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Minimally Invasive Therapy & Allied Technologies

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/imit20

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To cite this article: Mahdi Al-Taher, Bob Knapen, Manuel Barberio, Eric Felli, Sylvain Gioux, Nicole D. Bouvy, Laurents P. S. Stassen, Jacques Marescaux & Michele Diana (2020): Near infrared fluorescence imaging of the urethra: a systematic review of the literature, Minimally Invasive Therapy & Allied Technologies, DOI: 10.1080/13645706.2020.1826974

To link to this article: https://doi.org/10.1080/13645706.2020.1826974

Published online: 01 Oct 2020.

MINIMALLY INVASIVE THERAPY & ALLIED TECHNOLOGIES
https://doi.org/10.1080/13645706.2020.1826974

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REVIEW ARTICLE

Near infrared fluorescence imaging of the urethra: a systematic review of the literature

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ABSTRACT

Background: Urethral injury is a dreaded complication during laparoscopic, perineal and transanal surgery and is mainly a result of a failed visualization of the urethra. The aim of this systematic review is to provide an overview of the available literature on the near-infrared fluorescence (NIRF) imaging technique using contrast agents for the intra-operative visualization of the urethra.

Material and methods: A systematic review of the literature was conducted including studies on NIRF imaging using contrast agents to visualize the urethra. All studies describing a NIRF imaging technique and demonstrating visual findings of the urethra were included.

Results: Five studies were identified. Four studies examined indocyanine green, one of which also studied the IRDye® 800BK agent and one examined the CP-IRT dye. All studies showed that the NIRF imaging technique was feasible for an early identification of the urethra. No complications related to NIRF imaging were reported.

Conclusion: We conclude that the use of a NIRF imaging technique is feasible and that it can contribute to prevent iatrogenic injury to the urethra. However, based on the limited available data, no solid conclusion can yet be drawn and further translation to the clinical practice is necessary.

ARTICLE HISTORY
Received 28 April 2020
Accepted 9 September 2020

KEYWORDS
Fluorescence imaging; urethral visualization; fluorescent dyes; near-infrared; total mesorectal excision

Introduction

Urethral injury is a feared complication during laparoscopic, perineal and transanal surgery for urological or colorectal diseases [1,2].

The male urethra, which has a ten-fold higher risk of injury in comparison to women, is subdivided into an anterior and posterior part. The posterior part, which is most commonly involved in surgical iatrogenic urethral injuries consists of the membranous and prostatic urethra [3].

Urethral injuries and their postoperative consequences can be a source of significant morbidity [4]. In the acute phase, local tissue swelling and/or urethral disruption can cause acute urinary retention, which can lead to hydronephrosis, acute kidney injury, or acute renal failure if not adequately addressed [5]. In the long run, in general, all urethral injuries cause scar tissue formation which may lead to fibrosis, stenosis, and/or urethral stricture formation. Therefore, the prevention and direct recognition of iatrogenic injury is crucial to reduce the incidence and severity of subsequent complications [4,5].

In colorectal surgery, total mesorectal excision (TME) is the gold standard surgical treatment for mid-rectal and low rectal cancer [6]. However, it is associated with specific surgical difficulties, due to the complex anatomy and narrow pelvis, especially in males [7,8]. Transanal TME (TaTME) is a relatively new procedure which has been developed to overcome these difficulties through an enhanced visualization of the dissection plane. This could potentially result in a more accurate distal dissection, increasing the rate of sphincter-sparing procedures. However, despite the advantages of this procedure, iatrogenic urethral injury has a reported incidence of 1 to 6.7% during TaTME procedures [9–12].

In open urethra-sparing (Madigan) prostatectomy, surgeons must palpate the catheter to help guide the dissection and decrease urethral injury during

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removal of the adenoma [13]. However, this technique is challenging in laparoscopic and robotic surgery since the surgeon lacks tactile feedback, leading to up to 27% of urethrotomies [14]. Therefore, recognizing the structures and developing clear anatomical planes is paramount for urethra-sparing prostatectomies.

Thus, in order to reduce the incidence of iatrogenic urethral injury, enhancement of the urethral visualization is necessary.

Near-infrared fluorescence (NIRF) imaging during laparoscopic surgery has gained an increasingly growing interest over the last decade. It has been proven to be helpful in, among others, assessing perfusion in colorectal surgery and highlighting the biliary tract and ureteral anatomy [15–17]. In this review, we outline and investigate the currently available data on clinical and experimental NIRF imaging of the urethra for intraoperative recognition and consequently the prevention of iatrogenic injury.

Material and methods

Search strategy

This review is performed in compliance with the guideline from the preferred reporting items for systematic reviews and meta-analysis (PRISMA) group [18]. The search was independently conducted by two authors (MA, BK) on October 21, 2019. The search strategy is described in Appendix 1. There were no restrictions on study design. All studies, both clinical and pre-clinical, in which near-infrared fluorescence imaging was performed for the detection of the urethra were included. All titles and abstracts originating from the search were screened and assessed for eligibility. Additionally, the references of the selected literature were reviewed for possible additional articles. Any differences in the search were discussed between the two authors, and consensus was reached following a discussion. If no consensus was reached, a third author (MB) made the decision.

Clinical trial search

A systematic search of the literature was performed in the PubMed database, the Embase database, and the Cochrane library. Other sources were approached for relevant articles. These included https://clinicaltrials.gov, https://clinicaltrialsregister.eu, and https://trialregister.nl.

Key words, which were used to cover the subject, included the following: urethra, near-infrared, fluorescence imaging, and laparoscopic surgery.

Data extraction

All relevant data from the included articles were collected by two authors independently (MA, BK). Data, such as general study information, interventions, results, and the used dyes were collected and grouped.

Results

Figure 1 displays the PRISMA flow diagram. After removal of the duplicates, 324 articles remained after conducting the searches through different databases. Out of these, 310 were excluded after the screening of the titles and abstracts. The remaining 14 articles were completely screened for eligibility after which a total of five relevant articles were included in this review. Reasons for exclusion of the remaining nine articles are mentioned in Figure 1. In the included articles, a total of 24 subjects (23 males and one mouse model) were studied.

Dyes used

The included studies and their general characteristics are summarized in Table 1. In these five studies, three different fluorescence agents were used for urethral visualization: four articles mention the use of indocyanine green (ICG), in one article the dyes studied were IRDye® 800BK (LI-COR Biosciences, Lincoln, NE, USA) and ICG, and one article described the use of the CP-IRT dye. In each of the studies, different methods and materials for dye administration and urethral visualization were reported. The methods and materials are outlined in Table 2. The dosing, moment of application, and number of subjects were not always specified.

In the next section, we will discuss every article and the used dye separately.

Indocyanine green

Simone et al. [19] included a total of 12 male patients who underwent a urethra-sparing robot-assisted simple prostatectomy (US-RASP) performed using the da Vinci Si™ robotic surgical system (Intuitive, Sunnyvale, CA, USA). All procedures were performed through a transperitoneal approach. After prophylactic antibiotics administration and under general anesthesia, an 18 French urethral catheter was inserted.

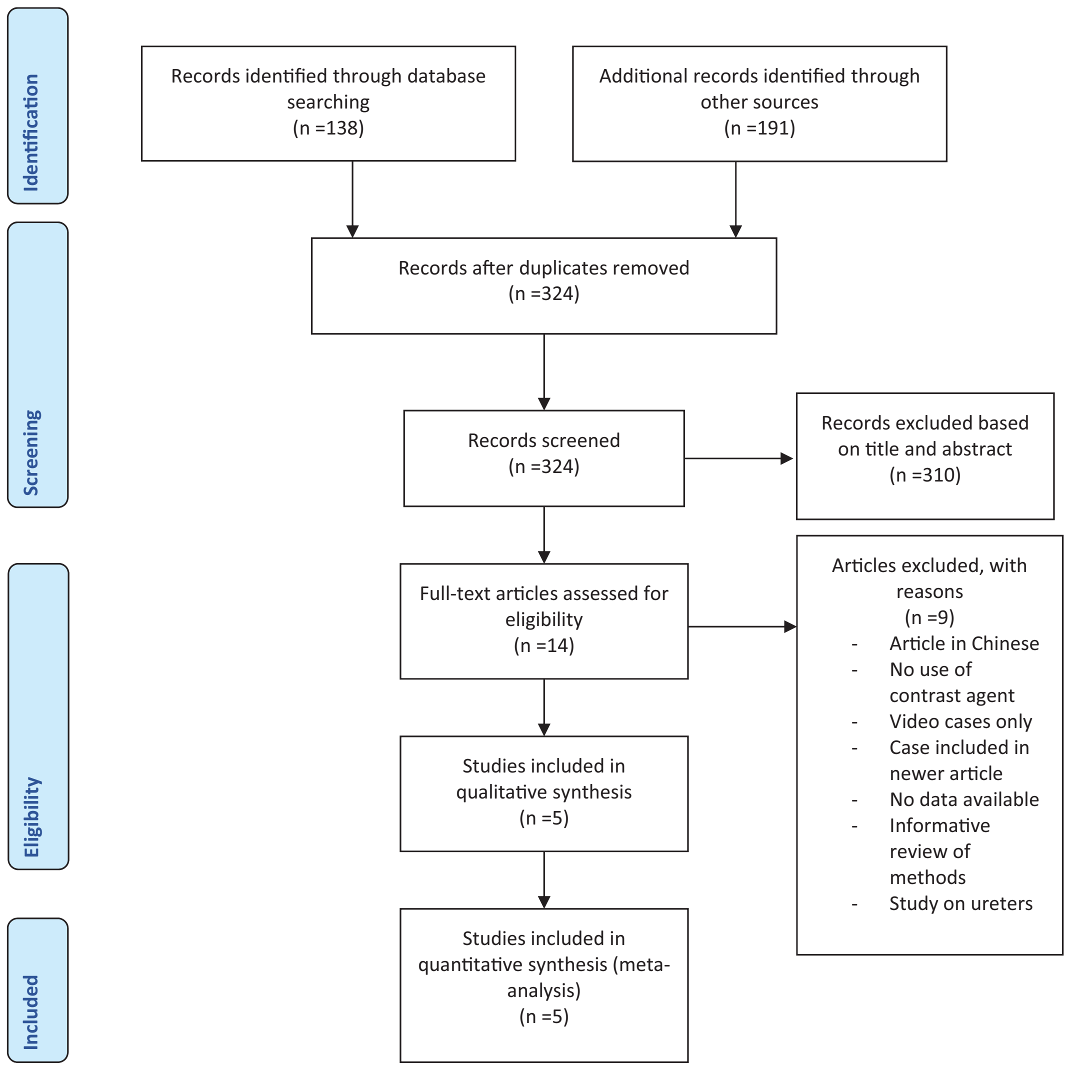

Figure 1. PRISMA 2009 flow diagram.

Table 1. Characteristics of the selected articles.

Authors	Country	Year of publication	Number of subjects	Contrast agent	System
Simone et al. [15]	Italy	2019	12 male patients	ICG	da Vinci Si^{TM}
Nitta et al. [16]	Japan	2019	1 male cadaver	ICG	IRIS ureteral kit
Barnes et al. [17]	UK	2018	2 male cadavers	ICG, IRDye 800BK	in-house manufactured
Wang et al. [20]	China	2018	NS, mice	CP-IRT dye	NS
Barnes et al. [19]	UK	2017	8 male cadavers	ICG	PINPOINT

NS not specified, *ICG* indocyanine green, *CP-IRT dye* click chemistry derived peptide-dye.

The catheter was then retracted to the navicular fossa and was filled with 50 ml of ICG; the dye concentration was not further specified. NIRF imaging was performed during the surgical procedure to identify the bladder neck and to prevent any damage to the urinary tract. Dissection of the paraurethral tissue in the prostatic fossa was done under NIRF, to prevent dissection of the proximal urethra. In two cases in which the urethra was damaged, NIRF imaging allowed an immediate identification and intraoperative repair of the injury. No intraoperative complications related to NIRF imaging were noted. Additionally, no urethral strictures or urinary incontinence were reported.

In a case report, Nitta et al. [20] successfully visualized the prostatic part of the urethra with ICG under endoscopic NIRF imaging, in a 58-year-old man who underwent a TaTME. Before starting the surgical procedure, a urethral catheter was inserted over a guide wire, after which the IRIS ureteral kit (Stryker, Kalamazoo, MI, USA) was used (a urologist

Table 2. Materials and methods for the administration of the dyes.

Study	Contrast agent	Dosage	Application moment	Administration method
Simone et al. [15]	ICG	50mL ICG, not further specified	During the US-RASP surgery	Intraurethral
Nitta et al. [16]	ICG	NS	During a TaTME	Intraurethral Indocyanine green Injection using the IRIS Ureteral kit
Barnes et al. [17]	IRDye 800BK	IRDye 800BK: 2.5mg dye mixed with 1mL of water and 10 mL of anesthetic and antiseptic lubricant.	During a TaTME IRDye 800BK: prior to dissection	IRDye 800BK was directly infiltrated into the urethra.
	ICG	ICG: 2mg of dye dissolved in 1mL of ethanol (100%) and mixed with 10mL of transparent silicone.	During a TaTME ICG: infiltrated into a 10 French one-way Foley catheter and set for 1 week. This is not further specified	ICG was infiltrated into a 10 French Foley catheter
Wang et al. [20]	CP-IRT dye	50μM CP-IRT probes were mixed with 200μL of PBS	At the start of non-invasive NIRF imaging	Intravenous
Barnes et al. [19]	ICG	ICG was reconstituted with saline and mixed with 10mL of Instillagel®. A urinary catheter (when possible) was inserted, and ICG was infiltrated adjacent to the catheter in the urethra with dose: 2.5, 5, 10, 12.5, and 25mg	NS	Intraurethral and infiltrated into the catheter

NS not specified, *ICG* indocyanine green, *TaTME* transanal total mesorectal excision, US-RASP urethra-sparing robot-assisted simple prostatectomy.

inserted the IRIS ureteral kit to guarantee safety). ICG was then injected intra-urethrally and the urethra was easily recognized under fluorescence imaging during a TaTME procedure. In this study it was not specified whether surgical dissection was needed for the first identification of the urethra. The perineal time of the TaTME procedure was 122 min.

Barnes et al. [21] performed a TaTME in a cadaver with NIRF imaging of the urethra using ICG. An ICG-silicone mix (2 mg of ICG was solved in 100% 1 ml ethanol and mixed with 10 ml transparent silicone) was injected into a 10 French one-way catheter. An in-house manufactured laparoscopic imaging system was used, previously described by Volpi et al. [22]. During the TaTME procedure, the membranous urethra was clearly visible in the transanal part of the procedure, with a signal-to-background ratio of 5.75. After removing the catheter, no residual fluorescence was seen, which indicated that there was no leakage of ICG-silicone.

In another and earlier study by Barnes et al. [23], eight cadavers were included. A PINPOINT laparoscopic system (Stryker, USA) was used for NIRF imaging. When feasible, a 14 French Foley catheter was inserted. This was successful in five cadavers. In that group, 10 ml of ICG was administered in the catheter in a total dose of 2.5, 5, 10, 12.5, and 25 mg, respectively. In the remaining 3 cadavers, 10 ml of ICG was directly administered in the urethra. In seven of the eight cadavers, the urethra was exposed using a transverse or vertical perineal incision. Similar levels of fluorescence were observed in comparison to the cadavers with and without a catheter. In the cadavers without a catheter, there was no ICG leaking to the bladder. In one cadaver, the prostate was mobilized during a TaTME. The urethra was clearly delineated, and thus no perineal incision was needed. It was not necessary to denude the urethra completely in any of the cadavers prior to successful NIRF identification. This study showed no correlation between the dose and the brightness of the fluorescence signal. The urethra was easily seen through overlying muscles to a depth of 2 to 4 cm. In addition, ICG leakage was observed after deliberately damaging the urethral wall. The ICG and Instillagel® (Farco Pharma, Cologne, Germany) were green under the white light and could be clearly seen without the need for NIRF imaging.

IRDye® 800BK. Barnes et al. [21], in the same publication describing the use of ICG, complemented the study by testing the IRDye® 800BK as a NIRF fluorophore, in a cadaver model of a TaTME.

A mixture made of 2.5 mg of IRDye® 800BK mixed with 1 ml of H_2O and 10 ml of anaesthetic antiseptic lubricant was injected directly into the urethra, as previously described by the same authors [23] using the same in-house manufactured laparoscopic imaging system. The surgeons defined a clear signal, after the incision of the perineal skin, in the location of the urethra with overlying fat, of approximately 2 cm in size. The signal-to-background ratio was 6.24 with the overlying fat and 6.61 without the fat.

CP-IRT dye

Wang et al. [24] studied molecular cancer imaging by using a renal-excreted fluorophore-peptide probe in mice [24]. For this study, a click chemistry derived peptide-dye (CP-IRT dye) probe was injected to target the CD133 stem cell tumor biomarker. The fluorescence imaging was performed in the second near-infrared window, which involved wavelengths between 1000 and 1700 nm (NIR-II). The CP-IRT dye was injected intravenously, and within three minutes the urethra was clearly visible through the intact tissue of the mouse with NIRF imaging. The used fluorescence imaging system was not described.

Discussion

This study presents an overview of intraoperative enhanced visualization of the urethra *via* NIRF imaging, possibly leading to a decreased risk of urethral damage.

Five studies reporting a fluorescence-based method for enhanced urethral recognition were found. In four out of five articles, the clinically available ICG was studied. ICG is the most commonly used dye for NIRF imaging. ICG is rapidly and exclusively excreted into bile and is approved for clinical use in the assessment of hepatic blood flow, ophthalmology and cardiology. These experiences with ICG have greatly facilitated its introduction as a NIRF fluorophore for several surgical indications [25].

In all studies exploring the use of ICG for urethral identification, the authors concluded that it provided a significant improvement as compared to the standard surgical approach.

Barnes et al. [23] demonstrated that the ICG emission easily penetrates the overlying muscles on the urethra to reach visualization up to a depth of 2 to 4 cm. This penetration depth is remarkably higher than the fluorescence penetration depth which has been described in other studies on intraoperative NIRF imaging, reaching a maximum penetration of 2 cm [26]. Future studies on NIRF imaging of the urethra should assess the reproducibility of this technique and the penetration depth of the fluorescence signal.

Simone et al. [19] showed that the use of ICG provides a significant improvement in the identification of the prostatic urethra. However, despite the improved recognition of the prostatic urethra, in two cases (16.6%) where a medial prostatic lobe was present, iatrogenic injury to the urethra could not be prevented due to the known technical challenges of this procedure. NIRF imaging however, demonstrated the benefit for the detection of urethral damage introaoperatively. Consequently, NIRF imaging with ICG may not only serve as a tool for enhanced recognition of the urethra, but also as a tool to recognize iatrogenic damage intraoperatively. Especially in cases with large lateral and/or medial prostate lobes protruding into the bladder neck, up to 27% of unintentional urethrotomies were described by Wang et al. [14]. At present, there is no prospective study evaluating NIRF imaging for the reduction of uretheral injuries in comparison to conventional imaging, which may be the focus of future studies.

The IRIS ureteral kit is a single use, flexible tube containing a fiberoptic bundle that emits light throughout its length, intended to be inserted into the ureter to facilitate the visualization of the ureter. Nitta et al. [20] demonstrated in a case report that it can also be used for urethral visualization and that it did not alter the length of the surgical procedure; the perineal time of the TaTME procedure was 122 min, compared to a mean of 128 min (±70; 15–467), as reported by the international TaTME registry. However, based on this study alone, it is yet not possible to conclude whether NIRF imaging significantly influences the length of the perineal procedure. In this study, the IRIS ureteral kit was used as it has FDA approval to transilluminate the ureter during open and surgical procedures. However, in this paper the IRIS Ureteral kit was used for urethral and not ureteral identification. It is not clarified whether the white light led of the IRIS kit was visible as a standalone device. The authors used the IRIS kit illumination in combination with ICG urethral instillation. Importantly, tissue penetration of white light is much lower when compared to the depth of penetration of the NIR light.

One study explored the use of IRDye® 800BK and ICG, showing a successful visualization of the urethra [21]. The IRDye® 800-BK was originally developed specifically for intraoperative NIRF visualization of the ureters. Due to its hydrophilic nature, it is primarily cleared by the kidneys and therefore it showed a great potential for real-time NIRF imaging of the ureter in preclinical studies [27,28].

The authors evaluating this dye for urethral imaging concluded that IRDye® 800BK could be a promising alternative to ICG, with a greater depth of penetration and target to background fluorescence when it comes down to visualizing the urethra [21].

Wang et al. [24], studied the CP-IRT dye in a mouse model. It was not primarily used to visualize the urethra, because the aim of the study was to test a dye for cancer imaging. It was an interesting secondary finding as the urethra was visualized with the CP-IRT dye, but no further information was provided. Consequently, the clinical relevance of this dye is uncertain for urethral recognition.

None of the studies reported side effects attributable to the used dye or imaging system.

An open-label feasibility clinical study (NCT03204201) using a direct instillation of ICG into the urethra intraoperatively for low rectal cancers by Barnes et al. [29] was terminated due to failure of the technique. The trial involved a single intervention taking place during the patient's operation. No data was provided concerning the reasons for terminating this study.

The methods used to administer the dye through direct instillation into the urethra or through a urine catheter, seem to be easily applicable and clinically reproducible in all included articles exploring these methods. However, the practicality of these methods should be further evaluated. Since most open and laparoscopic procedures in which urethral recognition is important require the insertion of an indwelling bladder catheter for urine drainage [30], it would be ideal if NIRF imaging did not interfere with the drainage of urine. As a result, the direct injection of a dye into the urethra with a urinary catheter in place may not be feasible. Besides, inserting the dye into the catheter may prevent the drainage of urine or will result in the washout of the dye during the procedure due to urine flow through the catheter which may result in a decrease of the fluorescence signal during the procedure.

Recently, our group developed a proprietary fluorescent coating, named NICE (Near-Infrared Coating of Equipment). This biocompatible paint has been engineered based on poly (methyl methacrylate) (PMMA) associated with a specially designed fluorescent dye, which exhibits optical properties rather similar to indocyanine green (ICG), but with higher brightness and stability. The NICE has been successfully used to coat gold fiducials [31] and magnetic anastomosis devices [32] under experimental settings. Inspired by the results of this review, we performed a successful feasibility study on human anatomical specimens [33]. In the experimental setting, it was possible to visualize the urethra using a NICE-coated indwelling urinary catheter, during a TaTME procedure. This might represent a good solution to be explored in clinical practice since it does not interfere with the drainage of urine and is completely removed from the body after urinary catheter removal.

The use of the NIRF imaging technique for urethral recognition appears to be a new field of interest, due to the limited amount of studies exploring this technique. Due to the promising results found in the studies described in this review and due to the increasing use of NIRF imaging techniques in the clinical practice, we expect a growing interest about urethral NIRF imaging in the near future.

Conclusion

Near-infrared fluorescence imaging techniques show promising results for the early recognition of the urethra intraoperatively. However, data is too limited to draw solid conclusions on its value for the prevention of urethral injury. Future studies are required to investigate the clinical applicability, reproducibility, and the right composition of the dye, before conclusions can be drawn.

Acknowledgments

Authors are grateful to Guy Temporal and Christopher Burel, professionals in Medical English proofreading, for their valuable help in revising the manuscript.

Declaration of interest

Jacques Marescaux is the President of both the IRCAD, which is partly funded by KARL STORZ and Medtronic. Laurents Stassen and Michele Diana are members of the board of Diagnostic Green (travel fees). Michele Diana is the recipient of the ELIOS grant. The remaining authors have no conflicts of interest or financial ties to disclose.

Funding

This work was funded by the ARC Foundation through the ELIOS (Endoscopic Luminescent Imaging for precision Oncologic Surgery) grant.

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References

[1] Cong J, Zhang H. [Mechanism and prevention of urethral injury during transanal total mesorectal excision. Zhonghua Wei Chang Wai Ke Za Zhi. 2019;22(3):233–237.

[2] Sylla P, Knol JJ, D'Andrea AP, et al. Urethral injury and other urologic injuries during transanal total mesorectal excision: an international collaborative study. Ann Surg. 2019.doi: 10.1097/SLA.0000000000003597

[3] Pichler R, Fritsch H, Skradski V, et al. Diagnosis and management of pediatric urethral injuries. Urol Int. 2012;89(2):136–142.

[4] Delacroix SE, Jr., Winters JC. Urinary tract injures: recognition and management. Clin Colon Rectal Surg. 2010;23(2):104–112.

[5] Chapple CR. Urethral injury. BJU Int. 2000;86(3): 318–326.

[6] Heald RJ, Ryall RD. Recurrence and survival after total mesorectal excision for rectal cancer. Lancet. 1986;1(8496):1479–1482.

[7] Grass JK, Perez DR, Izbicki JR, et al. Systematic review analysis of robotic and transanal approaches in TME surgery- a systematic review of the current literature in regard to challenges in rectal cancer surgery. Eur J Surg Oncol. 2019;45(4):498–509.

[8] Atallah S, Albert M, Monson JR. Critical concepts and important anatomic landmarks encountered during transanal total mesorectal excision (taTME): toward the mastery of a new operation for rectal cancer surgery. Tech Coloproctol. 2016;20(7): 483–494.

[9] Burke JP, Martin-Perez B, Khan A, et al. Transanal total mesorectal excision for rectal cancer: early outcomes in 50 consecutive patients. Colorectal Dis. 2016;18(6):570–577.

[10] Penna M, Hompes R, Arnold S, et al. Transanal total mesorectal excision: international registry results of the first 720 cases. Ann Surg. 2017;266(1):111–117.

[11] Rouanet P, Mourregot A, Azar CC, et al. Transanal endoscopic proctectomy: an innovative procedure for difficult resection of rectal tumors in men with narrow pelvis. Dis Colon Rectum. 2013;56(4): 408–415.

[12] Marecik SJ, Pai A, Sheikh T, et al. Transanal total mesorectal excision: save the nerves and urethra. Dis Colon Rectum. 2016;59(7):e410–e414.

[13] Dixon AR, Lord PH, Madigan MR. The Madigan prostatectomy. J Urol. 1990;144(6):1401–1403.

[14] Wang P, Xia D, Ye S, et al. Robotic-assisted urethra-sparing simple prostatectomy via an extraperitoneal approach. Urology. 2018;119:85–90.

[15] Schols RM, Bouvy ND, van Dam RM, et al. Combined vascular and biliary fluorescence imaging in laparoscopic cholecystectomy. Surg Endosc. 2013; 27(12):4511–4517.

[16] Slooter MD, Janssen A, Bemelman WA, et al. Currently available and experimental dyes for intraoperative near-infrared fluorescence imaging of the ureters: a systematic review. Tech Coloproctol. 2019; 23(4):305–313.

[17] van den Bos J, Al-Taher M, Schols RM, et al. Near-infrared fluorescence imaging for real-time intraoperative guidance in anastomotic colorectal surgery: a systematic review of literature. J Laparoendosc Adv Surg Tech A. 2018;28(2):157–167.

[18] Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Int J Surg. 2010; 8(5):336–341.

[19] Simone G, Misuraca L, Anceschi U, et al. Urethra and ejaculation preserving robot-assisted simple prostatectomy: near-infrared fluorescence imaging-guided madigan technique. Eur Urol. 2019;75(3): 492–497.

[20] Nitta T, Tanaka K, Kataoka J, et al. Novel technique with the IRIS U kit to prevent urethral injury in patients undergoing transanal total mesorectal excision. Ann Med Surg (Lond)). 2019;46:1–3.

[21] Barnes TG, Volpi D, Cunningham C, et al. Improved urethral fluorescence during low rectal surgery: a new dye and a new method. Tech Coloproctol. 2018;22(2):115–119.

[22] Volpi D, Tullis I, Laios A, et al. A novel multiwavelength fluorescence image-guided surgery imaging system. Proceedings of the SPIE 8935, Advanced Biomedical and Clinical Diagnostic Systems XII; 2014. 8935.

[23] Barnes TG, Penna M, Hompes R, et al. Fluorescence to highlight the urethra: a human cadaveric study. Tech Coloproctol. 2017;21(6):439–444.

[24] Wang W, Ma Z, Zhu S, et al. Molecular cancer imaging in the second near-infrared window using a renal-excreted NIR-II fluorophore-peptide probe. Adv Mater Weinheim. 2018;30(22):e1800106.

[25] Alander JT, Kaartinen I, Laakso A, et al. A review of indocyanine green fluorescent imaging in surgery. Int J Biomed Imaging. 2012;2012:940585

[26] Marshall MV, Rasmussen JC, Tan IC, et al. Near-infrared fluorescence imaging in humans with indocyanine green: a review and update. Open Surg Oncol J. 2010;2(2):12–25.

[27] Al-Taher M, van den Bos J, Schols RM, et al. Evaluation of a novel dye for near-infrared fluorescence delineation of the ureters during laparoscopy. BJS Open. 2018;2(4):254–261.

[28] van den Bos J, Al-Taher M, Bouvy ND, et al. Near-infrared fluorescence laparoscopy of the ureter with three preclinical dyes in a pig model. Surg Endosc. 2019;33(3):986–991.

[29] Barnes TG. Validation of ICG to identify the urethra during rectal surgery; 2017. https://clinicaltrials.gov/ct2/show/NCT03204201

[30] Gould CV, Umscheid CA, Agarwal RK, et al. Guideline for prevention of catheter-associated

urinary tract infections 2009. Infect Control Hosp Epidemiol. 2010;31(4):319–326.
[31] Kong S-H, Haouchine N, Soares R, et al. Robust augmented reality registration method for localization of solid organs' tumors using CT-derived virtual biomechanical model and fluorescent fiducials. Surg Endosc. 2017;31(7):2863–2871.
[32] Watanabe R, Barberio M, Kanaji S, et al. Hybrid fluorescent magnetic gastrojejunostomy: an experimental feasibility study in the porcine model and human cadaver. Surg Endosc. 2020;34(3):1393–1398.
[33] Barberio M, Al-Taher M, Forgione A, et al. A novel method for near-infrared fluorescence imaging of the urethra during perineal and transanal surgery: demonstration in a cadaveric model. Colorectal Dis. 2020.doi: 10.1111/codi.15156

Appendix 1. Search 21-10-2019

(("Fluorescence"[Mesh]) OR ("Microscopy, Fluorescence"[Mesh]) OR ((Diagnosis/Broad[filter]) AND ("Microscopy, Fluorescence"[Mesh])) OR ("Lasers, Dye"[Mesh]) OR (Near-infrared fluorescence imaging) OR (near-infrared) OR (near-infrared imaging) OR (fluorescence diagnosis) OR (fluorescence imaging) OR (near-infrared diagnosis) OR (NIRF imaging)) AND (("Urethra"[Mesh]) OR ("Urethral Stricture"[Mesh]) OR (Urethral) OR (Urethra) OR (urethral stricture)) AND (("Laparoscopy"[Mesh]) OR ("Surgical Procedures, Operative"[Mesh]) OR (Laparoscopic surgery) OR (surgery) OR (laparoscopic) OR (minimal invasive surgery) OR (operation) OR (abdominal surgery) OR (abdominal))