An Overview of Prostate Cancer Detection, Validation, Surveillance and Treatment Options – The Role of MRI for Early Detection of Prostate Cancer

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EARLY DETECTION through Screening

Population-Based Screening Studies

Screening for Prostate Cancer continues to be highly controversial, yet those controversies are diminishing thanks to rapid technological advances just in the last few years including improved chemical and genetic testing (PCA3, "4K" test and similar) as well as better prostate imaging through multi-parametric Magnetic Resonance Imaging (mp-MRI).

There has been a deluge of data collected from hundreds of thousands of men over the past two decades regarding prostate cancer screening and early detection. Unfortunately, the conclusions from many of these studies conducted over five years ago have been based upon tests and assumptions now proven to be outdated and inaccurate. We are going to review these tests of the past and compare them to those using today's most promising technologies. Further, we will update and revise older, outmoded conclusions that persist regarding prostate cancer early detection in the modern healthcare era among providers and insurance carriers.

Why Screen at all?

The following statistics and recommendations are reported by the American Cancer Society today. Prostate cancer is a pandemic disease and of roughly the same order of magnitude as breast cancer, yet it has received far less attention and publicity until recently. It is a relatively slow killer and can often be treated effectively, preventing painful complications and death while preserving quality of life if detected early enough and treated appropriately.

* Most common cancer among men after skin cancer with 1 in 6 men diagnosed with Prostate Cancer (PCa) in their lifetimes.

* Second Leading cause of cancer death in men (1 in 36), behind lung cancer. (In Sweden, where they do little Prostate Specific Antigen (PSA) testing or prostate cancer treatment, their prostate cancer death rate is 2 ½ times ours and prostate cancer mortality in Sweden is higher than lung cancer.)

* Although a serious disease, most men diagnosed with prostate cancer do not die from it, only about 1 in 6.

Screening Recommendations:

1) Men of average risk over age 50 should consider starting an early detection (screening) program.

2) Men age 45 of high risk (positive family history, African Americans) should start getting screened.

3) Men of age 40 with extreme risk (those with more than one first degree relative with PCa) should also start screening.

4) Men at age 40 can be offered a baseline PSA test to determine their relative prostate cancer risk. (Those with PSA less than 1 are considered low risk.)

5) Men over age 75 with normal PSA levels and those who have significant other health issues that reasonably limit their life expectancy to less than 10 years probably do not need prostate cancer screenings.

* Screening recommendations currently include:

o PSA (prostate specific antigen – blood test)

o DRE (digital rectal exam – finger in the rectum)

o TRUS Biopsy (Transrectal Ultrasound Guided Biopsies to confirm any suspicious lesions)

Comment: We DO NOT concur with the last recommendation as it was based upon the old technology of non-image guided biopsies.

In this review, we will present the evidence that logically led us to understand the tremendous value of using MRI as the ultimate Prostate Cancer screening tool, as a targeting guide for image-guided biopsies, and as a necessary component for the new, state-of-the-art focally ablative treatments for prostate cancer, such as High Intensity Focused Ultrasound (HIFU) and Focal Laser Ablation. These new minimally invasive prostate cancer treatments minimize side effects by treating only the cancerous areas which can only be reliably identified and imaged by advanced MRI technology. Before they become life threatening or debilitating, most prostatic cancers can be detected, measured and even viewed with the latest advanced MRI equipment. They can then be classified and targeted for biopsy or for organ-sparing definitive treatment.

We will provide peer-reviewed evidence that MRI is by far the leading biomarker for early detection of PCa. Prostatic MRI has not yet become the “standard of care” adapted widely by

the medical profession in the US although it is the standard in Europe. Such "standard of care" guidelines require both a thorough review of the scientific validity, value and reliability of any new test by the medical community as well as approval by health insurance carriers that is typically driven by "cost/benefit ratio" analyses and are often markedly delayed far beyond the point where they are generally accepted by physicians. We will demonstrate how this cost/benefit ratio requires updating based upon the latest scientific and clinical evidence in peer-reviewed medical journals and that Prostatic MRI is the most valuable, useful and most cost effective Prostate Cancer biomarker available.

Today, it remains rare that insurance will reimburse for Prostatic MRI; yet the industry routinely reimburses for non-image guided "blind" biopsies. We will demonstrate the cost-effectiveness of utilizing MRI as a targeting tool in lieu of blind biopsies, as an adjunct for independent PSA testing and as a necessary component of the new focally ablative therapies for Prostate Cancer.

Digital Rectal Exams (DRE) Proven to be Ineffective When Used Alone in Early Detection of Prostate Cancer

The National Comprehensive Cancer Network (NCCN) compiles data from researchers, academic institutions and experts throughout the world and offers an opinion based upon the consensus of its' "panel of experts".[1] It is considered an authoritative source of current cancer care guidelines and recommendations. Following are excerpts from this panel's 2015 release of guidelines for Prostate Cancer Early Detection.

According to the NCCN 2015 Guidelines panel of experts review, they "believe that the value of DRE as a stand-alone test for prostate detection is limited…Furthermore, the panel believes that DRE should not be used as a stand-alone test without PSA testing. Finally, the panel believes that DRE should be performed in all men with an abnormal serum PSA to aid in decisions regarding biopsy."1

Comments: Certainly, it is true that in many cases, the DRE is a test that does not produce clinically relevant results; in fact, many peer reviewed papers report the results of positive detection at below 25%.[1] While feeling a hard, suspicious nodule on DRE can be helpful in detecting some prostate cancers, the majority of cancers cannot be detected with a DRE alone. The decision to continue its use was based upon the historically limited available technologies and the accumulation of data over the past two decades. Unfortunately, the technology used to validate the efficacy of DRE and PSA was largely based upon the outcome of using non-image guided biopsies; which have since been proven to be only approximately 50% effective (discussed below).

PSA as an Early Warning Indicator of Prostate Cancer

PSA is a glycoprotein secreted by the prostatic epithelial cells, and its protease activity lyses the thick proteins in the ejaculate to enhance sperm motility. PSA enters the blood and is detectable using commercially available sources of PSA antibodies for serum tests.

"PSA is not a cancer-specific marker, and as such most men with elevated PSA levels do not have prostate cancer. In fact, only about 25% of men with PSA in the 4 to 10ng/mL range have a subsequent positive biopsy.[2] The NCCN added "Best evidence supports the use of serum PSA for the early detection of prostate cancer. However, in men with normal PSA, the positive predictive value (PPV) of DRE is poor (about 4-11%).[3,4]

Information from the National Cancer Institute and the Centers for Disease Control confirm that the mortality rate from prostate cancer has dramatically dropped by 44% since PSA testing became widely available in the US in 1992. This survival benefit cannot be explained by anything other than the introduction of PSA screening.

Overall, appropriate use of PSA testing alone can provide a diagnostic lead-time of 5 to 10 years, but the lead-time varies across studies, populations, and screening protocols.[5] Since the introduction of PSA testing, there has been a dramatic increase in the detection of early-stage, organ-confined disease and a substantial decrease in disease that is metastatic or advanced at the time of diagnosis.[6]

There is also good evidence that an initial PSA test at age 40 can be highly predictive of prostate cancer incidence and activity over the next 20-25 years.[31] At least 12 separate major studies, including the Baltimore Longitudinal Study, Department of Defense Serum Repository Study, Duke Prostate Database Report and the Malmo Preventive Project, show that an elevated PSA level in contrast to a Baseline PSA Test at Age 40 that is less than 1 is:

- A Stronger Predictor of Prostate Cancer Risk than Race or Family History.
- A Robust Predictor of Aggressive Prostate Cancer, Metastases and Disease-Specific Mortality even 25 years later.
- Useful in Risk Assessment and Subgroup Determinations.

Although PSA is far from perfect, it is a readily available, low-cost blood test that has served a productive purpose in saving men's lives through awareness and early detection. We'll demonstrate later how this early detection is a tremendous benefit in terms of lives saved as well as cost. It also serves as a way of providing a trigger point to initiate early detection protocols so that definitive treatment can be offered before these cancers progress and lead to far greater costs and morbidity.

We are already beginning to see an increase in incurable, metastatic and advanced disease due to a significant decrease in PSA testing in recent years. We believe it is essential to continue reasonable early detection protocols including PSA testing to reverse this trend before too many more men suffer unnecessarily from prostate cancer that could and should have been detected and treated earlier.

Recent studies are again showing a strong correlation between PSA and PCa that is potentially treatable with the newer, minimally invasive treatment technologies such as High Intensity Focused Ultrasound (HIFU), which was just approved by the FDA, and Focally Ablative Laser Therapy.[28]

Should Age be a Factor in Promoting PSA and MRI screening in PCa?

"Despite the predicted increase in prevalence of disease in the elderly, most studies investigating optimal treatment regimens have focused on men younger than 75 years of age. Ongoing prospective studies investigating the utility of PCa screening exclude patients older than age 75 years.[7,8] Likewise, the US Preventative Task Force (USPSTF) explicitly recommends against screening men age 75 years or older – yet this statement is based in large part on extrapolations from studies of patients younger than 75 years and does not account for health status or comorbidities. [9,10] It also does not account for the new focally ablative, minimally invasive treatment technologies that are becoming available.

Most older men with low-risk, localized disease are candidates for active surveillance, but selected patients with more aggressive tumors should not be denied the opportunity for potentially curative local (focal) therapies.[10] MRI can and should play a role in helping to follow men on Active Surveillance protocols so that more aggressive treatment can be started as soon as it becomes necessary. Men who are in reasonably good health and have an expectation of living 10 additional years or more should not be denied access to early detection programs or curative treatments

The Role of MRI in the Detection and Characterization of Prostate Cancer

MRI, and particularly multi-parametric MRI (mp-MRI), has been widely published in recent years as THE biomarker for PCa. From an overview of several years of recent European peer-reviewed literature, "Multi-parametric magnetic resonance imaging is an emerging imaging modality for diagnosis, staging, characterization, and treatment planning of prostate cancer….There is accumulating evidence suggesting a high accuracy of mp-MRI in ruling out clinically significant disease.[11-16] Although the precise definition of clinically significant disease widely varies, the negative predictive value (NPV) is very high at up to 98%."[17] Translation: **if a high quality mp-MRI interpreted by an experienced MRI radiologist does not detect a**

clinically significant prostatic malignancy, then one is reasonably assured with 98% confidence that they don't have significant cancer!

The European studies have been mirrored by many in the USA. This from a leading researcher, Dr. Dan Margolis, at UCLA: "MRI can identify most men who would not benefit from biopsy, and can identify the index lesion in most men who would."[18] Based upon an extensive literature review and presented in June 2015, this was the overview of the standard of care at the time.

Physical Exam (DRE) + Serum Analysis (PSA)

- If either are abnormal → systematic biopsies.

* >1M American men annually have an elevated PSA but negative biopsies

* False negative rate up to 47% depending on series

*Also risk of "over diagnosis": assuming low grade disease on biopsy belies hidden aggressive cancer or too easily leads to treatment of low risk disease best left untreated.

Overview of Pi-RADSTM: The American College of Radiology (ACR) Scoring System for Grading Prostatic Lesions on mp-MRI of the Prostate.

In 2007, the AdMeTech foundation organized the International Prostate MRI Working Group, which brought together key leaders of academic research and industry for the purpose of addressing critical impediments to the widespread acceptance and use of MRI in diagnosing prostate cancer. [22] They identified the excessive variation in the performance, interpretation, and reporting of prostate MRI exams, and resolved to bring additional standardization and consistency in order to facilitate multi-center clinical evaluation and implementation.

PI-RADSTM (Prostate Imaging, Reporting and Data System) Version 1 was drafted in 2012 by the European Society of Urogenital Radiology (ESUR) to respond to the Working Group's recommendations, and has since been validated in various clinical and research scenarios. [32]

The ACR, in conjunction with the ESUR and the AdMeTech Foundation, recently (late 2015) released PI-RADSTM Version 2 to address some limitations of the earlier guidelines resulting from rapid progress in the field.[33] The Steering Committee formed from this coalition consists of several working groups with international representation and used the best available evidence and expert consensus from around the world.

In short, PI-RADS is a 5 point assessment scale based upon the probability that a combination of mpMRI findings correlates with the presence of a clinically significant cancer for each lesion identified in the prostate gland. Any identified lesion is given a PI-RADS score of 1-5. Typically,

a PI-RADS score of 3, 4 or 5 is considered suspicious enough to warrant a biopsy, preferably image guided. Clinically significant cancer is generally defined on the pathology/histology of a Gleason score ≥ 7 (3+4, with the Gleason 3 being the predominant component), and/or volume ≥ 0.5cc, and /or evidence of extra prostatic extension.

The Gleason Score and Sum is a histological grading system based on architecture or cellular arrangements instead of individual cellular characteristics. It is only used in prostate cancer and has been found to be a more reliable predictor of prostate cancer aggressiveness than other histological methods. The predominant pattern (1-5) is listed first and the secondary pattern (1-5), if any, is then presented second; otherwise the predominant pattern is doubled. The two are added together for a sum. Any Gleason 4+3=7 or higher is considered "high risk", Gleason 3+4=7 is considered "intermediate" and any Gleason Sum of 6 or lower is considered "low risk".

PI-RADS Assessment Categories: Likelihood for presence of clinically significant cancer

1- Very Low (Highly unlikely)

2- Low: (Unlikely)

3- Intermediate (Equivocal)

4- High (Likely)

5- Very High (Highly likely)

VALIDATION: Transrectal Ultrasound (TRUS) vs. MRI-Guided Biopsy

Significant studies have compared the efficacy or accuracy of TRUS to MR and FUSION-Guided Biopsies and reported similar results about the substantive improvement of guided biopsy over systematic or blind biopsy.

In recent years, MRI or Fusion Guided biopsies have proven to deliver a 30-50% improved positive predictive value (PPV) as well as the same relative improvement in negative predictive value (NPV) over just Ultrasound guided (TRUS) or blind (no imaging guidance) biopsies.[18,20,21]

A comparison by Dr. Margolis of the methods and results of Systematic (blind or TRUS biopsies) to MRI-Guided biopsies was recently reported. [18] The list below is a summary of the differences in the recommended Current Standard of Care for Patients with an Elevated PSA and a Negative Systematic Biopsy (non-image guided) beginning with the fact that it Varies by Practitioner.

•Repeat Systematic biopsy (standard 6-14 core) within 6 weeks or up to 1 year.

•Trans-perineal biopsy.

•Saturation biopsy (20-100 cores) which usually requires full anesthesia.

•Biopsy using color power Doppler ultrasound.

•Trial of antibiotics for presumed prostatitis.

•MRI image guided, targeted biopsy.

MRI guided biopsies find definitive histological proof of cancer in >50% of men with initially negative TRUS biopsies!

Dr. Margolis reported that over a dozen groups have published improved yield using In-bore (MRI-targeted) and all methods of MRI-US image fusion guided biopsy over that of non-image guided biopsies – with the following summation of data:

Rate of lesion detection 73-96%.

Lesion positivity rates for any cancer: 22-55%.

Increasing suspicion score correlates with yield.

Although these numbers are impressively better than blind biopsy results, they raise the question as to why they varied as much as they did amongst the various researchers' results. This was discussed at the recent meeting of the ISMRM (May 2015) by an MRI Prostate Focus group of predominantly radiologists experienced with prostate MRI. The MRI Prostate Focus group overwhelming agreed that the results of lesion detection rate varied predominately due to the training and experience of the radiologist interpreting the MRI.[22]

A recent published review described the current situation this way: "The targeted biopsy "flight" has taken off and the benefits of targeted biopsy have been repeatedly shown in several studies. There is mounting evidence along with the recent literature suggesting that the effectiveness of mp-MRI when used along with PSA, followed by targeted biopsy of the MRI-visible lesion, is a better alternative to systematic TRUS biopsy in the diagnostic pathway for prostate cancer detection and therefore benefits the diagnosis of cancer. The largest benefit may come from a reduction of unnecessary biopsies (NPV of mp-MRI for clinically significant cancer), which could in turn prevent over-diagnosis and overtreatment. It also has the potential to decrease the number of missed clinically significant cancers and. As we move toward personalized medicine, use of MRI to biopsy each man's prostate differently rather than based on a pre-defined 12 core pattern seems to be supported in the recent literature".[23]

World-renown Prostate Cancer MRI researcher, Dr. Jelle Barentzs conducted a direct comparison of TRUS guided biopsy (TRUSGB) to MRI-guided biopsy (MRIGB) in 223 men with suspicious PSA levels. All men in the study have both biopsies performed: The MRI guided biopsies were done after allowing the men to heal after the TRUS guided biopsies. Of the 223 men in the study, 142 (63.7%) had PCa. TRUSGB detected 126 cases of PCa in 223 men (56.5%) including 47 (37.3%) classed as low risk. MRIGB detected 99 cases of PCa in 142 men (69.7%) with equivocal or suspicious mp-MRI, of which only 6 (6.1%) were low risk.

Conclusion: The MRIGB pathway reduced the need for biopsy by 51%, decreased the diagnosis of low-risk PCa by 89.4%, and increased the detection of intermediate/high-risk PCa by 17.7%. Over half of the biopsies conducted via TRUS alone were ultimately unnecessary as there were no viable targets of suspect cancer to biopsy. Thus, 51% of the blind TRUS biopsies were not warranted! This was supported by the 47 low-risk cancers that were biopsied unnecessarily – meaning, had they been characterized as low-risk by MRI, the men would not have been biopsied. Secondly, MRI targeting detected 12.6% more intermediate/high risk Prostate Cancers that were missed by TRUS guided biopsies. As stated by Dr. Barentzs, "We found that mp-MRI/MRIGB reduces the number of men requiring biopsy while improving the overall rate of detection of intermediate/high-risk PCa."[20]

These results were repeated in another study published in the Journal of Urology in 2014. "Among men with a previous negative biopsy but persistent suspicion, it (MRI) has the potential to increase cancer detection and reduce further repeat biopsies. Among men with cancer who are contemplating surveillance, MRI targeted biopsy potentially improves risk stratification and reduces the need for repeat biopsies." [24]

More on FUSION Guided biopsies

Fusion-guided biopsies utilize a high resolution mp-MRI image set which is superimposed in three dimensions on the prostate as visualized in real-time using ultrasound. Computer software continuously adjusts for accurate superposition of the two images and accounts for motion such as incurred by patient breathing. This enables the physician to use a visual representation of the target area on the ultrasound machine using the information from the MRI. The physician can then visually guide the biopsy needle or ablative technology directly into the target area for biopsy or treatment.

Transrectal Ultrasound-MRI Fusion guided biopsies present a less costly targeted biopsy option than MRI-guided biopsies, yet the accuracy is generally reported to be only 5-20% less than that of pure MRI-guided biopsies which is still far much more accurate than TRUS guided biopsies without MRI fusion.[25]

It is encouraging that innovative forms of technological solutions and advancements are evolving together as this spurs even faster improvements and controls costs by intense competition. It also provides millions of men increased access to advanced diagnostic tools that will ultimately be life-saving for some of them.

Cost Savings to the Healthcare System using MRI or Image – Guided Biopsies versus Blind TRUS.

It becomes obvious from the statistics summarized above that significant cost savings are realized by eliminating unwarranted biopsies by over 50% multiplied by the number of TRUS biopsies taken in the US each year, yields a potential estimated annual cost savings of up to $2.5 billion. This doesn't include the physician, technologist, and patient time wasted or lost opportunity costs.

Offsetting some of these savings is the increased MRI scanner usage required for in-bore MRI-guided biopsies. However, due to the much higher degree of accuracy of MRI screening, early detection, planning and treatment, MRI should ultimately save additional billions due to the anticipated reduction in definitive cancer treatments that would otherwise have been employed because the cancer was not detected early enough to use less costly and less invasive therapies.

ACTIVE SURVEILLANCE

The point or goal of active surveillance it to provide an option for men with low grade or suspected intermediate grade cancer (PI-RADS score of 3) – this indicated typically on mp-MRI and validated with an image guided biopsy.

"Active surveillance (AS) is an emerging treatment option for most low- and some intermediate – risk PCa patients with the aim of reducing overtreatment of indolent disease. Eligibility criteria in all representative AS protocols are based on standard clinic-pathological variables, which are inaccurate to predict "clinically significant disease." The risk of misclassification is, thus, a major problem. With this regard, MP-MRI could be a useful tool both to determine initial eligibility for AS and to monitor disease progression."[26]

Use of mp-MRI has already been shown to be a more accurate and cost effective means for active surveillance in men with prostate cancer. "Multiparametric MRI based nomograms may reasonably decrease the number of repeat biopsies in patients on active surveillance by as much as 68%".[27]

We see mp-MRI as a necessary and indispensable tool for all active surveillance protocols now and in the future, especially when combined with advances in genetic testing, such as the

Oncotype-DX and Prolaris tests that help identify those patients at higher risk of disease progression who need more careful monitoring.

TREATMENT OPTIONS

Until recent years, treatment options for prostate cancer have been very limited, with surgical removal (radical prostatectomy either open, laparoscopic or robotic) or definitive radiation treatment (external beam, brachytherapy (radioactive seed implantation) or combination therapy with both). Overall, robotic surgery has made the surgery less painful for the patient with reduced hospital time, but outcomes are still about the same as with traditional open surgery. Over half typically have some degree of incontinence, scarring or ED. Radiation therapy has about the same overall cure rate as surgery with reduced complication rates and it avoids the need for an anesthetic. But there are problems with radiation therapy including bleeding, bowel and bladder problems, ED, incontinence and scarring.

The holy grail of mp-MRI is that it has created an accurate visual representation of cancerous lesions and hence created the opportunity for minimally invasive, focally ablative treatments. Many clinical trials have been conducted or are in progress using these organ saving techniques which are intended to substantially improve the quality of life after PCa treatment through retention of full sexual and urinary control functions.[28]

Cryotherapy has been available for several years, but is typically relegated to salvage procedures or very high risk cancers due to irreversible side effects like ED (erectile dysfunction). Focal cryoablation is now being investigated as a possible localized treatment modality as the cryotherapy probes have become smaller and more manageable, but it is still considered investigational. Radical prostatectomies, particularly robotic, have been increasing in recent years.

One of the more promising organ saving treatments is focal laser ablation of targeted cancerous lesions. This technology employs MRI guidance of a laser probe directly into the target lesion with real-time computerized temperature controlled feedback to help ensure that only the cancerous lesion and immediately surrounding tissues are ablated (killed with heat) while sparing the outer and surrounding tissues.[29]

HIFU (High Intensity Focused Ultrasound) is another promising minimally invasive focal therapy that was recently approved by the FDA. Focusing ultrasonic waves allows them to create heat to ablate or kill cancer cells. They are imaged by using MRI guidance translated into a visual image on the ultrasound machine. Costs and side effects are relatively minimal and the procedure can be repeated if necessary; something that cannot be done with radiation therapy.

Focal laser ablation, HIFU and focal cryoablation are not without restrictions, as all men are not good candidates for these therapies based upon their general state of health, the disease manifestation (diffuse or focal, single or multi-focal, proximity to the erectile nerves, etc.) and clinical or pathological stage of the disease. Treatment selection for individual patients will depend on physician training and skill, equipment availability and target characteristics. Ideally, at least two of these options would be available. For example, focal laser ablation may be optimal when there are a limited number of clear targets, but cryoablation or HIFU may be better for more diffuse disease.

"Today, there is no consensus on choosing an appropriate candidate for focal ablation of prostate cancer. Some believe there is insufficient evidence to justify offering anyone this treatment option. Recognizing the spectrum of prostate cancer and the limitations of curative intervention (radical prostatectomy and radiation therapy) and active surveillance, we believe there are acceptable candidates, provided they are properly counseled about the limitations of the procedure and the limited short-term and total lack of long-term oncologic outcomes.

One of the major problems arising from the lack of specificity of PSA screening and random biopsy of the prostate is the detection of minute foci of prostate cancer which, if untreated, will cause no harm. These men should be offered AS and not focal ablation. Ideally, the goal should be not to diagnose these insignificant cancers. One strategy to minimize over-detection is to eliminate random biopsies in men with normal or minimally suspicious mp-MRIs."[30]

CONCLUSIONS

Evidence from researchers around the world has irrefutably indicated the clinical value of mp-MRI in cancer detection and treatment guidance. Cost and resistance-to-change remain the key issues why this proven science is not more widely adapted in the US. There is nearly unanimous consent amongst leading prostate cancer MRI researchers and physicians that we will ultimately prove a beneficial cost/benefit ratio by delivering better care to those who are willing to take part in research studies or pay directly for their improved healthcare benefits.

As scientists and physicians, we are obliged to continually collect and evaluate the data in order to gain both public and medical peer-reviewed acceptance. The use of mp-MRI as a relatively low cost prostate cancer early detection tool has not been directly compiled and reported. Most of the available data on this issue was derived or extrapolated from existing studies; we therefore intend to gather this data ourselves and publish it in the near future.

For now, we can only recommend reasonable guidelines for Prostate Cancer early detection and screening in patients who are in good enough health to benefit from treatment should a cancer be found, as reviewed earlier. Decreased PSA test screening has already started to increase the number of incurable, metastatic and advanced disease cases we are currently

seeing and this is unfortunately likely to rise in the near future. We believe that PSA testing and mp-MRI based early detection protocols, combined with targeted, image guided biopsies, advanced genetic prognostic testing, correct use of active surveillance and the appropriate incorporation of newer, minimally invasive – focally ablative cancer treatments, is the best way to save lives and control costs while minimizing patient side effects and morbidity.

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