NATIONAL PHOTONICS INITIATIVE

A BRIGHTER FUTURE: ELIMINATING CANCER THROUGH ADOPTION OF NEW AND ENHANCED TECHNOLOGIES AND A TRANSFORMED IT HEALTH SYSTEM

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National Photonics Initiative ⋅ www.lightourfuture.org

EXECUTIVE SUMMARY

Over the last several decades, the "war on cancer" has been characterized as a series of lengthy, hard-fought and costly campaigns resulting in a limited number of significant but narrow victories against a complex and ever-mutable foe. Progress in the treatment of cancer has resulted primarily from combining new drugs with diagnostic technologies that identify patient populations who will respond favorably to these new treatments. At the same time, improvements in early detection, predominantly using quantitative imaging technologies, have had a substantial impact on early intervention (Stage 0 – Stage I) when cancer is easier to treat or, in many cases, stratifying patients to active surveillance, thereby avoiding the costs and risks of unnecessary treatment.

Current treatment protocols remain broadly insufficient in their effectiveness for many cancer patients, and this is due, in part, to many of the diagnoses occurring at Stages III or IV when the disease is more difficult to cure. Despite advances in early detection of some cancers, early detection of the most lethal cancers including brain, lung, ovarian and pancreatic remains challenging. It is now widely recognized that new drug development directed at earlier stages needs to be partnered with improvements in diagnostic technology, and that therapies that are effective at treating early, or minimal residual, disease need to be investigated. Improvements in diagnostics that guide therapeutic development and advance early detection have the potential to significantly decrease the incidence of late stage cancer; reduce the severity of therapeutic side-effects; improve outcomes such that survival is more likely; stratify patients more precisely to their most effective course of therapy; and help monitor patients for treatment benefit and the earliest signs of recurrence.

This white paper focuses on new technologies for early detection, stratification between treatment and surveillance, effective early stage intervention, and sensitive techniques for recurrence monitoring. We provide a technology road map for the development of new, low-cost cancer detection technologies and treatment protocols. We believe our recommendations can benefit a wide range of cancer patients in community-based clinical practice, improve overall survivability, and decrease health care costs within the next five years. Finally, we include specific case studies of existing and new technologies that will impact patient outcomes throughout the stages of cancer management. Earlier and more effective intervention, as well as stratification to surveillance rather than unnecessary intervention, promises savings to the health care delivery network as well as better outcomes to the patient.

Enhancing Existing Technologies for Improving Early Cancer Detection

Current technology exists to significantly improve outcomes in some cancers but more clinical trial data are needed to conclusively demonstrate efficacy. One such example is the early detection of lung cancer using computed tomography (CT) imaging. Preliminary studies have shown existing CT imaging instruments can detect lung cancer in patients earlier, reducing mortality by as much as 20 percent over two annual rounds of CT follow-up. Instruments now installed in hospitals and clinics can be used effectively, however instrument calibration procedures need to be established to assure site-to-site reproducibility of quantitative image measurements. Technicians and radiologists will need feedback to ensure their performance is

providing reliable quantitative assessments of the CT imaging. The information technology (IT) infrastructure will need to be scaled so that image files from previous studies are routinely available for comparison, wherever follow-on imaging studies are performed, allowing quantitative image analysis of the CT data files to accurately assess changes in tumor volume. The data bandwidth required for this function can also be used to store complementary precision medicine data, such as tumor proteomic and genetic analysis, to enable broad national access to the full capabilities of 21st century oncology care.

Other examples where there is great potential for using the current generation of diagnostic instruments for early detection and effective intervention are: high-resolution magnetic resonance imaging (MRI) instruments for detection of early prostate cancer, quantitative image analyses (machine learning) for image-based phenotyping for predictive modeling of breast cancer subtypes (i.e., "virtual/digital biopsies"), point-of-care optical technologies for early detection of cancers at epithelial surfaces, and better methods for the detection and typing of tumor-derived circulating cell-free nucleic acids (RNA and DNA) in peripheral blood (plasma) for early diagnosis of a wide-range of cancers (i.e., "liquid biopsies").

Identifying and Developing New, Low-Cost Detection Technologies for Comprehensive Coverage

Although in some cancers effective technology already exists and can be directly employed, for other types of cancers technology needs to be improved or developed to achieve better outcomes. One example is early detection of ovarian cancer. Presently, no effective early detection screening methods exist for ovarian cancer patients, leading to high mortality rates for this disease. There are also no available biomarkers for subtyping these cancers that would guide therapeutic intervention. Therefore, developing new quantitative imaging diagnostic technologies and a new series of coordinated clinical trials is critical to detecting the earliest signs of cancer, and better identifying the molecular signatures indicating the most effective drug treatment at early stages of this disease. Moreover, by development of instruments that detect and monitor tumors at early stages, these diagnostic instruments would stimulate discovery of new drugs that specifically, and more effectively, treat early stage disease.

Eliminating Silos and Building a National Health IT Infrastructure

Just as important as realizing advances in new diagnostic instruments is the need to build the health IT infrastructure to collate quantitative image data, molecular and genomic data, patient histories and drug responses, in order to accelerate progress for better patient outcomes. Existing commercial cloud-based data centers and the interconnection bandwidths linking them to hospitals and caregivers already provide the necessary data and communication infrastructure to support a dramatic increase in data sharing and data analysis capabilities while ensuring HIPAA compliance and protections. Lacking today is a national program to organize and support the health IT infrastructure. The National Cancer Moonshot Initiative could create a coordinated program to develop common database structures, user interfaces for existing electronic medical records databases, quantitative instrumentation calibration protocols necessary for data entry, and reimbursement incentives to facilitate data access, encourage data sharing, protect patient privacy and enable actionable clinical meta-studies in HIPAA compliant studies.

Technology Recommendations for the National Cancer Moonshot Initiative

The National Cancer Moonshot is a call to arms. In response, the National Photonics Initiative (NPI), a collaborative alliance among industry, academia and government seeking to raise awareness of optics and photonics - the science and application of light - is coordinating a new multi-disciplinary effort that will identify technology advancements critical to the National Cancer Moonshot and provide a blueprint for effective public and private investments. The NPI has organized a Cancer Moonshot Task Force comprised of thought leaders and health care providers from leading academic institutions, patient organizations, hospitals and the medical device industry including the Lung Cancer Alliance, Prevent Cancer Foundation, Siemens, the Advanced Medical Technology Association (AdvaMed), the Medical Imaging and Technology Alliance (MITA), The Optical Society (OSA), the International Society for Optics and Photonics (SPIE), MD Anderson Cancer Center, Stanford University, Rush University Medical Center, University of Texas Health Science Center, University of Chicago and Rice University. This collaboration will leverage their annual investment in research in cancer diagnosis and therapeutics technologies - which exceeds $3 billion - to maximize both existing and new early detection and treatment technologies while also exploring cost-effective approaches amenable to community-based practices.

In concert with its collaborating partners, the NPI Cancer Moonshot Task Force has drafted the following recommendations as well as a high-level technology road map, and will convene workshops, focus groups and educational webinars to further identify and advance technologies critical for early cancer detection and leverage our partners' annual $3 billion investment.

- **Expand funding for clinical studies over the next five years employing existing noninvasive, and minimally invasive, imaging technologies and companion molecular tests for early detection of cancer.** The three most commonly used and most effective treatment options for cancer include surgery, radiation therapy and chemotherapy. These treatments can be used alone but are often combined. Examples of areas where existing imaging modalities could be employed are: lung cancer (CT), prostate cancer (MRI), breast cancer (MRI, ultrasound (US), optical), ovarian cancer (molecular US), colon and gastric cancer (CT, US and optical) and brain cancer radiation therapy (RT). A large number of molecular probes are available for use with a range of imaging modalities that improve the sensitivity and specificity of early detection and these should be evaluated in clinical studies.

- **Use coordinated public and private investments to expand funding for the development of new noninvasive quantitative imaging approaches for early detection and guided treatment of cancer where these technologies are needed.** Focus on low cost but highly precise early detection instruments and diagnostic assays, new automated and quantitative predictive models (which take advantage of quantitative image analyses and machine learning techniques), and treatment protocols which are scalable and replicable to provide widespread access to community-based care that serves the majority of our nation's cancer patients.

- **Provide the resources to develop a network for an IT medical infrastructure available to US health care providers and consumers**. Develop a national IT infrastructure to support patient, doctor and clinical researcher access to quantitative diagnostic medical data, and to enable more rapid, objective reporting of patient outcomes to facilitate reimbursement decisions and the entry of new impactful technologies into "standard-of-care" community settings. This infrastructure will provide access to complete medical records including quantitative imaging and genomic datasets, validated data analysis tools, instrumentation calibration protocols, and quality assurance and control methods to assure patient safety and data accuracy. This data resource must be accessible to all medical care sites that a patient may go to, to obtain care. A secure, cloud-based data storage system could serve as a national repository for such information and greatly accelerate the dissemination of precision care.

The National Cancer Moonshot's goal of doubling the rate of progress – to make a decades' worth of advances in five years - will require academia, industry and federal government engagement across the full spectrum of cancer management. The good news is that our country can make significant strides within the next five years with existing imaging molecular diagnostic technology solutions and quantitative image-based machine learning as well as make focused investments to develop new low-cost, precise, early detection technologies and treatment protocols. With regard to existing solutions, such hurdles to access as Centers for Medicare and Medicaid Services (CMS) coverage could be addressed as a priority. These coverage decisions can simultaneously provide access to the benefits of innovation and enable the ongoing collection of clinical evidence in real-life community practice. Public-private partnerships and coordinated investments will drive innovation in areas such as imaging instrumentation, companion biomolecular and image-based predictive assays, and bioinformatics infrastructure that will improve patient outcomes in each stage of cancer diagnosis and treatment, and significantly reduce medical costs. Advancements in optics and photonics technologies, molecular probes, new companion biomolecular assays and a national IT infrastructure are essential for ushering in these next generation tools that will benefit patients across the spectrum of cancer management.

CANCER TECHNOLOGY ROAD MAP

Effectively battling cancer will require engagement at all stages of the disease, from prevention and early detection, to determining the most effective therapy, monitoring for recurrence, and ensuring quality of life in survivorship. There are many stages of cancer management where existing and new technologies can dramatically improve the patient outcomes. For example, changes in lifestyle and the environment can significantly reduce the incidence of certain types of cancer. Understanding the effects of these environmental stressors on organ systems - i.e., understanding field carcinogenesis - will lead to new technologies for prevention and early detection. Existing imaging technology can screen for early signs of specific types of cancer (e.g., lung, colon and breast cancer) and lead to better outcomes though early intervention.

Once risk is assessed rapidly with molecular markers and imaging is used to locate the cancer, image-guided biopsy techniques can lead to more directed sampling of tissues for more informative analyses. This will enable novel image-based, quantitative typing of the cancer for a more complete profile (i.e., anatomic, and even microanatomic, linkages to genomics and proteomics). This emerging field is known as radiomics and is leading to radical new insights into tumor heterogeneity, and to integrated guidance approaches that improve outcomes for patients suffering from the most deadly cancers. New molecular analysis technology, using advanced optical technologies, has the potential to provide information to enable precision medicine, choosing the optimal therapy regimen for each patient. Image-guided surgery can remove diseased tissue while preserving healthy tissue in the most sensitive organs. Patient responses to therapy can be determined by measuring tumor volumes, as well as other tumor characteristics from image-based phenotyping, using quantitative 3D imaging technologies such as MRI and CT. And finally, monitoring for recurrence enables intervention at the earliest times with the most effective second line therapy.

Figure I illustrates the many stages of cancer detection and treatment that a patient experiences.
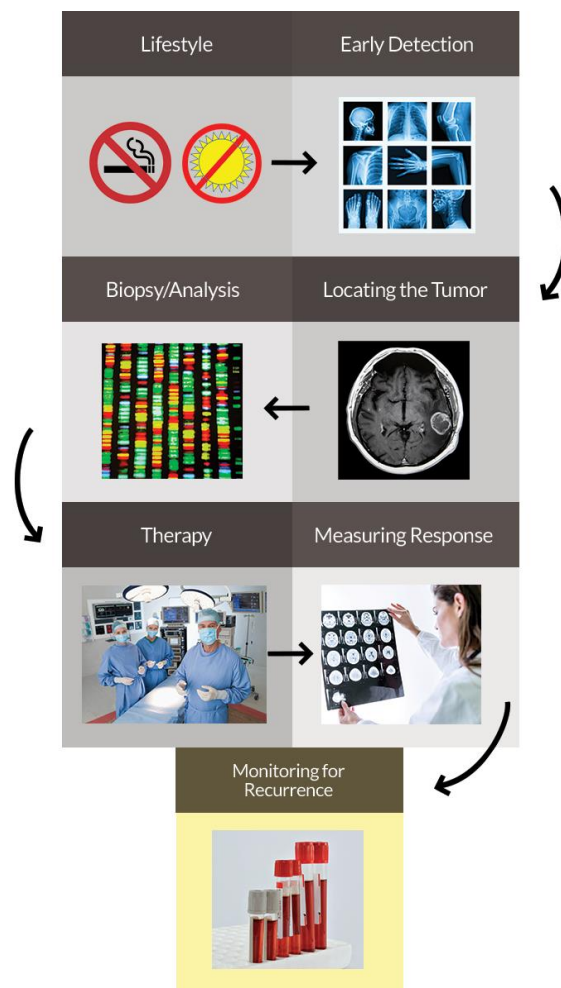
Figure I. Technologies impact patients across the cancer treatment spectrum, from prevention and early detection to treatment.

Figure II gives an overview of the different technologies that can have a significant impact on improving outcomes across the full spectrum of cancer management.

Figure II. Examples of technologies that could significantly improve outcomes and their effective employment in the cancer management spectrum.

The following sections review examples of the important potential roles that photonics-based technologies can play in accelerating progress in helping to prevent cancer and improve outcomes for patients with cancer.

ROLE OF NEW TECHNOLOGY IN IMPROVING MANAGEMENT AT ALL STAGES OF CANCER

I. Lifestyle and Environment

Improving lifestyle and environmental factors that impact an individual's probability of developing cancer can be viewed as the frontline in the war on cancer. Poor environmental quality is a significant risk factor, especially for lower income populations.

Smoking cessation counseling and cigarette reduction programs would significantly reduce the incidence of many types of cancer linked to smoking, including lung, breast, colon and prostate cancers. Smoking cessation counseling can be part of the screening protocol for individuals at high-risk for lung cancer. New optical methods are being developed that assess the level of risk for smokers and predict progression to malignancy.

Environmental pollutants, both inside buildings and in the atmosphere, are estimated to cause between 10 and 20 percent of all lung cancers. New technologies which monitor dangerous airborne, small particle pollutants can be deployed in highly polluted urban settings to provide real-time feedback of hazard levels. New optical methods for monitoring commonly found cancer-causing chemicals inside buildings, such as benzene and formaldehyde, can not only reduce hazard levels but can also save energy by increasing the efficiency of air exchange within buildings.

Over 70 percent of skin cancers are caused by excessive sun exposure. Inexpensive wrist-worn sun exposure monitors can provide information on when sun exposure has exceeded safe levels, particularly important for small children where excessive sun exposure has been shown to lead to an increased probability of skin cancer in later years.

II. Screening and Early Detection

Early detection of cancer by screening high-risk populations is one of the most effective methods to improve the efficacy of cancer treatments. When detected at an early stage, cancer is most successfully treated and is often curable. Recent results reported in the National Lung Cancer Screening Trials clearly demonstrate a significant (20 percent) reduction in lung cancer mortality by implementing screening for high-risk populations using quantitative data from CT scans and early intervention. Improved protocols using higher resolution CT instruments are expected to significantly improve these initial results by allowing precise detection of small growing lung cancer tumors. Likewise, screening for aggressive prostate cancer using high-resolution MRI imaging has been shown to enable earlier diagnosis of this progressive disease and increase patient compliance by reducing the number of painful biopsy procedures, which will also lower health care costs.

One of the most successful screening programs is Papanicolaou (PAP) smear testing for cervical cancer, which has resulted in an estimated tenfold decrease in the incidence of cervical cancer since its inception. New imaging methods for early detection of cervical cancer performed in conjunction with out-patient, simultaneous treatment methods for early stage cervical cancers can have significant impact, particularly for patients located in resource-limited areas where the

cervical cancer rates are much higher due to lower compliance for both screening and treatment.

Endoscopic screening for gastrointestinal (GI) cancers including malignancies of the esophagus, stomach and colon has been shown to detect early cancers and effectively reduce progression to deadly disease. It has been estimated that despite these improvements, 20 percent of cancer is currently missed during routine endoscopies and that use of molecular probes with optical signatures could improve endoscopic screens and lead to more effective interventions and improved outcomes.

Screening for oral cancers has become routine practice in most dental practices and despite advances in optical tools for early detection of oral malignancies, most of the screening is still done by visual inspection by dentists with a wide range of expertise. Use of the available tools would lead to more reliable and earlier detection that would eliminate the deformities left by surgical resection and dramatically reduce the costs of therapy.

III. Tumor Localization, Biopsy and Molecular Analysis

Noninvasive imaging methods (CT, MRI, optical, ultrasound and endoscopy) for determining the location and size of suspect tumors substantially improves the accuracy of obtaining reliable biopsies. Serial screening using quantitative 3D imaging methods (CT, US and MRI) provide precise information on tumor size and growth, and can at times be used to distinguish aggressive from indolent tumors. This allows doctors to avoid potentially unnecessary aggressive interventions and alternatively prescribe careful monitoring when appropriate, eliminating preventable costs, reducing patient morbidity and improving quality of life.

Molecular analysis of biopsy tissue using high-throughput genomic, gene expression and proteomic analyses can provide data for precision medicine and effective guidance on the most appropriate drug treatments for specific cancer subtypes. Genomic analysis can also identify whether a biopsy comes from the primary cancer location or is a metastatic tumor originating from a different organ site, which can help determine the optimal surgical or pharmaceutical intervention.

IV. Therapy

The three most commonly used and most effective treatment options for cancer include surgery, radiation therapy and chemotherapy. These treatments can be used alone but are often combined. New techniques for real-time imaging of tumor boundaries during resection allow more precise determination of the appropriate size of the resection, preserving critical healthy tissue in organs such as the brain, while helping to ensure appropriate removal of all affected tissue. For example, near-infrared imaging methods can indicate to the surgeon whether or not tumor cells have invaded tumor draining lymph nodes, reducing the number of cancer-free lymph nodes removed, minimizing the extent of surgery, and decreasing post-operative edema and other deleterious effects of extensive surgery. Real-time imaging combined with radiation therapy to guide the precise proton or gamma ray beams to the exact location of the tumor can also improve the efficacy of radiation treatment while dramatically reducing damage to surrounding tissues, particularly important in radiation treatment of sensitive organ tissue in brain, prostate and abdominal cancers.

New checkpoint inhibitor drugs are providing alternatives to aggressive chemotherapies with effective and long-lasting tumor responses in patients with certain types of melanoma, colon, brain and lung cancers. This new class of drugs mobilizes the patient's own immune system to attack the tumor cells, often providing a sustained disease-free response. Identifying patients who will respond to these new treatments remains a challenge. Determining which checkpoint inhibitor therapies are most appropriate could be facilitated by measuring tumor response using quantitative measurements of tumor volumes by employing high resolution quantitative CT, PET and MRI imaging. Using imaging technology, specifically PET and optical, to classify patients with tumors involving inflammatory immune responses may provide a key biomarker for treatment with checkpoint inhibitors. If no inflammation is detected by imaging, then checkpoint inhibitors can be combined with therapies that induce an immune response in these patients. Imaging for inflammation avoids the expense and suffering caused by tumor biopsy or lymph node dissection. Immune suppression pathways in the tumor can be pinpointed by analyzing circulating tumor cells (CTCs) in the patient's peripheral blood along with the cell-free molecular information in the plasma (liquid biopsy).

In order to expedite the translation of the molecular and genetic understanding of cancers and the ability to plan therapeutics and predict cancer response in patients, co-clinical trials are being conducted. In such trials, mouse models that can accept transplanted xenografts from human cancers, so-called patient derived xenograft (PDX) models, or that can replicate the mutational events observed in human cancers, are used in assessing treatment plans and predicting therapeutic responses. Imaging technologies at both the human and mouse model scales need to be developed and linked. In certain cases organoids from patient tumors can be grown in culture rather than in animals, and the optical tools for rapidly analyzing the response of organoids to therapy will improve their use in predicting patient responses and guiding therapy.

V. Measuring Response

Precise volume measurements of tumors allow for the assessment of drug response prior to surgical removal. This approach allows post-surgery drug regimens to be chosen more effectively. Now, in addition to tumor volume, imaging through "virtual/digital biopsies" with quantitative image analysis (computer vision and machine learning) can view and type (via radiomics) the entire tumor, potentially overcoming the limitations from cancer heterogeneity that are inherent in actual biopsies. Advances in computer power and machine learning algorithms are allowing for computer-extracted features from computer-aided diagnosis, quantitative imaging algorithms and deep learning to yield "radiomics," i.e., the high throughput conversion of complex imaging data sets into a multi-dimensional feature space with extractable characteristics. Investigators are phenotypically characterizing solid tumors to gain information on the underlying genetic makeup in patients with glioblastomas, lung cancer and breast cancer. For example, breast cancers are spatially heterogeneous and current MR imaging biomarkers of breast cancer for response to therapy includes only size and signal enhancement ratio (SER). Various genomic studies have demonstrated the heterogeneity of primary breast cancer tumors. Quantitative MRI phenotypes of the cancerous tumor can include size, shape, margin morphology, enhancement texture, kinetics and various kinetic phenotypes. For example, an enhancement texture phenotype can potentially characterize the

tumor pattern of the contrast-enhanced tumors, and thus quantitatively characterize the heterogeneous nature of contrast uptake within the breast tumor.

VI. Monitoring for Recurrence

Certain classes of patients respond so completely to drug therapies that detection of residual disease is difficult. Early detection of recurrence can be achieved by monitoring circulating tumor cells or by using ultra-high sensitivity gene expression measurements. Such tests allow the earliest detection of recurrence and the reestablishment of suppression protocols or the shift to new drug protocols, if necessary.

SPECIFIC CASE STUDIES

Case Study I

IMPROVING EARLY DETECTION: Quantitative imaging, big data and machine learning for improved methods to screen for and detect cancer at the earliest stages

The advent of digital mammography revolutionized the medical practice of breast cancer screening and diagnosis. Digital mammography, using x-rays, digital image sensors and computers, has yielded substantially improved mammographic images, as well as provided the potential for lower radiation doses. These improvements allow better visualization of dense breasts, digital data for computerized image analysis, the ability for digital storage and efficient image transfer between health care providers. Further incorporation of computer power, big data, and machine learning, with both computer-extracted tumor features and direct deep learning methods, will increase the information available to clinical interpretation as well as allow for the integration of information from multiple modality breast images such as digital mammograms, sonography and MRI. Meta-analysis of large databases of breast images will yield new cancer risk models, novel image-based prognostic markers and objective metrics for assessing response to therapy.

Case Study II

IMPROVING OUTCOMES AND REDUCING COST: Integrating imaging with blood tests and biopsy

The combined modalities of MRI and ultrasound (US) are useful in guiding biopsy needles to potentially cancerous nodules within the healthy prostatic tissue. In addition, multi-parametric MR (mpMR) assesses organ function as well as anatomical information, simultaneously reducing the risk of missing cancers by directing the needle to higher-grade nodules and reducing unnecessary biopsies when the nodules are all of low grade. Full adoption of currently available mpMR, and the Prostate Imaging and Reporting System (PI-RADS) prostate cancer scoring system, could eliminate 50 percent of the unnecessary biopsies in one million Americans, while also reducing the costs of later treatment of cancers missed early. Ongoing innovation offers the prospect of multi-parametric US, which could be less costly than mpMR.

PI-RADS scoring could also reduce by 50 percent the prostatectomies which are performed unnecessarily due to the poor prognostic qualities of the current Gleason scoring system used by pathologists. If widely adopted, PI-RADS could better stratify the aggressiveness of the cancer, thereby avoiding the direct costs of surgery and the indirect costs of associated adverse effects (such as incontinence and impotence) by channeling more men into "Active Surveillance" with confidence that, if the lesion does progress, it will be detected early using these same methods.

Another promising development is "liquid biopsies," genomic testing of DNA in peripheral blood samples. Together with PI-RADS, these minimally invasive biomolecular tests have the potential to surpass Gleason scoring in therapeutic decision-making. Combining these biomolecular tests with imaging data would allow correlation of these parameters and improve patient care, as well as provide valuable data for ongoing clinical research.

Once diagnosed, prostate cancer is staged for choice of therapy using Positron Emission Tomography/Computed Tomography (PET/CT). Awaiting approval by FDA are PSMA-based PET image enhancement agents specific to the prostate which will improve staging as well as detection of recurrence following prostatectomy.

These non-invasive methods for diagnosis also have therapeutic potential. PSMA carrying 177-Lutetium can deliver therapeutic doses of radiation to the site of action and US can ablate pathologic tissue. Both methods preserve healthy surrounding tissue.

In summary: wide adoption of currently available mpMR throughout the care pathway will improve outcomes *and* reduce costs. Innovations in diagnostic applications for US, PET and "liquid biopsy" are nearing clinical utility and will further improve outcomes and reduce costs. As innovations are introduced into patient care, clinical data should be aggregated in order to derive optimal patient benefit. In addition, the next generation of photonics will include non-invasive, targeted *therapeutic* applications for PET and US.

Case Study III

IMAGING LYMPH NODES PRE-EXCISION: Optical methods can improve surgical outcomes

Most cancers do not spread initially through the blood vasculature but rather through the lymphatics, an often forgotten vasculature. The lymphatic system evolved to circulate "lymph." Lymph consists of the excess fluid filtered from the blood vasculature and taken up by the initial lymphatics. Cancer cells primarily metastasize from tumors through the lymphatic vessels to what otherwise should be an inhospitable immune environment in lymph nodes. But for reasons we are only beginning to understand, it appears that the immune system in cancer patients has been hijacked, and tumor draining lymph nodes represent a cozy niche for metastatic tumor cells, which disseminate to the rest of the body. Currently, no medical imaging methods are available to detect cancer-positive lymph nodes pre-operatively. As a consequence, lymph nodes typically are removed and examined for tumor cells with the majority of excised lymph nodes found to be cancer-negative upon pathology. An emerging solution to reduce needless excisions is near-infrared fluorescence imaging technologies that offer a non-radioactive, low cost, point-of-care method to assess the tumor load at the molecular level in the lymphatics prior to excision. This kind of imaging could be performed both in the operating suite as well as in the oncologists' office.

Case Study IV

IMPROVING FOLLOW ON CARE AND TREATMENT: Optical methods can measure drug response and monitor for disease recurrence

Chronic myeloid leukemia (CML) normally starts with a relatively indolent chronic phase that can last for a number of years. If untreated, CML often progresses to an accelerated phase and ultimately to a typically fatal blast or acute phase with a median survival time measured in months. The disease is the result of a chromosome rearrangement that can be precisely diagnosed by optical microscopic examination of the chromosomes of the patient's white blood cells or by sensitive fluorescence-based genomic tests. Very effective drugs have been developed that interfere with the proliferative mechanisms that drive expansion of the subpopulation of

white blood cells that make up this disease. These drugs are so effective that they eliminate evidence of the disease and can allow the patients to stop taking the drug, potentially preventing undesired side effects. However, these patients must be monitored carefully for any signs of resurgence of the cell populations with the characteristic mutation. Improved detection, based on ultra-highly sensitive fluorescence methods needs to be developed with the sensitivity and specificity necessary to detect the recurrence of the disease at the earliest possible stage so that effective drug intervention can be resumed.

Case Study V

IMPROVING CARE IN RESOURCE-LIMITED SETTINGS: Imaging tools can improve efficacy and lower the cost of cancer detection and treatment

Cervical cancer was previously the leading cause of cancer-related death among women in the United States; however, incidence and mortality have decreased by more than 70 percent due to the introduction of screening programs to detect early cervical cancer and its precursors. In stark contrast, cervical cancer continues to be the first- or second-leading cause of cancer death among women in low- and middle-income countries (LMICs). Virtually all cases of cervical cancer are caused by persistent infection with high-risk types of human papillomavirus (HPV). This discovery led to the development of preventive HPV vaccines that have been commercially available since 2006. Although these vaccines hold promise to reduce the incidence of cervical cancer, the adoption of HPV vaccination has been poor; less than half of eligible children in the US undergo HPV vaccination, with fewer than 30 percent of those initiating vaccination completing the three vaccine series. In resource-limited settings in the United States and abroad, new point-of-care diagnostics are needed that enable combined detection and treatment of cervical pre-cancer in a single visit. To date, global attempts to implement "see and treat" protocols have been limited by the extremely low specificity of the three existing diagnostic approaches that can be used at the point-of-care. See and treat protocols based on imaging (colposcopy or visual inspection with acetic acid (VIA)) or biomarker detection (HPV DNA testing) result in high rates of overtreatment, subjecting patients to unnecessary procedures and wasting health care resources. Recent data suggest that a combination of optical imaging and biomarker detection can reduce the high false positive rate of current cervical screening tools. Non-invasive, high-resolution optical imaging can detect changes in nuclear morphology, one of the best-known phenotypic biomarkers of cervical pre-cancer. Similarly, low cost digital colposcopy can identify cervical pre-cancers and, when coupled with contrast agents targeted against biomarkers of neoplastic progression, may differentiate lesions likely to progress from those that do not require treatment. Optical imaging tools have the potential to provide clinicians in the United States and globally with robust, affordable, integrated, point-of-care tools to image phenotypic changes directly and detect molecular markers associated with the development and progression of cervical pre-cancer, addressing the poor specificity of current methods. Together, these tools could improve the efficacy and cost-effectiveness of early detection of cervical pre-cancer, allowing diagnosis and treatment in a single visit to prevent the development of invasive cervical cancer.

Case Study VI

BUILIDING AN IT INFRASTRUCTURE: Providing critical information to patients, health care providers and the medical research community

An essential component for optimizing the impact of an expanded early cancer detection capability is the establishment of an IT infrastructure that will assemble quantitative image data, molecular analysis results, genomic data and patient history into a widely-accessible and analyzable database. The importance of this IT infrastructure has been conclusively demonstrated by the impact of the International Early Lung Cancer Program (I-ELCAP) database of more than 75,000 participants from 72 institutions which represents a paradigm for future research collaborations. The database consists of baseline and follow-up meta-data (e.g., pertinent medical information, smoking history, quality of life measures), diagnostic reports (e.g., CT examination reports), diagnostic images (e.g., CT, MRI, PET), treatment information if performed (e.g., surgical, radiotherapy and chemotherapy procedures and results) and long-term follow-up of screenings and diagnoses. All data is entered into the I-ELCAP Management System, a web-based database that also provides for patient management and follow-up reports. This database has enabled seminal research on early lung cancer detection and treatment, and provided the key information for the development of national guidelines for efficient implementation of CT screening for lung cancer, which is now covered for high-risk smokers by the CMS. Data in the I-ELCAP database has been used in over 300 publications.

The I-ELCAP Data Repository collects the patient meta-data and images in a distributed system that provides participating institutions with a web-based interface to enter patient data and manage the follow-up of their participants/patients according to a common protocol. The system is hosted in a "private cloud" in a US datacenter, with backup systems in place at a separate location in the US. Each datacenter has multiple power and Internet connections to provide redundancy. The security and privacy of patient data is ensured by using industry-standard encryption technologies to protect the data between all the I-ELCAP institution and servers. The clinical meta-data can be directly entered into the system from any Internet-connected computer, and images are transferred from each institution's scanner or PACS (Picture Archiving and Communication System) to the I-ELCAP repository automatically. In addition to data collection, the I-ELCAP Management System provides for download of all data in a format that can be parsed by any statistical package and thus enables data analysis for research, patient follow-up, and quality image and data monitoring, both on an institutional and national/global level.

The I-ELCAP Data Repository has collected the metadata and images for over 75,000 patients, totaling approximately 40 TB of data. The average file size for an individual patient is less than one gigabyte. If all new patients diagnosed with cancer in the US (1.6 million per year) were included in a similar national database, the total storage required per year would be approximately one petabyte. This amount of data is easily handled by existing commercial cloud storage facilities. For comparison, approximately seven petabytes of photos are uploaded to Facebook accounts and six petabytes of videos are uploaded to YouTube every month.

ABOUT THE NPI CANCER MOONSHOT TASK FORCE

The NPI is bringing together thought leaders and experts in medicine and optics and photonics to identify technologies critical to the National Cancer Moonshot and to create a technology road map to achieve technology goals. The NPI Cancer Moonshot Task Force members include:

- Thomas Baer, PhD, Chairman, NPI Cancer Moonshot Task Force and Executive Director, Stanford Photonics Research Center, Stanford University
- Christopher Contag, PhD, Professor, Departments of Pediatrics, Bioengineering Radiology and Microbiology & Immunology, Stanford University
- Richard Frank, MD, PhD, Chief Medical Office, Siemens Healthcare North America
- Maryellen Giger, PhD, A.N. Pritzker Professor of Radiology, Committee on Medical Physics and the College; Vice-Chair for Basic Science Research, Department of Radiology, University of Chicago
- James Mulshine, MD, Acting Dean, Graduate College and Vice President and Associate Provost of Research, Rush University
- Rebecca Richards-Kortum, PhD, Malcolm Gillis University Professor; Professor of Bioengineering; Professor of Electrical and Computer Engineering; Director, Rice 360: Institute for Global Health; Director, Institute of Biosciences and Bioengineering
- Eva Sevick, PhD, Professor, Cullen Chair in Molecular Medicine; Professor and Director, Center for Molecular Imaging, University of Texas, McGovern Medical School

About the NPI

The NPI is a collaborative alliance among industry, academia and government seeking to raise awareness of photonics - the science and application of light - and drive US funding and investment in five key photonics-driven fields critical to US competitiveness and national security: advanced manufacturing, communications and information technology, defense and national security, energy, and health and medicine. The initiative is led by top scientific societies including the American Physical Society (APS), the IEEE Photonics Society (IPS), the Laser Institute of America (LIA), The Optical Society (OSA) and SPIE, the International Society for Optics and Photonics (SPIE).

The NPI organized the US optics and photonics community in support of an integrated photonics institute for manufacturing innovation led by the Department of Defense. On July 27, 2015, Vice President Joe Biden announced that a New York-based consortium – now named American Institute for Manufacturing Integrated Photonics (AIM Photonics) – was the sixth institute selected for the National Network of Manufacturing Institutes.

In the medicine and health care sector, the NPI formed a multi-disciplinary consortium of US companies to work with top researchers and program managers to develop the first Technology Road Map for the Brain Research Through Advancing Innovative Neurotechnologies (BRAIN) Initiative.

The NPI is pursuing endeavors with the administration and Congress in other areas, such as high performance computing and technician training opportunities. For more information on the NPI, please visit www.lightourfuture.org.