane. The assumption here is that all waves from the predetermined coronal plane arrive at the image plane at the same time.

1.2.2 Proof of lens based photoacoustic imaging concept

As the first step toward designing an in-vivo PA imaging system, a prototype PA imaging camera has been developed by the previous research team to detect any malignancies present in an excised tissue. The prototype is designed with a singlet element lens of a
39.8 mm focal length and a \( f/1.2 \). The radii of curvature of biconvave surface are \( \pm 33.5 \) mm on both sides (based on the sign convention of geometrical optics), with a refractive index of the material of 0.58. A 32-element 5 megahertz (MHz) linear array with 54.6% bandwidth, element size 0.7 mm by 1 mm and 0.7 mm pitch is used as the sensor. Our own 32 channel simultaneous data acquisition board is designed and fabricated with PA waves sampling at 30 MHz, 700 to 100 nm tunable laser, pulse width of 5 ns, and pulse repetition rate (PRF) of 10 hertz (Hz) is used to irradiate the tissue. Laser intensity is around 5 millijoules (mJ)/cm\(^2\), which is below the ANSI limit (25) for safe human use. Tests performed on 0.7 mm diameter graphite target placed in the focal zone showed that our system resolution in the C-scan plane was about 1 mm, in between C-scan plane 0.3 mm and in the B-scan plane estimated to be non-circular of size 0.3 mm \( \times \) 1 mm.

The project involves ex-vivo human tissues such as prostate, thyroid, kidney [21, 22, 23], and tailored various phantom experiments [13, 24, 25]. According to preliminary experimental results obtained by the team [25], in which six 2 to 3 mm diameter tapioca seeds were soaked in Indocyanine green (ICG) and embedded in a 3D gelatin phantom at depths ranging from 1 to 6 mm. The experiment was to test the camera’s ability of differentiating the target at different depth. The entire probe with the lens and the linear array was moved with a stepper motor to obtain C-scan images. The phantom was imaged with the prototype PA device at 790 nm which is the peak absorption wavelength of ICG. The ex-vivo preliminary results obtained using Fig. 1.1 PA setup shows that the system is able to resolve seed targets in the phantom located at different depths in individual C-scans, where a projection of reconstructed volumetric rendering of PA C-scan images acquired over the entire phantom thickness provides a better visualization of all the embedded targets.
1.2.3 Remaining work on photoacoustic imaging

Although the PA imaging system has been empirically verified feasible, it still lacks theoretical derivation support from the perspective of PA signal formation to propagation. Therefore, the project started with theoretical simulation of PA imaging using a third-part Matlab software, named k-Wave toolbox [26]. Based on \( k \)-space pseudo-spectral method, the toolbox simulates 2D propagation of PA waves in inhomogeneous media by calculating the first-order partial differential equation of linear acoustic. A schematic of the singlet lens system is shown below in Fig. 1.2, which follows all the parameters of the designed lens previously described in a 2D plane. The source position, \( i.e., \) point scatter in the prostate zone, corresponds to the location of the ex-vivo tissue organ. This is where the PA effect takes place. When the tissue organ is interacted with a NIR laser pulse, a very short pulse of PA signal will be generated accurately by the toolbox via the PA effect described earlier. The acoustic lens system then focus the waves to the image plane. The detailed simulation process, including the selection of parameters, the establishment of the simulation model, and the corresponding results will be described in Chap. 3.

![Figure 1.2: Introduction to the singlet lens based 2D PA imaging simulation with 4f imaging configuration.](image)

The Institute of Optics at the University of Rochester helped us design a more sophisticated multi-lens system, the layout of which is shown below in Fig. 1.3. The aim of
CHAPTER 1. INTRODUCTION

this design is to further eliminate the spherical aberration of the singlet lens system. Two lenses, respectively responsible for the wave focusing and the aberration corrections, are expected to improve image quality by providing better point spread function (PSF) for off-axis absorbers. The acoustic lenses were designed with Zemax, an optical lens software [27]. The multi-lens PA imaging system will be briefly evaluated in Chap. 4.

![Figure 1.3: Introduction to the multi-lens based PA imaging simulation, where two lenses are responsible for wave focusing and field curvature correction, respectively.](image)

1.2.4 Incorporation of ultrasound imaging

The novel, also the most challenging part of the study is to come up with a practical solution that could incorporate US imaging into our existing PA imaging probe in order to produce dual modality co-registered images, or simply put, to come up with an US source for backscatter imaging that preserves the PA framework of signal acquisition.

For PA imaging, as has already been discussed earlier, the laser beam exposes a finite volume of the tissue simultaneously and the PA signals are generated everywhere instantaneously. As shown below in Fig. 1.4, these PA signals that propagate within a solid angle subtended by the lens diameter get focused. Therefore, all sources of PA signal, i.e., NIR absorbers that lie on a plane perpendicular to the lens axis, arrive at the image plane almost simultaneously, enabling a good C-scan by using a short time gating. Furthermore, the signal arrival time can be converted to depth along the lens axis in the B-scan using
one way US travel time, as has been specified in Sect. 1.2.1.

For US imaging, the use of an US plane wave generator, i.e., a polyvinylidene fluoride (PVDF) film was proposed with its plane being perpendicular to the lens axis, the location of which throughout the system is indicated in the diagram of 1.4, where a 28 micron (µm) PVDF film is placed at approximately 1 cm right of the object plane. The red part of the diagram indicates PA imaging, including the incident laser beam and corresponding generated PA waves, while the blue part shows the US imaging mechanism, the key component of which is the PVDF film. A PVDF film produces US waves that propagate into two directions. The backscattered US signal from all US scatterers in the tissue, as shown in dotted blue line, will be effectively focused by the lens similar to its PA counterpart. The other signal from PVDF film that propagates directly to the sensor array, as marked by solid blue, is of no great significance to the study.

![Figure 1.4: Introduction to the US imaging incorporation. US signal generated by the PVDF film will propagate into two directions, with one propagating directly to the image plane, and the other one backscattered by the tissue first and then propagating through the PVDF film to the image plane with a time delay.](image)
The PVDF film is driven by a 0.5 volt (V) FM signal through a 50 Decibels (dB) power amplifier. The focusing and signal reception by linear array is kept similar to PA imaging setup described in Fig. 1.1. Given the typical active area of approximately 4 cm\(^2\) of the PVDF film, even the 3 to 4 cm deep areas of prostate gland will be safely in the near field, which ensures minimum diffraction and maintains plane wave nature of the incident wave up to required imaging depths. Acoustic impedance of about 4 megayls (MRayl) PVDF is also close to that of water of 1.5 MRayls. Therefore, backscattered wave propagating through the PVDF film will produce minimum distortion and multiple reflection artifacts. Its plane wave nature, focusing ability, and inconsequential distortion in back-propagation through PVDF have been confirmed in the experiment of the study. For the same reasons, a Piezo composite or crystal would be unsatisfactory. The setup of US imaging simulation, as shown in Fig. 1.5, is similar to that of its 1.2 PA imaging counterpart but with a PVDF film placed near the object plane to generate the waves as described earlier for US image generation.

Figure 1.5: Introduction to the singlet lens based 2D US imaging simulation with the PVDF film placed approximately 1 cm from the object plane, producing US waves propagating to two directions.

The incorporation of US imaging, including the simulation model, experimental US imaging system setup, and the corresponding results will be elaborated in Chap. 5. The experimental results of dual modality co-registered images of PA and US as well as future
improvements to the existing problems of the current probe will be discussed in Chap. 6.

1.2.5 Approach to low signal to noise ratio challenge

In order to improve the signal to noise ratio (SNR) of the backscattered US wave, pulse compression technique using linear FM signal has been proposed to increase penetration depth and improve SNR deep inside the tissue [28]. The axial resolution of an US imaging system improves with increasing frequency, but at the same time, due to the frequency dependent attenuation property of the tissue, the corresponding SNR degrades with increasing depth. Instead of using a short pulse as in conventional pulse echo system, the pulse compression technique uses a long duration FM signal as input, thereby distributing the total energy over the long duration input signal, and consequently reducing the requirements on the peak intensity. After receiving, the backscattered signal will be fed in to a matched filter which adjusts relative phases of the frequency components to produce the compressed pulse with improved SNR. The time duration of the compressed pulse is comparable to that of a conventional short pulse and thereby the axial resolution is maintained. More mathematics behind the technology will be derived in the following Chap. 2.

1.3 Project achievements

The objective of incorporating US imaging into our existing PA imaging probe and designing a practical dual mode imaging probe with emerging PA and US functional modality has been achieved in the study. The research was carried out in two phases: the first phase concentrated on the concept development, including evaluation of the existing PA imaging system and the concept of US imaging incorporation. The second phase took in the dual mode imaging system establishment and testing. The ultimate goal of the long-
term study is to provide researchers with an inexpensive and real-time imaging camera with synergistic modality of PA and US that can clearly distinguish the cancerous tissue from the benign ones.

Specifically, the achievements of the study are:

- **implementation of incorporating US imaging into our current PA imaging probe with SNR enhancement**: US imaging incorporation into our existing PA imaging probe for dual modality co-registered images production has been developed and implemented in both custom-designed simulation and experiment, in which an US source, i.e., a PVDF film, that does not interfere with but instead take advantage of the acoustic lens based PA focusing technology has been realized. The SNR of the US imaging counterpart has been improved by driving the film with FM pulses followed by pulse compression processing, the use of which in conjunction with acoustic lens based focusing is a novel and as yet an untested concept before the study. The SNR enhancement as a function of sweep bandwidth of the signal with weighting function considered for the sidelobe structure reduction has been investigated. Given the limits and trade-offs from PVDF film, linear array transducer and the backend electronics, 20 to 30 dB SNR improvement in amplitude has been demonstrated for image quality improvement in US imaging experiments, which is a lot higher than the conventional pulse echo systems.

- **production and testing of PA and US dual mode imaging prototype camera with positive preliminary results**: a transrectal dual mode of PA and US imaging probe which is capable of generating co-registered images suitable for prostate biopsy has been designed and fabricated by the interdisciplinary research team. PA and US imaging experiment on the tissue equivalent phantoms has been performed to validate the performance.
• **toolbox development for PA signal simulation and propagation:** results from optical ray tracing based optical software Zemax have been incorporated into a third-party Matlab software, namely k-Wave toolbox, for feasibility evaluation of the lens based PA imaging, in which Zemax ray tracing results are complemented by combining the characteristics of PA signal generation and propagation. The PA signal propagation from the prostate tissue to the linear sensor array through acoustic lens has been modeled in the software. The imaging systems performance metrics on PSF, off-axis behaviour, depth of field, and the modulation transfer function (MTF) have been evaluated. Combining optical ray-tracing results with k-Wave software to build a PA imaging camera gridded model that incorporates realistic PA signal generation and acoustic wave propagation is a also new contribution to PA imaging community.

1.4 Thesis organization

Building further on the innovation of acoustic lens based focusing technology and previous achievements for the fast PA imaging, the method and implementation to incorporate US imaging with SNR enhancement for a dual mode of PA and US transrectal prostate imaging probe are presented in this thesis. Specifically, Chapter 2 details the mathematics behind the pulse compression technique of FM signals. It is applied to improve the SNR of the US imaging component in systematic experiments, with the use of a PVDF film as an US plane wave generator. A detailed theoretical analysis of the trade-off between the resolution of the US imaging system and the side effects of the sidelobe structure are conducted from a mathematical point of view. Chapter 3 presents the development of a custom-designed acoustic simulation toolbox that combines Zemax and k-Wave open source software for the modeling of PA signal propagation. PSF based quality metrics
of the proposed PA camera system using the finite element wave propagation model is discussed in the chapter. **Chapter 4** gives a brief introduction about our multi-lens system from the perspective of optical design. **Chapter 5** experimentally demonstrates the feasibility of US imaging incorporation using a PVDF film, which is embedded in the prototype camera and designed for the potential dual mode use of PA and US. The investigation on the effect of signal time-frequency products on the image SNR is discussed. **Chapter 6** introduces the design and working principle of PA and US camera, and gives preliminary results of the dual mode imaging. **Chapter 7** summarizes the progress of the project and discusses future directions of the long-term study.
Chapter 2

Modulated excitation signals

2.1 Background

In order to improve the signal-to-noise ratio (SNR) of the backscattered ultrasound (US) wave, pulse compression technique using linear frequency modulated (FM) signal has been used in the past. It is now often used in medical US imaging systems, to increase penetration depth and improve SNR deep inside the tissue [28]. The axial resolution of an US imaging system improves with increasing frequency, but at the same time, due to the frequency dependent attenuation property of the tissue, the corresponding SNR degrades with increasing depth. Improving the SNR by increasing the peak intensity of the input signal is not a solution, as the peak intensity has to stay within the safety limit [29, 30]. Instead of using a short pulse as in conventional pulse echo systems, the pulse compression technique uses a long duration FM signal, also known as the chirp signal as input, distributing the total energy over the long duration input signal, thereby reducing the requirements on the peak intensity. After receiving, the backscattered signal is fed into a matched filter which adjusts relative phases of the frequency components to produce the
compressed pulse with improved SNR [31]. The time duration of the compressed pulse is comparable to that of a conventional short pulse, and therefore, the axial resolution is maintained.

The technology has been back to the focus of medical US community for only few decades. The foremost motivation for this move mainly comes from the fact that current widely used short pulse mechanism can barely meet the rapidly increasing demands on the US image quality. This expectation is mainly toward two aspects, the first of which is to further increase the wave penetration depth, one of the most commonly occurred problems in medical US imaging due to the signal attenuation. The other anticipation of the technology is more from practical reasons: in order to get real-time images of the vibrating structures, the frame rate needs to be high enough to capture every single movement. This is also one of the limiting factors of the current conventional US system. Despite some technical complexities in the hardware implementation, the main reason leading to the difficulty of its application in medical US is due to the complexity of the imaging environment of the tissue organ itself. The frequency dependence of the attenuation of US signals, as previously mentioned, is also a problem that cannot be avoided by any means, all of which dramatically increase the imaging pressure over a high dynamic range.

## 2.2 Medical ultrasound

This section particularly focuses on the underlying mathematics of the use of FM signal in medical US field. The theoretical analysis is provided in detail.

### 2.2.1 System overview

The received echoes from the target can be determined by several factors of the whole imaging system. This radio frequency (RF) A-line signal, denoted by $\psi_r(t)$, can be gen-
generally expressed as [32]:

$$\psi_r (t) = \psi (t) * [T_t (t) * T_r (t)] * [A_t (t) * A_r (t)] * f_{scat} (t) * M (t),$$  \hspace{1cm} (2.1)

where $\psi (t)$ is the generated signal with a window envelop of $w (t)$; $T_t (t)$ and $T_r (t)$ are the impulse response of the transducer in transmit and receive mode, respectively; $A_t (t)$ and $A_r (t)$ are the impulse response of the transmit and receive aperture, respectively; $f_{scat}$ is the scattering effect of the system, and $M (t)$ is the impulse response of the medium.

Particularly in our case, since the US signal is generated by the PVDF film, $T_t (t)$ can be ignored. The aperture effect $A$ and scattering effect $f_{scat}$ are also fixed once the lens is fabricated, consequently both of which are not in the scope of this study. The study exclusively concentrates on the generation of the FM signal $\psi (t)$ and the corresponding filter for signal compression. Specifically, this includes:

- the choice of the time-bandwidth product, \textit{i.e.}, sweep bandwidth and time duration of the generated FM signal $\psi (t)$;
- the choice of the tapering window function $w (t)$;
- the choice of compression filtering method.

### 2.2.2 Basic principles and anticipated profits

#### Time-bandwidth product

One of the key measurements of the FM signal is the time-bandwidth product, which directly affects the image quality after signal compression. The time-bandwidth product, as the name suggests, can be increased either by enlarging the duration of the signal, and/or the sweep bandwidth of the signal. For the conventional short pulse technique, the
only way to make full use of a broader available bandwidth is to shorten its time series, which obviously forms an inefficient solution to the problem as it always keeps the product a constant of an order of unity. Specifically, for a short pulse with an available bandwidth of $B$, the corresponding time duration of the pulse is

$$T = \frac{1}{B}.$$ (2.2)

This indicates the most essential difference between the conventional pulse and modulated pulse, as the latter always possesses a time-bandwidth product greater than one, making it unnecessary to reduce the pulse duration to make full use of the available bandwidth.

**Attenuation effect**

Frequency-dependent signal attenuation is another inevitable problem with medical US, in which attenuation of high-frequency signals is more severe than that of lower-frequency counterparts. In the simplest scenario where this attenuation is neglected, the received echo $\psi_r (t)$ is simply the time-shifted version of the generated signal $\psi (t)$:

$$\psi_r (t) = \psi (t - t_0),$$ (2.3)

where $t_0$ is the time for the signal to travel to the sensor elements.

With attenuation considered, the mean frequency of the modulated signal with a Gaussian envelop, according to Jensen’s discovery [33], yields a linear decrease by

$$f'_0 = f_0 - (\beta B^2 f_0^2) z,$$ (2.4)

where $f_0$ is the center frequency of transmitted signal, $\beta$ is the frequency-dependent at-
Another factor that affects the signal frequency is the Doppler shift. It is not common, but when the imaging involves moving organs, such as the heart, the Doppler shift of the signal will occur. Also known as Doppler effect, it refers to the phenomenon of the change in signal frequency for a target to be imaged moving relative to the transducer array. According to Misaridis [32, 34, 35], the magnitude of Doppler shift is about two orders less than the attenuation-caused frequency downshift, thus can be safely omitted when combined with the use of FM signals.

### 2.2.3 Linear frequency modulation

Table 2.1 lists several key notations which are of great importance for this mathematical investigation of the pulse compression technique using linear FM signals.

#### The signal

The complex expression of a finite duration FM signal can be represented as:

$$
\psi(t) = \tau(t) \cdot \left\{ m(t) \cdot \exp \left\{ j2\pi \left[ \left( f_0 - \frac{B}{2} \right) t + \frac{B}{2T} t^2 \right] \right\} \right\}, \quad 0 < t < T,
$$

where

<table>
<thead>
<tr>
<th>domain</th>
<th>Time signal</th>
<th>Spectrum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linear FM signal</td>
<td>$\psi(t)$</td>
<td>$\Psi(\xi)$</td>
</tr>
<tr>
<td>Matched filter</td>
<td>$\phi(t)$</td>
<td>$\Phi(\eta)$</td>
</tr>
<tr>
<td>Tapering window</td>
<td>$w(t)$</td>
<td>$W(\xi)$</td>
</tr>
<tr>
<td>Mismatched filter</td>
<td>$\varphi(t)$</td>
<td>$W(\xi) \cdot \Psi(\eta)$</td>
</tr>
</tbody>
</table>
where
\[ \tau(t) = \text{rect} \left( \frac{t}{T} \right) \] (2.6)
represents finite duration \( T \) of the signal with an amplitude of \( m(t) \), \( f_0 \) is the starting frequency of the signal, and \( B \) is the total sweep bandwidth. Particularly, \( \frac{B}{T} \) represents the sweep rate of the signal with a frequency range of \([f_0, f_0 + B]\).

**Matched filter**

The matched filter is the autocorrelation of the received signal with its transmitted counterpart. When the effect of frequency shift as indicated in Eq. (2.4) is ignored, \( i.e., \) no signal distortion during propagation, the received signal is simply the “matched” replica of the transmitted signal but with a time delay. Therefore, the impulse response of a matched filter is

\[
h(t) = \psi(-t) = \cos \left[ \left( f_0 - \frac{B}{2} \right) t - \frac{B}{2T} t^2 \right], \quad 0 < t < T. \] (2.7)

The output signal of the filter is

\[
\phi(t) = \int_{-\infty}^{\infty} \psi(\delta) \psi(t - \delta) d\delta. \] (2.8)

The real part of Eq. (2.5) gives

\[
\text{Re} \left[ \psi(t) \right] = \cos \left[ \left( f_0 - \frac{B}{2} \right) t + \frac{B}{2T} t^2 \right], \quad 0 < t < T. \] (2.9)

Substituting Eq. (2.9) to Eq. (2.8), the compressed signal can be generally represented
as:

$$\phi(t) = \int_{0}^{T} \cos \left[ (f_0 - B) \delta + \frac{B}{2T} \delta^2 \right] \cos \left[ (f_0 - B)(t - \delta) - \frac{B}{2T}(t - \delta)^2 \right] d\delta,$$

(2.10)

where the high frequency term \( (f_0 - B) \) in the equation can be safely omitted for practical reasons. By trigonometric expansion, a simplified version of a matched filter response can be acquired:

$$\phi(t) = T \cdot \sin \left[ \pi D_\frac{f}{T} \left(1 - \frac{|t|}{T}\right) \right] \cdot e^{j2\pi f_0 t},$$

(2.11)

where

$$D = TB$$

(2.12)

represents the time-bandwidth product of the signal.

There are two major discoveries from Eq. (2.11): first of all, the corresponding signal after compression is roughly with a shape of a sinc function. The significance of it is that it introduces the resulting sidelobe from the mathematical point of view, the side effect of which unquestionably forms the major problem in the application of this technology in the field of medical US. It is worth noting that this sidelobe is caused by the inherent characteristics of the technique that cannot be completely avoided under any circumstances. This, on the other hand, also indicates that the problem will never occur in the conventional short pulse technique, for the simple reason that post-autocorrelation is not involved in the mechanism. Misaridis et al. [32] found that the magnitude of the strongest sidelobes of the first pair is about −13.2 dB below that of the main lobe, which dramatically decreases the resolution of the image.

Further investigation on this issue gives the second insight of the compressed signal,
the first pair zeros of which is of a distance of

\[ d = \frac{T}{2} \left(1 - \sqrt{1 - \frac{4}{BT}}\right) \approx \frac{T}{2} \left[1 - \left(1 - \frac{2}{BT}\right)^2\right] = \frac{1}{B} \]  (2.13)

from the center of the main lobe. This distance, by definition, is the axial resolution of the system. Compared it to that of the image obtained by a short pulse excitation given in Eq. (2.2), two mechanisms approximately give the same axial resolution when the same bandwidth of the signal is used. The peak of every sidelobe is positioned \( \frac{1}{B} \) apart from each other with a fall-off rate at roughly 4 dB per interval.

**Fresnel integrals**

The sidelobe effect can be confirmed from another aspect by the spectrum of the finite-duration FM signal, from which the introduced spectrum ripples can be extracted from that of the infinite one, and consequently allows us to directly study the impact of mutations of the time domain signal on its spectrum.

Specifically, for a finite FM signal with a unit amplitude of \( m(t) = 1 \), the signal can be represented as:

\[ \psi(t) = \exp \left[j2\pi \left(f_0t + \frac{B}{2T}t^2\right)\right], \quad -\frac{T}{2} < t < \frac{T}{2}. \]  (2.14)
Its spectrum can be calculated as:

\[
\Psi (\xi) = \mathcal{F} [\psi (t)] = \int_{-T/2}^{T/2} \exp \left\{ j2\pi \left( f_0 t + \frac{B}{2T} t^2 \right) \right\} \cdot e^{-j2\pi ft} dt
\]

(2.15)

\[
= \int_{-T/2}^{T/2} \exp \left\{ j2\pi \left( (f_0 - f) t + \frac{B}{2T} t^2 \right) \right\} dt
\]

(2.16)

\[
= \exp \left\{ -j \frac{\pi}{(B/T)} (f - f_0)^2 \right\} \cdot \int_{-T/2}^{T/2} \exp \left\{ j \frac{\pi}{2} \cdot \frac{2B}{T} \left( t - \frac{f - f_0}{k} \right)^2 \right\} dt
\]

(2.17)

\[
= \frac{1}{\sqrt{2k}} \exp \left\{ -j \frac{\pi}{(B/T)} (f - f_0)^2 \right\} \left[ \int_{-Y_1}^{Y_2} \cos \left( \frac{\pi}{2} y^2 \right) dy + j \int_{-Y_1}^{Y_2} \sin \left( \frac{\pi}{2} y^2 \right) dy \right].
\]

(2.18)

where the substitution

\[
y = \sqrt{\frac{2B}{T}} \left( t - \frac{f - f_0}{k} \right),
\]

(2.19)

the lower limit

\[
Y_1 = \sqrt{2k} \left( \frac{T}{2} + \frac{f - f_0}{k} \right) = \sqrt{\frac{D}{2}} \left( 1 + 2 \frac{f - f_0}{B} \right),
\]

(2.20)

and the upper limit

\[
Y_2 = \sqrt{2k} \left( \frac{T}{2} - \frac{f - f_0}{k} \right) = \sqrt{\frac{D}{2}} \left( 1 - 2 \frac{f - f_0}{B} \right).
\]

(2.21)

The Fresnel integrals are introduced as:

\[
R (z) = \int_{0}^{z} \cos \left( \frac{\pi}{2} y^2 \right) dy, \quad I (z) = \int_{0}^{z} \sin \left( \frac{\pi}{2} y^2 \right) dy,
\]

(2.22)
from which the spectrum can re-written as:

\[
\Psi (\xi) = \frac{1}{\sqrt{2k}} \exp \left[ -\frac{j \pi}{(B/z)} (f - f_0)^2 \right] \cdot \{ R(Y_1) + R(Y_2) + j [ I(Y_1) + I(Y_2)] \}. \tag{2.23}
\]

The sidelobe effect of the modulated pulse can be observed very directly from the oscillating curves of the Fresnel integrals \( R(z) \) and \( I(z) \) as shown in Fig. 2.1(a), the values of which as a function of the upper limit \( z \) are indicated in the figure in solid blue and dotted red, respectively. The 2.1(b) counterpart shows the whole spectrum of the FM signal, \( \Psi (\xi) \) of Eq. (2.23), in terms of the relative frequency \( \xi \), in which the higher the time-bandwidth product \( D \), the closer the spectrum shape is to a rectangle, but more ripples will also be involved due to the steep signal boundaries in the time domain. Therefore, the goal of the tapering window \( w(t) \) is to maximally eliminate the sidelobe effects in the sinc-shape compressed signal, in order to further improve the image resolution, but this is at the cost of reducing the width of main lobe.

**The mismatched filter**

In addition to the previously described matched filters, mismatching filters are also suitable for signal compression. Based on the symmetry property of the signal, the tapering window function \( w(t) \) can be applied either in the time domain or in the frequency domain for the mismatched filter compression. For these two cases, the corresponding filter response can be calculated either by convolution or the inverse Fourier transform.

For the time domain tapering, the signal after mismatched filter compressing can be expressed as:

\[
\varphi(t) = \psi(t) \ast [\phi(t) \cdot w(t)], \tag{2.24}
\]

where \( \ast \) represents the convolution operation.
CHAPTER 2. MODULATED EXCITATION SIGNALS

(a) The Fresnel integral specified in Eq. (2.22)

(b) Signal spectrum as calculated in Eq. (2.23)

Figure 2.1: The Fresnel integrals and the spectrum of the frequency modulated signal. It can be observed from 2.1(a) that the Fresnel integrals, both real (in solid blue) and imaginary (in dotted red) parts, have a limit of 0.5. From the corresponding 2.1(b) spectra of linear FM signals with different time-bandwidth products, a more rectangular spectrum is shaped as this product goes up, while more Fresnel ripples are also involved.

For the frequency domain tapering, since the matched filter has a frequency response of

\[ \Phi (\eta) = F [\phi (t)] = F [\psi (-t)] = \Psi (-\xi), \]

(2.25)

the mismatched filter response of linear FM signal can be calculated by the inverse Fourier transform,

\[ \varphi (t) = \int_{0}^{\infty} \Psi (\xi) \cdot [R (\eta) \cdot W (\xi)] \cdot e^{j2\pi ft} dt \]

(2.26)

\[ = \int_{0}^{\infty} \Psi (\xi) \cdot [\Psi (-\xi) \cdot W (\xi)] \cdot e^{j2\pi ft} dt \]

(2.27)

\[ = \int_{0}^{\infty} |\Psi (\xi)|^2 \cdot W (\xi) \cdot e^{j2\pi ft} dt, \]

(2.28)
where $W(\xi)$ denotes the spectrum of the tapering window function.

## 2.3 Literature review

The study of pulse compression technique in medical US started few decades ago when Takeuchi [36] first investigated the time-bandwidth limitations of modulated signals in US imaging, but it was not until 1990s that this technique re-caught the attention of the field when Rao [37] made a breakthrough. Popular modulated signals among researcher’s interest include but are not limited to: pseudo-chirp signals [38, 39], m-sequences [40, 41], and Golay sequences [42, 43]. There is a also trend to combine several coding methods together [44]. Not much research has been done previously regarding SNR enhancement of the FM signal. Chiao and Hao [45] have investigated the trade-offs between penetration and resolution in US imaging with different code types, but no suggestion is given on the SNR improvements. Behar and Adam [46] have studied the excitation and compression scheme by exploring the best optimization parameters over imaging system with coded excitation. However, their study does not involve any acoustic lens systems which may make the result invalid for our research. Oelze [47] has come up with a new novel pulse compress technique, namely resolution enhancement compression, but it’s not real-time, and therefore not practical to our case.
Chapter 3

Singlet lens system

In this chapter, a novel imaging technology that can be used to acquire three-dimensional (3D) photoacoustic (PA) images that are reconstructed by focusing the PA signals in real time is discussed. It is based on an innovative concept of using an acoustic lens to simultaneously focus PA signals originating from all absorbers with a small volume, typically less than 5 cubic centimeters (cm$^3$), similar but not identical to optical focusing. The heart of the system is the acoustic lens. Therefore, a new methodology is outlined in this chapter which consists of initial lens design and optimization on an optical lens design software Zemax, as well as various ultrasound (US) based quality metrics evaluation using a finite element wave simulation modelling technique. In particular, the chapter first explains the concept and advantages of the acoustic lens based system, and then describes the lens design procedure using Zemax. It’s followed by the introduction of a finite element simulation model that is used to generate the point spread function (PSF) and the evaluation of the PSF based quality metrics of the lens. The system setup details, experimental results, and examples of possible applications are discussed at the end.
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3.1 Singlet acoustic lens design

3.1.1 Previous studies

PA imaging is an emerging, noninvasive and functional imaging modality. Many researchers are currently exploring its potential for cancer diagnosis. For PA imaging, one employs short laser light pulses in the near-infrared (NIR) to excite molecules in the tissue, producing localized heating and pressure increase that begins to propagate as US waves, also referred to as PA signal [48]. A valuable feature of PA imaging is its ability to discriminate among tissue constituents on the basis of optical absorption properties [49], allowing for PA imaging spectroscopy, which can detect biological function [48, 50]. PA imaging can map the concentration of deoxy and oxy-hemoglobin, as well as water and lipid in the tissue [48, 50, 51]. Research based evidence pointing towards its usefulness in cancer diagnosis and disease management is growing day by day [48, 50]. Many believe that PA imaging is poised to become the next major clinical imaging modality within a decade.

For the imaging purpose, PA signals originating in a 3D tissue volume are detected by one or more US sensor elements that are strategically placed at the volume surface. Typically, computer based image reconstruction algorithms are employed to focus the PA signals and generate B-scan, C-scan or 3D PA images [52, 53]. Such systems are expensive because they require dedicated hardware and software. The cost can increase exponentially as the number of sensor elements increases. In addition, image reconstruction is digital, requiring careful spatial and temporal sampling of the sensor data to avoid aliasing.

Many possible medical applications of multispectral PA imaging are being explored by researchers. Fast data acquisition and robust image reconstructions using photoacoustic tomography (PAT) methods are required for any PA imaging device. Currently available devices are very expensive and assembling a PAT system requires multidisciplinary exper-
tise. To the best of our knowledge, currently there are no commercial US scanners available that employ large area two-dimensional (2D) sensor arrays specifically designed for real-time C-scan imaging. Walker et al. developed a 2D US piezo electric transducer (PZT) array for PA imaging of vasculature at shallow depths [54, 55]. Their system performs synthetic aperture focusing (SAF) on the acquired B-scan image allowing reconstruction of a C-scan image. Schneider et al. developed a 2D polyvinylidene fluoride (PVDF) sensor array for US biometric applications [56]. C-scan imaging has been used in ophthalmology [57, 58, 59] and in photoacoustic microscopy [60], where C-scans are generated by extended scan time from the 3D US data rather than in real time.

### 3.1.2 Acoustic lens based focusing

As a cost effective alternative, a one-dimensional (1D) linear array of US transducers placed in the image plane with back-end electronics to acquire PA time signal from a larger range of axial distance, typically 2 to 4 centimeters (cm), could be used to generate focused B-scan image slices in real time. By scanning the linear array in the image plane, both C-scan and volumetric data set can be generated, though it will be at the cost of reduced image frame rate. There are many advantages to adopting this technology. The lens is performing the focusing task that would otherwise require billions of computer instructions per second on dedicated hardware and software, including US diffraction computed tomography [61], synthetic aperture focusing [62], and beamforming in receive mode [63]. The fabrication of acoustic lens using 3D printing technology significantly reduces the fabrication costs of the PA system and substitutes the required dedicated hardware and software. In addition, the lens uses zero electrical power and focusing happens in real time. Dispersion in typical acoustic lens materials is generally negligible at 1 megahertz (MHz) to 10 MHz frequencies. Therefore, a single lens is able to focus PA signals effectively over a wide range of frequencies, unlike PAT where different spatial and
temporal sampling design choices may have to be adopted based on the frequency content of the PA signal. Furthermore, a treasure of knowledge from optical lens design industry, such as a multi-lens system for correcting aberrations and zoom lens systems [64], can be utilized here with ease.

The technology that uses an acoustic lens to focus the PA signals simultaneously from multitude of absorbers within a given volume is proposed to be used in a PA imaging camera. The concept and schematics of acoustic lens based imaging system have been introduced in Sect. 1.2. Fig. 3.1 below more intuitively explains the acoustic lens based formation mechanism of PA image.

![Figure 3.1: Schematics of an acoustic lens based PA imaging camera. The system is based on 4f geometry, where both target and transducer array are set 2f from the lens. The stepper motor which controls the location of the transducer array is used for a 2D raster scan.](image)

Simply put, the tissue volume containing multiple random-distributed NIR absorbers is assumed to be placed on the left side of the acoustic lens at the 2f object plane. The entire intervening medium is water with an US propagation velocity of ~ 1500 meter/second.
(m/s). Subsequent to a short pulse of NIR laser exposure delivered to the tissue volume, the photoacoustically generated US waves, i.e., the PA signals, begin to propagate isotropically in all directions, with a small fraction within the lens field of view, as shown in the coloured conical area of Fig. 3.1 moving towards and getting focused. Similar to an optical imaging system, the appropriately designed single element acoustic lens accomplishes the focusing of these waves onto the right side of the lens to the image plane. According to the lens formula previously mentioned in Eq. (1.1), the PA signals originating from absorbers located on the focal plane at a distance $2f$ to the left of the lens should optimally focus at the image plane located at an equal distance to the right of the lens. This, according to geometric optics, is referred to as 4$f$ setup which gives an image magnification of $-1$. This forms the basic principle and the core of the acoustic lens based imaging idea.

Fig. 3.2 further illustrates the concept on which the design and operation of PA imaging system is based. The time for the PA signal to travel from focal plane to image plane is finite, in the range of microseconds ($\mu$s). Therefore, by placing an array of US sensors in the image plane and time gating the received PA signal at each sensor, coronal or C-scan focused image of absorbers can be generated in the focal plane. A given lens, based on its design has a certain depth of field. The implication of this is that a slightly defocused PA image of absorbers from a certain out of focus plane can also be captured by the same sensor array with a different time gate. Therefore, potentially 3D PA image data from a small 3D volume can be acquired in real time and displayed as either series of C-scan or B-scan images [48]. The variation of focusing effect within this volume can be characterized with the wave simulation technique that will be described later in this chapter.

3.1.3 Acoustic lens design and characterization

The initial lens design and optimization were performed using the optical design software, Zemax [27]. The Lens Maker’s Formula, as given below in Eq. (3.1) [19], plays a central
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Figure 3.2: Schematics of an acoustic lens based PA imaging camera, where red, green and blue point absorbers stand for on-axis, off-axis and out-of-focus cases, respectively.

In the equation, $f$ represents the focal length of the system, $n$ is the refractive index of the lens material, and $R_1$ and $R_2$ are the radii of curvature on both sides of the lens. The lens material is chosen to be a photopolymer, typically used for 3D printing with a refractive index of 0.58. Unlike the conventional converging lens whose index of refraction is usually greater than 1, this characteristic of the photopolymer causes the surface of the designed focusing lens to be concave. Taking into account the actual clinical needs and limitations, the bi-concave lens is designed of a diameter of 32 millimeters (mm) with radii of surface curvature of 33.5 mm on both sides. The working focal length $f$ under this configuration is 39.8 mm, as calculated from using thin lens formula Eq. (3.1) [65]. Again, the object plane and image plane are both set at $2f$ distance from the lens. Fig. 3.3 visually shows the shape of the lens as well as the ray tracing diagrams for the points located on axis, 5.0 mm off axis and 10 mm off axis, respectively, where they are correspondingly indicated.

\[
\frac{1}{f} = (n - 1) \left( \frac{1}{R_1} - \frac{1}{R_2} \right). \tag{3.1}
\]
in blue, green and red. The requirements for the acoustic impedance of lens material and the choice of its refractive index are elaborated in the next Sect. 3.4, both of which have been carefully thought over for the consideration of the actual working environment of the imaging probe.

Figure 3.3: Ray tracing diagram of the designed acoustic system from Zemax. The lens is with a diameter of 32 mm and radii of curvature of ±33.5 mm on two sides (based on the sign convention). The working focal length of the lens is 39.8 mm. The blue, green and red ray diagram correspond to the on-axis case, 5 mm off-axis and 10 mm off-axis cases, respectively. Note: the diagram is not drawn to scale.

Also worth mentioning here through this 4f configuration is the presentation of the data. The concept of B-scan and C-scan image is introduced here so that the reader can have a distinction between different types of US images presented in the following simulation and experiment. More details will be covered later in Sect. 5.2.1. Simply say, if the paraxial approximation is assumed, i.e., if the off-axis distance is presumed to be small compared to 2f, PA signals originating from any point in the focal plane will arrive at the image plane simultaneously, and they will all be focused at their conjugate locations in the image plane simultaneously by the same lens [66]. Correspondingly, by time gating the detected signals in the image plane and reading out the 2D pattern of detected values, the 2D mapping of the absorber distribution in the focal plane can be potentially generated. This is referred to as the C-scan PA image of the focal plane, which is also the way in
which our images are presented in experiments. In simulation, however, considering the computational burden, 3D simulation cannot be performed for our PA experiments. For this reason, all the simulation images obtained in this chapter are B-scans, which present the cross-sectional view of the target with one axis reflecting the depth information.

The PSF and the modulation transfer function (MTF) are associated with lens evaluation, which in part, are capable of quantifying the resolution of the imaging system. The degradation of the imaging of off-axis points with Fig. 3.3 setup is quantified in this way through determining the PSF and MTF of the system that are shown in Fig. 3.4, where 3.4(a) shows the predicted spot diagram collected at $2f$ image plane with the point source placed at different off-axis locations, while 3.4(b) shows its counterpart of MTF. The wavelength of US in water at 5 MHz is used for MTF calculation, corresponding to the center frequency of the intended sensor array to be used later in the system fabrication. The limited frequency reception range of the transducer is the key reason why the MTF plays such a crucial role in the lens design and subsequent system experiments. The following Sect. 3.3.2 will provide an in-depth analysis of simulation results based on system frequency response.

In the PSF and MTF graphs shown in Fig. 3.4 below, it is worth pointing out that the black circle shown in 3.4(a) indicates the system diffraction-limited spot size which is of a size of 936 micrometers ($\mu$m) in diameter. It is the theoretical limit of the imaging due to diffraction phenomenon. It is not difficult to find that the system imaging capability of on-axis point, as shown by the blue dot in 3.4(a), is very close to its theoretical limit, but the situation is clearly not the case for the off-axis points. The off-axis points, as shown in green for 5 mm off-axis and red for 10 mm off-axis source, produce MTFs that increasingly get worse, both in the sagittal (in dotted line) and transverse (in solid line) direction. This degradation is quantified through defining limiting spatial frequencies by intercepting a threshold at 0.2 on the MTF curves. The acquired spatial frequencies in this way are 0.88
cycles/mm, 0.74 cycles/mm and 0.37 cycles/mm, for on-axis, 5 mm and 10 mm off-axis points, respectively. Correspondingly, the predicted resolution degrades from 0.95 mm to 1.69 mm and 3.24 mm on the spot size. That is to say, from Zemax’s prediction of system imaging capability, the image of the 10 mm off-axis point source would be 3.4 times worse than that of its on-axis counterpart, where the further the point is away from the optical axis, the worse its image would be at the image plane. This degradation cannot be corrected within the framework of the singlet spherical lens system which prompted us to further improve the system performance by designing a more complex multi-lens imaging system, which will be briefly introduced in the next Chap. 4. Its main purpose is to improve the system’s imaging ability for the off-axis points by introducing another lens for field curvature correction.

![Spot diagram](image1.png) ![Modulated transfer function (MTF)](image2.png)

**Figure 3.4:** The spot diagram and MTF of the designed singlet lens system. The diffraction-limited spot size of the system is with a diameter of 0.936 mm, as shown in black circle in 3.4(a). The on-axis, 5 mm off-axis, and 10 mm off-axis point gives a PSF of 0.95 mm, 1.69 mm, and 3.24 mm in diameter, respectively. From the corresponding MTF diagram given in 3.4(b), the degradation of system performance for off-axis points (green for the source 5 mm off-axis and red for 10.0 mm off-axis point) can be clearly observed, in both the sagittal (in dotted line) and transverse (in solid line) directions.
3.2 Computer modeling of the acoustic lens

While the ray tracing based acoustic lens design of Zemax provides a preliminary estimate of lens performance, it still has two obvious flaws, the first of which is its solely ray-tracing-diagram based PSF prediction, making it impossible to indicate the intensity of PSF as in many other cases can be specified by the pixel value. Also, although the frequency of US signal has already been considered, it must also be aware that the wavelength range typically considered for the Zemax lens design is from 400 nm to 700 nm, which is within the range of human perception. This is another factor that cannot be ignored, since as a commercial lens design software, Zemax does not take into account any of the PA signal generation and propagation mechanisms, let alone the time-frequency range of the PA signal and medium attenuation. For this reason, a simulation technique that utilizes wave-theoretic formulation of propagating the PA signal through the lens has been developed. A third party Matlab k-Wave toolbox was used for this purpose for developing a simulation technique that is capable of simulating the generation and propagation of PA waves through the designed singlet acoustic lens based imaging system. The toolbox, as the name suggests, applies $k$-space pseudo-spectral method for solving the first order partial differential equations of linear acoustic [67], which is capable of PA wave field simulation in both homogeneous and heterogeneous media, in one, two and three dimension. The Zemax ray optics based results are proceeded here by further tested on full wave theory based simulations for the above reasons. Considering the needs of the study and underlying computation burden, the simulation is limited to a 2D environment. As previously described, the image obtained in the simulation in such a way is the B-scan image, with one direction reflecting the depth information.
3.2.1 Theoretical basis

The model calculates the pressure distribution by a transient laser pulse on a 2D plane \( p(x, y, t) \), or in 3D space \( p(x, y, z, t) \) by the inhomogeneous wave equation [68]:

\[
\frac{\partial^2 p(\vec{x}, t)}{\partial t^2} - c^2 \Delta p(\vec{x}, t) = \Gamma \frac{\partial}{\partial t} p_0(\vec{x}) \delta(t),
\]

(3.2)

where \( c \) is the speed of sound, \( \Gamma \) is the Grueneisen coefficient serving as the conversion factor, and \( S \) is the amount of energy released by the tissue under laser exposure. \( p_0(\vec{x}) \) denotes the initial distribution of pressure wave which depends on the light distribution resulting from the laser pulse and corresponding absorption coefficient within the tissue.

The solution of \( p(\vec{x}, t) \) to Eq. (3.2) lies in the forward problem of wave propagation which can be calculated through the Green’s function,

\[
p(\vec{x}, t) = \frac{1}{4\pi c} \cdot \frac{\partial}{\partial t} \left( \int_{|\vec{x} - \vec{x}'| = ct} \frac{p_0(\vec{x}')}{|\vec{x} - \vec{x}'|} d\sigma \right).
\]

(3.3)

The pressure wave at time \( t \) after the transit laser pulse absorption can then be calculated by integrating the surface at the sphere of the observation point of radius \( |\vec{x} - \vec{x}'| = ct \).

Correspondingly, in the \( k \) space, \( p(\vec{x}, t) \) can be calculated by

\[
p(\vec{x}, t) = \frac{1}{(2\pi)^3} \int \int \int [P(\vec{k}) \cdot \cos(\omega t)] \cdot e^{i\vec{k} \cdot \vec{x}} d^3k,
\]

(3.4)

where \( P(\vec{k}) \) represents the Fourier transformation of the initial distribution of pressure wave:

\[
P(\vec{k}) = \int \int \int p_0(\vec{x}) \cdot e^{-i\vec{k} \cdot \vec{x}} d^3\vec{x}.
\]

(3.5)

\( p(\vec{x}, t) \), through Eq. (3.4), can be briefly described in terms of the Fourier transform of the initial pressure wave of the PA signal \( P(\vec{k}) \) in the plane (or space), in which it is
located. By incorporating the propagator $\cos(\omega t)$, it is then subjected to an inverse Fourier transform for the distribution calculation of the pressure wave on the desired plane (or space) at a specific time $t$. The biggest advantage of the algorithm is its computational efficiency. Since it relies on the fast Fourier transform, it saves at least two orders of magnitude computation time than the time domain counterparts.

### 3.2.2 Simulation model

In order to best correspond our 2D simulation to the imaging probe used in the experiment which consists of a cylindrical body with the acoustic lens embedded inside, the entire model was sampled by a $640 \times 4096$ finite grid, with each one covering a $0.05$ mm by $0.05$ mm area for the finite element wave propagation. The choice of the grid size is based on achieving a compromise between avoiding spatio-temporal aliasing and excessive run time. The maximum supported frequency of the grid with this configuration can go up to 15 MHz, which is significantly higher than the US wave frequencies intended to use in simulation. For PA signal, it is well known that the dominant frequency content of photoacoustically generated signal upon exposure to nanosecond pulse of laser light depends largely on the size of the absorber. Therefore, the spectrum of the simulated PA signal should match its actual counterpart in experiment which is generally from 0.5 MHz up to 9 MHz. It is also established [69], and we have confirmed independently that the k-Wave toolbox [51, 67] is capable of accurately generating correct PA time signals whose frequency spectrum corresponds to the appropriate source size. The source size in the model was adjusted correspondingly before simulation runs by grouping different numbers of grids together, which were then assigned as source in the toolbox in order to match a reasonable spectral range of the signal [70]. Another aspect that is closely related to this signal spectrum is the filtering effect of the sensor, whose response is centered at 5 MHz with a $-6$ dB bandwidth of 2.745 MHz (54.9%). In view of these two considerations,
the source size is determined to be 0.1 mm in diameter, i.e., a 2 pixels by 2 pixels size, through the observation of the signal spectrum in a series of simulation of different absorber sizes. Fig. 3.5(a) shows the corresponding generated time PA signal, and 3.5(b) shows the generated PA signal amplitude spectrum (in black), as well as the spectrum of the signal received at the image plane before (in blue) and that after the signal is filtered through the sensor frequency response (in red). As can be seen, the duration of the generated PA signal is about 1 µs with low frequencies as its dominant frequency. The simulation with this architecture can effectively prevent potential aliasing problems of the simulated PA signal that may occur during the propagation. It is also noteworthy that in order to eliminate the adverse effect of the finite sensor size on the image resolution in the experiment, the point detector of 0.05 mm by 0.05 mm size, 10 times smaller than its experimental counterpart was used in the simulation. This allows us to exclude restrictions on the system hardware to more accurately evaluate the designed acoustic lens in the following series of simulations.

The schematics of simulation, including the 2D model representation of the camera design as well as snapshots of the propagating PA signal wavefront at different time stages after the laser excitation are clearly shown below in Fig. 3.6.

The location of the point source and the sensor strictly follows the previously described 4f structure, and is set at axial pixel number 452 and 3645, respectively, with the lens placed in the middle of the grid at pixel number 2048. The properties of the lens described in Sect. 3.1.3 are also introduced into the simulation in the same manner, including its curvature and size of the surface. The designed bi-concave lens is of a diameter of 640 pixels (32 mm) and radii of curvature 670 pixels (33.5 mm), with a distance between its back surface to 2f image plane of 1592 pixels (79.6 mm). The lens pixels, as shown in black in Fig. 3.6, are assigned with a sound velocity of 2590 m/s and a material density of 884.17 kg/m$^3$, same as the photopolymer material used for lens production. The remaining pixels
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(a) Time series PA signal

(b) Amplitude spectrum

Figure 3.5: (a) The generated time PA signal with a target diameter of 0.1 mm. (b) The amplitude spectrum of the generated PA signal (in black), the recorded signal without (in blue) and with transducer filtering (in red). The transducer has a response centered at 5 MHz with a $-6$ dB bandwidth of 2.745 MHz (54.9%).

Figure 3.6: Visualization of simulated PA signal propagation using third party Matlab k-Wave toolbox. The system model is set up with a 4$f$ imaging configuration, where the PA source, acoustic lens and sensor array are positioned at 2$f$ object plane, center of the grid and 2$f$ image plane, respectively.

marked with white are assigned values pertaining to water with a 1500 m/s velocity and a 1000 kg/m$^3$ density. The medium is presumed to be attenuation-free, and thus an 0 dB/cm/MHz attenuation is used. A 20 grid points thick perfectly matched layer to absorb the waves and prevent boundary reflections is applied to the edges of the model. It is set
to prevent the wavefront leaving one side of the domain to reappear from the opposite side. In this way, the entire simulation model, which is based on the actual imaging probe, is established.

### 3.3 Simulation results

There are several factors that are especially valued in the simulation experiment, the first of which is the best imaging plane. Considering the innovative use of the converging acoustic lens on PA signal focusing, the best imaging plane must be first investigated for the consistency check with the theoretical $2f$. Closely related to this is the system’s focusing ability on a range of signal frequencies, mainly due to the consideration of system versatility so that the performance is not subject to the sensor restriction. The imaging of off-axis points is another key factor. In view of Zemax’s imaging prediction of the singlet lens system and previous discussion of MTF in Sect. 3.1.3, system’s imaging capability of off-axis points would be significantly reduced due to the spherical aberration of lens. This degradation can also be quantified accurately by analysing the PSF obtained through simulation of entire propagation of PA signal. Last but not least, the depth of field of the system, which directly determines the effective 3D imaging region of the system. All of these are discussed in detail in this section.

#### 3.3.1 Best focal plane

In order to compare the performance prediction between ray tracing and wave-theoretic formulation, several simulation experiments were performed using the 2D model described above. The first set of experiments investigated the best focal plane of the system. The PA signal source was fixed on axis at the original $2f$ to the left of the lens. The sensor array, which consisted of a line of point detectors, was placed at 17 different distances around
the theoretical 2\(f\) imaging plane, varied from 2\(f - 2\) cm, \textit{i.e.}, 2 cm before 2\(f\), to 2\(f + 2\) cm, 2 cm after 2\(f\), with a step size of 0.25 cm. One full simulation experiment was performed for each location that consisted of the generation of PA signal, signal propagation through the lens to the sensor array, and envelop extraction of A-line signals received at each point sensor location [71]. The final B-scan image, which represents the system PSF pertaining to that image plane location, is displayed through the adjacent envelope detected A-line signal. Fig. 3.7 below shows 12 of these PSFs with their corresponding image plane location indicated at subcaption. Fig. 3.8 is its counterpart which represents the PSFs when the received sensor signal was filtered by the transducer bandwidth before the envelop extraction.

To quantitatively analyze the PSF results, the 1D profile through the maximum of each PSF in the lateral direction, \textit{i.e.}, perpendicular to lens axis, is taken, and its full width at half maximum (FWHM) is determined. The maximum signal values (in red) and the FWHM (in blue) of all the PSFs are plotted in Fig. 3.9 as a function of image distance relative to 2\(f\) distance. Based on the criteria that best focus is where the FWHM of the PSF is the smallest and the maximum PSF value is the highest, the best focal plane is determined to be not at 2\(f\) but at 0.25 cm before. At the best focus, the FWHM value is just under 1 mm, which represents the lateral resolution in the focal plane of this imaging system. Maximum PSF values are relative, as such at the best focus value is almost 3 fold higher, \textit{i.e.}, 1.65 versus 0.5, than that found just outside the focal zone. In particular, in order to compare the simulation results with those from Zemax described earlier in Sect. 3.1.3 for consistency check, the magnitude of the Fourier transform of 1D lateral profile of the PSF at best focus is calculated for the lens MTF. As shown in Fig. 3.10(a), it can be compared to the MTF obtained from Zemax which is shown in Fig. 3.10(b). The predicted diameter of the spot size is 0.954 mm from simulation which qualitatively is slightly worse than that from Zemax of 0.949 mm for on-axis source, but they still can be
Figure 3.7: PSFs collected at different positions without transducer filtering. Specifically, (f) corresponds to the PSF collected at the theoretical $2f$ image plane. As shown in (e), the best focal plane was found at 0.25 cm before the $2f$ with a detected lateral FWHM of 0.954 mm.
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Figure 3.8: PSFs collected at different positions with transducer effect. The transducer has a response centered at 5 MHz with a $-6$ dB bandwidth of 2.745 MHz. In particular, (f) corresponds to the PSF collected at $2f$ image plane. The best focal plane was found at 0.25 cm before the $2f$, as shown in (e).
Figure 3.9: Simulation based investigation on the best focal plane, where blue and red curve are the FWHM and the maximum signal value of each PSF collected at different position around the $2f$ image plane. The best focal plane, according to the result, occurs at 0.25 cm before the $2f$ image plane. The FWHM values within this region keep at the lowest level ($\sim 1$ mm) while the maximum pixel value remains the strongest ($\sim 1.65$).

considered as consistent with each other.

### 3.3.2 Frequency components

The variation of refractive index of acoustic lens material with PA signal frequency in low MHz range is negligible. For this reason, unlike optics, one does not need to worry about chromatic aberrations. The generated PA signal in the model has significant frequency content in the 1 MHz to 9 MHz range, which follows up with our initial requirements of the signal spectrum. Therefore, by bandpass filtering the focused A-line signals acquired at the best focal plane, the lens focusing characteristic can be generated as a function of center filtering frequency which further reveals the lens focusing ability over a wide bandwidth of US. Nine different bandpass filters were applied to the A-line data acquired
at the best focal point, each of which had the same \(-6\) dB bandwidth of 2.745 MHz (54.9%), but with its peak response varied from 1 MHz to 9 MHz, in steps of 1 MHz. The panel of 9 different PSFs with normalization are shown in Fig. 3.11, where the first panel corresponds to the wideband PSF without any filtering. The variation of lateral FWHM (in solid blue), axial FWHM (in dotted blue), and the peak amplitude value (in red) as a function of center frequency are shown in Fig. 3.12.

As expected, the variation of the peak value is dominated by the transducer frequency response. According to the theory of diffraction limited system, the lateral FWHM should vary linearly with wavelength or inversely with frequency \([72]\). And qualitatively, that is what can be observed from Fig. 3.11, with the FWHM going from 4.27 mm at 1 MHz to 0.55 mm at 9 MHz. Particularly, Fig. 3.13(a) shows lateral PSFs with different transducer filtering centered at 1 MHz (in blue), 3 MHz (in green), 5 MHz (in red), 7 MHz (in cyan)
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Figure 3.11: Frequency components of the best PSF acquired by the designed system. From left to right: bandpass filtered PSF with center frequency of 1 MHz to 9 MHz, respectively. The filters are with a 6 dB bandwidth of 2.745 MHz (54.9%).
Figure 3.12: Relationship of the FWHM along lateral (solid blue line) and axial (dotted blue line) directions as well as the peak PA signal value (solid red line) of PSF, versus the center frequency of the signal. 5 MHz bandpass filtering, which corresponds to the filtering response of the transducer applied in experiment gives the best PSF, in terms of the FWHM along the axial direction (1.258 mm) and PSF peak signal values (0.869). The FWHM along the lateral direction constantly decreases as the center frequency of the filter goes up.

and 9 MHz (in purple), while 3.13(b) shows the corresponding MTFs. The axial FWHM is theoretically expected to depend on the signal frequency bandwidth which was held constant at 0.5 MHz. While it bottoms out at 5 MHz transducer center frequency, it does show some increase above and below it. This is one of the reasons why a sensor with a center frequency of 5 MHz was chosen for experiment.

### 3.3.3 Off-axis performance

Five simulations were done to explore the off-axis performance of the system. Through the prediction of Zemax, the lens imaging capability of the off-axis points would be greatly degraded. However, the simulations based on PA wave equation show different results. Fig. 3.14 shows the simulation based measurement of the PSFs for 5 different PA sources at
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Figure 3.13: (a) Normalized signal value along the lateral direction of the center of the pattern with different bandpass filters; (b) Calculated MTFs

(a) Normalized signal value along the lateral direction of the center of the pattern with bandpass filters centered at 1 MHz, 3 MHz, 5 MHz, 7 MHz and 9 MHz; (b) corresponding MTFs, from which the decreasing spot size along lateral direction with increasing filtered center bandpass frequency can be observed. The cutoff spatial frequency of corresponding MTFs also increases with raising bandpass frequencies.

off-axis distance ranging from 2.5 mm to 12.5 mm, in steps of 2.5 mm, the same PSFs after filtering by the transducer frequency response are shown in Fig. 3.19. To quantitate the results, the lateral FWHM and the peak PSF value are plotted in Fig. 3.20 as a function of off-axis distance. Unlike Zemax prediction, the FWHM changes very little until getting to the edge of the lens. There are some visible degradations of the PSF that are difficult to quantitate, but the PSF peak values gradually drop for off-axis points and at the lens edge is almost 50% of on-axis value. This difference with the results from Zemax is mainly due to the fact that Zemax can only predict the imaging of a single frequency signal through ray tracing. Although three dominant wavelengths of the US signals have been considered, it still has great limitations which are reflected in its neglect of the PA signal’s generation and propagation mechanisms, including the heating process caused by the absorption of
light, corresponding changes in the fluid density, initial acoustic pressure distribution, and its isotropic propagation properties. However, it still served as a good starting point for launching the project.

Figure 3.14: PSFs collected at different off-axis position without transducer filtering.
Figure 3.15: PSFs collected at different off-axis position with transducer filtering.
3.3.4 Depth of field

A series of simulation experiments were performed in the same manner to investigate the depth of field of the acoustic lens system with the transducer array fixed at the optimal position discovered before at 0.25 cm before the $2f$ imaging plane. The on-axis sources were positioned around the $2f$ object plane at 9 different location, ranging from $2f - 2$ cm to $2f + 2$ cm, in steps of 0.5 cm. Fig. 3.21 shows the corresponding collected PSFs with the point placed at different depth, where the one in the middle matchups the absorber at $2f$. These PSFs are evaluated with the same analysis, i.e., FWHM and the peak signal value for assessment. Fig. 3.18 shows the variation of FWHM (in blue) and peak PA signal value (in red) with respect to the distance from the $2f$ object plane, respectively. An “arbitrary” but pragmatic definition of the depth of field is adopted for the system. It is chosen to be the range of object distance for which the FWHM of PSF remains within 60% of its best

Figure 3.16: Simulated based measurements for off-axis performance of the system. Two vertical axes correspond to the FWHM value (in blue) and peak PA signal value (in red), with respect to the off-axis distance (horizontal axis).
value. This seems to be the case for a distance range of approximately 0.50 cm before and 0.75 cm after the 2\(f\) object plane, leading to an approximately 1.25 cm depth of field for this system.

Figure 3.17: Simulation based PSFs for depth of field determination with the sources placed at 2 cm, 1.5 cm, 1 cm, 0.5 cm before the 2\(f\), and 0.5 cm, 1 cm, 1.5 cm, 2 cm after the the 2\(f\) object plane.
Figure 3.18: Simulation based measurements for the depth of field of the system. Two vertical axes correspond to the FWHM value (in blue) and peak PA signal value (in red), with respect to the off-axis distance (horizontal axis). Our depth of field was chosen to be the range of object distance for which the FWHM of point spread function (PSF) remains within 60% of its best value which led to a distance range of approximately 0.50 cm before and 0.75 cm after the 2\(f\) object plane.

### 3.3.5 Simulation summary

The singlet acoustic lens based camera system in 2\(f\) geometry is evaluated here with a 2D finite element wave propagation model that is capable of providing us the full A-line data at each sensor location, from which 2D PSF is constructed and evaluated for depth of field and off-axis performance. Signal detection with a 5 MHz center frequency and 50% bandwidth sensor array results in the best PSF with an axial and lateral resolution of about 1 mm. The depth of field, defined as the distance range around 2\(f\) object plane where approximate axial and lateral resolution degradation is within 60% of its best value is estimated to be about 1.25 cm. Along the off-axis, the resolution in the best focus plane does not deviate much up 1 cm. Assuming circular symmetry for the 3D PSF, the system
has the ability to image PA absorbers in a small volume \( \sim 5 \text{ cm}^3 \) with nominal resolution of 1 mm. If superior resolution has to be maintained at all depths, then the lens and sensor assembly can be moved together to keep the intended object plane always at \( 2f \) distance.

It is known that PA signal generated by different size absorbers generally covers a wide range of frequencies, from 0.5 MHz to well above 9 MHz. A digital PAT imaging system has to give careful considerations to spatial and temporal sampling of the sensor data, because image reconstruction quality may get affected by aliasing errors. Higher sampling rates, while desirable, will lead to added system cost. Acoustic lens based focusing idea mitigates this dilemma to some extent. It is demonstrated that a lens designed to be used with a 5 MHz and 50% bandwidth sensor can focus PA signal effectively over a wide frequency range, from 1 MHz to 9 MHz. This can happen because the lens material has negligible dispersion with respect to the velocity of propagation of US. This being a diffraction limited system, the resolution, especially the lateral resolution, decreases inversely with frequency, as has demonstrated with the simulations.

### 3.4 Experimental results

Experiments using our singlet acoustic lens based PA imaging camera are discussed in this section, which throughout the whole project, is one of the very crucial steps in exploring the feasibility of the dual-mode imaging cameras of PA and US. All the experiments presented here were completed by Bhargava Chinni, a research fellow at the University of Rochester Medical Center. In order to keep the consistency of the study, the same assessment is conducted, including the investigation of the best focal plane, off-axis performance and the depth of field of the system.

The PA imaging probe is aimed to allow medical professionals to detect and diagnose
disorders related to the prostate. Illumination of the prostate tissue by high-intensity optical radiation causes PA signals to be produced, which is imaged onto a detector such that a region of prostate tissue can be mapped. As shown below in Fig. 3.19, the laser is located at the bottom of the 3D-printed probe for generating the high-intensity optical signal. The returning acoustic signals is collected through an acoustic lens embedded inside the probe and focused onto a transducer array located at the top.

Figure 3.19: Working principle of the PA imaging probe: the laser is located at the bottom of the 3D-printed probe for generating the high-intensity optical signal. The returning acoustic signals is collected through an acoustic lens embedded inside the lens system and focused onto a transducer array located at the top.
The lens is $f/1.2$ and 3D printed using Somos Protogen 18430, the acoustic impedance of which matches that of water. It is worth noting that the wavelength of the acoustic signal being imaged is on the order of several hundred microns which is significantly longer than the wavelength of visible light. Because of this, the surface roughness of the lens induced by 3D printing technique [73] can be much greater while maintaining image quality. This characteristic makes 3D printing a viable manufacturing technique for our acoustic imaging lens. Specifically, midrange 3D printers can achieve resolutions of 30 µm which is sufficiently smooth for the acoustic signal. Similar to electronic systems where impedance mismatching may cause reflections at the interface which would reduce the available signal, it is important that the acoustic impedance of the selected materials matches that of water as it will be immersed in distilled water during the testing. The acoustic refractive index of the material, which is defined as the ratio of US propagation speed in the material to that in water, also matters. It is crucial that they are sufficiently different so that the acoustic lens can effectively focus the signal. Taking these two factors into account, the Somos Protogen 18420 was selected.

The experimental results are given below. The best imaging plane, as shown in Fig. 3.20(a), appears 0.25 cm before $2f$ with a FWHM of 0.98 mm, which is in agreement with the simulation result of 0.95 mm detected at the same location. Due to the 0.5 mm size limit of the sensor, the accuracy of the PSF obtained in the experiment is significantly lower than the simulation counterpart as given in Fig. 3.20(b). This leads to the slight difference of the results between the two. If the output of every 10 sensors in the simulation is uniformly averaged to achieve the same sensor size, the FWHM of the PSF, as shown in Fig. 3.20(c), will be reconciled with the experimental result of 0.98 mm with the same pattern of PSF.

Similarly, the off-axis performance and depth of field measurement follow similar approaches to simulation. However, due to the limitations of experimental hardware, the
CHAPTER 3. SINGLET LENS SYSTEM

Figure 3.20: PSF of the best focal plane experiment of PA imaging in comparison with those of the simulation counterparts, where 3.20(b) shows the original simulation result with a sensor size of 0.05 mm, while 3.20(c) is its averaged counterpart with a 0.5 mm sensor size, the same as used in the experiment.

off-axis performance was only measured at 2.5 cm and 5 cm. The FWHM, as shown in Fig. 3.21(b) and 3.21(c), is 1.12 mm and 1.15 mm, respectively. This is consistent with the simulation results of 1.10 mm and 1.13 mm with sensor averaging considered, both of which are of no significant degradation in comparison with the 3.21(a) on-axis measurement.

3.5 Summary

An innovative technology to simultaneously focus PA signals originating in a small volume has been evaluated in this chapter, through simulation and successfully incorporated into a prototype camera for practical applications. The acoustic lens system is at the heart of the system. The use of an optical lens design software, Zemax, to perform initial acoustic lens design has been demonstrated. How to build a PA imaging camera model using k-Wave
CHAPTER 3. SINGLET LENS SYSTEM

Figure 3.21: PSFs of off-axis performance experiment of PA imaging. No significant degradation of the off-axis performance is observed, where the FWHM of on axis, 2.5 mm off axis and 5 mm off axis absorbers is 0.98 mm, 1.12 mm and 1.15 mm, respectively.

Matlab toolbox is a new contribution that may be of interest to PA imaging community. Its use in evaluating the quality metrics of the lens, including the time-frequency content of the PA signal, has also been presented in this chapter.

A singlet lens design and characterization have been accomplished in the chapter. However, the methodology can also be used to design and test more complex lens systems. With a singlet lens and a 5 MHz US sensor array, the system has a nominal 1 mm axial and lateral resolution. Off-axis performance remains good up to 10 mm. The depth of field is around 12.5 mm. There are two options to image different depth planes in this type of camera. First is to time gate the focused PA signal so that only signal from the best focal plane is captured by the sensor array. To image other depth planes with the same resolution, we will have to move the lens and sensor planes in unison. The other alternative is to design a lens with finite depth of field. In this case, signals from different depth planes
are captured simultaneously by the sensor, but displayed separately by choosing different time gates. It is the latter that we aimed for and demonstrated in our study. There is a compromise in the resolution that one has to accept in this case but it can be estimated with the procedure we have described.
Chapter 4

Multi-lens system

Through previous simulation and experiment, it can be seen that the designed singlet lens system can effectively focus generated photoacoustic (PA) signals of on-axis absorbers, however, another problem also surfaced. According to the ray tracing diagram of Zemax, the system’s focusing ability for off-axis absorbers is significantly reduced. Although this degradation is not evident in the subsequent simulation and experiment, in order to further enhance the performance of the system, a team of undergraduate students from the Institute of Optics at the University of Rochester, helped us design a more sophisticated multi-lens system. The primary purpose of two lenses of the system is to provide focusing power, and to correct the field curvature aberration, respectively. This chapter gives a briefly introduction to this multi-lens imaging system. It is primarily intended for the reader to gain a deeper understanding of the lens design process. However, it is not the core of the study.
4.1 Limitation of singlet lens system

As has been mentioned, the relatively simple singlet lens based acoustic system suffers from field curvature aberrations, which limit the resolution of the image. This can be easily observed from the ray tracing diagram of Fig. 3.3, where the paraxial rays and the rays travelling through the edge of the lens do not meet at the same point at the $2f$ image plane. This degradation is also reflected in the corresponding modulation transfer function (MTF) diagram of Fig. 3.4(b), where the calculated MTF value of 0.2 for on-axis absorber, 5 millimeters (mm) and 10 mm off-axis absorbers, drops from 0.88 cycle/mm to 0.74 cycle/mm and 0.37 cycle/mm, respectively. The limitation of the singlet acoustic lens system, on the other hand, also reflects that of the original lens design: the heuristic design is solely based on the Lens Maker’s Formula as has been given in Eq. (3.1). This, however, is proved to be the optimal design in the hindsight, which provides an on-axis performance very close to the theoretical diffraction limit. Therefore, there’s no room left for us to further modify the lens surface with current diameters to minimize aberrations for off-axis points. This inspired us to improve the focusing accuracy of the system by having a completely new design. The goal of the multi-lens acoustic imaging system, consequently, is to provide a better imaging resolution system for off-axis absorbers, while satisfying the same design constraints.

4.2 Multi-lens system design

The layout of the multi-lens system is shown below in Fig. 4.1.

The primary purpose of the first lens is to provide focusing power to the system. It is located closer to the object plane than the $1\times$ static magnification design, as would be predicted by a first-order analysis. The second lens corrects for the introduced field
Figure 4.1: Ray tracing diagram of multi-lens based acoustic system from Zemax. The primary purpose of two lenses is to provide focusing power, and correct the field curvature aberration, respectively. The object plane is located 53.4 mm in front of the first surface, while the image plane is located 50.87 mm behind the last surface. The distance between them along the optical axis is 9.3 mm. The diagram shows the optical ray tracing for on-axis, 5 mm, 7.5 mm, 10 mm, and 11 mm off-axis point, respectively.

curvature aberration, and is located closer to the image plane. The aperture stop of the system is located just beyond the second surface of the first lens. Both lenses have a diameter of 24 mm, where the radius of two surfaces of the first lens is −27.03 mm and 21.05 mm, respectively. The second lens has the same surfaces on two sides, with each corresponding to two curvatures: −19.05 mm near the edge, and 23.66 mm at the center. The distance between two lenses along the optical axis is 9.3 mm. The corresponding object plane is 53.4 mm in front of the first surface, while the image plane is located 50.87 mm away from the last surface. The design under this specific distance settings gives a system magnification of −1. The optical design software, Zemax, was applied to vary the total four surfaces of the lens and their placement distance, so as to optimize the MTF for on-axis and up to 11 mm off-axis points.

Significant improvement on off-axis performance is evident in the corresponding ray tracing diagram as has been illustrated in Fig. 4.1. It is also reflected in the optimized MTF predictions as shown in Fig. 4.2(a), where the degradation of off-axis points is greatly alleviated, especially when compared to that of the singlet lens system as given in Fig. 4.2(b). However, on the other hand, we must also note that this is at the expense of sacrificing sys-
tem overall performance on a wider range of spacial frequency: MTF now attains a lower value of 0.25 at 0.7 cycle/mm compared to that of 0.3 for on-axis absorbers of singlet lens at the same spacial frequency – the improvement on system’s off-axis performance is at the cost of point spread function (PSF) based resolution.

![MTF comparison of multi-lens system and singlet lens system](image)

Figure 4.2: MTF comparison of multi-lens based system and singlet lens system. MTF consistency of on-axis and off-axis points has been greatly improved on the multi-lens system, but it’s slightly attenuated the on-axis performance which degrades from 0.3 from the single-lens counterpart to 0.25.

### 4.3 Simulation results

Since the major improvement of the multi-lens system is its better performance for off-axis points, this, consequently, becomes our main testing focus in both simulation and experiment. Similar to the previous simulation of singlet lens system where results from Zemax are only treated as a starting point, the optimized lens design parameters are integrated into a two-dimensional (2D) system simulation using a Matlab third party toolbox, namely K-wave toolbox, in order to acquire a more realistic PSF of the designed system. The toolbox, as the name suggests, is based on $k$-space pseudo-spectral time domain solution, and
is specifically designed for calculation of the acoustic wave propagation. Therefore, it is good for our use.

The simulation procedure for multi-lens system is similar to that of the previous singlet lens. As shown below in Fig. 4.3, a comprehensive 2D simulation is established based on the actual lens parameters, which incorporates PA signal generation, lens focusing, transducer reception, and corresponding frequency filtering. The same simulation setup parameters are assigned to the multi-lens model: 0.05 mm by 0.05 mm spacial grid size, 0.1 mm PA absorber diameter, velocity of 1500 meter/second (m/s) and impedance of 1.5 megarayls (MRayl) medium property; 2586 m/s velocity and 2.29 MRayls impedance lens material property. In particular, the frequency response of the transducer array is simulated to be centered at 5 MHz with a $-6$ dB bandwidth of 2.745 MHz. The transducer size in the simulation is 0.05 mm, 10 times smaller than the experimental one.

![Figure 4.3: Schematics of a multi-lens based PA imaging camera.](image)

Specifically, from a simulation point of view, the point source is generated at pixel number 752 along the wave propagating direction. The center of two lenses are located at pixel number 2048 and 2297, respectively, while the image plane is located at pixel number 3354 for A-line data collection.
To evaluate off-axis performance, point sources were placed at three locations in the object plane defined by Zemax, namely on-axis, 2.5 mm off-axis and 5 mm off-axis, for direct comparison with results from the single lens model. The corresponding PSFs for mult-lens and single lens system is given in Fig. 4.4, where 4.4(a) shows the result of multi-lens system, while 4.4(b) is its single lens system counterpart. The quantitative results are given in Table 4.1.

![Image](image.png)

(a) Singlet lens system  (b) Multi-lens system

Figure 4.4: Off-axis performance evaluation of the multi-lens system. Left to right: one axis, 2.5 mm off-axis, and 5 mm off-axis.

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<tr>
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Table 4.1: The spot diameter comparison of the singlet lens and multi-lens based simulation.
4.4 Conclusion

The multi-lens system design was initiated to overcome MTF based off-axis PSF degradation predicted by ray tracing results, as indicated in Fig. 3.4(b), for the singlet lens based imaging system. In the discussion here, a correspondence and an inverse relationship between the limiting spatial frequency have been assumed. On the singlet lens based MTF, the differences are small up to an off-axis distance of 10 mm, with major difference setting in at 11.2 mm. The simulations examined the PSF of multi-lens base system for only up to 5 mm off-axis distance, but the differences are small and do not indicate any trend. However, the overall MTF has gotten worse already compared to the singlet lens counterpart. The simulation FWHM values for on-axis and up to 5 mm off-axis for multi-lens design do not show any clear trend, but on average the FWHM is higher than singlet lens case as expected from the MTF data. With data acquired from simulation and experiment, it is concluded that the multi-lens system does not provide any measurable improvement over singlet lens, and therefore, is not chosen for the following research.
Chapter 5

Ultrasound image incorporation

Since the goal of the project is to incorporate ultrasound (US) imaging functionality into our existing photoacoustic (PA) imaging probe in order to produce a dual mode imaging camera, in this chapter, we validate through computer simulation and experiment, an acoustic lens based focusing idea for US imaging that eliminates synthetic aperture focusing typically used in conventional US imaging systems. The chapter is the core of the thesis which elaborates on the implementation of the project innovation. As has already been explained Sect. 1.2, a polyvinylidene fluoride (PVDF) film located on and perpendicular to the lens axis is used as an US plane wave generator. The US plane wave backscattered by the target gets focused by the acoustic lens onto the 16-channel linear transducer array. A linear frequency modulated (FM) chirp signal is used for signal-to-noise ratio (SNR) enhancement. The acoustic lens based imaging system is simulated using our custom-designed lens evaluation package. Preliminary system performance is tested through a prototype imaging camera. The US imaging modality of a dual mode imaging probe, which is designed for clinically potential use for both PA and US imaging, is presented at the end of the chapter.
5.1 Simulation results

The acoustic lens based imaging idea is illustrated in Fig. 5.1.

Figure 5.1: Schematics of an acoustic lens based US imaging camera. The system is based on the $4f$ geometry, where $f$ is the lens focal length of the system. The target to be imaged is placed at $2f$ distance to the left of the lens, and the sensor is placed at the same distance on the right side of the lens. This gives an image magnification of $-1$. The system is originally designed for PA imaging, where the tissue volume placed at $2f$ object plane is exposed to a laser beam of wavelength between 750 nanometers (nm) to 1000 nm, a PA wave is then generated due to the thermal expansion of the tissue volume. A small fraction of PA wave within the solid angle subtended by lens diameter propagates through the lens and gets focused onto the image plane. The generation of US image using
this acoustic lens based system follows the same idea. It needs to be noted that though the generation mechanisms of PA and US signal are quite different, they are exactly the same from propagation and sensor points of view, as both of which are mechanical waves, and consequently will get focused in the same manner. In the experiment, a stepper motor, as shown in Fig. 5.1 on the image plane, is used to precisely adjust the position of the transducer array for a two-dimensional (2D) raster scan. Its scanning method will be described in details in the following 5.2.1 Data Presentation Section.

In order to put in the US imaging functionality into our imaging system without disturbing our current structure of the PA imaging system, the use of a PVDF film has been proposed with its plane perpendicular to the lens axis. Choosing PVDF film for US signal generation mainly comes from practical reasons. The film itself is very thin, with a thickness of 28 microns (µm) and an active area \( \sim 2.25 \) square centimeters (cm\(^2\)). This fits in well with our current existing PA imaging probe, which is of a diameter of 3.2 centimeters (cm). The PVDF film emits US waves in both two directions, with the forward one propagating directly to the sensor, as shown in blue in Fig. 5.1, and the reverse one, shown in dotted red, backscattered by the target first and propagating through the film to the image plane with a time delay. Only the backscattered signal is used for US image generation. Given the close acoustic impedance between PVDF film of 4 megarayls (MRayl) and water of 1.5 MRayls, backscattered wave propagating through the film can be ensured to have the minimum diffraction and distortion. The distance between the target and PVDF film is supposed to be within the nearfield region of the film. Since the wave propagation speed doesn’t deviate too much in water (\(\sim 1500\) m/s) and lens (\(\sim 2590\) m/s), the US signals coming from the same plane perpendicular to the lens axis will get to the image plane almost simultaneously, thus the wave arrival time can be easily converted to the depth information.

A lens evaluation package with a third party Matlab k-Wave toolbox is used for system
Figure 5.2: Schematics of US imaging simulation. The wire target is placed at \(2f\) object plane with a line of US source placed 0.9 cm behind. Two waves will be generated by the line source and will arrive at the image plane with a time difference. Specifically, the wire target, line source, lens and sensor array are located at pixel number 452, 632, 2048 and 3595, respectively.

The PVDF film is simulated as a line source in simulation, with each pixel on the line serving as a point US source generating the chirp signal. It is noteworthy that k-Wave toolbox is specifically designed for PA wave generation, where the corresponding output PA waveform is solely determined by the size of absorber, as well as the duration and shape of the laser beam. For most cases, the output PA wave is of an ‘N’ shape. However, when a linear FM signal is applied to encode the laser beam, the corresponding waveform of output PA signal is almost exactly the same as that of the encoded laser beam. Again, PA signal and US signal are only different in the generation mechanism, but there is no substantial difference in the generated signal itself. The PA signal, to some extent, can be considered as an US signal in which the amplitude of the signal depends on the optical absorption rather than the elastic properties of the tissue. This is the reason why the toolbox can also be applied for US simulation in our case. The chirp output is used as the input US signal and fed to every pixel element of the line source. The simulation is based on a \(k\)-space pseudospectral time domain solution, where the wave pressure at each
grid point is calculated by solving the 1st order acoustic equations as has been discussed in Chap. 3.

The whole US simulation model consists of a one-dimensional (1D) US plane wave generator locating on and perpendicular to the lens axis. The wire target to be imaged is placed at $2f$ distance to the left of the lens. Focused image is formed at the same distance to the right of the lens, where A-line signals are captured by a linear transducer array. The discrete grid is 4096 by 640 points along the lens axial direction and transverse direction, with a 0.05 millimeter (mm) spacing. The corresponding maximum supported frequency under this configuration can go up to 15 megahertz (MHz). According to previous simulation of PA signal propagation using the same system (see Sect. 3.3.1 for more details), the best focal plane was discovered at 0.25 cm before the $2f$ image plane. The sensor is fixed at this location in the simulation. A line source, which simulates the signal generated from PVDF film, is placed 0.9 mm away from the wire target. It generates the signal propagating in two directions. The designed lens is of a bi-concave shape with a 32 mm diameter, 33.5 mm radii of curvature, and a 39.8 mm focal length. It simulates the photopolymer material of the lens, with a 2590 m/s velocity of sound and a 884.17 kg/m$^3$ density. The medium is simulated as water with a 1500 m/s velocity and a 1000 kg/m$^3$ density. In order to best match our experimental 16-channel transducer of a frequency response centered at 5 MHz with a $-6$ dB bandwidth of 54.9%, a bandpass filter is used to filter the signal recorded at each sensor element. The wire target simulating the material of steel is created with a 8000 kg/m$^3$ density and a 5790 m/s velocity. Considering the main purpose of the US image is to help locate the movement of the probe in real time during biopsies, three wire targets are created for this purpose. As shown below in Fig. 5.3(a), they are 5 mm, 7.5 mm and 10 mm in length, respectively, with a 2 mm width. In order to best simulate the experimental environment, these wire targets are embedded in a speckle medium with a mean density of 2000 kg/m$^3$ and a deviation of 0.2, all of
which are of a constant 1500 m/s velocity, the same as that of water. The visualization shown in Fig. 5.3(a) illustrates the corresponding density value represented by each pixel, from which several key values can be read: water medium with a density of 1000 kg/m$^3$ (in black), needle target of 8000 kg/m$^3$ (in white), and that of the nonuniform speckle environment around 2000 kg/m$^3$ (in gray).

It is known that the time-bandwidth product of the FM pulse directly determines the SNR of the signal after compression. Since no attenuation is considered in simulation, in order to best test the feasibility of this lens based US imaging idea with the use of chirp signal, this product is intentionally kept low. As shown below in Fig. 5.3(b), the generated signal is with a duration of 10 microseconds ($\mu$s) and a sweep bandwidth of 6.5 MHz, from 1 MHz to 7.5 MHz with a Gaussian envelope. The choice of Gaussian envelope is primarily intended to reduce the effect of the finite length signal on its spectrum, i.e., the Fresnel ripples effect introduced in Sect. 2.2.3. The frequency range of the signal is chosen to match the frequency response of transducer which is centered at 5 MHz.

In order to more intuitively observe in computer modelling, how the generated US signal interacts with medium and the target, the target is simplified to a single wire target with a 17 mm length and a 1 mm width for the visualization of wave propagation. The snapshots taken at four different times are shown in Fig. 5.4, in which the red and blue dotted lines represent the location of wire target and PVDF film, respectively. A two-direction propagating chirp signal can be observed in Fig. 5.4(a) and 5.4(b), with the one propagating to the target reflected back in 5.4(c), and generating the backscattered wave in 5.4(d). This is the signal that is of more interests to us, since that is the one needed for data post-processing. The reflection of the US waves by the speckle medium can also be clearly detected.

The received A-line time signal from the center transducer is shown in Fig. 5.5. Two chirp signals without compression can be visually observed in 5.5(a), though the backscat-
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(a) density value represented by each pixel
(b) the generated chirp signal

Figure 5.3: The phantom and chirp signal used for US simulation. The phantom, which is represented by the corresponding density value consists of a three-segment wire target embedded in the medium of speckle pixels, with a length of 5 mm, 7.5 mm and 10 mm, respectively. The generated chirp signal is with a duration of 10 µs and a sweep bandwidth of 6.5 MHz from 1 MHz to 7.5 MHz with a Gaussian envelope.

tered one is almost buried in noise. This problem will become more severe, as will be shown in the following experiment Sect. 5.3, when the SNR of the generated chirp remains at even lower level. There are four time points which are of greater importance for us: the arrival time of the direct and backscattered chirp, as well as that of the signal reflected by two phantom boundaries. The arrival time of these signals can be theoretically calculated through corresponding distance knowledge. These key time points are marked in dotted lines in the two subfigures of 5.5, where the red and blue lines mark the theoretical arrival times of the direct and backscattered chirp, respectively, and the black lines label those of the boundary signals. These uncompressed signals unquestionably alias as expected, in which the ones from the phantom boundary are no longer identifiable in 5.5(a). Its compressed counterpart, however, demonstrates a significant improvement in terms of the signal visualization, where four short pulses clearly stand out. It can be evidently seen in
Figure 5.4: Visualization of simulated US signal propagation. The chirp signal is generated by a line US source which propagates in two opposite directions, with one reflected by the target generating the backscattered signal. Signal reflections from speckle generating medium can also be clearly observed.
5.5(b) that the arrival time of these signals coincides with the corresponding theoretical calculations, which from another aspect, verifies the accuracy of the simulation. The SNR is used to quantify the results which is calculated by the averaged amplitude ratio of the signal versus that of the noise. The corresponding SNR of the signal, before and after compression, is 4.25 and 27, respectively. The SNR is enhanced by a factor of 6.

Figure 5.5: Simulated US signal before and after compression at the sensor end. The dashed lines in two figures indicate theoretical arrival time of each of the four following signals: the direct chirp, backscattered chirp, and the signal from the phantom boundaries. The simulation results are in agreement with the theoretical calculations.

The comparison of created wire target phantom and corresponding lens focused image are shown below in Fig. 5.6. The signal recorded at each sensor element on the best image plane is timegated in order to filter out the direct chirp received around 115 µs. The vertical axis of the figures represents the sensor direction, while the horizontal axis stands for the wave propagating direction, along which the wave arrival time has been converted to the depth information. It is worth mentioning that off-axis point has a longer optical path compared to its on-axis counterpart. Although this distinction is very small, but since the system has to be clocked in microseconds, any difference in the optical path length
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would be clearly presented on the lens-focused image. As presented below in 5.6(b), off-axis signals are received by the sensor at a later time compared with the on-axis ones. The further the point is away from the optical axis, the later it will be received by the sensor due to the difference of propagation distance. The $-1$ magnification of the system results in an upside down image, which is another factor that needs to be taken care of. They are both corrected in 5.6(c). Through comparison with the original phantom image given in 5.6(a), it can be seen that the 10 µs duration chirp is already able to generate a clear resolution of the phantom. It is worth mentioning that the image acquired through this 2D simulation is the B-scan image, in which the distance information along the horizontal axis is converted by the receiving time of the signal. Therefore, it is not the “face-to-face” image of the phantom. In the experimental Sect. 5.3 that will be described later, the data will be further processed for C-scan image acquisition – an “actual” plane-type view image of the target.

Another interesting finding from the simulation is that even as the time-bandwidth product of signal is kept as low as only 65, with a 10 µs duration and a 6.5 MHz sweep bandwidth, we are already able to focus a clear image through our acoustic lens based imaging system. It is our expectation that the focused image will be further improved in terms of SNR by applying signals with higher time-bandwidth product.

5.2 Prototype camera

A prototype US imaging camera has been built for the project in order to experimentally validate the acoustic lens based US imaging idea. As shown below in Fig. 5.7, the experiment follows the same setup as has been illustrated in Fig. 5.1. The center of the lens is placed 79.8 mm ($2f$ distance) behind the 16-channel transducer array. It’s followed by the PVDF film, and the phantom, which is placed at the same $2f$ distance behind the lens.
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(a) original phantom  (b) lens-focused image  (c) corrected image

Figure 5.6: Simulation results of US imaging.

The phantom and PVDF film is 1.0 cm apart from each other. The positional relationship of each device can be more clearly observed in Fig. 5.8, where 5.8(a) shows that of the transducer array, acoustic lens and the PVDF film, while 5.8(b) shows that of the lens, film and the phantom.

5.2.1 Data presentation

Due to underlying computation burden, a 2D simulation was chosen to model the system. Therefore, the image acquired in this way is actually the B-scan presenting image, where the horizontal axis displays the travel time of US waves which reveals the depth information, while the vertical axis corresponds to the position of linear transducer array. As shown in Fig. 5.9, the specific B-scan image shown in the picture shows the image acquired from time $t_1$ to time $t_2$. In the experiment, it is practicable for us to get a “chunk” of data which will contain A-line signals acquired at different transducer locations recorded from 0 to time $t$. This makes it possible for us to process corresponding C-scan images, presenting a plane-type view of the location and size of test specimen features. This can be done by timegating the data at a specific time. The specific C-scan image shown in Fig. 5.9, for example, is gated at time $t_3$. This allows us to image the target located at
Figure 5.7: Experimental setup of prototype US imaging camera. From left to right: the 16-channel transducer array, acoustic lens, PVDF film and the phantom to be imaged. The setup strictly follows the 4f configuration, where the distance between both phantom and sensor array to the center of acoustic lens is 2f of 79.8 mm. The phantom and PVDF film is 1.0 cm apart from each other. Specifically, the PVDF film is driven by the signal generated by a polynomial waveform synthesizer followed by a power amplifier of 50 dB. The experiment is done with the tank filling with water (not shown in the picture).
(a) the transducer array, acoustic lens and the PVDF film

(b) acoustic lens, PVDF film and the phantom

Figure 5.8: Other views of the prototype US imaging camera.
different depth.

![Figure 5.9: Schematics of US data presentation. B-scan image is based on the time axis which reflects the depth information of target (from $t_1$ to $t_2$), while the C-scan image is obtained by intercepting A-line signals at a certain time ($t_3$), capturing the “actual” plane-type view image of the target.](image)

5.2.2 The 1D transducer array

A 16-channel 1D transducer array was used for imaging, each element of a size of 0.5 mm by 0.5 mm with a 0.7 mm pitch between the adjacent two. Therefore, in order to cover a 2D area of imaging, the 16-channel transducer array needs to be subjected to a raster scan. Specifically for this experiment, 40 and 3 scans were carried out in the vertical and horizontal directions, respectively. As shown in Fig. 5.9, the 1D transducer array starts scanning from the lower right position, climbing to the highest position after 40 climbs and completes the data collection for the first column positions. The sensor then translates to the middle column and scans down for another 40 sets of data acquisitions. By analogy, at the lowest point of the middle column, the sensor translates to the third column and climbed for the final set of data acquisitions. It is worth mentioning that,
in order to improve the accuracy of the data, the data acquired at each location were collected 25 times, only the averaged data was taken as the corresponding acquisition result at the position. Although this greatly increases data acquisition time, it at the same time, significantly enhances the reliability of the data by performing multiple laser excitations at the same position of the phantom. This also eliminates the impact of minor vibration of the equipment during the data acquisition.

Synchronicity plays a crucially important role in this experiment, as the system has to be clocked in microseconds. Consequently, any time error in the data acquisition process would destroy its authenticity and bring serious consequences on the post data processing. Especially for the signal generation of the experiment, the signal generator is served as the “masterboard” which controls each imaging device, from which the chirp signal driving the PVDF film and the excitation signal for synchronizing the system are simultaneously generated. As shown in Fig. 5.10, the excitation signal (in red) is generated prior to the chirp signal (in blue). The generated chirp signal is input to a 50 Decibels (dB) signal amplifier before fed into the PVDF film, meanwhile, the excitation signal is sent to the sensor. Each time the sensor receives the excitation signal it starts to collect the data. Simultaneously, the PVDF film to which the chirp signal is input begins to produce the corresponding US waves. This ensures that the sensor begins timing and starts the data collection while the signal is being sent. In this way, the sensor and the signal generator could have the same “starting time”. Another device that must be synchronized precisely is the stepper motor which controls the location of transducer array. As shown in Fig. 5.10, this is a device that can precisely move up, down, left and right in a customizable manner. Since data acquisition is performed 25 times per acquisition location, the transducer array should move to the next position after receiving 25 activations. This process is precisely carried out by a computer program, through which the number of data acquisition taken at each location is controlled. Specifically for this
experiment, the motor moves the transducer array to the next acquisition position after receiving the 26th trigger signal. The stepper motor and transducer array then complete their time matching by reading input trigger signal exactly. Through such a connection, the entire imaging system would have a unified timing, so that each device, the PVDF film, transducer and stepper motor could be linked together for image acquisition.

![Signal synchronization diagram of the prototype US imaging camera](image)

Figure 5.10: Signal synchronization diagram of the prototype US imaging camera. Synchronization in the experiment is crucial. The chirp signal is introduced to the PVDF film for US signal generation, while at the same time, the trigger signal is sent to the sensor and the stepper motor, to ensure the correct signal starting acquisition time.

We have already noted the degradation of system’s off-axis performance in Sect. 3.3.3, when the performance of the PA system was examined. In order to eliminate the influence of the lens on the imaging resolution as much as possible for off-axis targets, the relative position of the lens and the sensor was fixed in the experiment, that is to say, the center transducer was always aligned with the center of the lens during data acquisition, both of which were moved through the stepper motor as a whole. This allows us to image all areas of the phantom through the central area of the lens, irrespective of whether they are
aligned originally. It is our expectation that through such an arrangement, the resolution of the image can be maximized.

In particular for our case, there is a 0.7 mm spacing between each two adjacent sensors. In order to ensure the resolution of the image to be processed, data collection for one experiment trial was divided into two groups: the first set of data was carried out according to the raster scanning method described earlier. The second set of data followed the same scanning method, but was shifted horizontally by 0.5 mm at the starting position compared to that of the first set of data acquisition. As shown below in Fig. 5.11, the red and blue box represent the relative position of each element of the transducer array during two data acquisitions. The two sets of data were cross-linked together in the data post-processing. This eliminates the signal loss caused by the spacing between adjacent transducers, greatly improving the efficiency of each data collection. Also, thanks to these denser data collection points, it greatly reduces the difficulty of post image processing.

Figure 5.11: Diagram of data cross-processing. In order to prevent signal acquisition loss due to the adjacent transducer spacing, each data acquisition is divided into two groups, with the second group shifted 0.5 mm horizontally from the first one in order to supplement the missing data points.

The data acquisition time under this setting is approximately 25 minutes. This corresponds to two sets of data acquisition, each of which has 25 data acquisitions per location and 120 (40 × 3) positions in total. That is, a total of 6000 (120 positions × 25 averaging × 2 sets) acquisitions were performed for each experiment. For the entire image chain, from
lens focusing to later imaging processing, all aspects are compact and complementary. Any lack of one component would cause difficulties for the subsequent ones. Consequently regardless of the hardware difficulties, the performance of every link in the experiment has been tried to be optimized as much as possible.

5.2.3 The PVDF film

The US signal generator used in the experiment is a PVDF film, as shown in 5.12(a). The film itself is very soft, making it very difficult to fix in the immersed experimental environment. Therefore, both sides of its edge were glued onto a plastic plate for fixing purpose. The film is 3 cm by 1.5 cm in size with a 1.5 cm square effective area in the center. Due to hardware constraints, the PVDF film was not controlled by the stepper motor, but was fixed on a pedestal located between the acoustic lens and phantom. The distance between the PVDF film and phantom was determined to be about 1 cm, mainly taking into account the 10 $\mu$s duration of the chirp to prevent the signal reflected by the target from being aliased with the one propagating directly to the lens. Theoretically, this should not affect the subsequent data processing since the processed signal after cross correlation would not be affected by its aliasing, but they were still separated in our prototype experiment in order to test the feasibility of our acoustic lens based US imaging system.

Also, the PVDF film is not a good US signal generator which makes it impossible to produce high-amplitude signals. This is why the use of pulse compression technique was proposed at the beginning of the study, in order to average the total energy of the signal over a “period” of time to maintain the same-level SNR. The PVDF film is supposed to be connected to a very high impedance device, typically larger than 1 megohm (M$\Omega$) receiver, which is not the case for our experiment as it followed a typical low-impedance ENI RF power amplifier. We experimented with the chirp with five different durations as
input from 10 $\mu$s to 30 $\mu$s, respectively, in steps of 5 $\mu$s. The film, however, was burned in an experiment when a signal of 30 $\mu$s was imported. Therefore, in order to ensure its safety, the duration of the signal input has to be limited to 10 $\mu$s with a conservative 1 millisecond (ms) pulse repetition time, in order to minimize the burden of PVDF film. As a consequence, we could only change the time-bandwidth product by changing the sweep bandwidth of the signal.

According to the user guide, the PVDF film maintains a high frequency response in the range up to 15 MHz. Considering the center frequency of the transducer element used in the experiment is only 5 MHz, the impact of the bandwidth of PVDF film on the generated signal can be safely omitted. The center frequency of the signal is fixed at 5 MHz, but with different scanning ranges for the maximum signal reception. In the following experiments for the imaging of phantom 2, they were carried out in four groups, corresponding to the sweep bandwidth of 4 MHz (3 MHz to 7 MHz), 3 MHz (3.5 MHz to 6.5 MHz), 2 MHz (4 MHz to 6 MHz), and 1 MHz (4.5 MHz to 5.5 MHz). That is, four
different time-bandwidth products at 40, 30, 20, and 10 were tried, respectively.

5.3 Experimental results

In order to test the feasibility of the acoustic lens based US imaging idea using PVDF film, three sets of experiments were conducted on different phantoms. The first set was for validation purpose, as well as investigation on the system depth of field. The second set of experiments was performed to detect the effect of the signal sweep bandwidth on the SNR of the image. It was carried out in four groups according to the experimental setup described above. That is, corresponding to the signal duration of 10 µs, attempts were made at four different sweep bandwidths in order to explore its impact on the resolution of the generated image, from 1 MHz to 4 MHz, in steps of 1 MHz. The third experiment was based on the former two, to detect the capability of the acoustic-lens based US imaging system on a multi-target phantom.

5.3.1 Phantom 1: single target

The first phantom, as shown in Fig. 5.13(a), is a needle inserted diagonally inside a 1.50 cm long by 0.85 cm width chicken breast. There are two main reasons for building this phantom: first, to investigate the signal intensity – whether the needle target is able to be displayed from the background, and if so, how “visually” clear the displayed image would be in the generated US image. Second, to validate system’s depth of field, as has already been tested in the previous PA experiment discussed in Sect. 3.3.4. The phantom used for this testing, as well as its corresponding size information are given in Fig. 5.8. In order to minimize the impact of ancillary equipment on the experiment, the phantom was fixed with glue on a polymorph plastic plate. Again, the size of the phantom is mainly to correspond to that of the active region of PVDF film which is approximately a 1.5 cm
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Figure 5.13: Phantom 1 for US imaging: a needle diagonally embedded in a slice of chicken breast of a size of 1.50 cm by width and 0.85 cm by height. The size was chosen to match the active area of the PVDF film.

In order to measure the depth of field of the US imaging system, the phantom was placed in five different positions from $2f - 0.5$ cm to $2f + 0.5$ cm, in steps of 0.5 cm. Each transducer, at each position to which it’s moved, recorded information from the beginning of the US signal transmission to the next 150 $\mu$s. Considering the 1 cm distance between the PVDF film and the phantom, and the $4f$ positional relationship among the components of the whole imaging system, the reflected signal should propagate to the transducer at the time

$$t = \frac{(39.8 \times 4 + 1) \text{ mm}}{1.54 \text{ mm/} \mu\text{s}} = 104.03 \mu\text{s},$$

which is sufficient for the transducer to record all signals reflected by the needle target. This also allows us not only to capture the C-scan image of the needle target itself, we are
also able to get the background image of the medium in the same manner by gating the A-line signal at different times. Here, as shown in blue in Fig. 5.14, one raw A-line signal data recorded at a particular acquisition location is extracted which contains the direct signal and the reflected signal that have been mentioned earlier. As in the actual experiment the US signal would face attenuation, scattering, and other unfavorable problems, it can be visually observed from Fig. 5.14 the degree of attenuation of the backscattered signal from the target, where the signal reflected by the target is too weak to be visually identified. However, the SNR after pulse compression, as shown in red, demonstrates a significantly improvement, from which the signal of the target evidently stands out from that of the noise, greatly enhancing the range resolution of the acquired C-scan US image.

![Figure 5.14: Experimental US signal before and after compression. The blue line shows the original signal, and the red line shows the signal after pulse compression, in which the substantially invisible backscattered signal is clearly displayed after compression.]

The setup of each device in the experiment is crucial, especially their relative positional relationships. The distance from the center of the lens to the phantom and the transducer array was measured precisely using a vernier calliper to ensure it is exactly the theoretical value of 2f (79.8 mm). The positional relationship of each device is of equal importance, since the parallel positional relationship of the planes on which each
device is located has to be confirmed, so as to ensure the PVDF film to produce planar US waveform to the phantom, lens accurately to focus and transducer array precisely to collect. Since the lens, transducer array, and the PVDF film were all firmly fixed by rod in the experiment and themselves carry some weight, they were not easy to be moved in the experiment, even when immersed in water. The phantom, however, is different. As shown above in Fig. 5.8(b), it is suspended from the top and held by a relatively soft polymorph plastic. The choice of polymorph plastic is mainly taken into account its smaller acoustic impedance so that the impact on the generated US signal can be minimized. It should be noted that, although attempts have been made to ensure the parallel relationship between suspended phantom and the PVDF film by visual inspection, there’s no guarantee that they were exactly parallel to each other, especially when there might be some slight displacements of the phantom during the experiment. The reason why this is particularly important is because that the transducer performs a data acquisition at each location every 0.017 µs, making our system extremely time-sensitive. Correspondingly, any slightest differences of wave arrival time could be presented in the different time-gated C-scan images. As shown in Fig. 5.15, which displays the normalized C-scan images taken from 103.6 µs to 105.0 µs with a 0.2 µs step, the system is able to accurately distinguish the targets from different depths.

It can be clearly seen from the figure that the upper left position of the needle is relatively forward (i.e., closer) to the lens so as to the rest part of the needle, so that its backscattered signal is firstly received. Signals from other parts are then subsequently received. The reason for such an accurate depth detection results from the fact that we are able to get more than 400 of the C-scan images of a 1-mm thick phantom, leading to the accuracy up to every 25 µm.

Through this experiment we once again investigated the depth of field of the system. Although it has been previously studied for the PA system with the same lens, but in view
Figure 5.15: C-scan results of the first phantom taken at different times.
of the mechanism differences of PA and US, five experiments were conducted to detect the depth of field of the US imaging system. The depth of the target was precisely adjusted by the vernier caliper, and was placed within 1 cm of the front and back 2\( f \) in steps of 0.5 cm.

In order to obtain all the needle target signal in a single C-scan image for easy comparison, 25 images before and after the theoretical C-scan of the target were superimposed together. The normalized image was used as corresponding processing result. As shown in Fig. 5.16, defocused images at non-2\( f \) positions can be observed, especially when the object distance is increased, from which it can be visually measured that the system maintains a good focus ability in the range from 2\( f \) – 1 cm to 2\( f \) + 0.5 cm. This is in agreement with the depth of field measurements of previous PA imaging system which is 0.75 cm before 2\( f \) and 0.5 cm after 2\( f \) (see Sect. 3.3.4 for details). The discontinuities in the imaged targets in 5.16(a) and 5.16(b) result from the slight displacement error that occurred when the transducer array moved from the first column of data acquisition positions to the second one during the raster scan, which has been illustrated in Fig. 5.9. This error may be due to the slight vibration of the experimental platform, or the displacement error of the stepper motor itself. Since each pixel covers a 0.5 mm square area, it can be visually observed that this error range is around 0.1 mm, which is very slight and can be ignored during the post data processing.

Compared to point targets, it is a little bit tricky to quantify the line target image, especially when the target has a certain angle. Therefore, the Radon transform is performed for each image at a specific orientation perpendicular to the direction of the imaged target for image quality quantification. This direction of the projection is believed to best map out the extent of spread of the target. Fig. 5.17 illustrates this quantification process well. As the phantom is relatively fixed in the experiment, the target tilt angle in the image would not be of much difference. It is measured as 114 degrees counterclockwise in the
horizontal direction, as shown in red dotted line in the figure. The plane perpendicular to it, as shown by the yellow line, is the plane along which the Radon transform is calculated. In this way, the line spread function (LSF) of the target (the black curve in Fig. 5.17) of each image is obtained. The full width at half maximum (FWHM) of LSF and the pixel maximum value were used to quantify the results. The corresponding LSF is shown in Fig. 5.18(a), and its statistical results are shown in Fig. 5.18(b), where blue and red curve respectively correspond to the FWHM and maximum pixel value measured at each object distance.

It’s interesting to note from Fig. 5.18(a) how the energy of the signal diverges gradually from the center of the target to its perpendicular direction at off–2f positions. This is reflected in two aspects: first, the center maximum value of the Radon transform at that
Figure 5.17: Schematics of depth of field quantification of US imaging. The red line represents the direction of the needle target which is measured as 114 degrees counter clockwise in the horizontal direction. The yellow line is the calculation direction of the corresponding Radon transform, perpendicular to the direction of the needle target. The black curve symbolically represents the calculated Radon transform in the described direction.

particular line slowly decreases; next, at the same time the energy is diffused to both sides of the target in the perpendicular direction.

5.3.2 Phantom 2: the “doughnut” phantom

In order to further quantify the impact of different signal sweep bandwidths on the SNR of generated image, a “doughnut” phantom, as shown in Fig. 5.19, was built. It’s also made of chicken breast but was cut into a concentric shape. The diameter of the outer circle is about 1.25 cm and that of the inner circle is about half of that of the outer one, 0.65 cm. As the overall area of the phantom is small without sharp corners, prior to investigate the impact of time-bandwidth product on SNR, we have to look at whether this acoustic lens based imaging system is capable of getting a detectable signal and identifying it in the
C-scan image. In this set of experiments, the input signal of PVDF was controlled at 10 µs in accordance with the experimental arrangement described earlier in this section, while experimenting with four different sweep bandwidths from 4 MHz to 1 MHz, in steps of 1 MHz.

As the time-bandwidth product of the signal is reduced, the sharpness of the C-scan image is visually decreased. As shown below in Fig. 5.20, when the time-bandwidth product drops to 10, the processed C-scan image does not have the capability to provide clear phantom information. This is reflected in two aspects: first, the noise in the central region has dramatically increased; furthermore, system’s imaging ability of the phantom has also been significantly distorted. Of course, these are only the initial visual recognitions of the image. In order to quantify the image quality for comparison, two regions of the image are carefully selected and used as the basis for detecting the SNR: the circular blank area inside the phantom, marked with a red circle in Fig. 5.21, and its outer ring area, marked with yellow, are chosen as the noise and signal detection area, respectively.

The relevant statistics are shown in Fig. 5.22, where the bar graph represents the signal
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Figure 5.19: Phantom 2 for US imaging: a concentric circle shape chicken breast with the diameter of the inner circle of 0.65 cm and that of the outer one of 1.25 cm.

Figure 5.20: C-scan results of the second using different sweep bandwidth signals: (a) 4M sweep bandwidth from 3M to 7M; (b) 3M, from 3.5M to 6.5M; (c) 2M, from 4M to 6M; (d) 1M, from 4.5M to 5.5M. The degradation of image resolution is obvious.
Figure 5.21: SNR evaluation of US imaging, where the circular blank area on the inside of the phantom (marked with a red circle) and its outer ring area (marked with yellow) are chosen as the noise and signal detection area, respectively.

and noise level at each sweep bandwidth, while the red asterisk shows the calculated SNR. It is clear from the trend of the curve that the SNR decreases almost linearly with the time-frequency product. Although the largest one used in the experiment was only 40, this was already sufficient to obtain a high resolution US C-scan image.

5.3.3 Phantom 3: multiple targets

Through previous two groups of experiments, it can be confirmed that the designed imaging system has the ability to provide high-quality US images. It further prompted us to continue to explore the system of multi-target recognition. Based on this purpose, the third phantom was built. Different from the first two, the thickness of this one has been significantly increased in order to have the capacity to accommodate two targets at the same time. As shown in Fig. 5.23, the first needle is diagonally embedded in the surface layer of the chicken breast, while the second one is inserted along the other diagonal direction at the bottom. Such an arrangement can effectively distinguish between the two in the post C-scan images. The chicken breast is with a shape of a cube, of a 1.25 cm
square size and a 1 cm thickness. The choice of 1-cm thickness is mainly due to the effective imaging area of the system, that is, the depth of the field that has been detected in the previous experiment. Also slightly different from the first two experiments, since the phantom has a certain volume and carries a little weight this time, we were unable to paste it on the plastic plate under the condition that the shape would not be changed during the experiment. A compromise solution was adopted with the phantom wrapped with transparent tape for the fixing. The attendant drawback of this is that the tape would generate a reflection of the US signal so that the signal energy reaching the phantom is weakened. However, we believe that since the resulting signal is pre-processed with a 50 dB amplifier, the signal energy across the tape can still remain within a significant range. The reflected signal from the tape can be intercepted by time gating the A-line signal. We indeed realized that this is not the best solution, but after weighing all the factors, especially the experimental conditions, we believe that this expedient can be accepted.
In this experiment, the bottom needle target was placed at about 0.25 cm after \( 2f \) so that the surface probe corresponded to the position about 0.75 cm before \( 2f \), in which way both can be relatively clearly imaged. Similarly, the arrival time of the reflected signal is calculated through wave propagation distance. C-scan images corresponding to several representative times are intercepted in Fig. 5.24. In order to better visualize the reception of the backscattered signal in 12 images, each of the following C-scan images are the normalization results of the adjacent 35 images.

![Phantom 3 for US imaging](image)

(a) phantom 3  (b) size information  (c) wrapped by tape

Figure 5.23: Phantom 3 for US imaging: the first target is diagonally embedded in the surface layer of the chicken breast, while the second one is inserted in the other diagonal way at the bottom of the chicken breast cube. The phantom is of a 1.25 cm square size and 1 cm thickness, and is wrapped by tape in the experiment.

It’s not hard to observe in Fig. 5.24 how the backscattered signal is chronologically transmitted back and recorded. Although the two targets are only 1 cm apart, the resolution of the system is sufficient to distinguish them. This is not only reflected in the 0.017 \( \mu \text{s} \) transducer receiving frequency, but also reflected in the corresponding 25 \( \mu \text{m} \) resolution on the distance. Consequently, within a distance of 1 cm we are able to obtain up to 400
Figure 5.24: C-scan images of the third phantom taken at different times.
C-scan images, while the below 12 images are only their highly condensed microcosm of them. It is foreseeable that, if this imaging technology can be applied clinically in the future, physicians will not have to rely on the traditional US images and use their experiences to diagnose the patient. This novel imaging technology will provide physicians with accurate and potentially real-time C-scan images to guide them to determine the disease more clearly.

5.4 The dual mode imaging probe: US modality

5.4.1 Probe design

After obtaining satisfactory results on the prototype camera, we continued to further validate the US imaging functionality using our 3D-printed imaging probe, in order to lay the foundation for the subsequent dual mode (PA and US) imaging experiment. As a potential product for future in-vivo imaging purpose, the imaging probe, which will be placed against the patient’s neck, is designed to be handheld and portable in order to allow physicians to diagnose problems within and around a patient’s thyroid gland, such as cancer, abnormal tissue masses, as well as circulation problems. In this section, we specifically focus on the US image acquisition using the probe, while the following chapter will further introduce the probe design to achieve dual mode (PA and US) imaging functionalities.

The shape of the entire probe is shown in Fig. 5.25(a), with relative position of each imaging component shown in the CAD file in 5.25(b).

The choice of probe configuration follows the same 4f geometry, as has already been described in the previous chapters. As shown in Fig. 5.26, the tissue phantom is placed at a distance of 2× the 39.8 mm focal length of the lens at bottom on the 2f phantom plane, while the transducer array is placed at the same 2f distance on the top, which
Figure 5.25: The design and implementation of the 3D printed PA and US dual mode imaging probe. The probe is designed with a square column shape, mainly due to the reason of less introduced uncertainty from misalignment and less tight tolerances from easier modification.
is located on the opposite side of the lens. This produces an approximately collimated acoustic beam incident on the transducer. The PVDF film is attached at the bottom of the probe for US signal generation. The detailed US propagation path using 3D printed probe is also shown below in Fig. 5.26, which includes the same previously mentioned two signals: the direct chirp (marked with blue solid lines), and backscattered signal reflected by the phantom (marked with red dashed lines). Considering the clinical use that the probe won’t be utilized tightly against patient’s neck, there’s a 6 mm distance left from the end of the outerprobe piece to the actual 2f focal plane. It is noteworthy that, unlike precious experiments using the prototype camera, this time the PVDF film is fixed at the bottom of the imaging probe which makes it possible to move along with the probe. This greatly increases the area we can image on the phantom, making it no longer a factor limiting the experiment.

The part that houses each imaging component was chosen to have a shape of a square column, mainly due to the reasons of less uncertainty that would potentially introduce to the system from misalignment, as well as easier modification and loose tolerances on the optical reflector for PA imaging which will be described in details in the following Chap. 6. The probe comprises of four main parts, all of which were 3D printed. As shown below in Fig. 5.27, they are innerprobe, outerprobe, lens tube filling and the lightguide coupler, respectively.

The main structure of this probe is the inner and outer probe, on which the lens tube filling and lightguide coupler are first installed. The innerprobe is the upper part of the probe which contains the embedded lens and a slot specifically designed for housing the 16-channel transducer array. The outerprobe is the lower half, including a thin plastic plate which acts as an optical reflector for subsequent PA experiments. The details of the design can be obtained from the top and bottom view of the probe in Fig. 5.27, from which the composition of each imaging component can also be clearly observed. The two
Figure 5.26: Schematics of the direction of US signal propagation within the probe. The PVDF, as shown in blue, is fixed at the bottom which can be moved together with the probe in the experiment. Two signals propagating in different directions will be generated, with the forward one, as shown in blue solid lines directly transmitting to the transducer array, and the other one reflected back by the phantom first and producing the backscattered signal, shown in red dashed lines. The phantom is placed at $2f$ plane which is 6 mm below the probe under the design.
Figure 5.27: Components of 3D printed imaging probe. The innerprobe and outerprobe are the two main components, where the innerprobe contains the embedded lens and a slot reserved for the transducer array on the top, while the outerprobe includes a thin plastic plate which will act as the optical reflector for subsequent PA experiments.
sub-probes, as also can observed through Fig. 5.25(a), is attached together with a very thin rubber sheet and joined by four screws on the side to make probe waterproof. In this way, the installation of the entire device is complete and ready for the experiment.

![Image](image1.jpg)

(a) top view (the slot for transducer array)  
(b) bottom view (embedded lens inside)

Figure 5.28: The top and bottom view of the 3D printed probe.

### 5.4.2 Experimental results

Since the experiment must be carried out in a water environment, the side and bottom of the probe are first sealed with glass to make it watertight as highlighted in Fig. 5.29(a) and 5.29(b). Since the probe remains an upright position in the experiment, water injection is done through the transducer slot on the top. The choice of glass is mainly to take into account its minimum impact on the US signal. As shown in 5.29(c), the PVDF film is fixed to the bottom of the sealed glass. Since it’s moving along with the probe as a whole in the experiment, the relative position with the film and transducer array is crucial. Alignment must be ensured so that the signal generated by the PVDF film can be correctly received by the transducer.

Fig. 5.30 further illustrates the progress of the experiment. Unlike the previous US
image acquisition using our prototype camera where the 2D scan of the phantom was
done through the overall movement of the transducer array and acoustic lens, this time
the entire imaging system, including the transducer array, lens, and the PVDF are fixed by
rod during the experiment, while the phantom to be imaged is placed on an experimental
platform, the position of which is precisely adjusted by the stepper motor. In other words,
the 2D area where the phantom needs to be imaged is realized by moving the phantom
itself this time. From the experimental setup in Fig. 5.30, the position of the imaging
probe can be easily observed as fixed. Fig. 5.30(b) also shows the movement path of the
entire experimental platform. The platform in which the phantom is placed is scanned
3 and 20 steps along the horizontal and vertical directions, respectively, at a rate of 0.5
mm each time. Likewise, two sets of experimental data are interleaved to cover the data
gaps due to spacing between two adjacent transducers. The scope of the scan under this
configuration can cover a 2.4 cm by 2 cm area which is good for our experiment. It is
also worth mentioning that before the experiment, the center of the probe and that of the
phantom was aligned to ensure the imaged target to be located at the center of the image.
The experimental platform was then moved by 10 steps and 1.5 steps, respectively to two
directions to start the experiment.

Figure 5.30: Experimental setup for US imaging using the probe. The imaging probe remains fixed throughout the experiment. Specifically, the phantom to be imaged is placed on the experimental platform which will be manipulated by stepper motors for a 2D raster scan, whose scanning path is explicitly marked in (b).

As the purpose of this experiment is to use our 3D printed probe to verify the results of the previous experiments, also taking into account the fact that the distance from the bottom of the probe to $2f$ phantom plane is only 6 mm, it’s not easy to image complex targets with certain thickness. As shown in Fig. 5.31(a), we simply used a needle as imaging target. This has two purposes: first, because the entire imaging probe and its embedded lenses were 3D printed out, although the same printing technology and lens parameters are used, the focusing function of this acoustic lens has not been actually tested. Therefore, the use of wire target would help us detect the LSF of the system; secondly, because the major role of US image in this project is to assistant physician to locate the probe in real time, this also meets the need of the project. We maintained the same experimental parameters in this experiment as before using the prototype camera: 25 consecutive data were collected for each data acquisition location and their mean value was used as the
final data acquisition result for that location.

(a) original phantom  
(b) imaged phantom

Figure 5.31: The phantom for US imaging using the probe.

The imaged phantom is shown in Fig. 5.31(b). The same Radon transform method was performed to quantify the result. The detected linear width of the imaged target is 7.5 mm. Compared to the previous $2f$ results using prototype camera (7.1 mm), the probe meets the imaging requirements and is good for following further experiments on both PA and US imaging functionalities.

5.5 Summary

This chapter is of great importance throughout the whole thesis. It explains in details how we experientially applied the PVDF film to our lens based imaging system to realize the US imaging functionality using our 3D-printed probe. This is one of the most crucial steps in our design and implementation of a dual mode PA and US imaging camera.

A Matlab third-party k-Wave toolbox was used first to computer model the experiment. We then built our prototype US imaging camera and successfully detected the depth of field of the system. Radon transformations were experimentally computed for data processing on the targets located at different depth in order to better quantify their defocus
phenomena. We specially made a “doughnut” phantom, a phantom made of chicken breast with a concentric shape to quantify the effect of different time-frequency products of signal on final imaging resolution. The results imply a linear decreasing relationship between signal-to-noise ratio of the image with decreasing time-frequency product of the signal. We have also been able to acquire high-resolution C-scan images of a multi-target phantom in the experiment. Last but not least, we turned our focus on the use of 3D printed probe to image the wire needle target and got the same satisfactory results. This is a very key step toward future potential clinical trials and will pave the way for our later-on dual function imaging cameras of PA and US. The corresponding experimental results indicate that our 3D-printed acoustic lens and probes is able to provide clear C-scan US image of the target with satisfy resolution.
Chapter 6

The dual mode imaging camera

This chapter, as the finishing of the project, focuses on the realization of the dual mode imaging camera of photoacoustic (PA) and ultrasound (US). Through previous work, PA and US images have been successfully acquired separately using our 3D imaging probe, in which the principle of realizing US imaging modality has already been described in detail in Sect. 5.4. This chapter continues this introduction of the dual mode imaging probe, but delves more into the working principle of its PA imaging counterpart. How to combine two imaging mechanisms into one single probe and make it clinically feasible will be the main focus of the chapter. The chapter analyses the preliminary experimental results obtained by the prototype imaging probe. It is our expectation that these analytical results will contribute to the improvement of the next generation probe design, and further lay the foundation for its future clinical commercialization. The further analysis of the existing problems of the imaging probe and the prospect of the project’s future development will be presented in the last Chap. 7.
6.1 The big picture

Presumably so far, the reader is no strangers to the principle of PA and US image generation. Here, in order to facilitate the introduction of the dual mode imaging camera, the generation mechanisms of two imaging modalities are plotted together in Fig. 6.1, where they are marked in red for PA imaging, and blue for US imaging, respectively. The system is built under the 4f framework, where both the object distance and image distance are set as 2f to ensure a 1 to 1 magnification ratio. As shown below in the red waveform, PA waves are produced resulting from the expansion of the tissue under a transient laser exposure, while US waves are simply generated by a polyvinylidene fluoride (PVDF) film which is located 0.6 cm behind the 2f object plane. The PVDF film generates US waves that propagate in two opposite directions: the direct waves, as indicated by blue solid lines, and the backscattered waves indicated by dashed lines. The latter one will be used for US image generation.

6.2 The dual mode imaging probe: PA modality

The most crucial part of the PA imaging is the laser delivery system which will be used for delivering laser light to the imaging probe. As shown below in Fig. 6.2 in red, the laser beam will be reflected by a coated plastic reflector. The backscattered PA wave from the target will be transmitted through it, and collected by the transducer array located at 2f image plane. The beam delivery is designed to have less than 50% power loss which is expected to be readily sterilized for use in-vivo. In terms of photons, this means that at a wavelength of 850 nanometers (nm), for example, the laser produces about $1.7 \times 10^{17}$ photons, and this number cannot be reduced to $7.85 \times 10^{16}$. Another factor that must be considered is its effect on the propagation of generated US waves – the backscattered
US signal cannot undergo a noticeable amount of refraction through the optical reflector. Also, due to the fact that the probe will be filled with water in the experiment, in order to allow for the maximum transmission of the signal, the material for this reflector needs to be a plastic with an acoustic impedance similar to that of water, which is around 1.5 megarayls (Mrayl). Given these considerations, a 0.52 millimeter (mm) thick piece of TPX plastic covered with a piece of Aluminium coated Mylar film was chosen, due to its high reflectance of laser light in the visible to near infrared spectrum and acoustic impedance matching with water.
Figure 6.2: The PVDF film and the optical reflector. The PVDF film, as shown blue, is immobilized at the bottom of the probe for US image generation. The optical reflector, shown in red in the figure, is designed to reflect the horizontally incident laser light to the vertical direction in order to excite the phantom placed at the $2f$ plane for PA image generation.
6.3 Experimental verification

6.3.1 Laser incidence problem

However, in the experiment, it is found that the coated plastic reflector did not effectively reflect the laser, whose main problem is the sharply reduced energy after the reflection which makes it impossible to provide enough signal to generate a PA image. Therefore, we were unable to simultaneously explore both of the two imaging modalities in one attempt. In order to investigate the dual mode imaging capability of the probe, a compromise was adopted, in which the PA and US imaging experiments were carried out separately by changing the initial incident direction of the laser. The imaging process of the US is the same as has been described in Sect. 5.4, where the PVDF film is attached to the bottom of the probe and the phantom is imaged through the backscattered signal. The PA image, however, is generated by the laser beam that is incident from the bottom of the probe, rather than through the previously designed reflector located at the center of the probe. In this way, two imaging modalities can be tested in the same probe. This one-to-two imaging compromise reduces the need for system synchronization, but at the same time increases the time required for imaging. However, its ability to investigate the feasibility of the dual mode imaging camera, which is the main purpose of the experiment, is beyond doubt.

6.3.2 Experimental setup

Fig. 6.3 shows the phantom designed for this verification experiment. Two targets, the pencil lead (left) and the needle (right) are embedded in a 2 cm long, 1.5 cm wide and 0.5 cm thick chicken breast which are used for PA and US imaging, respectively. It is noteworthy that in the experiment two targets were truncated to be embedded only in the chicken breast medium, as shown in the area within the red box in 6.3(b), with
other exposed part removed from the phantom. The illustration shown below is just for visualization purposes of the size and position of the target, which does exist some nuances from the actual phantom used in the following experiment.

![phantom and size information](image)

**Figure 6.3**: The phantom for PA and US dual mode imaging: a pencil lead and a needle target embedded in a chicken breast with a size of 2 cm by 1.5 cm and a thickness of 0.5 cm.

Fig. 6.4 further shows the experimental platform built for the experiment, from which the relative position of the phantom on the platform, as well as the mirror used to change the direction of the laser incidence from horizontal to vertical for PA signal excitation, can be clearly observed. The probe is placed vertically in the experiment, as demonstrated in Fig. 6.4(b), where the position of the lens and its focusing effect on the PA signal are also schematically indicated. The method of its US imaging counterpart is the same as has been described earlier in Sect. 5.4. It uses a PVDF film attached to the bottom of the probe for imaging. The 2D scanning of the phantom is completed through the movement of the experimental platform with 25 data taken at each acquisition location for the SNR enhancement.
6.3.3 Experimental results

A new colormap, HSV, is used here for a better presentation of the results of both PA and US. All the results shown here in Fig. 6.5 have been normalized to maximize the visual effect of the target, of which 6.5(a) is the US imaging result while 6.5(b) is its PA counterpart. The clearly discerned background signal depicted in the US image is the primary purpose of incorporating US image into the dual mode imaging camera. This information is able to provide the location of the needle target as well as to depict echoes from the soft tissue background in real time. This will improve physician’s ability to locate the suspicious cancerous region during biopsy. An interesting discovery is that the image of pencil lead can also be faintly distinguished from the US image. However, its signal strength is almost the same as that of the background which is not enough to provide sufficient information. The graphite pencil lead in the PA image, as shown in 6.5(b), is
more separated from the background compared to the US one. Again, it results from the fact that PA imaging provides optical absorption based contrast which gives high specificity and sensitivity to the prototype pencil lead target. Study has shown that it is also able to differentiate cancerous region from the normal tissue on the basis of the concentration of deoxy-hemoglobin and oxy-hemoglobin. However, PA imaging itself alone is not able to provide the anatomical cues, that are required to determine the position of the visualized suspect region relative to familiar prostate landmarks, such as capsule boundary, urethra, etc., which are often visible on US images. This is the main reason why a clinically useful dual modality of PA and US transrectal probe will have the potential to optimize cancerous region selection, encourage targeted biopsies and consequently reduce the unnecessary biopsies. Here, a “simpler” prototype version of tissue equivalent phantom was used to verify the concept of this co-registered image as well as the experimental feasibility of the dual mode imaging probe. A series of experiments on biopsy should be followed up for further clinical validation.

![Figure 6.5: Experimental results of PA and US dual mode imaging.](image)
Chapter 7

Future Work

This chapter, as the end of the entire thesis, briefly summarizes the overall progress of the project. The chapter also analyses existing problems of the current probe design and looks at some perspectives for its future clinical development.

First of all, the project has reached the goals set in the early stage. The concept of incorporating ultrasound (US) imaging into our existing photoacoustic (PA) imaging probe for a dual modality co-registered image generation has been validated in both simulation and experiment. It is accomplished with the use of a polyvinylidene fluoride (PVDF) film as an US plane wave generator, located on and perpendicular to the lens axis. The signal-to-noise ratio (SNR) of the US imaging component has been significantly improved in amplitude by driving the film with a frequency modulated (FM) pulse followed by pulse compression technique. The probe, which is fabricated through 3D printing, has demonstrated the potential of generating co-registered images that are suitable for prostate biopsy. The PA and US imaging experiments have been performed on the tissue equivalent phantoms for performance validation.

Of course, some existing problems with the probe design did emerge as the project
progresses. The first is the signal loading problem of the PVDF film, as mentioned in Chap. 5. The film currently only accepts signals up to 30 microseconds (µs). Therefore, the duration of the signal was controlled for 10 µs in the experiment to reduce its load on the film, which leads to the fact that, at current stage, the time-bandwidth product of the signal can only be reset by changing its sweep bandwidth. It is followed by the problem of signal attenuation within the probe, the phenomenon of which is evident, in particular, by comparing the experimental result of the prototype camera given in Sect. 5.2 with that of the 3D printed probe presented in Sect. 5.4. An average attenuation of 30% has been observed with the same amplitude signal as input. For the sake of the film protection, we were unable to load it with signals above 5 volts (V) in amplitude. Coupled with scattering of the signal by the medium of phantom, and further attenuation of it propagating in the probe, it is almost impossible to detect any signals on the sensor side. This prevented us from using the Multipurpose US Phantoms Box to further determine the quality metrics of the dual mode imaging probe. Therefore, the overall design of probe and its material selection need to be further optimized in the future research. Last but not least, the problem with the laser reflector, as discussed in Chap. 6. If the dual mode camera requires simultaneous data acquisition of both PA and US, finding a material that can efficiently reflect laser beam without interfering with the propagation of the resulting PA and backscattered US signal, will be a top priority for the final success of the project. Also, due to the difference in signal intensity of PA and US imaging, which can be clearly observed in Fig. 6.5 where both images have to be normalized for a visualization purpose, how to weight the signals acquired from different imaging mechanisms in practice in order to successfully provide physicians with the best combined image will also be a focus of clinical practice in the future. This requires the co-registered image to both depict echoes from the soft tissue background in US imaging as well as to demonstrate the signal from malignant tissue in its PA counterpart.
All in all, the project has taken the idea of a dual mode PA and US transrectal imaging probe from proof of concept to an actual working prototype. It is ready, at this point, for improvements of further in-vivo studies that will be necessary for the use in humans, such as faster real time frame rate and more uniform and higher lase intensity delivery to the tissue surface. We look forward to its ultimate success!
Bibliography


