BANGLADESH JOURNAL OF
UROLOGY
Bangladesh J. Urol. 2024; 27(1): 1-3
www.banglajol.info/index.php/BJU
DOI: https://doi.org/10.3329/bju.v27i1.71208

Editorial

ISSN : 2304 - 8514 (Print)
ISSN : 2304 - 8522 (Online)

Editorial on Evolution of Prostate Biopsy

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Prostate cancer (PCa) is the second most common cancer among men. It represents the 5th most frequent cause of cancer-related death. Among men alive today, it is estimated that approximately 1 in 8 (12.9%) will be diagnosed with prostate cancer, and 1 in 40 (2.5%) will die from this disease. Again, metastatic disease causes a huge financial burden for the patient, society, and the nation as well. So, early diagnosis and subsequent management is imperative to provide benefit to the affected individual.

A physical examination, including a digital rectal exam (DRE), is important. Induration or nodularity, if detected, must alert the physician to the possibility of PCa. Raised serum PSA is also suggestive of underlying malignancy. However, tissue diagnosis is considered to be imperative to confirm a diagnosis. Currently, the only way to make a definitive diagnosis of prostate cancer is a prostate biopsy (PBx) and the subsequent histopathological examination.

PBx to exclude cancer has been part of clinical practice since the beginning of the 20th century. These techniques have evolved to optimally address some of the unique issues of the procedure, including the awkward anatomical position of the prostate, the proximity of the biopsy tract to feces and urine, the risk of sepsis, the potential side effects affecting voiding and sexual function, heterogeneity of underlying cancer, the discrepancy in the appearance of significant lesions between the different imaging modalities, and finally difficulty in precisely targeting significant cancer. Whilst a digital rectal examination (DRE) to guide the decision regarding the need for PBx was critical in the early 1900s, the arrival of prostate-specific antigen (PSA) and ultrasound (US) into clinical practice in the 1980s and the evolution of multi-parametric magnetic resonance imaging (mpMRI) in the early 21st Century have driven the surgical art of PBx into a more scientific-based procedure.

The first PBx was performed using an open perineal technique in 1926. Patients required general anesthesia (GA), at least a week of postoperative stay in hospital and almost invariably had urinary incontinence (UI) and erectile dysfunction (ED), rendering the procedure ineffective. In 1937 finger finger-guided trans-rectal biopsy was described by Astraldi. Finger-guided TP aspiration PBx was first introduced by Kaufman in 1954, which involved the insertion of a needle through the perineum 1cm above the anus but guided by a digit in the rectum.

The transurethral biopsy suggested by Denton et al.in 1967, was of the view that an extensive transurethral prostatectomy (TURP) would nearly always confirm the diagnosis of PCa. However, Grabstald commented that TURP might be useful only in advanced tumors. By then, it was also well known that PCa was more frequently seen posteriorly, near the capsule, and thus was not easily reached with the resecting loop. Consequently, it was affirmed that the transurethral PBx should not be performed as a primary PBx technique for prostate cancer.

The development of ultrasound imaging gradually eclipsed the finger-guided prostate biopsy techniques. Takahashi and Ouchi first described the use of TRUS to evaluate the prostate in 1963. However, the image quality was too poor to be of any clinical use at that time. In 1974 Watanabe et al. were the first to demonstrate clinically useful TRUS images of the prostate. They used a 3.5MHz probe, which was considered to be state-of-the-art at the time. However, image quality continued to be unsatisfactory. It was only in the 1980s, with technological advances in probe manufacture and the development of an attachable biopsy needle guide, that TRUS became clinically useful for the diagnosis of PCa. A 7MHz probe was developed allowing a better definition of the structure of the prostate.

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The modern era of prostate biopsy started in 1989 by Hodge et al. In their first paper Hodge et al. described targeted TR PBx of palpable abnormalities, 90% of which had corresponding hypoechoic lesions on TRUS. In addition, they also took biopsies of isoechoic areas in the PZ and CZ. Although these biopsies were not systematic, they were positive in 66% of cases. Their second article, published later in 1989, was a landmark paper ushering in the modern era of PBx. Hodge et al. compared the TRUS-guided PBx taken from palpable or sonographic abnormalities with those taken in a random systematic fashion from six sites, the apex, middle, and base of each prostate lobe. This sextant technique detected 9% more cancers compared with the targeted method. The Hodge protocol of systematic sextant biopsy of the prostate thus came to be considered the gold standard for many years in an era when a raised PSA was an acceptable indication for PBX irrespective of DRE or imaging findings.

Gradually the technique and method of TR PBx became more elaborated. Initially, sextant biopsy was practiced but nowadays most centers perform twelve core biopsies. Initially, TR PBx was performed under G/A or spinal anesthesia, then urologists shifted to nerve block and now in many centers, it is done by surface anesthesia. Thorough bowel preparation was practiced earlier but nowadays limited rectal wash seems to be adequate.

The term 'saturation biopsy' was coined by Stewart et al. in 2001, in which 20 or more systematic cores were taken. These saturation biopsies have been offered to those who have had previous negative biopsies but continue to raise clinical suspicion for PCa usually through a rising PSA test. The trend to take more cores emerged with the current practice of TP PBx.

TP PBx via US guidance was first described in 1981 although finger-guided TP PBx was described in 1954. US-guided TP PBx was developed further, due to the key advantage that the TP approach has a far better sampling of both the anterior prostate and the apical region, in addition to the low risk of sepsis. A 2005 paper pointed out the importance of obtaining a large number of cores in TP PBx to improve the cancer detection rate. However, this is affected by differing prostate volumes. Ficarra's study found that in volumes less than 30cc, a scheme including as low as eight peripheral cores was not statistically different from higher core schemes, however, this difference became greater with larger volumes. Over 50cc, a 14-core scheme was still considered to be inadequate, therefore even more cores were recommended for larger prostate volumes. The perceived need for more biopsies led to the systematic TP biopsy using the brachytherapy grid. This systematic method gives increased analysis of the whole prostate and reduces the randomness of the original multiple core method, particularly allowing coverage of the apical and anterior regions as mentioned above. The emergence of focal ablation as a therapeutic option for PCa has increased the need for reliable and accurate localization of tumors within the prostate. The trans-perineal route appears more useful in this regard.

MRI scanning provides much higher spatial resolution than ultrasound and volumetric imaging capabilities in multiple planes. In addition to the commonly available 1.5-Tesla magnets, the 3-Tesla magnets have improved the resolution of multiparametric magnetic resonance imaging (mpMRI). With the introduction of mpMRI, the pathways for PCa diagnosis have changed. It is unique in that it can stratify risk for PCa and allow anatomical guidance for biopsy. The spatial information provided by mpMRI allows for precise mpMRI-informed targeted biopsy (TGBx).

There are currently three techniques for the MRI-targeted biopsy (TGBx): cognitive registration, fusion registration, and the in-bore biopsy. The earlier techniques of incorporating MRI into PBx involved taking the PBx in-bore in the MRI scanner. However, in-bore biopsies were found to be severely limited by patient discomfort, long procedure durations, high cost, lack of expertise, the need for specialist equipment, and a sophisticated radiology department in which to perform the biopsy. The difficulties of in-bore PBx led to the transfer of MRI information to TRUS PBx. Cognitive fusion guidance was the first of this type, in which the MRI is used to identify lesions initially and then, after reviewing the MRI images, the urologist attempts to manually guide a biopsy needle to that predetermined location using TRUS guidance. In cognitive registration, also known as visual registration, a prebiopsy mpMRI is performed to localize the suspicious lesions. However, the transverse plane slightly differs between MRI and TRUS, hence this requires significant experience and training.

MRI-TRUS fusion biopsy was the next advance in this technology and is currently rapidly developing. It is software-assisted in which an MRI is first taken separately but the MRI image is fused with a 3D

ultrasound image. When the TRUS probe moves, the fused MRI image also moves in the same way allowing the urologist to use the MRI image within a TRUS-guided PBx technique.

Very recently Fletcher et al. (2023) described 'Vector Prostate Biopsy'- a novel MRI/US image fusion TP biopsy technique using electromagnetic needle tracking under local anesthesia. There are also some new techniques featured in a recent EAU meeting including, ultrasound CT with artificial intelligence (AI-US-CT) targeted biopsy, a novel robotic device – the iSR'obot Mona Lisa – to perform MR-US fusion TP PBX and the Trimodal 18F-Choline-PET / mpMRI / 3D -TRUS targeted PBx. We will have to wait and see how these evolve into day-to-day clinical practice.

In this present scenario around the world, we need to concentrate on our state. Although the majority of the centers around the world still practicing TR PBx but actively thinking to shift in TP PBx, we are still practicing finger-guided biopsy in some centers. We hope robotic prostatectomy will be started in our country in the coming days although open radical prostatectomy is going on routinely. If urologists can improve the pickup rate, they can detect more localized diseases and can serve more people because we know five-year survival after radical prostatectomy for localized disease is almost ninety-nine percent.