SMALL ANIMALS

Evaluation of cystoscopic-guided laser ablation of intramural ectopic ureters in female dogs

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Objective—To describe and evaluate the short- and long-term outcomes in female dogs after cystoscopic-guided laser ablation of ectopic ureters (CLA-EU).

Design—Prospective case series.

Animals—32 incontinent female dogs with intramural ectopic ureters.

Procedures—A diagnosis of intramural ectopic ureters was made via cystoscopy and fluoroscopy in all patients. Transurethral CLA-EU (via diode laser [n = 27] or Holmium:yttrium aluminum garnet laser [3]) was performed to relocate the ectopic ureteral orifice cranially into the urinary bladder. All vaginal anomalies were treated with the laser concurrently. Follow-up evaluation was standardized and included urinary continence scoring, serial bacteriologic culture of urine samples, and a follow-up cystoscopy 6 to 8 weeks after CLA-EU.

Results—Ectopic ureteral orifices of all dogs were initially located in the urethra. Eighteen of 30 dogs had bilateral ectopic ureters, and 12 had unilateral ectopic ureters. All dogs had other concurrent urinary anomalies. At the time of last follow-up (median, 2.7 years after CLA-EU, [range, 12 to 62 months]), 14 of 30 (47%) dogs did not require any additional treatments following CLA-EU to maintain urinary continence. For the 16 residually incontinent dogs, the addition of medical management, transurethral bulking-agent injection, or placement of a hydraulic occluder was effective in 3, 2, and 4 dogs, respectively, improving the overall urinary continence rate to 77% (23/30 dogs). One dog had evidence of polypoid cystitis at the neoureteral orifice 6 weeks after CLA-EU that was resolved at 3 months.

Conclusions and Clinical Relevance—CLA-EU provided an effective, safe, and minimally invasive alternative to surgery for intramural ectopic ureters in female dogs. (*J Am Vet Med Assoc* 2012;240:716–725)

Ectopic ureters are a congenital anomaly of the urinary system where the ureteral orifice is inappropriately positioned caudal to the urinary bladder (ie, the urinary bladder neck, urethra, vagina, vestibule, or uterus).[1–4] This is the most common cause of urinary incontinence in juvenile female dogs, accounting for over 50% of affected dogs in 1 study,[5] compared with only 5% of incontinent adult dogs.

The embryological foundation of this condition is thought to result from the abnormal differentiation of mesonephric and metanephric duct systems, resulting in inappropriate ureteral tube termination and malposition of the ureteral orifice.[6–8] Abnormalities in the formation of the urogenital sinus, which becomes the urinary bladder and urethra, results in inappropriate termination of the ureters in the urinary bladder neck, prostate, or urethra.[8] Ectopic ureters are classified anatomically as tunneling either intramurally or extramurally, with > 95% reported to be intramural in dogs.[1,8–12] The typical intramural ectopic ureter will enter the distal aspect of the urinary bladder and trigone in a relatively normal position but fail to open into the urinary bladder lumen, traversing the urethra in the submucosa.

Although ectopic ureters have been reported for male and female dogs as well as both purebred and mixed-breed dogs, they seem to occur with greater frequency in female than male dogs as well as in certain breeds (ie, Siberian Huskies, Newfoundlands, Labrador Retrievers, Golden Retrievers, Terriers, Miniature Poodles, and Toy Poodles).[1,9,10] The most common clinical finding in these dogs is constant or intermittent urinary leaking since birth or weaning, although many dogs develop urinary leaking after a period of urinary continence and are incontinent only in certain positions.

Suspected concurrent urinary bladder and urethral functional anomalies, such as urethral sphinc-

Abbreviations

CLA-EU	Cystoscopic-guided laser ablation of ectopic ureters
Hol:YAG	Holmium:yttrium aluminum garnet

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ter mechanism incompetence, have been reported for 75% to 89% of female dogs evaluated.[10,13,14] Other associated urinary conditions such as urinary tract infections (64%),[12] renal agenesis (5%),[15] renal dysplasia, hydroureter (34% to 50%)[14] or hydronephrosis (15% to 27%),[14] short urethras (21%), persistent paramesonephric remnants (83%) or vaginal septum or dual vaginas (8%), hormonal imbalances, and ureteroceles have all been reported concurrently for female dogs with ectopic ureters.[1,3,4,9–11,13,14,16]

Various methods of surgical correction have been described,[1,10–12,14] all of which require a laparotomy, cystotomy, ureterotomy, and urethrotomy. The complication rates with surgery vary, and in 1 study,[14] there was a 14% complication rate overall, with 50% of dogs after ureteral reimplantation developing worsening hydroureter or hydronephrosis, 16% of dogs after the intravesicular transplantation technique having dysuria, and 8% of dogs with ureteronephrectomy developing renal failure. Unfortunately, the postoperative urinary continence rates reported for female dogs continue to be low, regardless of the surgical technique performed, ranging between 25% and 58% with or without concurrent medical management.[1,8,10–14,17] Because many of these dogs are relinquished or euthanized because of urinary incontinence issues, these disappointing outcomes made the search for other alternatives appealing.

The diagnostic imaging method of choice for evaluating dogs for ectopic ureters is now considered to be cystoscopy or computed tomography.[15,18] The CLA-EU procedure, first described in 1 female dog in 2006[19] and 4 male dogs in 2008,[4] provides a minimally invasive alternative to surgery in dogs with intramural ectopic ureters. Since that time, there have been a few descriptions of the procedure performed on small groups of dogs[4,a–c] and, more recently, a retrospective study[20] of 16 dogs. This procedure enables the diagnosis to be made while simultaneously performing a therapeutic intervention and also potentially avoids some of the complications and risks associated with the open surgical techniques described. The CLA-EU procedure uses cystoscopy and fluoroscopy to directly visualize the ureteral orifice and to assess for any other urinary anomalies (vaginal septum, persistent paramesonephric remnant, dual vagina, hydroureter, and hydronephrosis). During cystoscopy and fluoroscopy, a guided laser is used to ablate the tissue that forms the medial aspect of the ectopic ureteral wall, so the orifice can be repositioned into the urinary bladder neck. The purpose of the study reported here was to prospectively describe and evaluate the preoperative, operative, and postoperative findings in female dogs undergoing CLA-EU and provide consistent short- and long-term follow-up information for all enrolled patients, including evaluation of all ureteral tracts 6 to 8 weeks after the procedure. The hypothesis was that CLA-EU is safe, effective, and associated with minimal morbidity or complications.

Materials and Methods

Selection of cases—Female dogs examined by 1 author (ACB), with a diagnosis of intramural ectopic ureters from January 2006 to September 2009 determined by use of cystoscopy and fluoroscopy and treated by CLA-EU, were serially enrolled.

Inclusion criteria—Dogs were included in the study if the owners signed consent for the following: evaluation, cystoscopy, CLA-EU, and a 6- to 8-week postprocedural cystoscopy as well as serial follow-up phone calls during the course of the study. All enrolled patients had the cost of the procedure and follow-up cystoscopy subsidized by a grant obtained through Waltham Pet Nutrition. This study protocol was reviewed and approved by the Institutional Animal Care and Use Committee of the University of Pennsylvania.

Exclusion criteria—Patients were excluded if they had any previous surgical manipulation of their urinary tract prior to referral, did not have evaluation of renal and ureteral morphology via fluoroscopy and retrograde ureteropyelography, failed to undergo a 6- to 8-week cystoscopic reevaluation of the neoureteral orifice, had an inconsistent follow-up by the author (ACB), or had < 12 months' follow-up time.

Historical and laboratory data—All dogs had a CBC, serum biochemical profile, urinalysis, and bacteriologic culture of urine samples (followed by antimicrobial susceptibility testing if applicable) prior to the procedure. Data regarding signalment, urinary incontinence history, history of a urinary tract infection, previous imaging information, clinical signs, duration of signs, physical examination findings, and morphology of ectopic ureters (unilateral, bilateral, location of ureteral orifice, single or multiple fenestrations, presence of ureteral troughs, ureteral dimensions, renal anatomy or dimensions, length of the urethra, length of the ectopic tract that was laser treated, presence of an intrapelvic urinary bladder, urinary bladder shape, vaginal anatomy, presence of vaginal septums, stenosis, or paramesonephric remnants) were recorded.

CLA-EU—All cystoscopic laser procedures were performed by 1 author (ACB). Dogs were placed in dorsal recumbency, and the vulva was clipped of hair and aseptically prepared. Periprocedural antimicrobials were given (cefazolin, 22 mg/kg [10 mg/lb], IV) in patients that were not currently being treated with an antimicrobial for a previously diagnosed urinary tract infection. A rigid cystoscope[d–f] was advanced into the vestibule and urethral orifice in a retrograde fashion by the use of manual irrigation with saline (0.9% NaCl) solution. Each ureterovesicular junction was evaluated, and the ectopic ureters were identified and locations were confirmed and recorded (**Figure 1**). Evaluations for multiple fenestrations, urethral length, and urethral, vaginal, and vestibular defects were performed and recorded. Portable C-arm fluoroscopy[g] was used to confirm the presence of an intramural ectopic tract as well as to document the diameter of the ureter and renal pelvis via retrograde contrast ureteropyelography. An angled, hydrophilic-tip guidewire[h] was advanced up the ureter through the working channel of the cystoscope, under fluoroscopic and cystoscopic guidance. An open-ended ureteral catheter[i] was advanced over the guidewire into the distal portion of the ureter through the ureteral orifice. A retrograde ureteropyelogram was performed with 5 mL of iodinated nonionic contrast medium[j] (diluted 50:50 [vol/vol] with

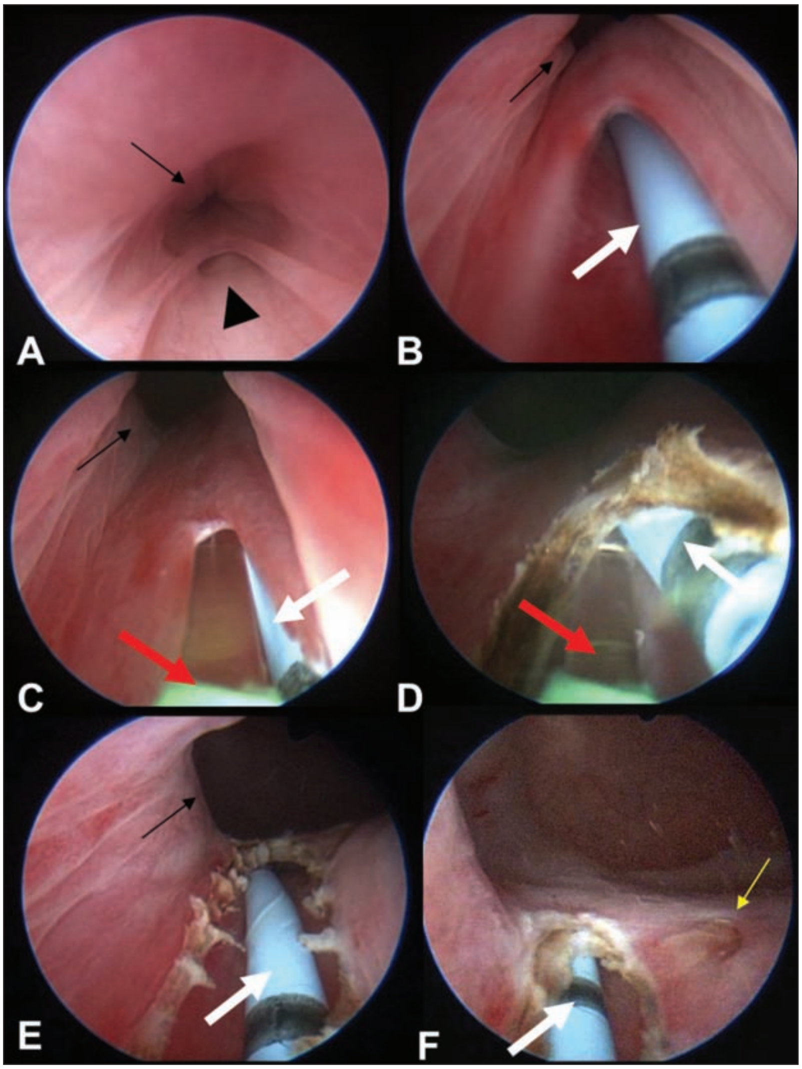

Figure 1—Endoscopic images of the lower urinary tract in a female dog with a right-sided intramural ectopic ureter. The patient is in dorsal recumbency while undergoing CLA-EU. A—The ectopic ureteral opening (black arrowhead) and urethral opening (black arrow) are evident. B—An open-ended ureteral catheter (white arrow) is placed within the ureteral lumen; notice this placement in relation to the urethral opening (black arrow). C—The diode laser fiber (red arrow) is positioned at the ectopic ureteral orifice. Notice the ureteral catheter (white arrow) and urethral opening (black arrow). D—The ectopic tunnel is cut with the laser (red arrow), and the ureteral catheter (white arrow) is protecting the lateral ureteral wall. E—Notice the ureteral catheter (white arrow) after the ureteral segment of the ectopic ureter is cut. The urethrovesicular junction (black arrow) is evident. F—The neoureteral orifice with a ureteral catheter (white arrow) inside the lumen as it enters the urinary bladder. Notice the location of the right neoureteral orifice is even with the normal contralateral left ureteral orifice (yellow arrow).

sterile saline solution) by retrograde injection through the ureteral catheter to identify the ureteral path through the urethral wall and determine the anatomic features of the ureter and renal pelvis. Then, approximately 2 to 10 mL/kg (0.9 to 4.54 mL/lb) of this mixture was injected into the urethra through the cystoscope for a retrograde cystourethrogram, allowing for a combination of an ureteropyelogram and cystourethrogram. This permitted evaluation of the urinary bladder trigone in relation to the ureteral orifice and the transition of the ureter from intramural to extramural **(Figure 2)**. Once an intramural ureteral tract was confirmed, the cystoscope was removed over the wire-catheter combination, and they were secured to the drape with a hemostat. The cystoscope was then reinserted into the urethra, next to the wire-catheter combination, and the laser fiber (600-µm diode[k] or 400-µm Hol:YAG[l]) was inserted into the working channel of the cystoscope and directed onto the ectopic ureteral orifice. The cystoscope was deflected toward the urethral lumen to angle the laser fiber tip toward the medial aspect of the ectopic ureteral wall, avoiding the lateral side of the ureteral wall and ureteral catheter. The medial aspect of the ectopic ureteral wall was then carefully cut in a continuous manner by use of the diode laser at 16 to 25 W or a pulsed manner by use of the Hol:YAG laser (10 to 12 Hz and 0.7 to 1.2 J at a pulse width of 700 milliseconds). When the neoureteral orifice was within the urinary bladder lumen or the ureter appeared to be diverging from its path alongside the urethra or urinary bladder lumen, suggesting the potential transition from its intramural to its extramural course, cystourethrography was performed to confirm neoureteral orifice location. This procedure was repeated on the contralateral side for patients with bilateral ectopic ureters.

Retrograde contrast urethrocystography and ureteropyelography were performed in each dog after CLA-EU to ensure there was no extravasation of contrast medium and to document the new location of the ureteral orifice relative to the urinary bladder trigone both cystoscopically and fluoroscopically (Figure 2). After completion of CLA-EU, the paramesonephric remnant or vaginal septum-dual vagina, if present, was laser treated to create a normal vaginal opening and lumen. Briefly, a guidewire-ureteral catheter combination was used to cannulate 1 side of the vaginal lumen and the cystoscope-laser combination was used to ablate the membrane until an open vaginal lumen was viewed. Dogs were given meloxicam (0.1 mg/kg [0.045 mg/lb], SC) upon recovery from the laser procedure if there was no concern of chronic kidney disease, and their urethras were infused with a bupivacaine (1 mg/kg [0.45 mg/lb]) and saline solution mixture (1:1) for local transurethral analgesia.

Postsurgical management—At the time of hospital discharge, owners were provided with an analgesic to be administered to their dogs for signs of pain as needed. This was typically an NSAID, meloxicam (11/30 dogs; 0.1 mg/kg, PO, q 24 h), to be administered for 2 to 3 days if dogs were nonazotemic or had no evidence of hydroureter or hydronephrosis. Otherwise, dogs received tramadol (19/30 dogs; 2 to 5 mg/kg [0.9 to 2.3 mg/lb], PO, q 8 h) for 24 hours. Dogs were also administered amoxicillin-clavulanic acid (15 mg/kg [6.8 mg/lb], PO, q 12 h) for 10 days. Bacteriologic culture of urine samples was performed at 2 to 4 weeks in all patients and recommended at 8 weeks, 3 months, 6 months, and then every 6 months thereafter.

Follow-up—For all dogs, cystoscopy was performed at 6 to 8 weeks after CLA-EU (**Figure 3**). All owners were contacted at 1, 2, 6, 8, 12, and 24 weeks after the procedure and every 6 months thereafter with a written questionnaire about the urinary continence status, quality of life, and medical conditions of their pet. Urinary incontinence was defined as any persistent or intermittent involuntary urination. Urinary continence was scored on a scale of 1 through 10, (1 = minimally continent or extremely incontinent [leaking urine all the time], 5 = moderately continent [only leaking urine when lying down or when the urinary bladder is full] but able to hold some urine between urinations, and 10 = perfectly continent with no urine leakage at all). Dogs were graded immediately after the procedure, prior to starting any supplemental medications (if necessary), or after any other intervention performed to aid in the preservation of urinary continence. All dogs had the same protocol for treatment of urinary incontinence, but not all owners committed to all supplemental procedures. At 2 weeks, if the dogs were still incontinent, they began receiving phenylpropanolamine (1 to 1.5 mg/kg [0.45 to 0.68 mg/lb], PO, q 8 h). If the dogs were still incontinent 2 weeks after beginning treatment with phenylpropanolamine and previously ovariectomized, it was recommended that they be given diethylstilbestrol (0.1 to 0.3 mg/kg [0.045 to 0.14 mg/lb], PO) once daily for 7 days, then once weekly. Not all owners were willing to have their dogs treated with diethylstilbestrol. If medical management failed, treatment with periurethral bulking agent injections[m,n] was offered. If this failed or was declined, treatment by placement of a periurethral hydraulic occluder device[o] was offered; this device was not placed until the patient was > 10 months of age.

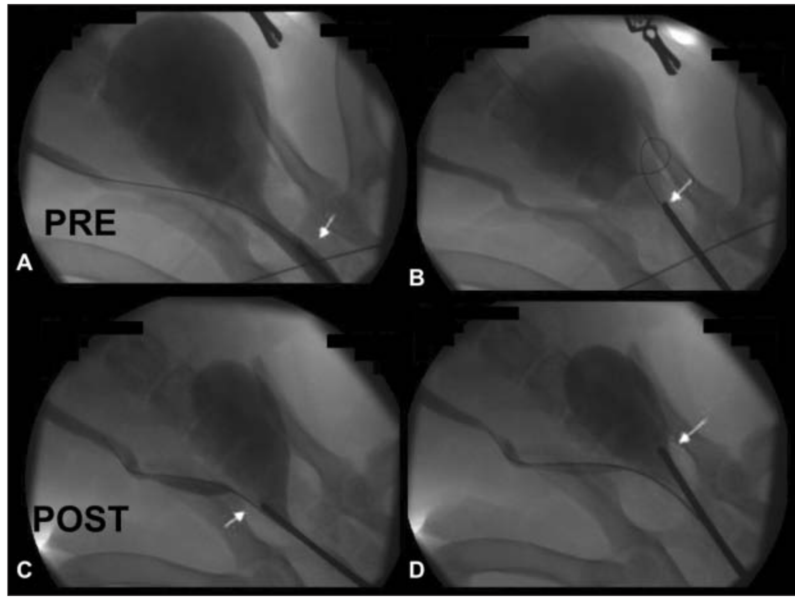

Figure 2—Fluoroscopic images of a female dog with bilateral intramural ectopic ureters during CLA-EU. Fluoroscopic images represent a combination of a retrograde ureteropyelogram and cystourethrogram. The patient is in dorsal recumbency. A—Rigid cystoscope at the level of the right ectopic ureteral opening (arrow) before (PRE) CLA-EU. The guidewire is within the right ureteral lumen, revealing the intramural nature of the ectopic ureter. B—Rigid cystoscope at the level of the left ectopic ureteral opening (arrow) before CLA-EU. The guidewire is within the left ureteral lumen. C—The rigid cystoscope is at the level of the right neoureteral opening (arrow) after (POST) CLA-EU, revealing that the cystoscope is within the urinary bladder lumen and there is no extravasation of contrast medium. D—The left neoureteral opening (arrow) after it was advanced into the urinary bladder.

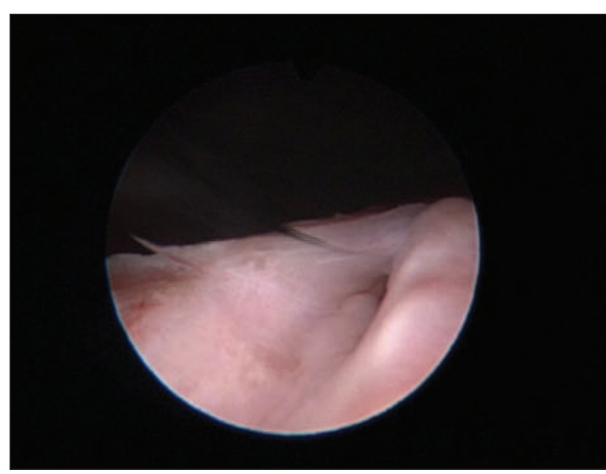

Figure 3—Cystoscopic image of a female dog in dorsal recumbency 6 weeks after CLA-EU. Notice the left neoureteral opening healed well inside the urinary bladder with a urine jet from the neoureterovesicular junction.

Results

Selection of cases—Thirty-two female dogs with intramural ectopic ureters were prospectively enrolled in the study. One dog was excluded because it was lost to long-term follow-up, and another dog was excluded because of lack of follow-up.

Historical and clinical data—Eight of 30 dogs were spayed females and 22 of 30 were sexually intact females at the time of the procedure. All dogs were ultimately spayed throughout the course of the study. Of the 30 dogs, 3 were mixed breeds and 27 were purebreds, including 9 Golden Retrievers, 4 Labrador Retrievers, 2 Pomeranians, 2 American Pit Bull Terriers, 1 Wheaten Terrier, 1 Miniature Poodle, 1 Havanese, 1 Jack Russell Terrier, 1 Rottweiler, 1 English Bulldog, 1 Border Collie, 1 Chihuahua, 1 Cairn Terrier, and 1 Shih Tzu. Median body weight at initial hospital admission was 14.4 kg (31.7 lb; range, 2.7 to 49.4 kg [6.0 to 108.7 lb]), and the median adult weight was 25 kg (55 lb; range, 4.55 to 49.4 kg [10.0 to 108.7 lb]). Median age at the time of the procedure was 5.5 months (range, 3.5 to 40 months). The age of onset of urinary incontinence was since birth in 15 of 30 dogs, unknown in 13 of 30 dogs, and after 1 year of age in 2 of 30 dogs (up to 15 months of age). No dog had any known history of other surgeries to the urinary tract. No dogs had a history of polyuria or polydipsia prior to their procedure.

Clinicopathologic and laboratory data—A preanesthetic serum biochemical analysis was performed for all dogs. Median BUN concentration was 13.5 mg/dL (range, 10 to 31 mg/dL; reference range, 5 to 20 mg/dL), and median serum creatinine concentration was 0.9 mg/dL (range, 0.5 to 1.5 mg/dL; reference range, 0.5 to 1.8 mg/dL). Median urine specific gravity was 1.030 (range, 1.019 to 1.051; reference range, > 1.030 for healthy and hydrated dogs). No other abnormalities were detected on urinalysis or serum biochemical analysis. A history of positive bacteriologic urine culture results was documented for 25 of 30 (83%) dogs, with *Escherichia coli* predominating in urine samples from most dogs. All dogs had a negative bacteriologic urine culture result immediately prior to the procedure, with negative results obtained for some dogs only after appropriate antimicrobial treatment was initiated.

Imaging—Cystoscopic evaluation confirmed the location of each ureteral orifice. Eighteen of 30 (60%) dogs had bilateral ectopic ureters and 12 of 30 had unilateral ectopic ureters, totaling 48 ectopic ureteral units. Of the dogs with unilateral ectopic ureters, 10 of 12 were left sided and 2 of 12 were right sided. Forty-two of 48 ectopic ureteral units originated within the urethra (17 proximal, 4 mid, and 21 distal), 5 of 48 ectopic ureteral units originated at the urinary bladder neck-proximal portion of the urethra, and 1 of 48 ectopic ureteral units originated at the level of the urethral vestibular junction. No ureteral orifice was found in the vagina. One dog had evidence of a ureteral stricture at the ectopic ureteral orifice, and this dog also had hydroureter and hydronephrosis on the ipsilateral side. Four of 48 ectopic ureteral units had multiple fenestrations, and 5 of 48 ectopic ureteral units had evidence of a ureteral trough. All ectopic ureters were intramural in nature on the basis of retrograde ureteropyelography and cystourethrography findings (Figure 2).

Fourteen of 30 (47%) patients had a short urethra and intrapelvic urinary bladder determined on the basis of cystourethrography. The median urethral length was 4.0 cm (range, 2.5 to 8 cm). Five of 30 (17%) dogs had evidence of a subjectively hypoplastic urinary bladder based on visible urinary bladder size and capacity.

A retrograde ureteropyelogram was performed for all renal units regardless of ectopia. Twenty-three of 48 (48%) ectopic ureteral units had hydroureter, and 23 of 48 (48%) ectopic ureteral units had hydronephrosis or pyelectasia. One dog had hydroureter and another had hydronephrosis without evidence of an ectopic ureter on the ipsilateral side. Twenty-eight of 30 (93%) dogs had evidence of a vaginal defect including a persistent paramesonephric remnant (26/30), paramesonephric remnant with a vaginal septum (5/30), paramesonephric remnant with a dual vagina (4/30), a vestibulovaginal stenosis (1/30), and a vaginal membrane covering the entire vaginal orifice (1/30). Evidence of prominent lymphoid follicular hyperplasia in the vestibule, urethra, or urinary bladder was documented in 12 of 30 (40%) dogs, not all of which had previous urinary tract infections.

CLA-EU—The diode laser with a 600-μm end-fire laser fiber was used in 27 of 30 dogs (median, 20 W [range, 16 to 25 W]), and a Hol:YAG laser with a 400-μm end-fire laser fiber was used in 3 of 30 dogs (median, 10 W; 1 J at 10 Hz [range, 10 to 12 W and 0.7 to 1.2 J]) to ablate the medial aspect of the ectopic ureteral wall, as described. Median procedure time was 45 minutes for all dogs (range, 20 to 125 minutes). All dogs were discharged from the hospital either the same day or the morning following the procedure. There was no postoperative evidence of dysuria or discomfort in any dog. Five dogs had mild hematuria that lasted < 12 hours, with 1 of 5 dogs having had the Hol:YAG laser used (1 of 3 Hol:YAG-treated patients) and 4 of 5 having the diode laser used (4 of 27 diode-treated patients).

Immediate complications—No major complications were encountered. In 1 dog, there was concern that CLA-EU was performed slightly too proximally, where urinary bladder wall dissection with the laser was evident during cystoscopy. There was no evidence of contrast medium extravasation on cystography, but a urinary catheter was left in place overnight to keep the urinary bladder decompressed. No ill effects were seen after catheter removal or at the 6-week reevaluation.

Follow-up—At the 6- to 8-week cystoscopic reevaluation, all 48 neoureteral orifices were located within the urinary bladder, cranial to the urinary bladder trigone. A single orifice in 5 dogs was cranial to the urinary bladder trigone, but slightly more caudally located than desired. Ureteral orifices in these 5 dogs were able to be advanced 2 to 5 mm cranially at the time of reevaluation. During the initial CLA-EU procedure, all 5 of these dogs had poorly defined urinary bladder trigone regions, 3 of which were hypoplastic, so the ureteral orifice was created in a safe location to avoid the risk of extravasation. Once the urinary bladder was able to fill and expand more appropriately, the new trigone was more defined at the 6- to 8-week reevaluation. One dog had a polypoid type of proliferation seen along the laser tract and around the neoureteral orifice. The tissue was biopsied, and lymphoplasmacytic polypoid cystitis was the histopathologic diagnosis. The orifice was patent with a strong urine stream, and no evidence of hydroureter was evident on retrograde ureteropyelography. This same patient had a repeat cystoscopy 8 weeks later during an ovariohysterectomy and hydraulic occluder placement, and the polypoid reaction was no longer present. The 1 dog with severe hydroureter and hydronephrosis secondary to the ectopic ureteral stricture had dramatic improvement in the ureteral-pelvic dilation on the retrograde ureteropyelogram. All dogs with hydroureter or hydronephrosis had either stable or improved measurement at the 6- to 8-week reevaluation (**Figure 4**).

Bacteriologic culture of urine samples was performed as described, and 11 of 30 (37%) dogs had at least 1 positive bacteriologic culture result after CLA-EU. Seven of 30 dogs had positive culture results at 2 to 4 weeks, 0 of 30 had positive results at 8 weeks, 4 of 30 had positive results at 3 months, 4 of 30 had positive results at 6 months, and 4 of 30 dogs had positive culture results thereafter. Nine of 30 (30%) dogs had > 1 urinary tract infection after correction of ectopic ureters. Only 2 of these 9 dogs were persistently incontinent.

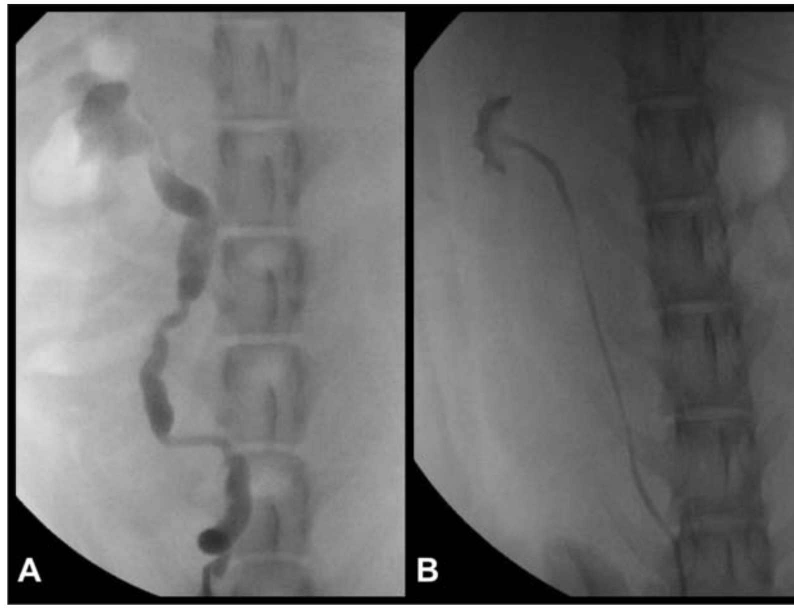

Figure 4—Fluoroscopic images of the urinary tract in a female dog with a right-sided ectopic ureter undergoing retrograde ureteropyelography. A—Notice the right-sided hydroureter and hydronephrosis evident before correction via CLA-EU. B—Eight weeks after CLA-EU, notice that the ureter is now a normal size and the renal pelvis has mild pyelectasia with a slightly abnormally shaped renal pelvis.

Postprocedural follow-up time was a median of 2.7 years (range, 12 to 62 months). According to the owner questionnaires and telephone conversations, 23 of 30 (77%) dogs became completely continent after CLA-EU and with additional treatment as needed (**Table 1**). The median urinary continence score prior to the procedure was 3 of 10 (range, 1 to 7). At 2 weeks after the procedure, the median urinary continence score was 10 of 10 (range, 3 to 10), and at 6 weeks, the median value was also 10 of 10 (range, 3 to 10). Overall, complete urinary continence from the procedure alone was seen in 21 of 30 (70%) patients at 1 week after the procedure, which decreased to 17 of 30 (57%) patients at 6 weeks, prior to starting supplemental treatment.

At the time of last follow-up, 14 of 30 (47%) dogs did not require any other treatments (medications, bulking-agent injection, colposuspension, or placement of an artificial urethral sphincter [ie, hydraulic occluder]) to maintain urinary continence. In 16 residually incontinent dogs, medical management was implemented; phenylpropanolamine (1 to 2 mg/kg, PO, q 8 to 12 h) was effective in 3 of the 16 dogs, whereas diethylstilbestrol (0.1 to 0.3 mg/kg, q 24 h for 7 days, then once weekly) was not effective in any of the 5 patients it was tried on. Therefore, medical treatment improved the urinary continence rate from 47% (14/30 dogs) to 57% (17/30 dogs). Transurethral bulking-agent injections (bovine collagen, 5 dogs; hydroxyapatite, 2 dogs) were performed in 7 of 13 residually incontinent patients after adjunctive medical management failed and were effective in 2 of these 7 dogs, improving the overall urinary continence rate to 63% (19/30 dogs). Five of 11 residually incontinent patients that failed medical or bulking-agent intervention had a hydraulic occluder placed. This was effective in 4 of 5 dogs, improving the overall urinary continence rate to 77% (23/30 dogs). Two patients had a colposuspension performed during the course of the study, and neither procedure was effective long term.

Owners considered the outcome for their dogs either moderately improved (2/30), good (2/30), or excellent (26/30), with no reports of a poor outcome or minimal improvement. All owners felt that if faced with the same clinical situation, they would elect to have CLA-EU performed again on their pet. At the time of long-term follow-up, all patients but 1 were still alive. The 1 dog that was deceased was ultimately euthanized for aggressive behavior issues > 3 years after the procedure.

Table 1—Urinary continence score* based on information from owner questionnaire for 30 incontinent female dogs with intramural ectopic ureters before and after CLA-EU.

Urinary continence score*	No. of dogs (%)		
	Before CLA-EU	Six weeks after CLA-EU alone	After CLA-EU with additional treatment
1	10 (33)	0	0
2	4 (13)	0	0
3	7 (23)	1 (3)	0
4	5 (17)	0	0
5	2 (7)	4 (13)	1 (3)
6	1 (3)	3 (10)	3 (10)
7	1 (3)	2 (7)	0
8	0	3 (10)	3 (10)
9	0	0	0
10	0	17 (57)	23 (77)

*Scores are as follows: 1 = minimally continent (leaking urine all the time without being able to make a puddle), 5 = moderate (leaking urine when lying down or walking and playing but can make a puddle of urine during micturition), and 10 = fully continent (not leaking urine at all).

Discussion

Results of the present study suggested that treatment of intramural ectopic ureters in female dogs via CLA-EU is safe, is associated with few complications, and produces similar treatment outcomes to those previously reported for open surgical management of ectopic ureters in female dogs. The long-term urinary continence rate following CLA-EU alone was 47% and up to 77% with the addition of medical, cystoscopic, or surgical interventions. Considering that not all patients with refractory urinary incontinence had supplemental treatments, this overall urinary continence score could potentially be higher. All owners were satisfied with the procedure, and 87% (26/30) considered the outcome excellent.

Traditional surgical techniques for the treatment of ectopic ureters include the following: neoureterostomy with ligation of the distal ureteric tunnel, neoureterostomy with urethral-trigonal reconstruction, neoureterocystostomy or ureteral transposition, and ureteronephrectomy.[1–3,5,8–12,14] These procedures require a laparotomy, cystotomy, urethrotomy, and ureterotomy or the removal of the affected kidney and ureter. Considering the low reported postsurgical urinary continence rates in female dogs (between 25% and 58%),[1–3,5–12,14] we investigated CLA-EU as an alternative, less invasive technique, which can be performed simultaneously with a diagnosis of the ectopic ureters.[1,10,11]

In a study[11] comparing neoureterostomy with ligation of the distal portion of the tract and neoureterostomy with urethral-trigonal reconstruction, significant differences between the success of these 2 techniques were unable to be detected; however, a better result with ligation (50% urinary continence rates) over reconstruction (29% urinary continence rates) was found. The suggested benefits of dissection of the distal portion of the ureteral tract inside the urethra, to try to restore an internal sphincter, diminish urinary stasis in the ureteral tunnel, and decrease the risk of recanalization,[1] may not be substantial. This may be why the patients with ligation alone as well as the patients that underwent CLA-EU in which the urethra and distal ureteral tracts were minimally manipulated did similarly better than did those with dissection and reconstruction. It has been suggested that manipulation of the urethral sphincter during reconstruction (in dogs with sphincter mechanism urinary incontinence; 75% to 89% of female dogs with ectopic ureters) may worsen the outcome by causing further damage to this already incompetent sphincter mechanism.[4,11,13] The benefit of the CLA-EU over the neoureterostomy with ligation is that the entire distal ectopic ureteral tunnel is ablated, preventing urinary stasis, pooling, and recanalization, without the muscular manipulation of the urethra that is encountered during the urethrotomy for surgical fixation.

As supported by results of previous studies, most dogs with ectopic ureters described in the present study were large breeds and purebreds. Golden and Labrador Retrievers were overrepresented. It has been suggested in the literature[1,5,14] that female dogs > 20 kg (44 lb) have a higher lifetime risk of urinary incontinence than do those < 20 kg.

Dogs with ectopic ureters commonly have urinary tract infections,[1,11] and results of the present study support this finding, considering that 83% (25/30) of dogs had positive bacteriologic culture results prior to CLA-EU. Interestingly, most dogs had an *E coli* infection, and nearly all were susceptible to routine antimicrobial treatment. The rate of infection decreased in the lifetime of the animal after undergoing CLA-EU (83% vs 37%). Those that had recurrent urinary tract infections were not more likely to be persistently incontinent, although during an infection, some dogs would revert to temporary urinary incontinence. This would suggest that all dogs with a history of ectopic ureters, regardless of outcome, should be routinely tested for urinary tract infections.

Of the 7 persistently incontinent dogs, 3 were unilaterally affected and 4 were bilaterally affected, and of the 14 dogs that were cured by CLA-EU, 50% were unilaterally affected and 50% bilaterally affected, supporting results of the previous studies,[1,5,11,14] which suggested that outcome is likely not associated with unilateral versus bilateral ectopic ureters. Ectopic orifice location was more commonly found in the distal portion of the urethra in 6 of 7 persistently incontinent dogs. In the dogs that were fully continent following CLA-EU, 6 of 14 were proximal and 8 of 14 were distal in location.

The normal functional urethral length has been previously reported to be approximately 5 cm, regardless of patient size.[13] Urethral length is suggested to be shorter in dogs with ectopic ureters on the basis of the experience of many endoscopists. This length was measured in each patient, with the median length being 4 cm (range, 2.5 to 8 cm).

Of the 14 (47%) dogs with documented intrapelvic urinary bladder and short urethra, only 3 were immediately continent after CLA-EU, and 9 were continent after medications or supplemental interventions. This may suggest that dogs with an intrapelvic urinary bladder and short urethra have a stronger likelihood of failure of the procedure and will likely need supplemental support to achieve urinary continence.

The difference between the diode laser and Hol:YAG laser is the wavelength. The Hol:YAG laser works at a wavelength of 2,100 nm, and it is best for the fragmentation of stones. It can also be used for tissue ablation but works in a pulsed fashion and can result in more hemorrhage during ablation. The diode laser works at 980 nm and is best for tissue ablation, which usually provides both coagulation and cutting, with essentially no hemorrhage. The laser fiber is larger for the diode, making it much harder to manipulate during flexible cystoscopy.[4] The authors prefer the diode laser because the continuous cutting mode provides an ablation that is typically fast and exact. The Hol:YAG laser can be used as well, but has a pulsed activity that results in more of an intermittent surge of pulsing energy, which causes a jumping type of ablation, and the mild amount of hemorrhage can obscure the cystoscopy image. To avoid excessive bleeding with the Hol:YAG laser, contact mode should be avoided and the laser fiber instead should be situated 0.1 to 0.5 mm from the desired tissue to be ablated to allow for the power to coagulate, rather than cut the tissue directly. Since the advent of laser lithotripsy, more veterinarians have an Hol:YAG laser available, making this a reasonable alternative. The postprocedural hematuria that was seen did not seem to be associated with the type of laser used, given that 1 of 3 Hol:YAG patients and 4 of 27 diode patients had evidence of mild hematuria within 24 hours after the procedure. This could have been due to the cystoscopy alone, the ureteral catheterization, or the lasering of the ureter or vaginal membrane.

The patients of the present study were all imaged with cystourethroscopy and vaginoscopy as well as retrograde ureteropyelography and cystourethrography. The authors found that, in combination, all genitourinary anomalies, including both upper and lower urinary tract and vaginal defects, were able to be documented during the procedure. This allowed an accurate assessment of concurrent anatomic anomalies without the need for multiple diagnostic procedures, saving time and expense. In the present study, all dogs had a concurrent urinary tract anatomic anomaly other than the ectopic ureter, most commonly a paramesonephric remnant, followed by hydronephrosis, hydroureter, intrapelvic urinary bladder, hypoplastic urinary bladder, and a vaginal septum or dual vagina.

Nearly half of the patients had evidence of hydroureter, hydronephrosis, or both on the affected side, which is slightly higher than previously reported.[1,3,8,14] This supports the recommendation that finding evidence of dilation on ultrasonographic examination in a young incontinent dog should encourage further investigation for ectopic ureters, but they should still be considered in cases where no dilation is present. The exact pathogenesis is not clear, but these findings may be secondary to functional or physical ureteral obstruction. Other suggested causes include congenital anatomic abnormality, urine reflux during urination, lack of peristalsis, and chronic pyelonephritis.[1,18] All dogs described in the present report had either improvement or stabilization of hydroureter or hydronephrosis at the follow-up ureteropyelogram, supporting improvement after ectopic ureteral correction. Progressive hydroureter or hydronephrosis can result in irreversible renal damage,[21–26] which further supports ectopic ureteral correction as early as possible.

Most patients described in the present study had a vaginal defect. All abnormal vaginal tissue was ablated to prevent vaginal pooling and chronic infections. This is the first study, to the authors' knowledge, of endoscopic and laser correction of a dual vagina, which was seen in 13% of cases. The literature is not clear on whether vaginal defects contribute to persistent urinary incontinence or recurrent infections,[27–29] but prior to cystoscopy, the defects were not always diagnosed, and with traditional surgical correction, they are typically not fixed because of the need for invasive surgery (vaginectomy). With the ease of laser ablation during vaginoscopy, this is now considered a routine addition to the procedure, and correction of all defects should be considered whenever possible. A vaginal septum or remnant was not considered synonymous with vestibulovaginal stenosis, which has been previously reported on the basis of contrast vaginoscopy.[27–29] These patients can have very similar-looking vaginogram studies, but on cystoscopy, the membrane seen is longitudinal rather than concentric as described for vestibulovaginal stenosis. A large number of dogs were also documented to have lymphoid follicular hyperplasia throughout the vestibule or urinary bladder. This is classically seen in dogs with chronic urinary tract infections.

The entire procedure was typically short (median time, 45 minutes), including both diagnostic testing and treatment of both the ureter and vaginal defect, with most dogs being discharged from the hospital the same day as the procedure. This was considered ideal for the combination of both diagnosis and treatment of ectopic ureters in these dogs.

Follow-up cystoscopy performed at 6 to 8 weeks following CLA-EU showed no evidence of ureteral stricture, recannulization, or vaginal defect regrowth. During the reevaluation, it is possible that the neoureteral orifice could appear caudally displaced within the urinary bladder neck, which was seen in 5 of our patients. The urinary bladder shape can become more apparent as it is allowed to fill after ectopic correction. As the previously hypoplastic urinary bladder stretches, the trigone becomes better defined, making the ideal location for the new orifice more obvious. During follow-up, the orifice was advanced when necessary. Since the time of the present study, the authors recommend repeating the cystoscopy only in dogs that are persistently incontinent to see whether advancement is necessary, at which time either a transurethral bulking agent can be injected or a urethral hydraulic occluder can be placed if necessary. Interestingly, of the 5 dogs that had their ureters advanced, only 1 dog was ultimately continent, and this was not secondary to advancement of the ureters but was instead achieved with the addition of a hydraulic occluder, suggesting that advancing the ureters a few millimeters more cranially in dogs that fail the procedure is likely not tremendously beneficial in outcome.

In the present study, there were very few short- and long-term complications seen. The surgical literature suggests a 6% to 25% complication rate[11,14,17] most commonly associated with ureteral stricture at the surgical site, resulting in progressive hydroureter and hydronephrosis. In the largest veterinary study[14] to date, 50% of the dogs that had their ureter reimplanted had evidence of progressive hydroureter and hydronephrosis, also suggesting possible ureteral stricture development at the ureterovesicular junction. Sixteen percent of the dogs in that same study[14] had postprocedural dysuria. All dogs described in the present study with previously documented hydroureter and hydronephrosis had either improvement or resolution in their dimensions at their reevaluation. The polypoid type of proliferation seen in 1 dog along the laser tract resolved 8 weeks later without treatment. This was of no consequence clinically or anatomically at the subsequent reevaluation. In an additional dog, which was excluded from the study because of the lack of consistent follow-up, the 6-week reevaluation showed a similar proliferative reaction around the neoureteral orifice with progressive hydroureter and hydronephrosis, suggesting that this reaction resulted in a ureteral obstruction. This was subsequently seen 1 additional time in approximately 60 cases by the authors to date. This is likely an unusual reaction to either the laser or to an infection. In a recent retrospective study[20] that used CLA-EU to treat 16 dogs, 1 dog had evidence of a neoureteral orifice reaction to the laser. The authors currently recommend that all patients, regardless of treatment modality (surgery or CLA-EU) should have a follow-up ultrasonographic examination to ensure there is no evidence of progressive hydronephrosis, which could suggest neoureteral orifice stricture or reaction.

On the basis of the careful follow-up and long-term assessment by owners, all dogs had a clinical improvement in their urinary continence scores from a median of 3 of 10 to 10 of 10. Forty-seven percent of dogs did not require any other supplemental procedures. In the 16 residually incontinent dogs, medical management was implemented and effective < 20% of the time. The dose of phenylpropanolamine was limited typically to 1 to 2 mg/kg, PO, 3 times daily, and there are reports[13] of doses as high as 3 to 4 mg/kg (1.4 to 1.8 mg/lb) 3 times daily, which could have been more effective. It would be important to monitor for adverse effects at such a high dose. Transurethral bulking-agent injections were performed in nearly half of the dogs in which CLA-EU and medical treatment failed and were effective in < 30% of them. When a hydraulic occluder was placed, it was effective in 80% of patients, suggesting further investigation of its use in dogs with refractory urinary incontinence. If owners are set up for staged procedures if necessary, particularly if a hydraulic occluder can be placed during a spaying procedure, necessitating only 1 open surgery, then the authors would predict much higher overall urinary continence scores.

Persistent urinary incontinence is likely attributable to concurrent urethral, sphincter, and vesicular abnormalities and often necessitates additional medical intervention (eg, phenylpropanolamine, diethylstilbestrol, and oxybutynin), transurethral injections of a submucosal bulking agent, or further surgery (eg, colposuspension, urethropexy, cystopexy, or the placement of an artificial urethral sphincter [ie, hydraulic occluder]). Urinary continence was reported previously to be restored with medications in 32% to 38% of dogs after surgery,[10,11] although the rate was only 18.75% in the present study. In dogs with primary sphincter mechanism urinary incontinence without ectopic ureters, bulking agents can be effective in 50% to 83% of cases.[10,30] It is not known whether urethral bulking agents are equally efficacious in persistently incontinent dogs that have ectopic ureters versus those dogs with primary urethral sphincter mechanism incompetence without ectopic ureters, but in the authors' experience, bulking agents are less effective in dogs with previous or concurrent ectopic ureters, and only 28.5% of dogs in the present study had successful outcomes after injections. These dogs have very wide and short urethras, so achieving urethral luminal closure was very difficult.

The primary limitation of the present study was the small number of patients, the variable anatomy of each patient, and the variable supplemental treatments each patient had. Each patient had the procedure performed by the same clinician and was followed up carefully and extensively. Because all imaging and follow-up was consistent, the true incidence of anatomic abnormalities, procedural complication rates, short- and long-term urinary continence rates, and ultimate satisfaction was obtained, contrary to the variability in other studies on ectopic ureters.

Unfortunately, no urethral pressure profilometry studies were conducted, and this information would have been helpful in characterizing sphincter incompetence before and after CLA-EU and potentially associated urethral sphincter mechanism incompetence with outcome.

In conclusion, the use of CLA-EU is safe and at least as effective as the traditional surgical techniques previously reported. This procedure is met with few complications and can be considered at the time of the diagnosis of ectopic ureters. This procedure allows the clinician to avoid invasive surgery until it is known whether the procedure was successful, at which time the patient can undergo supplemental correction procedures at the time of routine ovariectomy or ovariohysterectomy.

a. Berent A, Mayhew P. Cystoscopic-guided laser ablation of intramural ureteral ectopia in 11 dogs (7 female, 4 males) (abstr). *Vet Surg* 2007;36:E3.
b. Berent A, Mayhew P. Cystoscopic-guided laser ablation of intramural ureteral ectopia in 12 female dogs (abstr). *J Vet Int Med* 2007;21:600.
c. Smith AL, Radlinsky M, Rawlings C. The use of cystoscopic guided laser ablation for the treatment of intramural ureteral ectopia: a retrospective evaluation. (abstr). *Vet Surg* 2009;38:E46.
d. Rigid endoscope, 4-mm 30° lens, Karl Storz Endoscopy, Culver City, Calif.
e. Rigid endoscope, 2.7-mm 30° lens, Richard Wolf, Vernon Hills, Ill.
f. Rigid endoscope, 1.9-mm 30° lens, Karl Storz Endoscopy, Culver City, Calif.
g. ISO-C, Fluoroscopy, Siemens, Malvern, Pa.
h. Weasel Wire 0.025- or 0.035-inch hydrophilic angle-tipped guidewire, Infiniti Medical LLC, Menlo Park, Calif.
i. 4-5F open-ended ureteral catheter, Cook Medical Inc, Bloomington, Ind.
j. Omnipaque, Iohexol 240 mg/mL, GE Healthcare, Princeton, NJ.
k. 600-µm diode laser fiber and 25-W diode laser, Lumenis Inc, Santa Clara, Calif.
l. 400-µm Hol:YAG laser fiber and 30-W Hol:YAG lithotrite, Convergent Inc, Alameda, Calif.
m. Contigen, Bard Medical, Covington, Ga.
n. Coaptite Injectable Implant, Boston Scientific Corp, Natick, Mass.
o. Hydraulic Occluder, DocXS, Ukiah, Calif.

References

1. McLoughlin MA, Chew DJ. Diagnosis and surgical management of ectopic ureters. *Clin Tech Small Anim Pract* 2000;15:17–24.
2. Tattersall JA, Welsh E. Ectopic ureterocele in a male dog: a case report and review of surgical management. *J Am Anim Hosp Assoc* 2006;42:395–400.
3. Steffey MA, Brockman DJ. Congenital ectopic ureters in a continent male dog and cat. *J Am Vet Med Assoc* 2004;224:1607–1610.
4. Berent AC, Mayhew PD, Porat-Mosenco Y. Use of cystoscopic-guided laser ablation for treatment of intramural ureteral ectopia in male dogs: four cases (2006–2007). *J Am Vet Med Assoc* 2008;232:1026–1034.
5. Holt PE. Urinary incontinence in dogs and cats. *Vet Rec* 1990; 127:347–350.
6. Owen RR. Canine ureteral ectopia—a review. 1. Embryology and aetiology. *J Small Anim Pract* 1973;14:407–417.
7. Owen RR. Canine ureteral ectopia—a review. 2. Incidence, diagnosis and treatment. *J Small Anim Pract* 1973;14:419–427.
8. Dean PW, Bojarab MJ, Constantinescu GM. Canine ectopic ureter. *Compend Contin Educ Pract Vet* 1988;10:146–157.
9. Mason LK, Stone EA, Biery DN, et al. Surgery of ectopic ureters: pre and postoperative radiographic morphology. *J Am Anim Hosp Assoc* 1990;26:73–79.
10. McLaughlin R, Miller CW. Urinary incontinence after surgical repair of ureteral ectopia in dogs. *Vet Surg* 1991;20:100–103.
11. Mayhew PD, Lee KC, Gregory SP, et al. Comparison of two surgical techniques for management of intramural ureteral ectopia in dogs: 36 cases (1994–2004). *J Am Vet Med Assoc* 2006;229: 389–393.
12. Stone EA, Mason LK. Surgery of ectopic ureters: types method of correction, and postoperative results. *J Am Anim Hosp Assoc* 1990;26:81–88.
13. Lane IF, Lappin MR, Seim HB III. Evaluation of results of preoperative urodynamic measurements in nine dogs with ectopic ureters. *J Am Vet Med Assoc* 1995;206:1348–1357.
14. Holt PE, Moore AH. Canine ureteral ectopia: an analysis of 175 cases and comparison of surgical treatments. *Vet Rec* 1995;136:345–349.
15. Cannizzo KL, McLoughlin MA, Mattoon JS, et al. Evaluation of transurethral cystoscopy and excretory urography for diagnosis of ectopic ureters in female dogs. *J Am Vet Med Assoc* 2003;223: 475–481.

16. Hays HM. Breed associations of canine ectopic ureter: a study of 217 female cases. *J Small Anim Pract* 1984;25:501–504.
17. Holt PE, Gibbs C, Pearson H. Canine ectopic ureter—a review of twenty-nine cases. *J Small Anim Pract* 1982;23:195–208.
18. Samii VF, McLoughlin MA, Mattoon JS, et al. Digital fluoroscopic excretory urography, digital fluoroscopic urethrography and helical CT and cystoscpy in 24 dogs with suspected ureteral ectopia. *J Vet Intern Med* 2004;18:271–281.
19. McCarthy TC. Transurethral cystoscopy and diode laser incision to correct an ectopic ureter. *Vet Med* 2006;101:558–559.
20. Smith AL Radlinsky MG, Rawlings CA. Cystoscopic diagnosis and treatment of ectopic ureters in female dogs: 16 cases (2005–2008). *J Am Vet Med Assoc* 2010;237:191–195.
21. Wen JG, Frokiaer J, Jorgensen TM, et al. Obstructive nephropathy: an update of the experimental research. *Urol Res* 1999;27:29–39.
22. Coroneos E, Assouad M, Krishnan B, et al. Urinary obstruction causes irreversible renal failure by inducing chronic tubuointerstiital nephritis. *Clin Nephrol* 1997;48:125–128.
23. Wilson DR. Renal function during and following obstruction. *Ann Rev Med* 1977;28:329–339.
24. Fink RW, Caradis DT, Chmiel R, et al. Renal impairment and its reversibility following variable periods of complete ureteric obstruction. *Aust N Z J Surg* 1980;50:77–83.
25. Kerr WS Jr. Effect of complete ureteral obstruction for one week on kidney function. *J Appl Physiol* 1954;6:762–772.
26. Vaughan ED Jr, Sweet RE, Gillenwater JY. Unilateral ureteral obcclusion: pattern of nephron repair and compensatory response. *J Urol* 1973;109:979–982.
27. Wang KY, Samii VF, Ches DJ, et al. Vestibular, vaginal and urethral relations in spayed dogs with and without lower urinary tract signs. *J Vet Intern Med* 2006;20:1065–1073.
28. Crawford JT, Adams WM. Influence of vestibulovaginal stenosis, pelvic bladder, and recessed vulva on response to treatment for clinical signs of lower urinary tract disease in dogs: 38 cases (1990–1999). *J Am Vet Med Assoc* 2002;221:995–999.
29. Kyles AE, Vaden S, Hardie EM, et al. Vestibulovaginal stenosis in dogs: 18 cases (1987–1995). *J Am Vet Med Assoc* 1996;209:1889–1893.
30. Barth A, Reichler IM, Hubler M, et al. Evaluation of long-term effects of endoscopic injection of collagen into the urethral submucosa for treatment of urethral sphincter incompetence in female dogs: 40 cases (1993–2000). *J Am Vet Med Assoc* 2005;226: 73–76.