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CURRENT MAGNETIC RESONANCE IMAGING-BASED DIAGNOSTIC STRATEGIES FOR PROSTATE CANCER

General Surgery

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ABSTRACT

Recent developments in multiparametric MRI and MRI-targeted biopsy have made it possible to detect clinically significant cancers more accurately and efficiently than ever before. Furthermore, software that enables easy MRI/US image fusion has been developed and is already available on the market, and this has provided a tailwind for the spread of MRI-based prostate cancer diagnostic strategies. Such precise diagnosis of prostate cancer localization is essential for highly accurate focal therapy. In addition, a recent large-scale study applying MRI to community screening for prostate cancer has reported its usefulness. By contrast, concerns about overdiagnosis and overtreatment, the existence of inter-reader variability in MRI diagnosis, and issues with current MRI-targeted biopsy have emerged. In this article, we review the development of multiparametric MRI and MRI-targeted biopsy to date and the current issues and discuss future directions.

KEYWORDS

Clinically Significant Cancer, MRI, Prostate Cancer, Targeted Biopsy.

INTRODUCTION

Prostate cancer (PCa) has traditionally been diagnosed by transrectal ultrasonography (TRUS)-guided systematic prostate biopsy (SB),1,2. However, this procedure has been linked to overdiagnosis of clinically inconsequential PCa (cisPCa) and missed diagnoses of clinically significant PCa (csPCa). Furthermore, there is a rare downgrade or upgrade in the cancer diagnosis at the time of radical prostatectomy (RP).3,4 But with the advent of multiparametric magnetic resonance imaging (mpMRI) in the last ten years, the diagnostic strategy for PCa has changed dramatically.5. According to recent research, mpMRI is the best imaging method for identifying and locating questionable csPCa regions..6–9 In addition, the role of mpMRI is growing to include reduced detection of low-grade disease, precise clinical staging, planning for surgery and radiation therapy, decreased detection of csPCa through MRI-targeted biopsy (MRITB), appropriate candidate selection, and follow-up support for active surveillance (AS). While many of the benefits and drawbacks of using mpMRI in conjunction with SBs are well documented, there are still some unanswered questions around the technology. This article's goal is to examine the state of MRI-based PCa diagnostic techniques at the moment.

ROLE OF MULTIPARAMETRIC MRI

Since the 2000s, a number of studies have shown how effective mpMRI is at identifying csPCa.1,10 As a result, since the 2010s, the European Association of Urology (EAU) Guidelines (https://uroweb.org/guidelines/) have drastically altered the function of MRI. 2015 saw Before a second biopsy, MRI was advised just for those whose first biopsy came out negative. In 2016, however, prior to a confirmation biopsy, patients under active monitoring were encouraged to have an MRI. Furthermore, it was made clear in 2019 that MRI imaging is advised even in circumstances where there hasn't been a biopsy history prior to the initial biopsy. MRI technology has also advanced significantly as a result of the creation and broad application of PI-RADS (Prostate Imaging Reporting and Data System), a standardized reporting technique.11, 12 based on a 1-4 risk scale for having csPCa, stratifies suspected PCa into low- and high-risk groups [PI-RADS v2.1 Guidelines 2019]. As per the latest meta-analysis published by According to Other et al., the cancer detection rates (CDRs) for PI-RADS 1 were 6% (0%–20%), PI-RADS 2 had 9% (5%–13%), PI-RADS 3 had 16% (7%–27%), PIRADS 4 had 59% (39%–78%), and PI-RADS 5 had 85% (73%–94%). Higher CDR was shown to be significantly correlated with high categories ($p = 0.001$). 13 The International Society for Urological Pathology (ISUP) grade > 2 cancers can be detected and localized with MRI with good sensitivity, according to correlation with total prostatectomy specimens. Prostate cancer size and volume are predictive factors for MRI delineation, particularly when the cancer's diameter is greater than 10 mm.14–17 It's important to recognize the limitations of mp MRI tumor identification, though. According to Le et al., mp MRI misses' lesions in almost 20% of instances with a Gleason score of 3 + 4 or above.17 According to Bratan et al., MRI imaging is likewise less sensitive in detecting ISUP grade 1 PCa. About thirty percent of ISUP grade 1 tumors smaller than 0.5 cm in size were found in RP tissues according to histopathologic examination.16 These results are significant and call for careful consideration of MRI imaging in AS procedures and future local therapy.

Dynamic contrast enhanced MRI (DCE MRI) can currently enhance PI-RADS 3 lesions in the peripheral zone to PI-RADS 4 lesions, following PI-RADS V2.12 Biparametric The benefits of MRI (bpMRI) include lower prices, faster acquisition times, and no dangers from contrast chemicals. Consequently, a great deal of research has contrasted the accuracy of mpMRI with bpMRI.18–20 For the identification of csPC utilizing PI-RADS v. 2.1.21, bpMRI's interobserver reliability and diagnostic performance in Japan were comparable to those of mpMRI. The right patients must be chosen for targeted therapy of localized prostate cancer using mpMRI and MRITB.22

MRI-TARGETED BIOPSY

There are two different ways that MRI results can be applied to improve the yield of prostate biopsies and reduce the number of unneeded diagnoses.7. The first is known as the "combined biopsy pathway," in which patients who have MRI abnormalities with low probability undergo planned SB, and those who have MRI findings with higher probability undergo both scheduled SB and MRITB.24 The second is the "MRI pathway," where men with substantial MRI abnormalities undergo MRITB alone (no systematic cores) while men with negligible MRI findings do not receive any biopsy. The benefit of the MRI approach is that, among men with substantial MRI results, it decreases the number of men who need biopsies and the total number of biopsy cores, lowering the overidentification of cisPCa.25 Figure 1 illustrates a novel MRI-based diagnostic approach. Adapt screening and risk if the initial prostate biopsy result is negative. Each person should have a revaluation. Individualized mpMRI should be carried out if there are any significant indicators of csPCa during follow-up, such as an elevated PSA or abnormal results from a digital rectal examination.

PROMIS demonstrated the advantages of MRITB. By using mpMRI prior to biopsy, 27% of patients were able to skip the procedure, which led to a 5% decrease in cisPCa and an 18% rise in the number of csPCa cases detected.1. Furthermore, the study's mpMRI's negative predictive value (NPV) was high, suggesting that the absence of csPCa may be reassured by negative mpMRI results. Two further prospective multicenter trials assessed MRITB in individuals who had never had a biopsy.

The mpMRI method is less likely to detect cisPCa and has a high sensitivity for csPCa, which should assist reduce overdiagnosis and avoidance of needless biopsies. In our earlier research, when no significant mpMRI findings were found (PI-RADS <3), the NPV for csPCa was as high as 82%. An NPV of 100% was obtained by using the two factors "regression test for the first negative biopsy" and "PSA density <0.15" in the study.26 When comparing the MRITB group to the SB group, the length of <6 mm, which is considered an inconsequential finding, was much lower (5.6% vs. 19.5%, $p < 0.0001$),9 suggesting that MRITB without SB greatly reduced the overdiagnosis of low-risk disorders.

Significance Of Combining Mritargeted Biopsy With Systematic Biopsy

Although the improved detection of csPCa by MRITB has been established, the debate on whether MRITB should be used in combination with SBx persists.9 Several studies have directly compared the ability of MRITB and SB to detect csPCa and the significance of their combined use. In the prospective, randomized PRECISION study, Kasivisvanathan et al. found that MRITB might be an alternative to conventional SB.2 The study demonstrated that MRITB alone was superior to SB for identifying csPCa (+12% for ISUP grade group 2 or higher tumors) and decreased detection of cisPCa (_13% for ISUP grade group 1) in 500 biopsy-naive men with MRI findings of PI-RADS 3–5. Another systematic review also revealed that MRITB alone can detect more csPCa than SB while detecting less cisPCa.6

Ahdoot et al. did, however, emphasize how crucial it is to combine MRITB and 12 core SB.27 Their examination of information from 2103 patients with notable MRI anomalies, SB, and 8.8% of patients with ISUP Grade Group 3 or above would have gone unnoticed if either approach had been used alone, according to MRTB. Further analysis of 404 patients who had complete prostateectomy revealed an upgrade rate of 16.8% with SB alone and 8.7% with MRITB alone to ISUP Grade Group 3 or higher. When the two approaches were combined, the percentage dropped to just 3.5%.

To date, the combination of MRITB and SB has the lowest rate of missed csPCa 28 and is recommended in biopsy-naive men even with positive MRI findings. Omitting SB and performing MRITB alone might be an option only for highly selected MRI-positive patients with a prior history of negative biopsy.

MRI/US IMAGE-FUSION BIOPSY

There are currently three methods available for conducting MRITB. The first method is known as cognitive registration, in which MRI images are acquired before the TRUS biopsy is performed, and the surgeon uses these images to navigate the biopsy while recognizing the target in his or her mind. The second method is in-bore MRI, where the patient undergoes biopsy in real time in an MRI machine. During this procedure, special unmagnetized needles are guided to the target using T2-weighted images.29 In-bore MRITB can be conducted using either manual or robot-assisted needleguide systems.30,31

The third technique is MR/US image fusion, which uses specialized software to virtually merge MRI and TRUS images in real time in order to guide biopsy. The efficiency The MR/US fusion biopsy has been shown to be dependable and is expanding globally.32 There were no discernible variations in the three techniques' diagnostic accuracy according to the FUTURE study.33 An additional piece of equipment is not needed for the typical approach of cognitive registration, but the surgeon's ability and experience are crucial.23 Because in-bore MRITB is laborious and time-consuming, it is not yet widely used. Since MR/US fusion biopsy is now covered by public health insurance, more facilities in Japan are using this technology, despite its relatively high cost. This is because it allows for more precise biopsies.

Utility Of Mri And Mri-targeted Biopsy In Prostate Cancer Screening

The idea of using MRI as a screening tool for PCa has generated a lot of discussion. Using mpMRI to triage biopsy-naive males with PSA levels below 15 ng/mL, a multicenter, paired-cohort, confirmatory trial was carried out. It was discovered that 27% of patients were able to avoid a first biopsy, leading to 5% fewer occurrences of cisPCa.1. More recently, MRI and MRITB were used in a sizable trial conducted in Sweden to screen for PCa.35 12 750 males between the ages of 50 and 74 with PSA levels above 3 ng/mL were enrolled in this population-based, non-inferiority trial, and 1532 of them were randomly assigned to the Experimental-biopsy group (N = 929) or the Standard-biopsy group (N = 603). Negative MRI findings in the Experimental biopsy group eliminated the requirement for The additional cost of less frequent biopsies and possible financial savings from less overtreatment could more than make up for the nMRI 37 The diagnostic pathway's use of molecular markers and risk calculators may improve the suitability of MRI for PCa screening.38

Current Issues Of Mri-based Diagnostic Pathway

Many factors affect the accuracy of MRI and MRITB in identifying and localizing csPCa. The significant variation across earlier research emphasizes the necessity of verifying the based on numerous variables.23

MRI and image processing

The PI-RADS article describes in detail not only the evaluation methods but also the appropriate MRI imaging supplementation methods.11 Furthermore, it should be recognized that a limitation of MRI itself is that it is difficult to detect all csPCa, and even after expert review, some csPCa with genetic mutations, such as those often seen in advanced cancer, may not be detected by mpMRI.39

PI-RADS scoring system

The PI-RADS scoring system has been updated, and the accuracy, especially in the transition zone, is reported to be higher in version 2 than in version 1.40–42 However, many issues related to the current PI-RADS scoring system itself have been identified, and it is not perfect.42

MRI interpretation

The accuracy of different imaging modalities is known to vary amongst readers, and the diagnosis of PCa by MRI is not an exception. We discovered a statistically significant difference between radiologists with experience in prostate imaging and those without, in terms of the overall cancer detection rate (63% vs. 35%, p = 0.001) and the csPCa detection rate (47% vs. 27%, p = 0.027) in MRI score 4-5 lesions.43 It has been reported that radiologists are expected to report at least 100 prostate mpMRI images under expert supervision following a particular training session, albeit the requisite experience has not been confirmed.44, 45 Therefore, care should be used when implementing the results of big randomized controlled trials, which usually depend on MRI diagnoses that are interpreted by exceptionally talented radiologists, to our daily clinical work.14 Nonetheless, it has been demonstrated that MRI and MRITB accuracy significantly increases with time thanks to PI-RADS updates, feedback on pathology results at multidisciplinary conferences, and the application of organized reporting templates.13, 46, 47

Targeted biopsy

The precision of the biopsy outcome itself is directly correlated with the operator's prostate contouring and target marking in MRI/US image-fusion biopsies. This is because, even with software-based fusion technologies, contouring and marking are usually done by hand.6,23 If targeting is not achieved, taking more cores per lesion. may somewhat offset the biopsy's error, although the ideal number of cores per lesion is still up for discussion.48 It was also recently noted that biopsies performed samples taken from within and outside of MRI lesions have a higher sensitivity for detecting cancer than samples taken from the lesion alone.49

Overdiagnosis/overtreatment

The majority of the factors used now to choose a prostate cancer treatment plan are typically derived from the outcomes of traditional SBs. Consequently, using these standards in the MRITB period could be susceptible to over diagnosis and over treatment.14 The nomogram that is used to assess if extended pelvic lymph node dissection (ePLND) at RP is necessary for localized PCa is one example. When MRITB data are incorporated into a nomogram designed during the conventional SB period, the proportion of positive cores may increase and patients who don't actually require ePLND may experience it. A fresh, distinct nomogram that is appropriately based on the findings of MRITB should be employed to prevent such overtreatment.50, 51 Additionally, a brand-new categorization based on MRITB has been put forth to forecast.

CONCLUSIONS

Recent developments in mpMRI and MRITB have enabled more efficient and accurate identification of csPCa. The achievement of such precise localization of csPCa makes targeted focal therapy, which treats smaller areas, a promising and realistic approach. In other words, we are entering an era in which targeted focal therapies that treat only the target lesion and a small surrounding safety margin can provide both better cancer control and better quality of life. Furthermore, incorporation of risk calculators and biomarkers into mpMRI may increase the potential use of MRI as a screening tool.

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