



It's hard to believe

that almost a year ago the Peter Michael Winery was dangerously near catastrophe as the North Bay fires raged swiftly through the Wine Country.

The looming threat of disaster really puts life into perspective – in a flash, all of it could be gone. Thanks to the extraordinary dedication of winery staff and fire fighters, we are incredibly fortunate to have everything on the property intact and thriving. It has been inspiring to see the community coming together to support one another through the chaos and uncertainty.

When he founded it 35 years ago, my father-in-law, Sir Peter made a philosophical promise that the winery would operate as “100 x 100”: 100 percent family owned for 100 years. It is still family-owned and will remain so with three generations of the Michael family now involved today. The winery and surrounding land have become a cherished home from home for our family and an integral part of our lives.

We were deeply touched by the support we received from many of you in person, over the phone and emails. The fires were a reminder how quickly one's life can change forever. It can be the loss of a home, a job, a family member or being told you have cancer. Your life is changed in an instant. We are blessed to have such wonderful support from so many people including you reading this.

If you or any of your family need cancer support in the form of information or a referral, please know we are here to help you.

We're all in this life together.

Emily Michael, Founder



Martina De Santis, Walter Menzel & Jenny Koehler

Many of you may not know that the Peter Michael Foundation is a team of three people working together daily in a modest one-room office over a bike store in Southern Marin County, California.

As each year passes quickly, we see growing evidence of the Foundation's expanding impact and progress in prostate cancer clinical research and improved patient care. We began in 2004 with one fundraising event and this year we are hosting an unprecedented seven Stars dinners. The initial funds were used to underwrite one prostate cancer project at UCSF and we are now partnered with and funding six leading cancer institutes across the country.

We know full well that this progress and impact is due to the continued efforts, committed support and contributions of the hundreds of people who comprise the extended Peter Michael family.

It is with pleasure and pride that we report on the Foundation's accomplishments to you. Jenny, Martina and I are a small team with a big impact thanks to you.

PROSTATE CANCER (PCa) ACCOMPLISHMENTS

UCSF Helen Diller Family Comprehensive Cancer Center

PMF has been supporting immunotherapy research for several years at UCSF under the expert guidance of Dr. Larry Fong. Dr. Fong opened the first immunotherapy clinic for patients in the US. He and his team have researched and identified biomarkers believed to predict a positive response to PCa immunotherapy treatments. Immunotherapy only works in 10-20% of patients and produces dramatic results when it does. However, the high cost of immunotherapy discourages payers from reimbursement because of the majority of non-responding patients. The ability to confidently predict patient response will revolutionize all cancer care. *(See page 17)*

Memorial Sloan Kettering Cancer Center

Dr. Hedvig Hricak, Chair of Radiology, is a world leader in improving and refining MRI and its various combinations in the detection and management of PCa. Dr. Hricak has greatly strengthened the sensitivity and specificity of MRI in PCa and she has driven the adoption of MRI in the Active Surveillance protocol and the utilization of MRI prior to and during biopsies. Additionally, thanks to Hedi, many brilliant young PMF Postdoctoral Fellows have remained in science and medicine for their careers. *(See pages 18 - 19)*

Stanford Cancer Institute

Dr. Sam Gambhir, Chair of Radiology, and the PMF Postdoctoral Fellow have developed the second generation photoacoustic imaging device treating human patients in the lab. This is a "theranostic" which combines a diagnostic device with a therapeutic agent to treat prostate cancer at the cellular level. That means killing cancer cells while sparing healthy cells thereby providing life-affirming benefits to men. *(See pages 20 - 21)*

cont.

Miami Cancer Institute

This is the first year the Foundation has supported the Miami Cancer Institute which is a member of the Memorial Sloan Kettering Cancer Alliance. Dr. Michael Zinner is Founding CEO and Executive Medical Director of MCI. The Foundation's initial grant was applied to research on improving prostate cancer patients' PCa quality of life outcomes, cancer specific outcomes and prognostic markers. MCI and Dr. Zinner have a focused goal of effectively treating all cancers while maintaining or enhancing quality of life in the process. *(See pages 22 - 23)*

PERSONAL PATIENT REFERRALS AND SUPPORT

The Peter Michael Foundation receives one request a week on average for help with a cancer issue. It used to be just prostate cancer. Now the calls come from both men and women with a variety of different and in some cases, exceedingly rare cancers. We are not physicians and do not provide medical advice. But we do help patients and their families gain access to the top specialists at the leading medical centers in the US and in Europe if need be. The expressions of gratitude from the patients and their families are directed to us but really are due to the support and involvement of all of you.

YOU MAKE ALL THIS HAPPEN!

These results are due to the hundreds of you who support the Foundation's mission and work. Your energy, inspiration, commitment, counsel, and support is what drives us and helps the lives of others.

The Michael Family

Sir Peter has a long history of charitable work. He established the PELICAN Foundation twenty-five years ago in the UK. PELICAN is an acronym for Pelvic and Liver Cancer. In 2002, he decided to shift the focus of his US foundation onto prostate cancer exclusively. Emily and Paul Michael are carrying the mission forward with their active involvement and attendance at Foundation events throughout the US. The family's passion for the Winery and the Foundation is evident to all.

Peter Michael Winery Colleagues

The Foundation would be nothing without the support of the Winery which donates every bottle of wine served at the dinners, as well as the wine for the auction lots. Winery staff are at all of the Foundation events and are critical to the annual flagship event—Stars Knights Valley at Côte Deux Mille, the mountaintop aerie at the Estate. They are true, valued partners.

Foundation Friends

We are not fond of the term "donors." You are much more than donors. You are true supporters and deeply valued friends. Regarding our dinners, we say "Come as a guest. Leave as a friend." You are friends of the foundation and friends of the family. You truly are the ones that make it all happen and we are eternally grateful. *(See list pages 15 - 16)*

Board of Directors and Board of Strategic Advisors

The Foundation is a non-profit that's run like a business. The Foundation adheres to good governance principles and takes counsel from extraordinarily helpful, committed women and men on its two boards. The Board of Directors consists of an attorney, an accountant, and the President of the Winery. The Board of Strategic Advisors consists of two MDs (an oncology surgeon and a trained GP), two venture capitalists, two attorneys, three financial advisors, and an entrepreneur. All are successful and multi-tasking in multiple roles in various industries. *(See list page 24)*

cont.

Physicians and Scientists

The Foundation is blessed to have the opportunity to engage with the leaders in Urology, Radiology and Oncology who are both medical practitioners and accomplished scientists. Their direct ongoing patient care informs their scientific work in the labs. They all speak at the Stars dinners and more than a few of the guests are or have been patients in their care. They are truly inspirational to all of us.

Corporate Partners

From the outset, the Foundation has been blessed to have the engagement of the world class firms of the Bonhams Group for auctions and O'Melveny & Myers for legal counsel. Numerous senior Bonhams executives—the Co-Chairman, the Co-CEO, VPs and sector heads are all auction maestros. Guests say they've not seen such fun auctions. O'Melveny & Myers has provided wide-ranging, valuable governance and business counsel. OMM established the Foundation's pioneering business model that allows the Foundation to do both non-profit work and for-profit work concurrently in prostate cancer. Established five years ago, the PMF business model is being adopted by more 501(c)(3)s now. Silicon Valley Bank is the third firm that supports the Foundation thanks to its relationship with Sir Peter Michael and its leadership in the wine industry.

(See list page 24)

PMF Ambassadors

A cadre of experienced volunteers help implement the Stars dinners and live auctions. Among them is a group of uber volunteers acknowledged as Peter Michael Foundation Ambassadors. They are more than volunteers at the events. They are continually promoting the Foundation to their friends, introducing it to new hosts in new markets, and encouraging their friends to attend the Stars dinners.

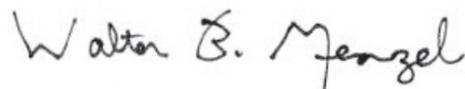
(See list page 24)

Chef Partners

Since the publication of the *Hands and Hearts* culinary arts book in 2004, the Foundation has partnered with many Michelin-starred chefs for the dinners and live auctions around the country. As well, the Foundation is constantly looking for up and coming chefs to work with. Our dear friend, Drew Nieporent has officially become the Peter Michael Foundation Culinary Advisor. Drew owns the Myriad Restaurant Group in New York and is in partnership with chefs and celebrities in his restaurants such as Tribeca Grill, Nobu, and Bâtard. Drew is instrumental in opening doors to new chefs for us.

Peter Michael Foundation is performing seven Stars dinners around the US in 2018. Please contact us for more information at any time.

Thank you all!



Walter B. Menzel
Executive Director



Friends of the Foundation

Greg and Lisa Boyce; Scottsdale, Arizona



Greg Boyce, Emily Michael & Lisa Boyce at Stars Knights Valley 2017

We met Emily and Paul Michael in 2000. Emily's brother, George, was the relocation officer for our move to the UK. George liked the neighborhood where we choose to live and he mentioned it to Emily and Paul as a possible good spot for them. We lived across from one another with a beautiful tree in the center of our Sunningdale community.

It was a quirky gathering of neighbors and fortunately the Michaels and Boyces become fast friends. Our oldest daughter Laura was like the 'Pied Piper' for the gaggle of kids from the surrounding homes and we all adored Elliot Michael. The kids would play till nearly dusk; create and perform talent shows and fashioned all sorts of games to play. Laura loved the opportunity to babysit Elliot. On weekend afternoons we often gathered to watch whatever 'theatrical' endeavor the kids would put on. Often a bottle of wine and little bites would make their way to the picnic area, then perhaps another bottle... it would be dark and past bedtime by the time we all would return to our homes. So many fun times! Paul and Emily still remember the 'ugly' wine we brought, a white zinfandel. They still tease us about it!

On 9/11, as I walked in the house the phone was ringing. It was Emily and she said "Lisa, turn on the TV and I'll be right over." Emily and Paul gave us such support and kindness as the horror in America unfolded. I will never forget her holding my hand and I am forever grateful.

When Emily was pregnant with Anna, Laura and I gave her a baby shower, which at that time was not a common practice. We had so much fun. When it came time for us to return to America, Emily organized the most amazing going-away party – a very special memory!

We attended the first Foundation dinner in 2006 on the mountaintop at Côte Deux Mille. We have attended six more Foundation dinners there since. We were also fortunate to be in Knights Valley for the first picking of Ma Belle-Fille a special wine in honor of a very special lady and friend.

For my 60th birthday a few girlfriends and I visited Downton Abby and had a beautiful evening at The Vineyard Hotel with Emily and Paul. It was the highlight of a very special trip indeed!

Finally, in June 2017 Emily was our first house guest in our new home in Scottsdale, Arizona. It was our daughter's wedding and having Emily there was so very, very special for our family. We are forever indebted to Paul for helping to make that happen. We hope our paths continue to cross for family events, wine events, foundation events and other life milestone moments.

Stars Miami 2017

Chef José Andrés



Maria & Dr. Sergio Gonzalez-Arias



Lori Calleja & Maria Beguiristain



Alysia Casebeer, Walter Menzel, Chef José Andrés, Jenny Koehler, Martina De Santis



Dr. Michael Zinner & Nancy Brinker



Andrea Kostanecki, Heather Murray, Martina De Santis, Jenny Koehler



Maryellen McKee & Jim MacGilvray



Dean Dennis & Cecil Flamer



Miranda & Dr. Jose Martin



Lorena & Dr. Ramón Quesada



Carving Jamon



Cecil & Sheryl Flamer



Jacob & Mariana Gadala-Maria



Interior of Bazaar Mar by José Andrés



Dr. Michael & Julie Jacobs



Dr. Felipe & Monica Del Valle



California "Funnel Cake": seaweed funnel cake, avocado, blue crab, tobiko, mayo, cucumber



Stars New York 2017

Chef Daniel Boulud



Sheri & Jimmy Rosenfeld



David Ingles & Ellen Fair



Cynthia & Bob Hay, Joia & Howard Haber,
Sue & Dave Quackenbush, Bill & Kristina McLaughlin



Jenny Koehler, Anne Yamamoto, Drew Nieporent



Robin Mathews, Michael Meyers,
Dan Mathews, Chad Labenz



Francesco Scattone



John Christopher, Jason Kinander, Ray Pirrello



Jaclyn Bogue



Sy Sternberg



Andrea Kostanecki, Paul & Kimberley Tanico



Daniel Boulud & Laura Pirrello



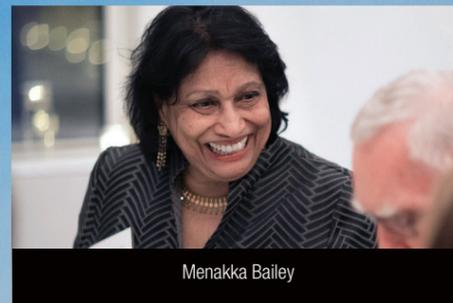
Dr. Hedvig Hricak



Chad Labenz



Karl, Meredith & Walter Menzel,
Lauren Ridenhour, Lisa Millman



Menakka Bailey



Martina De Santis, Ellen Fair, Walter Menzel, Paul & Emily Michael,
Chris Ehrlich, Dr. Hedvig Hricak, Jenny Koehler



Mike Kwatinetz



Blair & Wendy Van Zetten



Lisa Millman



Blair & Wendy Van Zetten



Lisa Millman

Stars Knights Valley 2017

Chefs Rupert & Carrie Blease



Sir Peter Michael, Chef Rupert Blease, Paul Michael



Michelle Monhoff & Kathryn Soter



Aaron Gershenberg & Julia Massa



Aaron Gershenberg, Julia Massa, Peter & Amy Wagner, Beverly & Arvind Sodhani



Walt & Gayla Wood



Richard and Linda Slade



Gary & Beth Goldberg, Laura Sparks-Boyce, Jennifer Sparks-Boyce, Lisa & Greg Boyce, Sharon & Dale Fiehler



Loretta & David Doon



The Umbrella at Côte Deux Mille



Michele Grasso-Dennis, Dean Dennis, Emily Michael, Katie & Mickey Miller



Stephanie & Jack Koraleski



Dennee Frey & Mike Eagle



Stephanie & Jack Koraleski, Bob & Polina Schlott, Pam Smith, Wallace Cunningham



Paul & Emily Michael, Sir Peter Michael, Chef Rupert Blease, Jenny Koehler, Walter Menzel, Martina De Santis



Gary & Beth Goldberg



Kim Wight, Chuck Allen, Jenni Hamill



Alisa & Ryan Bauer, Doug Fisher, Chris & Sara Ehrlich, Sachiko & David Eckert



Randall & Donna Melby



Chef Rupert Blease



Andy & Molly Mercy, Teke & Liz Kelley

Stars San Francisco 2017

Chef Thomas McNaughton



Shanti Brien, Allison White, Anja Hart, Nicki Gilbert



Eliot & Cynthia Fried



Katie & Spencer Fast



Jay Reinemann, Tom Whiteaker, Ryan Gilbert



Charlene & Vinny Lingham



Erik Muller, Jodi Steel, Amanda Wulfstat, Matt Wulfstat



Aaron Bastian, Dr. Lawrence Fong



Beth & Patrick Heron



Ilan & Cori Zipkin, Allison Abta



Lisa & Don Douglas



Albert & Cheryl Cha



Rochelle & David Ludwig, Chris & Sara Ehrlich



Greg Grunberg, Kristi Dravland-Grunberg, Ron Abta



Nathalie Shami, Michelle McKechnie, Martina De Santis, Jenny Koehler, Gabriela Shultz



Kate & Jeff Perkins



Richard Leider & Erik Muller



Jay & Annika Reinemann



David White, Nicki Gilbert, Allison White, Chris Hart



Eliot Fried, Jeff Ehrlich, Bill Newell



Alison Chaput, Chris Ehrlich, Matt Wulfstat



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Heather Murray
Emily Sabo
Gabriela Shultz
Nathalie Shami
Kathryn Soter
Jennifer Young

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Chefs Rupert & Carrie Blease
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Chef Daniel Boulud
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Feast and Fêtes
Lauren Ridenhour
Lord Stanley
Morlet Family Vineyards
Ne Timeas Restaurant Group
O'Melveny & Myers
Peter Michael Winery
Ram's Gate Winery
SLS Brickell

In Honor Of

In Honor of Don Macrae
In Honor of Dave Mortara
In Honor of Kevin White

In Memory Of

In Memory of Steve Bergren
In Memory of Charles E. Colander
In Memory of Dan G. Elmore
In Memory of Edith & Leo Multack
In Memory of William C. Nolan, Jr.

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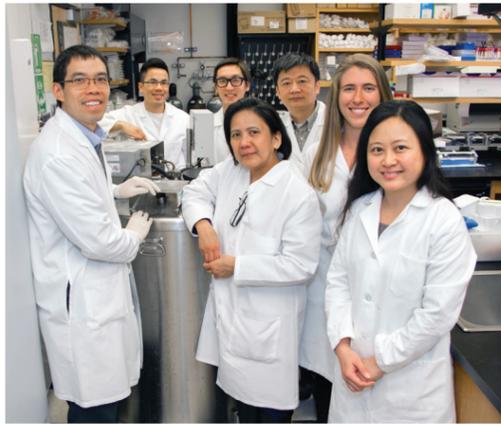
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Geoffrey & Sasha Meyerson
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Carl E. Wynn Foundation
York Family Giving Fund
Michael Zinner
Ilan & Cori Zipkin

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notify us of any
errors, omissions
or misspellings
for us to correct.





UCSF Helen Diller Family
Comprehensive
Cancer Center

Mentor: Lawrence Fong, M.D. (far left)
*Efim Guzik Distinguished Professor in Cancer Biology
Leader, Cancer Immunotherapy Program*

Fellow: Serena S. Kwek, Ph.D. (far right)

The group at University of California San Francisco is developing new immunotherapy approaches to prostate cancer. They currently have immunotherapy trials for men with localized, relapsed and advanced prostate using a combination of different treatments including immune checkpoint inhibitors.

Developing Biomarkers to Guide Cancer Immunotherapy

With the first-in-man clinical trial with an anti-CTLA4 antibody (ipilimumab) and granulocyte-macrophage colony stimulating factor (GM-CSF) combination therapy in prostate cancer, our PMF-funded fellow, Serena Kwek showed that different as well as a greater number of antibodies to tumor antigens were induced by these treatments (Kwek et. al., 2012). Furthermore, she also observed that pre-existing immune profiles of the patients' blood, specifically expression of an inhibitory protein, PD-1 in CD4 non-regulatory T cells, are related to overall survival in the same clinical trial (Kwek et. al., 2015; Spitzer et. al., 2017).

Discovery of biomarkers in the blood versus the tumor has the added advantages of being less invasive, increased safety and easier access. The current objectives of Dr. Kwek are to determine firstly if the signaling pathway in PD-1-expressing CD4 non-regulatory T cells differ from other CD4 T cells not expressing PD-1; and secondly if other biomarkers are differentially expressed in these cells in patients with shorter overall survival compared to patients with longer overall survival and cancer-free controls. They are extending this work to both develop this into a potential biomarker of response, and also to discover other novel immunotherapeutic targets. They are applying novel approaches such as single cell RNAseq, single cell T cell receptor sequencing, and combined RNA expression and protein sequencing assay (REAP-seq) for thousands of cells in combination with validation by multiparameter flow cytometry to tease out how these immunotherapies are working in men with prostate cancer. With this research, we hope to rapidly translate new scientific discoveries into tangible clinical benefits for patients.

Dr. Lawrence Fong leads the Cancer Immunotherapy Program of the Helen Diller Family Comprehensive Cancer Center, is an Efim Guzik Distinguished Professor in Cancer Biology and is also the genitourinary cancer specialist at the UCSF Medical Center.

Dr. Serena S. Kwek is the senior scientist and project manager of the laboratory of Dr. Fong and the Cancer Immunotherapy Program. She received her Ph.D. from the University of Illinois, Chicago in 2001 and completed her postdoctoral fellowship at the University of California San Francisco with grant funding awarded from the Department of Defense breast cancer fellowship program.

References:

1. Kwek SS, Dao V, Roy R, Hou Y, Alajajian D, Simko J, Small EJ, and Fong L. Diversity of antigen-specific responses induced in vivo with ctla-4 blockade in prostate cancer patients. *J Immunol.* 189(7): 3759-66, 2012.
2. Kwek SS, Lewis J, Zhang L, Weinberg V, Greaney SK, Harzstark AL, Lin AM, Ryan CJ, Small EJ, Fong L. Preexisting Levels of CD4 T Cells Expressing PD-1 Are Related to Overall Survival in Prostate Cancer Patients Treated with Ipilimumab. *Cancer Immunol Res.* 3(9):1008-16, 2015
3. Spitzer MH, Carmi Y, Reticker-Flynn NE, Kwek SS, Madhiredy D, Martins MM, Gherardini PF, Prestwood TR, Chabon J, Bendall SC, Fong L, Nolan GP, Engleman EG. Systemic Immunity Is Required for Effective Cancer Immunotherapy. *Cell.* 168(3):487-502, 2017.



**Memorial Sloan Kettering
Cancer Center**

Mentor: Hedvig Hricak, M.D., Ph.D., Dr. h.c.
*Chairman, Department of Radiology
Carroll and Milton Petrie Chair
Professor, Gerstner Sloan Kettering Graduate School of Biomedical Sciences
Professor of Radiology, Cornell University*

Fellow: Dr. Andreas Wibmer

Dr. Hedvig Hricak was a pioneer of prostate MRI in the 1980s and has remained a leading investigator in the field ever since. The work of her research team has been critical in achieving growing acceptance of prostate MRI as a valuable tool for prostate cancer detection, characterization, staging and treatment follow-up around the world. With support from the Peter Michael Foundation, her team continues to refine and help standardize the use of MRI for evidence-based cancer management and explore new applications of advanced prostate MRI and related technologies. This year, three PMF-funded fellows at MSK are contributing to highly innovative studies that are establishing MRI as a powerful prostate cancer predictive biomarker and exploring new technologies pushing the field forward.

With help from PMF fellow Dr. Andreas Wibmer, the MSK Department of Radiology is leading a multi-institutional study that aims to integrate clinical and imaging data for more precise diagnosis of extracapsular extension—a feature that influences the initial prostate cancer stage and is often associated with the failure of localized treatment. A dozen European and American institutions have agreed to submit data on 100 patients each; the analysis will be performed in collaboration with Dr. Michael Kattan of the Cleveland Clinic, a statistician who is internationally renowned for developing nomograms (i.e., predictive models) that can be applied in routine patient care. Preliminary results are expected to become available in the second half of 2018.

Dr. Wibmer is also involved in a large-scale, longitudinal study of the prognostic value of MRI that now includes more than 3,000 patients who underwent radical treatment (surgery or radiation) for localized prostate cancer at MSK during the early 2000s. The goal of the study is to establish phenotypic characteristics of prostate cancer on MRI that are associated with the likelihood of disease recurrence after treatment as well as cancer-specific mortality, independently of established prognostic factors (i.e. clinical, laboratory, and biopsy data).

In other studies, the MSK research team is applying radiomics—a cutting-edge computer-based approach—to the analysis of prostate images. In this approach, mathematically defined “radiomic” features not discernible to the human eye (describing, for example, tumor texture, shape or heterogeneity) are automatically extracted and then correlated with clinical and or genomic data to determine whether they hold meaningful predictive value. The term “radiogenomics” is often used to describe studies that correlate radiomic features with genomic data. A recent radiogenomic study on the association of prostate cancer MRI features and cell cycle gene expression levels led by Dr. Wibmer demonstrated that specific MRI features indicated the presence of a more aggressive genotype of prostate cancer. This finding could help to select candidates for genetic testing, optimize pre-therapy risk stratification, and enable more individualized management decisions. The results of this study were presented at the European Congress of Radiology 2018, * and a manuscript is currently under review.

cont.

PET/MRI, a hybrid modality only recently introduced to clinical practice, produces images that simultaneously reflect a variety of metabolic, functional and anatomic properties. This makes PET/MRI data highly attractive for radiomic analysis. At present, however, it is unclear if PET/MRI radiomic data can be compared between different centers. Dr. Marius Mayerhoefer, another PMF-funded fellow at MSK, is involved in a study to evaluate differences in PET/MRI radiomic features obtained with different equipment at two centers (MSK and the Medical University of Vienna) and develop strategies to standardize the measurements. In addition, Dr. Mayerhoefer is initiating a study at MSK that will analyze quantitative (including radiomic) features of two highly promising PET and MRI techniques: PET with a radiolabeled prostate-specific membrane antigen (PSMA) ligand, which has been shown to improve the detection of local and distant prostate cancer spread and aid in image-based radiotherapy planning; and diffusion-weighted MRI, a widely used technique for prostate imaging that indirectly reflects cell density (a marker of malignancy and of cancer aggressiveness). Specifically, the study will examine the potential of features derived with these PET and MRI techniques to predict (a) the development of metastases and (b) progression-free survival.

Furthermore, the interdisciplinary team at MSKCC is continuing their groundbreaking clinical research study imaging prostate cancer patients with hyperpolarized MRI (HP-MRI). This safe and highly promising technique, still confined to the research realm, allows metabolic dynamics to be observed in patients in nearly real time. As previously reported, the team demonstrated a link between increasing Gleason score and the conversion of hyperpolarized pyruvate to hyperpolarized lactate, indicating that the latter is a potential biomarker of prostate cancer aggressiveness. Recently, Dr. Kristin Granlund, an electrical engineer and PMF fellow whose work has been crucial to the implementation of clinical HP-MRI at MSK, has been developing a processing technique (abbreviated as HyperSIFT) that reduces noise in HP-MRI data and thereby makes it easier to interpret and compare across patients (see Figure). Dr. Granlund will present this work at the annual meeting of the International Society of Magnetic Resonance in Medicine in June.

* 24th European Congress of Radiology (ECR), February 28 - March 4, 2018, Vienna, Austria. Cell cycle progression genomics and MRI features of prostate cancer: radiogenomic correlation and prognostic synergism. A. G. Wibmer (Presenter), N. L. Robertson, B. Ehdai, S. Stone, M. Brawer, H. Hricak, H. Vargas; New York/USA, Salt Lake City/USA, Irvine/USA

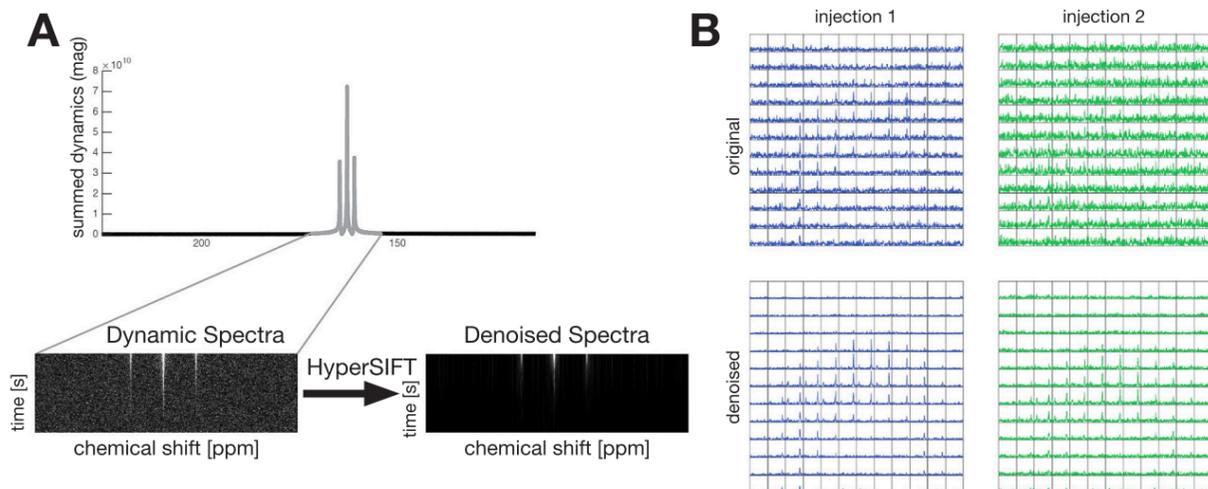
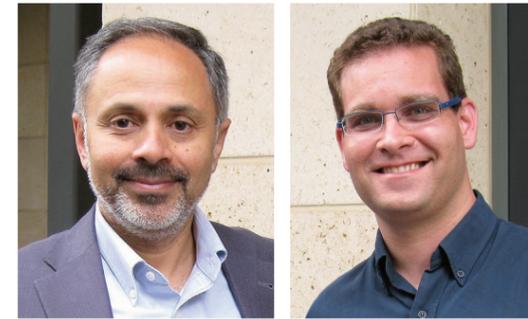


Figure showing the effects of HyperSIFT. **A)** With the application of HyperSIFT, the signal of interest becomes more conspicuous. **B)** In a patient injected twice for testing and re-testing, the lower polarization level of the second injection makes the lactate peaks difficult to measure. Denoising the data allows comparison of the lactate production between the two injections.



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Fellow: Idan Steinberg, PhD

A. Progress on Dual Modality Transrectal Ultrasound and Photoacoustic Imaging of Prostate:

In recent years, we have developed and translated bench-to-bedside an integrated transrectal ultrasound and a photoacoustic device that synergizes the strengths of transrectal ultrasound and photoacoustic imaging based on capacitive micro-machined ultrasonic transducer array. While we are in the process of obtaining an FDA approval for our photoacoustic specific agent targeting the gastrin-releasing peptide receptor (Bombasin), the current device was used to image patients with suspected prostate cancer with non-specific Indocyanine green (ICG) contrast agent for assessing the device capabilities. Delay and sum algorithms were used to provide real-time imaging for both photoacoustic and ultrasonography albeit with a relatively low contrast to background ratio.

During the past year, we have developed a 2nd generation device and reconstruction algorithm aim to markedly improve the contrast and sensitivity of images. Our new device is based on a commercial piezo-composite 192-element concave ultrasound array, integrated with a split-light guide that allows multiple illumination directions. The device is shown in Fig. 1a and comprises a functional unit and detachable parts that allows for multiple applications. Fig 1b illustrates the split light-guide and Fig 1c shows the functional unit. The new algorithm, which was developed for photoacoustic imaging, uses a non-negative model-based reconstruction technique. On the ultrasound side, a synthetic aperture approach was taken. Fig 2 (a-d) shows the results of imaging a wire phantom. It demonstrates the improvement in resolution as well as a contrast-to-background ratio for both ultrasound and photoacoustic images by 30 dB and 15 dB, respectively.

To conclude, we have developed new reconstruction algorithms to improve both photoacoustic and ultrasound reconstruction. Using those algorithms we have shown a marked improvement in the reconstruction of data which was previously acquired with the first generation device. Those results were presented at scientific meetings and we are now in the process of publishing those. In addition, we are in the final stages of manufacturing a new transducer and back-end hardware that intended to outperform the previous generation markedly. Those will assist us to overcome the existing limitations of standard transrectal ultrasound and offer new diagnostic and prognostic insights into the prostate cancer screening and management.

cont.

B. Future Directions:

We are in the process of finalizing our new system and reinitiating clinical trials:

- The final device will be ready within a few weeks. We will then test it, optimize the various imaging parameters and calibrate it to assure smooth operation during clinical trials.
- We are in the process of developing a new algorithm for quantitatively assess chromophore concentration based on multiple illuminations, now available with the new device.
- To support the continuation of this research we will image another 24 prostate cancer patients with ICG administration. We are in the process of obtaining all the necessary approvals.

C. Figures

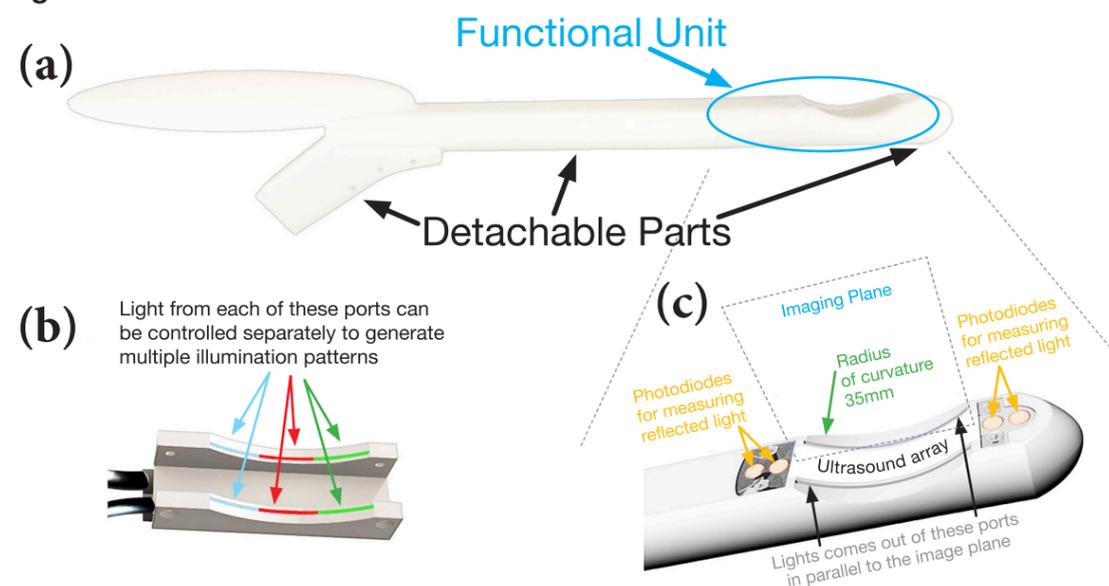


Figure 1: 2nd generation combined photoacoustic and ultrasound imaging transducer

(a) The device body, which was 3D printed from a biocompatible resin. Such a material has the advantage of being strong, chemically resistant and optically reflective to avoid photoacoustic signal generation within the device. The device includes a watertight functional unit that can be detached from the device body and be used for other applications. (b) The light guide head implemented within the device. The head is divided into multiple separate ports, which can be controlled independently. This allows for multiple illumination patterns, which will be utilized to achieve a more quantitative imaging. (c) The device head, which includes a side looking concave ultrasound array, photodiodes for calibration and measurement of the reflected light as well as the light-guide ports.

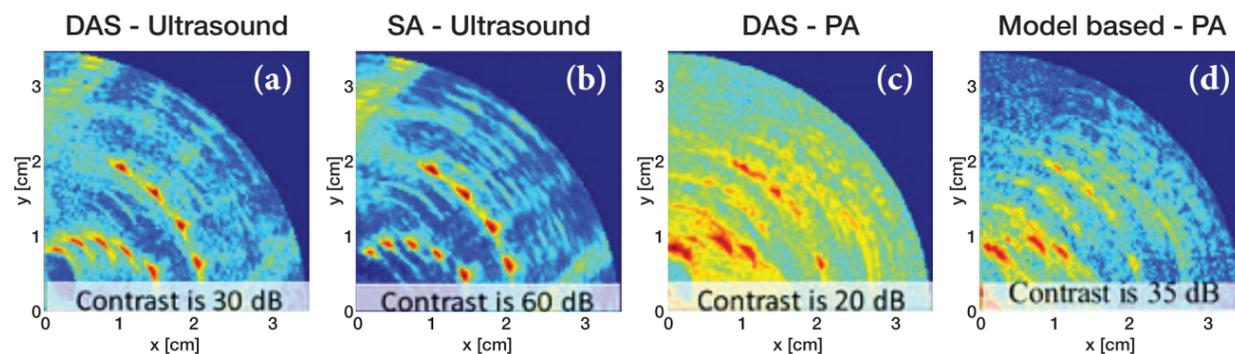


Figure 2: New reconstruction algorithms

(a) Ultrasound image of 100-micron black wires in water using conventional Delay and sum (DAS) reconstruction. The contrast between the wires and their surroundings is about 30 dB (~30 fold) (b) the same but with Synthetic Aperture (SA) reconstruction. The contrast between the wires and their surroundings is about 60 dB (~1000 fold). Both 'a' and 'b' are displayed in log-scale with an 80 dB range. (c) Same as 'a' but with photoacoustic Delay and some reconstruction. The contrast between the wires and their surroundings is about 20 dB (~10 fold) (d) The same as in panel 'c' but with model-based reconstruction. The contrast between the wires and their surroundings is about 35 dB (~55 fold). Both 'c' and 'd' are displayed in log-scale with a 60 dB range.



Prostate Cancer Research

About Prostate Cancer:

Prostate cancer forms in the tissues of the prostate, a male gland just below the bladder and in front of the rectum. Prostate cancer is the second most common type of cancer among men in this country. A man in the U.S. has a one in five chance of being diagnosed with prostate cancer in his lifetime.

If diagnosed early, prostate cancer has a good chance for successful treatment. In some cases, prostate cancer does not pose a significant threat to a man's life and can be observed cautiously instead of treated immediately.

Prostate Cancer Risk Factors:

Most men who develop prostate cancer are over age 50, and about two of every three prostate cancers are diagnosed in men over age 65. African-American men are nearly twice as likely as Caucasian men to be diagnosed with the disease. Eating a diet high in fats, particularly animal fats, and having a family history of prostate cancer, especially involving a father, brother or son, raises your risk.

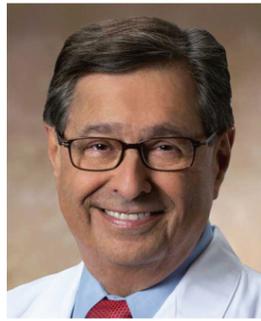
Some healthy lifestyle habits may help lower your risk of prostate cancer. These include eating five or more servings of fruits and vegetables daily, eating less red meat, decreasing fat intake, exercising regularly and maintaining a healthy weight.

Research Funding:

The Prostate Cancer Research fund will focus on a creating a robust prostate cancer outcome database. The support from part time database staff is crucial to properly measure and evaluate prognostic markers. This will be part of an ongoing project that will help improve the quality of life for our patients as well as support cancer specific outcomes.

The funding will also help support investigator initiated clinical studies. An example of these studies is the utility of pre-operative Auximin PET CT which predicts lymph node involvement in patients with high risk prostate cancer undergoing Robotic radical Cystectomy.

cont.



Michael Zinner, M.D.
*Founding Chief Executive Officer & Executive Medical Director
Miami Cancer Institute*

Dr. Zinner is a world-renowned cancer surgeon and researcher. He was named founding CEO and executive medical director of Miami Cancer Institute at Baptist Health South Florida in October of 2015.

An expert in pancreatic-hepatobiliary diseases, Dr. Zinner joins Miami Cancer Institute from Dana-Farber/Brigham and Women's Cancer Center in Boston, where he was Clinical Director and Surgeon-in-Chief at the Brigham and Women's Hospital. He is also the Moseley Professor of Surgery, Emeritus at Harvard Medical School and founder of Harvard's Center for Surgery and Public Health.

Dr. Zinner was co-founder and co-director of the Gastrointestinal Cancer Center at Dana-Farber Cancer Institute, a multidisciplinary clinical program of surgeons, oncologists, radiation therapists, radiologists and pathologists. The author of more than 230 academic papers, he is a member of the editorial boards of Annals of Surgery, Journal of Gastrointestinal Surgery and the Journal of the American College of Surgeons.

From 2008 to 2010, Dr. Zinner served as Chairman of the Board of Governors of the American College of Surgeons (ACS), which has more than 80,000 members. Today he serves as Vice Chairman of the Board of Regents of the College and as Chairman of the Health Policy and Advocacy Committee.

Throughout his distinguished career, Dr. Zinner has been widely recognized for his extraordinary clinical accomplishments, his contributions to cancer treatment and research and his mentorship to students, physicians and researchers worldwide.

A Miami native, Dr. Zinner received his M.D. degree from the University of Florida and conducted his surgical residencies at The Johns Hopkins Medical Institutes in Baltimore.



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