Optimising prostate biopsies and imaging for the future – a review

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Abstract

Conventionally, transrectal ultrasound guided prostate biopsy (TRUS-Bx) was the main technique used for the diagnosis of prostate cancer since it was first described in 1989 [1]. However, the PROMIS trial showed that this random, non-targeted approach could miss up to 18% of clinically significant cancer (csPCa) [2]. Furthermore, risk of sepsis post TRUS-Bx can be as high as 2.4% [3]. Understanding the demerits of TR-biopsy have led to the introduction of transperineal prostate biopsy (TP-Bx). The incorporation of mpMRI revolutionised prostate cancer diagnostics, allowing visualisation of areas likely to harbour csPCa whilst permitting some men to avoid an immediate biopsy. Furthermore, the advent of prostate specific membrane antigen-positron emission tomography (PSMA-PET) is highly promising, because of its role in primary diagnosis of prostate cancer and its higher diagnostic accuracy over conventional imaging in detecting nodal and metastatic lesions. Our narrative review provides an overview on prostate biopsy techniques and an update on prostate imaging, with particular focus on PSMA-PET.

Keywords:

Prostate cancer, transperineal prostate biopsy, magnetic resonance imaging (MRI), prostate specific membrane antigen (PSMA), positron emission tomography (PET)

Introduction

Prostate cancer is the second most diagnosed cancer in men. According to GLOBCAN, 1.4 million cases of prostate cancer were diagnosed in 2020, accounting for 14.1% incidence of all cancer in men [4]. In United States, it is estimated that more than 288,000 new cases will be diagnosed in 2023 alone [5]. Prostate biopsy is the cornerstone of establishing a definitive diagnosis of prostate cancer. TRUS-Bx was the gold standard technique, however post-biopsy sepsis could be as high as 2.4% [3]. Results published from TREXIT (EXIT from Transrectal Prostate biopsies) showed that a switch from transrectal to transperineal approach can lower the sepsis rate to as low as 0.4% [3].

Despite best efforts from TRUS-Bx, the PROMIS trial showed that this approach was associated with 18% underdetection of csPCa (Gleason score ≥4 + 3 or a maximum cancer core length 6 mm or longer) [2]. The trial also validated the benefit of pre-biopsy multi-parametric magnetic resonance imaging (mp-MRI) in prostate cancer diagnostics. Results of another landmark trial PRECISION shortly followed, validating the superiority of MRI-targeted biopsy to TRUS-Bx [6]. Research interest in pre-biopsy imaging modalities and image-fusion technology grew since these landmark studies. Our narrative review aims to provide an overview and update on techniques for prostate biopsy, pre-biopsy imaging and image guided targeted biopsy.

Materials and Methods

A comprehensive electronic literature search of peer-reviewed journal articles was conducted in this review. The PubMed database was queried with the following search terms: “prostate biopsy” “transrectal,” “transperineal,” “68Ga-PSMA,” “prostate specific membrane antigen”, “PSMA” and “multiparametric MRI”. The identified articles were further screened and assessed for eligibility. Selected articles were manually searched to generate additional eligible citations. International guideline from European Association of Urology (EAU) [7] was consulted.

Transrectal ultrasound guided prostate biopsy (TRUS-Bx)

TRUS-Bx was first described in 1989. This technique involved using a spring-loaded biopsy gun, aligning a transrectal ultrasound to areas of palpable prostate nodularity to guide biopsy. Areas of palpable nodularity are seen as hypoechoic defect on ultrasound, and these areas corresponded to more cancer detection [1]. When compared to digitally targeted prostate biopsy, the addition of transrectal ultrasound increased accuracy in diagnosing prostate cancer in the man with a palpable abnormality of the prostate.

Furthermore, a study that compared random systematic TRUS-biopsy versus targeted TRUS-biopsy at areas of hypoechoic defects showed that systematic biopsy picked up 9% of cancer missed by targeted biopsy [8]. Equally, targeted biopsy found cancer missed by random systematic biopsy in 5%. Therefore, a combination of systematic and targeted biopsy is recommended to improve accuracy of diagnosing prostate cancer through minimising sampling errors [8]. A common protocol used traditionally for TRUS-Bx was 12-core sexant biopsy [1,8], which involved sampling the transitional zone in the apex, mid and base as well as the peripheral zone bilaterally.

Shift towards transperineal prostate biopsy (TP-Bx)

Concerns regarding sepsis risk post TRUS-biopsy led to the gradual transition to TP-Bx. Passage of a biopsy trocar from dirty to clean via the transrectal approach risk the passage of rectal bacterial flora into the bloodstream. Sepsis following TRUS-Bx can be life-threatening, with sepsis-related mortality rate as high as 0.13% [9]. Although the use of prophylactic antibiotics can minimise such risk, rising antibiotics resistance concerns many who have now switched to the transperineal, cleaner approach. One such example is the ‘TRexit’ movement initiated by urologists at Guys’ Hospital in London in 2017, with the intention to roll out TP-Bx and replace TRUS-Bx across all London network by mid-March 2019 [10,11]. This target was achieved ahead of time in early March 2019. Results from the recently published PREVENT trial

reaffirms the safety of TP-Bx without use of prophylactic antibiotics, which is noteworthy given rising antibiotic resistance. The trial randomised 658 patients to TP-Bx without prophylaxis antibiotics and TRUS-Bx with targeted prophylaxis (based on rectal flora). They showed an absence of post biopsy infection for TP-Bx group and 1.4% in TRUS-Bx group, although no statistical significance was found (p=0.059) [12].

There are various schemas that divide the prostate into zones to facilitate transperineal systematic biopsy. The Barzell template technique was established in 2003 and modified in 2008. Using this technique, systematic TP-Bx is performed via the aid of a brachytherapy grid that divides the prostate into 24 zones, spaced 5mm apart. The use of brachytherapy grid allows precise and systematic sampling of the prostate under guidance of real-time transrectal ultrasound, reducing human sampling error [13]. Barzell's team showed that this technique is associated with a high biopsy positive rate (78%), increased detection of prostate cancer and superior staging information compared to TRUS-Bx. The median number of cores taken in the study was 46 [14]. However, given the higher number of cores taken with this technique, cost related to processing all biopsies and procedure related morbidity such as increased risk of retention was inevitably higher (8%) [14]. Furthermore, a new puncture to the perineum is required for each biopsy which can be associated with pain, and therefore requires the procedure to be performed under general anaesthesia [15,16]. These drawbacks have limited its utility and wider adoption. This led to the proposal of another technique in 2013, the Ginsburg protocol [17]. The Ginsburg protocol targets the peripheral zone and divides it into the anterior, mid and posterior sector whilst avoiding the transition zone and periurethral zones. The rationale of the latter is to reduce glandular oedema around the urethra, and therefore the risk of retention, especially when incidence of prostate cancer in transition zone is low (<4%). This divides the prostate into 12 anatomical sectors. For prostate glands smaller than 30ml, the protocol recommends 2 biopsies to be taken from each sector, totally 24 systematic cores. For prostate glands larger than 30ml, additional basal cores are recommended. The protocol also recommended 2 MRI targeted biopsy to be taken in addition to the systematic cores, with targeted biopsies taken prior to systematic biopsy to prevent movement of lesions on imaging. Studies which utilised this technique showed no major complications, 96% overall cancer detection rate, with clinically significant cancer missed in only 3.6% of cases [18-20].

The free-hand TP-Bx technique overcomes the need for a brachytherapy stepping unit and general anaesthesia. It involves one or two punctures to the perineum through one or two common access cannulas. Local anaesthesia can be infiltrated around the puncture sites, therefore allowing the procedure to be performed under local anaesthesia. The puncture site via the cannula acts as a pivot point through which the biopsy needle can be directed to different parts of the prostate. A large cohort study on 1287 patients showed that free-hand TP-Bx was tolerated well by patients under local anaesthesia, with acceptable complications and low (0.3%) infection rate [21]. However, with free-hand TP-Bx, the puncture needle is dissociated from the transrectal ultrasound probe and therefore requires frequent realignment to visualise the biopsy needle.

Figure 1: Image of PrecisionPoint Transperineal access system (Permission to use image granted from Perineologic)

The development of transperineal access system such as PrecisionPoint (Perineologic, Cumberland, Maryland) revolutionised TP-Bx [Figure 1]. This transperineal access system consists of a needle holder, a 15 Gauge access needle and a clamp which allows attachment to the transrectal ultrasound probe. The biopsy needle is stabilised after clamping the access system to the transrectal ultrasound probe and aligns with the probe. Unlike techniques which involve piercing the perineum multiple times, the PrecisionPoint uses two access points on each side of the prostate only.

Transition to such transperineal approach has been of success in London, with a 'clean break' from TRUS-Bx (TREXIT) announced in September 2017 and achieved early March 2019. Within one year of its transition, 678 cases of TP-Bx were performed with either PrecisionPoint or stepper with or without MRI fusion technology in Guy's Hospital, London. Most cases (60%) were performed under local anaesthesia. All patients had one dose of pre-operative antibiotics, with only one case of sepsis reported (0.16%) [22]. Many further studies have shown 0% sepsis rates post TP-Bx using PrecisionPoint irrespective of whether pre-op prophylactic antibiotic was used, demonstrating its safety [23-25]. The EAU 2023 Guidelines recommend performing prostate biopsy using the transperineal approach due to the lower risk of infection [7].

TRUS-Bx and TP-Bx have equal diagnostic accuracy. A meta-analysis compared the diagnostic accuracy of TP-Bx versus TRUS-Bx. Data from seven observational studies (RR 1.01, 95% CI 0.87–1.18) and four randomised controlled trials (RR 0.94, 95% CI 0.81–1.10) showed no significant difference in diagnostic accuracy between those two approaches [26]. However, the transperineal route allows more cores to be taken for diagnostic purposes without an increased risk of sepsis [26], unlike the transrectal route where there is an association between the number of cores taken and risk of sepsis ($p<0.001$) [28].

mp-MRI prior to biopsy

PROMIS was the first study that validated the use of mp-MRI prior to TP-Bx. The study compared the diagnostic accuracy of mp-MRI versus TRUS-Bx, using template prostate mapping biopsy as a reference. The study showed that mp-MRI had higher sensitivity (93%) and negative predictive value (89%) compared to TRUS-Bx for csPCa (Gleason ≥ 4+3 or maximum cancer core length 6mm or longer). A negative mp-MRI therefore implies a high probability of absence of csPCa. Furthermore, PROMIS showed that if mp-MRI was used as a triage system pre-biopsy, 27% of men could avoid a biopsy and 5% less cases of clinically insignificant prostate cancer diagnosed. Overall, mp-MRI helps to improve the detection of csPCa and reduces the diagnosis of clinically insignificant prostate cancer [2]. The EAU 2023 guidelines strongly recommend MRI to be performed before prostate biopsy for biopsy-naïve patients [7].

Introduction of mp-MRI pre-biopsy has changed the way urologists diagnose and monitor prostate cancer. It provides a diagnostic tool to target lesions and helps urologist select patient for prostate biopsy. With growing research interest with mp-MRI, it became apparent that some lesions are inconspicuous on mp-MRI. Post-hoc analysis of the data from PROMIS showed that between 4-17% of prostate cancer could be overlooked by mp-MRI, depending on how one defines csPCa (Gleason ≥4+3 versus Gleason ≥3+4). Post-hoc analysis also identified clinical factors which predict MRI-undetected cancers, such as low Gleason score (Gleason ≤ 3+4), short cancer core length and low PSA density. Overall, none of the aggressive cancers were overlooked by MRI [29]. Results of the PRECISION trial in 2018 validated the use of mpMRI before prostate biopsy in biopsy-naïve men. The study showed that in a biopsy naïve setting, for patients with clinical suspicion of prostate cancer, risk assessment with mpMRI with or without targeted biopsy increased the number of csPCa diagnosed and reduced the diagnosis of clinically insignificant prostate cancer when compared to TRUS-Bx. Results from the PRECISION trial had significant impact on international guidelines, with both EAU and NICE guidelines in 2019 recommending MRI to be performed before prostate biopsy in biopsy-naive men [7,30].

Study, Sample Size	Study Design	Summary of study	Summary of Findings
Ahmed etal., (2017) **PROMIS** *N= 740*	Prospective, multi-centre study	Compared diagnostic accuracy of mpMRI versus TRUS-biopsy, using template prostate mapping biopsy as a reference.	Using mpMRI as a triage before prostate biopsy, 27% of men could avoid a biopsy and 5% less cases of clinically insignificant prostate cancer diagnosed. mpMRI has superior sensitivity (93%) and negative predictive value (89%) compared to TRUS-Bx for csPCa.
Kasivisvanathan etal., (2018) **PRECISION** *N= 500*	Prospective, multi-centre study	Evaluated mpMRI and mpMRI targeted biopsy compared to targeted TRUS-biopsy in men with clinical suspicion of prostate cancer who had not undergone biopsy	mpMRI with or without targeted biopsy was superior to standard TRUS guided biopsy. mpMRI targeted biopsy diagnosed fewer men with insignificant prostate cancer (9% vs 22%, p<0.001) and more men with csPCa (38% vs 26%, p=0.005) than TRUS-Bx.

Table 1: Overview of studies that validated the use of mpMRI for prostate cancer diagnosis

Image-guided fusion vs cognitive-guided targeted prostate biopsy

The aim of targeted biopsy is to improve the diagnose csPCa whilst not over-diagnosing clinically insignificant prostate cancer. Results from PRECISION trial led to the introduction of mpMRI as a guiding tool for increasing the precision of prostate biopsy. The interpretation and reporting of prostate mpMRI has been standardised with the adoption of Prostate Imaging-Reporting and Data System (PIRADS) [31]. PIRADS assigns a score of 1 to 5 based on mpMRI findings, correlating with the likelihood of csPCa for each lesion present in the prostate gland. PIRADS 1 corresponds to very low likelihood of csPCa whilst PIRADS 5 corresponds to very high likelihood csPCa. The introduction PIRADS helps to improve the detection of csPCa, benign disease that does not warrant a biopsy and helps reduce diagnosis of clinically insignificant prostate that are unlikely to cause problems in a man's lifetime. There are 3 ways that targeted biopsies can be performed when mpMRI detects a suspicious lesion. Cognitive targeted prostate biopsy is the simplest approach. The operator reviews suspicious lesions on mpMRI prior to the procedure and aims the biopsy needle at the prostate where the suspicious lesion is. The second approach is fusion software target biopsy. This approach was first described in 2002 [32]. In this approach, prior mpMRI imaging is fused with ultrasound via a specialised software to provide real-time information to target areas suspected of having prostate cancer. The last approach, also the least common approach, is in-bore MRI-guided prostate biopsy. Prostate biopsy is performed simultaneously with MRI, to ensure that the biopsy needle reaches target lesions. In-bore MRI guided biopsy is often used for academic purposes only.

The EAU guidelines 2023 does not specifically recommend an approach for targeted biopsy as there does not seem to be a clear superiority of one image-guided approach over another [7]. A systematic review and meta-analysis in 2020 comparing MRI-ultrasound image guided fusion biopsy versus cognitive biopsy for

the detection of prostate cancer and csPCa did not establish any statistical significance between these two approaches [33]. A retrospective study on 510 patients who had MRI showing suspicious lesions who underwent either cognitive or MRI-ultrasound image guided biopsy in addition to concurrent 12- core systematic biopsy did not show any significant difference in rates of csPCa [34]. Therefore, which targeted approach is adopted depends on centre preference, availability of fusion software, cost and operator skill.

PSMA PET/CT

Patients with localised prostate cancer are often treated definitively with radiotherapy or radical prostatectomy. Unfortunately, biochemical recurrence can occur in 20-50% of patients with prostate cancer within 10 years of receiving definitive treatment [35]. Conventionally, imaging in the form of computed tomography (CT) and whole-body technetium bone scintigraphy have been used in the assessment of clinical progression in patients with biochemical recurrence. However, use of such imaging is of limited value in oligometastatic patients with low PSA (<10ng/ml), with positive bone scan and CT scan found in 4.5% and 14% of patients with biochemical recurrence only [36]. Furthermore, bone scintigraphy has low diagnostic yield (3.5% with serum PSA values ≤10 ng/mL, 6.9% with serum PSA between 10 and 20 ng/mL, and 41.8% with serum PSA >20 ng/mL) [37] and are not adequate at distinguishing benign osteoblastic activity versus prostatic bone metastasis. Limitations of bone scintigraphy have prompted research interest in alternate imaging modality with better specificity, particularly for patients at earlier stage of their disease, with low PSA levels. One such modality is prostate-specific membrane antigen-positron emission tomography (PSMA-PET).

Prostate-specific membrane antigen (PSMA) is a type II membrane protein with folate hydrolase activity produced by the prostate epithelium. A study using immunohistochemical analysis showed that PSMA can also be found in other areas of the body such as duodenum and kidney. It studied the expression of PSMA in primary prostate adenocarcinoma, prostatic lymph node and bone metastasis, and found that 33 of 35 primary prostate adenocarincoma, 7 of 8 lymph node metastasis and 8 of 18 prostatic bony metastasis expressed PSMA [38]. Another immunohistochemical study showed that expression of membranous-PSMA (mPSMA) was associated with higher Gleason grade, worse overall survival and increased expression in metastatic castration-resistant prostate cancer [39]. Higher ^{68}Ga-PSMA uptake is also associated with more aggressive cancer [40]. Therefore, application of PSMA to imaging may further aid detection of bone metastasis and optimise accuracy of prostate biopsy.

PSMA conjugated with radionuclides 68-gallium (^{68}Ga) and 18-fluroide (^{18}F) have been used successfully in the clinical diagnosis of prostate cancer [41], with ^{68}Ga being the radiotracer most used for PSMA PET/CT. A meta-analysis compared ^{68}Ga-PSMA PET/CT and ^{99}mTc-labeled methylene diphosphonate bone scintigraphy (^{99m}Tc-MDP BS) at detecting bone metastasis in patients with prostate cancer. It showed that the diagnostic performance of ^{68}Ga-PSMA PET/CT was superior to bone scintigraphy in both pooled sensitivity and specificity ($p<0.001$).^{68}Ga-PSMA PET/CT identified bone metastasis in patients where bone scintigraphy showed a negative result and identified more metastasis in patients with oligometastases, changing oncological management [42]. Another retrospective multi-centre head-to-head comparison study using PSMA-PET as a reference standard showed that the positive predictive value of bone scintigraphy at initial staging was low at 43%. They showed that 27% with bone metastasis shown on bone scintigraphy were negative on PSMA-PET [43]. This has oncological implications. The CHAARTED trial showed that in patients with high volume metastasis, defined as presence of visceral metastasis or ≥ 4 bone lesions, addition of docetaxel to standard androgen-deprivation therapy (ADT) resulted in significantly longer overall survival compared to ADT alone [44]. The STAMPADE trial showed that for patients with low metastatic burden, defined as 3 or fewer bone metastasis, addition of prostate radiotherapy to androgen deprivation therapy and docetaxel improved overall survival at 3 years [45]. These studies highlight the importance of accurate assessment of metastatic burden with imaging.

Furthermore, PSMA PET/CT may also have a role in primary diagnosis of prostate cancer. The PRIMARY trial [46] prospectively evaluated the negative predictive value and sensitivity of combined mpMRI and PSMA-PET/CT vs mpMRI alone for the detection of csPCa (defined as International Society of Urology Pathology grade group ≥2). All 296 men in the study with clinical suspicion of prostate cancer based on abnormal PSA < 20ng/ml or abnormal digital rectal examination underwent mpMRI, pelvic-only PSMA and systematic ± targeted biopsy. The PRIMARY trial showed that a combination of PSMA-PET/CT and MRI had a synergistic effect, with a higher negative predictive value compared to MRI alone (91% vs 72%, p<0.001). Sensitivity of combined PSMA-PET/CT and MRI was as high as 97%, compared to 83% with MRI alone (p<0.001). Results from the PRIMARY trial is promising. It might be that patients with negative findings on PSMA-PET/CT with MRI could avoid a biopsy in the future. However, further randomised trials will need to confirm its clinical application. A retrospective study showed that PSMA-PET/CT is most useful for patients with high-risk prostate cancer, with a higher detection compared to mpMRI; whilst for patients with low and intermediate-risk prostate cancer, mpMRI provided superior diagnostic confidence [47]. In recent years, there has been increased research interest in the application of PSMA-PET/CT targeted prostate biopsy. A prospective study of 125 men with clinical parameters for high-risk prostate cancer were evaluated by mpMRI and ^{68}Ga-PSMA PET/CT. Patients with mpMRI showing PIRADS ≥3 and/or standard uptake value (SUVmax) ≥8 in ^{68}Ga-PSMA PET/CT had targeted TP-Bx (4 cores) followed by systematic TP-Bx. They showed that PMSA-PET/CT had higher diagnostic accuracy than mpMRI (92% vs 86.2%) in the diagnosis of csPCa [48]. A novel technique for ^{68}Ga-PSMA PET/CT guided biopsy via the transgluteal approach has been described. This involves pre-biopsy pelvic CT/PET to identify the index lesion, simulating the puncture path, angle, and depth via these images. Under local anaesthesia, a 17G biopsy trocar is introduced through the gluteus maximus, ischial anal fossa and anal elevator muscle to the target point. This technique was shown to be well tolerated by patients, with lower complication rates compared to TRUS-GB [49].

Lastly, PSMA-PET may be a useful tool for monitoring response to High-Intensity Focused Ultrasound (HIFU) for patients with localised prostate cancer. mpMRI post HIFU is often difficult to interpret because of the signal alterations of treated prostate gland. Areas that are treated with HIFU show focal high signal on T1 images from haemorrhage, and dark central zone on T2 from central necrosis [50]. These changes make detection of residual prostate cancer challenging. These challenges could be overcome with PSMA-PET. ^{68}Ga-PSMA PET/MRI has been shown to detect recurrent disease not seen on routine mpMRI post HIFU treatment and correlated significantly to tumour burden and volume (p<0.001) [51]. It can also monitor and predict biochemical response post-HIFU treatment. A prospective study on patients with localised prostate cancer who received HIFU showed that there was a significant correlation between SUV variation (PSMA PET response) and PSA response at 12 months post-HIFU (p=0.021) [52].

Study, Sample Size	Study Design	Summary of study	Summary of Findings
^{68}Ga-PSMA PET/CT vs bone scan			
Zhao etal., (2022) *5 studies, N=546*	Meta-analysis	To compare the diagnostic performance of ^{68}Ga-PSMA PET/CT and ^{99m}Tc-MDP BS for the detection of bone metastasis in patients with prostate cancer.	Pooled sensitivity and specificity were both significantly higher for ^{68}Ga-PSMA-11 PET/CT than ^{99}mTc-MDP BS (both $p < .001$). Findings from ^{68}Ga-PSMA-11 PET/CT changed management in 67 patients through the detection of bone metastases in patients with negative BS, or by identifying more bone metastases in patients with oligometastases on BS.
Hope etal., (2023) *N=167*	Retrospective study	All patients with prostate cancer were imaged with bone scan and PMSA PET. The study evaluated the ability of bone scan to detect bone metastasis using PMSA PET as a reference standard.	Positive predictive value of bone scan was low at initial staging with 47% of positive bone scans being false positive.
^{68}Ga-PSMA PET/CT vs mpMRI			
Emmett etal., (2021) *N= 296*	Prospective study	All patients with clinical suspicion of prostate cancer based on abnormal PSA (<20ng/ml) or abnormal digital rectal examination underwent mpMRI, pelvic-only PSMA and systematic ± targeted biopsy. The study evaluated and compared the negative predictive value and sensitivity of mpMRI alone vs combined PSMA-PET/CT and mpMRI.	Combining PSMA-PET/CT and mpMRI improves negative predictive value (91% vs 72%) and sensitivity (97% vs 83%) compared to mpMRI alone for detection of csPCa.
^{68}Ga-PSMA PET/CT guided prostate biopsy			
Pepe etal., (2023) *N=125*	Prospective study	All patients with clinical parameters for high-risk prostate cancer were evaluated by	^{68}Ga-PSMA PET/CT had higher diagnostic accuracy compared to mpMRI (92% vs 86.2%)

		mpMRI and ^{68}Ga-PSMA PET/CT. Patients with mpMRI showing PIRADS ≥3 and/or standard uptake value (SUVmax) ≥8 in ^{68}Ga-PSMA PET/CT had targeted TP-Bx (4 cores) followed by systematic TP-Bx. The diagnostic accuracy of ^{68}Ga-PSMA PET/CT vs mpMRI targeted biopsy were compared.	in the diagnosis of clinically significant prostate cancer (Gleason ≥3+4 =7).

Table 2: Overview of studies evaluating diagnostic accuracy of ^{68}Ga-PSMA-11 PET/CT versus bone scan and mpMRI.

Conclusion

Prostate biopsy has evolved significantly in the past decades. The ideal prostate biopsy technique should be of low cost and risk to the patient, be minimally invasive and of high sensitivity. TP-Bx has largely replaced TRUS-Bx in London, since the TREXIT movement which demonstrated a much lower sepsis rate compared to TRUS-Bx. The PROMIS trial validated the importance of pre-biopsy mpMRI and is now recommended by EAU Guidelines for biopsy naïve patients. The future of prostate biopsy might lie on ^{68}Ga-PSMA PET/CT targeted prostate biopsy, with current research showing its diagnostic superiority when used in combination with mpMRI and to mpMRI alone for patients with csPCa.

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