PhotoMedicine Labs

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# PROGRESS REPORT OF 2020

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# Overview

The PhotoMedicine Labs is a research group within the Department of Systems Design Engineering at the University of Waterloo. Principle Investigator (PI), Professor Parsin Haji Reza, formed the PhotoMedicine Labs in September 2018, with the vision to nurture and grow this group into a major hub within the fields of biomedical optics and medical imaging. Throughout 2020, our lab has received significant notoriety and has been the source of several innovative discoveries.

We at the PhotoMedicine Labs are focused on designing and developing novel engineering systems for clinical and pre-clinical biomedical applications. These technologies aim to provide clinicians and researchers with novel tools and information which are presently difficult or impossible to obtain with existing techniques. Our philosophy involves translation of research from bench to bedside through investigations into fundamental biomedical imaging technologies with relevant real-world applications. Supported by our skilled interdisciplinary research team, we investigate, design, and develop our own in-house hardware and software systems.

This includes but not limited to research activities in state-of-the-art optical imaging systems, photoacoustic, nonlinear optics, optical sensing, fiber-optics, data acquisition, electronics, software development, image processing, machine learning, artificial intelligence, ultrasound, instrument control, analytical modeling and numerical modeling. We also design, perform and analyze significant pre-clinical and clinical experiments.

The PhotoMedicine Labs aim to offer innovative medical imaging techniques in the field of digital pathology, oncology, pre-clinical research, drug discovery, and ophthalmology. The central goal is to physically build, optimize, and characterize novel hardware and software imaging systems capable of recovering diagnostic cellular-scale information in-situ. The developed hardware and software systems will be used toward imaging in human tissues, including benign and malignant tumors, and imaging within the human eye. This will involve development from applications of fundamental physical phenomena into physical devices that are intended for use as a clinical tool. To progress along this path, we will continue to grow our extensive collection of interdisciplinary talents from graduate students, postdoctoral fellows, scientists, engineers, and clinicians.

In spite of the challenges that we all faced and several months of being locked down, 2020 was an amazing year for the PhotoMedicine Labs. We have achieved ground-breaking accomplishments throughout the year and are blessed and honoured to have some of the most hardworking, dedicated, and talented students and staff on our team that makes what we do each and everyday possible.

Currently, the PhotoMedicine Labs have two state-of-the-art optical and hardware design labs (Discovery and Imaging labs) and an image processing & machine learning lab. In addition, we have a pre-clinical imaging lab, in which we perform cell culture and pre-clinical model studies. We have also established the necessary ethics approval to work on freshly resected human tissues (healthy and cancerous). To that end, we have also been working on extramural collaborations, securing lab spaces with major local hospitals such as Grand River Hospital in Kitchener, Ontario and Southlake Regional Health Centre in Newmarket, Ontario. Following the COVID-19 pandemic, we will start our oncology research program within these hospitals. This will allow us to test our hardware, software, and pre-clinical developments in a real clinical setting to compare our results with the current gold standard methods. We are also in the process of securing infrastructure and ethics approval to start our Eye Disease and Blindness research program with the University of Waterloo Optometry School.

The track-record of the PhotoMedicine Labs this last year shows that our team is on the right path to push the boundaries of biomedical optics and medical imaging. With the support of our donors, colleagues, department, and faculty, our lab will continue to focus on biomedical breakthroughs, and attract top talents in the field. Within this report you will discover the substantial progress that the PhotoMedicine Labs has made in 2020. If you wish to follow our process along the way, please check out our website (https://www.photomedicinelabs.com/) or follow us on our LinkedIn (https://www.linkedin.com/company/photomedicine-labs).

# Research Accomplishments

In 2020, the PhotoMedicine Labs achieved several major research accomplishments.

- First in-vivo, non-contact photoacoustic images of ocular tissues.
- First report of H&E-like histological imaging methods using a non-contact optical absorption-based modality.
- First dual wavelength and "true" PARS® H&E images targeting both DNA and cytochromes.
- First non-contact photoacoustic imaging to show histology-like images in human tissue samples.
- First report of histology- like images using PARS® microscopy in various human samples: brain, skin, breast, gastrointestinal and many more.
- First report of a label-free non-contact H&E like imaging technique that can image all the intermediate histopathology steps (FFPE blocks and slides, frozen sections, and fresh unprocessed tissues).
- First report of a fully non-contact optical absorption spectrometer.
- The first 3D non-contact optical resolution photoacoustic microscopy.
- The first real-time non-contact optical resolution photoacoustic microscopy.
- First report demonstrating that PARS® imaging can be incorporated into the standard histopathological processing stream without affecting staining and further processing.
- First rapid high-resolution mosaic acquisition for non-contact photoacoustic imaging methods.

# The PhotoMedicine Labs Research Team

Our research team is made up of some of the best and brightest minds in the field. All the work that we accomplish would absolutely not be possible without each and every one of our staff and students paving the way for amazing research to take place. It is truly their hard work and dedication towards making the world a better place that makes PhotoMedicine Labs such a sought-after research lab to work for. The atmosphere in the group is full of passion and knowledge which welcomes everyone coming through its doors. There are always new changes and challenges taking place, and the team that we have built allows us to work through them together.

As the principal investigator, Parsin Haji Reza's strong desire to teach motivated him to create and grow the PhotoMedicine Labs to what it is today. Our lab aims to provide a unique research experience for all those who work with us. By doing so, we are able to assist everyone in discovering their strengths, help them to grow, and find purpose in life. We hold the teaching philosophy that learning can be impactful and can impart the desired knowledge and skills to students. We create relationships with our team members that motivates them. We believe, students should know what they have to learn, why they have to learn it and how they can apply their creativity.

Every year we receive many requests and applications from eager students who have a passion for research. These bright minds seek to work with our lab to receive an experience like no other. We at the PhotoMedicine Labs are passionate about teaching young minds from all backgrounds who value the importance of hard work, creativity, dedication, and fun within research.

The global pandemic issued some challenges for our lab. We took them head on, working with available resources to the best of our abilities. In 2020, we were able to provide research opportunities for nine Undergraduate Research Assistants (URA), and one co-op student. We also brought on board, three masters students, two PhD students and one Postdoc, one research associate and one research assistant.

This year also brought a bittersweet moment. We had the honour of seeing three of our team members pursue new adventures in their careers. Two of our master's students completed their degrees and graduated, while one of our Postdocs also received a job offer from an engineering company in the United States.

Overall, the PhotoMedicine Labs since January 2019 (effective start date) have worked with in total, 20 URAs, 6 co-op students. 7 masters students, 3 Ph.D. students, 2 post-docs, 1 research assistant, 1 research associate and 1 visiting scholar.

# The PhotoMedicine Labs Research Team

## Since September 2019

- Kevan Bell
- Zohreh Hosseinaee
- Marian Boktor
- Nicholas Pellegrino
- Layla Khalili
- Benjamin Ecclestone
- Lyazzat Mukhangaliyeva
- Alkris Warren
- Shahid Haider
- Saad Rasheed Abbasi
- Jasmine Chan
- Nima Abbasi
- Alex Tummon Simmons
- Auguste Koh
- Muhammad Mohsin
- Furqan Syed
- YanYan Tran
- Anne Mei
- Sheen Thusoo
- Martin Le
- Chandu Subramaniam
- James Tweel
- Daniel Javaheri-Zadeh
- Moujan Saderi
- John Quinto
- Aysegul Alpay
- Natasha Willis
- Yun Kim
- Bazil Lorenzo Sonier
- Amir Mohammad Farzaneh
- Cassandra Maxwell
- Amanda Hope
- Maggie Zhang
- Karam Danial
- Serene Abu-Sardanah
- Mikaela MacMahon

# Awards

Our entire team worked extremely hard and was highly dedicated to their research activities. This paid off as shown by the number of different awards and accomplishments multiple members received in 2020. We are proud to recognize the following awards received by the PhotoMedicine Labs team.

Awards earned by our principal investigator:

- Our PI, Dr. Parsin Haji Reza received the Faculty of Engineering Distinguished Performance Award from the University of Waterloo.

Awards earned by our graduate students:

- Saad Abbasi our master's student received the Optical society of America (OSA) Student Paper Award from OSA Biophotonics Congress: Biomedical Optics.
- Benjamin Ecclestone our master's student received the Engineering Excellence Fellowship.
- Benjamin Ecclestone our master's student received the Dean's Entrance Award.

Awards earned by our undergraduate students:

- Three of our undergraduate students received the President's Research Award to work in the PhotoMedicine Labs.
- One of our co-op students won the NSERC Undergraduate Student Research Award (USRA) to work in PhotoMedicine labs.

# News

In 2020, the PhotoMedicine Labs and its research was highlighted by multiple news agencies.

May 2020:

- New Frontiers in Research Fund (NFRF) awarded to SYDE Professor Parsin Haji Reza and PhotoMedicine Labs. This research fund awards $46.3 million for Exploration projects that push research boundaries in Canada. Read more here.

June 2020:

- Our paper "All-optical Reflection-mode Microscopic Histology of Unstained Human Tissues" presented by graduate student Saad Abbasi at the 2020 OSA Biophotonics Congress: Biomedical Optics has been awarded the OSA Student Paper Award. Read more here.

August 2020:

- Our paper "Deep non-contact photoacoustic initial pressure imaging" is one of the top downloaded papers in the field of Biophotonics over the last two years from Optica.

October 2020:

- "New laser imaging could precisely guide doctors during brain surgery."
  Researchers have taken an important step in the development of a microscope to precisely guide doctors during surgery to remove brain tumors. Our newest news article featured on the University of Waterloo's - Waterloo Stories.

November 2020:

- Nikon Instruments recently highlighted the publication in scientific reports led by Professor Parsin Haji Reza and his team. Read the full story here.

# Grant Applications

The PhotoMedicine Labs received several prestigious grants from some of the top funding agencies in the country. In 2020, we received ~ $1.2M in funding from sources including New Frontiers in Research Fund (NFRF), Industry Partnerships, and Canada Foundation for Innovation (CFI), to name a few.  To date, the PhotoMedicine Labs has received a total of ~$2.3M in funding since our start date (September 2018).

The highlight of these grants is that from the New Frontiers in Research Fund (NFRF). This research fund was given to only 186 recipients nationally, a success rate lower than 3 to 5%, from various fields of research. The NFRF is a federal research funding program that fosters world-leading discovery and innovation by encouraging Canadian researchers to explore, take risks, lead, and work with partners across disciplines and borders. It supports research that defies current paradigms, bridges disciplines, or tackles fundamental problems from new perspectives.

The NFRF's Exploration stream addresses gaps in the federal funding system to innovation. It supports research that defies current paradigms, bridges disciplines, or tackles fundamental problems from new perspectives. The Exploration grants support a wide range of research topics—from developing ultrasound and photoacoustic technologies for detecting cancer, to supporting Inuit youth environmental leaders, to using drone-aided networks for communications in remote communities. The topics all share a unique interdisciplinary approach and the potential for game-changing outcomes in social, cultural, economic, health-related, or technological areas that may benefit Canadians.

For the NFRF, principal investigator (PI) and director of the PhotoMedicine Labs, Prof. Parsin Haji Reza and his team proposed working towards the next generation of surgical microscopes for real-time virtual histopathology. This would allow the ability to accurately distinguish between cancerous and healthy tissue, which is currently impossible in intraoperative conditions (during surgery). For decades, histology has been the gold standard for post-operative margin analysis, taking several days or weeks depending on the case and specimen. The proposed research brings together engineering and medical experts to advance Photoacoustic Remote Sensing (PARS®) Microscopy, a non-contact, high-resolution technology that can image the margins of a surgical cavity in real-time. Unlike conventional histopathological tools, PARS® may provide imaging feedback while tissues are still in situ, meaning pathologic analysis can be done in a matter of seconds. The outcome would be dramatically shortened operation times, increased throughput of surgeries per day per operating room, improved patient prognosis, and decreased anesthetic complications for patients. New techniques to skew the battle against cancer will benefit patients, clinicians, and the healthcare system.

# Collaborators

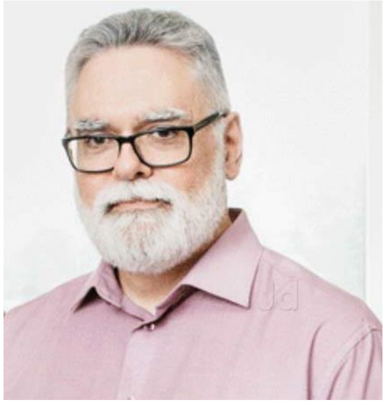
Our research team is made up of some of the best and brightest minds in different fields of research and medicine. All the work that we accomplish would absolutely not be possible without each and every one of our collaborators.

## Professor John Mackey, MD

Professor and Director, Clinical Trials
Department of Oncology
Division of Medical Oncology
University of Alberta

## Dr. Deepak Dinakaran, MDCM, PhD

Resident Physician
Department of Oncology
Division of Radiation and Experimental Oncology
University of Alberta



## Dr. Gilbert Bigras, MD, PhD

Associate Professor
Department of Laboratory Medicine & Pathology
Faculty of Medicine & Dentistry.
Division of Anatomical Pathology
University of Alberta

## Dr. Paul Fieguth, PhD

Professor and Vice-Dean
Policies and Resources; Interim Associate Dean, Outreach
Faculty of Engineering
Department of Systems Design Engineering
University of Waterloo

## Dr. Muba Taher, MD

Clinical Professor of Medicine
Department of Medicine
Division of Dermatology Fellow
American College of Mohs Surgery
University of Alberta

## Dr. Frank K. H. van Landeghem, MD

Associate Professor
Department of Laboratory Medicine & Pathology
Division of Anatomical Pathology
University of Alberta

## Dr. Hamid Tizhoosh, PhD

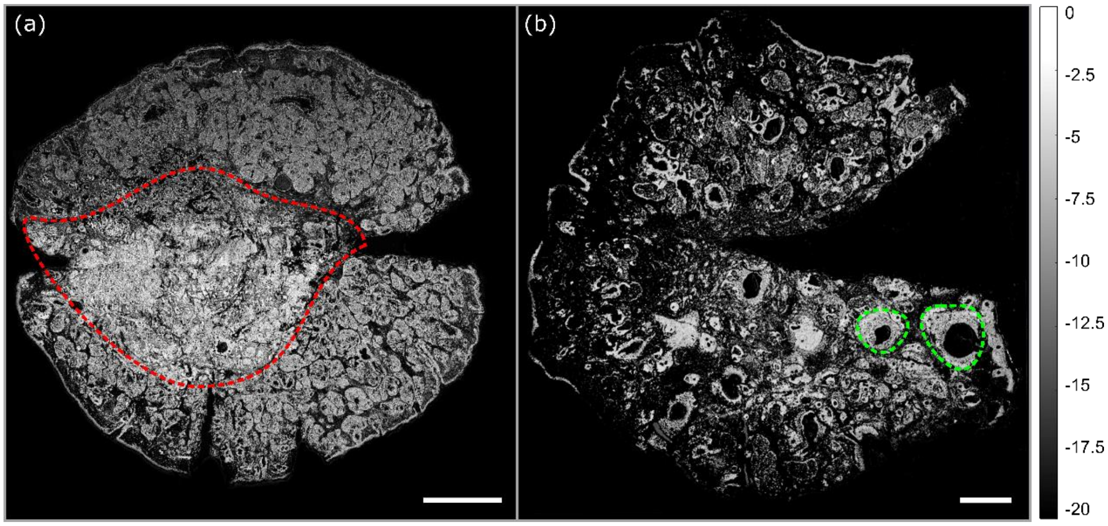
Professor
Faculty of Engineering
Department of Systems Design Engineering
University of Waterloo

# Published Manuscripts

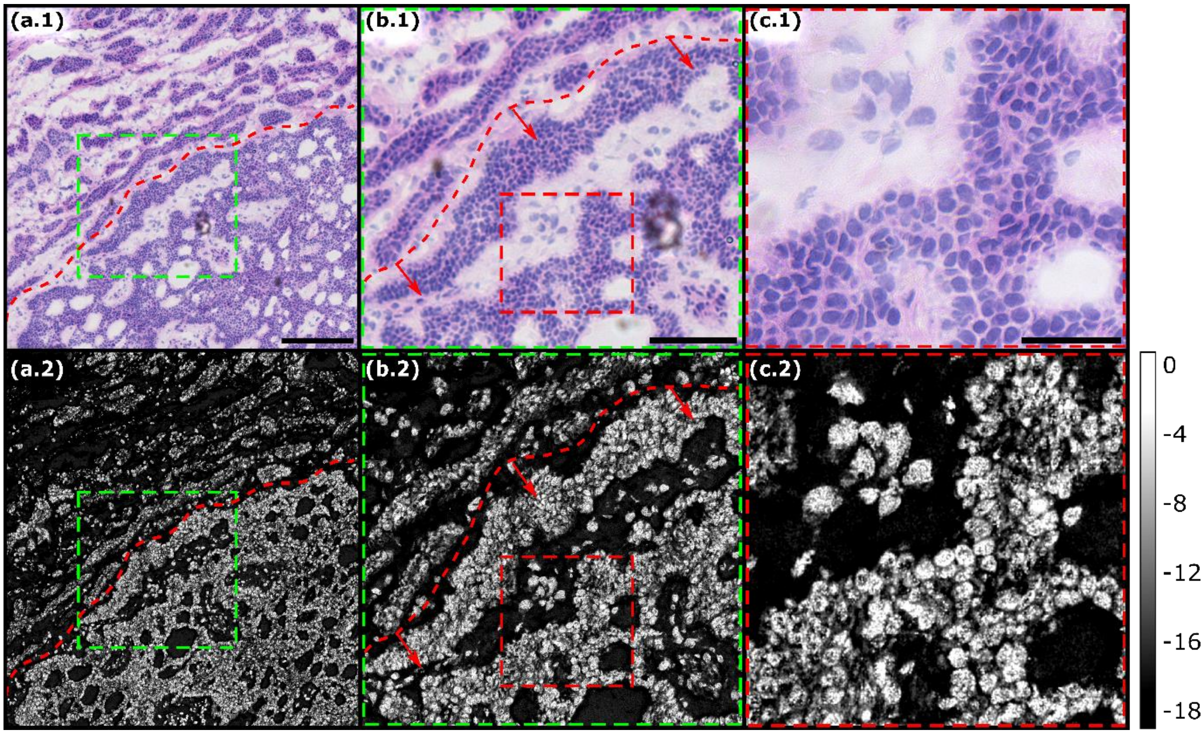
2020 was an amazing year for publications at the PhotoMedicine Labs. This year, the PhotoMedicine Labs had 11 publications in the field of biomedical optics and biophotonics within multiple reputable journals, such as Quantitative Imaging in Medicine & Surgery, Optics Letters, Photoacoustics, Scientific Reports, and Sensors. Each one of these published papers supports an incredible novelty and advancements in the field of Biomedical Imaging and our PARS® technology.

*1. Benjamin R. Ecclestone, Kevan Bell, Saad Abbasi, Deepak Dinakaran, Muba Taher, John R. Mackey, Parsin Haji Reza," Histopathology for Mohs Micrographic Surgery with Photoacoustic Remote Sensing Microscopy," Biomed. Opt. Express, 2020. (Accepted).*
[https://arxiv.org/abs/2009.08337](https://arxiv.org/abs/2009.08337)

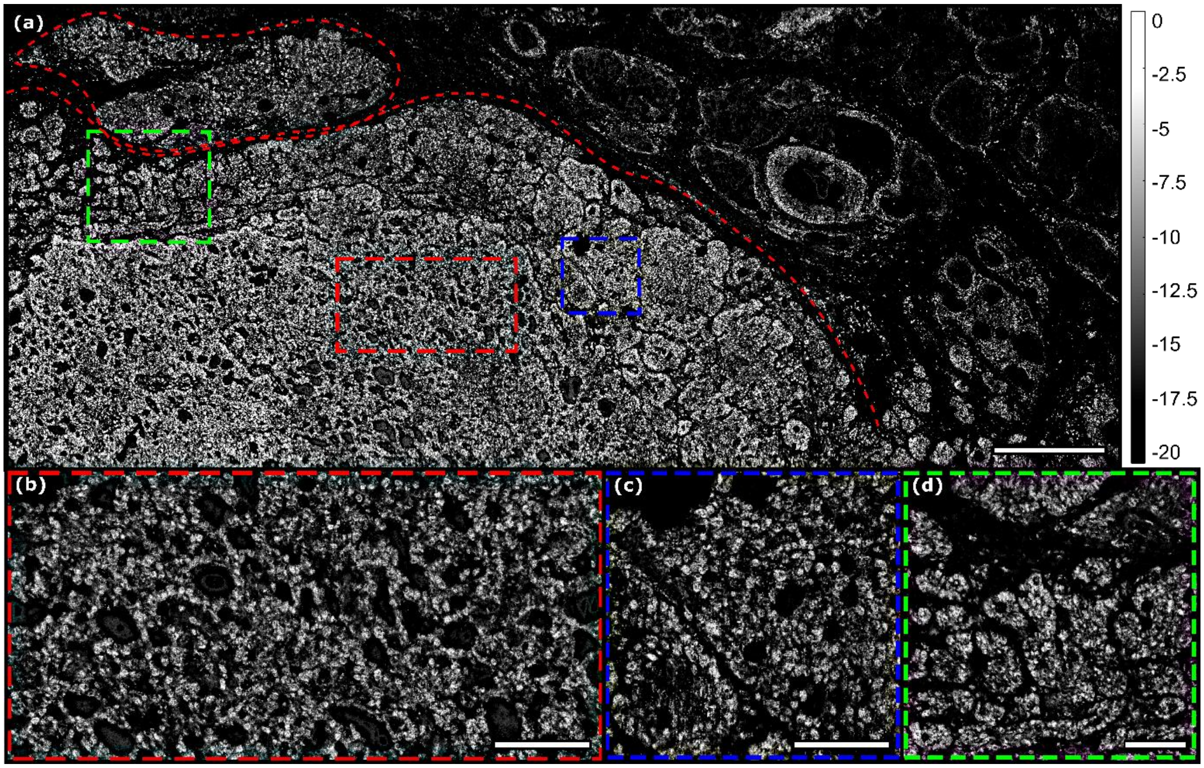
In this article several key milestones were achieved. First, this presented the first true one-to-one comparison between the same pieces of human tissue imaged both with a UV-excitation PARS® and conventional histopathological techniques. This was accomplished by taking frozen sections from MMS procedures, imaging them with our PARS® system and then staining the same piece of tissue followed by imaging with a conventional pathology microscope. These comparisons demonstrate that the same morphological elements can be extracted between the two methods. Another highlighted aspect is that PARS® can be incorporated into the standard histopathological processing stream without affecting downstream staining and further processing. Imaging with a PARS® device did not appear to adversely impact future tissue processing.




Wide field of view PARS® images of entire Mohs excisions. a) 13 mm by 13 mm PARS® image of human skin tissue with basal cell carcinoma (red outline) shown by the increased cellularity in the middle (deep) margin causing invasion and architectural distortion of the normal skin (scale Bar: 2 mm). b) 10 mm by 10 mm PARS® image of human skin tissue, where two examples of hair follicles are circled in green (scale Bar: 1 mm). Both a & b feature a 4 µm lateral step size. The notch in the tissue signifies the superior margin and aids in orientation. (Dynamic range presented in decibels).



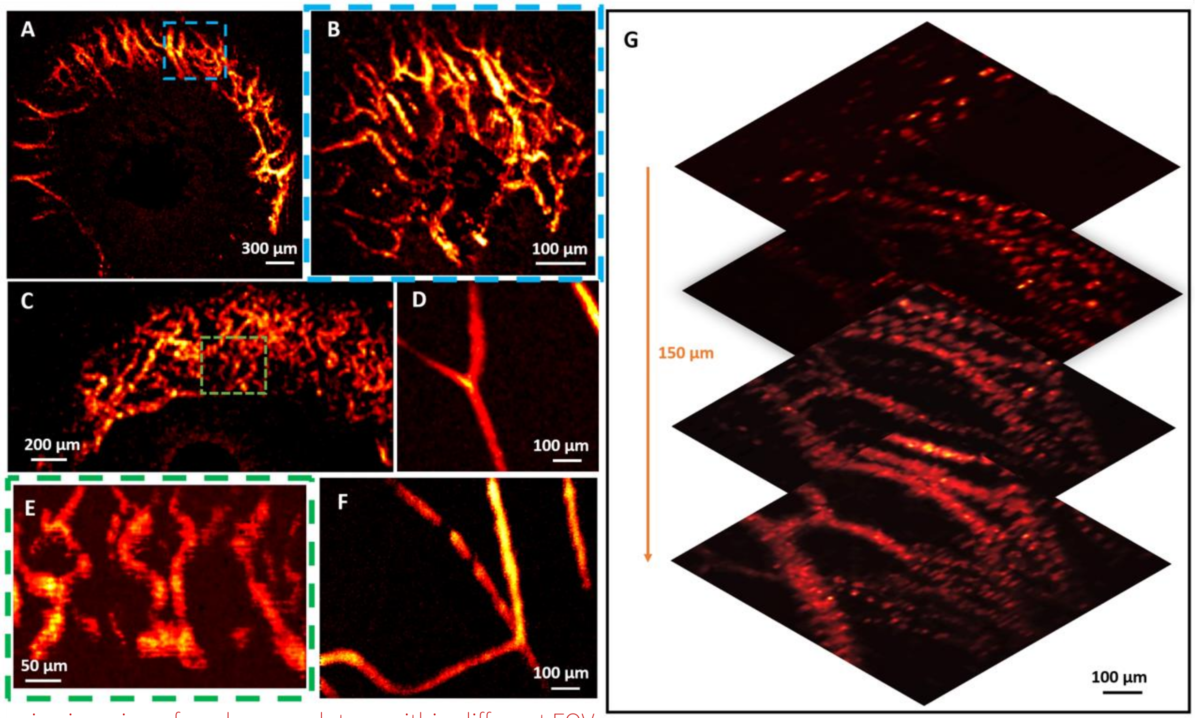

True one to one comparison of PARS® and bright-field images of hematoxylin and eosin (H&E) stained human skin tissue with basal cell carcinoma (BCC). a) (1) 5x bright field image of tissue with BCC demonstrating the border of invasive cancer (bottom of red border) versus normal tissue (top of red border). (2) PARS® image of the same unstained sample with BCC, the same red border denotes the cancer boundary. Scale Bar: 200 µm b) (1) 20x bright field image demonstrating the same cancer margin as in (a.1, a.2). (2) Enlarged section (green box) of the PARS® image (a.2) compares the disorganized cellular architecture seen in the light microscopy (b.1) and PARS® images (the same red border separates cancerous and normal tissues). Scale Bar: 100 µm c) (1) 20x bright field of tissue with clearly identifiable atypical nuclear morphology, size and distribution. (2) Enlarged section (red box) of the PARS® image (b.2), providing a near perfect match to the brightfield histology image (c.1). Scale Bar: 40 µm. (Dynamic range presented in decibels).




Large area high resolution PARS® image of human skin tissue with basal cell carcinoma. (a) A series of four PARS® images stitched together (112-megapixel image, 16000 by 7000-point scan, 250 nm step size) with hypercellularity and nuclear content. Evident disorganized cellular architecture denoting cancerous tissue is enclosed in the red border on the left side with normal tissue in the top and right. Scale Bar: 400 µm (b) Cropped and enlarged section (red box) of the PARS® image shown in (a) Scale Bar: 100 µm (c) Cropped and enlarged section (blue box) of the PARS® image shown in (a) Scale Bar: 100 µm (d) Cropped and enlarged section (green box) of the PARS® image shown in (a) Scale Bar: 100 µm. (Dynamic range presented in decibels).

*2. Zohreh Hosseinaee, Layla Khalili, James A. Tummon Simmons, Kevan Bell, Parsin Haji Reza, "Label-free, non-contact, in-vivo ophthalmic imaging using photoacoustic remote sensing microscopy," Opt. Lett. 45, 6254-6257 (2020).* [https://doi.org/10.1364/OL.410171](https://doi.org/10.1364/OL.410171)

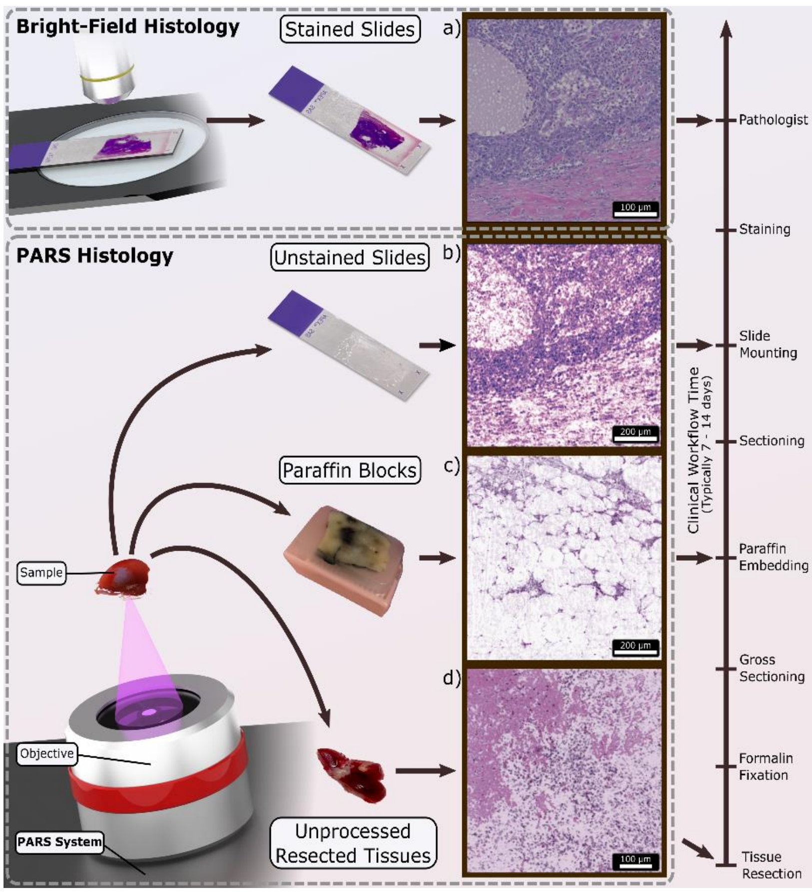
This paper represents the first study showing non-contact photoacoustic imaging conducted on in-vivo ocular tissue, which has been a long-lasting desire in the field of photoacoustic microscopy and ophthalmic imaging. In ocular imaging, one of the significant limitations of photoacoustic microscopes arises from their need to be in physical contact through a coupling media. This physical contact may increase the risk of abrasion, infection, and patient discomfort, additionally, involuntary eye movements may affect the coupling efficiency and degrade image quality. In small animal imaging, immersion in water significantly complicates the procedure and commonly results in sacrificing the animal. PARS® microscopy can overcome these limitations by providing non-contact detection of photoacoustic signals. To make PARS® microscopy suitable for ophthalmic imaging, we made significant modifications to the system. These modifications include employing, eye-friendly 830 nm detection wavelength, suitable scanning pattern and interpolation algorithm, focusing optics and live feedback during in-vivo imaging. The 830 nm probe beam improves photoacoustic signal detection in the ocular environment by having lower absorption in water. Additionally, it reduces the amount of chromatic aberration in the system by having close spectral bandwidth to the 532 nm excitation beam. The PARS® microscope reported in this study, for the first time has employed a telecentric pair, which provides a uniform image intensity and improves the effective imaging field of view (FOV) of the optical scanning. We have also showed the first live feedback imaging in the eye which is beneficial for accurate alignment and to select the right imaging location. The system is used for imaging different regions of the ocular tissue including, iris, scleral and retinal vasculature. We believe that PARS® microscopy has the potential to advance the diagnosis and treatment of ocular diseases



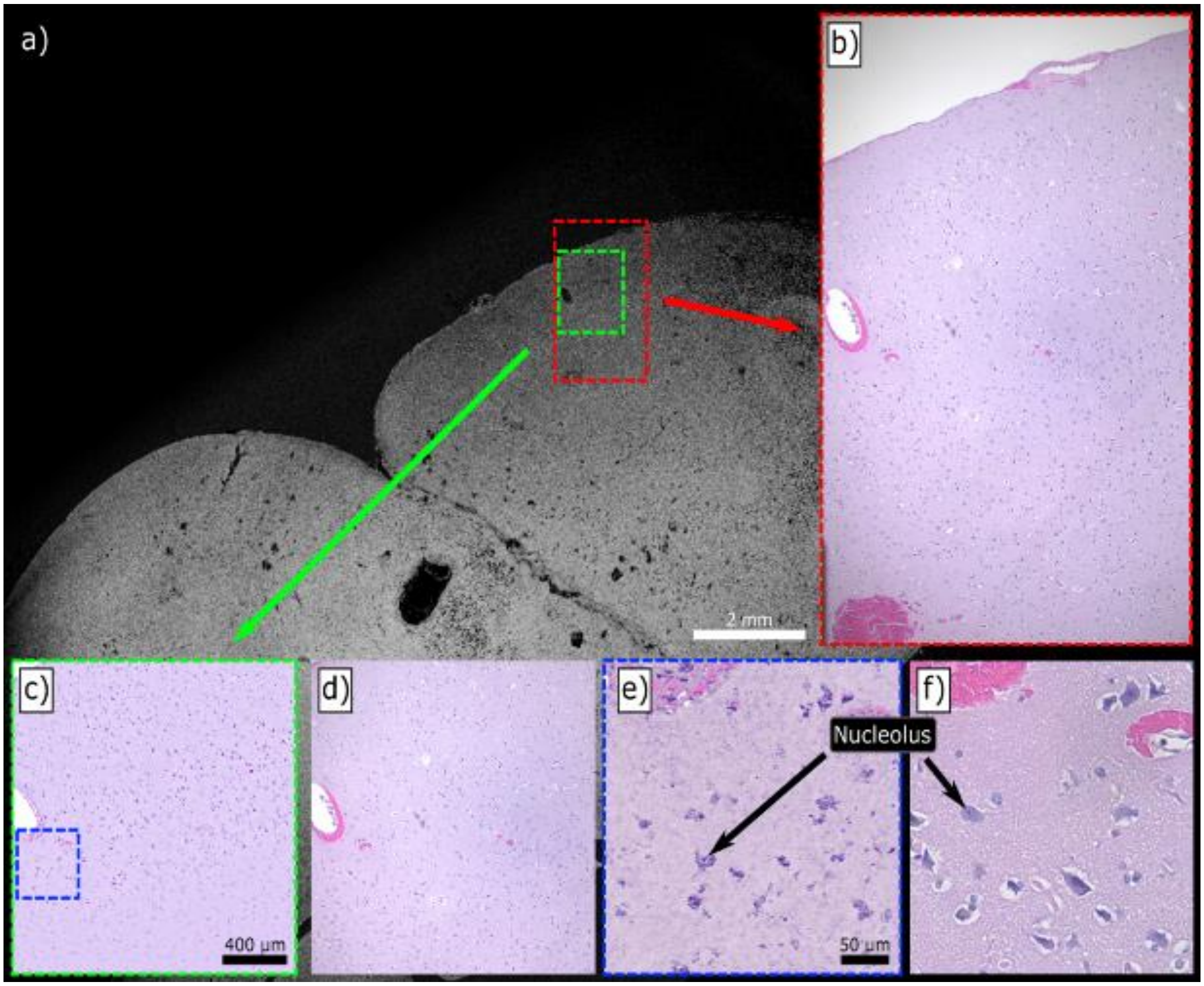

In-vivo imaging of ocular vasculature within different FOVs.

*3. Kevan Bell, Saad Abbasi, Deepak Dinakaran, Muba Taher, Gilbert Bigras, Frank K.H. van Landeghem, John R. Mackey, Parsin Haji Reza, "Reflection-mode virtual histology using photoacoustic remote sensing microscopy," Scientific Reports, 10, 19121 (2020).* [https://doi.org/10.1038/s41598-020-76155-6](https://doi.org/10.1038/s41598-020-76155-6)

This article represents the first concise study which compares the use of UV-excitation PARS® imaging across a wide range of tissue preparations (FFPE blocks and slides, frozen sections, and fresh unprocessed tissues) which is capable of recovering qualitative clinically relevant morphology. One of the central goals of this work was to demonstrate the broad applicability of the technique with minimal-to-no systematic changes between sample type. Although not the first publication on this technique, some of the presented results use the first two-color PARS® imaging system. This took advantage of our tunable hyperspectral PARS® to target both the 250 nm absorption peak of DNA, and the 420 nm hemeprotein absorption peak facilitating visualization of cytoplasmic structure. As well, wide field-of-view regions were captured using our faster histological imaging platform providing cm-scale bulk scanning. Human tissues were compared against adjacent regions which had undergone conventional histological processing providing broad morphological matching.



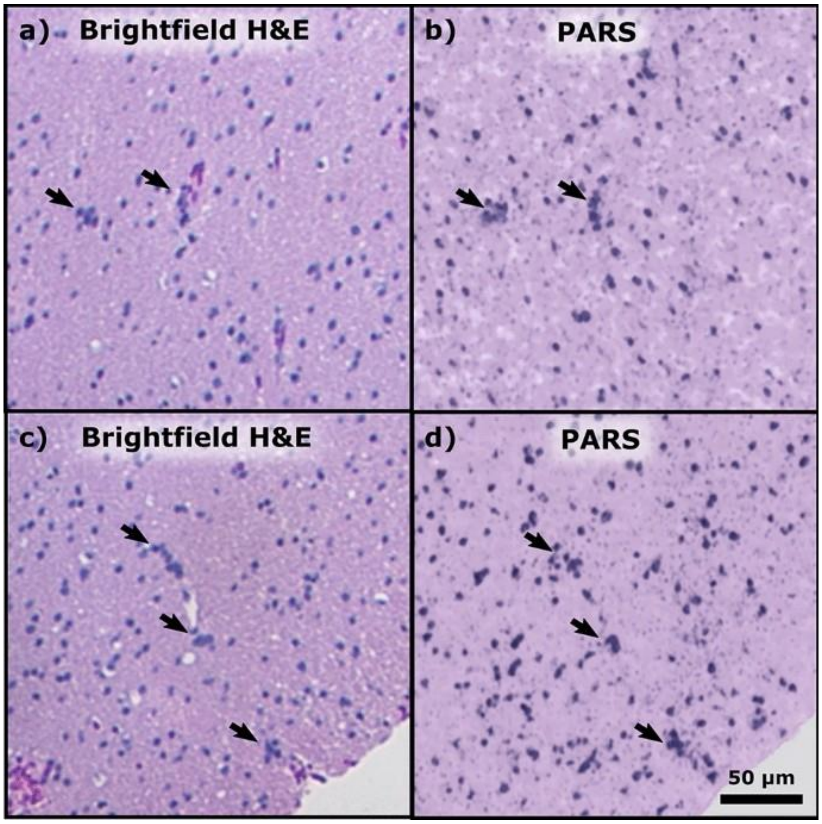

Overview of PARS® histologic imaging workflow as compared to conventional light microscopy. (a) Conventional imaging of H&E-stained slides is performed on a bright-field microscope where the Hematoxylin (purple hues) and Eosin (red hues) stains block light from a white source. PARS® may image (b) unstained FFPE slide preparations, (c) unstained FFPE blocks and (d) unprocessed tissues by taking advantage of the intrinsic optical absorption provided by the cell nuclei (DNA) and the surrounding cytoplasm (cytochrome). We image each intermediate step along the FFPE process in this paper using a single system configuration to show the versatility of PARS®. No other reported technique has reported all of these capabilities in a single modality.



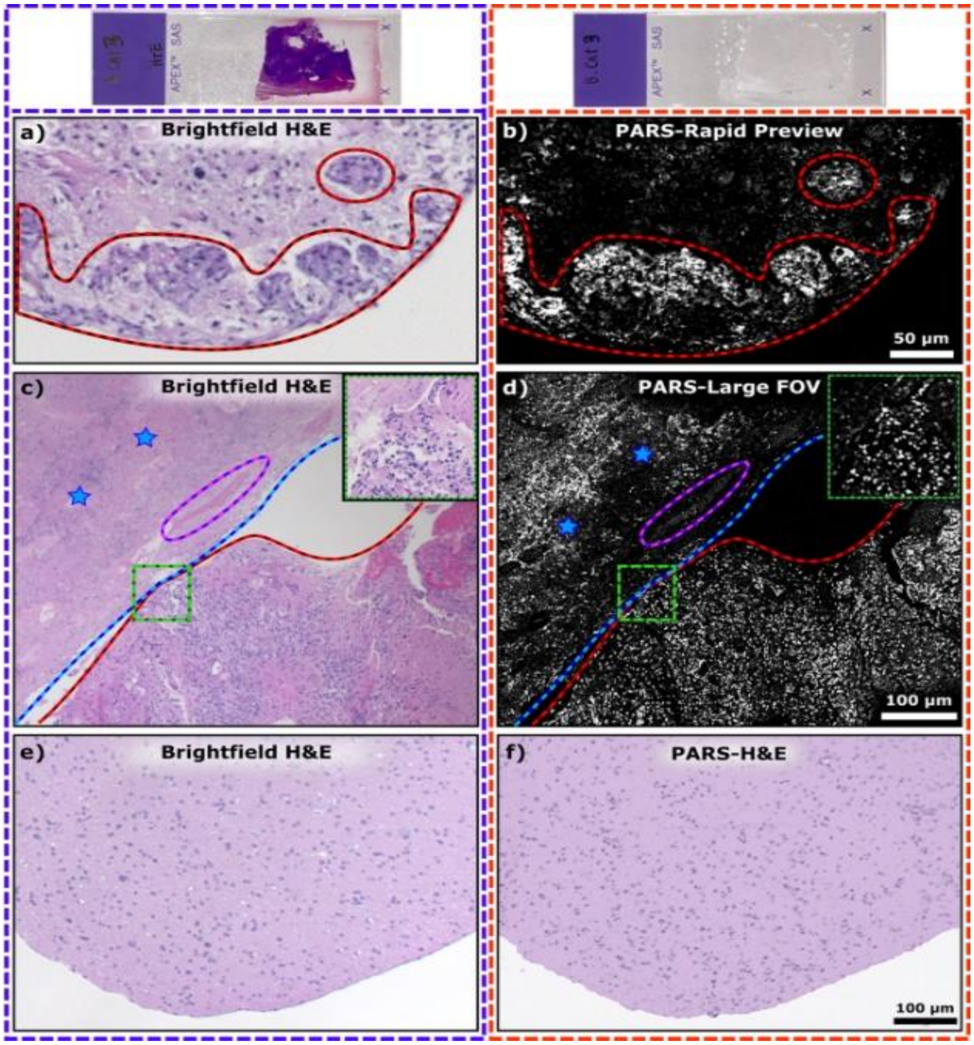

Several comparisons between PARS® and conventional bright-field images of FFPE slides of human brain tissues. a) A wide field of view (WFOV) scan using 266 nm excitation with b) a matching wide field image of the adjacent slide which has been H&E stained. c) A two-color (250 nm and 420 nm) PARS® with a false-colour map applied to match d) the adjacent H&E region. Finally, e) and f) likewise show a two-color PARS® and bright-field image respectively in higher detail.

*4. Benjamin R. Ecclestone, Kevan Bell, Saad Abbasi, Deepak Dinakaran, Frank K.H. van Landeghem, John R. Mackey, Paul Fieguth, and Parsin Haji Reza, "Improving Maximal Safe Brain Tumor Resection with Photoacoustic Remote Sensing Microscopy," Scientific Reports, 10, 17211 (2020).* [https://doi.org/10.1038/s41598-020-74160-3](https://doi.org/10.1038/s41598-020-74160-3)

This article represents the first report of our two-color PARS® imaging system and its application on imaging of FFPE human brain tissues. The two-color architecture facilitated the first reported dual-stained PARS® images which aims to replicate the look of conventional H&E staining. This took advantage of our tunable hyperspectral PARS® to target both the 250 nm absorption peak of DNA, and the 420 nm hemeprotein absorption peak facilitating visualization of cytoplasmic structure. As well, wide field-of-view regions were captured using our faster histological imaging platform providing cm-scale bulk scanning. Another important milestone featured in this publication are the first PARS® images of positive surgical margins where tumors could be clearly delineated from healthy tissue regions. As well, other more subtle clinically relevant features such as oligodentrocytes, necrotic regions, microvascular proliferations, and thrombotic vessels were identified.



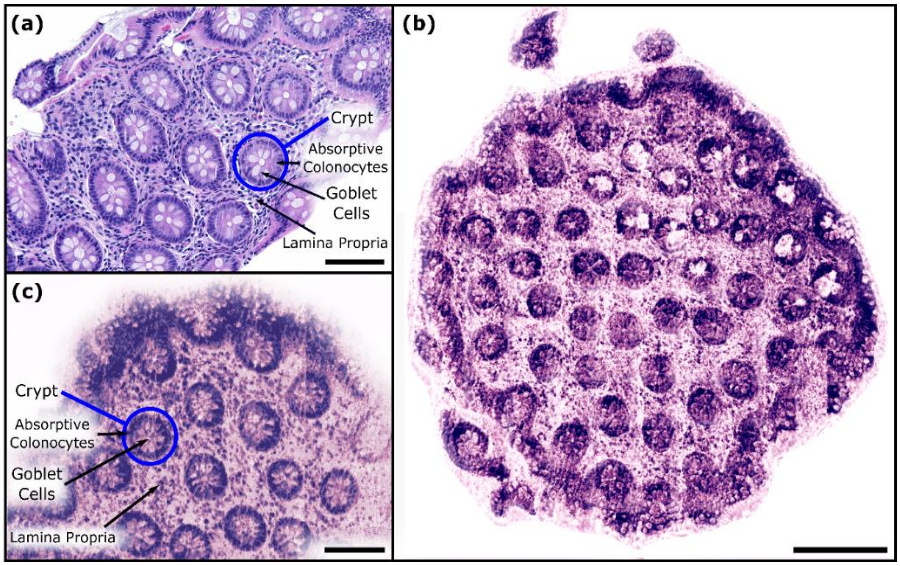

Standard brightfield histology, compared to PARS® H&E. (a, c) Small field of view standard H&E processed white matter tissue with gliosis; perivascular oligodendrocytes are indicated by the black arrows. (b, d) High fidelity PARS® emulated H&E images of adjacent tissue sections showing the same clusters of perivascular oligodendrocytes, marked with black arrows.



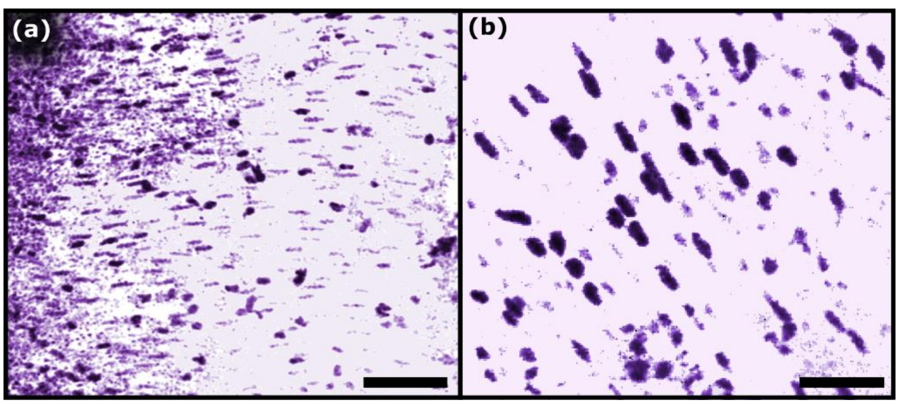

PARS® H&E images of unstained tissue in comparison to their standard histopathological preparations. (a) A conventional bright field H&E image of glioblastoma with solid tumor and microvascular proliferations (red outlines). (b) A rapid acquisition PARS® image of the adjacent unstained brain tissue sample, with the region of solid tumoral tissue, and microvascular proliferations (red outlines), as in (a). (c) A standard bright field histopathological H&E image of a glioblastoma sample with a largely necrotic region (blue lines and stars), a thrombotic vessel (purple outline), and a region of solid tumor with microvascular proliferations (red outline). (d) A PARS® image acquired in a rapid acquisition mode of the same section of glioblastoma tissue, with the largely necrotic region (blue line and stars) and thrombotic vessel (purple outline), and the solid tumor region with microvascular proliferations (red outline), as in (c). A close-up of tumor cells and microvascular proliferations at the boundary between these regions is shown enclosed in the green boxes. (e) A standard bright field histopathological H&E image of a brain tissue sample with infiltrating tumor cells, adjacent to solid tumor shown in (a)–(d). (f) A PARS® multiwavelength simulated H&E image of the same section of brain tissue.

*5. Benjamin R. Ecclestone, Kevan Bell, Saad Abbasi, Deepak Dinakaran, John R. Mackey, and Parsin Haji Reza, "Towards virtual biopsies of gastrointestinal tissues using photoacoustic remote sensing microscopy," Quant Imaging Med Surg (2020).* [http://qims.amegroups.com/article/view/51162](http://qims.amegroups.com/article/view/51162)

This work presented the first PARS® imaging in FFPE human GI tissue blocks along with the first report of PARS® histological imaging within unprocessed freshly resected tissue samples. Wide field-of-views using our older mosaic-based approach were presented of normal colonic mucosa prepared as FFPE tissue slides. Volumes of FFPE tissue blocks demonstrated optical sectioning capabilities. PARS® imaging of freshly resected murine small intestine was presented demonstrating visualization of various tissues such as smooth muscle structure.



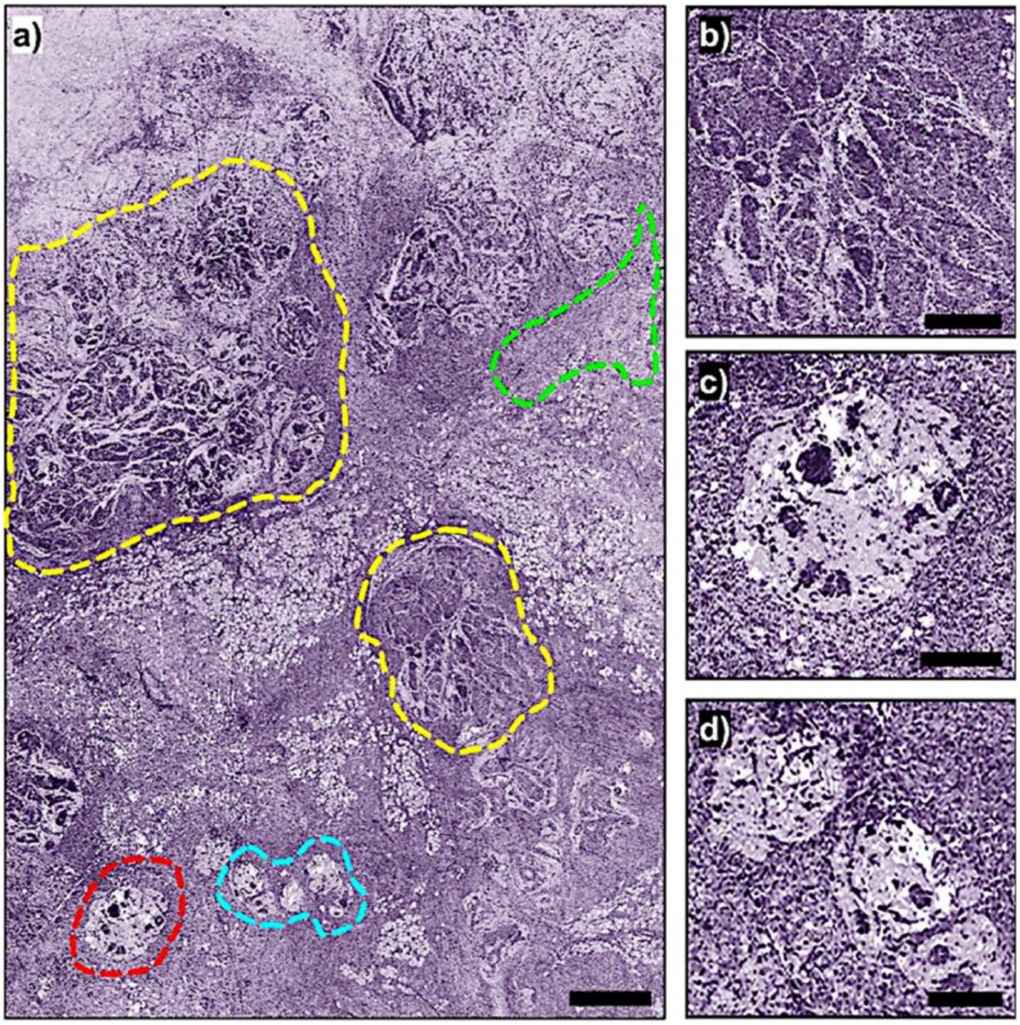

(a) Bright field H&E image of a normal colonic mucosa in sectioned formalin fixed paraffin embedded (FFPE) form. Scale bar: 100 µm (b) Wide field of view PARS® image of unstained sectioned FFPE normal colonic mucosa biopsy. Scale bar: 200 µm (c) Small field PARS® image of unstained sectioned FFPE normal colonic mucosa biopsy. Scale bar: 100 µm. Artificial H&E-like coloring has been applied to the PARS® images.




PARS® images of freshly resected mouse small intestine, highlighting smooth muscle structure (a) Large field of view image. Scale bar: 200 µm (b) Small field of view image. Scale bar: 75 µm

*6. Saad Abbasi, Deepak Dinakaran, Gilbert Bigras, John R. Mackey, and Parsin Haji Reza, "All-optical Label-free Human Breast Tissue Block Histology using Photoacoustic Remote Sensing," Opt. Lett. 45, 4770-4773 (2020).* [https://doi.org/10.1364/OL.397223](https://doi.org/10.1364/OL.397223)

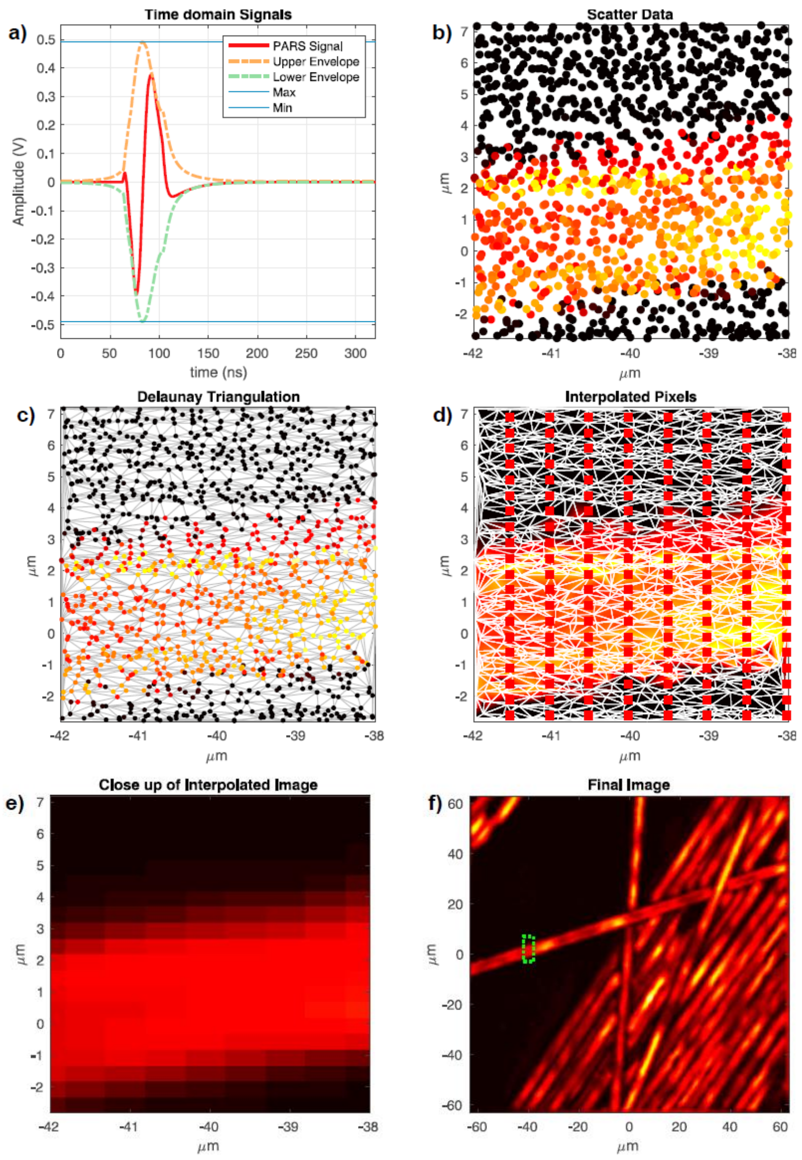
This article represented the first detailed study involving PARS® imaging of unstained FFPE blocks of human breast tissues, highlighting salient features. It was the first report of our wide field-of-view histological imaging platform. Clinically relevant features such as hyperplasia, connective tissues, healthy glands, and ducts were extracted. 3D volumes of FFPE tissue blocks were also presented demonstrating optical sectioning capabilities of the approach.




(a) Wide FOV of a FFPE tissue block with human breast tissue showing ductal hyperplasia (yellow outline), connective tissue (green), normal gland (red), and ducts (blue), scale bar 1 mm. (b) Close up of an abnormal duct, scale bar 400 µm. (c) Normal gland, scale bar 350 µm. (d)Normal duct, scale bar 250 µm.

*7. Saad Abbasi, Kevan Bell, and Parsin Haji Reza, "Rapid High-Resolution Mosaic Acquisition for Photoacoustic Remoting Sensing," Sensors 20(4), 1027; (2020).* [https://doi.org/10.3390/s20041027](https://doi.org/10.3390/s20041027)

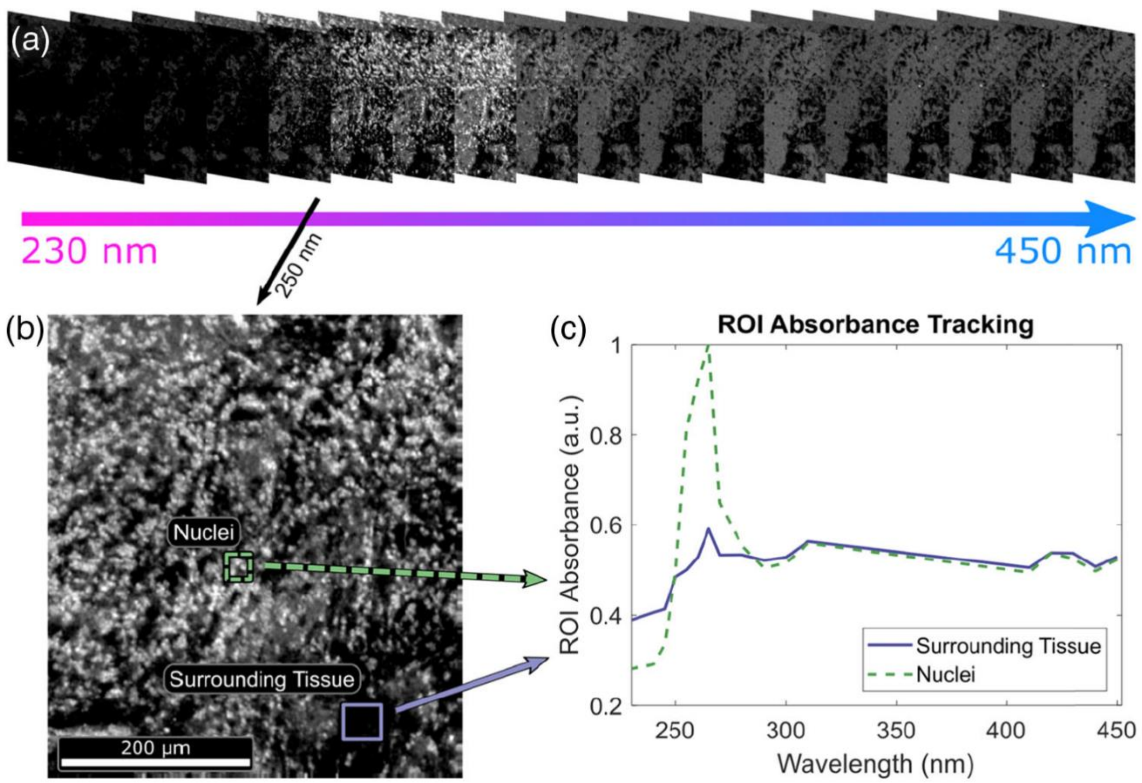
This was a technical article which focused on acquiring large field-of-views from a collection of smaller optical scans through a mosaic-based acquisition approach. It presented details for extracting PARS® signals informing PARS® images. This also discussed methods for implementing rapid real-time PARS® acquisitions. Large acquisitions of carbon fiber networks (400 frames, 20 x 20, covering 9 mm$^2$) were presented.




(a) PARS® time-domain signal with upper and lower envelopes (b) raw scatter data (c) Delaunay triangulation (d) cartesian grid imposed on Delaunay triangulation (e) closeup of interpolated pixels (f) reconstructed image.

*8. Kevan Bell and Parsin Haji Reza, "Non-contact Reflection-mode Optical Absorption Spectroscopy Using Photoacoustic Remote Sensing," Opt. Lett, 45(13), 3427-3430 (2020).*
*https://doi.org/10.1364/OL.394637*

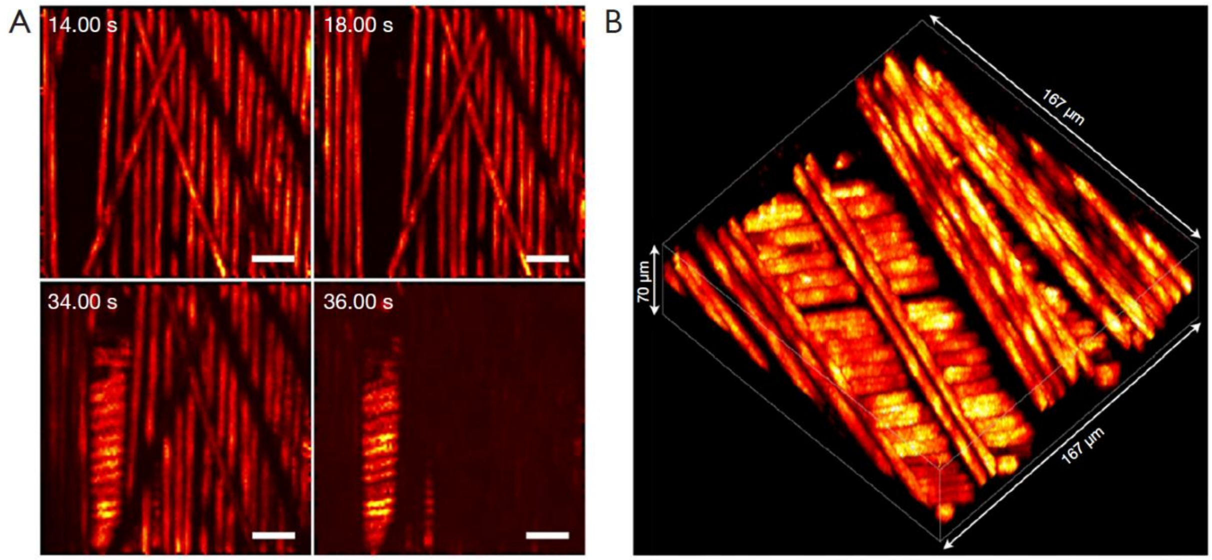
This article represents the first report of a fully non-contact optical absorption spectrometer. This device also represented the first report of a PARS®-based optical absorption spectrometer and the first report of a PARS®-based imaging spectrometer. Our tunable source was operated between 210 nm to 680 nm providing a wide range of characterization wavelengths. The work included discussion of analytical basis for calibration of such a device. Presented were the first PARS® absorption spectra of several substances including three India ink colors, paraffin, histone, DNA, and reduced cytochrome C. Alongside this, the first PARS® imaging spectra taken from FFPE slides of human breast tissue were also presented.




Outline of hyperspectral PARS® imaging with ROI tracking. (a) Set of images acquired on an unstained formalin-fixed paraffin-embedded human breast tissue slide. The same region is imaged consecutively while sweeping the excitation wavelength from 230 to 450 nm. (b) Shows the 250 nm frame from the set and provides one example for nuclear regions and the surrounding tissue regions. (c) The means signal in these ROI are then plotted against wavelength.

9. *Saad Abbasi, Kevan Bell, Benjamin R. Ecclestone, and Parsin Haji Reza, "Live feedback and 3D photoacoustic remote sensing," Quantitative Imaging in Medicine and Surgery (2020).* [*http://qims.amegroups.com/article/view/54005*](http://qims.amegroups.com/article/view/54005)

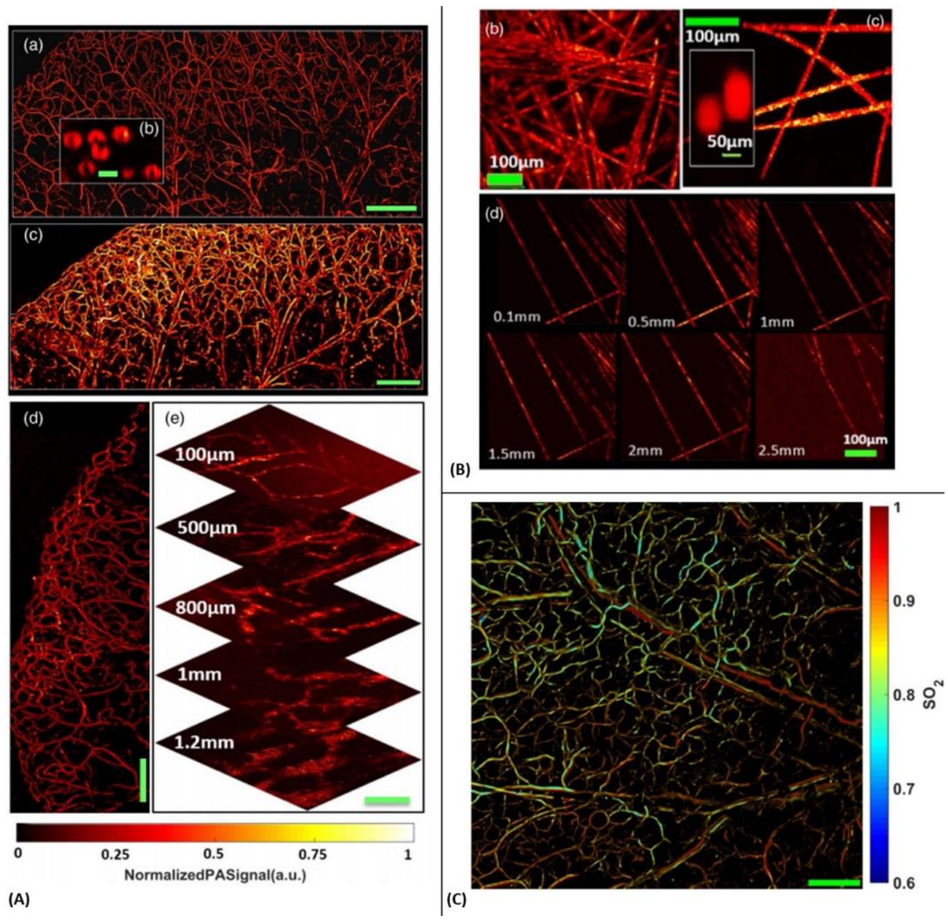
This was a technical article which presented newly improved acquisition methods for use in Photoacoustic Remote Sensing (PARS®) microscopy which are also applicable to other laser-scanning microscopic devices. The focus on these improvements involved facilitating real-time acquisitions and capturing 3D images. Volumes of carbon fiber networks and mouse ear vasculature were presented.




Real-time and 3D imaging of carbon fiber networks. (A) Live display of carbon fibre networks Individual frames extracted from a screen capture of the live display. Time stamp is annotated in the top left corner of each frame. Scale bar: 25 µm. (B) 3D reconstruction using the same method. Field of view is 167 µm2, total depth 70 µm.

*10. Zohreh Hosseinaee, Martin Le, Kevan Bell, and Parsin Haji Reza, "Towards non-contact photoacoustic imaging [review]," Photoacoustics, 20, 100207 (2020).*
[https://doi.org/10.1016/j.pacs.2020.100207](https://doi.org/10.1016/j.pacs.2020.100207)

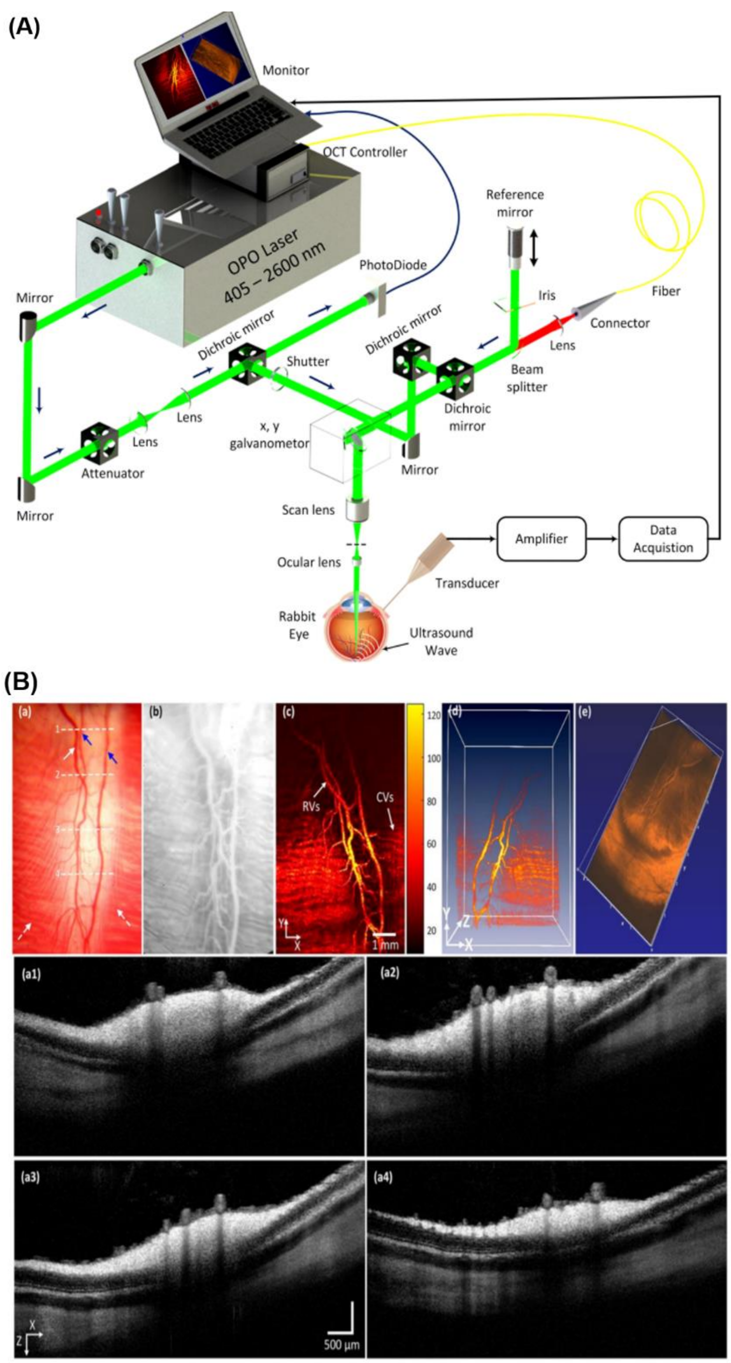
This was a review on the topic of non-contact photoacoustic imaging. It discussed the importance of non-contact photoacoustic techniques in medical applications and provided an overview of previously reported approaches. Topics included air-coupled photoacoustic signal detection, speckle pattern analysis, heterodyne interferometry, and photoacoustic remote sensing microscopy.




(A) In vivo PARS® microscopy structural images. (a) Image of en face microvasculature in mouse ear using the high-resolution mode (Scale bar: 500 µm) (b) In-vivo image of red blood cells in the mouse ear using the high-resolution mode (Scale bar: 5 µm) (c) Image of mouse ear vasculature using the deep-penetrating mode (Scale bar: 500 µm) (d) Image of en face microvasculature in the tip of a mouse ear using the high-resolution mode (Scale bar: 500 µm) (e) Images of back flank of mouse at various depths using the deep penetrating mode (Scale bar: 100 µm) (B) Image of carbon fiber networks using the deep penetrating imaging mode. (c) Image of carbon fiber networks using the high-resolution imaging mode, as well as an inset image of 100-nm gold nanoparticles. (d) Images of carbon fiber networks at various depths in tissue-mimicking solution. (C) Functional images SO2 measurement of en face microvasculature in the ear of an 8-week-old nude mouse. Reprinted with permission.

*11. Zohreh Hosseinaee, James A. Tummon Simmons, Parsin Haji Reza "Dual-modal photoacoustic imaging and optical coherence tomography [review]," Frontiers in Physics, Accepted. (2020).*

This article is a review on the subject of dual-mode photoacoustic imaging and optical coherence tomography (OCT). It discusses the basic mechanisms of the two individual modalities along with their current applications. Challenges of such devices which must be overcome to proceed to a clinical environment are also discussed.




(A) Schematic diagram of the integrated PAM and OCT systems for multimodal retinal imaging. Reprinted with permission from [147]. (B) images of retinal blood vessels in rabbits: (a) color fundus photography of retina. (b) Fluorescein angiography image showing retinal, choroidal and capillaries. (c) Corresponding maximum amplitude projection PAM images of retina. (d,e) volumetric PAM and OCT image, respectively. (a1–a4) Cross-sectional OCT images acquired along the scanning lines from Figure (a). Reprinted with permission from [148].

# International Scientific Conference Presentations

In 2020, the PhotoMedicine Labs had the pleasure to present at three international conferences.

- ❖ The first conference was at the SPIE Photonics West 2020 that ran from February 1-6, in San Francisco, California, United States.

SPIE Photonics West showcases the latest in applications, technologies, and discoveries in optics and photonics, with three major conference tracks: BiOS, highlighting new research in biophotonics, biomedical optics, and applications of medical imaging; LASE, with its focus on the laser industry and applications; and OPTO, showcasing optoelectronics, photonic materials, and related devices. SPIE BiOS is the most important biomedical optics conference in the field. Topics include biomedical optics, diagnostics, and therapeutics, biophotonics, new imaging modalities, optical coherence tomography, neurophotonics, optogenetics, tissue optics, and nanophotonics.

<u>Presentations were given on the following topics:</u>

- Saad Abbasi*, Martin Le*, Serene O. Abu-Sardanah*, Benjamin R. Ecclestone*, Kevan Bell*, Deepak Dinakaran, Gilbert Bigras, John R. Mackey, and Parsin Haji Reza, "All-optical reflection-mode microscopic histology of unstained human tissues." SPIE Photonics West (2020). (Talk)
- Serene O. Abu-Sardanah*, Chandu Subramaniam*, Saad Abbasi*, and Parsin Haji Reza, "A comprehensive characterization of a stimulated Raman scattering fiber-laser source for multi-wavelength dependent photoacoustic microscopy techniques" SPIE Photonics West (2020). (Talk)
- Benjamin R. Ecclestone*, Amir M. Farzaneh*, Kevan Bell*, and Parsin Haji Reza, "Deep optical resolution photoacoustic remote sensing microscopy" SPIE Photonics West (2020). (Talk).
- Nicholas Pellegrino, Saad Rasheed Abbasi, Kevan Bell, Deepak Dinakaran, Gilbert Bigras, John R. Mackey, Paul Fieguth, Parsin Haji Reza, "Chromophore selective multi-wavelength photoacoustic remote sensing." SPIE Photonics West (2020). (Talk).

<u>Posters were shown on the following topics:</u>

- Benjamin R. Ecclestone*, Saad Abbasi*, Kevan Bell*, and Parsin Haji Reza, "Detection and excitation defined systems in photoacoustic remote sensing microscopy." SPIE Photonics West (2020). (Poster).
- Saad Abbasi*, Nicholas Pellegrino*, Serene O. Abu-Sardanah*, Benjamin R. Ecclestone*, Kevan Bell*, Paul Fieguth, and Parsin Haji Reza, "Real time & 3D photoacoustic remote sensing." SPIE Photonics West (2020). (Poster).

❖ The second conference we attended was the OSA Biophotonics Congress – Biomedical Optics 2020 that ran from April 20-23, in Fort Lauderdale, Florida, Unites States. Due to the COVID-19 pandemic, this year's conference was held virtually online. Our PI, Dr. Parsin Haji Reza was a committee member and presider at this conference. The focus for this year at the Biomedical Optics was on technological solutions to medical challenges and medical applications. Engineers, optical and medical scientists, physicians, as well as junior researchers and graduate students, presented and engaged in optical methods to advance discovery and application of medical science leading to the translation of these methods to clinical practice.

<u>Presentations and posters were given on the following topics:</u>

- Saad Abbasi*, Martin Le*, Serene O. Abu-Sardanah*, Benjamin R. Ecclestone*, Kevan Bell*, Deepak Dinakaran, Gilbert Bigras, John R. Mackey, and Parsin Haji Reza, "All-optical reflection-mode microscopic histology of unstained human tissues." OSA Biophotonics Congress: Biomedical Optics (2020). (Talk).
- Kevan Bell*, Saad Abbasi*, Nicholas Pellegrino*, and Parsin Haji Reza, "Hyperspectral Photoacoustic Remote Sensing Microscopy," OSA Biophotonics Congress: Biomedical Optics (2020). (Talk)

<u>Posters were shown on the following topics:</u>

- Saad Abbasi*, Kevan Bell**, Benjamin R. Ecclestone#, and Parsin Haji Reza, "Real Time & 3D Photoacoustic Remote Sensing," OSA Biophotonics Congress: Biomedical Optics (2020). (Poster).
- Martin Le*, Saad Abbasi*, Kevan Bell*, and Parsin Haji Reza, "All-Visible Non-Interferometric Pulsed Detection Photoacoustic Remote Sensing Microscopy," OSA Biophotonics Congress: Biomedical Optics (2020). (Poster).

❖ The third conference was at the EMBC 2020 that ran from July 20-24 in Montreal Quebec, Canada via the EMBS Virtual Academy, where our PI, Dr. Parsin Haji Reza gave an invited talk.

The IEEE Engineering in Medicine and Biology Society had their 42nd Annual International Conference of the IEEE Engineering in Medicine and Biology Society in conjunction with the 43rd Annual Conference of the Canadian Medical and Biological Engineering Society. This conference was offered virtually. The theme of the conference was "Enabling Innovative Technologies for Global Healthcare". As the world's largest international biomedical engineering conference. A broad array of scientific tracks will cover diverse topics of cutting-edge research and innovation in biomedical engineering, healthcare technology R&D, translational clinical research, technology transfer and entrepreneurship, and biomedical engineering education. In addition to the high-profile keynotes, the conference program featured mini- symposia, pre-conference workshops, special sessions, research presentations, sessions for students and young professionals, sessions for clinicians and entrepreneurs, and a virtual exhibit hall.

A presentation was given on the following topic:

- Parsin Haji Reza, “Photoacoustic remote Sensing”, 42nd Annual International Conferences of the IEEE Engineering in Medicine and Biology Society. Montreal Canada (2020). (Talk).

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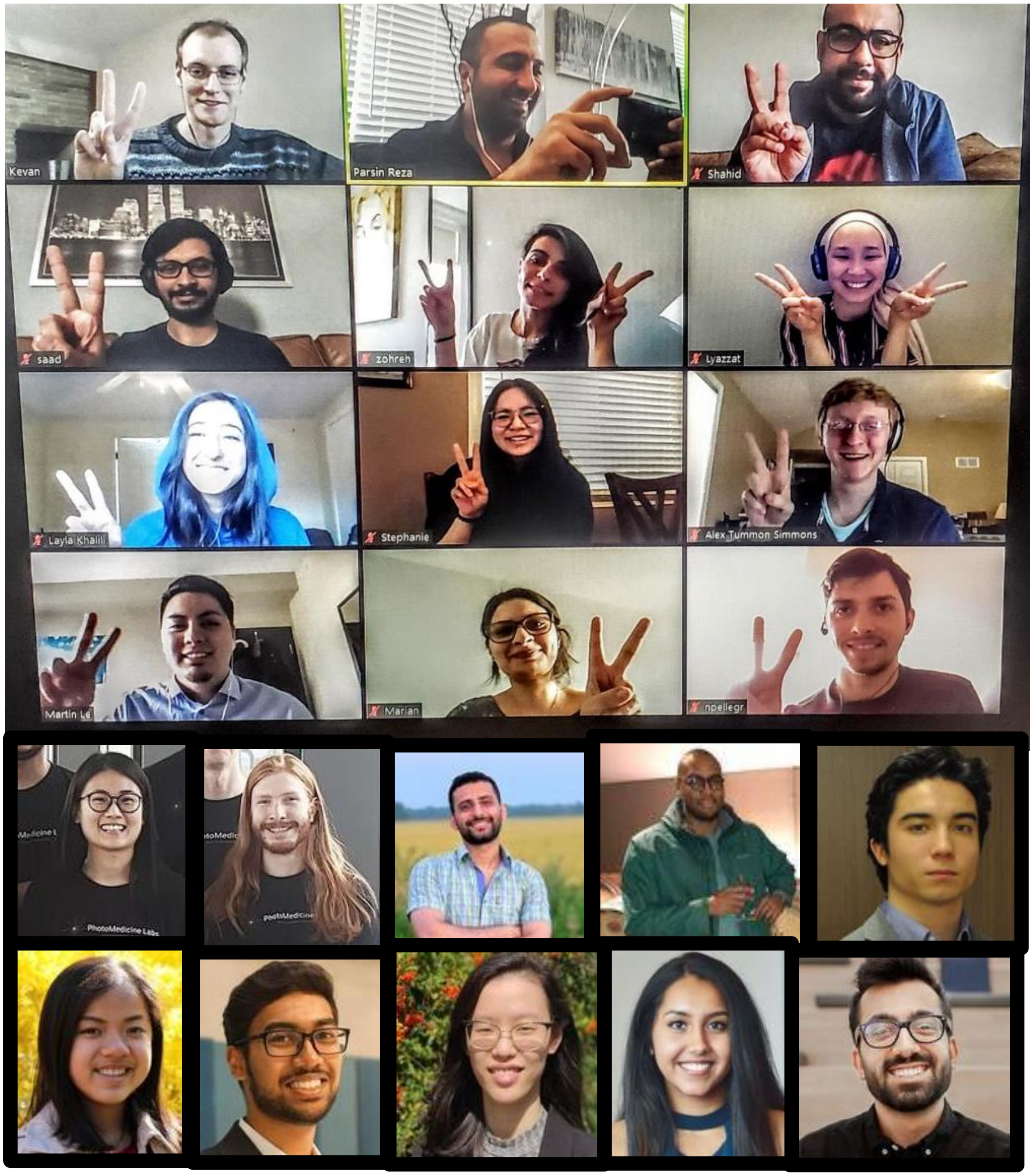
# PhotoMedicine Labs – Group Photo




We at the PhotoMedicine Labs are committed to making the world a better place with our research. We are so proud of everyone who has had the honour of being a part of our team and are immensely excited to see what big things the future holds