

MRI



Prostate MRI: Information for Patients and Families

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Prostate cancer affects nearly all of our lives, but it affects different people in different ways. Sometimes an abnormal blood screening test (for PSA, prostate specific antigen) will suggest cancer, but none is found at biopsy. Sometimes a decision has to be made whether to treat what appears to be a very small amount of cancer and risk the associated side effects. Sometimes a patient who is thought to be a good surgical candidate will turn out to have cancer that cannot

No other imaging technique is as good as MRI for delineating the prostate and surrounding tissues and detecting cancer within the prostate

be treated surgically. One new consideration is, with stereotactic radiosurgery and robotic-assisted laparoscopic surgery, can we formulate a more accurate treatment plan ahead of time? All of these are issues where prostate MRI (magnetic resonance imaging) can potentially provide value.

We all know that prostate cancer is the most common (non-skin) cancer and second leading cause of cancer death in American men, but it has relatively low mortality (death rates) compared with many other cancers such as lung, breast, and colon(1). In other words, most men die with prostate cancer, but not from it. The challenge, then, is to try to find all prostate cancer but treat only that cancer which is aggressive. Currently, the standard of care is to screen men with a blood test and physical examination (digital rectal examination) and perform “sextant” biopsies, or two biopsies each on the right and left side of the prostate at

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each of the three levels (apex, midgland, and base). The difficulty is that aggressive prostate cancer may only be found in a small proportion of the prostate, such that biopsies, which sample only a very small proportion of the prostate, may find only non-aggressive cancer or none at all. Because we do not want to let anyone die of prostate cancer, even a small amount of aggressive cancer is considered a reason to consider treatment.

Prostate MRI is not designed to replace the current practices (at least not yet). However, it can be helpful for physicians in specific situations. Some uses been well studied at academic medical centers and have become part of the work-up of prostate cancer at these centers. Other indications are rather new and relatively unproven, with few supportive studies in the medical literature, but many show promise and may enter the standard clinical arena soon.

There are 4 ways that prostate MRI has been shown useful in the work-up of prostate cancer

1. **Surgical Planning**
2. **Suspicious PSA, Negative Biopsies**
3. **Radiation Therapy Planning**
4. **Abnormal PSA After Surgery or Radiation Therapy, “Biochemical Failure”**

Surgical Planning

Although most surgeons neither use nor really need MRI for surgical planning, there are certain cases where it is useful. For the most part, a surgeon’s ability to palpate, or feel, the location of cancer tells him or her where to cut. Most surgeons will try to cut out all of the cancer but, if at all possible, spare the nerves next to the prostate which are important for continence and erectile function. The prostate tissue will be examined by a pathologist, and this report will help the surgeon decide if radiation therapy is needed after surgery.

In some cases, it can be determined prior to surgery from the PSA level and biopsies that there is an intermediate chance that the patient would need radiation therapy regardless. In these cases, it might make sense to proceed directly to radiation therapy and spare the additional risks of surgery. MRI can be used to determine if all of the cancer is confined within the prostate, which is necessary to prevent the need for radiation therapy(2).

With advent of interest in robot-assisted laparoscopic prostate surgery, or “robotic surgery,” surgeons have an immense improvement in control over the surgical field, and are able to see and cut with much finer detail. The only drawback is the loss of palpation, such that surgeons cannot “feel” where the cancer lies. Many will simply cut as close to the nerves as is safe. However, some surgeons are using MRI as a road map,



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in lieu of palpation, to determine how to plan their surgeries. This way, they can decide to cut closer to the prostate when it is safe which improves the chances of preserving nerve function, or to give the prostate a wide berth, in those cases where the cancer extends to the edge of the prostate or even slightly beyond. Surgeons can even vary the surgical technique between right and left if one side is safer than the other(3).

Suspicious PSA But Negative Biopsies

One of the most frustrating and anguishing situations for patients and physicians alike is when the PSA blood test is suspicious, because it is high or rising rapidly, but the biopsies are negative. In this case, the concern is that the biopsies missed the cancer. However, in some cases, the blood test is abnormal because of a benign condition, *(Continued on page 10)*

such as BPH (benign prostatic hyperplasia) or inflammation referred to as prostatitis. Because it is so important to determine whether or not a patient has aggressive (or any) cancer, some patients would undergo up to three or four repeat biopsies. MRI can find a suspicious area in the prostate in many if not most cases for targeting(4). Some centers can even biopsy a suspicious area during an MRI scan, although this is usually scheduled as a second scan because the hardware is different.

Radiation Therapy Planning

External-beam radiation planning is usually done with a CT scan. Some centers, which use stereotactic body radiation therapy (SBRT) that combines image-guided and intensity-modulated (IGRT and IMRT) techniques, use a CT scan to plan where to irradiate after metallic beads, “fiducial markers,” have been placed. However, the prostate appears as a gray blob on CT scan. MRI can delineate the prostate in exquisite detail, which is useful in guiding the radiation beams to treat just the cancer and spare the adjacent structures such as the rectum, bladder, and nerves. MRI can also be used to identify suspicious bone lesions and enlarged lymph nodes which could also be treated(5).

Conventional brachytherapy, a technique in which radioactive seeds are placed in the prostate, is a well-established treatment for early stage prostate cancer. High-dose brachytherapy instead uses rods, called catheters, which are inserted into the prostate through which highly radioactive seeds are temporarily placed into the prostate and then removed. It has the advantage

that specific areas in the prostate can be targeted. This has a very low incidence of side effects but is only effective for cancer confined to the prostate. MRI can be used to help determine which are the most suspicious areas in the prostate that need a “boost” of radiation, and to confirm that the prostate cancer is all confined to the prostate.

“Biochemical Failure,” Abnormal PSA After Therapy

Successful treatment of prostate cancer should result in a “negative” or undetectable blood level of PSA. In some cases, the PSA begins to rise again. This suggests that some prostate cancer may be left. Treatment choices at this point are limited, and it becomes important to determine where the cancer might be. MRI is sensitive for prostate cancer which may have survived radiation therapy, both in the prostate and in the pelvic lymph nodes and bones, and can sometimes find recurrence in the pelvis after the prostate is surgically removed. Other types of scanning (CT, PET, ultrasound) are less sensitive.

There are also 3 methods which are being actively investigated but are not widely available.

1. Active Surveillance
2. Biopsy Planning
3. Focal Therapy Planning

Active Surveillance

One choice for men who only have a very small amount of non-aggressive prostate cancer is active surveillance, previously called “watchful waiting.” Rather than

treating the prostate cancer right away, these patients return at regular intervals for a repeat physical examination, blood test, and (usually at longer intervals) repeat biopsy. Despite some confusing and alarming suggestions that biopsies can actually make cancer worse, this has never been proven. However, biopsies are uncomfortable and have the common risks involved with any invasive procedure, and the inflammation from repeat biopsies can make eventual surgery difficult.

MRI has two advantages for active surveillance. First, it can identify areas in the prostate that are suspicious for aggressive cancer that might have been missed by the biopsies(6). This would indicate the need for a targeted biopsy of the suspicious area to ensure that immediate treatment is not necessary. Additionally, MRI can be used for follow-up instead of biopsies, which is much safer and less uncomfortable.

Biopsy Planning

MRI has already been shown useful for locating prostate cancer when the blood test is abnormal but biopsies are negative. Some physicians have advocated for performing MRI *before* the biopsy, in order to target the most suspicious area the first time. Not only does this make biopsies more straightforward, but it lessens the likelihood of “undersampling,” the term used when the biopsies miss the aggressive cancer and only find non-aggressive cancer. This risk of undersampling is the basis by which we recommend treatment of non-aggressive prostate cancer, over the concern that more aggressive cancer may have been missed.

Biopsy planning is a rapidly developing area. Previously, the MRI images and report would describe the area in question, which the physician performing the ultrasound-guided biopsy would then try to locate using anatomic landmarks. Now, new software is trying to fuse the MRI and ultrasound images, so the physician can see the corresponding MRI images of the needle trajectory. Other centers are developing a dedicated MRI setup for MRI-guided biopsies.

Focal Therapy Planning

Current conventional treatment for prostate cancer consists of chemotherapy including hormonal therapy, surgery, radiation therapy and cryotherapy. New techniques which have been proposed include HIFU (high intensity focused ultrasound, where sound waves agitate and heat tissue, destroying tumor cells), HIFU (high intensity focused ultrasound, where sound waves agitate and heat tissue, destroying

tumor cells) and IRE (irreversible electroporation, where an electric current selectively destroys tumor cells). These techniques are very promising, but none have really gained clinical acceptance, and the last is not yet clinically available. One of the components of these focal techniques, which can pinpoint areas to treat in and around the prostate, is that they require imaging guidance. Because no technique is as good as MRI for delineating the prostate and surrounding tissues and detecting cancer within the prostate, it is the logical choice. MRI has the advantage that it can also measure temperature for both freezing and heating techniques(7).

What Does Prostate MRI Involve?

The basic physical principles behind MRI have been the subject of two Nobel prizes. MRI takes advantage of the fact that each hydrogen atom functions like its own spinning magnetic compass. By sending a fluctuating magnetic field through a patient and then

detecting eddies in the resultant magnetic field, one can (using some quite complicated mathematics that involves terms like “inverse Fourier transform” and “spin-lattice relaxation”) generate a picture of the tissues of the human body. Prostate MRI uses this amazing property and adds up to three additional techniques to optimize detection of prostate cancer.

T2-weighted imaging is the standard “tissue contrast” imaging we use to identify the prostate and surrounding structures such as the seminal vesicles, bladder, and neurovascular bundles. Cancer and some other conditions appear similar on T2-weighted imaging, so we have to use the other techniques to determine which areas are truly suspicious. T1-weighted imaging is primarily used for detection of hemorrhage, which can confuse the appearance of T2-weighted imaging and diffusion-weighted imaging.

Diffusion-weighted imaging uses the principle of Brownian motion, or the movement of free water molecules. Water motion is more restricted in densely packed cells, such as prostate cancer. MRI can use directional pulses to detect the degree to which free water motion is restricted. This has been shown to be highly sensitive for detection of prostate cancer, although it is lower resolution than standard MRI tissue imaging(8).

Perfusion imaging, or dynamic contrast enhancement, takes advantage of the fact that MRI imaging is completely safe for patients with normal or near-normal kidney function and no implanted iron or electronic devices. One can repeatedly scan (Continued on page 12)

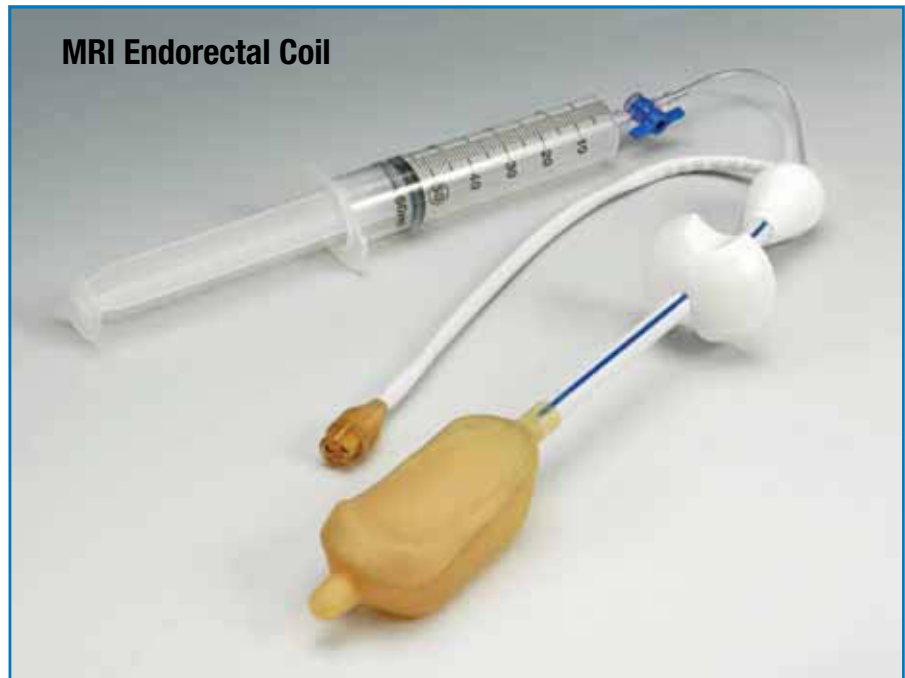
Combine 5 MRI Techniques for Best Cancer Detection	
T1 weighted imaging	Mainly used to detect hemorrhage
T2 weighted imaging	Standard “Tissue Contrast” imaging
Diffusion-weighted imaging	Highly sensitive for cancer detection, but lower resolution
Perfusion imaging or Dynamic Contrast Enhancement	Localizes cancer based on its disordered blood supply
Magnetic resonance spectroscopic imaging (MRSI)	Has the poorest spatial resolution, but is the most specific test for identifying aggressive prostate cancer

the same area. When a contrast dye containing the rare earth element gadolinium is injected intravenously, the blood vessels light up. By mapping which areas light up first and brightest, and which wash out earliest, one can localize cancer based on its disordered blood supply(9).

Technically, the dynamic contrast enhancement images are also T1-weighted, but they are analyzed by a workstation to generate the perfusion maps.

Finally, magnetic resonance spectroscopic imaging (MRSI) allows for the measurement of small molecules throughout the prostate. The molecules of interest are citrate, a normal component of prostate cells which is consumed in high metabolic states such as cancer, and choline, which is elevated during rapid cellular membrane turnover, also common in cancer. When the ratio of citrate to choline flips, this is an indication of aggressive cancer. Although MRSI has the poorest spatial resolution, it is the most specific test for aggressive prostate cancer(10).

Spectroscopy is tricky. No multicenter study has shown benefit, but many single-center studies at “centers of excellence” have shown benefit from MRSI (12,13,14, 15). Therefore, one should only get spectroscopy done where there are specialists in its use for prostate cancer. Fortunately, dynamic contrast enhancement and diffusion-weighted imaging mostly compensate for the lack of spectroscopy in most cases. Some prostate MRI is acquired



MRSI (Magnetic Resonance Spectroscopic Imaging) is the most specific test for identifying aggressive prostate cancer

using a special “coil,” which is the name for the antenna that listens to the echoes in the magnetic field. If very high spatial resolution is necessary, a specially designed coil is placed in the rectum adjacent to the prostate. This coil is actually just a loop of wire, but it has a small balloon around it that helps hold it in place. In some cases, mostly those where the lining or “capsule” of the prostate does not need to be accurately outlined and when spectroscopy is not ordered, imaging can be done without the special coil at a cost of some loss of resolution(11).

Prostate Endorectal Coil offers significantly higher signal-to-noise ratio

The MRI itself is otherwise relatively uneventful. Most patients will receive an injection of a hormone called “glucagon” in a shoulder muscle which will prevent the rectum from spasming for about an hour. There are no lasting effects of this medicine, but because it can interfere with insulin, diabetics who take insulin must not receive it. Otherwise, one lies on ones back for about 45 minutes. The scan is noisy, but other than the injection of contrast, patients do not feel anything during the exam. It is important that the hips remain perfectly still, as the scans are planned based on the initial images.

Because prostate MRI scans consist of multiple components, processing the information can take up to 24 hours. Afterwards, the referring physician will have access to the report and, in most cases, the images.

Most insurance, including Medicare, will cover a pelvic MRI with contrast, which is how insurance companies think of prostate MRI. However, many insurance companies (again, including Medicare) will not cover spectroscopy. Spectroscopy is much harder to do well, and there is no simple way for insurance companies to know that they are getting their money's worth when they pay for it, so in general, they will not. Most imaging centers will allow patients to pay out-of-pocket for this component, but it can cost hundreds of dollars. If it is not covered, the patient and referring physician must decide if it is worth it.

How Does One Know If Prostate MRI Is Necessary?

Like many medical tests, prostate MRI is ordered by a physician – a patient cannot schedule a scan without a doctor's order. This is a legal requirement, but it also means that patients must have a discussion with their physician in order to determine if prostate MRI is necessary, and what kind of MRI the physician should order. Prostate MRI is only a part of the diagnosis and management of prostate cancer and is only necessary in specific cases. However, both the technology behind prostate MRI and the understanding of its uses are improving every day, so cases which might have benefitted from MRI in the past might all but require it now. In some cases, the doctor treating the prostate cancer will need to discuss the matter with a radiologist, a specialist in medical imaging, in order to determine what kind of MRI is best and when it would be useful, and to make certain the necessary hardware and software is available. This is a relatively young technology and we are

only beginning to understand how to use it in patient management, but it holds tremendous potential to finally help distinguish patients with non-aggressive cancer who do not need treatment from those with aggressive disease who do.

There are certain cases where prostate MRI should not or must not be done. Patients with implanted medical devices, like pacemakers, cannot undergo MRI. Some new device designs purport to be MRI-compatible, but none are commercially available. Patients with metal in their bodies, especially those who have been exposed to welding or

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lathe work, must be screened for implanted metal in the eyes or other exposed regions. Patients with hip replacements or metal screws in the hips or pelvis can often be imaged, but the metal can cause artifacts on the image, and distort the magnetic field such that diffusion-weighted imaging and spectroscopy cannot be performed. Also, most MRI units have a weight limit, usually between 250-400 lbs. Older high-field magnets often have more stringent weight limits, but low-field and open magnets are not powerful enough to give the kind of information needed for prostate imaging. Finally, patients with kidney failure might not be able to receive contrast, depend-

ing on how much kidney function is left. Claustrophobia is a “relative contraindication” as it can often be treated by a sedative prescribed by the referring physician. Most imaging centers are not set up to sedate patients once they arrive, but patients can take medicine prescribed by their referring physicians.

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