Statement of
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Chairman Towns, Ranking member Issa, and honorable members of the committee, it is my pleasure to testify at today's hearing regarding prostate cancer screening and the efforts to improve the health of men with prostate cancer. By way of background, I am Professor and Chair of the Department of Radiation Oncology and Molecular Radiation Sciences at The Johns Hopkins University School of Medicine (URL: http://www.radonc.jhmi.edu/), and I am also a Professor of Urology and Oncology. For more than 15 years, I have dedicated my life to the treatment of men with prostate cancer and have treated over 2000 men diagnosed with this disease. I have also directed a laboratory over this same period of time that investigates how prostate cancer responds to radiation therapy and chemotherapy. I am intimately involved in research to develop new tests to diagnose prostate cancer and therapies to effectively treat the disease. I believe these experiences provide me a unique perspective on the problem of prostate cancer and the need for improvements in imaging and genetic analyses to enhance prostate cancer screening, diagnosis, and treatment. My goal today is to provide a background on the gaps in screening and treatment approaches, explain why more robust research funding is needed, and suggest policies that may help protect prostate cancer patients as we progress forward.

As you all know, major advances have been made in the past 25 years to reduce the suffering and death caused by prostate cancer. Since the mid-1970s when federal support was initiated, the death rate from prostate cancer in the United States has been reduced by about 30%. Despite that impressive figure, we can do even more to fight this disease. Among the most important advances in the screening for prostate cancer was the development of the prostate specific antigen (PSA) blood test. This blood test, typically combined with a digital rectal examination of the prostate, has served as the primary means of screening men for prostate cancer. The problem is that the PSA test is not cancer specific, it is only prostate specific. As such, not only can prostate cancer result in suspicious changes in PSA, but so can benign growth of normal prostate tissue and other non-cancerous conditions like infection. Moreover, the PSA typically does not indicate exactly how aggressive the cancer will be in any individual patient. This problem has produced great confusion for physicians and patients alike.

While it may sound odd, it is now generally accepted that many prostate cancers will never progress to cause harm to the patient or result in death from the disease. While refinements in our understanding of how to properly use the PSA test have certainly been made, significant

changes in the PSA level typically result in a biopsy of the prostate to determine if cancer is present in the organ. This is problem one—some men do not need to be biopsied because they really do not have cancer, only an abnormal PSA. However, we cannot tell which patients have cancer from those that do not. In addition, while the PSA test allows us to find some cancers earlier than we might without using the test (sometimes termed "lead time"), we find many prostate cancers that would never have been diagnosed in the patient's lifetime without screening, would never have been a problem for the patient, and do not need treatment of any sort (sometimes termed "over diagnosis" and "over treatment").

Even when diagnosed, we presently do not have adequate genetic markers to definitively determine which cancers are potentially lethal and, thus, demand treatment. This is not to say that our present screening and biopsy methods are useless. In fact, many men have had their cancer detected early enough to receive care that was life saving but this has been at the cost of finding many more men with cancer that never needed treatment. It is estimated that for every man that benefits from prostate cancer treatment, about 30-50 men who do not need treatment still receive it. Obviously, this approach is problematic in that it exposes many patients to the unnecessary risk of treatment-related side effects, and these treatments are associated with real economic cost.

Once a patient receives the news of an abnormal PSA test, the anxiety and fear associated with a potential cancer diagnosis begins. As noted earlier, the only definitive way to determine if the patient has prostate cancer is a biopsy of the prostate. This biopsy is done by inserting a biopsy device into the rectum which then guides needles into different areas of the prostate. Typically, 12 separate needles are placed through the rectum into the prostate in order to "sample" the organ. Hence, the second problem—the biopsies are done in a so-called "blinded fashion". That is, unlike virtually any other organ we biopsy for cancer, we do not have effective imaging that is or can be routinely used to guide the biopsy needles to suspicious areas in the prostate. We cannot see the cancer. Thus, it is very possible that biopsy needles placed into the prostate may miss cancer cells. Even if the needles hit cancer cells in one area, it may be that the needles miss a more aggressive cancer elsewhere in the prostate which then goes undiagnosed and, thus, the appropriate management for that more aggressive cancer is not employed. In fact, different therapies are used for different levels of prostate cancer aggressiveness. Many studies have been completed which document the benefit of more aggressive therapies, like high precision radiation therapy combined with hormonal therapy, which have resulted in improvements in survival for men with more aggressive prostate cancer.

As you can imagine, as more men are diagnosed with prostate cancer, the choice of the best treatment for a specific patient becomes critical. Currently, there are four options for prostate cancer patients with localized disease: prostatectomy (surgical removal of the prostate), external beam radiation therapy, brachytherapy (which is the insertion of radioactive seeds into the prostate), and watchful waiting. While these four options are generally equivalent for many men, there are specific reasons why a particular patient is a good candidate for one of these options rather than another. For example, a patient with a large prostate may not be a good candidate for brachytherapy; a patient with a history of bowel issues may not be a good

candidate for external beam radiation. In order to reduce the risk of overtreatment as well as to determine who should be treated and which treatment might be best for a given patient, more refined screening and genetic analyses applied to the problem are required.

I believe that because we do not have the type of the refined screening and genetic analyses that we need, strange treatment practices have emerged. Across the country, including in my community, new business arrangements are forming that produce strong incentives for one type of treatment (external beam radiation), while the use of other clinically appropriate, significantly less expensive treatments, such as radiation seed implants, or "watchful waiting," have declined or disappeared. I am concerned that the financial incentives are so great, that patients are not being given their full range of treatment options. I believe that high-quality, efficient patient care and informed patient choice supersedes financial benefit, and I hope this Committee will investigate and stop these perverse financial incentives.

These data make it easier to understand why and how our present prostate cancer screening and diagnostic strategy is not optimal and has actually resulted in treatment decisions that are not always in the patient's best interest. These facts demonstrate that our present approach can result in the over diagnosis and over treatment for many patients; under diagnosis in some men resulting in less optimal therapy because an aggressive prostate cancer was not biopsied; while some patients are left undiagnosed because the biopsy completely missed the cancer. Finally, our ability to accurately determine which prostate cancers in which patients are likely to be lethal is limited.

Taken together, a strong case can be made that significantly improved prostate cancer imaging and genetic markers are needed. With improved imaging, one would no longer have to biopsy the prostate blindly but instead, would have images to help guide the placement of biopsy needles to the most appropriate and suspicious sites. This would help to insure that all the cancer in the prostate is evaluated and that no lesion is missed. In addition, advanced imaging and genetic analysis of blood and urine may allow us to actually determine if a patient has the type of prostate cancer that will never cause harm and, thus, avoid a biopsy all together. Such optimized imaging and genetic analyses is also likely to allow us to determine which therapy would be most effective for a particular patient, avoiding unnecessary treatment for some men while directing more aggressive treatment to only those that will clearly benefit by it. Finally, it should be pointed out that most imaging and genetic analysis techniques that are contemplated are non- or minimally-invasive which tends to reduce the fear of the test and reduces the likelihood of complications.

It is my contention that our present prostate cancer imaging techniques are not adequate to meet the challenges we face and, thus, do not allow us to develop the robust genetic markers of aggressiveness that we need. Routine ultrasound imaging has not proven useful in identifying cancer in the prostate. CT scans have limited resolution and, thus, cannot be used for detecting cancers in the prostate. MRI scans with spectroscopic analysis are better and have improved our ability to detect some cancers in the prostate. Unfortunately, these scans also suffer from limited resolution and are not able to routinely detect the frequent, small

cancers with which most patients present. Standard PET and SPECT scans (which are similar in certain ways to PET scans) and their associated imaging agents have also proven to have limited utility in prostate cancer screening and diagnosis. Thus, a need exists for improved technology and academic institutions along with the government and private industry must play a role in creating these advances. It is fortunate that new imaging agents for PET scans, SPECT scans and MRI continue to be developed and show early promise. This also includes development of nanoparticles that preferentially target to areas of cancer and molecular-based imaging techniques that indicate cancer aggressiveness. While exciting, more support for development, testing and deployment of these and other approaches is necessary.

Despite these concerns, I am quite optimistic about the opportunities our present prostate cancer imaging situation affords. Studies using combinations of advanced imaging studies, performed on large networks of patients and employing uniform evaluation criteria could begin relatively soon, and I believe these studies would result in a much improved evaluation of our present imaging techniques. While such studies are laborious and relatively expensive, they are critical to moving closer to our goal. In addition, incorporation of novel, directed biopsy techniques (e.g. robotic) to obtain tissue for critical genetic analyses would more rapidly advance the evaluation and validation of these imaging studies over time and help in the development of tests to more accurately determine which cancers threaten the patient's life. It is critical that funding agencies demand and support genomic analysis of blood cells, normal prostate and prostate cancer tissue from all patients enrolled in these imaging studies in order to correlate genetic information with imaging data, which will in turn guide development of better imaging techniques, improved imaging agents and, ultimately, optimized biomarkers and treatment.

I remain devoted to my patients with cancer and continue to strive to develop better diagnostic and therapeutic techniques to help them. I fully support the notion that greater resources need to be directed toward the problem of prostate cancer screening, imaging and therapy. Positive steps forward that policy planners should consider include the following:

1) increase NIH research funding to support prostate cancer imaging, genetic and biomarker research and clinical trial development by at least 100% in these areas over the next two fiscal years
2) support the creation of an NIH request for proposal that would specifically encourage study of imaging, biomarkers and genetic analyses from patients in large patient networks so that uniform analysis of these techniques and genetic evaluation tools can be performed
3) urge the NIH to make these initiatives a priority and request a public report on progress by 2011 that involves outside experts in the analysis

Significant opportunities in each area exist. Federal research funding has already resulted in improved care for patients with prostate cancer and the 30% decline in the death rate from the disease is likely a result of both screening and better treatment. With enhanced research support for prostate cancer, I am confident further progress for our patients will be made.

Thank you all for your attention and consideration of my testimony.