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Imaging guidance in minimally invasive prostatectomy

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Abstract

Minimally invasive prostatectomy, such as laparoscopic and robot-assisted prostatectomy, has become more popular, with similar short-term outcomes as open radical retropubic prostatectomy series. The purpose of this article is to review different imaging modalities that have been developed with a goal of further improving the surgical outcomes in minimally invasive prostatectomy.

Keywords

Prostatectomy; Laparoscopic; Robotic; Imaging; Transrectal ultrasound; Elastography; Optical coherence tomography

Introduction

The surgical approach for a clinically localized prostate cancer has undergone significant transition in the past several decades. In 1982, Walsh and Donker discovered that the cavernous nerves, forming a neurovascular bundle (NVB) with capsular arteries and veins of the prostate, travel outside the prostatic capsule and fascia [1]. Based on this discovery, Walsh developed nerve-sparing anatomic radical retropubic prostatectomy (RRP) [2]. Wide application of this surgical technique, along with early detection of prostate cancer, resulted in improvement in cancer control and postoperative quality of life. Subsequently, Guillonnet and Vallancien developed laparoscopic radical prostatectomy (LRP) with improved visualization and decreased blood loss [3]. In the past decade, the introduction and dissemination of the da Vinci surgical robot (Intuitive Surgical, Inc., Sunnydale, CA) led to a rapid growth in robot-assisted laparoscopic prostatectomy (RALP) [4,5]. Regardless of the surgical approach, however, the ultimate goals of radical prostatectomy remain the same; to achieve cancer control and to preserve urinary continence and sexual potency [6].

A common criticism of minimally invasive approaches of radical prostatectomy has been that they do not allow for tactile feedback that is afforded in open surgery and may result in a compromise in cancer control. However, recent evidence from centers of excellence suggests that minimally invasive prostatectomy can achieve comparable outcomes as open prostatectomy series [7]. Further advancement of surgical technique that allows visualization of the periprostatic anatomy may result in improved oncologic result.

The preservation of the NVBs around the prostate gland is critical in recovery of sexual potency following radical prostatectomy. However, it can be challenging to visualize NVBs during surgery because of the periprostatic connective tissues and intraoperative

hemorrhage, even with the use of surgical loupes during open surgery or laparoscopic magnification during minimally invasive prostatectomy. To identify the course of the cavernous nerve fibers and to better preserve them during open RRP, the CaverMap Surgical Aid (UroMed, Boston, MA) with intraoperative cavernous nerve stimulation and real time tumescence monitoring was developed [8,9]. However, because of the low specificity, this device did not become widely accepted [10].

With a wide application of minimally invasive radical prostatectomy, there has been a renewed interest in image-guided navigation techniques that could potentially be used to supplement the tumor resection and the visualization/preservation of the NVBs. Although this area of research is still in infancy, these imaging techniques hold significant promise in achieving ultimate goals of radical prostatectomy. This article will review these imaging techniques, their utilities, and practical application to the minimally invasive radical prostatectomy.

Imaging modalities

Transrectal ultrasound with Doppler function

In 2006, Ukimura and Gill used transrectal ultrasound (TRUS) to guide the surgical dissection during LRP [11,12]. In their study, Doppler ultrasound was used to identify the blood flows within the NVBs. The authors found TRUS with Doppler to be helpful in visualizing the NVBs during release of prostatic apex, identifying hypoechoic prostatic nodules, guiding at areas of suspected extracapsular extension for wider excision, and facilitating transection of the posterior bladder neck [11,12]. They also reported a lower rate of positive surgical margins with the use of TRUS during LRP [11–13]. They suggested that visualization with TRUS during laparoscopy allowed for a more complete dissection and better cancer control as well as improved potency recovery [11].

This approach, while innovative, posed several challenges. For example, the TRUS probe was manipulated by a human assistant during LRP, compromising image stability. Also, in RALP, which now is more commonly performed than LRP, there is a limited space between the da Vinci surgical robot and the patient, not enough for a human assistant. Finally, the precise positional information of the TRUS probe was not incorporated in interpreting TRUS images.

Most recently, investigators developed a novel, compact robotic instrument (TRUS Robot) that accurately and steadily maneuvers a TRUS probe to acquire images [14]. This TRUS Robot can be safely placed and maneuvered in a limited space between the da Vinci surgical robot and the patient. In addition, it intrinsically measures its coordinates, providing the exact location and orientation of two-dimensional (2D) ultrasound images. Robot motion scans the volume of the gland providing image-position pairs used for three-dimensional (3D) image reconstruction. In this tandem robot-assisted laparoscopic Prostatectomy (T-RALP), both TRUS robot and 3D reconstruction/navigation software were used in tandem with the da Vinci surgical robot during RALP. In this feasibility study, the accompanying blood vessels in the NVB were visible with a Doppler ultrasound and served as a macroscopic landmark to localize the microscopic cavernous nerves in the NVBs [14]. Also, the prostate was scanned with the TRUS robot to reconstruct the 3D images of the prostate gland with adjacent NVB. Although there was no associated complications reported in this limited clinical study, additional studies are needed to prove clinical benefit of this promising technology.

Ultrasound elastography

Ultrasound elastography is an emerging imaging modality that generates a map of tissue elasticity [15,16]. Elastography can be considered as a quantified palpation of the tissues. The underlying principle of elastography is to apply mechanical stress to the tissue and measure the resulting strain from which the elasticity of the tissue is estimated. When the tissue is compressed, generating uniform stress within the tissue, the stiffer mass deforms less. By measuring the magnitude of this deformation in the images, relative stiffness between the regions of the tissues can be estimated. Because elasticity is derived from displacement evaluations taken from an image, elastography can be used in conjunction with numerous imaging modalities, including ultrasound.

Glandular architecture loss, disordered growth, and increased cell density are known to occur in neoplastic tissues, which cause a change in tissue elasticity and stiffness [17]. The addition of elastography can be used to distinguish nodules that are otherwise invisible or difficult to observe in a typical ultrasound. Studies have already demonstrated promising results for breast cancer and liver fibrosis detection [18,19].

Several recent studies investigated ultrasound elastography for prostate cancer. In the study comparing sextant biopsy with elastography, 84% of biopsy-proven prostate cancer foci had abnormalities noted on elastography [15]. In the study comparing elastography and 10-core template biopsy, sensitivity and specificity of elastography were 86% and 72%, respectively [20]. Interestingly, the investigators noted a trend toward higher sensitivity for higher grade cancers [20]. In 2010, Aigner et al. compared elastography-targeted and 10-core systematic biopsy in men with low serum PSA levels [21]. They noted that the cancer detection rate per core was 4.7-fold greater for elastography-targeted than for systematic biopsy [21]. The results from these studies suggest a potential role of elastography as a complement to minimally invasive surgery, especially to detect areas of extracapsular extension [22].

Image-fusion and augmented reality

Fused imaging combines the advantages of the 2 imaging techniques to create a single image [23]. For example, real time virtual sonography (RVS) simply fuses the image of real time ultrasound with preoperative CT or MRI [23]. Augmented reality uses digital imaging techniques to project these superimposed images onto endoscopic view, which brings this technology into the operating room for a minimally invasive surgeon [23]. Ukimura and Gill demonstrated the feasibility of using image fusion augmented reality in endoscopic procedures [24], such as cryoablation of renal tumors and laparoscopic prostatectomy.

Although this technology has significant potential to better steer the endoscopic dissection during prostatectomy to improve both cancer control and quality of life, some challenges exist before its clinical application. For example, Ukimura and Gill noted that there was a learning curve that is associated with image fusion and augmented reality [24], which is one more skill for a minimally invasive surgeon to master. For the surgeon, it involves looking at a combined view of a color coded fused image and the surgical field, while guiding the dissection. The extent of the learning curve will have to be addressed before widespread use of this technology.

Optical coherence tomography

Optical coherence tomography (OCT) is a noninvasive imaging technique that can provide high resolution, real-time, cross sectional imaging in biological system [25]. Analogous to ultrasonography, OCT measures backscatter near-infrared light, rather than sound, obtaining images of tissues with resolutions greater than that achieved with ultrasonography [26]. In addition, OCT can be delivered in a compact, fiberoptic system that can be potentially

integrated in minimally invasive surgeries. OCT has already been used clinically in ophthalmology and cardiology.

In urology, OCT has been applied to visualize structures, including prostate and bladder [27–29]. For minimally invasive prostatectomy, several investigators suggested the application of OCT to improve tumor resection [30] and nerve sparing [31]. Most notably, Rais-Bahrami et al. studied the use of OCT to visualize cavernous nerves in a rat model [31]. They visually identified and confirmed the cavernous nerve physiologically by electrical stimulation. Then, OCT images of cavernous nerves were correlated with the histologic findings in differentiating them from the underlying prostate glandular structure. This study demonstrated the feasibility of the OCT application in identifying cavernous nerves in an animal model. However, the investigators acknowledged that a layer of fascia around the human prostate impairs visualization of nerves by OCT and poses a significant challenge in implementing OCT into real-time intraoperative mapping and sparing of the NVBs during minimally invasive prostatectomy [27]. With further improvements in technology, OCT could potentially be used in the future to image the prostate gland and surrounding structures including NVBs.

Multiphoton microscopy

Multiphoton microscopy (MPM) involves illuminating with pulsed long-wavelength light to excite fluorophores within a target tissue. Compared with confocal microscopy, MPM offers deeper tissue imaging up to 500 μ with less phototoxicity [32]. As a result, MPM has become an essential tool for observing cellular events, especially in neuroscience. It has been used to study processes such as neuronal dynamics, Alzheimer's plaque progression, and tumor biology and growth [32].

Typically, extrinsic fluorophores such as fluorescein are used in MPM for labeling [33]. Although the use of extrinsic fluorophores improves the image quality, there is a concern about potentially increased phototoxicity in the live tissue. To circumvent this potential limitation of extrinsic fluorophores, Yadav et al. performed MPM with excitation of intrinsic fluorophores on prostate from a freshly euthanized rat [34]. They were able to identify nerve in the periprostatic region in this rat model. Similar to OCT, human anatomy, including periprostatic fascia with intertwined blood vessels around the nerves, poses a potential barrier that MPM should overcome before it can be fully implemented in minimally invasive prostatectomy.

Fiberoptic confocal fluorescent microscopy

Antegrade or retrograde axonal tracers have been used to specifically identify the afferent or efferent neurons that innervate tissues [35]. Recently, Boyette et al. used a fluorescent retrograde tracer optimized for axonal labeling (the B subunit of cholera toxin conjugated to AlexaFluor 488 [Invitrogen, Carlsbad, CA]) to label the cavernous nerves after intracavernous injection in a rat model [36]. They utilized a fiberoptic confocal fluorescent microscopy to visualize cavernous nerves. Their study demonstrated the use of these agents can increase cavernous nerve visualization up to 9 days without measurable toxicity [36]. However, the safety of these injectable fluorophores has not been determined in humans. In addition, the field of view in this microscopic probe was rather small. However, this is a promising imaging modality that can potentially be incorporated in minimally invasive prostatectomy if further human trials can clarify these limitations.

Conclusions

There are several promising imaging modalities that can potentially enhance the minimally invasive prostatectomy. Transrectal ultrasound with Doppler function is one of the most readily available and therefore most studied. The reported surgical outcomes using this technology have been promising in cancer control and NVB sparing. Ultrasound elastography, image-fusion with augmented reality, optical coherence tomography, multiphoton microscopy and fiberoptic confocal fluorescent microscopy are relatively recently developed and have shown significant promise in visualizing cavernous nerve in neurovascular bundles or improving cancer detection. With additional improvements in technology and further human testing, these imaging modalities could be integrated into both minimally invasive prostatectomy and open prostatectomy to achieve improved cancer control and quality of life.

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