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Evaluation of Age- and Radical-Prostatectomy Related Changes in Male Pelvic Floor Anatomy Based on Magnetic Resonance Imaging and 3-Dimensional Reconstruction

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Purpose: Puborectalis muscles (PRM) and ischiocavernosus muscles (ICM) play important roles in urinary continence and male erectile functions. Understanding of anatomy and surgical-injury related changes to these muscles is critical to monitor changes in continence or erectile function. Anatomical description of these muscles has undergone revisions because these conclusions were derived from cadavers. Our objectives were to: (i) elucidate male pelvic muscles by *in-vivo* magnetic resonance imaging (MRI) and 3-dimensional (3-D) reconstruction of these images and (ii) compare PRM and ICM thickness in healthy volunteers and symptomatic patients.

Materials and Methods: Healthy young male (mean age, 25 years; n=5), older male (age, 65–70 years; n=5), and post-prostatectomy patients with erectile dysfunction and urinary incontinence (age, 65–70 years; n=5) were scanned on a 3T-magnetic resonance scanner. Images were acquired from slices above urinary bladder base to urethra entry into penis. Pelvic bone, bladder/urethra, corpus cavernosum, ICM, PRM, and prostate were segmented. 3-D models of each structure were generated and assembled into composite images, and ICM and PRM thicknesses were calculated.

Results: We successfully reconstructed 3-D male pelvic floor anatomy including ICM, PRM, bladder, urethra, bulbospongiosus, corpus cavernosa, prostate and bones from the two groups. We documented significant reduction in PRM and ICM thickness in older men.

Conclusions: This is perhaps the first 3-D reconstruction of male pelvic floor structures based on *in-vivo* MRI in healthy and symptomatic patients. Observed reduction in PRM and ICM thickness is possibly due to age-related atrophy.

Keywords: Aging; Atrophy; Erectile dysfunction; Urinary incontinence; Urologic surgical procedures

INTRODUCTION

There are an estimated 218,000 new cases of prostate cancer each year in the United States in men over the age of 50 years making it the most common type of cancer. Despite significant advances in surgical tech-

niques, a significant number of men develop urogenital complications following surgical therapy (radical prostatectomy, RP) for prostate cancer [1-3]. Urinary incontinence (UI) and erectile dysfunction (ED), the inability to maintain adequate erections during intercourse, are well recognized post-surgical complications, which can be exacerbated by the aging process [1-3]. UI has been reported in about 31% of these men, and normal erectile function will never be regained in about 20% to 80% of men after surgical intervention for prostate cancer [4,5]. Risk of UI is greatly increased by surgical damage to the urethral sphincter complex, whereas damage to penile neural innervation and/or erectile tissue contributed to ED [6,7]. Pelvic floor muscles (PFM) such as puborectalis muscles (PRM) and ischiocavernosus muscles (ICM) play important roles in the regulation of continence and erectile mechanisms [8-10]. Fig. 1 shows schematics of the role of PRM and ICM in maintaining urinary continence and erectile functions. Briefly, urinary continence is maintained by a triple mechanism, namely: 1) lissosphincter or internal sphincter, 2) rhabdosphincter or external urethral sphincter, and 3) PRM [11]. After prostatectomy, rhabdosphincter function is affected and becomes less effective, and the contribution for maintaining urinary continence depends on strong PRM closure function. ICM is known to restrict venous outflow and aid in achieving high intracavernosal pressure (ICP) during penile erection. A weak ICM contraction could potentially contribute to venous leak, a common problem observed in post-prostatectomy men [8,12]. The exact contribution of PFM to the etiology of post-RP-related ED and UI still remains unclear despite significant research in this area, partially due to the limited knowledge of the normal anatomy of the male pelvic floor. Previously, several research groups have employed two-dimensional magnetic resonance imaging (MRI) on cadavers to assess the anatomy of the male pelvic floor [13-19]. A potential advantage of 3-dimensional (3-D) imaging is the quantification of muscle thickness, which could be useful for the evaluation of pelvic floor disorders. A clear understanding of the interaction between muscles and other anatomical structures of the perineal and pelvic regions is of paramount importance to the ongoing investigations of age and surgical injury-related urogenital problems. This includes anatomical structures implicated in current mechanisms of urinary continence and erectile functions, such as the external urethral sphincter [20], the

membranous urethra [17], and the PFM [18].

The delicate complexity of the pelvic region is evident in the numerous revisions made to pelvic anatomy in the past half-century, many of which are
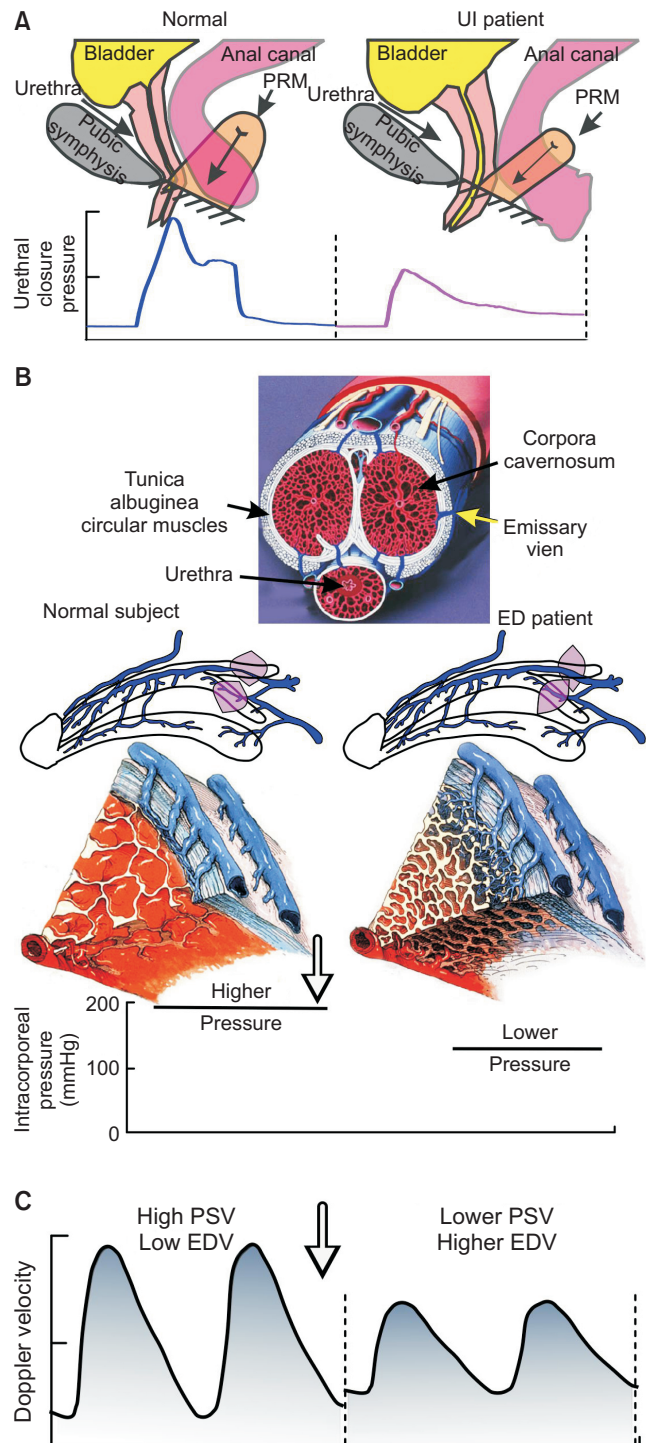

Fig. 1. Schematic of (A) puborectalis muscles (PRM) regulation of urethral closure pressure and (B, C) ischiocavernosus muscles regulation of intracavernosal pressure. UI: urinary incontinence, ED: erectile dysfunction, PSV: peak systolic velocity, EDV: end diastolic velocity.

due to limitations of cadaveric studies. Cadaver fixations and subsequent dissections have been known to yield distorted views of pelvic anatomy due to both the disfigurations made during dissections as well as preservation methods such as formaldehyde injections. To avoid such artifacts and misinterpretations of pelvic anatomy, a 3-D reconstruction of the Visible Human Dataset was created by utilizing histological images taken at 0.5 mm intervals from a male cadaver [13]. This reconstruction corrected multiple errors in the literature, such as bladder placement, continuity of the trigone and anterior fibromuscular stroma of the prostate, and musculoskeletal dynamics of the levator ani muscle, also known as the PRM [13]. While the 3-D reconstruction of the Visible Human Dataset study made substantial contributions to the knowledge of male pelvic anatomy, there are still some limitations. First, the Visible Human Dataset was still taken from a cadaveric specimen, which may have had altered myo-architecture. Second, the Visible Human Dataset only studied a single 38-year-old male cadaver [19], and studies have shown fluctuations in pelvic anatomy from person to person, as well as differences caused by invasive surgeries such as RP.

To overcome these limitations, we designed this study to perform MRI and reconstruct the pelvic floor anatomy of live male healthy subjects as well as post-RP patients with urogenital complications from these MRIs, using Amira (ver. 6.3; Thermo Fisher Scientific, Waltham, MA, USA), a novel volume and surface rendering software. With this approach, we anticipate fixation-related inaccuracies found in cadaver studies will be eliminated. Furthermore, this method will provide the pelvic anatomy of multiple normal subjects and post-RP patients, and any differences in pelvic anatomy should be well-visualized and evident. In addition, through the utilization of ImageJ, we were able to calculate and compare the thicknesses of the PRM and ICM in our study population.

MATERIALS AND METHODS

1. Patient population and ethics statement

All subjects signed an informed consent approved by the human use committee before enrollment into the study. The present study protocol was reviewed and approved by the Institutional Review Board of San Diego VA Healthcare Systems (H150076). Healthy continent male (mean age, 25 years; n=5), asymptomatic older male (age, 65–70 years), and post-RP patients with UI/ED symptoms (age, 65–70 years; n=5) were scanned. The post-RP patients had sustained UI and ED despite several years post RP based on the brief interview performed by one of the investigators (MRR) during the consenting process prior to MRI.

2. Magnetic resonance imaging protocol

Subjects were scanned on a 3T GE magnetic resonance scanner (GE Healthcare, Waukesha, WI, USA), using a multi-channel cardiac coil, lying supine, feet-first. Before taking images, subjects were asked to empty their bladders. Axial morphological proton-density scans were acquired using fast-spin-echo, 2-D, fat-saturated PD images, with 11.5-ms echo time, 5,500-ms repetition time, 256×192 image matrix, 15-cm field of view, 2.5-mm slice thickness, and 0.4-mm spacing. Images were taken from a few slices below the base of the bladder, extending to beyond the entry of the urethra into the penis. Approximately 18–22 slices were taken depending on the pelvic anatomy and height of the subject [21].

3. Three-dimensional reconstruction and puborectalis muscles and ischiocavernosus muscles measurement

Discrete anatomical structures, including the pelvic bone, bladder/urethra, corpus cavernosum, ICM, and PRM were segmented from the axial proton density images [22]. Using Amira 6.3, a volume and surface rendering software, 3-dimensional models of each structure were generated and assembled into composite figures (all images are color coded so that each color identifies with the one structure). PRM thickness was assessed by using ImageJ to measure the widest distance between the iliococcygeus muscles and the rectal wall on axial images. ICM thickness was assessed in a similar fashion, by taking the widest segment of the ICM muscle on axial images, also using ImageJ. Measurements were taken by one investigator (JWT), who was blinded to the clinical status of patients and normal subjects.

RESULTS

We first compared the proton-density MRIs from young, healthy volunteers with a pelvic floor cross-

section from the 38-year-old male pictured in the Visible Human Dataset, in order to identify the PRM and ICM, which are shown highlighted in pink (Fig. 2C, 2D). The cross-sectional MRIs taken from post-RP patients (Fig. 2G, 2H) were used for segmentation (Fig. 2I–2L). These 2-D proton-density images were then used to generate 3-D reconstruction models which show the spatial orientation of the pelvic bone, the bladder and urethra, the bulbospongiosus muscle, ICM, and PRM (Fig. 3, 4). Fig. 4 shows additional structures, corpus cavernosa and bulbospongiosus muscle in four different patients. Fig. 5, 6 show the 3-D surface-rendered male pelvic muscles and bone from a normal continent subject (Fig. 6A, left panel) and in a symptomatic patient after RP (Fig. 6A, right panel). Both PRM and

ICM thicknesses were also measured using the ImageJ software (Fig. 5, 6). PRM thickness was decreased by 38% in post-RP patients compared to controls, which may be indicative of age-related muscle atrophy as the post-RP patient group was older than controls on average. Additionally, ICM thickness was also significantly decreased which also may be due to age-related muscle atrophy. Such decreases in muscle thickness may contribute to UI and ED following RP. However, when comparing post-RP patients to aged-matched controls, there was no significant difference in PRM and ICM thicknesses (Fig. 5, 6). Thus, while the thinning of the PRM and ICM in isolation does not lead to UI and ED, it may predispose aged patients to be more susceptible to UI and ED post-RP.
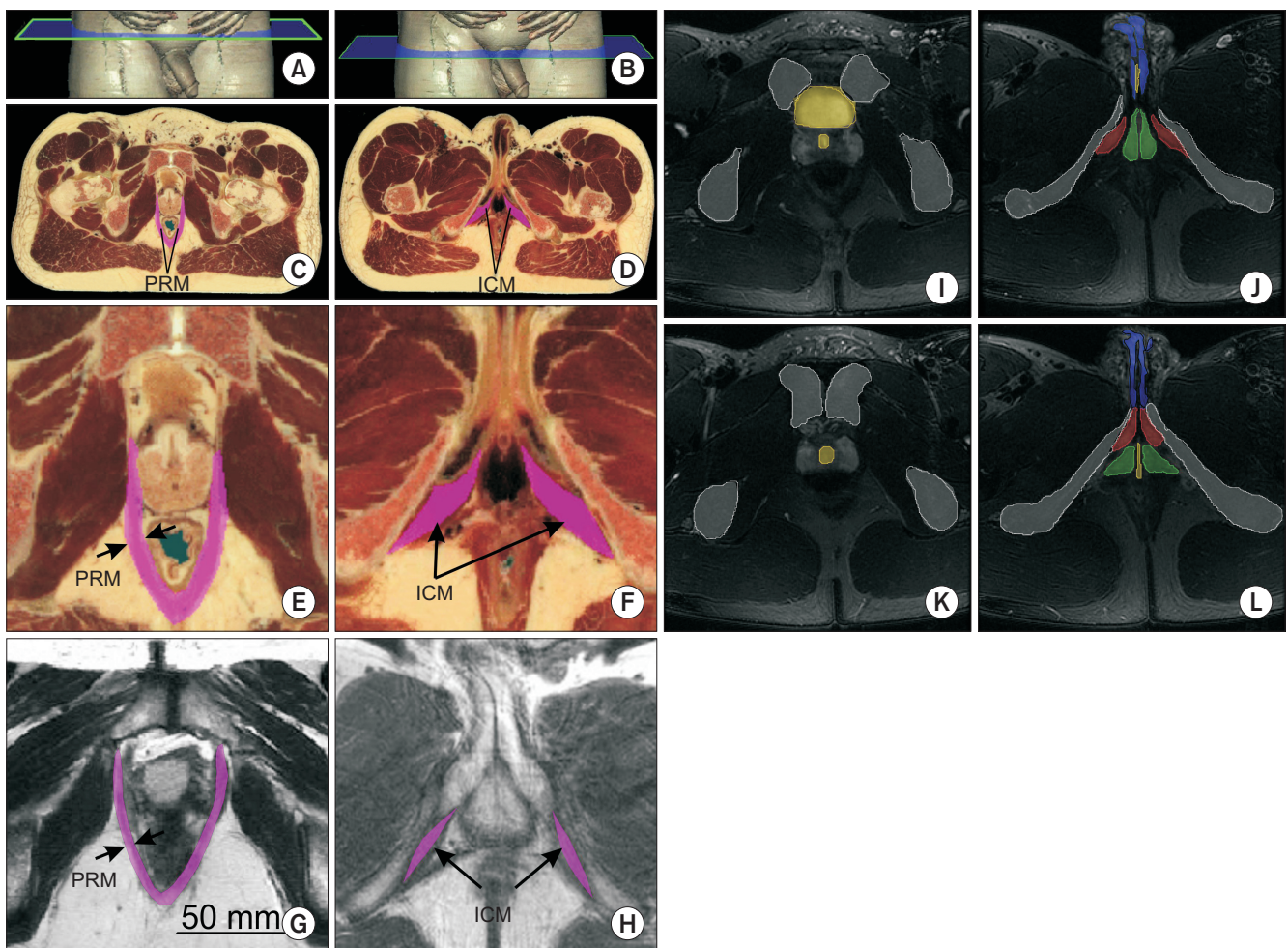

Fig. 2. (A, B) The figures depict a pelvic floor cross-section from a 38-year-old male pictured in the Visible Human Dataset. (C, D) Cross-sections of the pelvic floor at the level shown in panels A and B, respectively. Ischiocavernosus muscles (ICM) and puborectalis muscles (PRM) are highlighted in pink. (E, F) Higher magnification of images seen in panels C and D. (G, H) The figures are magnetic resonance imagings from a post-radical prostatectomy patient, with PRM and ICM highlighted in pink. (I–L) The figures are cross-sectional axial proton density images used for segmentation and 3-dimensional reconstructions, shown in colors corresponding to the structures: white, bone; yellow, bladder and urethra; red, ischiocavernosus muscle; green, bulbospongiosus muscle; blue, corpus cavernosa.
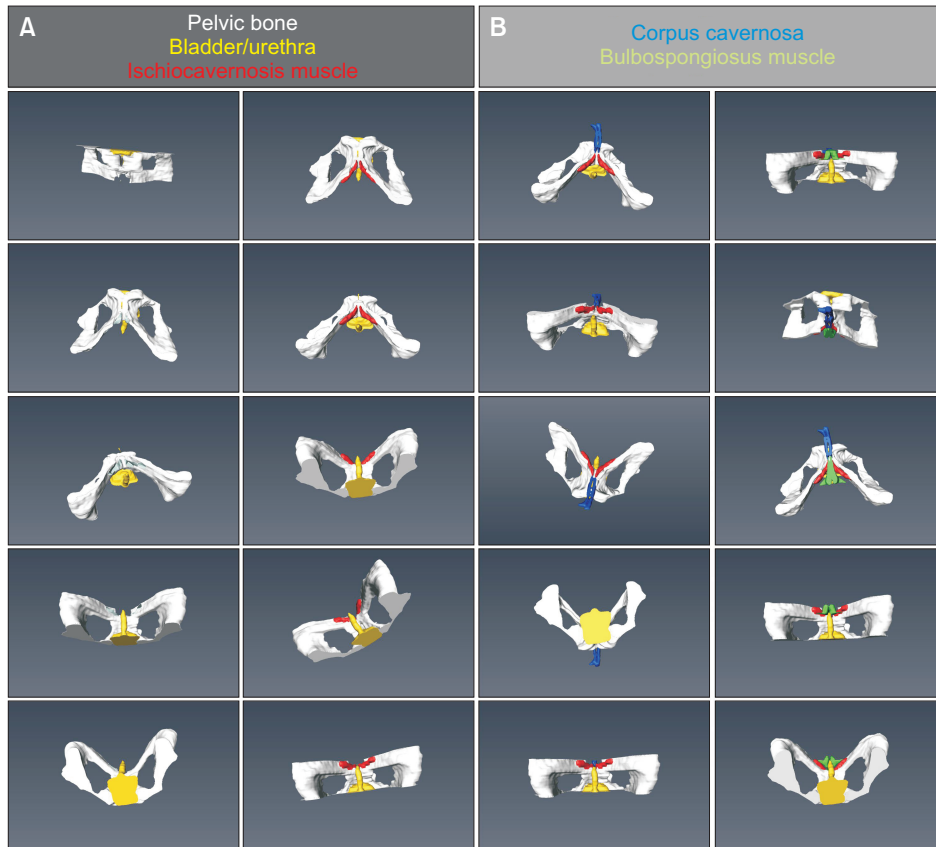
Fig. 3. Several projections of 3-dimensional reconstruction of pelvic floor structures reconstructed from magnetic resonance imagings based on segmentation shown in Fig. 2. (A) The figures show pelvic bone, bladder/urethra and ischiocavernosus muscle to clearly show these structures. (B) The figures add to the same subjects' corpus cavernosum and bulbospongiosus muscle.

Fig. 4. Four projections (columns) of four patients (rows) of 3-dimensional reconstruction of pelvic floor structures reconstructed from magnetic resonance imagings. All structure are visible and spatial projections are clearly seen. White, bone; yellow, bladder and urethra; red, ischiocavernosus muscle; green, bulbospongiosus muscle; blue, corpus cavernosa.
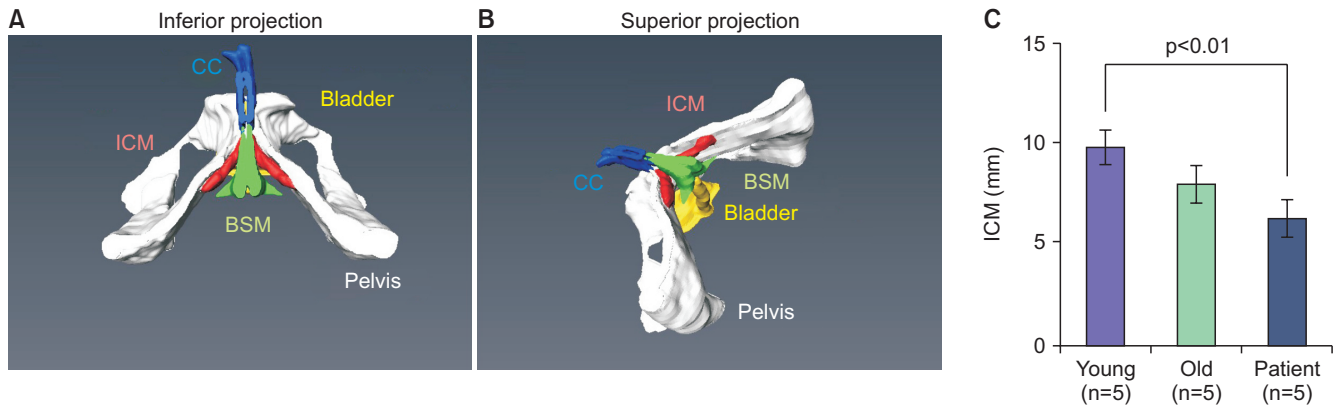
Fig. 5. Inferior (A) and superior (B) projections in one subject showing all pelvic structures with their spatial relationship. (C) The graph shows a bar graph of ischiocavernosus muscle (ICM) thickness in normal young as well as old subjects and symptomatic patients. CC: corpus cavernosum, BSM: bulbospongiosus muscle.
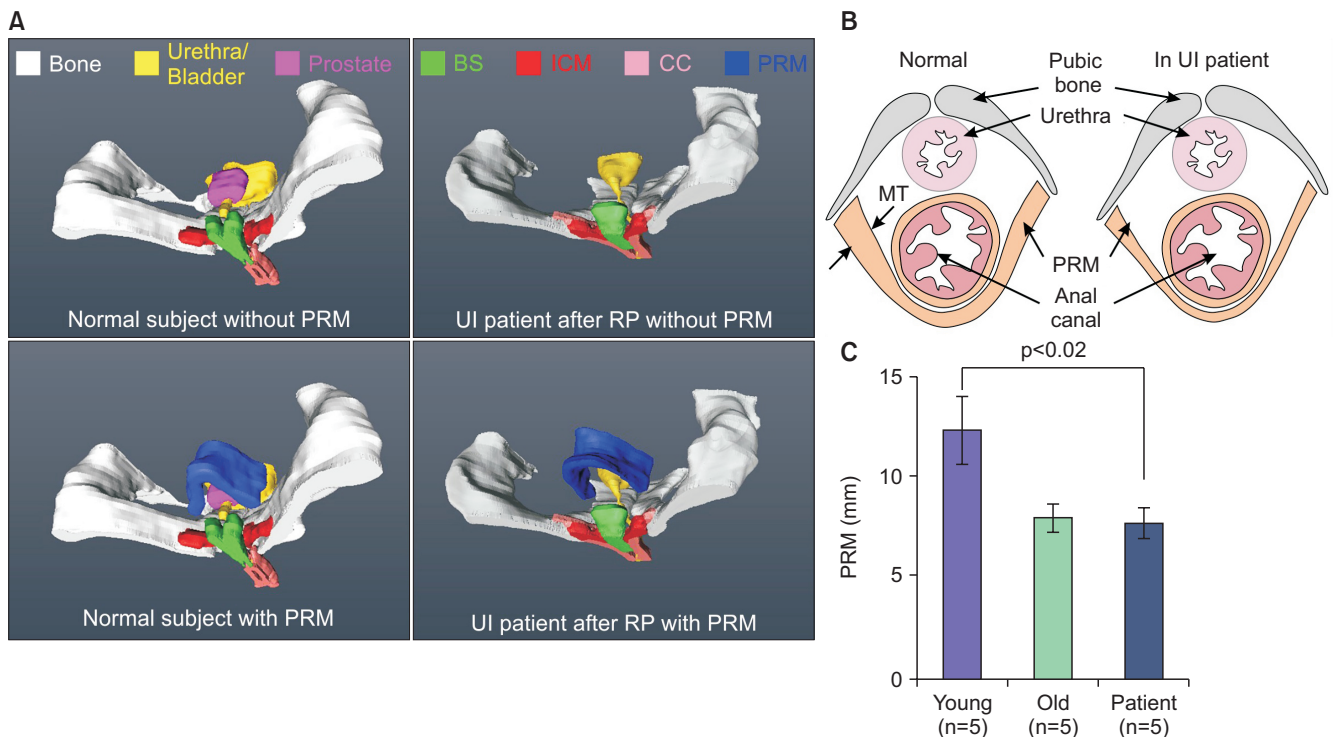

Fig. 6. (A) The figures show 3-dimensional surface-rendered male pelvic muscles and bone from a normal healthy subject (left panels) and from symptomatic urinary incontinence (UI) patient (right panels) with (top) and without (bottom) the puborectalis muscles (PRM). (B) The figure is a schematic of the PRM, showing a reduced thickness in an incontinent patient. (C) The graph shows a bar graph of PRM thickness in normal young as well as old subjects and incontinent patients. BS: bulbospongiosus, ICM: ischiocavernosus muscle, CC: corpus cavernosum, MT: muscle thickness.

DISCUSSION

To the best of our knowledge, this is the first *in vivo* 3-D reconstruction that compares the PFM of male healthy subjects and symptomatic patients using MRIs. Female pelvic floor anatomical studies using MRI have been reported [14,16,23]. In the present study, 3-D mod-els were created from MRIs to depict spatial relation-ship and quantify the thickness of two important male PFM, namely PRM and ICM, in order to get a better understanding of age and prostate surgery-related changes to these muscles. It is widely accepted that UI and ED following RP negatively affects patients' qual-ity of life. However, there has been limited research

towards understanding the exact etiology and specifically delineating the contribution of PFM.

In most men, UI may reduce progressively up to a year, but 2% to 7% of these patients develop long-term UI after open RP [24]. When the prostate is completely removed, damage to external urethral sphincter (EUS) during surgery can result in post-RP UI [6,25]. Because the bladder neck and prostatic mechanisms are nearly significantly/entirely diminished and possibly suffer from denervation, continence becomes solely dependent on the EUS/PRM. PRM is a U-shaped muscle which starts from the pubic rami and traverses dorsally, creating a sling around the rectum and urethra. Rajasekaran et al [9] confirmed the role of PRM in urethral closure, as well as anal sphincter closure function in a rabbit model. Since PRM surrounds both the urinary and anal canals, the contraction of this muscle squeezes both urethra and rectum towards the pubic bone, leading to their collapse/closure. Thus, the contraction of the PRM is hypothesized to contribute to both urinary and fecal continence functions [9,26]. Additionally, clinical studies suggest that injury to PFM such as the PRM impacts urinary continence in women [27,28]. However, the exact role of the PRM and its function in urinary continence in males after RP remains unclear. Both asymptomatic older men and RP patients with symptoms exhibited significant reduction in PRM thickness when compared to the young controls. Thus, the observed changes in older patients' continence function following RP is most likely a combination of age-related atrophy and surgical procedure related impact. A few studies have shown conflicting results in male PRM thickness in continent and incontinent patients after RP [18,29]. However, such studies relied upon measurements from 2-D MRIs alone, while our study places the measurement of PRM thickness in the context of each individual patient's 3-D pelvic reconstruction.

Another common complication of RP is development of ED, despite the use of nerve-sparing techniques [3]. During penile erection, ICP increases to 85% of systolic blood pressure [30]. During the rigid erection phase, ICM/tunica albuginea contractions cause the ICP to increase above systolic pressure [8,30]. Human trials have shown that the ICM electrical stimulation leads to an increase in ICP [10]. As shown in Fig. 1, ICM contributes to venous occlusion function during erection [8]. While strong contraction of ICM aids in venous occlu-

sion, a weak/atrophied ICM could lead to insufficient constriction of the dorsal vein and venous leakage contributing to the development of ED not responsive to therapeutics (such as phosphodiesterase type 5 inhibitors) that cause increased arterial inflow but have no impact on outflow.

In the present study, we used MRIs to determine PRM and ICM thickness. Our findings indicate that reduction in PRM and ICM thickness in post-RP patients are likely due to age-related atrophy. As such, the thinning of the PRM and ICM structures due to age is unlikely to be the primary driver of UI and ED post-RP. Possible direct causes of UI and ED due to RP include neurological damage, smooth muscle cell apoptosis, and vascular injury [31,32]. Indeed, even with nerve-sparing techniques, stretching and other trauma induced by the RP procedure may affect nerve function [33]. However, given the importance of the PRM and ICM in continence and erectile function, it is possible that age-related atrophy of these muscles may predispose older men to UI and ED following RP and perhaps increase the symptom severity. For example, patients with thinning of the PRM and ICM may be less able to compensate for damage to other mechanisms involved in continence and erectile function. A limitation of our study, however, is the lack of a patient sample post-RP which do not have lasting symptoms of UI and ED following surgery. Analysis of the PRM and ICM thickness in such patients would yield further insight as to whether PRM and ICM thickness correlates with the time for recovery from post-RP UI and ED. Furthermore, measurement of additional parameters to determine the extent of neurological damage and vascular injury would allow us to fully explore the importance of PRM and ICM thickness in relation to canonical causes of post-RP UI and ED.

Recently, MRI has become a strong, non-invasive tool for studying PFM function and morphology. Surgical planning can benefit from the more accurate representation of the relationships among PFM structures to account for variation in pelvic anatomy from patient to patient. Indeed, Di Carlo et al [34] recently utilized preoperative 3-D MRI reconstructions to guide surgical reconstruction of bladder exstrophy. Visualization of landmark pelvic bone and muscle structures including the PRM allowed intraoperative guidance of dissection into the pelvic floor. While the use of 3-D MRI reconstructions are beginning to be appreciated in urological

procedures, similar protocols have already been established for use in other fields including neurosurgery [35] and the treatment of hepatobiliary diseases [36]. Given the complexity and sensitivity of pelvic anatomical structures, 3-D MRI reconstructions should prove useful in a variety of urological procedures. Moreover, rapidly improving computer hardware and software tools may soon make 3-D imaging faster and more cost-effective. If such imaging becomes a reality, it could provide information such as muscle morphology, bulk, and signal intensity to guide appropriate treatment. Finally, the use of 3-D reconstructions will also benefit medical education and shed light on the previously ambiguous anatomy of the male pelvic region [37]. Moreover, changes in pelvic anatomy following procedures such as RP can be intuitively visualized using such models, especially when compared to 2-D images. Finally, our measurements derived from healthy young men will provide a baseline to which symptomatic men can be compared in future studies.

A limitation of our study is the lack of correlation of imaging findings with physical examination. A second limitation of our study is the small sample size, which limits statistical power. A third limitation of the study is our lack of pre- and postoperative 3-D reconstructions using the same patients. Ideally, future studies will be able to pair such 3-D reconstructions from the same patients before and after RP to elucidate the precise changes in pelvic musculature while normalizing for variation in pelvic anatomy between patients. In addition, comparison between patients with and without ED and UI after prostatectomy would shed light on causative anatomical changes. While we do not have this data now, we will include such a group in our future studies. Finally, our approach, namely 3-D reconstruction and PFM (ICM and PRM) thickness measurements are of very limited utility in predicting post-RP complications such as ED and UI. However, these findings may help in predicting patients who may benefit from PFM exercise program to strengthen these muscles.

CONCLUSIONS

This finding of this study will open the door to more 3-D reconstruction studies, which are better-suited to evaluate the subtle nature of spatial relationships among PFM in males as opposed to 2-dimensional, pla-

nar images. Based on our limited data, we believe the observed reduction in muscle thickness in post-prostatectomy patients is possibly due to age-related atrophy rather than due to prostatectomy. The observed significant differences in PRM and ICM thickness between healthy and symptomatic patients suggest age-related atrophy, and these findings warrant further exploration in future studies.

ACKNOWLEDGEMENTS

Conflict of Interest

The authors have nothing to disclose.

Author Contribution

Conceptualization: MRR, VB, MA. Data curation: JWT, MRR, VB. Formal analysis: MRR, VB, IT. Funding acquisition: MRR. Investigation: MRR, VB. Methodology: MRR, VB. Resources: MRR, SRS, VB. Software: MRR, JWT, VB. Writing – original draft: JWT, MRR, VB, SRS. Writing – review & editing: MRR, SRS, KS, MA.

Data Sharing Statement

The data required to reproduce these findings cannot be shared at this time as the data also forms part of an ongoing study.

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