Technology Advances for Prostate Biopsy and Needle Therapies

In 2012 an estimated 241,740 new prostate cancers (PCas) will be diagnosed in the United States alone.[1] A large number of them represent indolent tumors unlikely to limit the life span of the patient due to competing comorbidities. A recent study has shown that it is necessary to treat 48 men to prevent 1 death from PCa, suggesting that significant overtreatment exists.[2] Still, many PCas are aggressive, causing an estimated 28,170 mortalities this year.[1] Therefore, a comprehensive approach is urgently needed to increase the diagnostic accuracy of PCa.[3]

Freehand transrectal ultrasound (TRUS) guided prostate biopsy is the most frequently performed biopsy means for diagnosing PCa with more than 1.2 million procedures performed annually in the United States. However, standard grayscale ultrasound provides minimal PCa specific information, being unreliable in differentiating normal prostate gland from cancer tissue. Accordingly, biopsies do not specifically target cancer suspicious regions of the prostate (CSR). Instead, cancer detection and characterization rely on nontargeted, systematic, sextant biopsy schemata. However, executing the schema with freehand TRUS is a challenging procedure that is beyond typical hand-eye coordination and quality control is subjective. As such, samples are often clustered, miss regions and do not follow the biopsy schema.[4,5] Over diagnosis of clinically insignificant cancer and under diagnosis of potentially lethal cancer exist in the population at risk.[3]

Novel genomic, proteomic and image biomarkers are currently being investigated for the assessment of PCa aggressiveness. However, their gold standard validation relies heavily on pathology results from prostatectomy specimens, which provide single-step stage information in the progression of the disease. Instead, biopsy specimens could provide information with time for longitudinal progression studies but they are typically unreliable due to localization errors.

In short, the common TRUS guided prostate biopsy represents a critical barrier in the field. Clinically, it creates diagnosis and localization uncertainty, which are directly related to the current overtreatment of PCa. Its low repeatability increases the complexity of active surveillance and focal therapies. In research it makes it difficult to monitor the response of biomarkers and chemopreventive agents, and correlate novel PCa imaging modalities with gold standard pathology results from biopsy specimens.

Several novel biopsy devices are currently being investigated or are under development. They apply to biopsy and also to needle ablative therapies, such as brachytherapy and cryoablation. The most common needle paths are transrectal and transperineal. Approaches are gland distributed sextant schemata or targeted biopsies. The most common image guidance modality remains TRUS but registration (image fusion) to pre-acquired PCa images, such as multiparametric magnetic resonance imaging (MRI) and even direct MRI guided systems, are emerging. Biopsy guiding devices are based on 3-dimensional (3D) TRUS, probe position tracking and robotic technologies. Robots can handle the probe and/or a needle guide. Few systems automate needle insertion.

Using 3D TRUS alone for guiding the biopsy is difficult because the unsegmented prostate is difficult to observe and 3D images are not in real time. At the same time, automatic real-time prostate segmentation from TRUS is an active area of research. Several probe tracking (continuously measuring) methods have been developed for 3D as well as 2-dimensional (2D) ultrasound. With special navigation software they show the location of the probe in the image space as it is used freehand by the urologist, so that he or she can apply this feedback to guide the intervention. Several commercial systems are already available with probe tracking accessories, such as the LOGIQ® E9 system.

A TRUS tracking system developed purposely for prostate biopsy is the Artemis (Eigen®). The Artemis system tracks a 3D TRUS with a 4 df encoded passive arm. An important advantage of this mechanical approach is that the arm can be locked in place to support the probe while performing the biopsy.

Another commercial system is TargetScan®. This motorizes the insertion motion of the TRUS probe for ultrasound scanning. Because TargetScan was designed for prostate brachytherapy, it is readily applicable to transperineal biopsy but difficult to use for common transrectal biopsy.

Perhaps one of the most active areas of new technology clinical trials in urology is MRI fused TRUS

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guided biopsy. Interventional TRUS and pre-acquired MRI volumes are registered to each other at the beginning of the biopsy procedure.[5,6] This enables CSR identified in MRI to be targeted under TRUS guidance. Studies suggest that biopsy targeting improves PCa detection. Current limiting factors remain the challenging cross-modality image-to-image registration, deformable registration methods and the limited means of verifying the registration, especially after the initial alignment.

Robotic systems have also been proposed for biopsy. In addition to tracking, robots may perform automated motion for scanning with 2D TRUS and automated needle targeting. A robot that manipulates the TRUS probe with the same 4 df available when used freehand[7] was developed and applied for intraoperative ultrasound based prostatectomy navigation.[8] The BioXbot robot (BioBot Surgical, Singapore) handles a 2D TRUS probe, similar to TargetScan, but includes a robotic transperineal needle guide that angles the guide to target zones of the prostate that otherwise are difficult to access.[6,9]

An interesting and original way to measure the location of TRUS for biopsy navigation is used by the KOELIS prostate biopsy system (La Tronche, France). Using a 3D probe and recording a full prostate scan, the relative location of the TRUS probe is determined by co-registering the scanned prostate volumes. In other words, rather than using a probe tracker, the system calculates the location of the probe from the images. The system applies to biopsy quality control but it has been difficult to use to guide the biopsy.

Nevertheless, in this issue of the Journal Long et al (page 1369) from the University of Grenoble, the technology founder, report the development of the Prosper robot for transperineal needle access.[10] Similar to the BioXbot, Prosper can change the direction of the needle to avoid pubic arch interference. In addition, this performs automated needle insertion and spinning, shown to reduce targeting errors.[11] The key novelty is its ability to track prostate motion, which allows the depth of needle insertion to be adjusted interactively during insertion, further reducing targeting errors.

Several novel types of robots are currently under development for direct MRI guided biopsy. The MrBot robot (URobotics, Johns Hopkins Medicine, Baltimore, Maryland) is an MRI safe (ASTM F2503–08) system that goes alongside the patient in the MRI scanner and orients a needle guide under direct MRI guidance.[12] Compared to pre-acquired images, direct image guidance eliminates image fusion errors, provides interventional PCa imaging feedback and may decrease prostate motion and deformation errors.[13]

In conclusion, numerous technologies are under development and being investigated clinically to address the current limitations of prostate biopsy technology. While they require further validation, clinical studies suggest substantial improvements over the standard of care. Under TRUS guidance, the prostate motion and deformations inherently induced by the TRUS probe remain a major potential source of targeting errors that are typically unhandled. The research presented by Long et al in this issue is the first to use prostate tracking software during biopsy. Further directions of research are related to MRI-TRUS image fusion validation, prostate displacement and deformation tracking with compensation software and/or robotic hardware means of minimizing these deflections, transrectal biopsy TRUS guided robots, MRI safe robots for direct targeted biopsy and focal therapy, and other techniques based on novel biomarker research.

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