Light and Life

Wellman 40th Anniversary Celebration

October 30, 2015

Wellman Center
for Photomedicine

Light and Life

1974
- First gift from Mr. Arthur Wellman

1975
- Wellman Labs established by John Parrish in the Department of Dermatology, MGH; located in Warren Building, fifth floor

1976
- Laboratory space occupied on Edwards Research Building, 2nd floor
- Warwick Morison joins the faculty

1979
- PUVA multicenter trial begins
- Office space opens in basement of the "temporary building;" site now under more recent MGH buildings

1981
- First radiation transfer theory applied to light transport in human skin
- R. William Gange and Irene Kochevar join the faculty
- Laboratory space expands on Edwards Research Building, 2nd floor
- Warwick Morison leaves Wellman to join the Johns Hopkins dermatology department

1982
- PUVA approved by FDA
- Feasibility of selective photothermolysis (SPT) for port wine stains demonstrated in animal studies
- Gift received from Mr. and Mrs. Wellman
- Name changes to Wellman Laboratories for Photomedicine

1983
- Feasibility of SPT for telangiectasias, tattoo removal and pigmented lesions demonstrated in animal studies
- Alan Oseroff joins the faculty

1984
- Laboratories move into newly constructed Wellman Building, 2nd floor
- Feasibility of laser lithotripsy demonstrated
- Human studies of portwine stain treatment by SPT
- Thomas Deutsch, Tayyaba Hasan and Richard Granstein join the faculty

1985
- Portwine stain treatment using SPT receives FDA approval
- First funding received from Department of Defense for Medical Free Electron Laser research
- Laboratories extended to Bartlett Extension Building, 6th floor
- Thomas Flotte joins the faculty

1986
- Kidney stone treatment by laser lithotripsy receives FDA approval
- Photopathology laboratory opens on 2nd floor of Edwards Research Building
- Alan Oseroff leaves Wellman to become Professor of Dermatology, Tufts New England Medical Center

1987
- Laser Applications Laboratory opens on Bartlett Extension Building, 6th floor
- Norman Nishioka and Kenton Gregory join the faculty

1988
- Telangiectasia treatment by SPT receives FDA approval
- Human studies for removal of tattoos using SPT
- Human studies using diode laser for retinal photocoagulation
- Human studies for laser lipotripsy of biliary stones
- Lynn Drake joins the faculty and Susan Weeks joined as chief administrator

1989
- Tattoo removal treatment by SPT receives FDA approval
- Laser treatment of biliary stones receives FDA approval
- Diode laser retinal photocoagulation receives FDA approval
- Human studies using SPT for pigmented lesions
- Human studies for selective laser ablation of athermoma
- Human studies for laser treatment of angiodyspasia
- Human studies for laser induced fluorescence to identify colonic polyps
- Reginald Birngruber and Nikiforos Kollias join the faculty
- Laboratory space expands to Bartlett Hall, 8th floor

1990
- Pigmented lesion treatment with SPT receives FDA approval
- Human studies for dyed scleral laser sclerostomy
- Apostolos Doukas joins the faculty

1991
- R. William Gange Lectures initiated (and continue for 20 years)
- Funding received from the Department of Energy to develop Laser Center of Excellence
- Kenton Gregory leaves Wellman to become the founding Director of the Oregon Medical Laser Center

1992
- FDA approves laser sclerostomy for glaucoma
- Human studies for psec pulsed photodisruption
- Human studies of PDT for skin cancers
- Robert Redmond joins the faculty

1993
- FDA approves psec pulsed photodisruption
- Human studies for Turbo PUVA
- Human studies for laser burn surgery and burn depth diagnostics
- Human studies for laser coronary thrombectomy
- Human study for PDT for vulvar cancer
- Robert Webb joins the faculty

1994
- Human study for endometrial ablation using PDT
- Michael Hamblin and Charles Lin join the faculty

1995
- Feasibility of laser hair removal demonstrated
- First laser confocal microscope for human use
- Feasibility of selective laser trabeculoplasty demonstrated
- Human studies of BPD PDT treatment of wet AMD
- Wellman laboratory space expands to Bartlett Hall, floors 6 and 7
- Richard Granstein leaves Wellman to become Professor of Dermatology, Weill Cornell Medical College

1996
- FDA approves pulsed CO_2 erbium laser for resurfacing

1997
- FDA approves pulsed laser trabeculoplasty
- FDA approves permanent hair removal using ruby and diode lasers
- Brett Bouma joins the faculty

1998
- FDA approves confocal microscope for skin imaging
- FDA approves diode array laser treatment of leg veins
- Human studies for GI endoscopic OCT

1999
- Laboratories extend to entire 2nd floor, Edwards Research Building
- Nik Kollias leaves Wellman to join Johnson and Johnson as Senior Research Fellow

2000
- Gift received for optical diagnostics research
- FDA approves Visudyne – PDT treatment of wet AMD
- Human studies of intracoronary OCT

(Continued on inside back cover)

Welcome to the Wellman 40th Anniversary Celebration!

YOU are the Wellman Center for Photomedicine. What follows is a very brief history, a very brief update, and a very brief look to the future.

Forty years ago, Dr. John Albert Parrish started a small laboratory in an MGH building so humble, that its official name was Temporary. The lab was to be dedicated to his own twist on photobiology – "photomedicine" – the good, bad and ugly of how light affects us, and especially how it might help us if we could just understand the possibilities deeply enough. At the time, John and his colleagues had just breathed new life into the world's oldest light-activated drug. Using high-power UVA lamps to activate 8-methoxy psoralen, a compound extracted from plants used at least 3,500 years ago in combination with sun exposure, they had come up with a potent "new" treatment for psoriasis (Parrish JA, Fitzpatrick TB, Tannenbaum L, Pathak MA; N Engl J Med 1974;291;1207-1211). One of their patients was the former Miss Sweden, no longer quite so beautiful because psoriasis covered her body. She responded so well that her husband, Arthur O. Wellman, gratefully offered to support some of Dr. Parrish's research.

At that moment forty years ago, the Parrish laboratory became the Wellman Laboratories. John was, and is, an amazing academic empire builder. A mix of independent and interacting faculty from chemistry, physics, immunology, bioengineering, medicine and surgery were recruited. The Wellman building, now Thier, was completed in 1984, which was about when John decided to redefine dermatology as "the skin, and everything in it!" By the turn of the century, out came a host of target-selective lasers that transformed the practice of dermatology, laser lithotripsy that is used in almost every hospital world-wide, the first laser-based microscope for human imaging, permanent laser hair removal, the first drug treatment for macular degeneration, and a widely used selective treatment for glaucoma. For every successful project, there were at least a few spectacular failures – which of course continues today. Bona fide research programs grew steadily from human photobiology to include mechanisms of photosensitization, molecular design of light-activated drugs, high power laser tissue interactions, tissue optics, optical coherence tomography for a host of breakthrough applications, other novel imaging strategies, optical nanoparticles, bio-inspired optical materials, genetics of melanoma, and others.

In 2004, Wellman Laboratories became the Wellman Center for Photomedicine (WCP), one of five non-departmental thematic research centers at MGH, and I became the director.

Light and Life

Beginning in 1998, Dr. Parrish had increasingly focused his efforts on CIMIT, a broad program that he created and still directs, which facilitates technological solutions to medical problems. In the past decade, the Wellman Center has about tripled in size and output. In essence, we were given a hunting license by MGH to actually solve medical problems, innovate, collaborate, translate, discover, teach and learn without regard to traditional boundaries. We launched effective new laser treatments for scarring, light-activated tissue repair, a popular non-invasive treatment to reduce body fat, incredible high-speed OCT imaging of coronary arteries, microscopes you can swallow (instead of a large endoscope, thank you), the world's first living cellular laser, surprising insights about stem cells, novel strategies for wound healing, promising optical treatments for brain trauma, and several point-of-care optical diagnostics. Marjorie Bullock, daughter of Mr. Wellman, fully endowed a competitive research fellowship. We recycle our patent royalties to support infrastructure in the form of four shared research resources (pathology, synthetic chemistry, computation and translational research cores). We are strongly affiliated with MIT, actively support graduate students, and teach new courses – including a robust Summer Optics Institute for undergraduates. There is a world-wide family of former and current Wellmanites. Our faculty and every lab group at the Wellman Center exemplify diversity of intellect, culture, gender, and age. The wonderful culture of academic freedom is alive and well at WCP.

We are now the world's largest research center in this field, with an annual budget of nearly $30 million, but size is a poor measure of worth. This 40th birthday is a celebration of the dream of Dr. Parrish and an excellent opportunity to look forward. Broadly and specifically, what might be the most promising next chapter in the evolution of "photomedicine"? With awe, we must admit that many fundamental effects of light on humans remain poorly understood. We will almost surely be able to extend the principles, and the diagnostic and therapeutic capabilities of what we already know into essentially every organ system. The marriage of two robust WCP capabilities looks promising: high-speed optical imaging and various optical treatments. Nanotechnology strongly beckons with about half of our labs exploring possibilities. Medical economics poses a sticky, compelling set of new problems worth solving. Moreover, we are not limited to using light. Indeed, some of our recent examples of medical impact are non-optical. Without restraint – what problems should we attack? What would you like to see in the future of the Wellman Center?

R. Rox Anderson
Director, Wellman Center for Photomedicine

John A. Parrish, MD
Professor and Founder

R. Rox Anderson, MD
Professor

Brett Bouma, PhD
Professor

Conor L. Evans, PhD
Assistant Professor

Michael R. Hamblin, PhD
Associate Professor

Tayyaba Hasan, PhD
Professor

Irene E. Kochevar, PhD
Professor

Charles P. Lin, PhD
Associate Professor

Seemantini Nadkarni, PhD
Assistant Professor

Robert Redmond, PhD
Associate Professor

Guillermo (Gary)
Tearney, MD, PhD
Professor

Hensin Tsao, MD, PhD
Professor

Benjamin Vakoc, PhD
Associate Professor

Mei X. Wu, MD, PhD
Associate Professor

Seok-Hyun (Andy) Yun, PhD
Associate Professor

Former Wellman Faculty

Johannes deBoer, PhD, was a Wellman faculty member from 2001 to 2008. He is currently Professor of Physics and Group Leader for Biophotonic and Medical Imaging at Vrije Universiteit Amsterdam in the Netherlands

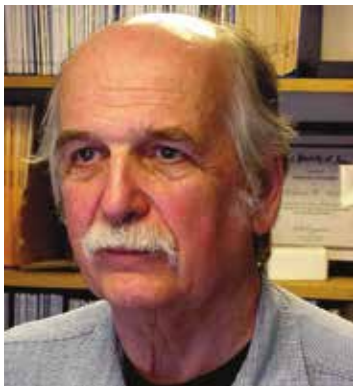
Thomas Flotte, MD, joined the Wellman faculty in 1985 and left in 2007. His current positions at the Mayo Clinic are Consultant for Anatomic Pathology, Professor in the Department of Laboratory Medicine and Pathology and Director of the Pathology Research Core of the Center for Individualized Medicine.

Kenton Gregory, PhD, was on the Wellman faculty from 1987 to 1991. He is currently the Founding Director of the Oregon Health Science University (OHSU) Center for Regenerative Medicine, Professor of Biomedical Engineering at OHSU, Staff Cardiologist in addition to several officer positions in biotech companies.

Nikiforos (Nik) Kollias, PhD, was a member of the Wellman faculty from 1989 to 1999. He joined Johnson and Johnson as Senior Research Fellow and retired in 2011.

Warwick L. Morison, MD, FRCP, was very early member of the Wellman faculty, from 1978 to 1981. He is currently Professor of Dermatology at the Johns Hopkins Medical School.

Emeritus Faculty



Robert Webb, PhD, Associate Professor of Dermatology and Ophthalmology, joined the Wellman faculty in 1993. Prior to joining Wellman, Rob was a Senior Scientist at the Schepens Eye Research Institute where he invented the scanning laser ophthalmoscope (SLO) for viewing the retina of the living human eye. At WCP he developed a confocal microscope (the VivaScope, Lucid, Inc.) for live, noninvasive imaging within skin and other organs. Rob's experience and wisdom was highly valuable to Wellman as it transformed from John Parrish's leadership to the current shared leadership management style. His technical advice was also sought by, and generously given to, numerous junior and senior researchers. Rob Webb retired in 2014.

Apostolos Doukas, PhD, Assistant Professor of Dermatology, was a member of the Wellman Center for 15 years starting in 1990. Stemming from his prior experience on spectroscopy of biological molecules and his experimental physics background, Apostolos' research focused on the use of pressure waves for drug delivery and in vivo spectroscopic markers that report on physiological conditions. He served as a resource on laser safety and optical measurements in tissue for a wide variety of projects. Apostolos Doukas just retired in 2015.

Team Assistant Professor

Tianhong Dai, MD, PhD, Hamblin group

Instructors

Clemens Alt, PhD, Lin goup

Walfre Franco, PhD, Anderson group

Michalina Gora, PhD, Tearney group

Zeinab Hajjarian, PhD, Nadkarni group

Yingying Huang, PhD, Hamblin group

DongKyun Kang, PhD, Tearney group

Zhiming Mai, PhD, Hasan group

Srivalleesha Mallidi, PhD, Hasan group

Martin Purschke, PhD, Anderson group

Imran Rizvi, PhD, Hasan group

Fernanda Sakamoto, MD, PhD, Anderson group

Mohd Shahid, PhD, Wu group

Joshua Tam, PhD, Anderson group

Martin Villiger, PhD, Bouma group

Affiliated Faculty

Mathew Avram, MD, JD
Department of Dermatology, HMS and MGH

Reginald Birngruber, MD, PhD
Institute for Biomedical Optics and
Medical Lasercenter Luebeck

Jonathan Celli, PhD
Department of Physics
University of Massachusetts Boston

Henry Chan, MD, PhD, FRCP
Visiting Scientist, MGH

Daniel Cote, PhD
Université Laval and Centre de Recherche de
l'Institut en Santé Mentale de Québec

Johannes F. deBoer, PhD
Department of Physics
Vrije Universiteit Amsterdam

Merete Haederdsal, MD, PhD
Department of Dermatology
Bispebjerg University Hospital Copenhagen

Farouc Jaffer MD PhD
Department of Medicine, HMS
Cardiology Division, MGH

James Kobler, PhD
Department of Surgery, MGH

Edward V Maytin, MD, PhD
Departments of Dermatology and
Biomedical Engineering
Cleveland Clinic

Norman Nishioka, MD
Department of Medicine, HMS and MGH

Brian Pogue, PhD
Departments of Engineering and of
Physics & Astronomy,
Dartmouth College

Mark Randolph, MAS
Department of Surgery, HMS and MGH

Giuliano Scarcelli, PhD
Department of Bioengineering
University of Maryland

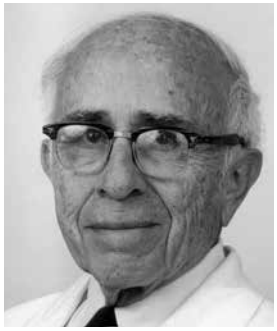
Melissa Suter, PhD
Department of Medicine, HMS and MGH

Zeina Tannous, MD
Department of Dermatology, MGH

Yukako Yagi, PhD
Department of Pathology, HMS and MGH

Anna Yaroslavsky, PhD
Department of Physics
University of Massachusetts Lowell

In Memoria



Irvin H. Blank, PhD, (1902–2000) was a member of the Wellman Labs from the very beginning and continued to come in daily until 1994, although he officially retired from HMS in 1968! His original expertise in skin physiology, especially skin hydration, bacteriology, percutaneous absorption and effects of topical agents, laid the basis for the development of multiple topical skin therapies. In the Wellman he contributed to basic studies of cutaneous photobiology and, possibly more importantly, provided sage advice to numerous WCP researchers – from technicians to professors.

Thomas F. Deutsch, PhD, (1932–2006) was an early member of the Wellman faculty, arriving in 1984 and bringing great expertise in laser technology to the lab from his former work at the MIT Lincoln Laboratory. He was a pioneering investigator of the mechanisms for tissue ablation using UV excimer lasers and contributed to the development of their medical applications. His work on ablation extended to different lasers and established greater understanding of their potential uses as well as the mechanisms of associated tissue damage. Tom's contributions to photomedicine also included in-depth studies of the use of laser-induced fluorescence for diagnosis of abnormal tissues. Tom retired as an Associate Professor from the Wellman Center and Harvard Medical School in 2006.

R. William Gange, MD, (1945–1991) headed an active research group investigating cutaneous photobiology in the Wellman Labs, beginning in 1984. He was an excellent and compassionate clinician, rising to Associate Professor in the HMS Dermatology Department. His research contributed greatly to our understanding of the different mechanisms for the effects of UVA and UVB radiation on skin, an area that was poorly understood at the time. His subtle sense of humor and sincere kindness, along with his intelligence and commitment, made him an ideal collaborator and friend.

Franz Hillenkamp, PhD, (1936–2014) was a long-term consultant to the WCP, initially advising John Parrish on establishing laser photomedicine as the lab's direction. Wellman researchers benefited greatly from his critiques, probing questions and vision. Franz was a professor at Goethe University Frankfurt and later on the Medical Faculty of the University of Münster. He had a highly distinguished career in mass spectrometry and was most well known, with his colleague Michael Karas, as the inventor of MALDI, an ionization method used in mass spectrometry that is now universally used for analysis of proteins and other labile macromolecules. Franz was a very generous mentor and was relentless in insisting that every research project include methods to probe underlying normal and abnormal physiologic response.

Allan Oseroff, MD, PhD, (1943–2008) was a member of the Wellman faculty from 1983 to 1986, when he moved to the Department of Dermatology at Tufts University School of Medicine. In 1989 Allan joined the Dermatology Department at the University of Buffalo and at the Roswell Park Cancer Institute, where he became chairman of both departments. He began his investigations of photodynamic therapy as a cancer treatment at Wellman and became an internationally recognized expert on its application to skin cancers. Allan was a dedicated translational researcher, devoting his laboratory to projects designed to improve clinical care. Allan was also widely respected for his compassion and thoughtfulness to patients and colleagues.

Administrative and Research Cores

Gabriela Apiou, PhD, Assistant Professor, HMS; Director of Translational Research Core

Brian Battersby, MS, Director of Computational Core

Brijesh Bhayana, PhD, Director of Synthetic Chemistry Core

Lynn Drake, MD, Lecturer, HMS; Director of Government Relations; Director of Business Development

Nancy E. von Hone, MS, CRA, Director of Finance & Strategic Planning

Jie (Jenny) Zhao, MD, PhD, Director of Photopathology Core

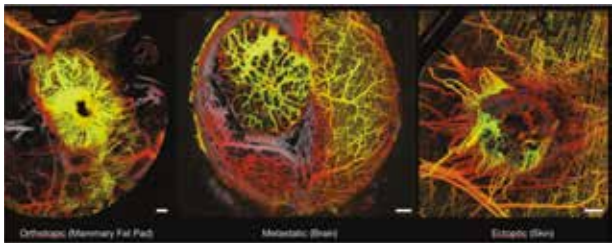
Not pictured:

Susan A. Weeks, MS, Administrative Director

Research Programs

Ben Vakoc Laboratory

Angiographic Optical Coherence Tomography
Optical coherence tomography (OCT) has been used with great success to image the microstructure of tissue. Soon after the development of structural OCT, it was recognized that through integration of Doppler methods OCT could also be used to image blood vessels. Initial Doppler OCT systems validated this principle. However, the angiographic images using these techniques were limited by poor sensitivity, high artifact rates, and slow imaging speed. Because the need for wide-field angiographic imaging was not being addressed by alternative microscopies, there was a strong rationale to improve the angiographic methods in OCT and enable its adoption in vascular research. In response, we developed robust, high-speed techniques for implementing vascular contrast in OCT. Through collaboration with the Steele Laboratory of Tumor Biology, we demonstrated the utility of angiographic OCT technology in cancer investigations, specifically in studies of tumor angiogenesis and in the evaluation of anti-angiogenic therapies (see image). After this, we have worked with additional collaborators and industry to broadly translate OCT-based angiography into biological research.



Angiographic OCT images of a breast cancer tumor grown in, from left, the mammary fat pad, brain and skin of a mouse.

Our current efforts in this area focus on two themes. The first is bringing angiographic imaging to clinical applications where patient motion is more pronounced and imaging times are reduced. Initial work is focusing on dermatology and ophthalmology with a long-term goal of enabling robust endoscopic angiography by OCT. The second theme is enabling quantitative blood flow velocity measurements within wide-field angiography datasets. Existing methods (like that used to generate the images shown) provide the morphology of the vascular network but cannot be used to quantify flow. With the development of new statistical methods for analyzing signal correlation properties in OCT, we have made significant progress toward enabling flow quantification at each voxel within a three-dimensional image.

Charles Lin Laboratory

We are developing advanced optical techniques for in vivo cell tracking and molecular imaging studies, concentrating in the areas of hematopoietic stem cell transplantation, hematologic malignancies, and inflammation. Our goal is to understand the in vivo cell biology by imaging cell homing, migration, interactions with the micro-environment, and response to therapy. To facilitate these studies, each student or posdoctoral fellow (most of them have a background in optics) builds his or her own microscope, or inherits a microscope from a previous lab member and reconfigures it for their specific purposes. This way each lab member gets to “own” a machine and becomes an expert in its design and operation. For example, one of the microscopes is coupled to a new fiber laser source that is able to output femtosecond pulses at multiple wavelengths (through soliton generation) in order to extend the spectral coverage of multiphoton excitation. Another microscope is developed for measuring local oxygen concentration in the bone marrow of live mice by two-photon phosphorescence lifetime microscopy. One system has simultaneous imaging, laser ablation, and optical trapping capabilities that are used to cut into bone and deliver single cells into the bone marrow with optical guidance. All systems have unique open architectures to allow modification and implementation of new technology. My laboratory has also developed a scanning laser ophthalmoscope that is optimized for imaging the mouse retina and an in vivo flow cytometer for real-time detection and quantification of fluorescent cells in the circulation, eliminating the need for drawing blood samples. We are actively engaged in multidisciplinary collaborative studies with experts across the fields of stem cell biology, immunology, and cancer biology.

Seemantini Nadkarni Laboratory

The research activities in my laboratory are directed towards the innovation and translation of optical technologies to address major challenges in medicine and biomedical sciences. Towards this end, our research focuses on four key areas of investigation.

Intracoronary Laser Speckle Imaging (ILSI)
My laboratory has pioneered the development of a new approach, ILSI, for identifying unstable coronary plaques that cause myocardial infarction. We have conducted the first demonstration of ILSI in living swine through the development of a novel optical catheter. This work has demonstrated for the first time that laser speckle fluctuations measured from the coronary wall provide unique biomechanical signatures of plaque stability.

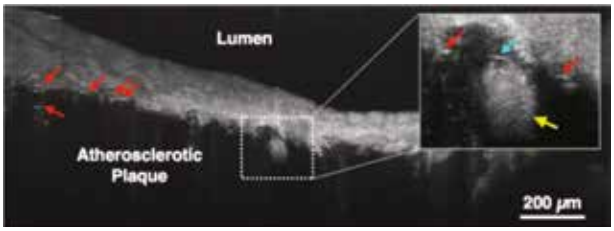
Optical Coagulation Sensing
Optical Thromboelastography (OTEG), a new optical technology invented in my laboratory can comprehensively measure the coagulation status of patients within minutes using a drop of whole blood. In collaboration with clinical colleagues in the Pathology service at MGH, we are leading studies to investigate the diagnostic accuracy of the OTEG approach for detecting patients with defective coagulation status. We are further developing methods to detect platelet abnormalities with a drop of whole blood, opening the opportunity for multi-functional coagulation assessment at the bedside. The OTEG technology is expected to have far-reaching clinical impact and may help identify patients with coagulation and platelet defects early so that they may be treated prior to the onset of hemorrhage and acute thrombosis.

Laser Speckle Microrheology (LSM)
My group is leading the development of another new optical device, LSM, that quantifies tissue stiffness with microscale resolution without physical contact. Through new collaborations with cancer biologists at MGH, this new technology will help address key questions on the role of extracellular matrix mechanics in modulating malignancy and drug resistance in tumors.

Polarization-sensitive Optical Coherence Tomography (PSOCT)
Through ongoing collaborations with the Bouma laboratory, our team is continuing to push the PSOCT technology forward to clinical translation. We are leading studies to address critical questions on whether collagen birefringence in coronary plaques measured by PSOCT is modulated by hyperlipidemia followed by subsequent lipid lowering and whether reduced collagen birefringence is associated with the risk of unstable angina in patients.

Gary Tearney Laboratory

Coronary Artery Imaging
The assessment of human coronary atherosclerosis to prevent and treat myocardial infarction has been one of the most important yet difficult problems in medicine. Current imaging technologies do not have sufficient resolution to evaluate the microscopic features of the coronary wall that are critical for identifying high risk atherosclerotic plaques and evaluating response to therapy. The Bouma and Tearney Labs developed and demonstrated in living patients a new catheter based imaging technology termed intravascular optical coherence tomography (IVOCT) that provides three-dimensional images of the coronary wall with a level of detail that is 10x greater than the previous state of the art. IVOCT has been commercialized by multiple companies, is now a mainstream imaging modality in intravascular cardiology, and is being used regularly around the world to improve the management of patients with coronary artery disease.



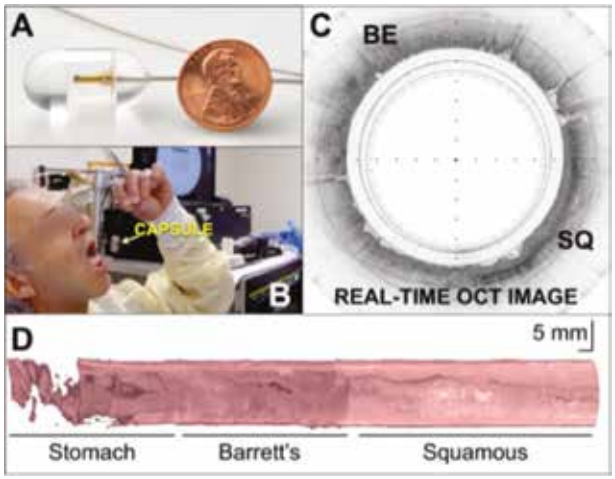
μOCT image of a cadaver coronary plaque showing crystals, seen as highly reflecting linear structures (red arrows). Inset (3x magnification) demonstrates crystals (red arrows) and a macrophage (yellow arrow) engulfing a crystal (cyan arrow).

The Tearney Lab also recently developed new forms that combine the structural imaging capabilities of IVOCT with compositional and molecular information obtained through spectroscopy and fluorescence, as well as a high-resolution form of OCT termed μOCT that enables the imaging of cells and subcellular structures in human coronary arteries.

Gastrointestinal Imaging
The state of the art for managing patients with Barrett's esophagus (BE), the precursor to esophageal adenocarcinoma (EAC), continues to be problematic due to its reliance on random endoscopic biopsy. A major focus of my laboratory has been to solve this problem by conducting comprehensive OCT imaging of the entire esophagus so that biopsy may

be based on in vivo microscopy morphologic features. The Bouma and Tearney Labs were the first to demonstrate endoscopic OCT for BE, then developed the criteria for interpreting these images and showed that it is possible to comprehensively image the entire distal esophagus with OCT by utilizing a balloon-centering catheter. We also have demonstrated a laser cautery technique that can be implemented through the same balloon that marks dysplastic and cancerous regions in patients so that they can be biopsied endoscopically. This technology has been commercialized and is being used to improve the management of patients with BE.

Recognizing a clinical need for less expensive and better-tolerated tools for screening for a variety of upper gastrointestinal diseases (BE, eosinophilic esophagitis, celiac disease) the Tearney Lab has recently developed a technique for conducting OCT and high-speed confocal microscopy through a tethered pill that can be swallowed. We have now demonstrated tethered capsule endomicroscopy (TCE) in approximately 100 patients and have shown that this technology enables comprehensive three-dimensional microscopic imaging of the entire esophagus and duodenum in vivo. The procedure is performed in unsedated subjects by a nurse or technician, takes approximately 5 minutes, and is preferable to endoscopy by the vast majority of subjects. These unique features of TCE make it a promising technology for screening for a wide variety of gastrointestinal disorders based on microscopic architectural and cellular morphology.



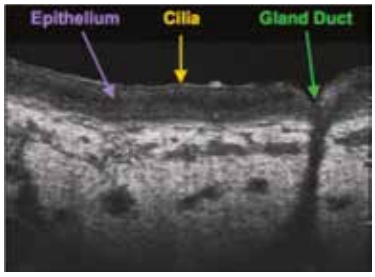
A. Photograph of the capsule and tether adjacent to a penny for scale. **B.** Photograph of an unsedated study subject swallowing an OCT TCE device. **C.** Real-time OCT image showing microscopic information throughout the full thickness and full circumference of the esophageal wall (ticks, 1mm). **D.** Three-dimensional rendering of TCE dataset from a patient with Barrett's esophagus.

Respiratory Cilia Imaging

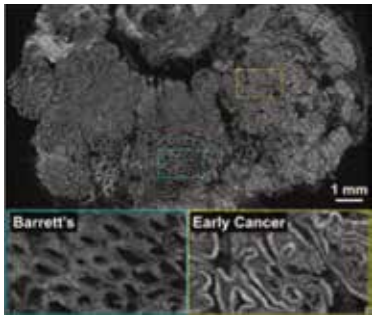
Cystic fibrosis is a condition that is characterized by abnormal mucociliary clearance and infection that is caused by aberrant function of respiratory epithelial cilia. However, studies of motile cilia have been limited by the absence of an imaging technology for visualizing the living respiratory mucosa at the cellular level. In collaboration with the Rowe Lab at University of Alabama, we have leveraged the high frame rate and resolution of μOCT to visualize and quantify ciliary motion and mucus clearance in respiratory cells, tissue culture, and animals in vivo. Our capability to visualize and quantify cilia with such detail has resulted in new discoveries about this important clearance mechanism.

Spectrally Encoded Imaging

The Tearney Lab has invented a technique for conducting confocal microscopy and endoscopy using a single optical fiber that is 100-1000 times faster than conventional beam scanning methods. As a result of this invention, it is now possible to image large regions of the esophagus at 1-μm resolution and to perform endoscopy using a device with a diameter as small as that of an optical fiber (diameter of a human hair). This technology is in the process of being commercialized and will be used for new diagnostic endoscopy indications.



High resolution OCT image of respiratory mucosa, showing the respiratory epithelium, cilia, and other architectural features such as gland ducts. Tick marks, 50 μm.



Spectrally encoded confocal microscopy (SECM) image of an esophageal resection specimen showing regions of Barrett's esophagus and early cancer.

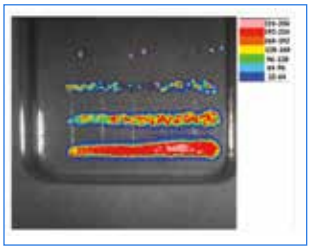
Robert (Bobby) Redmond Laboratory

Photochemical Tissue Passivation (PTP)
Expertise in photochemical reaction mechanisms was exploited by Redmond and Kochevar in the early 2000's to develop novel approaches to wound closure in a variety of tissues, including nerve, blood vessel, cornea, vocal fold, tendon, bowel and skin. Known as photochemical tissue bonding (PTB), the wound closure produced was based on basic research observations of protein crosslinking initiated by visible light and photoactivated dyes. Wound healing was consistently observed to involve far less inflammation than standard suture repair and was initially thought to be due to the lack of a potential foreign body (suture). However, it gradually became apparent that crosslinking generated at tissue surfaces during PTB also reduced inflammatory responses. This has led to a new technology and applications that address clinical scenarios where inflammation and aberrant scarring consequences can have unwanted consequences, including scarring, post-surgical adhesions, and capsular contracture. This process, called photochemical tissue passivation (PTP), was shown in early demonstrations to reduce capsular thickness in breast implant models and reduce post-surgical adhesions in Achilles tendon repair and in bowel anastomosis.

Additionally, PTP can be used to modify the biomechanical properties of tissue in circumstances where an increased strength or stiffness is of clinical benefit. Medical uses include stiffening the cornea to retard the progression of keratoconus and stiffening the outer layers of veins. The latter process reduces vein distension under arterial pressure that leads to endothelial damage, intimal hyperplasia, stenosis and failure when used as bypass grafts or in arterio-venous (AV) fistulas for vascular access in end-stage renal failure patients that requiring dialysis. Research in pre-clinical models has shown the remarkable ability of PTP to stiffen the vein exterior to prevent acute distension and its sequalae. As diabetes and vascular disease are increasingly prevalent in modern societies this technology has a tremendous potential for clinical impact and is on the verge of human studies and commercialization.

Michael Hamblin Laboratory

Our research interests broadly are in the area of phototherapy for multiple diseases. Photodynamic therapy (PDT) is a relatively new and exciting approach for treating cancers, infections and other diseases. Non-toxic dyes known as photosensitizers are administered systemically, locally or topically and accumulate in the tumor or other lesion. Illumination with (otherwise harmless) visible (usually red light, frequently from a laser) excites the sensitizer, which in the presence of oxygen, produces reactive oxygen species that mediate cytotoxic effects. Undesirable cells such as infectious microbial cells or malignant cancer cells can be selectively killed by this approach. My lab has set up collaborations with several chemistry groups that provide novel photosensitizers for testing both in vitro and in vivo such as bacteriochlorins, functionalized fullerenes and synthetic dyes.



Serial dilution of bioluminescent Pseudomonas aeruginosa growing on an agar plate

In recent years the Hamblin lab has developed an interest in elucidating the photochemical mechanisms that operate during PDT, focusing on the difference between Type I (hydroxyl radicals) and Type II (singlet oxygen) pathways and the factors that govern the balance between them. We also use optical imaging of infections caused by genetically engineered bioluminescent microbial cells. This allows us to test the effectiveness of PDT against infections in real time non-invasively in mouse models. In other studies we have shown that anti-tumor immune response occurs after PDT in some small animal models of cancer. There is a complex interplay between factors such as the tumor type and whether it contains a recognizable antigen, the strain of mouse and its population of host suppressor cells, the type of PDT and the acute inflammatory response it causes. Combination of PDT with certain immunostimulants can produce highly synergistic benefits including regression of distant untreated tumors.

Low-level light therapy (LLLT) or photobiomodulation can stimulate healing, prevent tissue death and relieve pain and inflammation. The molecular

and cellular mechanisms that underlie this effect are under investigation. We believe that reactive oxygen species are also involved and cause activation of redox sensitive transcription factors. Stem cells are particularly susceptible to the effects of light and can be induced to differentiate and proliferate. Light-sensitive ion channels are another possible cellular pathway. Applications of LLLT to healing and treatment of traumatic brain injury are being studied. Results from these studies have suggested that transcranial near-infrared (NIR) light may have wide applications to a diverse range of brain disorders, including stroke, neurodegenerative diseases such as Alzheimer's and Parkinson's, psychiatric disorders such as depression, anxiety, PTSD, autism, and addiction.

Rox Anderson Laboratory

We try, and sometimes even succeed, to solve diagnostic or therapeutic medical problems through novel strategies. It is fun and challenging to actually solve medical problems – which often requires a shift in strategic thinking, new technology, and some stewardship with industry when a hard-earned project leaves our lab. The current research team of about a dozen people includes an effective mix of talent in physics, engineering, biosciences and medicine. We often initiate collaborations, and we welcome you to contact us.

New Optical Treatments

This lab launched many of the now well-accepted lasers for dermatology, and a few in ophthalmology and laryngology, based on selective photothermolysis (SP). These include target-specific lasers for treating vascular birthmarks, scars, pigmented lesions, tattoos, hair removal, early glaucoma, and laryngeal tumors. Over the years our understanding of SP has greatly improved, and yet some implications from theory remain to be explored. For example, we are working on targeting lipid-rich cells as a potential cure for acne (#1 skin disease), using SP to selectively damage sebaceous glands. Theory led us to perform a successful confirmatory study, using optical pulses at infrared wavelengths that are preferentially absorbed by lipids. New high-power diode and fiber lasers have recently become feasible for this application in practice, which we are now avidly pursuing. An alternative strategy for SP as an acne treatment, is to deliver light-absorbing substances to the target. We recently published the first successful acne therapy based on this strategy, using gold nanoshells forced into the sebaceous glands, in a series of laboratory, animal and human studies. This collaboration included work at three universities, two countries, and a startup company research effort led by a former Wellman Center graduate student. The work is likely to lead to the first FDA approved example of this strategy, and perhaps the first non-drug cure for acne.

When we first "declared war" on acne over a decade ago, we simultaneously investigated two optical strategies for targeting sebaceous glands – SP (as above), and photodynamic therapy (PDT) using a then-experimental drug (aminolevulinic acid). We first introduced PDT for acne, which is very effective at high doses but produces significant side effects. Recently we devised a way to reduce those side effects by inhibiting epidermal phototoxicity, with promising results in a recent human study at the Wellman Center. Recently, we also devised and published the first-in-man test of an entirely different, non-optical strategy for acne treatment using controlled skin cooling. The sebaceous gland is an integral part of human hair follicles. Like our invention 20 years ago of permanent laser hair removal (now the most popular medical use of a laser), there are good reasons to expect that sebaceous gland targeting can be a cure for acne. We published this work, including a collaborative study with Conor Evans' laboratory at the Wellman Center.

Our laboratory also conceived fractional laser treatment, which has been highly successful in practice. Fractional laser treatment is not "target-selective" (although our next iteration of it will be!). The simple principle behind fractional laser treatment is that even deep micro-scale wounds are able to heal by the biologic process of tissue remodeling, unlike large wounds that heal only by scarring. Using a tightly focused surgical laser and scanner system, we showed that a large volume fraction of the skin can be ablated, forcing the tissue to rapidly remodel without scarring. A successful company was launched, fractional lasers became popular, and they are now widely used around the world. Surprisingly, even scar tissue can be stimulated this way to remodel, becoming closer-to-normal skin. Fractional laser treatment is fast becoming a leading treatment for burn scars. Dr. Anderson is leading a multicenter study of burn scar treatment at Wellman Center, Air Force, and Shriner's Hospital.

Wound Healing
Our fractional laser experience raised a new possibility: is it possible to make even a large wound heal rapidly, with minimal scarring, by converting it into the equivalent of many very small wounds? We are now pursuing a novel wound-healing strategy that uses robotic micro-scale needles to harvest skin from a donor site, then transfer a matrix of the harvested skin onto a wound. In theory, both the donor and recipient sites could potentially heal rapidly, without scarring. With grants from DARPA and DOD, we made prototype machines, showed that the donor sites heal without scarring, and that this form of skin grafting is superior to the present standard of split-thickness skin grafting. We are working on a full "skin copy" strategy, and have successfully copied human skin onto animal wounds.

Lipid-selective Treatments
Non-invasive, selective removal of body fat is another practical success from our laboratory. It is a good example of when "the second mouse gets the cheese". We first studied a laser treatment strategy that heats subcutaneous fat. It worked, but in practice the treatment was expensive, slow and painful – a poor substitute for liposuction. Rather than giving up, we attacked the problem differently. In a rare condition seen by dermatologists, babies exposed to cold will sometimes selectively lose fat. We figured out the mechanisms involved, optimized the conditions for fat removal in adults, and created a startup company to develop the equipment. "Cryolipolysis" is now a popular alternative to liposuction, with over a million patients treated.

The underlying principle of cryolipolysis can probably be applied for other medical problems. At about 10°C (above the freezing temperature of water), intracellular lipids crystallize, causing cell stress and apoptosis. For example, visceral (intra-abdominal) fat is highly associated with diabetes, hypertension, cancer and death. Using small animal models, we have found that cryolipolysis of visceral fat appears to be safe and effective, and are presently working on strategies for controlled visceral fat cooling. Around the world, other laboratories and companies have paid attention. In Germany, there is a group aiming to treat fatty atherosclerotic plaques using cold. Others are working on cryolipolysis as a potential treatment for sleep apnea, which is highly associated with fat near the airway. Here, we are studying whether controlled cooling can be used as a treatment for pain. A common, unexpected and harmless side effect of cryolipolysis for fat removal, is reduced skin sensation for 1-2 months. As with fat, myelinated nerves have high lipid content. We recently completed a human study, to determine exactly which sensory functions, which kinds of nerves are affected, and how they recover. We hope to use this knowledge to come up with long lasting, non-drug treatments for chronic pain – one of mankind's most vexing problems.

Optical Diagnostics
This lab has also contributed to the fundamental understanding of tissue optics, including the first mathematical models for optical radiation transfer, and some useful diagnostics. Two decades ago, the first laser confocal microscope for human imaging was developed in a collaborative effort led by Robert Webb at the Wellman Center. This device was cleared by the FDA, commercialized and is now used for research and in practice to image skin cancers. An imaging project presently in our lab is exploring UV autofluorescence imaging as a diagnostic. Tryptophan, collagen and elastin all exhibit ultraviolet excitation and emission. Tryptophan fluorescence in particular offers the possibility of functional imaging, because it correlates well with cell proliferation. We are validating this imaging strategy to monitor cancer, wound healing, psoriasis and other proliferative tissues.

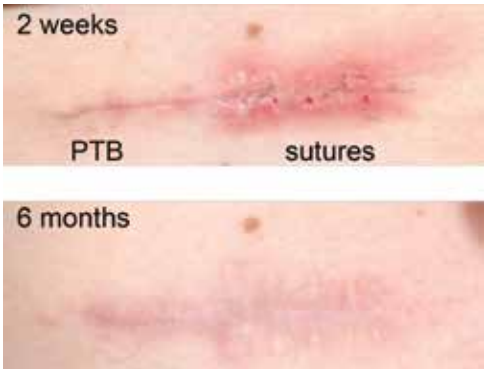
Irene Kochevar Laboratory

For many years the Kochevar research group investigated the photochemical and photobiological mechanisms underlying the effects of UV radiation on skin, especially the roles of reactive oxygen species in cell signaling initiated by UVA radiation and in the development of elastosis, a sign of UV-induced skin aging. More recently, in collaboration with the Redmond laboratory, the group's research focus shifted to fulfilling a clinical need for a method that rapidly and effectively seals wounds with only minimal scarring or fibrosis. Photochemical crosslinking of proteins was used to develop an effective technology for this need.

The process, termed Photochemical Tissue Bonding or PTB, is rapid and simple, involving application of an FDA-approved photosensitizing dye (Rose Bengal) and a few minutes of exposure to green light. Photochemical reactions then initiate formation of crosslinks (covalent bonds) between tissue proteins, which are mainly collagen in connective tissues. When the covalent crosslinks bridge between proteins on the surfaces of two tissues that are in contact, a continuous molecular-level seal bonds the tissues together. The first in vivo demonstration of wound sealing with PTB was for incisions in rabbit cornea; PTB sealed the wounds so strongly that they resisted opening even when the internal pressure was 10-fold greater than normal intraocular pressure.

Since then, PTB has also been demonstrated in vivo to seal surgical wounds in skin and vocal fold as well as to reattach severed blood vessels, tendons, colon and peripheral nerves with little scarring or fibrosis compared to sutured closure. The minimal inflammation and scarring after PTB treatment was clearly seen in a clinical study of sealing skin excision wounds in which one-half of the wound was sealed with PTB and the other half with superficial sutures (see image below). Research is ongoing as PTB is applied to further situations including bonding non-tissue materials.

When the dye is applied to intact tissue, then irradiated with green light, protein crosslinking within the tissue can modify tissue properties, such as stiffness. Keratoconus is a disease in which the cornea becomes less stiff, causing the cornea to bulge forward in response to the normal intraocular pressure. Consequently, vision is severely distorted.



Closure of a surgical wound with PTB (left half) or with superficial sutures (right half) showing that PTB elicits markedly less inflammation after 2 weeks and much less scarring after 6 months.

Photo-crosslinking collagen within cornea using Rose Bengal and green light has been shown to stiffen the cornea without damaging corneal cells or retina, and may be a treatment for arresting keratoconus.

Hensin Tsao Laboratory

The Skin Cancer Genetics Laboratory focuses on cutaneous malignant melanoma (CMM), a highly lethal form of skin cancer. In particular, our program is interested in (i) how inherited variants and ultraviolet radiation predispose us to CMM, (ii) how somatic mutations drive the progression of CMM and (iii) how acquired genetic changes modulate sensitivity of CMM to various therapies. Our major contributions to date include:

Identification of novel susceptibility loci in melanoma

Our laboratory has been interested in translating information about heritable variants for clinical use. We constructed the first computational model for estimating germline CDKN2A probability (MelaPRO). We have also been actively involved in uncovering new genes in familial melanoma. We were also one of the key laboratories on the international team which demonstrated that the MITF(E318K) variant is an important melanoma susceptibility allele. More recently, we established a role for germline BAP1 mutations in familial ocular/cutaneous melanoma and in the susceptibility for metastatic ocular melanoma. Our more recent functional analyses have confirmed that BAP1 in cutaneous melanomas have unexpected survival effects, which are contrary to the tumor suppressive genetic fingerprint. Cancer Res. 2010 Jan 15;70(2):552-9; Nature. 2011;480(7375):99-103; PloS One. 2012;7(4):e35295; J Invest Dermatol. 2015 Apr;135(4):1089-97

Elucidating mechanisms of photodamage in melanocytes and melanoma

Through our early work, we identified a p53 transcriptional footprint within the UV signature in melanocytes. We also developed the first permissive photocarcinogenesis mouse model of melanoma and showed that neonatal UV irradiation in murine pups can lead to activating mutations in the RAS pathway later in life. Finally, we more recently found that long-wave UVA exposure leads to a strong flux of ROS which elicits a high bystander oxidative stress, a finding that has dramatic deleterious implications for UVA-based tanning

beds. J Invest Dermatol, 2006; 126(11):2490-2506; Cancer Res, 2007; 67(12):5649-5657; Hum Mutation, 2007; 28(6):578-588; J Invest Dermatol. 2014;134(4):1083-90

Understanding melanoma progression and its attendant programs

We have been interested in programs which contribute to the progression of melanoma. Earlier in my career, we undertook several studies to understand melanoma biology in the context of molecular programs in the context of UVR response, senescence and outcome. Arch Dermatol. 2003;139(3):282-8; J Invest Dermatol. 2006;126(11):2490-506; Cancer Res. 2009;69(23):9029-37; Clin Cancer Res. 2012;18(15):4026-36

Leveraging RAS and p53 pathway interactions for therapy

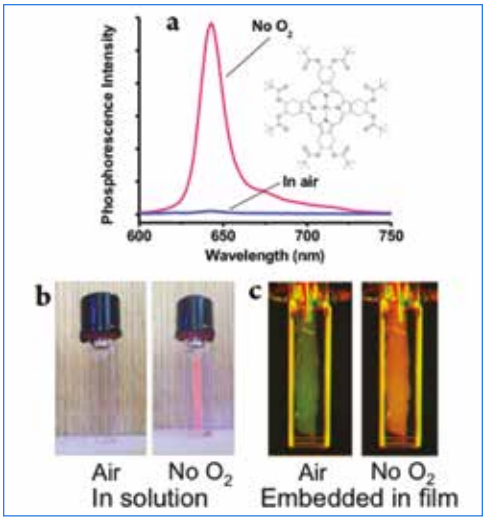
When mutations in the first melanoma oncogenes and tumor suppressors were described (e.g. NRAS, BRAF, PTEN, CDKN2A and TP53), little was known about the interactions between the changes. Furthermore, the broader implications of the MAPK and p53 pathways in melanoma therapeutics had not been recognized. Our laboratory was the first to describe PTEN mutations in melanoma. Subsequently, through our systematic analyses of NRAS, BRAF, PTEN, CDKN2A and TP53 loci, we developed a strong rationale for combining anti-MAPK therapy with p53 reactivation, provided pre-clinical substantiation of this approach; currently, clinical trials have been initiated in melanoma to test this strategy. Cancer Res, 2000; 60: 1800-1804; J Invest Dermatol, 2004;122:337-341; J Invest Dermatol. 2012;132(2):356-364; Clin Cancer Res; 2013;19(16):4383-91.

Understanding the role of EphA2 in melanoma formation and therapeutic resistance

Although EphA2 upregulation has been described in several cancers, its role in melanoma has been largely unknown. Using whole-genome expression analysis, we identified EphA2 as a critical UV-induced gene in melanocytes an oncogenic driver in melanoma. More recently, our laboratory also showed that EphA2 activation mediates resistance to BRAF inhibitors. In collaboration with Nathanael Gray at the Dana Farber Cancer Institute, we were able to develop several novel first-in-class small molecule inhibitors of EphA2 and overcome resistance. Cancer Res. 2008;68(6):1691-1696; Oncogene 2011;30(50):4921-4929; Cancer Discov. 2014 Dec 26; Cancer Discov. 2014 Dec 26

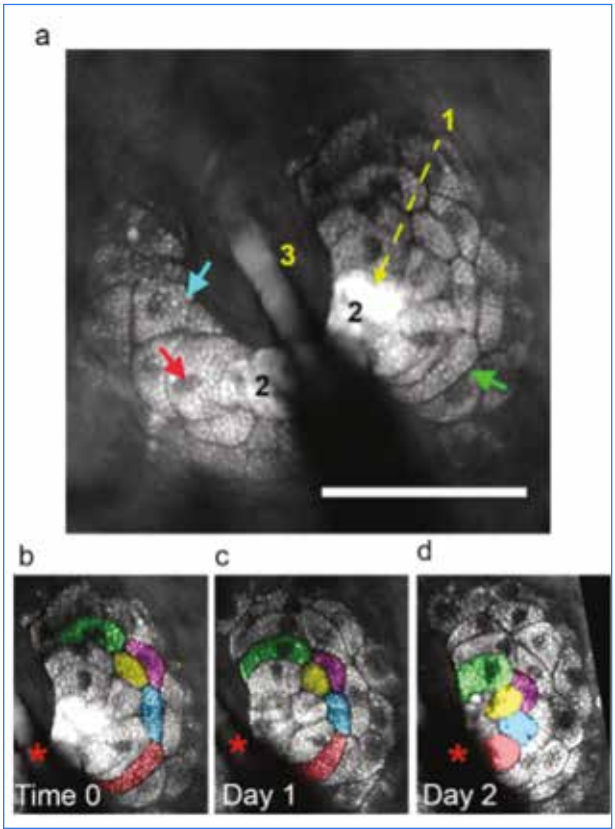
Conor Evans Laboratory

The Evans laboratory focuses on the development and application of optical toolkits to quantify and optimize treatment response. The main application areas are currently in cancer, specifically melanoma and ovarian cancer, dermatology, and wound healing. The team primarily employs spectroscopic and microscopy techniques, ranging from light scattering, fluorescence and phosphorescence measurements to advanced microscopy tools including stimulated Raman scattering and fluorescence lifetime imaging.



Response of platinum porphyrin to different oxygen levels. a) Phosphorescence spectra in dichloromethane, under room air and following deoxygenation. b) Platinum porphyrin in dichloromethane under room air (left) and in the absence of oxygen (right), The porphyrin was excited with a handheld LED flashlight. Emission was captured by a smartphone camera. c) Palladium porphyrin was embedded in a liquid bandage formulation along with a green-emitting, oxygen-insensitive fluorophore, and the film's emission was recorded with a color camera equipped with filters, under room air (left) and in the absence of oxygen (right).

The team has major efforts in the dermatology space in close collaboration with David Fisher, chief of Dermatology, in understanding the role UV- and chemical-induced reactive oxygen species play in the development of cancer. A Bridge Project funded research program is focused on the identification of key optical signatures of melanoma, and is currently translating one promising endogenous optical measurement method towards clinical application. Collaborations with Rox Anderson and his team have successfully used coherent Raman imaging to follow the dynamics of sebaceous glands and cold treatment methods to treat acne. These studies have since branched to examining the impact of cold therapy on nerves in skin. Additional research aims to characterize and understand skin barrier function and structure via coherent Raman imaging for future clinical translation of Raman toolkits to the clinic.



CARS imaging of normal sebaceous glands. (a) A sebaceous gland showing intracellular lipid granules (blue arrow), nuclei (red arrow) and cell membranes (green arrow). (1) CARS signal intensity increases as sebocytes approach the gland duct, corresponding to lipid accumulation as sebocytes mature. (2) Sebocytes near the duct show the highest CARS signal and lose cellular structures corresponding to cell death and lipid content release. (3) Hair shafts are coated with secreted lipid. (b-d) Sebocyte migration in the same sebaceous gland shown in (a) over 3 consecutive days. As the sebocytes migrated to the gland duct (*), there is a loss in intracellular structures and a concomitant increase in CARS signal. Scale bar: 50 μm.

The Evans lab is also actively developing toolkits for the measurement and quantification of tissue oxygenation. Due to the sustained efforts of chemists in the team, especially Manolis Roussakis, the group has successfully developed a new class of ultrabright porphyrin oxygen sensors that can report oxygen tension even in brightly lit environments. When coupled with dendrimer chemistry and advanced microscopy, these porphyrin oxygen sensors are now being used to map, in three-dimensions, oxygen tension on the microscale in models of cancer. In the wound healing space, the Evans lab is translating these probes toward Sensing, Monitoring, And Release of Therapeutic (SMART) bandages that can quantitatively display tissue properties and release therapeutics on-demand. The oxygen-sensing SMART bandage currently under development can report tissue pO2 maps across wound beds, and is being prepared for first-in-man studies.

In a relatively new research program, the lab is working closely with a new startup company to develop simple blood tests based on plasmonics for the detection of cancer in whole blood. This promising platform is in the early stages of development, and when successful, can be translated not only for ovarian cancer, but towards breast and pancreatic malignancies.

Mei Wu Laboratory

Utilization of Cosmetic Lasers to Enhance Skin Vaccinations

Several laser technologies invented at Wellman are now used worldwide for skin cosmetic applications, include the ablative fractional laser (AFL), non-ablative fractional laser (NAFL), and selective photothermolysis. We are exploring novel applications of these widely used clinical laser technologies to vaccinations.

Vaccination is the most cost-effective way to control infectious diseases. The most successful vaccine in medical history is smallpox vaccine, which is delivered by scarification because antigen presenting cells abundantly reside in the skin. Scarification is no longer used in today's immunization owing to the unacceptable skin lesion. To circumvent scarification, we deliver

vaccines into many microchannels generated with an AFL by applying a powdered vaccine array patch onto AFL-treated mouse skin. Fractional delivery of vaccine into many well separated microchannels greatly reduces vaccine-induced skin reactions without compromising the vaccine efficacy. Likewise, we used NAFL to generate an array of microinjured zones and the laser-damaged cells send "danger signals" to the immune system, inducing sterile inflammation in a microscale fashion. The transient sterile inflammation resolves quickly without causing obvious skin inflammation, but greatly enhances the immune responses induced by various vaccines. Moreover, a combination of NAFL with dissolvable microneedle arrays comprised of influenza vaccine leads to lesion- and needle-free, painless, and very effective skin vaccination.

Apart from AFL and NAFL, a modified form of selective photothermolysis was also investigated for facilitating delivery of malaria vaccines through mouse skin. A promising malaria vaccine, called radiation-attenuated sporozoite (RAS) vaccine, confers great protection in human volunteers by intravenous injection but not by intradermal or subcutaneous injection because RAS must be delivered via the bloodstream into the liver, the only organ that supports limited growth of RAS. Intravenous immunization is not a clinically acceptable route of immunization due to a large variation in delivering efficacy. To facilitate entry of RAS into blood vessels, we treat the inoculation site with a low power laser at 532 nm, delivering 1 J/cm^2. This treatment selectively injures capillaries, increased permeability of blood vessels beneath and significantly enhanced skin-to-liver delivery of RAS injected intradermally. The laser-mediated enhancement of skin-to-liver delivery of RAS resulted in much stronger immune responses and conferred protection against malaria infection nearly as effectively as IV immunization. Our investigations provide proof-of-concept evidence that cosmetic lasers hold great promise for safely augmenting skin vaccination.

Andy Yun Laboratory

Biological Lasers

Since Theodore Maiman demonstrated the first laser in 1960, stimulated emission and lasing have made a tremendous impact on modern science and technology. Typical lasers use engineered optical gain materials, such as semiconductors and doped crystals. Biological materials and living organisms had not been explored as materials for lasers. Our lab's research led to the development of the first laser based on fluorescent proteins as the gain medium [Gather & Yun, Nature Photonics 2011, Nature Communications 2014] and subsequently developed "cell lasers"—tiny lasers that can be embedded in and carried by a cell [Humar & Yun, Nature Photonics 2015, Fan & Yun Nature Methods 2014]. Biocompatible micro- or nano-lasers that are injectable into the body represent a paradigm shift in how we generate and use coherent light in living systems. Such lasers may one day open new pathways for disease diagnosis, imaging, and therapeutic intervention. This work has received considerable public exposure through numerous news media, including CNN Live interview, New York Times, BBC News, and Top 10 Breakthroughs in Physics. Dr. Yun is credited as the inventor of the first "living laser" in the Guinness record book, as displayed in the MGH Paul S. Russell, MD, Museum, and has been selected as one of the most remarkable breakthroughs in "MGH: Two Centuries of Discovery."

Brillouin Microscopy

Inelastic light scattering by acoustic phonons was first reported by Léon Brillouin in 1922. Our lab brought this hundred-year-old principle of Brillouin light spectroscopy to the biomedical community in 2008 [Scarcelli & Yun, Nature Photonics 2008]. The invention led to a Brillouin microscope that can map the mechanical properties of biological samples with optical resolution without physical contact. In human studies, Brillouin microscopy provided the clinical evidence for the heterogeneous degradation of corneal tissue stiffness in advanced keratoconus. This technology has been licensed to a startup company for commercialization. Besides diagnostic imaging, Brillouin microscopy is useful for the studies of cellular biomechanics [Scarcelli & Yun, Nature Methods 2015].

Tayyaba Hasan Laboratory

In October of 1982, I came to the Wellman Laboratories of Photomedicine as a one-year experiment, intending to move on to an industry job where I had what seemed like exciting and attractive offers at the time. Thirty-five years later, it has been a long one year! In that time, the transformation in both my scientific mind-set and my research focus, as a result of being at the

Massachusetts General Hospital and Wellman Center for Photomedicine, has been profound.

When I arrived, I had minimal experience in biomedical research. My training had been very physical sciences oriented, studying chemical reaction mechanisms using kinetics and modeling of transition states through vibrational analysis and kinetic isotope effects. Now, my laboratory operates under a very translational ethos, even in the research that may outwardly seem basic. Broadly, our group works on photochemistry-based approaches (photodynamic therapy, or PDT) for the treatment and diagnosis of disease. PDT is increasingly being used to treat a wide number of diseases and involves the photoactivation of a light-responsive chemical, or photosensitizer, upon exposure to an appropriate wavelength of light. Photoactivation initiates photochemical reactions that generate highly cytotoxic reactive oxygen species that then interact with proximal biological molecules (photosensitization).

We leverage the distinct mechanisms of these photochemical approaches to strategically develop molecular mechanism-based and optical imaging-guided combination treatment regimens, where one treatment arm involves near-infrared activation of a photosensitizer, while the other arm(s) modulate rationally-selected cellular and molecular targets that have been identified through mechanistic studies. These treatments can be fairly disease-specific and often require designing novel formulations, such as multi-agent nanoconstructs (Figure 1) and photoimmunoconjugates, for optimal photochemical treatment effects. In cancer, the focus malignancies within my group are ovarian, prostate, pancreatic and head and neck cancers. In infections and infectious diseases, efforts are targeted toward developing microbial-enzyme-specific photoactivatable molecules for use in PDT. Target organisms of infectious diseases are leishmaniasis (Figure 2), Mycobacterium tuberculosis and methicillin-resistant Staphylococcus aureus.

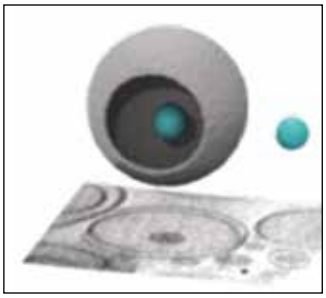


Figure 1. 3D rendering of a multi-agent nanoconstruct containing a lipid bilayer-incoprorated PDT agent and polymer-encapsulated biologic inhibitor of c-Met and VEGF pathways (blue).

Many of the treatment combinations are complemented or guided by the development of optimal imaging strategies with target-specific molecular probes that allow for both improved tumor detection and therapy monitoring (Figure 3), as well as in situ tracking of cellular processes during treatment for a better understanding and design of therapeutic response mechanisms (Figure 4). The abilities both to establish the mechanistic basis of a given

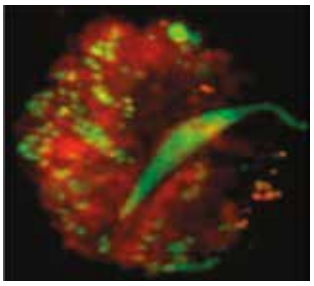


Figure 2. A promastigote Leishmania parasite homing to a macrophage.

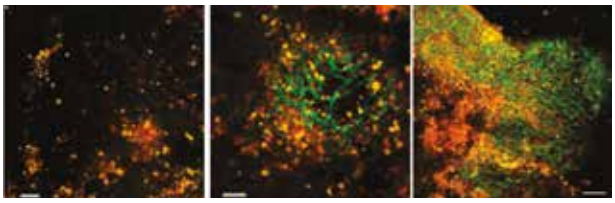


Figure 3. Distribution and localization of a photoimmunoconjugate (PIC, red) that penetrates through ovarian cancer nodules with varying levels of vascularity (green).

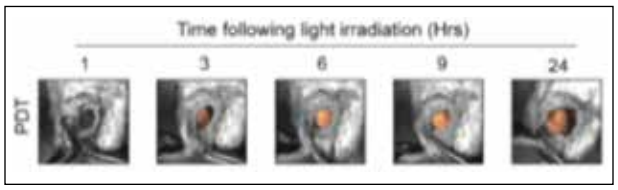


Figure 4. In vivo monitoring of changes in VEGF expression following PDT in an orthotopic mouse model of prostate cancer.

treatment and to subsequently make engineered nanoconstructs that can interfere with these deleterious pathways allow us to specifically inhibit them, thereby controlling tumor development and metastasis. However, it also opens up the possibility of numerous permutations of treatment combinations. Thus, in order to determine the best combination of agents efficiently, we are also developing in vitro tumor arrays that restore tumor architecture and have tunable ratios of cell types and extracellular proteins, so as to provide insights into the optimal sequences and combinations for clinically relevant subpopulations of heterogeneous disease (Figure 5).

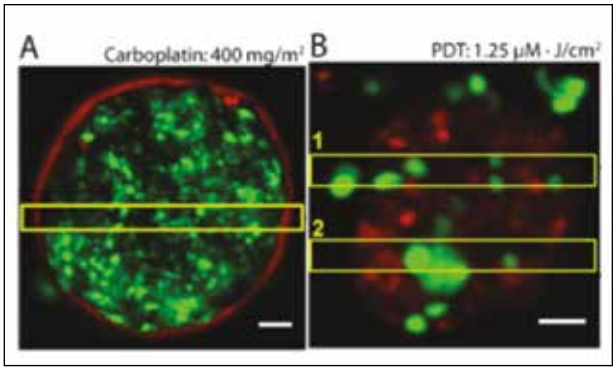


Figure 5. 3D micronodules of ovarian cancer allow for evaluation of differential patterns of cytotoxicity to different treatments.

Collaboratively, as part of two programmatic NCI grants, the laboratory studies described above are being translated into the clinic. A Phase I/II study of verteporfin-PDT for pancreatic cancer has been completed, led by Dr. Stephen Pereira at University College London. The next phase involves exploration of (i) patient customized PDT in collaboration with Dr. Brian Pogue at the Thayer School of Engineering at Dartmouth College and (ii) combinations of PDT with nanoconstructs incorporating topoisomerase inhibitors in collaboration with an industry partner. Additionally, a pilot investigation on the role of molecular modulation of actinic keratosis and psoriasis was completed and is being continued for skin cancers. Finally, low-cost PDT of oral cancers is being developed, in collaboration with Dr. Jonathan Celli at University of Massachusetts Boston, for patients in India as part of an NCI initiative on global health.

Short History

Origins

The Wellman Laboratories came into being in 1975, emerging from Dr. John Parrish's Photomedicine Unit laboratory in the Dermatology Department at MGH. Dr. Parrish had been working with Dr. Thomas B. Fitzpatrick and others in the department to develop a new, highly effective, light-activated treatment for psoriasis, called PUVA. Initial funding for the Wellman Laboratories was received from Mr. Arthur Wellman, the husband of a grateful patient, Gullan Wellman. Dr. Parrish has published a detailed account of the development of PUVA and the establishment of the Wellman Laboratories (J Invest Dermaol, 2012:132, 1042-49). The Laboratories, which were on the fifth floor of the Warren Building, moved to the Edwards Research Building in 1976, sharing space with Dr. Irvin Blank. Dedicated office space became available in 1979 in the basement of the "Temporary Building." This space is now under more recently built MGH buildings. The total laboratory and office area in 1980 was 1400 sq ft.

The Wellman Laboratories, still called the Photomedicine Unit in the early years, consisted of Dr. Parrish plus technicians and physicists including Rox Anderson, Dan McAuliffe, Chris Shea, Mary Stuart and Joanne Wimberly. The staff numbered only 4 in 1980. In collaboration with members of the MGH dermatology department including Warwick Morison (who joined the Wellman faculty), Lewis Tanenbaum, Robert Stern, Ernesto Gonzales, Madhu Pathak, Thomas Fitzpatrick and others, 60 original research papers on photomedicine were published from 1976 through 1981. Many of the studies focused on patient responses to PUVA for psoriasis or investigated application of PUVA to other skin diseases. Basic research studies in cutaneous photobiology were published including those defining quantitative UVB and UVA-induced responses in skin, establishing UV effects on immune responses (photoimmunology) and on the optics of skin. The results of these studies were the foundation for development of many current UV phototherapies in dermatology. The first publication from the Wellman Laboratories of laser-initiated effects on skin appeared in 1976 and described responses to nitrogen laser radiation at 337 nm.

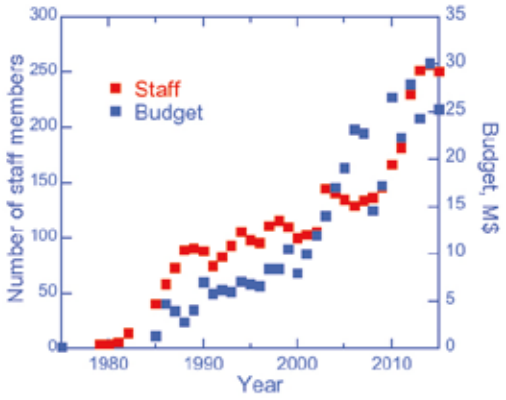
PUVA light box for treating psoriasis

First long-pulse dye laser for treatment of port-wine stains, circa 1983.

How Wellman Grew, 1975-2015

The Wellman Center staff increased steadily from 4 in 1975 to about 250 in 2015, with significant escalations around 1988 and 2010. Twenty-five research faculty were recruited in this period, many of whom established research groups, acquired independent funding and recruited additional research staff. An administrative and finance core was created in the 1980's. The current 18 members of the core provide essential (and excellent) support for the research activities. Creation of highly valued technical cores that serve the entire Wellman Center were initiated by formation of a Pathology Core in 1986. More recently cores were established for Synthetic Chemistry (2009),

Translational Research (2011) and Research Computation (2012).

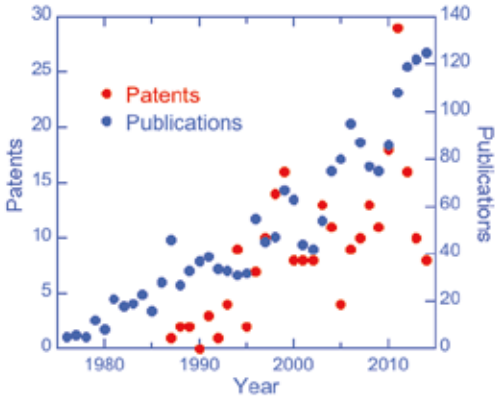


Wellman staff members and budget

Financial support necessarily increased substantially from the first philanthropic gifts in the early years to support from multiple governmental and non-governmental sources. Initially, one NIH grant and philanthropic gifts from Mr. Wellman largely supported the research efforts of the Wellman Laboratories. A large rise in funding began in 1985 with the receipt of peer-reviewed funds from Department of Defense (DOD) for Medical Free Electron Laser research. At first this program supported investigations of potential applications of short pulse, high peak power lasers in medicine. A version of this program still continues and now supports research on light-mediated diagnostic and therapeutic applications directed toward military medicine problems.

The need for additional laboratory and office space was met by expanding on the 2nd floor of the Edwards Building (1981 and 1999), then occupying space on the 2nd floor of the Wellman (later changed to Their) Building (1984) and the 6th floor of the Bartlett Extension Building (1985). Space was gained on several floors in Bartlett Hall: 3rd (2000), 4th (1988), 7th (2000) and 8th (1989). More recently, the Wellman Center gained laboratory and office space on the 8th floor of the Simches Building (2006), at 65 Landsdown Street in Cambridge (2011) and in Building 149 of the Charlestown Navy Yard (2014). The main Administrative and Finance offices were established at 125 Nashua Street in 2015.

From 1975 to 2015 hundreds of students, research and clinical fellows, technologists, engineers, faculty, other scientists and support staff have contributed to the Wellman Center research activities. Their efforts produced a multitude of new ideas that were tested, and the results subsequently published or used to substantiate patent claims. Partial evidence of their creativity, skills and determination is shown by the number of papers published and patents issued, which grew steadily in this period. Additional evidence is the significant number of commercialized clinical devices that arose from their research and development work



Wellman publications and patents

Wellman Center in 2015

The Wellman Center for Photomedicine (name changed in 1982) now has 251 members: 14 faculty directing research groups, 16 instructors and lecturers, 18 affiliated faculty, 78 research and clinical fellows, 23 research scientists, 31 technical staff, 18 administrative and financial staff, 16 visiting scientists, 29 graduate students and 6 undergraduate students. The Wellman Center utilizes 38,000 sq. ft. of space for research and administration in four contiguous buildings on the MGH main campus plus four other MGH buildings.

Recent Wellman annual budgets average $26 million. Research grants to individual investigators from NIH and NSF support the largest portion (41 percent) of the current budget. Inventions patented from Wellman research produce revenue, which is used to support further research. This year 23 percent of the budget was derived from this revenue. DOD funding, mainly as a large research grant to the Wellman directed toward military medicine, supported 16 percent

of the budget. Industry contracts supported 11 percent and investment income, foundations and philanthropy supported 9 percent of the annual budget.

The recent scientific and clinical impact of Wellman Center activities has been substantial. In the last 5 years, research by Wellman Center investigators led to 7 FDA approved clinical treatments or devices, 81 issued US patents and 560 original research papers.

Education and training remain cornerstones of the Wellman Center. Innumerable researchers from high school and graduate students to post doctoral fellows and visiting scientists have gained technical skills, as well as perspective on applications of their expertise and technologies to medical problems in the Wellman Center. In 1991, funding received from the Department of Energy to develop a Laser Center of Excellence was used largely to support training of MD and PhD fellows in laser medicine. Wellman investigators started graduate courses at MIT, and teach in courses at Boston area universities as well as participating in the teaching and training programs established and supported by the Wellman Center. These include:

- **Graduate student program —** Designed to support students carrying out their thesis research in the Wellman Center, this program provides stipend support to select graduate students. Since 2002, 20 students have benefited from this program.
- **Bullock Fellowship —** Created in 2007 through generous contributions from Marjorie and Bill Bullock, this fellowship is designed to support research by MD, PhD or MD/PhD fellows and to foster interactions between researchers from diverse fields of science and medicine. This highly competitive fellowship has been awarded to 20 fellows.
- **Summer Institute for Biomedical Optics —** This program began in 2003 to support and inspire talented college students to pursue advanced research, education, and careers in science and engineering. Now NSF-supported for US students, the program has also expanded internationally to support students from KAIST (Seoul, Korea) and the University of Tokyo (Japan).
- **Biomedical Optics course —** Taught since 2003 as part of the Harvard MIT Health Sciences Technology program, this course is an introduction to physics and engineering of optical technologies and their applications in medicine and biology.
- **Lasers in Dermatology —** A popular, annual CME course on Lasers in Dermatology began in 2005 and is attended by more than 150 practitioners each year.
- **Laser accreditation course —** Offered as a service to the MGH, this course is designed to educate MGH clinicians, researchers and staff who use lasers on their safe operation.
- **Lectures and tutorials —** A lecture series is held weekly that features Wellman Center researchers-in-training, Wellman faculty and additional outside speakers. The Wellman Center also co-sponsors with MIT the Lester Wolfe Photomedicine Workshops.

Impact on Medicine and Biology

The impact of the Wellman Center's research and inventions is multi-disciplinary with contributions to medical diagnostics and treatments, and insights into biological science. Well over a million people per month are treated or diagnosed with Wellman inventions. Moreover, a bona fide field arose, with Wellman largely leading it, now called biomedical optics. Hundreds of career scientists and physicians have been mentored, trained, nurtured and supported at Wellman. A multi-billion dollar industry was fostered from Wellman research that now includes medical lasers, other therapy devices, photodynamic drugs and diagnostic optical imaging.

Dermatology

Wellman research has had a wide-reaching impact on the practice of dermatology. In the early years of Wellman, John Parrish and co-workers determined an action spectrum for treatment of psoriasis. That knowledge launched "narrow-band UVB" therapy, which is still a mainstay for treatment of psoriasis. A recent variant, excimer laser treatment, also came from Wellman. Lasers have transformed the practice of dermatology, and nearly all of these treatments have roots in Wellman. This revolution started with Anderson and Parrish's notion that pulses of light can selectively heat and destroy microscopic structures, called selective photothermolysis (SP).

This concept was put into practice: long-pulsed dye lasers were invented specifically for treating children with port-wine stain birthmarks, without scarring, by targeting blood vessels. This treatment is still the gold standard. Tattoo removal without scarring and treatments for benign pigmented lesions are both applications of targeting with SP, as is permanent laser hair removal, which is now the most popular medical laser application.

Fractional laser treatment, which is not a targeted therapy, was invented to stimulate skin remodeling. It is rapidly becoming the leading method for scar normalization. Mei Wu's lab discovered recently that fractional lasers can also stimulate a robust response to immunization and she plans clinical studies in the near future. After a laser strategy failed, Rox Anderson's lab invented and launched cryolipolysis, a very popular treatment that uses controlled cooling to remove unwanted body fat. An automated device for epidermal skin grafting was also invented in the Anderson lab and is used for vitiligo, wounds and burns. Other studies demonstrated that photodynamic therapy is an effective treatment for acne.

Economics is one way to measure impact. At least $10 billion of medical device sales arose from Wellman inventions in dermatology, and there is much larger economic impact from the use of these devices. Wellman's pipeline of practical dermatology innovations is still full, including a potential cure for acne, novel treatments for pain and itch, and ways to "copy" the skin with all its component parts.

Ophthalmology and Urology

Research in the Wellman Center has had substantial impact also in ophthalmology, urology and other fields of medicine. Photodynamic therapy for macular degeneration, the leading cause of blindness in this country, came from Tayyaba Hasan's laboratory. It was the first, and for several years the only, approved treatment and has been used in millions of patients. Selective laser trabeculoplasty, a leading option for glaucoma treatment, came from Wellman. Optical coherence tomography (OCT) was not invented in the Wellman Center, but Wellman inventions have greatly improved its speed and resolution, leading to new medical applications. Laser lithotripsy, which allows urinary and other stones to be removed without surgery, was an early invention that is now in most hospitals throughout the developed world.

Optical Diagnostics

Wellman's impact in optical diagnostics has been substantial, but small compared to the devices and applications currently emerging from the research of several Wellman research groups. Early studies of polarized light imaging led to an extremely useful dermatoscope; almost every dermatologist now keeps one in their pocket. Rob Webb and colleagues invented the first laser confocal microscope for skin imaging, which is now used in clinical care and research. Currently, game-changing technologies are being launched: live microscopy will change pathology forever because, unlike biopsies that destroy tissue and pose risks, optical imaging is fast, safe and non-destructive. Live microscopy will be the means to guide treatments very precisely in the future and is now revealing the inner workings of organisms, tissues, and cells. Optical point-of-care diagnostics will improve care while reducing cost and saving lives.

NvisionVLE® Imaging System. Advanced OCT for evaluation of human tissue microstructure.

Since Tom Deutsch's early studies about 30 years ago, Wellman Center inventions have taken OCT, live microscopy, and optical diagnostics far forward. Gary Tearney and Brett Bouma invented, made and deployed microscopic imaging systems in the heart, airway, esophagus, upper GI tract, and other live tissues. Underlying these advances, are hard-won new technologies and strategies to push speed, resolution, depth, signal-to-noise ratio, and image analytic software. OCT microscopes you can swallow were launched, and recently FDA approved, as an alternative to endoscopy. Ben Vakoc developed a technology to image the microvasculature in exquisite detail that is proving to be very useful in studies of cancer, brain injury and other tissues. Andy Yun built the world's

first microscope capable of imaging mechanical properties of tissue and is currently being used to develop diagnostics for the lens and cornea. Charles Lin has developed unique microscopes to image the microenvironment and movements of cells in situ, leading to discoveries about how stem cells behave, how bone marrow grafting works and how cancer metastasizes. Seemantini Nadkarni is developing a novel point-of-care optical diagnostic for analysis of blood clotting, a problem that accounts for millions of deaths. Conor Evans is using coherent anti-Stokes Raman microscopy to study lipids, sebaceous gland activity, cancer growth and drug distribution in vivo.

Photochemical Effects and Treatments

Wellman has had substantial impact from pursuing of two persistent questions – what does light do to us, and what else can it do for us? Photochemistry underlies the benefits and risks of sun exposure, as well as providing a tool for therapies. Hensin Tsao discovered that a UV responsive gene drives the growth of some human melanoma cancers. Mike Hamblin's lab is studying the mechanisms and applications by which visible and near infrared light rescues tissue after injuries, promotes wound healing and improves human physical performance. Irene Kochevar contributed much to our understanding of photosensitivity, and of photoaging, a complex process that makes our sun-exposed skin look and act old. She and Bobby Redmond are now developing a photochemical method for bonding tissues together for reconstruction after injury or surgery that minimizes scarring and fibrosis. They recently introduced the concept of photochemical passivation, using light-induced protein crosslinking to stabilize tissue against unwanted strain, inflammation and scarring, that has multiple medical applications.

Summary

These are only a sampling of the large number of new technologies and applications under development, and of the multiple scientific advances that are emerging from Wellman research programs. Many are likely to have significant future impact.

Annual Photographs

1. Tayyaba Hasan
2. Irene Kochevar
3. Mike Moran
4. Norah Chen
5. Martin Price
6. John Parrish
7. Yaron Hefetz
8. Irwin Blank
9. Glen LaMuraglia
10. Kenton Gregory
11. Dom Bua
12. Elizabeth Siebert
13. Richard Granstein
14. Terry Kneisley
15. Anthony Cincotta
16. Ralph Delatorre
17. Richard Straight
18. Rox Anderson
19. Tom Deutsch
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21. Susan Weeks
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25. Peggy Hardy
26. Sima Ortel
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32. Peggy Sherwood
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54. Paul Bleicher
55. Joanne Wimberly
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1. Mike Moran
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6. Remy Nazareno
7. Lisa Buckley
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12. Sue Kopeckne
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73. Yakov Domankovitz

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58. Maire Doyle

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1. Beverly Dammin
2. Kirsty Swindells
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23. A. Kim Palli
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27. David Lin
28. Christine Dierickx
29. Gesa
30. Wooseok Koh
31. Judy Runnels
32. Bernhardt Ortel
33. Joanne Wimberly
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35. Mike Hamblin
36. Albrecht Kastein
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38. Sylvie Kossodo
39. Peggy Sherwood
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59. Robert Redmond
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61. Yacov Domankevitz
62. Beth Shulman (now Beth Scott)
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1. Tayyaba Hasan
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23. Vanessa Campo-Ruiz
24. Rieko Tachihara
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32. John Demirs
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35. Dom Bua
36. Milind Rajadhyaksha
37. Bernhardt Ortel
38. Michael Hamblin
39. Kevin Schomacker
40. Eugene Vanderpool
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7. Irene Kochevar
8. Peggy Sherwood
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12. Clemens Alt
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16. Misbah Khan
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19. Alok Sinha
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22. Mehran Poureshagh
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36. Gary Tearney
37. Brett Bouma
38. Gladys Ouedraogo
39. Anna Yaroslavsky
40. Tom Flotte
41. Milind Rajadhyaksha
42. John Demirs
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44. Eliot Battle
45. Costos Pitsillides
46. Barry Cense
47. Hyle Park
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50. Rob Webb
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52. Larry Booth
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55. Salvador Gonzalez
56. Maritza Middlekamp
57. Mark Pierce
58. Charles Lin
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62. Sylvie Kossodo
63. Peter Waterman
64. Melissa Cohen
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66. Eugene Vanderpool
67.

1. Peggy Sherwood
2. Tom Deutsch
3. Tayyaba Hasan
4. John A. Parrish
5. Irene Kochevar
6. Rox Anderson
7. Bernhard Ortel
8. Alok Sinha
9. Mary Beth Nolan
10. Les Lipkind
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12. Milen Shishkov
13. Michael Hamblin
14.
15. Jeremy Stern
16. Susan Weeks
17. Beverly Dammin
18. Johannes deBoer
19. Giuseppe Nigri
20. Dieter Manstein
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23. Mehron Poureshagh
24. Rieko Tachihara
25. Yasuhisa Nakayama
26. Leyda Bowes
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29. Imran Rivzi
30. Caroline Boudoux
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32. Brett Bouma
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34. Costas Pitsillides
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36. Glenda Best
37. Chelvi Rajadura
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39. Gene Vanderpool
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41. Tom Flotte
42. Mark Pierce
43. Rob Webb
44. Apostolos Doukas
45. Pal Selbo
46. Chris Ammen
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55. Barbara Chen
56. Clemens Alt
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58. Melissa Cohen
59. Anna Yaroslavsky
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61. Susi Astner
62. Hensin Tsao
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65. Bill Farinelli
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67. Bill Rice
68.
69. Denise
70. Hirotaka Akita
71. Bjorn Carle

Wellman Stories

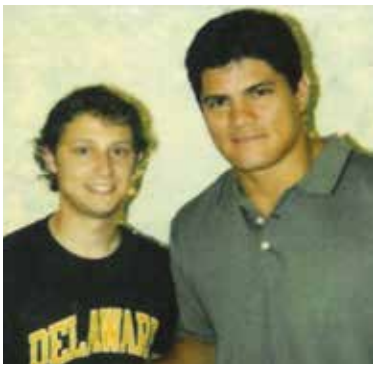
David Aghassi, MD, Clinical Fellow, Anderson Lab, 1998-1999

I was at Wellman for my fellowship 1998-99 and worked most closely with Rox Anderson and Salvador Gonzalez on confocal microscopy. Wellman is an amazing place; most of the ideas that lead to our new devices are generated there.

I do have a funny story: When I was at Wellman, Rox had a parrot that flew around the lab. One day, I was faxing something and "Photon" landed on my shoulder and said "What are ya doin?" I was so surprised, I hit my head on the fax machine – I wasn't hurt, just surprised. I always laugh about that incident whenever I think of the lab.

Ken Bujold, MD, Research Technician, Redmond and Kochevar Labs, 2004-2007

My position in Bobby Redmond's and Irene Kochevar's lab was my first "real-world" job. Starting straight out of college, I wasn't quite sure what to expect working in a Harvard research laboratory, but I quickly realized what it meant to work in Wellman. They immediately told me to call them Bobby and Irene, which was a bit of shock, but it was comforting to know they began to view me as a peer not as a underling or minion. Our lab had an open door policy, which was wonderful. Well, Irene's was always open and Bobby's meant moving things, usually stacks of paper, out of the way to open it for you.


Ken Bujold and Teddy Bruschi

Many of the lasting memories of Wellman center around the activities and personalities in the lab. I did some work with Mark Randolph and his team. In the lab, there were visiting surgeons from Ireland doing research and each summer medical students would be paired with members in the lab. Occasionally, the overzealous medical student and the surgeon would collide and usually it happened in the OR. One memory that sticks out was a student who was observing the surgeon operating on a rat nerve. The repair required hair-fine sutures and viewing through a microscope. The student, who couldn't see what was happening through the double-headed scope, decided to look more closely with his bare eyes thus obscuring the field of vision and inducing the ire of the surgeon.

Our lab was focused on food and ate many lunches together. The "fishbowl" was our common hang out even for some after hours drinks. Each holiday season, the lab made an annual trip to Penang in Chinatown for a group meal courtesy of the bosses. Nearly 7 years later, I returned to Boston to help transport a sick newborn to the Floating Hospital and brought the EMT crew to the same restaurant for lunch. We ordered "to go" and ate in the ambulance on our return trip to Springfield.

The photochemical tissue bonding (PTB) project involved trying to bond different types of tissues. Pretty much if you name a tissue, we tried to bond it. The ex vivo experiments worked best with fresh tissue, which meant harvesting or road trips to Super 88 to obtain tissue. The most interesting was tissue that was obtained through a guy who had connections at a slaughterhouse. I placed an "order" and a black BMW with tinted windows pulled up at the entrance facing Shriner's. The window rolled down, a black bag of fresh cow parts was exchanged for $40 and the car sped off.


Maki Yamaura, Elaine Rafferty, Min Yao, Bobby Redmond, Yin Chu Chen, Antonio Valencia, Chelvi Rajadurai, Asima Chakraborty, and two summer students

One of the best memories was in 2004. I had just moved to the city and as a HUGE Red Sox fan, I was able to witness history with their first World Series in 86 years. The best part was the bet made by George Taylor, the mail guy. He was a die-hard Yankees fan. He was so confident, he bet that if the

Red Sox won, he would wear a pink Red Sox hat in exchange for his Yankee's hat for a full day at work. He held true to his word, but the look on his face was priceless when he saw himself wearing the pink hat.

Even through residency and fellowship interviews, everyone has been fascinated with the PTB project. It was a great opportunity to become comfortable in helping plan projects. I am forever thankful to Bobby and Irene for giving me the opportunity in their lab and being a part of their work. It was truly a great time in my life.

Rehab Amin, PhD, Research Fellow, Hasan Lab, 2013-2014

I am a faculty member at National Institute of Laser Enhanced Sciences, Cairo University, Egypt. I joined the Wellman Center as a Fulbright scholar in 2013. Dr. Tayyaba Hasan gave me the opportunity to work in her lab. She introduced me to Dr. Tianhong Dai who helped me a lot during my stay. I appreciate the roles of both Dr. Hasan and Dr. Dai in developing my research career. Currently, I am still collaborating with Dr. Dai.

In my country I worked at an equivalent institute that deals with light applications in different fields such as medical, biological, environmental and industrial. However, the Wellman Center is characterized by being multidisciplinary. All facilities at the Center are linked with those at the Massachusetts General Hospital and at Harvard Medical School. This combination offers a great opportunity to the staff members to update their knowledge and develop their skills.

My project investigated the potential resistance development of P. aeruginosa to antimicrobial blue light. We identified endogenous porphyrins in P. aeruginosa cells and tested the effectiveness of antimicrobial blue light inactivation of P. aeruginosa in a mouse model of nonlethal skin abrasion infection using a bioluminescent strain. We concluded that endogenous photosensitization using blue light should gain considerable attention as an effective and safe alternative antimicrobial therapy for skin infections.

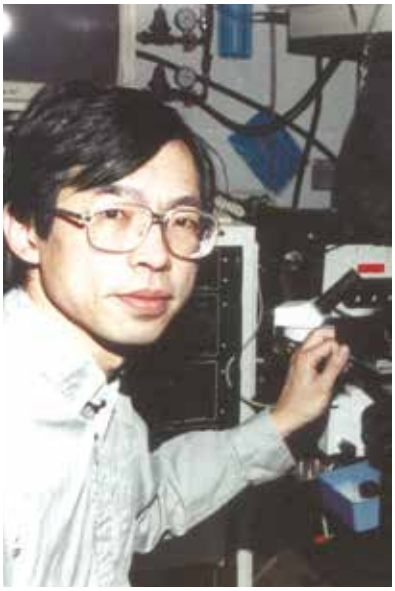
I gained new technical skills at Wellman, one of which is working with animals. I was impressed with the Center for Comparative Medicine (CCM). I used to work in my country in vitro and after I had joined the Wellman, I transferred my research to in vivo studies. Because of this change Fulbright approved my extension request to continue my training and my research study.

Wellman Center is one of the unique multidiscipline photo-research centers all over the world. It would be a great idea if the Center developed an international exchange program for visiting faculty/staff for training photomedicine scientists all over the world.

The best thing about Wellman is the learning opportunities as workshops and training courses that enhance the professional and personal development of faculty and staff. My most interesting memory is the New Year celebration party with all Wellman members, it was one of the memorable days in my life.

Charles Lin, PhD, Associate Professor; joined Wellman in 1994

I did my PhD at the University of Chicago on magnetic resonance spectroscopy, and my postdoctoral work at Princeton on coherent laser spectroscopy. By the end of that period, I was ready to leave the field of molecular spectroscopy and move on to something closer to the real world. A wise professor at Princeton told me to "go to Boston – doesn't matter what you do there, just get your foot in the door." So I came to Boston.



Charles Lin

On the day of my first interview with Dr. Carmen Puliafito at the Massachusetts Eye and Eye Infirmary, I walked into his laser lab on the top floor of the MEEI building, and met a very friendly gentleman with a German accent. It turned out to be Dr. Reginald Birngruber. He was working on selective laser targeting of the retinal pigment epithelium (RPE), a project I would later pursue myself. Subsequently I also met Dr. Franz Hillenkamp at MEEI, who gave me pages and pages of hand-written differential equations describing excimer laser ablation of the cornea. He wanted me to experimentally verify his calculations but I never got around to completing it.

So I had my foot in the door at MEEI, but the two doors I was most interested in getting in were the ones at Wellman and at Schepens Eye Research Institute (where I had heard about the fabulous work of Dr. Rob Webb with the scanning laser ophthalmoscope). Little did I know that the two doors would become one as Dr. Webb soon moved to Wellman.

I remember very well the conversation with Rox Anderson that finally got me into Wellman. It was outside Tufts Electro-Optics Technology Center (the building has since changed names) where Rox was coming in to give a guest lecture for a class that Tom Deutsch and I were teaching together. In the parking lot, I showed Rox a high-speed image I had taken with a laser-irradiated melanosome particle, showing a shock wave propagating outward and a cavitation bubble forming at the center. I think this image earned me my job at Wellman. When I came in for my formal interview with Dr. John Parrish (not in the parking lot), I was pleasantly surprised to see not just Rox Anderson but also Rob Webb in John's office.

At that time we did not have start up packages. Rox gave me an optical table on BHX-6 and a Q-switched Nd:YAG laser to play with. That was my start up package. Eventually I took over a second optical table and got funding to buy a Ti:sapphire laser to start building a two-photon microscope. I was inspired by the in vivo confocal microscopy work by Rob Webb, Rox Anderson, and colleagues, but I wanted to expand it beyond reflectance imaging to include fluorescence and other nonlinear contrast mechanisms, and apply it to cell tracking in animal models. I had in mind to study leukocyte trafficking in skin (multiphoton) and retina (confocal). A chance visit by Dr. David Scadden around 2002-2003 changed all that, and got me to devote most of my subsequent career to the studies of hematopoietic stem cell niche in the bone marrow. Tracking stem cells was never in my plan.

The ceiling of the BHX-6 lab used to leak all the time, such that every time it rained my first student Mike Kelly and I had to come in to make sure all the optics were safe, even nights and weekends. It was not just rain – condensation from the AC would also drip down onto the optical table. We hung up a large plastic sheet under the ceiling to protect the stuff below, but still lost a microscope (which was built on an open platform) because all the optics were ruined by the dripping water.

When Professor Sunney Xie developed the CARS microscope, he wanted to apply it to in vivo imaging. He sent a postdoc (Eric Potma) and a graduate student (Conor Evans), who brought their CARS laser system to my lab and carefully routed the CARS laser beams around my two-photon laser beams so both experiments could go on by flipping just a couple of mirrors. The optical table became a huge maze, but it worked and we got the first video rate CARS images on a live animal this way. Later when Conor became an independent faculty member at Wellman, he inherited this CARS laser system.

There was one major regret from those early days. In the late 1990s, as part of a collaboration with Dr. Irene Kochvar on selective photochemical excitation of the cell plasma membrane, I had built an evanescent wave microscope, and had thought about a simple modification to reduce the excitation beam below the critical angle. I would have created the light sheet microscope then, but I never pursued it because I could not envision how to use it for in vivo imaging.

Adriana Gabriela Casas, PhD, Research Fellow, Hasan Lab, 2002

I am currently a Researcher at the National Research Council of Argentina (CONICET). I visited the Wellman Center for 3 months in 2002, funded by an Argentine charity, the Bunge y Born Foundation, and under the supervision of Tayyaba Hasan. It was a wonderful experience, which helped me greatly to get my present position. Moreover, we have continued to collaborate with Tayyaba until now, and we have recently been awarded a NIH-CONICET travel grant to keep on working together.

Adriana Casas and Pål Selbo

What I remember most about that summer in Boston is the nice working group, and the fact that I really had a lot of fun during my stay. I also remember the food / the meals after the seminars and talks! I´d like to share some photos of

Tayyaba Hasan and Adriana Casas eating barbecue at Tayyaba´s home,

my Norwegian friend Pål Selbo, (the tall one) and me (the short one) at the Wellman Center. And a photo documenting that Tayyaba turned out to be a great cook!

By the way, I'm happy to inform you that after 13 years, I am coming back to the Wellman this year, funded by our collaboration grant. I hope to see you all!

Wikunda Limpiangkanan, MD, Research Fellow, Anderson Lab, 2011-2013

I first came to Wellman in June, 2011 and spent almost 2 years in Prof. Anderson's group. Our project was to develop a new technique to change the shape and to predictably move soft tissue in a particular direction using lasers. We modified fractional ablative laser treatment and followed by closure of microscopic holes. The results of our in vivo swine and ex-vivo human skin experiments supported the hypothesis that reducing skin area and moving skin in a preferred direction without causing a scar was feasible.

Wikunda Limpiangkanan

This application could be useful in treating some skin conditions such as relieving tension on burn scars, closing a wound or treating skin laxity in the near future. I would like to thank Prof. Anderson, my mentor who gave me a great chance, Bill Farinelli who was always there to give us a hand, and all of Wellman who made my wonderful memory there. Looking forward to seeing all of you again someday!

Joani Blank, Dr. Irvin Blank's Daughter

I appreciate getting the announcement of this important event, and would appreciate being kept on the mailing list for announcements like this. However, I moved to Northern California a mere 44 years ago, and I still live here on the Left Coast. So I am sending my congratulations to the Wellman Center with this email, and, if my sister attends the celebration, she can represent both of Irv Blank's daughters.

You may or may not recall something that was said about our Dad at the lovely memorial you created for him at MGH in 2000. John Parrish said in his eulogy that our father, when introducing himself at work-related social events, used to say, "Hello, I'm Dr. Blank; still trying to make a name for myself"

My memory is that both my sister and I dropped our jaws and looked at one another, thinking, "Our father never would have said anything like that." Since our dad wasn't there to defend himself, we had to accept John's assertion that he was telling the truth. And I, at least, felt that it was a good line whether or not my father actually said it. Since I have never used any surname other than Blank, I keep looking for chances to use the line, and in all these years, and I've found only two. Still, it's a good story.

Hyle Park, PhD, Research Fellow, deBoer Lab, 2005-2008

I primarily worked with Johannes deBoer. But among the people currently at Wellman, I also worked with Brett Bouma, Gary Tearney, Andy Yun, Ben Vakoc, Seemantini Nadkarni, and Melissa Suter.

After being away from Wellman for a while now, I have a much higher level of appreciation for the depth of expertise there. Almost no matter what I wanted to explore, there was someone right around the corner that was either an expert or at least knew enough to point me to an expert in the field. And that was just as true for more complex scientific concepts as it was for how to machine a block of aluminum. While I'm sure the same could be said at a number of other places, the level of expertise and the generosity with which it was given is just extraordinary at Wellman.

It's hard to understate how important my time at Wellman was to me and my career. I started at Wellman early in graduate school, and continued there as a postdoc and Instructor, 8 years in total. And so it had a huge impact on defining and setting my career.

Daniel McAuliffe, MS, Biomedical Technician, Parrish Lab, 1977–1997; Medical Laser Tech, Anderson Lab, 1998–1999

I have two Wellman stories.

Circa 1979, I was told that this guy, Mr. Wellman, had met TBF (Dr. Thomas B Fitzpatrick, Chair of Dermatology) at a country club in Florida. They got to talking. TBF mentioned he was the head of Derm at MGH. Mr. Wellman mentioned his wife had psoriasis. One thing led to another and Mrs. Wellman ended up at MGH getting PUVA treatments for her psoriasis. It was probably Chris Shea, Paul Levins or Ezra Matzinger who treated Mrs. Wellman. Anyway,
Mr. Wellman used to come by the lab where I was testing the blood of PUVA patients for PUVA's effects on immune response. I would explain all the tests I was performing – he seemed truly interested. One day he came by with a blood lab slip in his shirt pocket. He mentioned that he had to go to the Hematology Lab to get his blood drawn. I looked at the slip and told him that these are the same tests I perform for PUVA patients, and I could phone in the results to his doctor if he wanted me to do the blood tests. So I did. I drew his blood once or twice again while he and Gullan were up in Boston. The day before Mr. Wellman was leaving to go back to Texas he asked me if we needed any help with equipment, etc. I said yes, and he asked how much. I said around $20K for a centrifuge, microscope, incubator, etc. (At the time Warrick Morison and I were using Dr. Bloch's space up on the fourth floor right next to the Ether Dome.)


Daniel McAuliffe

Mr. Wellman donated $20K for the PUVA research. I never heard about Mr. Wellman again until I picked up the Sunday Globe in 1981. Front page, bottom right was the story of how Mr. Wellman donated $15M cash to the 1981 MGH Capital Campaign, and this led to the Wellman Building.

Circa 1998, Steve Zeitels and I got a CIMIT award for $75K to explore laser spot-welding of the epiglottis and trachea to provide an airway for stroke patients whose epiglottis had been impaired by the stroke. It didn't work because there wasn't enough protein in the trachea to make a strong weld. However, in the many conversations and meetings with Steve, Rox, Bill, et al., Steve wondered if there was a laser to treat vascular lesions in the vocal folds. Duh. Dermatologists had been using the pulsed dye laser (PDL) to treat vascular lesions in skin for many years, but Steve had never talked to anyone in Dermatology until then. I had a PDL in Eng Lo's lab in Charlestown that I had used for the primate stroke model studies. I asked Rox if I could use that laser, but Rox had another project in mind for that laser, so I contacted Jim Boll at Cynosure. Jim gave us a PDL and six weeks later Bill and I were in the MEEI OR running the laser for Steve. The patient had Verrucous Keratosis – something like slimy psoriasis on the vocal folds. We had agreed to treat only the top third of one vocal fold. Bill and I had no idea how much energy to use, so I believe we set the PDL pretty low and fired only 5 or 10 pulses. Anyway, we saw purpura, the desired endpoint in skin, in the treated area of the vocal fold. Steve said: "Bill, Dan what should I do now?" Bill didn't say anything, so I told Steve the tissue that had lifted off the vocal fold after the treatment looked like the shell of a shrimp after it was cooked, so why don't you try to peel it off. Steve cut it off with those little tiny scissors they use, then he looked at it through the microscope. "This is exactly where I would have tried to cut this off." And we know the rest of this story. I was told that Steve used this laser procedure to save Adele's career and she gave a shout out to Steve at the Grammy's a few years ago when she won all those awards. Steve was there in the audience as her guest.

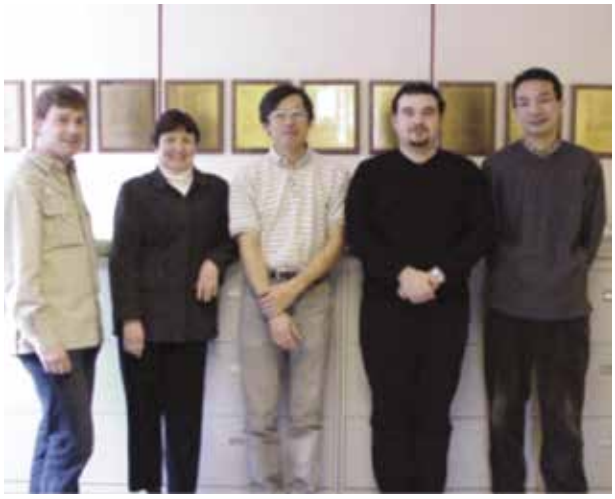
Carsten Framme, MD, Research Fellow, Lin Lab, 2001-2002

I was working in Charles Lin´s group together with Clemens Alt on selective laser treatment of the retinal pigment epithelium with a laser scanner. It was a fabulous stay and very interesting research work together with an enthusiastic group. The impact of the project was great and, being an ophthalmologist, this topic is still of clinical interest in spite of the fact that this new treatment modality has not yet made its way into clinics. However, SRT machines have been built and patients have been treated and we still await these lasers to come into the market. I guess that doing research at Wellman was one of the most important milestones to become a director of an university eye hospital in Germany. I´m still glad that I had the chance to join the Wellman team for a certain time working together with Clemens and Charles.

Carsten Framme

For the future it might be very interesting, if ophthalmologic research questions are be raised again and if US funding would be available for such projects and – maybe – I had the chance to send young interested ophthalmologists from my department to your institute for research projects.

With best greetings to all of you and especially to Charles and Clemens. I appreciate still having good contact and maybe there is a chance to enhance this contact in the future.



Clemens Alt, Judy Runnels, Charles Lin, Costa Pitsillides, Xun Bin Wei

Peggy Sherwood, MS, Photopathology Laboratory, 1986-2015

I was at Wellman for 28 years and worked with only 2 bosses, Tom Flotte for 22 of those years and Jenny Zhao for the last 6. I enjoyed my time with Tom, initially helping to set up the Photopathology Lab, serving as it's lab manager, and also as Tom's research assistant. With Jenny, the lab took a different turn, with 3 areas of service. I was responsible mainly for the electron microscopy aspect. The Photopath team is a service lab supporting the research projects of the Wellman investigators. Our role was (and still is) to guide them in the best approach to their projects so they would achieve the desired results. Under Jenny Zhao's guidance we helped establish new staining protocols and methodology.

My fondest memories of Wellman are the people I worked with over the 28 years, and the friendships I made. I had many enjoyable collaborations and have many people that I call friends to this day. I even dubbed the term W.O.W. (Women of Wellman) and now, M.O.W. (Men of Wellman). To this day, we keep in touch and get together periodically for dinner. There were a lot of fun times, especially in the early part of my tenure: we had parties (i.e., Halloween) and Sharky's on Fridays after work, where people would gather in the fishbowl to drink, do karaoke, be silly and let off steam.

Tom Flotte was the person who helped me most at Wellman. He always supported his team and particularly supported me: giving me many opportunities to take on projects. He insisted that his team members always got the credit they deserved in publications, etc. My tenure at Wellman was the longest of my working career. I grew tremendously as a person and as a researcher. I gained confidence in what I achieved and could achieve, and know I contributed substantially to the research at Wellman.

What makes Wellman unique is the diversity of the people and the working environment, which fosters collaboration among groups. I was always amazed how much people communicated and got along with each other despite the large size of the Center.

The best thing about Wellman: it's diversity and collaboration. The worst thing: sometimes losing sight of the contributions of each individual. I enjoyed my tenure at Wellman tremendously. I believe Wellman has some of the most dedicated and brightest researchers who care passionately about their work and where it will take medicine in the years to come.

My advice to Wellman is to never lose sight of the contributions of its members. To value and appreciate everyone that works there. To listen to everyone's ideas. Everyone contributes and should be recognized for their role. For several years Wellman had a luncheon for its staff just to say 'thank you" for all you do. It meant a lot.

Malte Gather PhD, Research Fellow, Yun Lab, 2009–2011

I'm sending an image of Andy Yun and myself explaining our work on living lasers in a CNN live interview. This was probably for me the most memorable experience at Wellman, even though working with so many great colleagues and friends was, of course, overall much more rewarding than the 2 min adrenaline kick at CNN.

Andy Yun and Malte Gather

Sally Ibbotson, MD, Research Fellow, Kochevar Lab, 1995-1996

I am keen to convey that I had the best time ever at Wellman! I was Irene Kochevar's research fellow and worked closely with Chris Lambert, Bobby Redmond, Mary Lynch, Mike Moran and many others. I thoroughly enjoyed every minute including the many hours of applying benzoyl peroxide to the backs of hairless mice and the trypan blue cell counting!!

Wellman is unique as it has such a close team feel to it and I felt very welcome right from the outset. The work I did there helped me to secure my academic photodermatology career path and as such I am now Head of the Photobiology Unit, at Ninewells Hospital & Medical School, University of Dundee. I now supervise scientists as part of my role and doing 15 months of full time lab work gave me inside knowledge and immense respect for the dedication and commitment required to be a laboratory scientist!

Of course the other main love I developed there was running – all due to Irene – and also to triathlons!! Running at lunchtimes along the river escalated me to doing ridiculous open water triathlons in lakes and the ocean at Cape Cod and elsewhere in New Hampshire and Vermont. I also recall going up to Mary's pad in New Hampshire and cross country skiing for the first time.

Altogether Wellman is an amazing place and it gave me an incredible 15 months that helped me hugely career-wise and in all aspects of life. I loved it and of course Boston is just the most incredible place that I had the good fortune to live in for 15 months. I lived in the North End and can still remember the cannolis!! I hope you have a wonderful celebration.

Neena Phillips, PhD, Research Fellow, Kochevar Lab, 1995-1997

I worked with Irene Kochevar's group on a photoaging project. The focus of Wellman on Photomedicine was unique. My experience there facilitated my academic career and progress to Professor. I especially remember the Wellman picnic in New Hampshire and enjoyed all my shuttle rides to and from the CBRC. My advice for Wellman would be to apply photomedicine to replace steroids and immunosuppressants for therapy.

Misbah Khan, MD, Research Fellow, Anderson Lab, 2000–2003

I worked with Rox Anderson and Salvador Gonzalez on fractional photothermolysis. I think the most unique thing about Wellman is its ability to provide opportunities to its fellows so that they can work in close association with highly qualified mentors. The understanding I gained at Wellman of laser physics and its interaction with skin has had the biggest impact on my life and my career.

My best memory about Wellman is meeting new people and getting to work with them.

My biggest help came from Bill Farinelli, Bev Dammin and Susan Weeks who were always there for me. The funniest


TB Fitzpartrick, Misbah Kahn, Salvador Gonzalez

Mehran Poureshagh, Leyda Bowes, Francisca Ruis, Kazu Nakano, Misbah Khan, Anna Yaroslavsky, Xun Bin Wei

thing at Wellman was that once I and my friend Leyda Bowes decided to play a prank on one of our friends by sending fake invites to all other fellows and faculty that there was to be a sushi party happening at his place. We placed flyers everywhere in Wellman and outside as well. He had no idea.

My advice is to take advantage of every moment at Wellman because you won't get this opportunity anywhere else in the world. The worst part is being a fellow there is that it has to come to an end.

Mary Stuart, BS, Research technician, Parrish Lab, 1980-1981, Gange Lab, 1985-1988

I was hired by John Parrish in 1980 who plucked my name from the applications because I went to Duke, as did he, and I had a work study job with his good friend Gerald Lazarus (head of Dermatology at Duke). I worked under Kosrow Momtaz, MD in the first period as a research tech/assistant. He was a kind, wonderful, gentle man. He was very patient and funny and had a great relationship with everyone. We were located in the temporary building and we did clinical studies on volunteers with psoriasis documenting results using different combinations UV light, soaking skin, and psoralens. I met so many really nice people who unfortunately had really bad psoriasis. We had great success with the treatments. We also had paid volunteers with no skin disease and we did many studies, mostly utilizing the buttocks (an untanned area). I met some very interesting people! The lab was a close knit group and we socialized a lot together. I am still good friends with some of these people and I have great memories of all from that period.

I came back to work in 1985 for Bill Gange who was also a kind, wonderful, gentle man. How lucky was I? I still worked in clinical studies but mostly on paid volunteers without skin disease. I also did work studying the effects of UV on the cellular level. We were in the Wellman Labs at that point, although I was in the Bartlett building. There were many of the same people but also LOTS of new people and again, we had a wonderful work environment with many of us being very close and always having a great time socializing. We had some GREAT parties in the Wellman first floor conference space and we did a lot outside of work. We also had many GREAT gatherings at John Parrish's house.

I left in 1988 when I had my first child. I was fortunate to be able to stay home while raising my children but visited often as I really missed everyone. I still get together with several people and we have such a great time and such great memories of working at Wellman. I think John set the tone where everyone felt like they were a very important part of the Lab and it made for a great work environment.

It may sound like I got more out of the social experience than the work experience and I am not sure I can argue that (and those who know me might agree). I was young and I never minded going to work!

Penggao Yang, MD, Research Fellow, Kochevar Lab, 2010-2011

I lived in Boston and worked in the Wellman for one year as part of Irene Kochevar's group. I have beautiful memories about that year as I reminisce writing this note. Great thanks to Irene, her group members and my other friends.

Penggao Yang

Godwin Mbagwu PhD, Visiting Scientist, Kochevar Lab, 1990-1991

My former student, Raymond Farmer, and I came to Wellman from Virginia State University (VSU), a Historically Black College and University, supported by the Medical Free Electron Laser Program (MFEL). We worked with a dedicated and supportive team led by Irene Kochevar and included David Dunn, Mike Moran, Ivo Gut. We also interacted with Tayyaba Hasan and Susan Weeks.

Wellman definitely had a direct positive impact on my career advancement. Our university is primarily a teaching institution. The experience and skill sets I gained at Wellman helped as I assisted, as Associate Dean for Graduate School and the Director of the Office of Research and Sponsored Programs, in developing a climate of faculty collaboration and research program excellence involving undergraduates, graduate students, and postdocs.

Through my research at Wellman, my student and I were exposed to new frontiers in photochemistry, photobiology and photomedicine, as well as to new skills and techniques. The project that developed partially from our time in Wellman enhanced our ability to access and successfully compete and receive funding from various federal agencies and these grants and contracts greatly improved our university's teaching, research and outreach capabilities. The project significantly transformed my student Raymond from a young man who grew up in an underserved and underrepresented minority community of Camden, New Jersey, to an excited, highly motivated contributor to the scientific world. Raymond went on to earn his BS in chemistry and a doctorate degree in Pharmacy and now works as a pharmacist at one of the major hospitals in Washington DC.

I cherish numerous wonderful memories from our time at Wellman. The one that stands out most is the weekly Friday Evening Social Hour that provided us the opportunity to interact informally with different research scientists from culturally diverse backgrounds across the world. One special memory is our introduction to the internet. At that time, our university did not have connections to the internet or e-mail. A few days after our arrival, my student and I watched with amazement, almost in disbelief, as one of our Wellman Lab colleagues, Ivo Gut, retrieved some online research information using the internet!

Wellman is almost like a miniature United Nations since scientists from diverse cultural backgrounds and different countries collaborate on cutting-edge research with potential significant global impact. Equally important is the great collegial working environment, which is nurturing, supportive and encourages team leaders to be receptive to new ideas and suggestions. This "Wellman culture" often results in enhanced creativity and productivity. Diversity represents a major strength and perhaps untapped resource of Wellman. Possibly the Wellman faculty and staff could develop engaging biomedical research and educational outreach mentoring activities to benefit Middle and High School students and their teachers from traditionally underrepresented and underserved minority communities.

Ivo Gut, Irene Kochevar, Mary Lynch, Mike Moran, student, Godwin Mbagwu, Joe Bouvier, James Davenport, Raymond Farmer, John Stith, George Henderson

Margaret Lee MD, Research student and Technologist, Anderson Lab, 1990–1994

Joining the Wellman Labs for an MIT undergraduate research opportunity had everything to do with my decision to apply to medical school and become a dermatologist who still aspires to honor what I learned from Rox and so many others at Wellman about scientific discovery, collegiality and selfless mentorship.

Jason Clark MD, Clinical and Research Fellow, Anderson Lab, 2012-2014

Shortly after I learned I had been accepted as a fellow, Ms. Dammin graciously arranged for me to meet with Rox at the AAD annual meeting in San Diego to discuss potential research projects.

Jason Clark, Matt Avram, Arisa Ortiz, Rox Anderson

Ms. Dammin tasked me with escorting Rox from one meeting area to another. It seemed straightforward, but everyone knew Rox! Every few steps people stopped him – former fellows, researchers, device company executives, well-wishers. It was literally like shuttling a rock star through a press tent. When we found a quiet area to discuss my research interests, I shared that I was passionate about building on my keloid genetics research with NIH. Rox replied, "I have no problem with that … I don't know anything about keloid genetics, but you should pursue a project you're passionate about." This formed one of my earliest impressions of Wellman. Rox was so busy, yet so open. It says a lot about Wellman as an institution and Rox as a leader. This is still one of my favorite Wellman memories.

Maria M Tsoukas MD PhD, Anderson Lab, 1991-1995

It was 1991 when as a visiting medical student at MGH, I first met with Dr. Rox Anderson who told me I could possibly return as a research fellow to work on Photodynamic Therapy. Dr. Anderson's and Dr. Parrish's "illuminating" achievements and leadership at the Wellman Laboratories of Photomedicine, had the most significant impact ever on my decision to work hard and pursue post graduate training in the US. My training and career wouldn't have been possible without these truly unique mentors and role models.

I was a research fellow for 3 solid years (1992-95) working on PDT dosimetry on skin under the direction of Dr. Anderson. I worked under the supervision of Dr. Kollias as well. I arrived as a novice and was fortunate to learn from the brightest, most prominent and talented teachers and colleagues! Research at Wellman was the most challenging, meaningful and rewarding experience ever! Everyone was committed, heart and mind, to excellence!

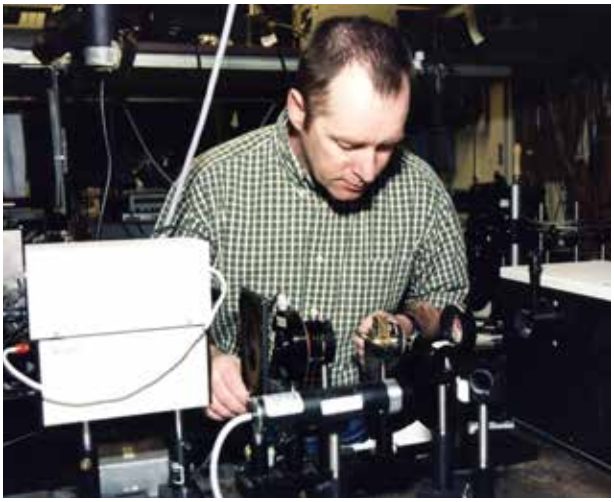
Being part of Wellman was "once in lifetime experience" that not only shaped my career as a dermatologist but also enlightened my entire life!

"Man is a being in search of meaning."
Plato

Thank you very much again for this invitation! Looking forward to seeing you soon!

Jay Walsh

Joanne Wimberly



Bobby Redmond

Elaine Rafferty and Chelvi Rajadurai

John Parrish, Lynn Drake, Senator Robert Dole and Rox Anderson

Brett Bouma

Rick Granstein

Jay Walsh

Ehsan Kamrani

Chris Shea

Peggy Sherwood and Tom Flotte

Kevin Schomacker

Franz Hillenkamp

Eleonora Reginato, Tomoharu Koiso, Marcelo Sousa, Cleber Ferraresi, Daniela Vecchioa

Beverly Dammin, Santa and Bill Farinelli

- Wellman space extended to Bartlett Hall, 3rd floor
- Dr. Blank retires from the faculty of Dermatology Department and Wellman
- Les Lipkind joins as Director of Finance and Strategic Planning

2001

- MGH Hereditary Melanoma Registry initiated to collect DNA samples from individuals with familial melanoma
- Human studies of PDT for Barrett's oesophagus
- Johannes deBoer, Gary Tearney and Hensin Tsao join the faculty

2002

- First demonstration of antimicrobial PDT in vivo using bioluminescent bacteria
- First demonstration of sealing wounds in vivo with photochemical tissue bonding

2003

- Name changes to Wellman Center for Photomedicine (WCP)
- WCP established as a Thematic Center at MGH
- FDA approves SPT treatment of laryngeal dysplasia and papillomas
- First demonstration of optical frequency domain imaging (OFDI)
- Summer Institute for Biomedical Optics initiated with NSF-NIBIB funding
- Mei Wu joins the faculty

2004

- Feasibility of fractional laser skin treatments
- Rox Anderson becomes Director of the WCP

2005

- FDA approves fractional laser for skin resurfacing (Fraxel)
- FDA approves treatment of melasma with Fraxel
- Human studies of OFDI balloon probe for esophagus
- Seok-Hyun (Andy) Yun joins the faculty

2006

- FDA approves treatment of skin scars with Fraxel
- FDA approves OCT coronary catheter
- Human studies of intragastric blue light for Helicobacter pylori infection

2007

- Bullock Postdoctoral Fellowship program initiated
- Feasibility of selective cryolipolysis demonstrated
- Human studies of GI and coronary OFDI
- Tom Flotte leaves Wellman to become Professor, Department of Laboratory Medicine and Pathology and Consultant, Anatomic Pathology at the Mayo Clinic

2008

- Human studies for transcranial NIR light for major depression and anxiety
- Human studies for PDT combined with chemotherapy for cholangiocarcinoma
- Human studies of OCT probe for biliary structure imaging
- First demonstration of Brillouin optical microscopy
- Synthetic Chemistry Core established
- Johannes deBoer leaves Wellman to become Professor of Physics, Vrije University Amsterdam

2009

- First demonstration of angiographic optical frequency domain imaging (OFDI) for preclinical cancer
- Human studies of PDT combined with differentiation therapy for actinic keratosis
- Human studies of OFDI for duodenal imaging in celiac disease
- Human studies of OFDI for assessing colonic polyps
- Benjamin Vakoc, Seemantini Nadkarni and Conor Evans join the faculty

2010

- FDA approves OFDI GI endoscopic
- FDA approves selective cryolipolysis
- FDA approves treatment of actinic keratosis with Fraxel
- Human studies of sealing skin wounds with photochemical tissue bonding (PTB)
- Human studies for Brillouin imaging of the lens
- Human studies of PDT for pancreatic cancer
- Human studies for image-guided biopsy of esophagus
- Discovery of the role of tumor specific antigens in anti-tumor immunity after PDT

2011

- Human studies for corneal Brillouin imaging
- Human studies of OFDI capsule for esophagus imaging
- First demonstration of single-cell biological laser based on fluorescent protein
- First in vivo demonstration of intracoronary laser speckle imaging in animals
- First demonstration of efficacy of transcranial LLLT for traumatic brain injury in mice
- Translational Research Core established
- Andy Yun's lab expands to Cambridge, 65 Landsdowne Street

2012

- FDA clearance for esophageal imaging with advanced OCT
- Research Computational Core is established

2013

- FDA approves balloon catheter-based esophageal OFDI
- FDA approves OFDI-NIRAF coronary catheter
- Human studies of OFDI capsule imaging and marking for guiding esophagus biopsy
- Human studies of OFDI capsule for duodenum
- Human studies of whole esophagus confocal microscopy (SECM)
- First demonstration that flow shifts ovarian cancer cells to a more aggressive phenotype
- Conor Evans' lab moves to Charlestown Navy Yard, Building 149
- Nancy von Hone joins as Director of Finance and Strategic Planning

2014

- Human studies using transcranial NIR light for acute traumatic brain injury
- Human studies for OCT imaging of non-melanoma skin cancer borders
- Human studies of polarization-sensitive OCT imaging of the retina
- Human studies of multimodality OCT-fluorescence in coronary arteries
- Feasibility and FDA approval of fractional epidermal suction blister grafting
- Feasibility of CT-based patient customized, photodynamic treatment of pancreatic cancer demonstrated
- First demonstration of light-triggered drug release and suppression of multiple treatment escape pathways using a single nanoconstruct
- First proof-of-principle in vivo for SMART bandage
- Development of rapid-assembly dendrimer chemistry for facile "click" oxygen sensing
- NSF-funded research experience for undergraduate (REU) site established in the Summer Institute
- Rob Webb retires from the Wellman faculty

2015

- FDA approves OFDI-NIRS coronary catheter
- Exome sequencing of nearly 400 hereditary melanoma patients completed in a collaboration between the MGH, MEEI and Broad Institute
- Human studies to monitor CNS inflammation by noninvasive imaging of the retina
- First demonstration of intracellular lasers
- First demonstration of a video-rate optically subsampled OCT camera system
- Apostolos Doukas retires from the Wellman faculty

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