0022-5347/05/1743-1110/0
THE JOURNAL OF UROLOGY®

Vol. 174, 1110–1114, September 2005
Printed in U.S.A.
DOI: 10.1097/01.ju.0000168620.36893.6c

POTASSIUM-TITANYL-PHOSPHATE LASER LAPAROSCOPIC PARTIAL NEPHRECTOMY WITHOUT HILAR CLAMPING IN THE SURVIVAL CALF MODEL

ALIREZA MOINZADEH, INDERBIR S. GILL,* MAURICIO RUBENSTEIN, OSAMU UKIMURA, MONISH ARON, MASSIMILIANO SPALIVIERO, KESTER NAHEN,† ANTONIO FINELLI, CRISTINA MAGI-GALLUZZI, MIHIR DESAI, JIHAD KAOUK AND JAMES C. ULCHAKER

From the Section of Laparoscopic and Robotic Surgery, Glickman Urological Institute, and Department of Anatomic Pathology, Cleveland Clinic Foundation, Cleveland, Ohio

ABSTRACT

Purpose: Laparoscopic partial nephrectomy (LPN) with hilar clamping represents the various challenges associated with warm ischemia. We tested the feasibility, and acute and chronic outcomes of LPN using a potassium-titanyl-phosphate (KTP) laser without vascular hilar clamping in the survival calf model.

Materials and Methods: Six Jersey calves weighing 76 to 94 kg underwent a total of 12 staged bilateral transperitoneal laser LPNs of the mid/lower pole using an 80 W KTP laser, including left kidney chronic LPN with 1-month followup in 6 and right kidney acute LPN with immediate sacrifice in 6. Two techniques (ablative vaporization in 5 subjects and wedge resection in 7) were evaluated. Renal parenchymal resection and hemostasis were achieved only with the laser without any adjunctive hemostatic sutures or bioadhesives. Retrograde pyelography, renal arteriography and histological analyses were performed.

Results: All 12 procedures were successful performed laparoscopically without open conversion and 11 (92%) were done without hilar clamping. Mean total operative time was 2.9 hours (range 1.5 to 5) and mean blood loss was 119 cc (range 25 to 300). Mean lasing time was 56 minutes (range 20 to 100) with an average energy use of 54 kJ. Mean preoperative and postoperative hemoglobin (10.38 and 10.52 gm/dl) and serum creatinine (0.46 and 0.4 gm/dl, respectively) were similar. At 1-month followup there was no evidence of urinary leakage or arteriovenous fistula.

Conclusions: This initial study of laparoscopic KTP laser partial nephrectomy without hilar clamping confirms its technical feasibility in most cases and good short-term outcomes. This success of laser LPN in the robust survival calf model with its human-sized kidney holds promise for future clinical application.

KEY WORDS: kidney, laparoscopy, nephrectomy, lasers, cattle

Approximately 35,000 new cases of renal tumors were diagnosed in 2004.[1] Given the increased use of sophisticated radiographic imaging, many of these tumors are small and amenable to partial nephrectomy. Laparoscopic techniques for partial nephrectomy are well described.[2] Hemostasis represents a primary challenge during the procedure and, hence, clamping the renal vasculature is often required to allow precise removal in a bloodless field. The resultant warm ischemia places significant time constraints on the laparoscopic surgeon for tumor excision and parenchymal reconstruction, making the procedure technically challenging. The potassium-titanyl-phosphate (KTP) laser has been used successfully with durable 5-year followup for the surgical vaporization of benign prostatic hyperplasia.[3,4] We investigate the technical feasibility and short-term outcomes of KTP laser laparoscopic partial nephrectomy in the robust calf model.

MATERIALS AND METHODS

The study was approved by our institutional Animal Review Committee and performed using 6 Jersey calves weighing 76 to 94 kg. All animals initially underwent KTP laser laparoscopic partial nephrectomy of the interpolar or lower pole of the left kidney with the aim of excising or ablating approximately 20% of the parenchyma. The animals were survived and 1 month later they underwent KTP laser laparoscopic right partial nephrectomy, followed by immediate sacrifice with ex vivo assessment. Thus, the 6 left partial nephrectomies provided 1-month chronic data and the 6 right partial nephrectomies provided acute data.

The 80 W quasicontinuous wave KTP laser (GreenLight PV, Laserscope, San Jose, California) with a 600 μ bare tip end firing laser fiber was delivered through a 5 mm suction irrigation tube hand piece (A5653, Olympus, Hamburg, Germany). The hand piece served 2 purposes. 1) It allowed stabilization of the laser fiber. 2) Smoke evacuator tubing connected to the hand piece served as integrated high flow suction. An on/off foot pedal controller along with variable power settings allowed the optimal control of desired laser power delivery for the ablation/resection vs the coagulation of bleeders.

Following broad-spectrum prophylactic antibiotics and general endotracheal anesthesia the animals were placed in the lateral flank position. Using a 4 or 5 port transperitoneal technique the left kidney was mobilized, maintaining upper pole attachments. En bloc dissection and preparation of the left renal hilum were performed in case of urgent need for

Submitted for publication December 22, 2004.
Study received institutional Animal Review Committee approval.
Supported by Laserscope.
* Correspondence and requests for reprints: Section of Laparoscopic and Robotic Surgery, Glickman Urological Institute, Cleveland Clinic Foundation, 9500 Euclid Ave., A-100, Cleveland, Ohio 44195 (FAX: 216-445-7031; e-mail: gilli@ccf.org).
† Financial interest and/or other relationship with Laserscope.

hilar vascular control. The hilum was not clamped. Using J hook electrocautery the renal capsule was incised over the proposed resection area at the mid/lower pole kidney. The 80 W KTP laser generator (532 nm wavelength) was set to 80 W for parenchymal resection. Partial nephrectomy was then performed by 1 of 2 techniques, as determined randomly preoperatively. 1) For ablative vaporization the laser fiber was used to vaporize the targeted renal parenchyma to the proposed size and depth, analogous to the use of KTP lasers in the prostate. No surgical specimen was obtained by this approach since the laser was "painted" over the desired area of resection, completely vaporizing the entire target tissue. 2) For wedge resection the laser was used as a cutting knife to precisely excise the targeted portion of the mid/lower pole kidney, thus, retrieving an intact partial nephrectomy specimen. The laser was used to create and deepen the parenchymal groove from a medial-to-lateral direction (figs. 1 and 2). This medial-to-lateral technique minimized the chance of inadvertent injury to adjacent bowel loops. The suction/irrigation system, which was held in the surgeon nondominant hand, was used to retract the cut portion of the kidney, allowing better visualization. In the event of hemorrhage the laser power setting was decreased to 40 W or the laser beam was defocused on the high power setting to enhance its hemostatic effect. We did not use vascular clips, monopolar or bipolar electrocautery, argon beam coagulation, parenchymal suturing or bioadhesives for hemostasis during any of the procedures.

Given the considerable smoke generated from vaporizing parenchymal tissue during our initial procedures, it became obvious that a dedicated smoke evacuator (Stackhouse Vital Vac ST-3000, Viasys, Wheeling, Illinois) would be necessary. The tubing from the evacuator was spliced in 2 parts and the tubes were connected to a dedicated trocar and the laser hand piece, allowing an evacuation capability of approximately 15 l per minute. A foot pedal controller with on/off functionality allowed the assistant to perform smoke evacuation in short bursts. To counteract the loss of pneumoperitoneum during smoke evacuation 2 insufflators were used to maintain a high CO_2 inflow of approximately 14 to 16 l per minute. More smoke was generated with the ablative technique than the wedge resection technique.

In 6 cases (left and right kidney in 3 each) in which the collecting system was visually entered watertight running suture repair with 2-zero poliglecaprone was performed purely laparoscopically after laser resection or ablation. The specimen was extracted intact in an EndoCatch™ bag. In cases that involved specimen excision the retrieved specimen was measured, weighed and fixed in formalin for histological analysis. Complete blood count and serum creatinine were determined preoperatively, immediately postoperatively, and at 1 and 2 weeks.

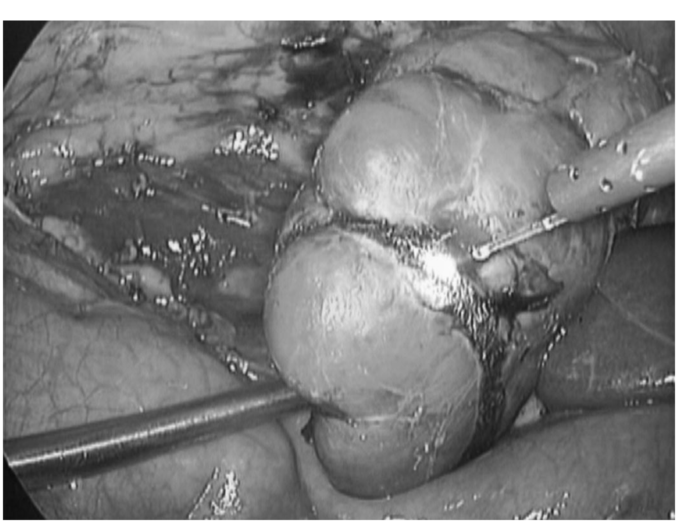

FIG. 1. Lower pole LPN resection technique

FIG. 2. Acute specimen of renal remnant after laser resection of lower pole (arrow).

At 1 month laparoscopic laser right partial nephrectomy was performed in similar fashion. Upon the completion of right acute partial nephrectomy the animal was sacrificed. Gross examination of the left chronic kidney was performed to assess evidence of gross hemorrhage or urine leakage. The kidneys were measured, weighed and grossly examined to assess the laser effect and depth of laser resection relative to the kidney surface. Ex vivo retrograde pyelogram and arteriogram were performed in the 6 chronic kidneys to assess collecting system integrity as well as any evidence of arteriovenous fistula. One genitourinary pathologist (CM-G) evaluated all tissue specimens. Hematoxylin and eosin sections, including the resected bed as well as normal adjacent parenchyma, were examined to assess acute and chronic laser effects.

RESULTS

All 12 KTP laser laparoscopic partial nephrectomies (LPNs) were performed successfully without open conversion. Seven cases (58%) were performed using the wedge resection technique (chronic in 3 and acute in 4) and 5 (42%) were performed using the ablative vaporization technique (chronic in 3 and acute in 2). Mean operative time was 2.9 hours (range 1.5 to 5), including a mean lasing time of 56 minutes (range 20 to 100). Average lasing time for the wedge resection and ablative vaporization techniques was similar at 56 and 57 minutes, respectively. Average blood loss was 119 cc (range 25 to 300) in the resection group vs 58 cc (range 20 to 150) in the ablative group for a mean blood loss of 119 cc for all procedures. Mean total energy use for all procedures was 53.9 kJ.

Of the 12 cases 11 (92%), were completed without hilar clamping. One case of left wedge resection required 20 minutes of hilar clamping due to hemorrhage from a centrally located blood vessel, which could not be controlled with laser while the kidney was unclamped. After hilar clamping the laser was used to coagulate the parenchymal bleeder, achieving hemostasis. Weight of the resected kidney tissue in this case was 11 gm with a specimen size of $4 \times 2.5 \times 2$ cm and an estimated blood loss of 300 cc.

Complications included 2 cases of bowel puncture injury during initial needle access to achieve CO_2 pneumoperitoneum. In these 2 initial cases we used a Veress needle for access, which resulted in puncture entry into the stomach.

TABLE 1. *Operative parameters and study results in 12 kidneys*

Parameters	Mean Overall (range)	Mean Ablative Vaporization	Mean Wedge Resection
No. kidneys	12	5	7
Total operative time (hrs)	2.9 (1.5–5)	2.3	3.5
Lasing time (mins)	56 (20–100)	57.2	55.5
Energy used (kJ)	53.97	48	57.8
Estimated blood loss (ml)	119 (25–300)	58	160
Specimen wt (gm)	7.7	Not available	160
Kidney wt (gm)	235 (200–300)	229	255
Preop/1-wk postop:			
Hemoglobin (gm/dl)	10.4/10.5*	10.2/10.9	10.5/10.1
Creatinine (mg/dl)	0.5/0.4*	0.4/0.4	0.6/0.4

* Normal values not available.

These complications were repaired laparoscopically by an intracorporeal figure-of-8 stitch without sequelae. Subsequently due to the large size of this multiple stomach chamber in the bovine animal model we elected to achieve initial pneumoperitoneum access with the Hassan technique without further complications. There were no complications related to the laser partial nephrectomy procedure per se.

In the 7 cases involving wedge resection mean specimen weight was 7.7 gm (range 3 to 11) with a mean specimen size of 4 × 3 cm. The mean measured depth (kidney surface to deepest part of the parenchymal bed) of the partial nephrectomy site with resection or ablation was 1.9 cm. Average weight of the kidney at autopsy was 235 gm (range 200 to 300). Preoperative and postoperative hematocrit and serum creatinine did not differ in the animals (table 1).

Gross examination of the kidney and surgical bed site revealed no evidence of urinoma or hematoma formation. Ex vivo retrograde pyelogram of the 6 chronic kidneys did not demonstrate any evidence of urinary leakage. Ex vivo arteriogram of the 6 chronic kidneys did not show any evidence of arteriovenous fistula. Hematoxylin and eosin stained histological sections of the acute kidneys revealed a superficial necrotic zone of parenchymal thermal damage that was 0.2 to 0.8 mm thick (coagulation zone). Congested small blood vessels were noted in proximity to the coagulation zone (fig. 3, *A*). A zone of vacuolization approximately 1 mm thick with intravascular fragmented blood vessels was present beneath the coagulation zone. These changes were related to tissue conductivity.

Histological examination of the chronic partial nephrectomy bed revealed a superficial layer of necrotic debris intermixed with fibrin and blood. A layer of granulating tissue resting on fibrosis, ranging in thickness from 0.1 to 1 cm was present beneath the necrotic debris, intermixed with foreign body type giant cell reaction (fig. 3, *B*). The underlying renal parenchyma demonstrated superficial interstitial fibrosis and focal chronic inflammation. These findings were related to the repair process occurring in tissue after the injury induced by the procedure. The giant cell reaction was in response to the foreign material used.

DISCUSSION

The first use of laser technology for organ surgery in the animal model occurred more than 30 years ago.[5] Since this initial use of the CO_2 laser, there has been significant improvement in laser technology as well as in understanding the laser mechanism of action. An important part of this understanding has been the realization that not all lasers are the same. The specific wavelength of each laser allows different interaction with the tissue that it is directed against. Scattering as well as absorption of laser light in water and hemoglobin governs the penetration depth of each wavelength in tissue. For example, the Nd:YAG laser, which has a wavelength in the infrared region (1,064 nm), interacts with water and blood. It penetrates tissues up to a depth of 5 to 10 mm. The KTP laser, which was in this study, has a shorter

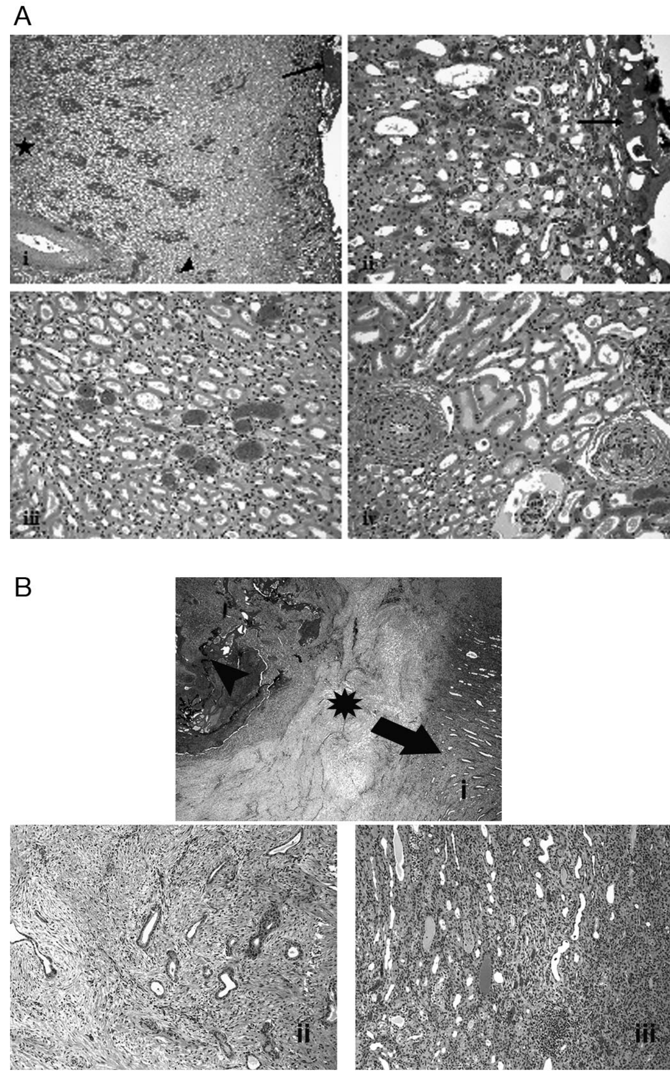

FIG. 3. *A*, acute kidney laser effect. *i*, low power view of kidney parenchyma section following acute laser treatment. Arrow indicates coagulation zone. Arrowhead indicates congestion of small vessels. Star indicates medium-sized arteries. Reduced from ×10. *ii*, high power view of coagulation zone (arrow). Coagulation zone depth was 0.2 to 0.8 mm with minimum carbonization effect. Parenchyma adjacent to coagulation zone (arrowhead), which was ± 1 mm thick, shows tissue vacuolization and intravascular red blood cell fragmentation. Reduced from ×20. *iii* and *iv*, vascular congestion (arrowhead) 3 to 4 mm from surface. Reduced from ×20. *B*, chronic laser kidney effect. *i*, low power view of kidney parenchyma after laser treatment. Arrowhead indicates superficial necrotic tissue intermixed with fibrin clot, granulation tissue and inflammatory infiltrate, which was 0.1 to 1.0 cm thick. Star indicates area of superficial fibrosis, which was 0.2 to 0.5 mm thick. Reduced from ×4. *ii*, area of superficial fibrosis. Reduced from ×10. *iii*, underlying kidney parenchyma with focal chronic inflammation. Reduced from ×10.

wavelength (532 nm), resulting in 200 times higher light absorption in hemoglobin than that of the Nd:YAG laser and, hence, a shallower tissue penetration of only 0.8 mm.[6] At the same time the KTP laser beam is virtually not absorbed by water. The selective uptake of KTP laser energy by hemoglobin leads to hemostasis, which has been effectively applied for tissue vaporization for benign prostatic hyperplasia.[3]

Laser partial nephrectomy using various lasers has been described (table 2).[5,7–12] Initial animal experiments were performed open surgically, most with hilar clamping. More recently 3 studies from the University of Texas-Southwestern described laser use for LPN.[11–13] Using a 980 nm diode laser[11] 5 farm pigs underwent bilateral LPN. Mean operative time was 126 minutes, including a mean lasing time of 84 minutes. Adjunctive hemostatic clips were required in 3 cases to control the larger, more centrally located vessels. Fibrin glue was used in all cases and, therefore, the sealing effect of the laser on the collecting system could not be determined. Histological analysis of chronic specimens revealed a necrotic margin of 3 to 5 mm at 2 weeks. Subsequently this group used the 2,100 nm wavelength pulsed Ho:YAG laser clinically to perform LPN in 3 patients, including a man with a complex cyst, a pediatric patient with a nonfunctioning lower pole duplicated system and a man with a 2.5 cm exophytic renal tumor.[12] Estimated blood loss in the 2 adults was less than 50 and 500 cc, respectively. Fibrin glue, oxidized cellulose and an argon beam coagulator were used and hilar clamping was not performed. No complications were reported. Thereafter, these investigators tested the feasibility of laser tissue welding for LPN in 5 pigs.[13] Ogan et al created an in-house solder consisting of 30% human serum albumin that was concentrated to 50%. Indocyanine green, a chromophore, was added to allow selective absorption of an 810 nm diode laser. After hilar clamping the lower pole of the porcine kidney was resected with cold endoscopic shears. The albumin solder was dripped onto the cut surface of the kidney and laser soldering was performed. Reportedly an albumin mixture covering was created over the treated surface of the vessels as well as the collecting system. Estimated blood loss was 43 cc with a warm ischemia time of 11.7 minutes. None of the chronic kidneys had evidence of urinary leakage on ex vivo retrograde pyelogram at 2 weeks. Gross and histological examination revealed solder adherent to the parenchymal surface. Acute extension of the cauterized area into the renal parenchyma was 0.5 mm. Data on the extent of cautery on the chronic specimen were not provided.

In our study we used the KTP laser to perform LPN in the more robust calf model. Since calves are considerably larger (in this study mean body weight 82 kg), their larger kidneys (in this study mean weight 237 gm) bleed more profusely in pulsatile fashion, similar to the human kidney. This is in contrast to the cats, dogs and pigs used in prior studies, in which parenchymal hemorrhage was less severe and easier to control. Since these smaller animals do not accurately replicate the clinical scenario, outcomes and hemostasis have been disappointing when the techniques are extrapolated clinically. As such, we believe that the calf model is more representative of the human kidney in terms of vascularity, laparoscopic technical difficulty and the potential for hemorrhagic complications.

At the outset we hypothesized that the KTP laser would provide certain advantages over other lasers previously tested. Given its 532 nm wavelength, the KTP laser has selective uptake by hemoglobin, thus, conferring a hemostatic advantage. This theoretical advantage was realized in practice since we completed 11 of the 12 procedures (92%) without hilar clamping or the use of any adjunctive hemostatic agents whatsoever. In addition, the shorter wavelength and, hence, lesser penetration produces a shallower rim of coagulation that is only 0.2 to 0.8 mm, thus, potentially making the photoselective KTP laser more attractive for partial nephrectomy. Finally, minimal hemorrhage resulted in almost negligible backsplatter, which is a significant practical disadvantage of certain pulsed lasers such as the Ho:YAG, which induce strong thermomechanical ejection of ablation products.[12]

Some shortcomings were noted. Unlike KTP vaporization of the prostate, in which cystoscopic irrigation fluid counteracts any smoke production, laser LPN does not lend itself to underwater performance. Hence, considerable smoke is generated that is not irrigated away from the working field. This issue was particularly noted during ablative procedures compared with the resecting technique. Although we used a smoke evacuating device for this purpose, visibility was nonetheless limited at times, increasing operative time and necessitating 2 insufflators to achieve the requisite higher CO_2 inflow rates. As such, a more efficient smoke evacuator system is desirable. However, we anticipate that smoke evacuation would be less of a problem in the clinical setting, given the smaller peritoneal volume in humans (approximately 3 l) compared with calves (approximately 10 l).

Possible theoretical inadequacies may exist with human application. Although the KTP laser has a 1 mm depth of penetration, evaluation of a resected margin may be hampered by the use of energy near the tumor compared with the cold endoscopic shears used with conventional laparoscopy. Limitations or risks of the ablative technique would include

TABLE 2. *Literature review of laser partial nephrectomy*

References	Animal vs. Human Model	No. Subjects	Acute vs Chronic	Open vs Laparoscopic	Laser	Hilar Clamping	Comments
Hughes and Scott[5]	Canine	7	Chronic	Open	CO_2	Yes	Suture ligatures necessary for adequate parenchymal hemostasis
Meiraz et al[7]	Feline	20	Chronic	Open	CO_2	Yes	Total of 16 cats survived for interval followup, no evidence of urinary leakage or hemorrhage
Benderev and Schaeffer[8]	Canine	6	Chronic	Open	Nd:YAG	Yes	Urinary leakage in 2 dogs, parenchymal necrosis depth 4–7 mm
Landau et al[9]	Canine	20	Acute	Open	Nd:YAG	Yes	No advantage noted over standard partial nephrectomy, vessel suture ligature required
Taari K et al[10]	Porcine	9	Acute	Open	Nd:YAG	Yes	Laser vs knife partial nephrectomy, similar blood loss, more suture ligatures needed for knife partial nephrectomy
Ogan et al[11]	Porcine	5	Chronic	Laparoscopic	Diode	No	Clip ligation required in 3 pigs due to insufficient hemostasis
Ogan et al[13]	Porcine	5	Chronic	Laparoscopic	Diode	Yes	
Present series	Bovine	6	Chronic	Laparoscopic	KTP	No	
Lotan et al[12]	Clinical	3	Not applicable	Laparoscopic	Ho:YAG	No	

a lack of histopathology beyond initial core biopsies, lack of pathological staging, increased smoke production and theoretical risks associated with tumor cell vaporization.

Adequate closure of the collecting system appears important. In our chronic cases any pelvicaliceal entry was efficiently suture repaired laparoscopically with a running polyglactin stitch. As noted previously, others have used fibrin glue or laser solder for this purpose. Currently to our knowledge there is no proof or reason to assume that the KTP laser can seal the collecting system upon entry. Further study is necessary in this regard.

CONCLUSIONS

KTP laser LPN without hilar clamping is technically feasible in most cases using the robust calf model. Further refinement is necessary in regard to smoke evacuation and flexible instrumentation for easier angulation of the laser fiber. The hemostatic properties specific to the KTP laser show a real potential for clinical application.

REFERENCES

1. Jemal, A., Tiwari, R. C., Murray, T., Ghafoor, A., Samuels, A., Ward, E. et al: Cancer statistics, 2004. CA Cancer J Clin, **54:** 8, 2004
2. Finelli, A. and Gill, I. S.: Laparoscopic partial nephrectomy: contemporary technique and results. Urol Oncol, **22:** 139, 2004
3. Malek, R. S., Kuntzman, R. S. and Barrett, D. M.: High power potassium-titanyl-phosphate laser vaporization prostatectomy. J Urol, **163:** 1730, 2000
4. Malek, R. S. and Kuntzman, R. S.: Photoselective vaporization of the prostate: 5-year experience with high power KTP laser. J Urol, suppl., **169:** 390, abstract 1457, 2003
5. Hughes, B. F. and Scott, W. W.: Preliminary report on the use of a CO 2 laser surgical unit in animals. Invest Urol, **9:** 353, 1972
6. Stein, B. S.: Laser physics and tissue interaction. Urol Clin North Am, **13:** 365, 1986
7. Meiraz, D., Peled, I., Gassner, S., Ben-Bassat, M. and Kaplan, I.: The use of the CO2 laser for partial nephrectomy: an experimental study. Invest Urol, **15:** 262, 1977
8. Benderev, T. V. and Schaeffer, A. J.: Efficacy and safety of the Nd:YAG laser in canine partial nephrectomy. J Urol, **133:** 1108, 1985
9. Landau, S. T., Wood, T. W. and Smith, J. A., Jr.: Evaluation of sapphire tip Nd:YAG laser fibers in partial nephrectomy. Lasers Surg Med, **7:** 426, 1987
10. Taari, K., Salo, J. O., Rannikko, S. and Nordling, S.: Partial nephrectomy with a combined CO2 and Nd:YAG laser: experimental study in pigs. Lasers Surg Med, **14:** 23, 1994
11. Ogan, K., Wilhelm, D., Lindberg, G., Lotan, Y., Napper, C., Hoopman, J. et al: Laparoscopic partial nephrectomy with a diode laser: porcine results. J Endourol, **16:** 749, 2002
12. Lotan, Y., Gettman, M. T., Ogan, K., Baker, L. A. and Cadeddu, J. A.: Clinical use of the holmium: YAG laser in laparoscopic partial nephrectomy. J Endourol, **16:** 289, 2002
13. Ogan, K., Jacomides, L., Saboorian, H., Koeneman, K., Li, Y., Napper, C. et al: Sutureless laparoscopic heminephrectomy using laser tissue soldering. J Endourol, **17:** 295, 2003