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J. S. Wolf Jr. · R. Marcovich

Laparoscopic tissue approximation

Abstract Although many extirpative urologic laparoscopic procedures are starting to be generally accepted, there is limited application of recontructive urologic laparoscopic procedures. Difficulties with laparoscopic tissue approximation account for a large portion of the slow development of recontructive laparoscopic urology. In this paper, the current state of laparoscopic tissue approximation is reviewed, research efforts in this area are summarized, and future directions are considered. The discussion addresses available techniques and devices, as well as those in development for future application.

Nearly a decade ago, the introduction of laparoscopy to the specialty of urology was greeted with initial enthusiasm followed by general skepticism. Acceptance of the new modality has gradually occurred, but only for select, relatively simple operations. Few at that time would have envisioned the strides taken by laparoscopic urologists over the past 10 years. Yet now, laparoscopy is standard of care for a variety of indications at several large centers.

While laparoscopic urology has undoubtedly expanded, with mainly ablative and extirpative procedures at the forefront, reconstructive laparoscopy has thus far seen less exuberant growth. The challenges of intracorporeal tissue approximation bear the major responsibility for this fact. While surgeons specializing in laparoscopy can become quite adept at intracorporeal suturing with a free needle and suture, the majority of urologists, who do not have the luxury of performing a large volume of such procedures, may be unable to gain the necessary skills to efficiently undertake complex reconstructive surgery. Thus, development of new methods of tissue approximation is requisite for the continued acceptance, and indeed expansion, of laparoscopic urology.

J. S. Wolf Jr. (✉) · R. Marcovich
1500 East Medical Center Drive, Section of Urology, TC 2916, University of Michigan, Ann Arbor, MI 48109-0330, USA
e-mail: wolfs@umich.edu
Tel.: +1 734-764-8397; Fax: +1 734-936-9127

The purpose of this paper is to review the current state of laparoscopic tissue approximation, to summarize research efforts in this area, and to consider future directions. The discussion will address available techniques and devices, as well as those in development for future application.

Indications for laparoscopic tissue approximation

In general, several different sets of maneuvers necessary in surgery may be conceptualized as tissue approximation. The two most obvious are anastomosis, or "the operative union of two hollow or tubular structures" [21], and wound closure, as exemplified by repair of cystotomy. Less obvious are fixation of an organ to another structure, as in nephropexy or colposuspension, and hemostasis, which is merely the approximation of vascular tissue to itself in order to arrest hemorrhage. Table 1 summarizes indications for laparoscopic tissue approximation.

Unfortunately, the laparoscopic environment is inherently hostile to traditional methods of tissue approximation. The surgeon must work in an enclosed space, relying only on two-dimensional imaging. Fixed angles of approach and decreased tactile feedback hamper efficient action. Even the simplest of tasks, such as loading a needle onto a driver, can be frustratingly daunting through the laparoscope. Given these obstacles, the catalogue of laparoscopic reconstructive procedures accomplished to date is impressive. Table 2 provides a list of such operations; this table is intended to be a representative sampling of procedures rather than an exhaustive index.

Methods of laparoscopic tissue approximation

Five methods of laparoscopic tissue approximation have been applied to date, either clinically or experimentally (Table 3). Table 4 compares the advantages

Table 1 Indications for laparoscopic tissue approximation

1. Anastomosis	
	Pyeloplasty
	Ureteroureterostomy
	Ureteroneocystostomy
	Ureteroenterostomy
	Enterocystoplasty
	Urethrovesicostomy
	Bowel anastomosis
2. Wound closure	
	Ureterotomy
	Repair of vesico-ureteral reflux (extravesical)
	Cystotomy
	Pyelotomy
3. Fixation	
	Nephropexy
	Colposuspension
	Urethropexy
4. Hemostasis	

and disadvantages of each method. Except for only a few reports of the clinical use of tissue glue for tissue approximation (as opposed to sealing, for which tissue glues are commonly applied), only modalities based on standard open techniques, i.e., use of sutures, clips, and staples, have thus far been applied in humans.

Standard modalities – sutures, clips, and staples

The challenge has been to develop effective and increasingly efficient modes to deliver these implements, which are simply tools adapted from open surgery. Historically, the first method of laparoscopic tissue approximation was free-needle suturing, with securing by extracorporeal knot-tying. This prompted the development of a variety of pre-tied knots and pushing devices. This technique is inefficient, however, because it requires multiple passages through the trocar and does not allow the surgeon to control the knots already at the tissue when the next knot is thrown. Extracorporeal knot-tying has thus, for the most part, fallen by the wayside in urologic laparoscopy.

Intracorporeal suturing and knot-tying have now become the laparoscopic "gold standard", to which future innovations in tissue approximation will be compared. Intracorporeal suturing was initially undertaken without specialized laparoscopic grasping instruments. Increasing efficiency in performing this task has occurred through the commercial design of specialized instruments, as well as insight into the kinematics of intracorporeal technique. Implements developed specifically to improve the ergonomics of intracorporeal free-needle suturing (IFNS) include pin-vise graspers, as well as curved-jaw drivers modeled after microsurgical instruments, such as the Szabo-Berci set (Karl Storz Endoscopy, Tuttlingen, Germany) (Fig. 1). These devices have addressed the problem of appropriate torque application for driving needles through tissues and are a significant improvement on standard graspers. The availability of several varieties of drivers without finger rings has improved the fluidity of suturing and reduced wear and tear on the surgeon's hands.

A multitude of procedures have been performed clinically with IFNS in the last 10 years, including procedures for female stress urinary incontinence, nephropexy, pyeloplasty, repair of vesico-ureteral reflux, ureteroureterostomy, cystotomy repair, and most recently, urethrovesical anastomosis after radical prostatectomy (see Table 2).

IFNS has seen significant use in the laboratory setting as well. In 1993, Atala and coworkers [7] first reported the laparoscopic repair of vesicoureteral reflux in minipigs using IFNS to create a Lich-Gregoir type of reconstruction, which has subsequently been performed clinically in limited series. In 1997, McDougall and associates [35] compared IFNS and the Endo-Stitch device (United States Surgical Corp, Norwalk, CT, USA.) for laparoscopic pyeloplasty in 16 mini-pigs. There were comparable satisfactory results in both treatment arms. More recently, Dechet et al. [13] performed laparoscopic transureteroureterostomy (TUU) in pigs using IFNS, with operative times ranging from 2.5 to 6 hours, and an 89% radiographically-determined success rate.

In the ongoing attempt to improve ease and efficiency of intracorporeal suturing, and to reduce operative times, mechanical suturing devices have been introduced. The most widely used such apparatus is the Endo-Stitch (Fig. 2), which is essentially a laparoscopic sewing machine. A needle with suture loaded at the midpoint is passed back and forth between the two arms of the device, using a toggle switch on the instrument's handle to release one end of the needle and grasp the other end [2]. Table 4 summarizes the advantages and disadvantages of this implement. The Endo-Stitch is commonly applied when intracorporeal suturing of significant lengths of tissue is required. Docimo and colleagues [14] reported the first purely laparoscopic gastrocystoplasty, in which the Endo-Stitch was used for anastomosis of the stomach patch and the bladder. Despite use of this mechanical device, the procedure required almost 11 h to complete. In 1998, Wolf and Taheri [64] reported the first laparoscopic urinary undiversion; the Endo-Stitch was used to accomplish the ileovesicostomy, for which the operative time was 5 h. Cadeddu and coworkers [10] reported on their experience with laparoscopic repair of enterocele. Three women underwent a modified Moschcowitz repair with obliteration of the hernia sac by approximation of the posterior vaginal fascia to the rectum using the Endo-Stitch. Operative time ranged from 3 to 5 h. Bauer et al. [8] have reported the largest series of laparoscopic pyeloplasty to date, in which all intracorporeal suturing was performed with the Endo-Stitch. In this study, the outcome of the procedure, as measured radiographically, was equivalent to that of a cohort that underwent open pyeloplasty. Although operative

Table 2 Reports of laparoscopic reconstructive procedures in the literature[a] (*FNS* free-needle suturing)

Investigator	Laparoscopic procedure	Methods
Human studies		
Abbou et al. 1999 [1]	Urethrovesical anastomosis	Intracorporeal FNS
Antiphon et al. 1999 [6]	Burch colposuspension	Intracorporeal FNS, mesh, clips
Bauer et al. 1999 [8]	Pyeloplasty	Endo-Stitch
Cadeddu et al. 1996 [10]	Enterocele repair	Endo-Stitch; Lapra-Ty
Docimo et al. 1995 [14]	Gastrocystoplasty	Endo-stitch
Ehrlich et al. 1994 [16]	Vesico-ureteral reflux repair	Intracorporeal FNS
Fornara et al. 1997 [17]	Nephropexy	Suture, tied extracorporeally
Gatti et al. 1999 [18]	Percutaneous trigonoplasty	Intracorporeal FNS
Guillonneau et al. 2000 [20]	Urethrovesical anastomosis	Intracorporeal FNS
Hubner et al. 1994 [22]	Nephropexy	Staples
Kerbl et al. 1993 [25]	Bladder closure	Endo-GIA stapler
Kozminski and Partamian 1992 [27]	Ileal conduit	Intracorporeal bowel stapling; extra-corporeal ureteroenterostomy
Lakshmanan et al. 2000 [29]	Vesico-ureteral reflux repair	Intracorporeal FNS
Lorenzo et al. 1997 [31]	Appendicovesicostomy	Extracorporeal anastomosis
McDougall 1996 [34]	Bladder neck suspension	Intracorporeal FNS; Lapra-Ty
Nakada et al. 1995 [37]	Pyeloplasty	Intracorporeal FNS; Lapra-Ty
Nezhat et al. 1992 [38]	Ureteroureterostomy	Intracorporeal FNS
Ou and Rowbotham 1999 [40]	Burch colposuspension	Clips & mesh
Parra et al. 1994 [42]	Cystotomy closure	Intracorporeal FNS
Polascik et al. 1995 [43]	Burch colposuspension	Intracorporeal FNS; Lapra-Ty
Rassweiler et al. 1999 [47]	Urethrovesical anastomosis	Intracorporeal FNS
Strand et al. 1997 [55]	Cutaneous ureterovesicostomy	Lap-assisted; extracorporeal suturing
Urban et al. 1993 [59]	Nephropexy	Intracorporeal FNS
Vancaille et al. 1991 [60]	Bladder neck suspension	Intracorporeal FNS
Vara-Thorbeck and Sanchez-de-Badajoz 1994 [61]	Ileal conduit	Extracorporeal ureteroenterostomy
Wolf and Taheri 1998 [64]	Ileovesicostomy	Endo-Stitch
Won et al. 1999 [65]	Burch colposuspension	Intracorporeal FNS vs "Tacker" & mesh
Animal studies		
Anderson et al. 1995 [3]	Colon pouch urinary diversion	Lap-assisted; extracorporeal uretero-enterostomy; no bowel anastomosis
Anidjar et al. 1996 [5]	Ureteroureterostomy	Fibrin glue
Atala et al 1993 [7]	Vesico-ureteral reflux repair	Intracorporeal FNS
Beduschi et al. 1999 [9]	Cystotomy repair	Fibrin glue
Cisek et al. 1999 [12]	Vesicourethral anastomosis	Clips with stay sutures
Dechet et al. 1999 [13]	Transureteroureterostomy	Intracorporeal FNS
Kerbl et al. 1993 [25]	Bladder closure	Endo-GIA stapler
Marcovich et al. 1999 [32]	Cystotomy repair	Cyanoacrylate glue, fibrin glue
Maxwell et al. 1998 [33]	Ureteroureterostomy	Nonperforating staples
McDougall et al. 1997 [35]	Pyeloplasty	Intracorporeal FNS, Lapra-Ty, Endo-Stitch
McKay et al. 1994 [36]	Ureteroureterostomy	Fibrin glue
Seibold et al. 1996 [50]	Ureteroureterostomy	Fibrin glue
Shalhav et al. 1999 [51]	Partial bladder replacement	Endo-Stitch, Lapra-Ty
Sung et al. 1999 [56]	Pyeloplasty	Robotic-assisted intracorporeal suturing
Wolf et al. 1997 [63]	Ureterotomy closure	Fibrin glue, laser, Endo-Stitch

[a] Larger series and/or initial reports

time was not discussed, this group's previous report of laparoscopic pyeloplasty had a mean operative time of 4.3 h [11].

Use of the Endo-Stitch in animal studies has been reported by Wolf and colleagues [63] in a trial of various methods of porcine ureterotomy closure, and by Shalhav and coworkers [51] for partial replacement of the bladder with biodegradable materials in pigs. In the former study, closure of ureterotomy with the Endo-Stitch was accomplished in an average time of 24 min, versus 40 min for closure with IFNS. The Endo-Stitch closures were found to leak less often and resulted in better histology than repairs with IFNS. In the latter study, anastomosis of synthetic patch material to the opened bladder was performed with the Endo-Stitch in an average of 121 min.

In the study of Shalhav and coworkers, Lapra-Ty clips (Ethicon Endo-Surgery, Cincinnati, OH, USA) (Fig. 3) were used to secure the four corner stitches of the patch. Lapra-Ty clips are locking, absorbable clips that are used to secure a suture to prevent it from pulling through the tissue, as an alternative to a knot of suture. Application of a Lapra-Ty clip is much easier and more rapid than laparoscopic knot-tying. Use of the Lapra-Ty has been reported as an adjunct to suturing in a number of clinical and investigational studies (Table 2). Sutures secured with this device have been shown to withstand supra-physiologic tension. [4]

Table 3 Methods of laparoscopic tissue approximation

Suture
Free-needle
Suture clip (e.g., Lapra-Ty)
Suture loom (e.g., Endo-Stitch)
Clips
Occlusive clip appliers (e.g., EndoClip, EndoPath, AcuClip)
Biting clip appliers (e.g., EndoUniversal 65, EndoPath EMS & EAS, Tacker)
Staples
Automatic linear staplers (e.g., EndoGIA, EndoPath, Articulator 35)
Cutting
Non-cutting
Tissue adhesives
Fibrin glue
Cyanoacrylate glue
Gelatin-resorcinol-formaldehyde glue
Laser welding

Fig. 1 Szabo-Berci needle driver and assisting forceps for laparoscopic free needle suturing (Photo courtesy of Karl Storz Endoscopy, Tuttlingen, Germany)

Another alternative to intracorporeal knot-tying with a free needle is the Suture Assistant (Ethicon Endo-Surgery), a reloadable unit that delivers knots on a suture placed intracorporeally.

One way in which surgeons have obviated the rigors of intracorporeal suturing and stapling has been to rather ingeniously perform the reconstructive portions of laparoscopic procedures extracorporeally, by bringing the target tissues out through trocar ports or sites, or through incisions later used for stoma creation. This technique has been quite useful in reconstructive procedures using bowel, especially for ureteroenterostomy in ileal conduit formation [27, 61]. To date, a laparoscopic *intracorporeal* sutured ureteroenterostomy has not been reported, but Anderson and colleagues [3] performed sutured extracorporeal laparoscopic-assisted

Table 4 Advantages and disadvantages of various methods of tissue approximation

Method	Advantage	Disadvantage
Suture		
Free-needle	Gold standard – emulates open technique	Time consuming
	Predictable tissue response	Instrumentation awkward
	Bio-absorbable	Hampered by 2-dimensional view
		Knot-tying difficult
		Need to re-grasp and position needle after each throw
Lapra-Ty	Obviates knot-tying	Same as Free-Needle except for knot tying
Endo-Stitch	Eliminates needle re-grasping and positioning	Needle hole always wider than suture
		Lack of articulation
	One instrument to both pass and catch needle	Tissue must be positioned between instrument arms
	Simplifies knot-tying	Straight needle not optimal for some purposes
		Cost
Clips	Eliminates tying/suturing vascular structures	Non-absorbable foreign body
		Applications limited
	Short learning curve	Cost
Staples	Simplifies bowel resection	Non-absorbable foreign body
	Hemostasis of vascular pedicles	Cost
Adhesives		
Fibrin glue	Biodegradable	Rapid fibrinolysis
	Easy of application	Lack of tensile strength
	Decreased tissue reactivity compared to suture	
	Hemostatic, Sealant	
Cyanoacrylate	Excellent bond and tensile strength	Biodegradable formulas not yet available
	Ease of application	Significant tissue reactivity
	Bacteriostatic	Not approved for internal use
		No experience in human laparoscopy
Laser weld	Causes fusion of tissues	Albumin tissue solder not FDA-approved
	Minimal inflammatory response	Limited experience in human laparoscopy
	No foreign substance present	Cost
	Immediate watertight seal	

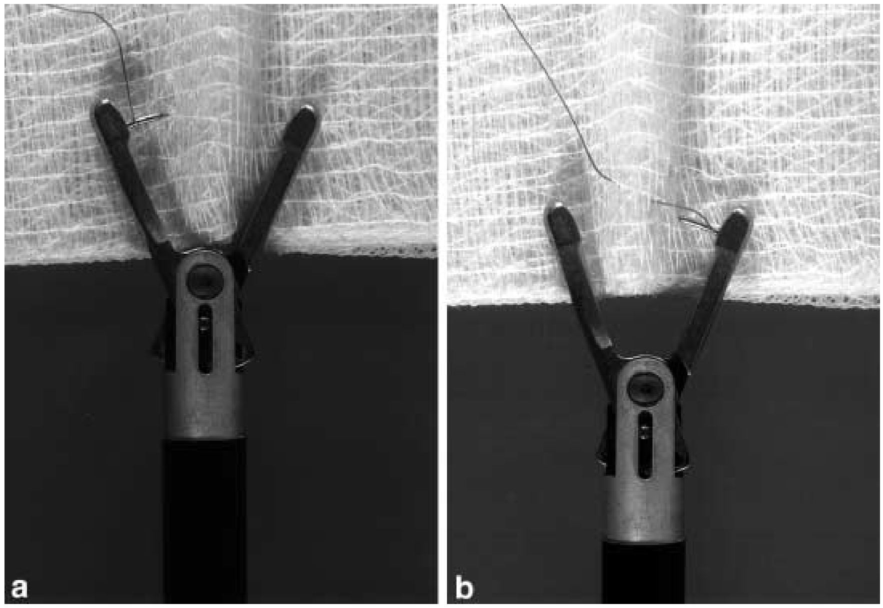

Fig. 2a, b Endo-Stitch (United States Surgical Corp, Norwalk, CT, USA). **a** Needle on left-sided jaw, poised to be inserted through tissue (represented by gauze). **b** After passing needle through tissue by closing jaws, a toggle on the instrument's handle is flipped and then the jaws are opened, which pulls the needle through the tissue on the right-sided jaw

ureteroenterostomy in pigs by "dunking", rather than tunneling, a 1-cm segment of distal ureter into the bowel. This technique resulted in a lower incidence of postoperative stricture and reflux than the comparative standard, tunneled anastomosis. The dunking technique might facilitate intracorporeal ureteroenterostomy.

One innovation, which might simplify the suturing of fragile tissue with small diameter thread as is necessary for ureteral work, is a "suturescope", in which an optical device runs down the barrel of the instrument and allows for a straight-on view of the tissues to be aligned. This type of implement has been described [19], but further work has not been published. Joining the concepts behind this device and those of the Endo-Stitch might yield a very useful instrument.

Absorbable and non-absorbable clips have gained acceptance in laparoscopy because of their ease of delivery. In appropriate situations, they can replace suture and greatly reduce the time necessary to approximate tissue. The major role for clips thus far has been in hemostasis (occlusive clips), but the advent of "biting" or "tacking" clips (Table 3) has facilitated procedures requiring fixation of one structure to another. Tacking clip applicators with articulating heads (Fig. 4) are very useful for fixation of material or tissue in settings where the presence of permanent clips is not problematic.

Tacking clips have found significant use in bladder neck suspension procedures, especially in combination with mesh. Antiphon and associates [6] found that a laparoscopic procedure combining a Burch repair with sacral colpopexy, performed with mesh and clips, yielded a 90% objective success rate in patients whom they treated for stress incontinence. Ou and Rowbotham [40] recently published their results with laparoscopic

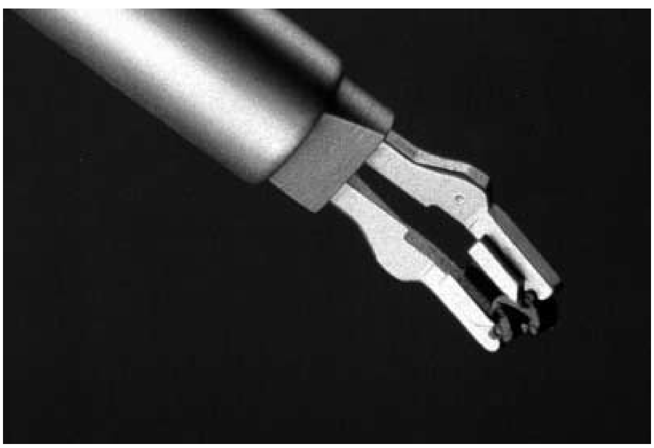

Fig. 3 Absorbable Lapra-Ty clip is locked onto sutures to secure them, using a dedicated re-useable applier (Photo courtesy of Ethicon Endo-Surgery, Cincinnati, OH, USA)

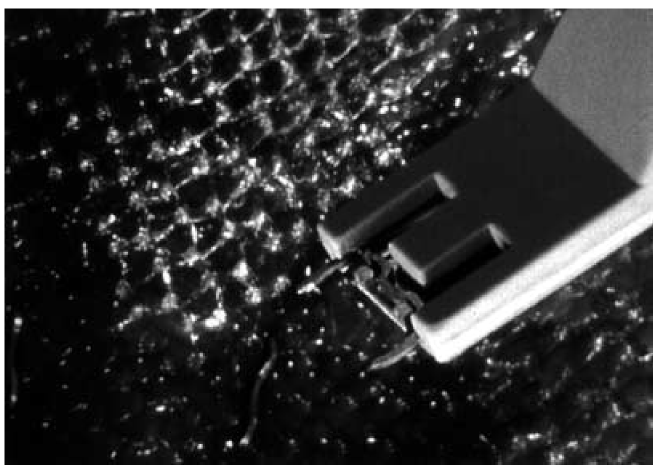

Fig. 4 EndoUniversal 65, a tacking clip-applier with an articulating head (Photo courtesy of United States Surgical Corp, Norwalk, CT, USA)

bladder neck suspension, using titanium surgical clips and Prolene hernia mesh in 34 patients. With a minimum 5-year follow-up, these investigators reported a success rate of 88%. Of the four patients who failed in this Series, three began leaking immediately after the procedure, indicative perhaps of a lapse in technique, rather than lack of long-term durability of the repair.

A recent innovation in fixation clip technology is the Tacker (Origin Medsystems, Menlo Park, CA, USA), a helical metal screw that is driven into tissue with a disposable 5 mm device. Won and colleagues [65] recently compared laparoscopic Burch operations, in which the Tacker device and mesh were used for fixation in one group of patients, while intracorporeal suturing was used in the other. Operative time in the Tacker patients averaged half that in the suturing group (77 vs 140 min), while success rates at a mean follow-up time of nearly 3 years were identical.

The main advantage of clips, which is their ease and rapidity of application, has been exploited in the laboratory as well. Maxwell and associates used titanium vascular closure clips to perform laparoscopic uretero-ureterostomy in pigs [33]. These anastomoses were performed quickly. Radiographic and pathologic follow-up indicated that the anastomoses were patent. The group noted no evidence of encrustation, stone formation, or intraluminal clips. More recently, Cisek and coworkers [12] reported preliminary results of their work, using titanium clips for vesicourethral anastomosis in dogs. In these experiments, the investigators performed total prostatectomy in six dogs, and after securing the urethral stump with two stay sutures, they completed the vesicourethral anastomosis with titanium vascular closure clips. After removal of the urinary catheter at 1 week, animals were followed clinically and with cystourethroscopy, and at 6 months with pathologic analysis of the anastomosis. There were no urinary leaks and no anastomotic strictures. Continence was normal and, despite erosion of clips into the urethral lumen in three animals, only one had evidence of deposition on the clip at 6 months.

This last finding prompted the group to test a variety of closure materials in rabbits for lithogenic risk when exposed to the intraluminal urinary tract [39]. Several interesting conclusions resulted from this study. First, alkaline urine was associated with the most deposition, and treatment to acidify the urine altered the frequency of stone formation. Next, even absorbable materials, especially chromic and polyglactin, were prone to deposition within 1 month, prior to their breakdown. Finally, it appeared that titanium had the lowest degree of deposition, significantly better than silk, chromic, polyglactin, and stainless steel. Polydiaxanone was not significantly different from titanium. Tews et al. [57] have used polydiaxanone clips for laparoscopic closure of the fallopian tube after removal of ectopic pregnancies in humans.

Automatic staplers, which deliver multiple clips with the ability to divide the intervening tissue, have found several applications in laparoscopic urology. The variety of staples includes cutting and non-cutting models. Some models incorporate articulation as well (Fig. 5). Staples have been used for vascular pedicle division, ileal conduit formation, bladder closure, and a variety of other applications. Kozminski and Partamian [27] described laparoscopic ileal conduit formation in which the bowel anastomosis was accomplished using automated stapling. They reported decreased operative time with intracorporeal stapling in comparison to extracorporeal bowel anastomosis. They also noted that increased body wall thickness, which can render extracorporeal bowel manipulation difficult, is not a significant hindrance when performing intracorporeal stapled bowel anastomoses. Anderson and colleagues [3] performed laparoscopic-assisted continent urinary diversion in pigs, by bringing a mobilized segment of colon up to a trocar site and then detubularizing the segment by extracorporeal application of a 6 cm cutting pneumatic linear stapler. Kerbl and associates [25] had previously used a similar instrument for laparoscopic resection of a cuff of bladder during nephroureterectomy, with simultaneous closure of the bladder both in the laboratory in pigs, and clinically in humans. In the animal experiments, urothelium completely covered the staple line at 6 months and there was no incidence of stone formation. In the human subjects, staples were seen intraluminally on postoperative cystoscopy in two of three patients initially, but in subsequent exams the staples had disappeared and stone formation did not occur.

Overall, despite significant advances that have occurred in technique and instrumentation for laparoscopic delivery of sutures, clips, and staples, important limitations still exist, particularly in terms of operative time and application of these implements to tissues of variable thickness and geometry. Now that the feasibility of performing nearly every major urologic procedure through a laparoscope has been established, the time is

Fig. 5 Articulator 35, a linear cutting stapler with a 45° articulating head (Photo courtesy of Imagyn, Irvine, CA, USA)

ripe for the introduction of newer, more efficient methods of tissue approximation.

The new frontier – tissue adhesives and laser welding

Cyanoacrylate tissue adhesives have existed for decades [58]. Their action derives from spontaneous polymerization when they contact liquids or bases. [46] Methyl-2-cyanoacrylate was tested in 1964 for closure of 3-cm-long cystotomies in dogs, [66] but its use was associated with significant postoperative urinary leakage and calculus formation. Vargas and associates [62] used fluoroalkylcyanoacrylate with some success in 1977 to reinforce the suture line in canine ureteroureterostomy. However, early cyanoacrylates were removed from distribution because of rapid in vivo degradation into cyanoacetate and formaldehyde, [58] resulting in significant tissue toxicity and inflammation. Longer alkyl chain cyanoacrylates (i.e., butylcyanoacrylate) have much slower degradation rates and therefore minimal tissue toxicity [58]. N-butyl-2-cyanoacrylate has been used clinically in Europe and Canada, but an oft-criticized study implicating the isobutyl form of the adhesive in carcinogenicity in rats [48] caused its distribution to be interrupted for clinical investigation in the United States. Additionally, butylcyanoacrylate has significantly lower tensile strength than suture at 1 day after repair [46].

2-Octylcyanoacrylate glue (OCG) (Dermabond, Ethicon, Somerville, NJ, USA) is a longer chain cyanoacrylate which has been tested and approved for skin wound closure by the United States Food and Drug Administration (FDA). Prior to its approval in the United States, it had been used for this indication widely in Canada and Europe. Its breaking strength is four times greater than that of butylcyanoacrylate, and it remains flexible and resists splintering after drying [46].

The mechanism of action of fibrin glue (FG) is a recapitulation of the final steps of the clotting cascade [53]. Most formulations employ two components, one containing fibrinogen and the other thrombin, that are mixed in situ, using a variety of delivery devices to produce a flexible clot (Fig. 6). Fibrin glue has found use in urology as a hemostatic agent in renal trauma and partial nephrectomy [28, 30], as well as in vasovasostomy [54]. Sutureless bowel anastomoses have been performed with fibrin glue in animals [67]. One commercial preparation, several of which have long been available worldwide, is now approved for clinical use in the United States (Tisseel, Immuno AG, Vienna, Austria).

To date, only one group has investigated the use of OCG experimentally in the urinary tract and compared its performance with FG [32]. In this study, OCG and FG were used for open and laparoscopic repair of large (7.5 cm) cystotomies in pigs. At 2 days after open cystotomy repair, neither OCG nor FG was able to withstand a burst pressure of 200 mmHg, applied by filling the bladders with saline. However, all bladders

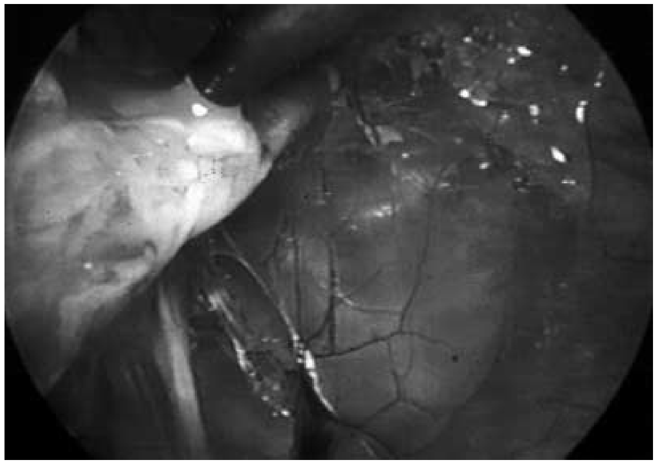

Fig. 6 Laparoscopic application of fibrin glue onto ureter (porcine model)

closed with OCG and tested at 4 weeks, including two closed laparoscopically, remained intact up to 200 mmHg. In contrast, of six animals closed with FG (two laparoscopically) and intended for pressure testing at 4 weeks, three animals died of urinary extravasation (including both closed laparoscopically) within one week; and of the three which survived to be tested, only two withstood application of 200 mmHg pressure. Furthermore, because urinary catheters were not used postoperatively in these studies, and because all OCG animals survived for 4 weeks until testing, the investigators concluded that OCG could withstand both physiologic bladder pressures early in the healing process as well as supra-physiologic pressures later on.

Fibrin glue did not perform nearly as consistently as OCG for closure of large bladder wounds in the above-noted study. Other reports, however, indicate that fibrin glue is effective for closure of smaller bladder wounds (i.e. less than 3.5 cm) [9], ureterotomies [63], and ureteral anastomosis [36]. In other words, fibrin glue may be adequate to bond tissue together in situations in which tissue edges are short, tension between the target tissues is minimal, and intraluminal pressures are negligible. The sealant and hemostatic properties of fibrin glue are excellent, and it has been useful in this regard in such applications as laparoscopic pyeloplasty and partial nephrectomy [15, 24]. While the main disadvantage of fibrin glue is lack of tensile strength, its advantages include biocompatibility and resultant minimal inflammation and fibrosis [32, 63]. In contrast, current formulations of OCG are not biodegradable, and result in inflammation and fibrosis too extensive for successful use in ureteral surgery (Wolf et al. unpublished data). Another drawback of OCG is that if it infiltrates the wound edges, effective tissue bonding will not occur, and healing may be impaired. Thus, close attention must be paid to the technique of application. Preliminary results in the authors' laboratory with an experimental, biodegradable formulation of cyanoacrylate glue has shown

Fig. 7 Laparoscopic laser tissue welding, using the KTP laser and albumin solder doped with fluorescein dye, to close ureterotomy (porcine model)

minimal inflammation without compromise in tensile strength. Toxicity data for all new formulations of OCG will have to be determined before intracorporeal use in humans can be considered. Current ongoing laboratory experimentation with tissue adhesives is directed at performing vesicourethral anastomosis and augmentation enterocystoplasty.

Laser tissue welding (Fig. 7) has thus far mainly been applied in the laboratory setting, although some clinical (non-laparoscopic) uses have been reported. Monochromatic light energy generated by the laser heats target tissues by absorption in pigments or water. This heating causes structural changes in tissue collagen, fibronectin, and other extracellular matrix proteins, which results in covalent bonding of these molecules in target tissues. Unlike other modalities which merely approximate tissues to facilitate healing, this process actually causes molecular bonding of tissues – the two tissues become one. Unfortunately, the surfaces to be bonded must usually be approximated with another technique (usually stay sutures) unless the length of the closure is short.

Several shortcomings of the laser have been addressed. Problems included thermal damage to tissue adjacent to the welding line, as well as lack of an objective "end point" for completion of welding. Development of protein solders, [44] which are applied to the tissue edges prior to laser welding has improved tensile strength significantly, and has allowed for decreased peripheral tissue damage, theoretically because the solder acts as a heat sink. Albumin-based solder has been found to be the most effective [45], although human albumin is not yet FDA-approved for this indication [49]. Another technological advance which has decreased peripheral tissue damage and promoted optimal thermal delivery, is a system which senses surface temperatures via an infrared sensor and then, via a feedback loop, adjusts the laser power delivered to the tissues [49]. Further protection of peripheral tissues has been made possible by the introduction of chromophores to the welding process. These substances are dyes which absorb certain wavelengths of light and serve to increase the heat capacity of the protein solder [41], thereby reducing peripheral heat absorption.

Laser tissue welding in urology has been applied to vasovasostomy, urethroplasty, ureteroneocystostomy, ureteral anastomosis, and enterocystoplasty, mainly in the laboratory setting [49]. Human application of laser welding has been limited to vasovasostomy, pyeloplasty, and hypospadias repair, but has required the use of adjunctive sutures in all cases [26, 52]. Nevertheless, many of studies have found that the tensile strength of the laser weld was greater than that of sutured closures. In addition to providing a water-tight seal, laser welding has been noted to improve healing, reduce fistula formation, and decrease operative time in comparison to standard techniques [49].

Laparoscopic laser welding has thus far been very limited. Using a laparoscopic laser-solder delivery system (Laserscope, San Jose, CA, USA), Wolf and associates performed ureterotomy closure in pigs, and compared this technique to closure with fibrin glue and intracorporeal suturing with the Endo-Stitch [63]. Laser ureterotomy closure was facilitated by longitudinal traction on the ureter with a grasper, thus obviating the need for stay sutures. Fluorescein dye, which emits some of its absorbed energy as visible light, was used as a chromophore to enhance directed uptake of the laser energy. Laser welding proved to be the most rapid method of closure, and yielded better histology than suturing, but was no better than fibrin glue. The authors concluded that, given the expense of laser systems, laser welding would have to offer significant advantages in operative time and tissue healing in order to find a place in routine clinical use [63].

We have thus come to an interesting point in laparoscopic tissue approximation. Modalities based on open surgical tools – suture devices, clips, and staples – are full-fledged and have found their niche in laparoscopy – they have become "standard". Yet, at the same time, this field is still in its developmental stages. Devices are far from ideal. As we stand poised to enter the third millennium, the stage is set for further advancement. Not only will more exposure to laparoscopy during training result in more efficient application of current tissue approximation methods, but the experimental modalities discussed above will continue to be refined until they achieve clinical use. Advances in robotic surgery, [56] remote surgery, mechanical devices which mimic the human hand, [23] and even virtual reality, may one day all serve to completely change the way tissues are brought together laparoscopically.

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